**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 5, 2018**

# 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)** |

**(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 September 5, 2018, 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 September 5, 2018, 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 September 5, 2018 |

**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 5, 2018

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


## H. C. Wainwright 20th Annual Global Investment Conference

**Aoife Brennan, M.B., B.Ch., Interim President and CEO, & CMO**

September 5, 2018

# 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: 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 August 9, 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:
## A Novel Class of Living Medicines

### Synthetic

- **Engineered** bacteria
- With **designed genetic circuits**
- To **degrade metabolites** that induce disease or **synthesize substances** to treat disease

### Biotic: *E. coli* Nissle as chassis:

- Widely-used **oral probiotic**
- **Leverage the safety** of probiotic
- Found within natural human **microbiome**
- **Amenable to genetic manipulation**

**Synthetic Biology + Bacteria = Synthetic Biotic Medicine**

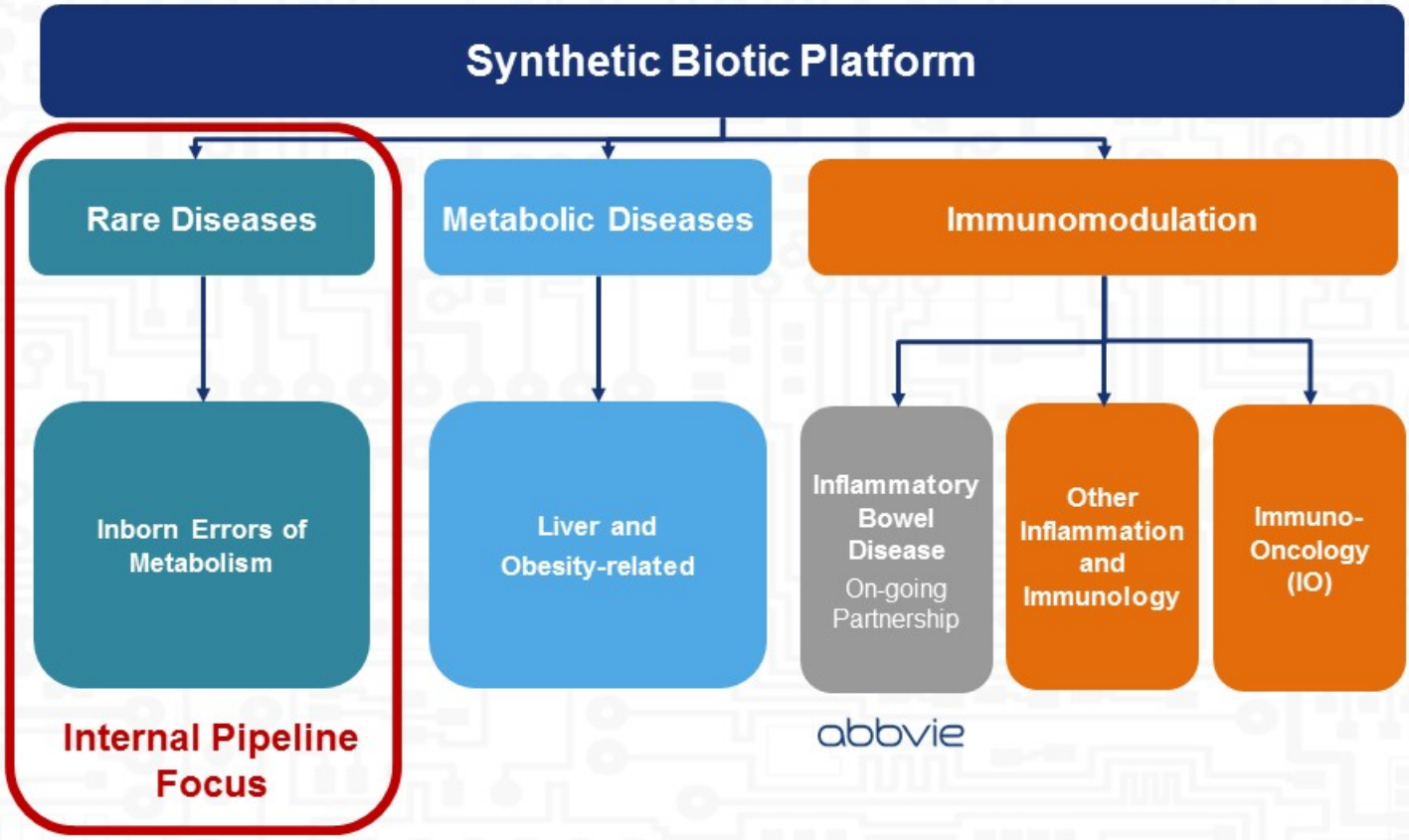
**Therapeutic** delivered locally to treat systemic diseases

# Advantages of a Synthetic Biotic Approach: Unique Mechanisms to Treat Systemic Metabolic and Immune Dysfunction

- Can program bacteria to execute
  - an entire metabolic pathway
  - multiple therapeutic functions
  - with potency
  - and generate biomarkers of activity
- Switches provide ability to control or "tune" functions
- Local delivery of therapeutic function is possible
  - may reduce systemic toxicity
- Single strain has advantages
  - for rapid understanding and deployment of the platform; and
  - development of robust and reproducible manufacturing processes

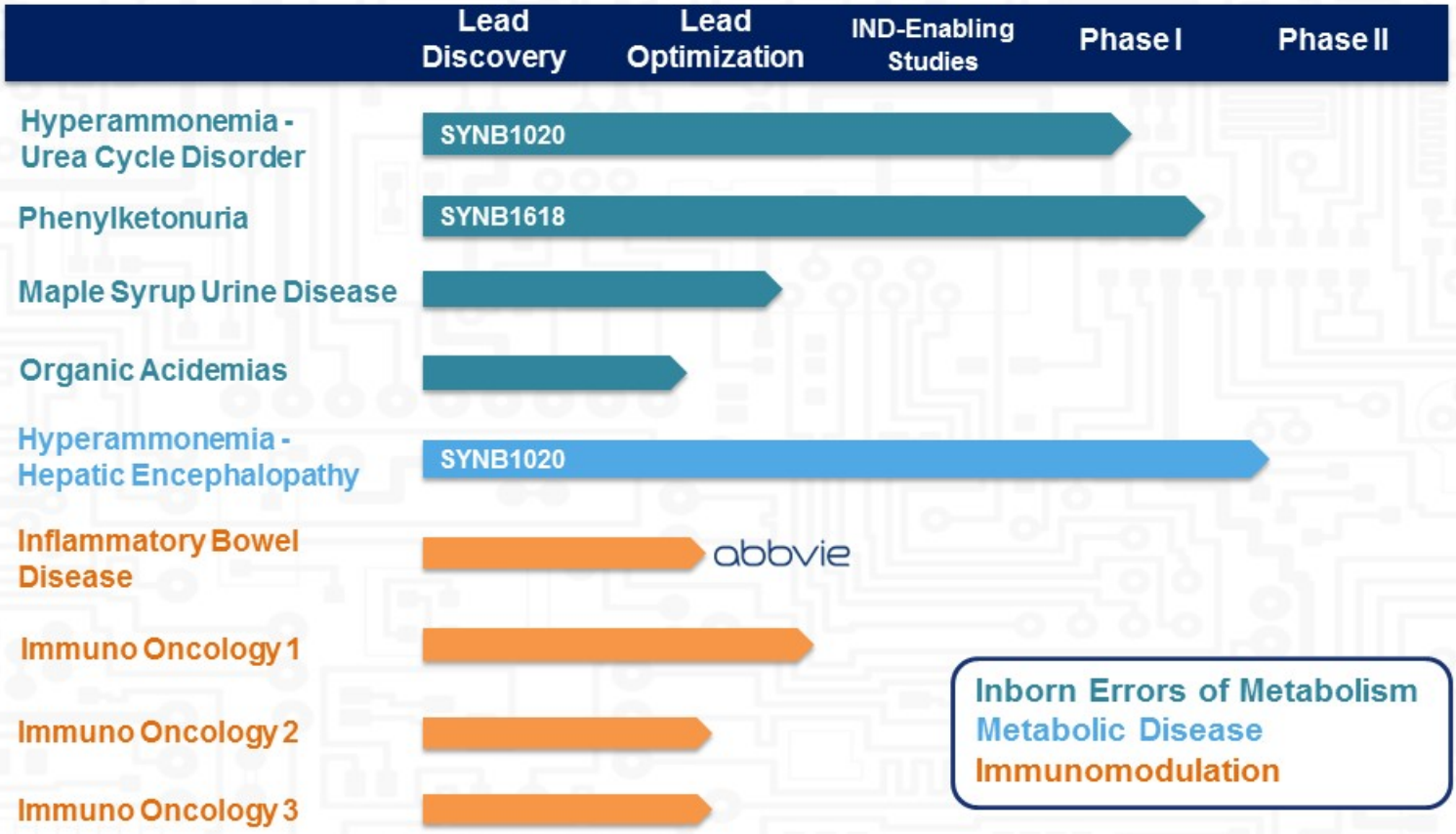
# Synthetic Biotic Platform Breadth and Potential:

## Initial Clinical Focus on Orphan Metabolic Diseases



# Synthetic Biotic Platform Breadth and Potential:

## Current Pipeline



# Initial Synthetic Biotic Programs:

## Designed to Evaluate Different Sites of Action

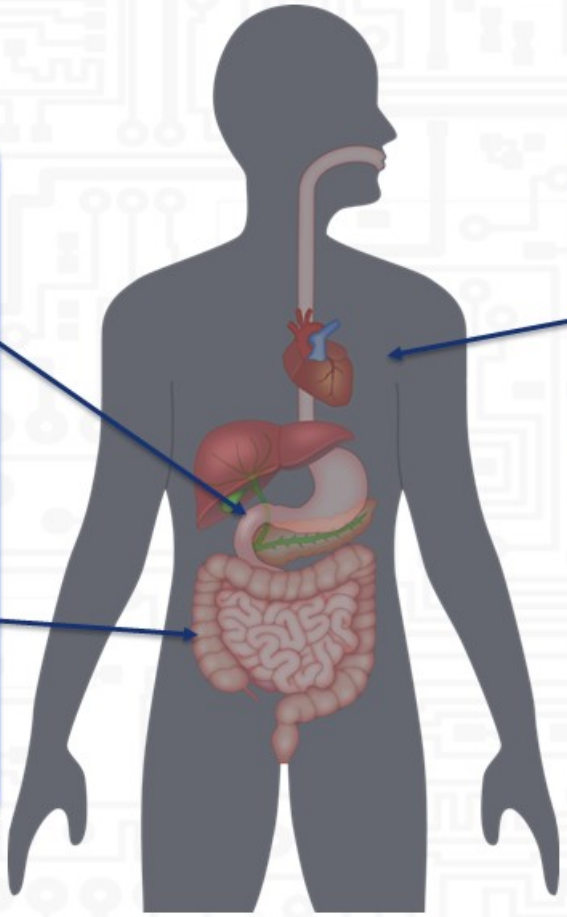
**Oral Administration**

***SYNB1618 for PKU:***

- Site of action = small intestine
- Other indications:
  - MSUD
  - IVA

***SYNB1020 for hyperammonemia:***

- Site of action = Colon
- Other indications:
  - PA
  - MMA



**Intra-tumoral Administration**

IO program: Site of action = “Cold” solid tumors

# SYNB1020 for Hyperammonemia Indications:

## Urea Cycle Disorders (UCD) and Hepatic Encephalopathy (HE)

*Both diseases are characterized by systemic ammonia accumulation*


### Urea Cycle Disorders

- **Genetic defects in Urea Cycle**
  - Deficiency in one of the six enzymes
  - Nitrogen accumulates as toxic ammonia → HE crisis
- **Patients:**
  - ~2,000 diagnosed in US; similar in EU
- **Treatment:**
  - Ammonia scavengers: buphenyl, Ravicti®
  - 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

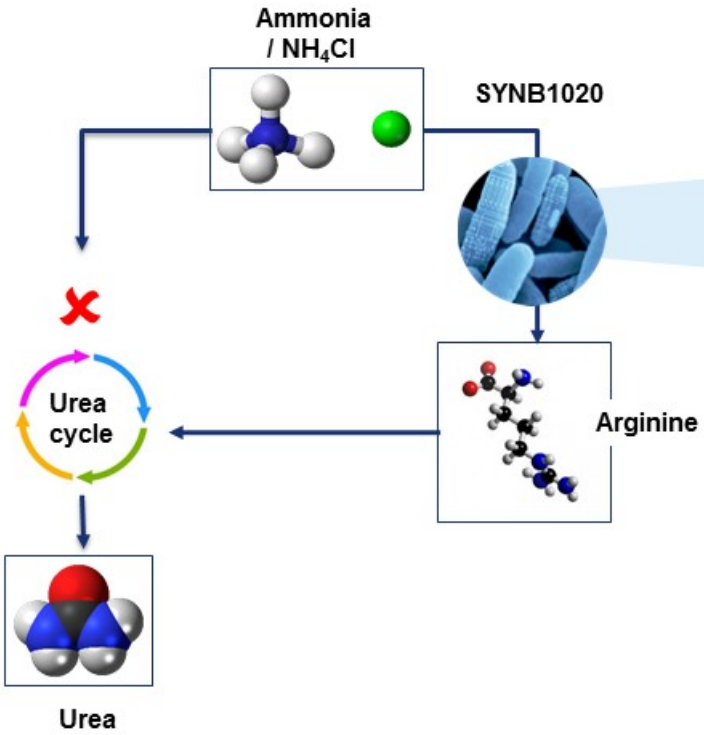
### Hepatic Encephalopathy

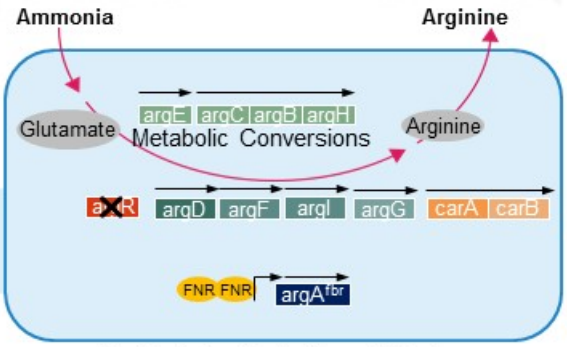
- **Neuropsychiatric complication in patients with end-stage liver disease (cirrhosis or hepatitis)**
  - Liver dysfunction leads to ammonia accumulation
  - Toxic to brain, leading to HE crisis & hospitalization
- **Patients**:
  - 165,000 diagnosed overt patients in US
  - Up to 70% of cirrhotic patients characterized as covert
- **Treatment**:
  - Lactulose: laxative - significant side effects
  - Rifaximin reduction in overt HE recurrence

- **Target Profile to Address Unmet Need:**
  - Reduce episodes of hospitalization
  - Improve cognitive outcomes, QoL

# SYNB1020 Mechanism of Action:

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



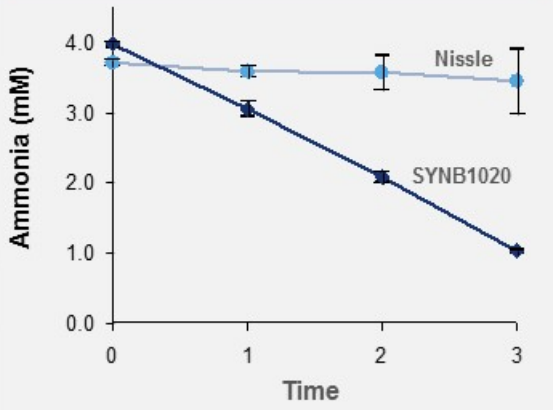

*Probiotic bacteria: E. coli* Nissle

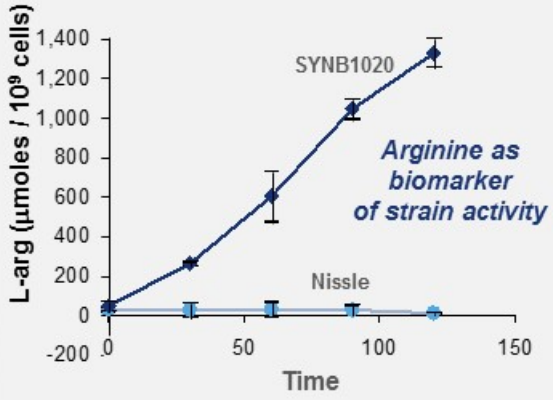
- Under normal conditions, **urea cycle metabolizes ammonia into urea**
- Where ammonia is not efficiently metabolized via urea cycle, **SYNB1020 provides an alternative mechanism**

# SYNB1020 Preclinical Characterization:

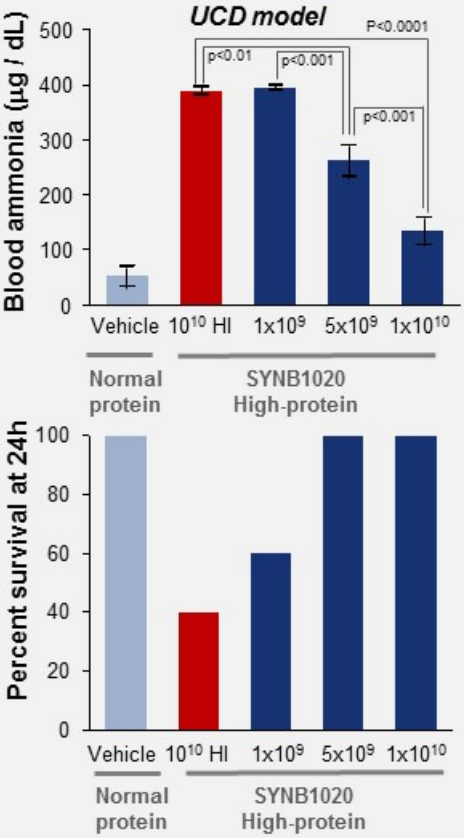
## Potent and Efficacious Ammonia Reduction and Improved Survival

### Potency *in vitro*



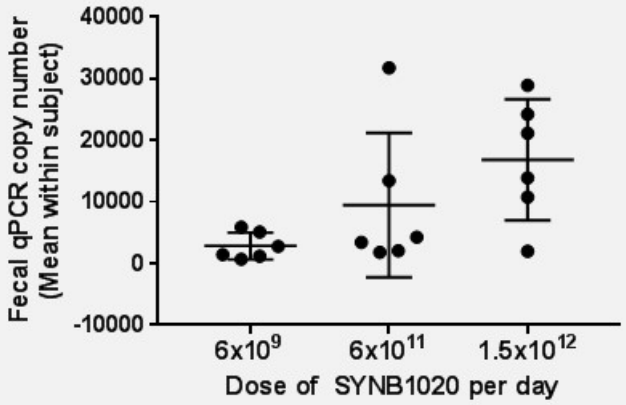




### Dose dependent survival and ammonia lowering *in vivo*



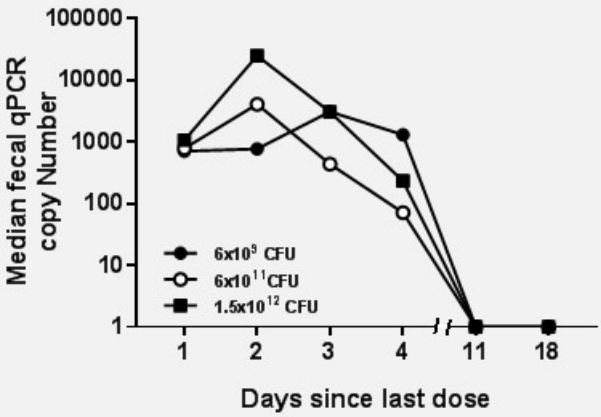
# Clinical Data SYNB1020 in Healthy Volunteers: Dose-Dependent Increase in SYNB1020 in Feces, Clearance on Cessation of Dosing

## Dose dependent steady-state SYNB1020 qPCR




- Steady-state qPCR copy number increases with increasing SYNB1020 dose

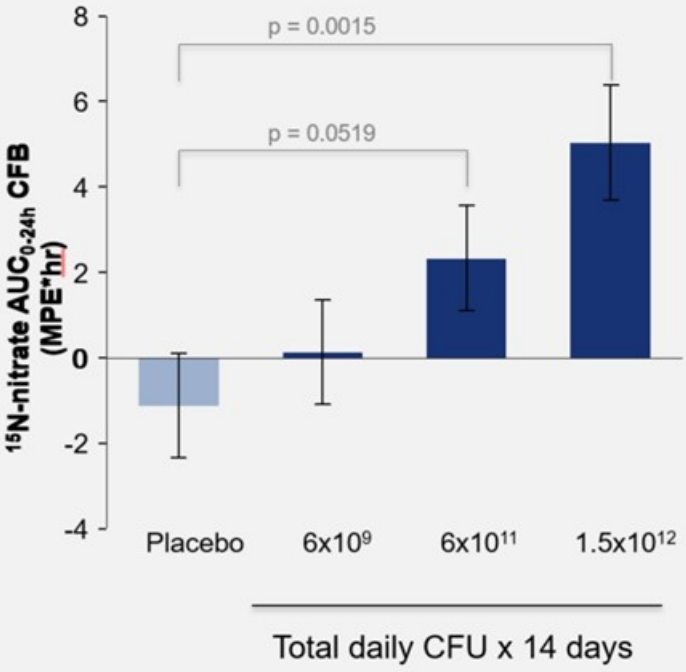
## SYNB1020 clearance within 2 weeks following completion of dosing



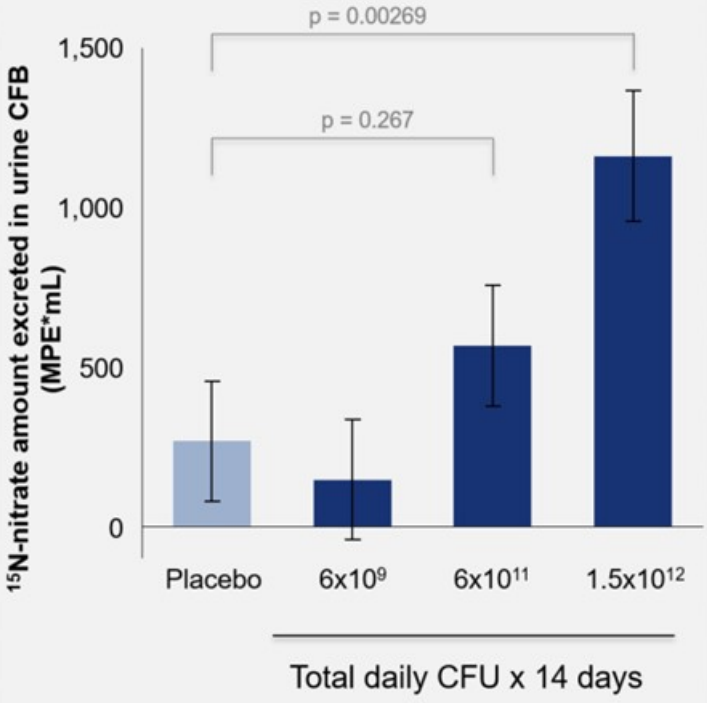

- SYNB1020 Clearance from Feces post-dosing

# Nitrate as a Biomarker for SYNB1020 Activity

## Plasma nitrate



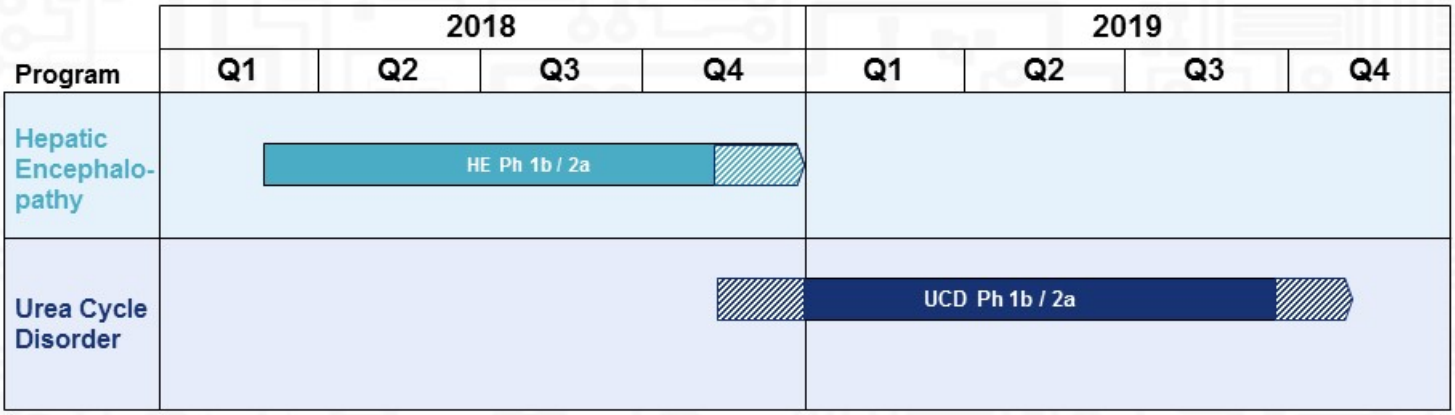

## Urinary nitrate



# SYNB1020 Clinical Development:

## Next Steps: HE and UCD Patient Studies – HE study initiated

***We are pursuing HE and UCD Ph 1b/2a with the goal of obtaining proof of concept data for both indications***




### Hepatic Encephalopathy

- Study open, initiating multiple sites in the US
- **Phase 1b/2a**: Randomized, double-blind placebo-controlled
- **Primary outcome**: establish safety/tolerability in hepatic insufficiency - patients with cirrhosis and HE
- **Secondary outcome**: reduction of ammonia

### Urea Cycle Disorders

- **Demonstrate safety/tolerability** in adults with late onset UCD
- Initiate Phase 1b/2a at multiple metabolic clinical sites

# SYNB1618 for Phenylketonuria (PKU):

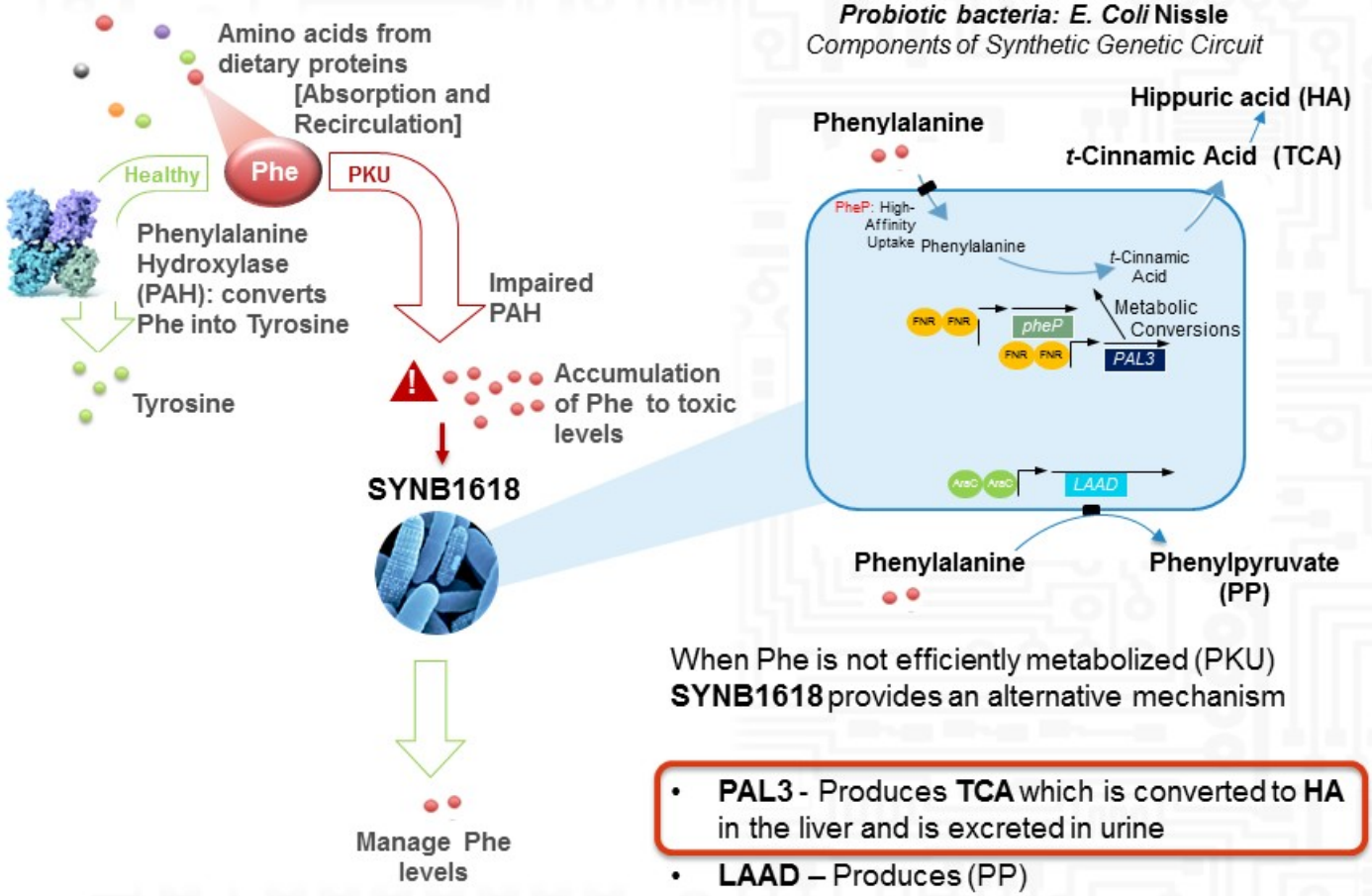
## Goal: Managing Plasma Phe Levels to Enable Increased Intake of Natural Protein

- **PKU is a rare inherited amino acid metabolism disorder**
  - Causes build up of amino acid phenylalanine (Phe) in the body
  - Phenylalanine is found in all proteins
- **Diagnosed:** 16,500 in US, similar in EU5
  - If left untreated, symptoms include cognitive impairment, convulsions, behavior problems, skin rash
- **Treatment:**
  - Low protein diet (no meat, dairy, nuts, eggs)
  - Kuvan: PAH cofactor. 20-40% of patients
  - Palynziq: injectable, pegylated, bacterial enzyme (PAL) (Adults)

- **Target Profile to Address Unmet Need:**
  - Manage Phe: Currently < half adults at target (120 - 360 mmol / L, source: NPKUA)
  - Increase natural protein intake (less than 10g typically)
  - Oral dosing without systemic toxicity

# SYNB1618 Mechanism of Action:

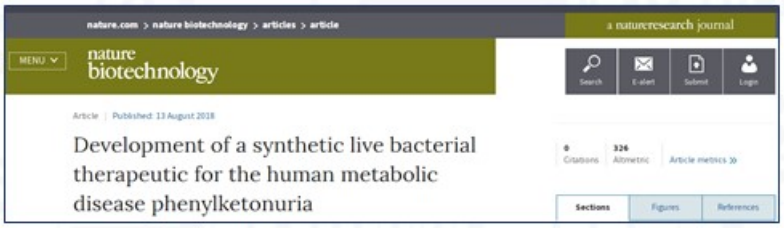
## Designed to Convert Toxic Phenylalanine to *trans*-cinnamic Acid



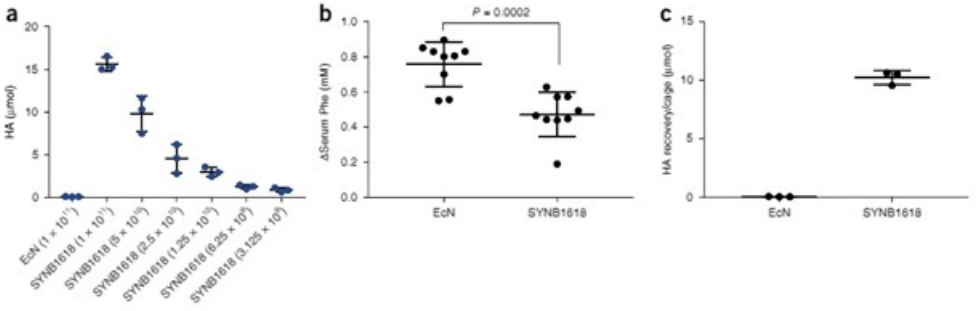

When Phe is not efficiently metabolized (PKU) **SYNB1618** provides an alternative mechanism

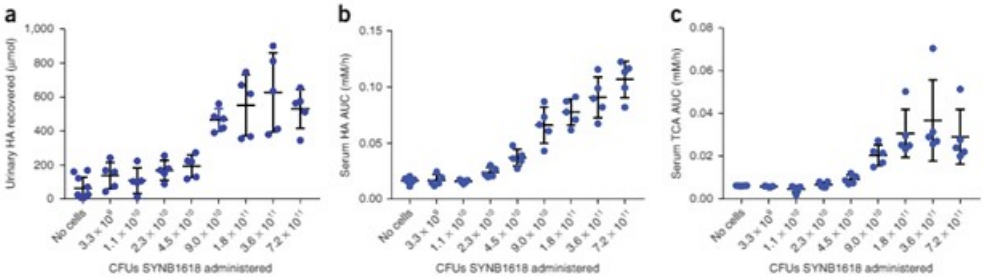
- **PAL3** - Produces **TCA** which is converted to **HA** in the liver and is excreted in urine
- **LAAD** – Produces (PP)

# **Preclinical data:** Biomarkers demonstrate activity of SYNB1618 in mouse model of PKU and healthy NHPs




*In vivo* activity and efficacy of SYNB1618 in mouse model of (PKU) Pah$^{enu2/enu2}$



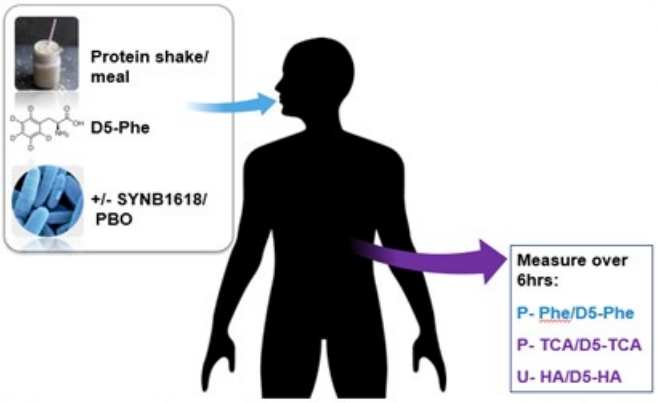

Dose response and PD of SYNB1618 in healthy NHPs

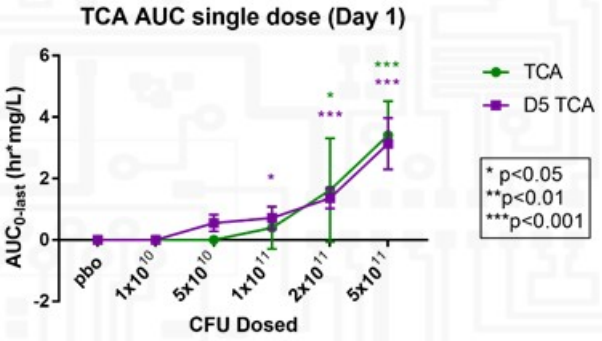
# SYNB1618 in the Clinic: Safety

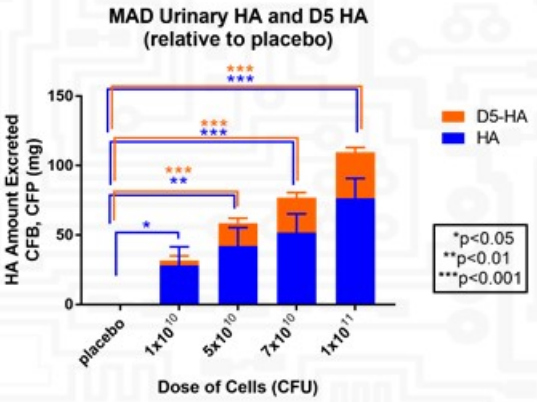
## Interim Analysis of Phase 1/2a SAD/MAD Study Healthy Volunteer Cohorts

- The study enrolled 56 healthy volunteers, all of whom received at least one dose of SYNB1618 or placebo. The subjects were predominantly male Caucasians and the age range of enrolled subjects was 18-62 years
- 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 AEs were GI-related
- All subjects cleared the bacteria. There was no evidence of colonization, and no subject required antibiotics
- Single dose MTD was defined as $2x10^{11}$ CFU. Doses above this level were associated with dose-limiting GI adverse events
- Based on pharmacodynamic data and tolerability profile a dose was identified for the second part of the study in PKU patients

# SYNB1618 in the Clinic: Statistically significant dose-dependent activity of SYNB1618 in healthy volunteers



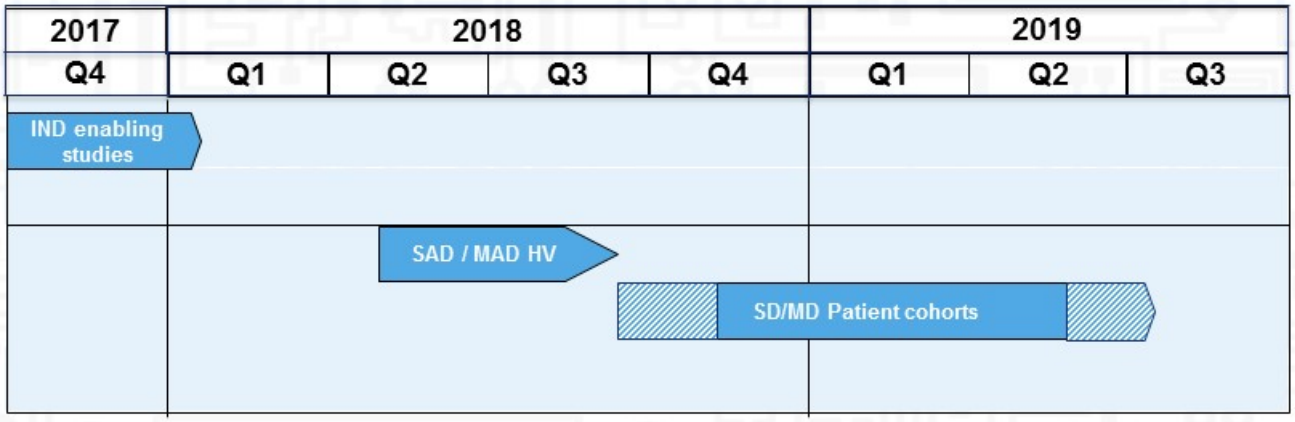




HA=hippurate, D5-HA= labeled HA,
CFB=change from baseline, CFP=change from placebo

# SYNB1618 in the Clinic:

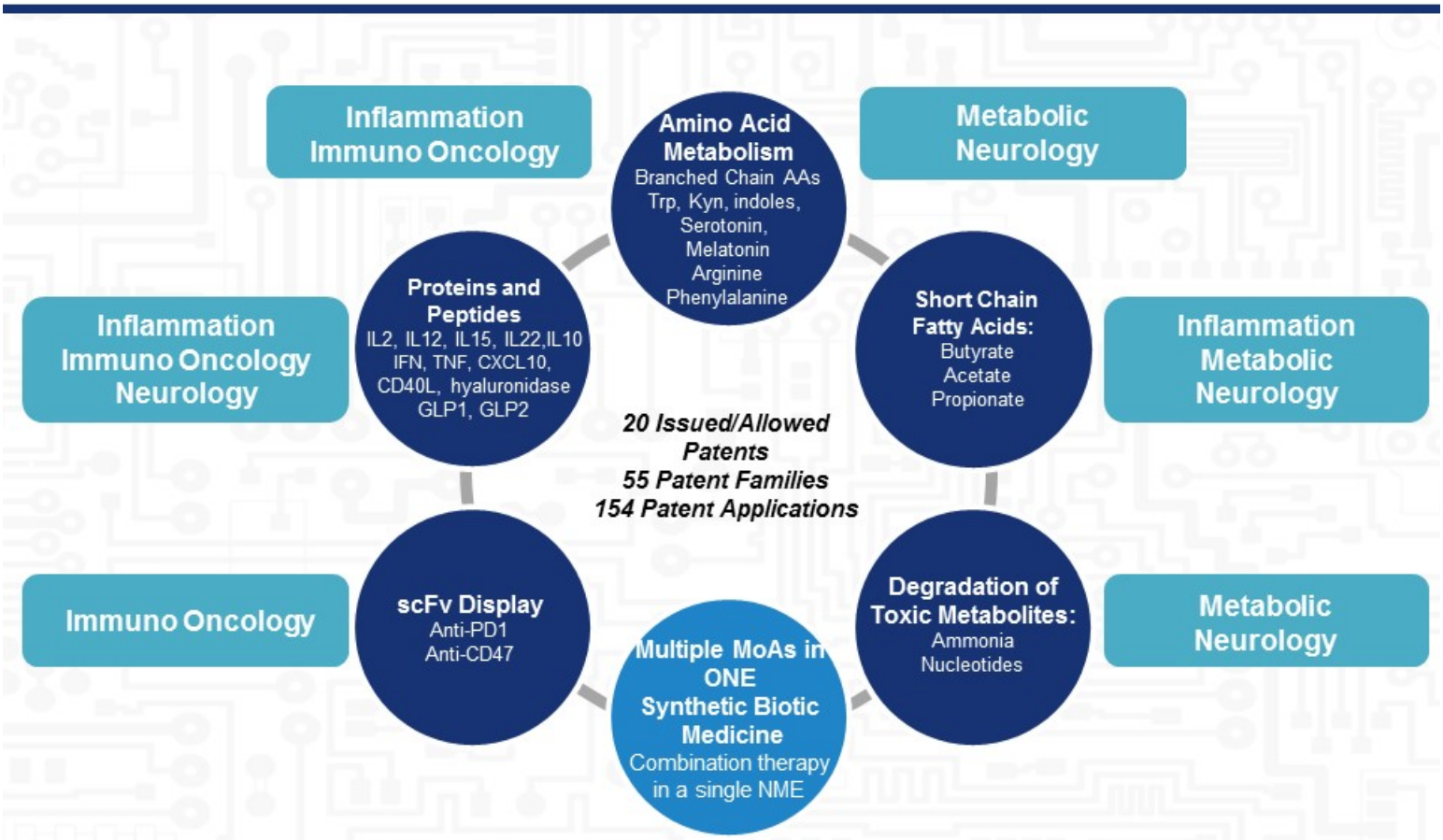
## Phase 1/2a SAD/MAD in Healthy Volunteers with Patient Cohort




- **Goal:** assess safety, tolerability and kinetics in healthy volunteers across a range of doses
  - Includes cohorts of SD/MD PKU patients
- **Interim read**: *trans*-Cinnamic acid and Hippuric acid production in healthy volunteers
- **Study duration**: ~12 months

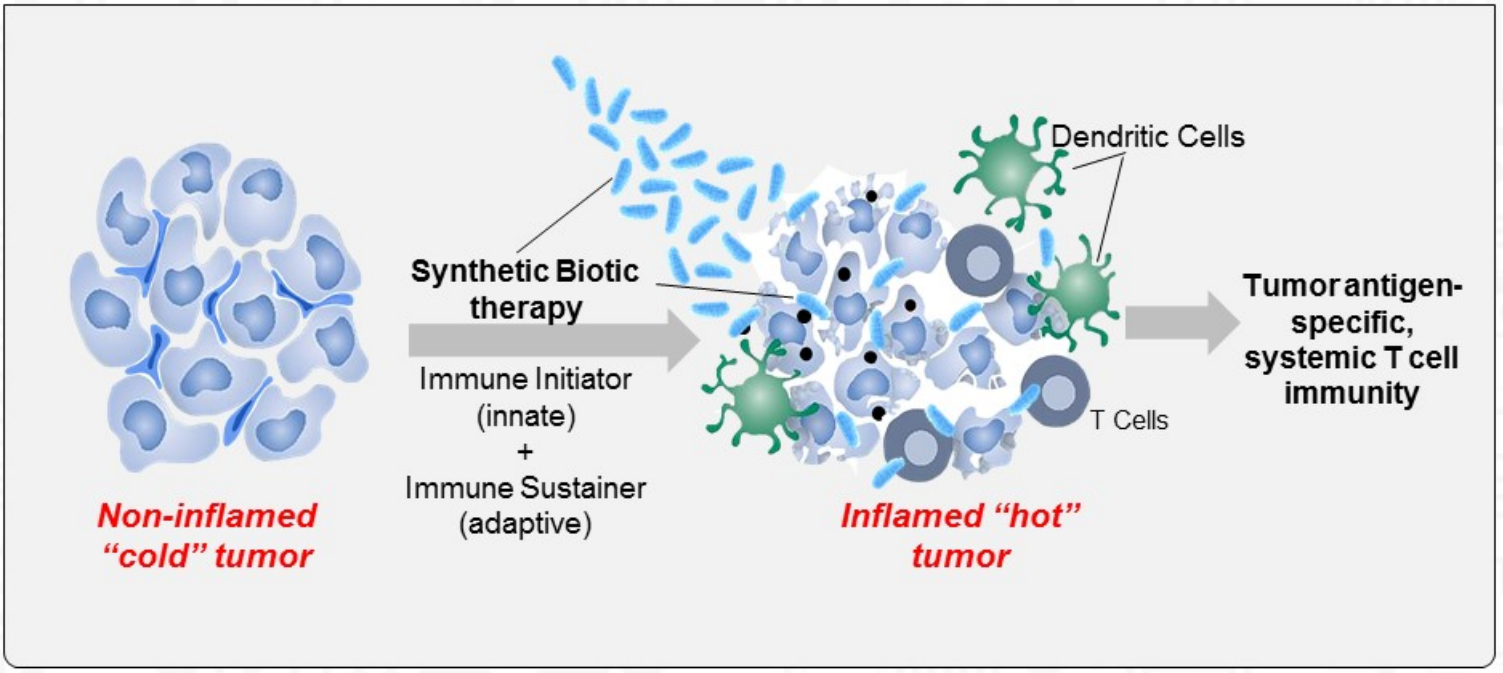
# Synthetic Biotic Medicines:

## Applicability Beyond Rare Disease Across Multiple Pathways



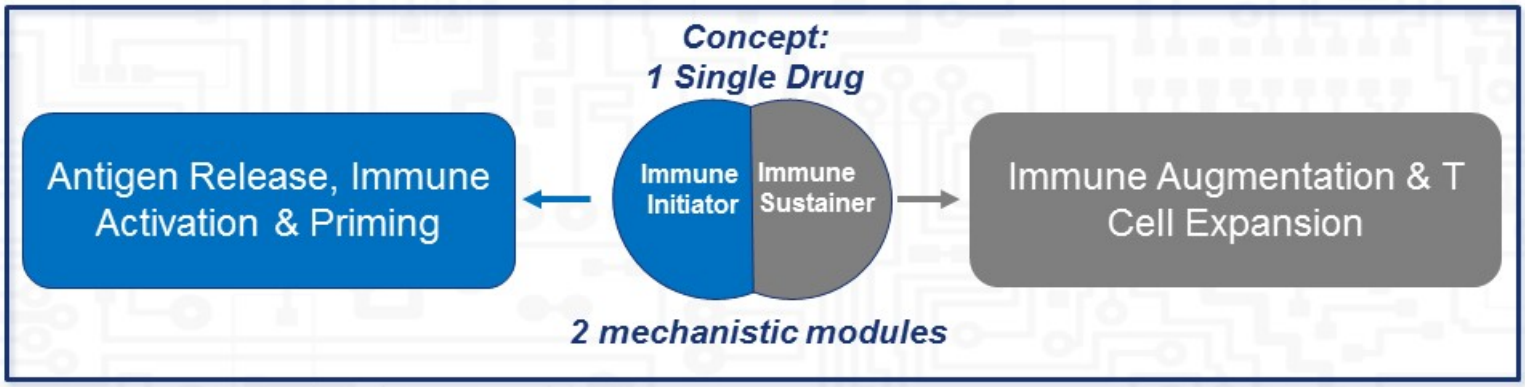
# Synlogic Vision for Immuno-Oncology:

## Living Medicines to Turn a "Cold" Tumor "Hot"



# Synlogic Vision for Immuno-Oncology:

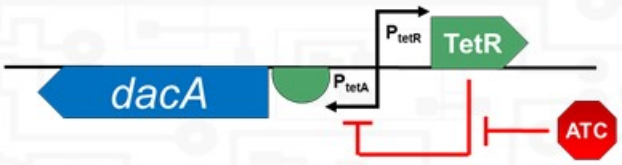
## Living Medicines with High Response Rates and Abscopal Effect as Single Agents



# Design of Initiator SYN-STING and Sustainer SYN-Kyn

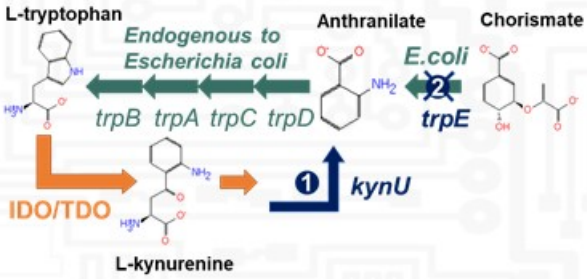
**Antigen Release, Immune Activation & T cell Priming** ← **Immune Initiator** | **Immune Sustainer** → **Immune Augmentation & T Cell Expansion**


## Tetracycline Inducible STING Agonist




***dacA*, a diadenylate cyclase gene from *Listeria monocytogenes*, driven by Ptet**

## Constitutive Kynurenine Consumption

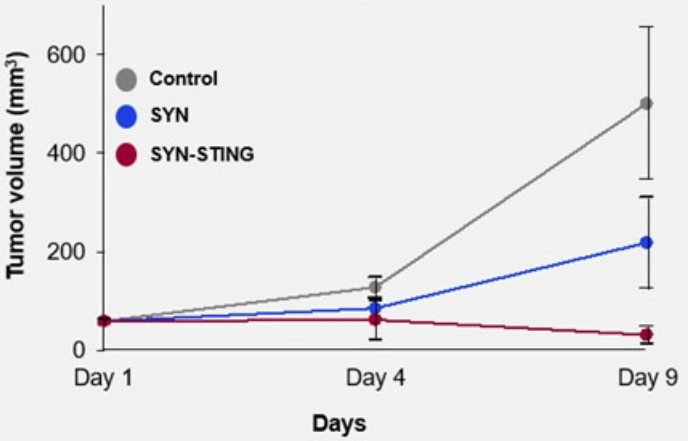



***kynU*, a kynureninase gene from *Pseudomonas fluorescens*, constitutively expressed**

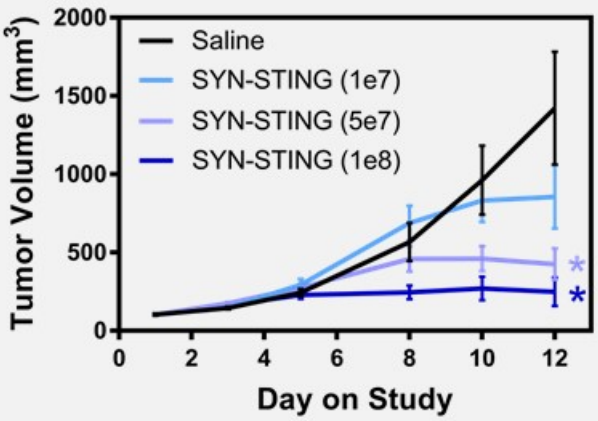
# Initiator (STING) Module Characterization:

## STING Agonist Producer with Anti-tumor Activity as Single Agent

**Tumor regression by day 8 following SYN-STING intra-tumor injection**

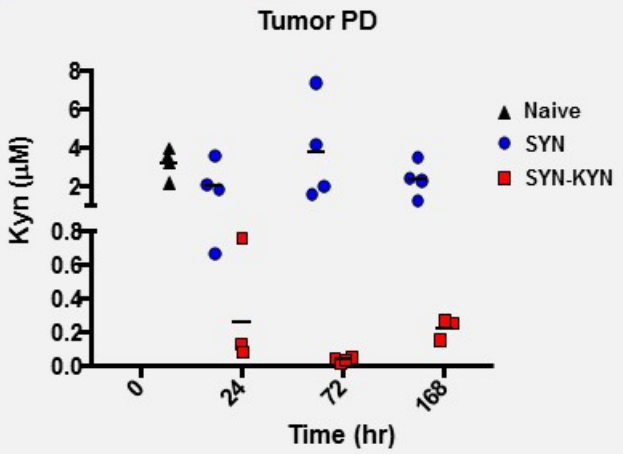



**Dose-dependent inhibition of tumor growth (A20)**

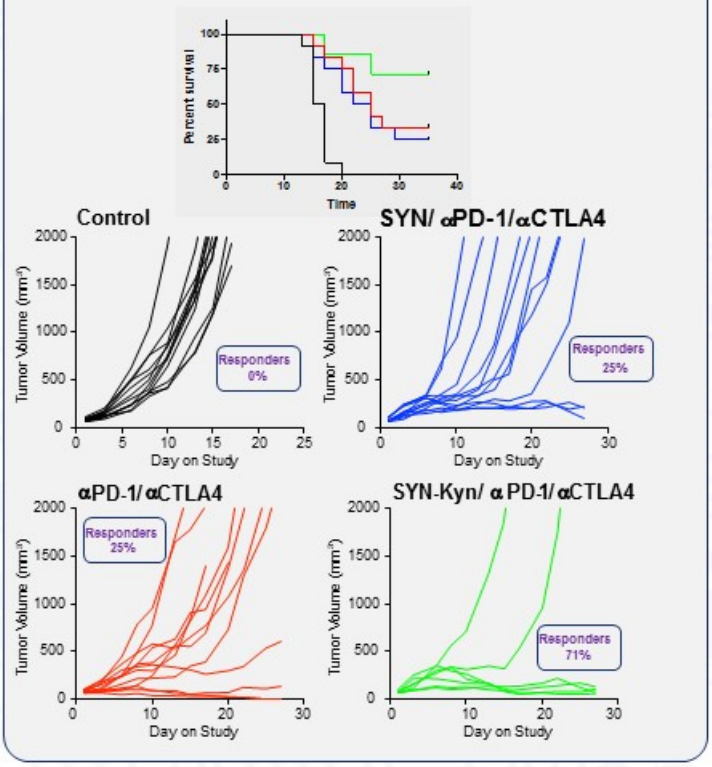


# Sustainer (Kyn) Module Characterization : Consumes Kynurenine - Arrests Tumor Growth in Combination; Increased Response Rates as Triple Combo

## Kyn-consuming strain reprograms the tumor microenvironment by depleting kynurenine

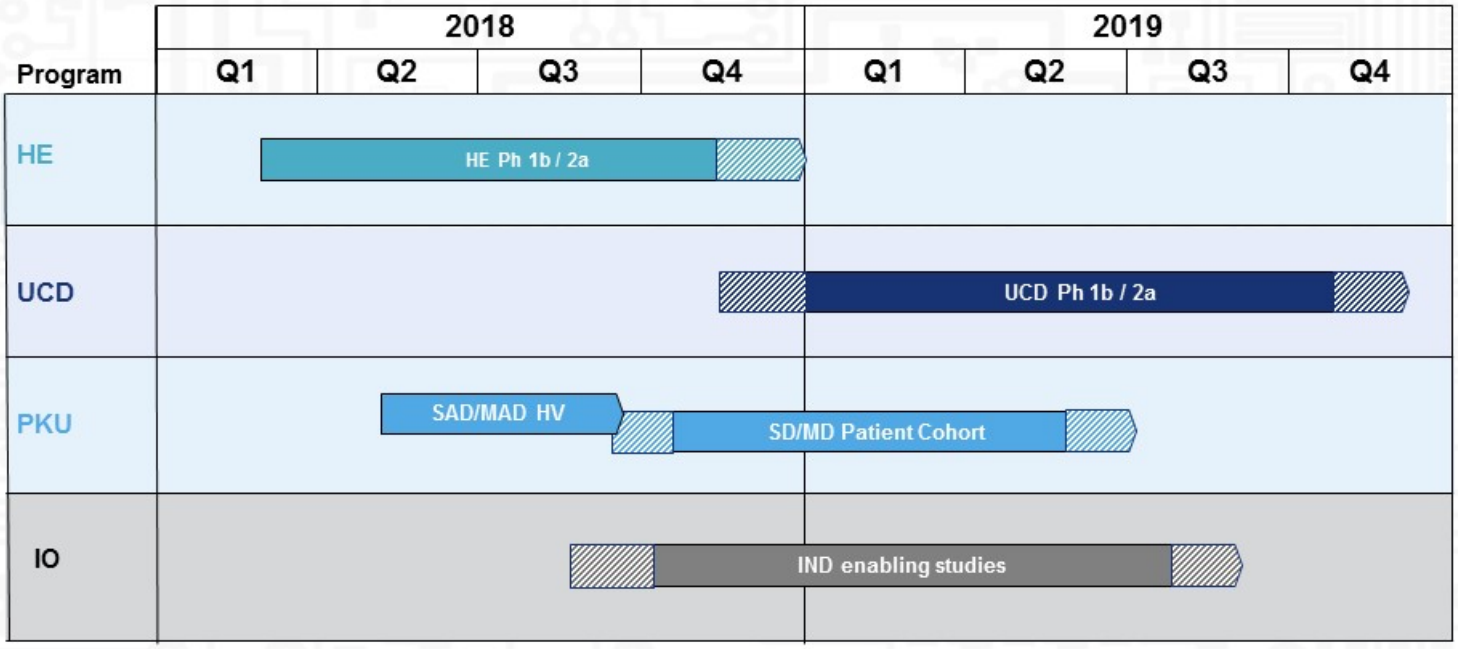



## Metabolite reprogramming in the TME, early T cell activation and reversal of T cell exhaustion drive tumor rejections



# Synlogic Development Pipeline:

## Programs' Timelines Summary



# Synlogic Synthetic Biotic Platform:

## Bringing Rational Drug Development to the Microbiome

### Build Potency

**Rational design:**

- Synthetic biology tools applied
- Engineer potency
- Exceed endogenous bacterial activity

### Apply Pharmacological Principles

**Pharmacologically tractable:**

- Non-colonizing
- Measurable dose-response

### Develop Reliable Manufacturing

**GMP manufacturing:**

- Single strain
- Reproducible yield
- Formulation & delivery
- Control switches
- Portfolio applicability


synlogic