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 8, 2018

SYNLOGIC, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**001-37566**	**26-1824804**
(State of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
200 Sidney St., Suite 320 Cambridge, MA		**02139**
(Address of principal executive offices, including zip code)		**(Zip Code)**

Registrant's telephone number, including area code: (617) 401-9947

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:

☐ 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. ☒

Item 7.01 Regulation FD Disclosure.

Synlogic, Inc. has prepared an investor presentation to be used in connection with general corporate presentations, a copy which is attached to this Current Report on Form 8-K as Exhibit 99.1.

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 2018.

SIGNATURE

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.

Dated: January 8, 2018

SYNLOGIC, INC.

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

Corporate Overview

January 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 November 13, 2017. 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:

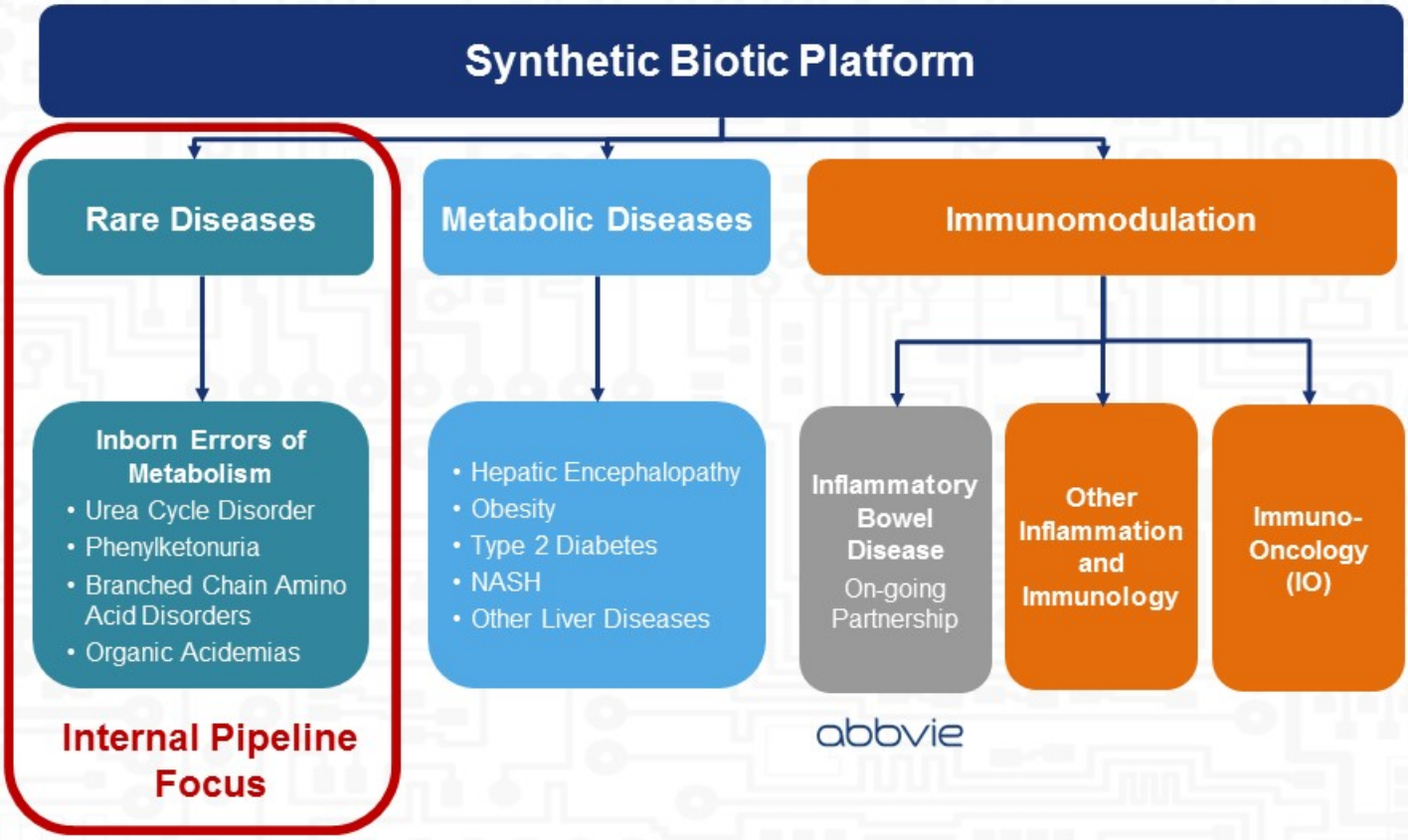
- Widely-used **oral probiotic**
- **Leverage the safety** of probiotic
- Found within natural human **microbiome**
- **Amenable to genetic manipulation**

Synthetic Biology + Bacteria = Synthetic Biotic Medicine

Therapeutic delivered locally to treat systemic diseases

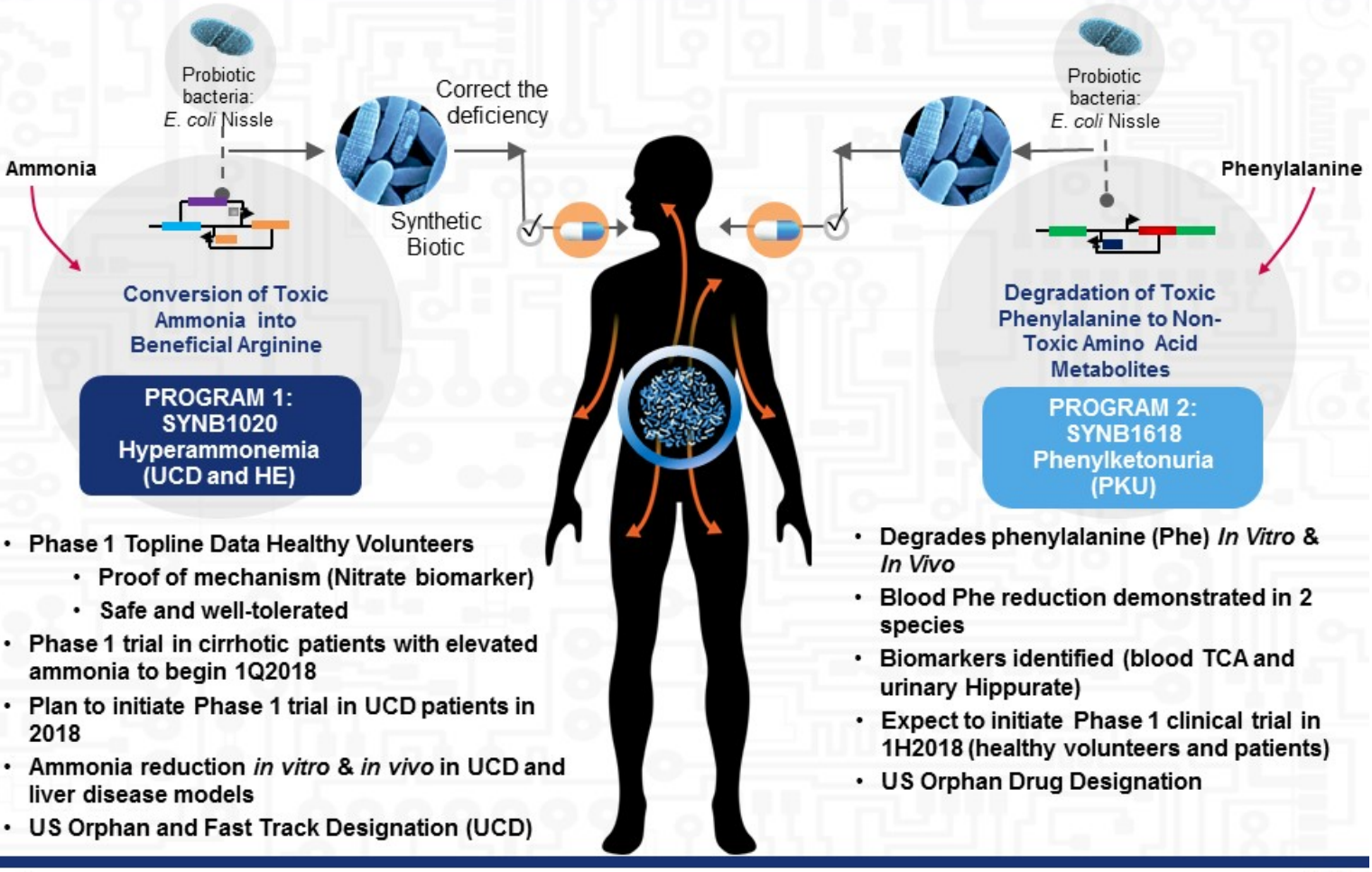
Synthetic Biotic Platform Breadth and Potential:

Initial Clinical Focus on Orphan Metabolic Diseases



Rare Diseases:

Hyperammonemia and Phenylketonuria Programs in Clinical Trials in Patients in 2018

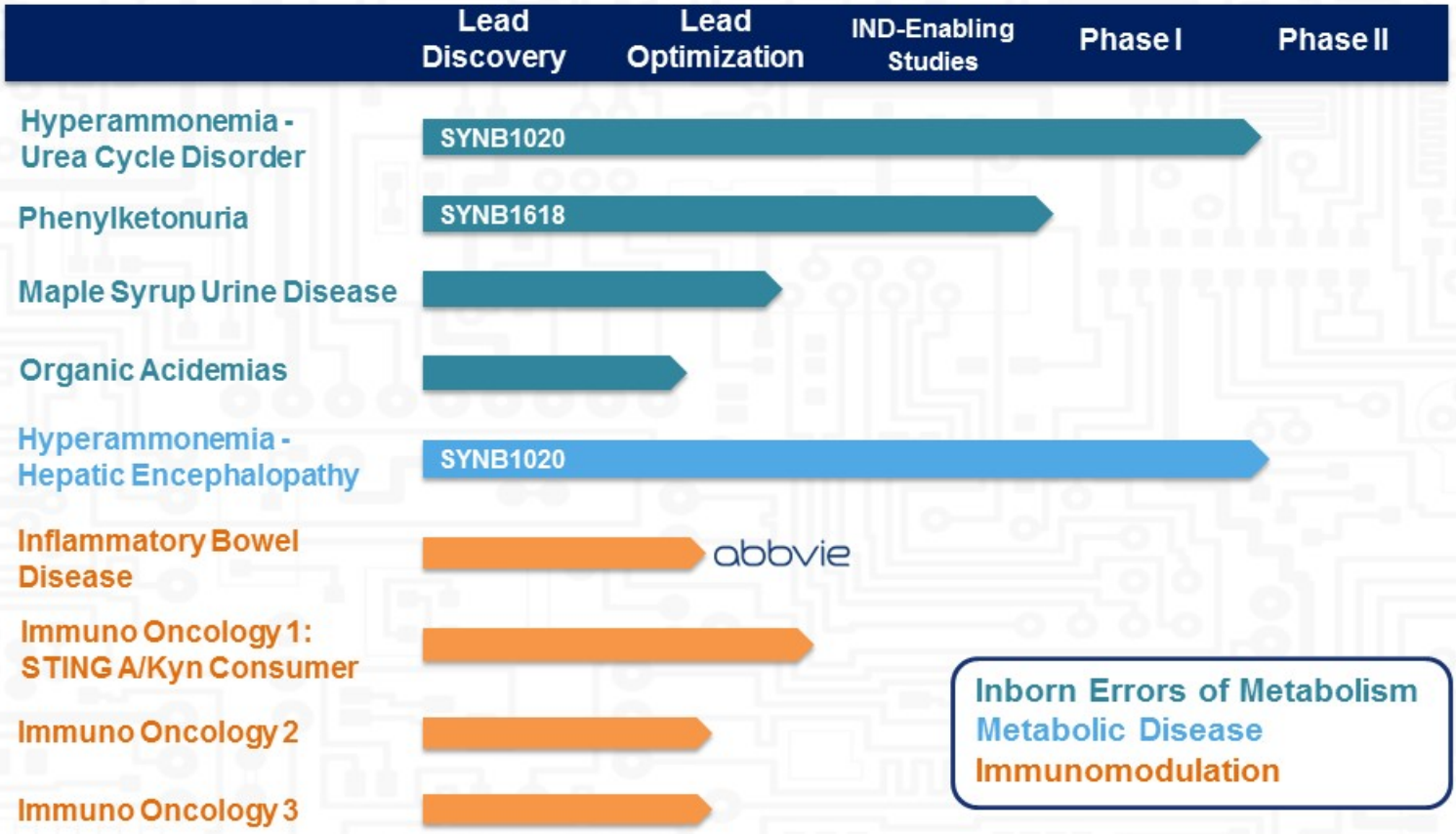


- Phase 1 Topline Data Healthy Volunteers
  - Proof of mechanism (Nitrate biomarker)
  - Safe and well-tolerated
- Phase 1 trial in cirrhotic patients with elevated ammonia to begin 1Q2018
- Plan to initiate Phase 1 trial in UCD patients in 2018
- Ammonia reduction *in vitro* & *in vivo* in UCD and liver disease models
- US Orphan and Fast Track Designation (UCD)

- Degrades phenylalanine (Phe) *In Vitro* & *In Vivo*
- Blood Phe reduction demonstrated in 2 species
- Biomarkers identified (blood TCA and urinary Hippurate)
- Expect to initiate Phase 1 clinical trial in 1H2018 (healthy volunteers and patients)
- US Orphan Drug Designation

Synthetic Biotic Platform Breadth and Potential:

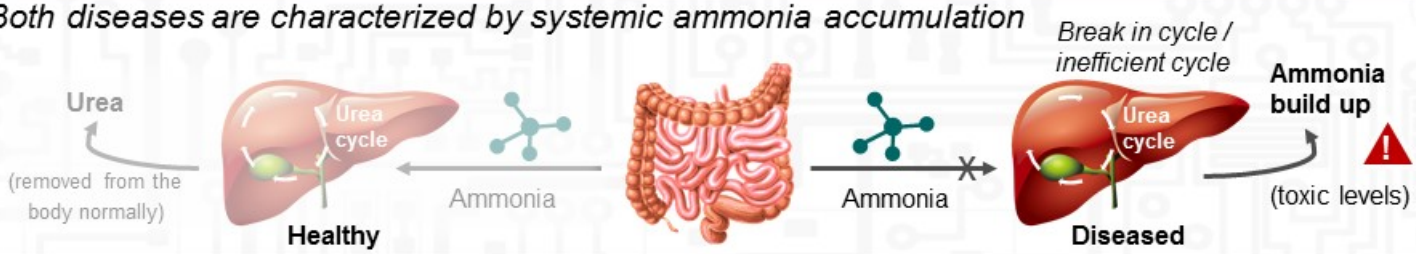
Current Pipeline



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**
  - Results in 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 grams per day
  - Oral administration

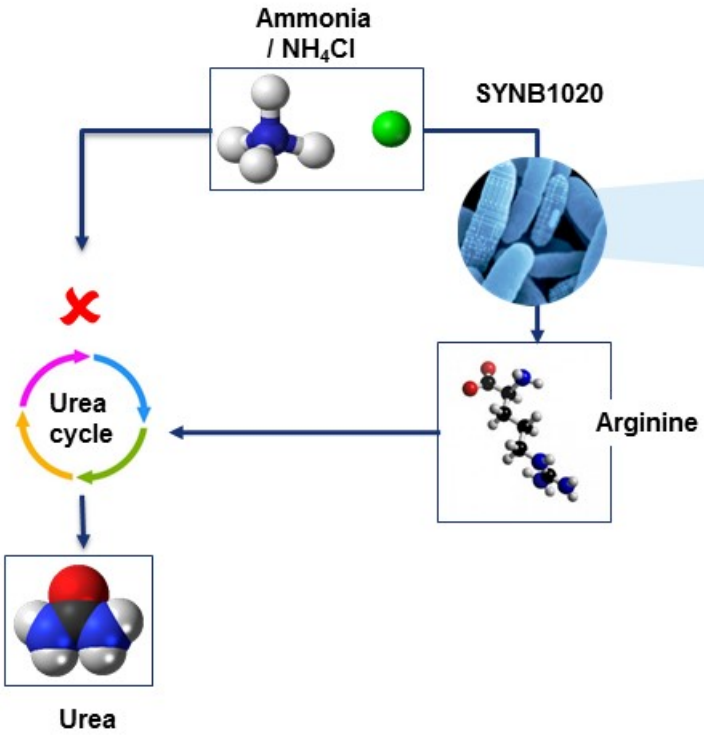
Hepatic Encephalopathy

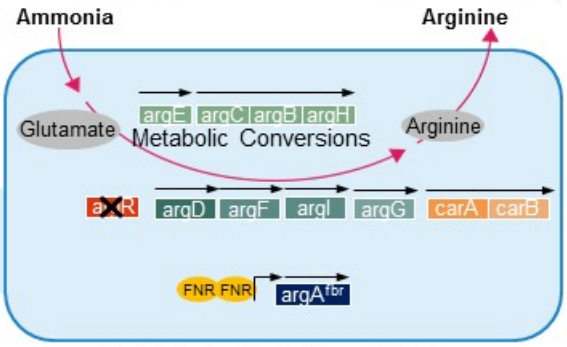
- **Neuropsychiatric complication in patients with end-stage liver disease (cirrhosis or hepatitis)**
  - Liver dysfunction leading to ammonia accumulation
  - Toxic to brain, leading to crisis & hospitalization
- **Patients**:
  - 165,000 diagnosed overt patients in US
  - Covert in up to 70% of cirrhotic patients
- **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





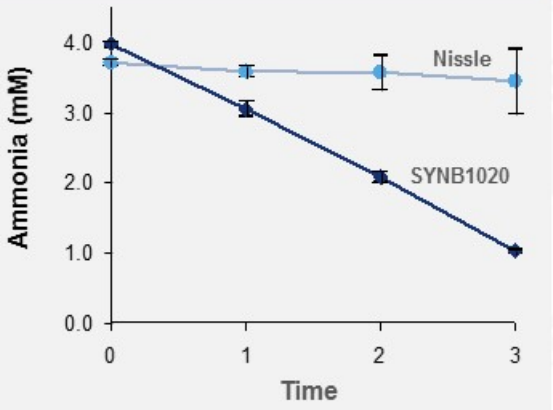
Probiotic bacteria: E. coli Nissle

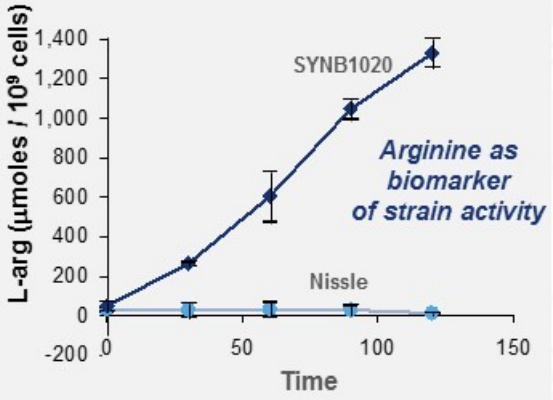
- Under normal conditions, **urea cycle metabolizes ammonia into urea**
- Where ammonia is not efficiently metabolized via urea cycle, **SYNB1020 provides an alternative mechanism**

SYNB1020 Preclinical Characterization:

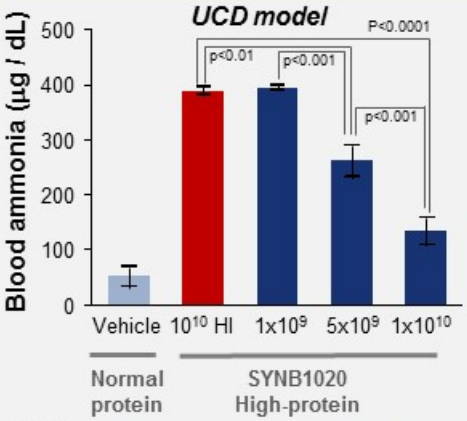
Potent and Efficacious Ammonia Reduction and Improved Survival

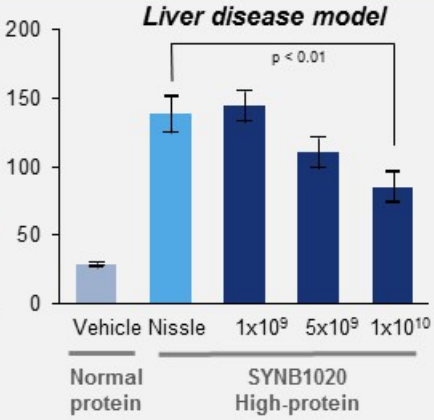
Potency *in vitro*

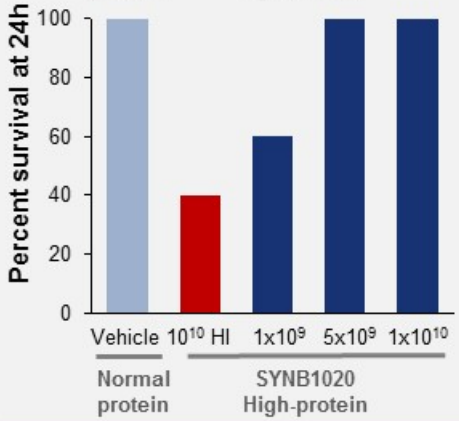


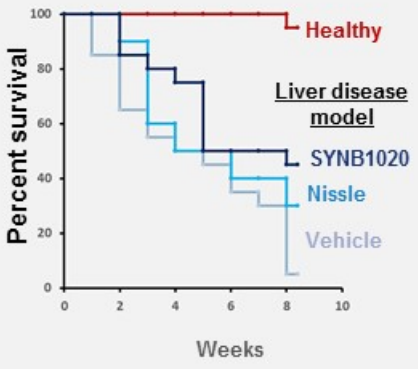


Dose dependent survival and ammonia lowering *in vivo*



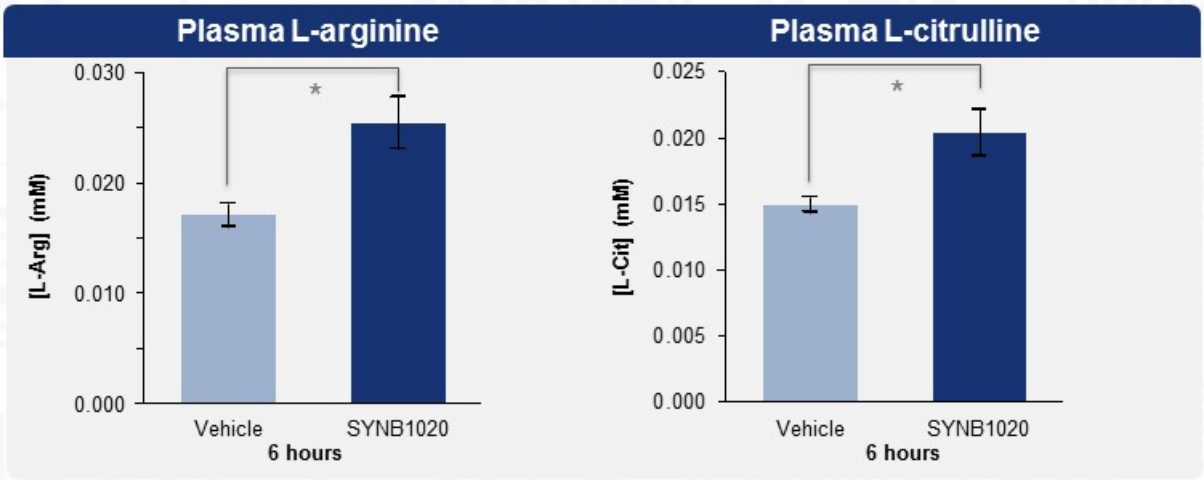


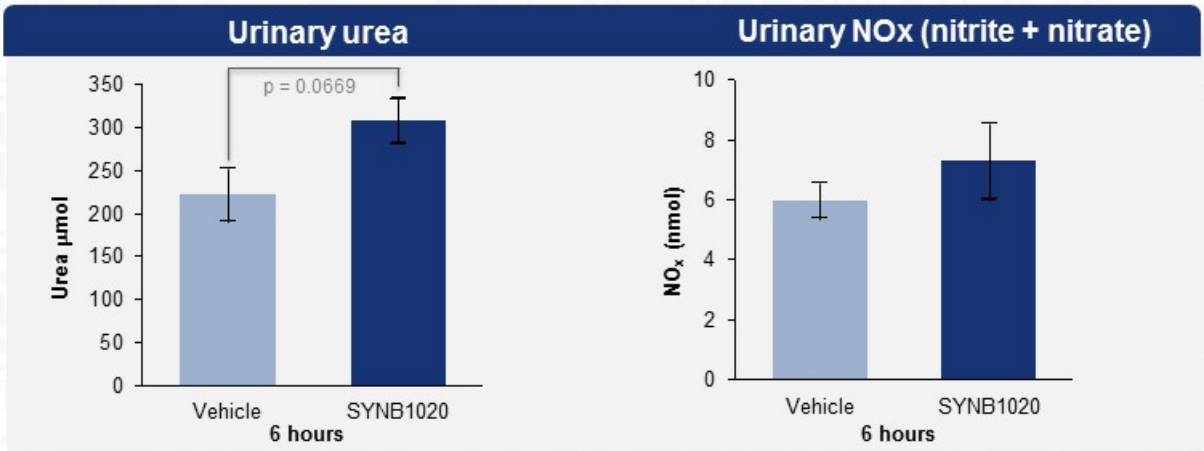




SYNB1020 Biomarkers of Mechanism:

Increase of Plasma and Urinary Biomarkers and Improvement in Urea Cycle in Mice

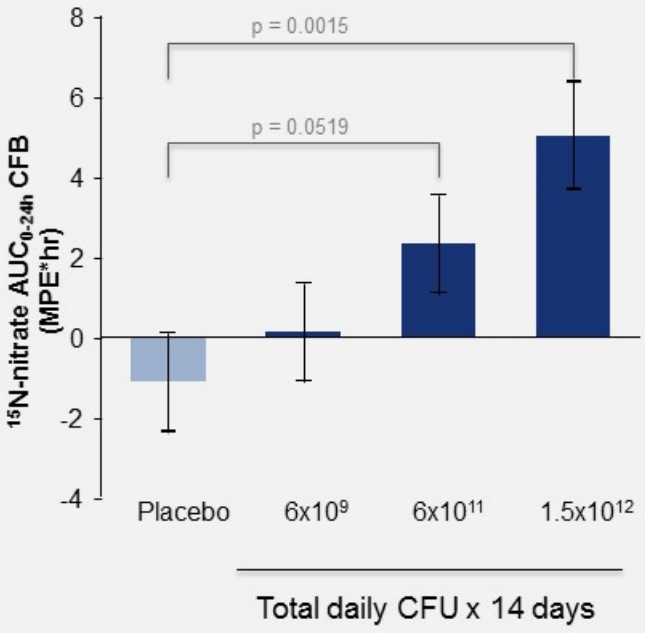




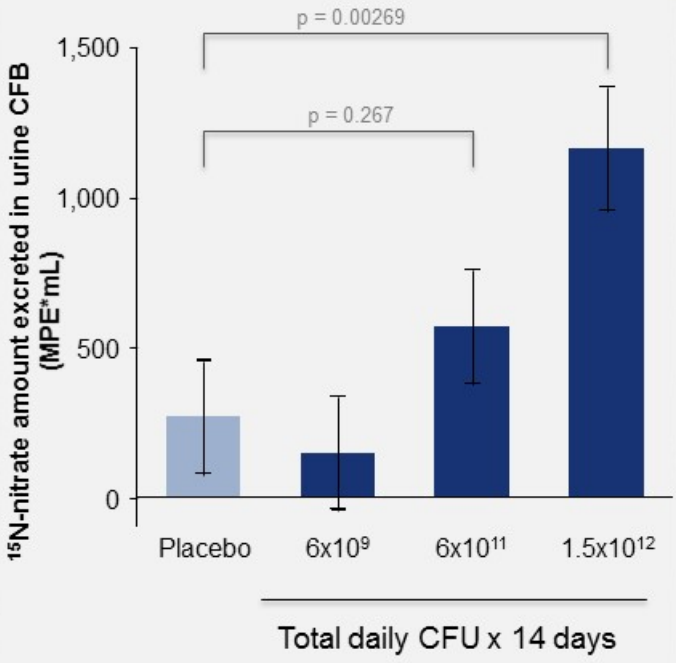
SYNB1020 Biomarkers in Phase 1 SAD / MAD Study:

Significant Dose-Dependent Effect on Plasma and Urinary ^{15}Nitrate

Plasma nitrate



Urinary nitrate

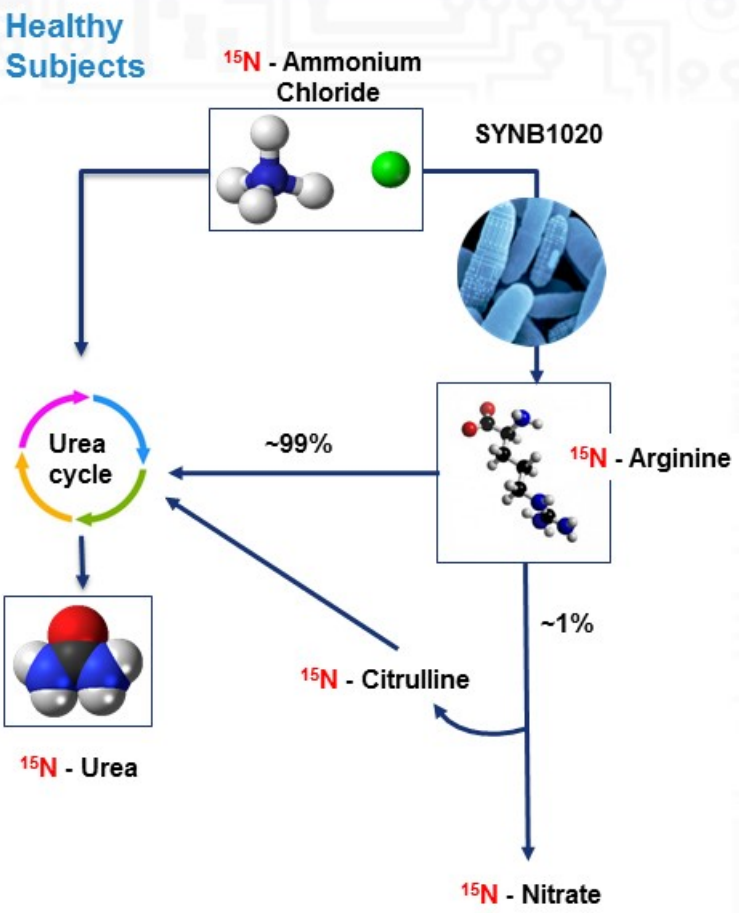


SYNB1020 Biomarkers in Phase 1 SAD / MAD Study:

Summary of Biomarker Strategy

- Healthy humans have a robust urea cycle
  - Rapidly convert excess ammonia into urea
  - Maintain consistent ammonia levels
- In the **Phase 1** study of healthy volunteers, an oral dose of $^{15}NH_4CL$ was followed by blood and urine sampling over 24 hours:
  - Tested for ^{15}N-labeled urea, citrulline, nitrate
  - Change in levels compared to baseline as measure of *in vivo* strain activity

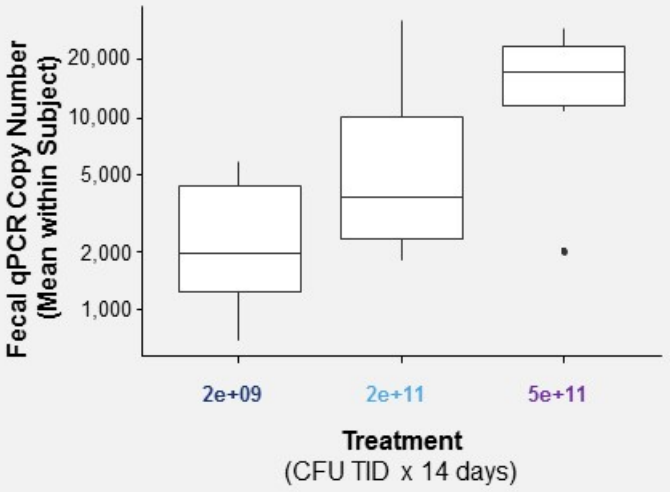
- In UCD / HE patients, *in vivo* activity is expected to translate to lower ammonia levels (vs baseline)



SYNB1020 Phase 1 SAD / MAD Study:

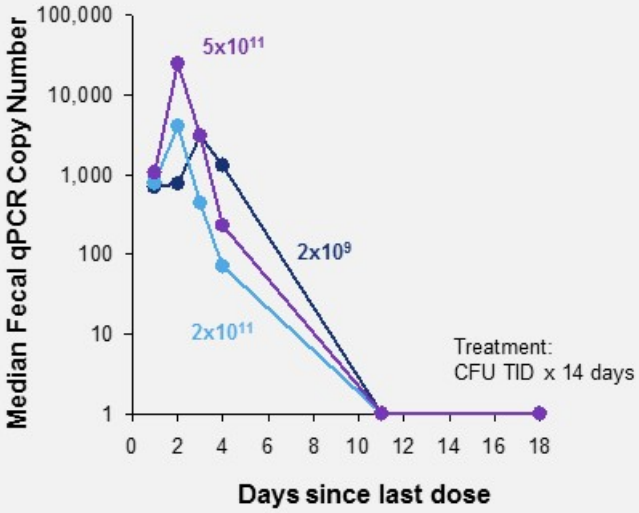
Safe & Well Tolerated with Dose-dependent Exposure Relationship and Fast Clearance

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

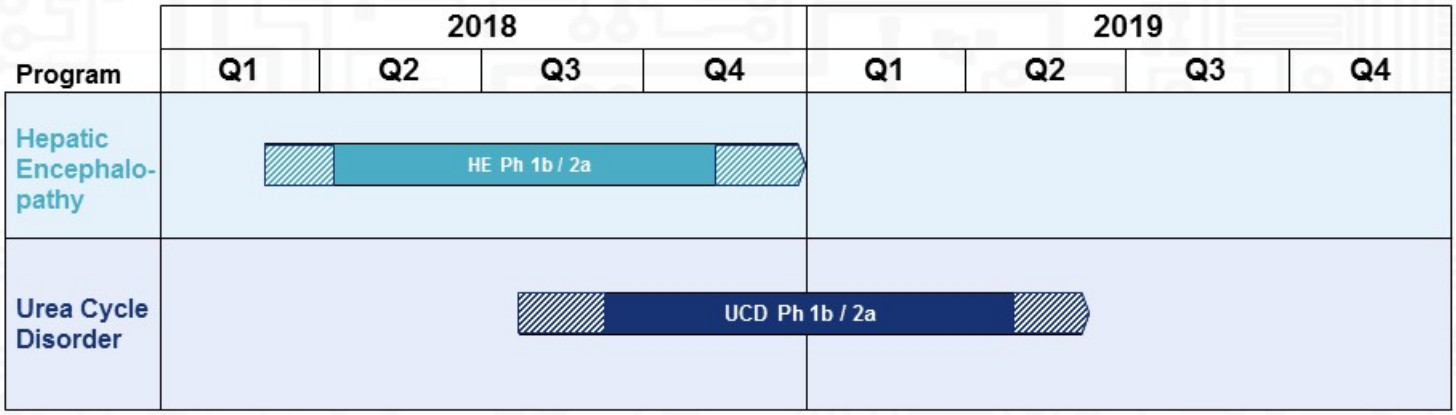


- Following discontinuation of dosing, fecal qPCR load fell rapidly

SYNB1020 Clinical Development:

Next Steps: HE and UCD Patient Studies in 2018

We are pursuing HE and UCD Ph 1b/2a in 2018 with the goal of obtaining proof of concept data for both indications



Hepatic Encephalopathy

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

Urea Cycle Disorders

- **Demonstrate safety/tolerability** in adults with late onset UCD
- Initiate Phase 1b/2a in H2 2018 at multiple metabolic clinical sites

SYNB1618 for Phenylketonuria (PKU):

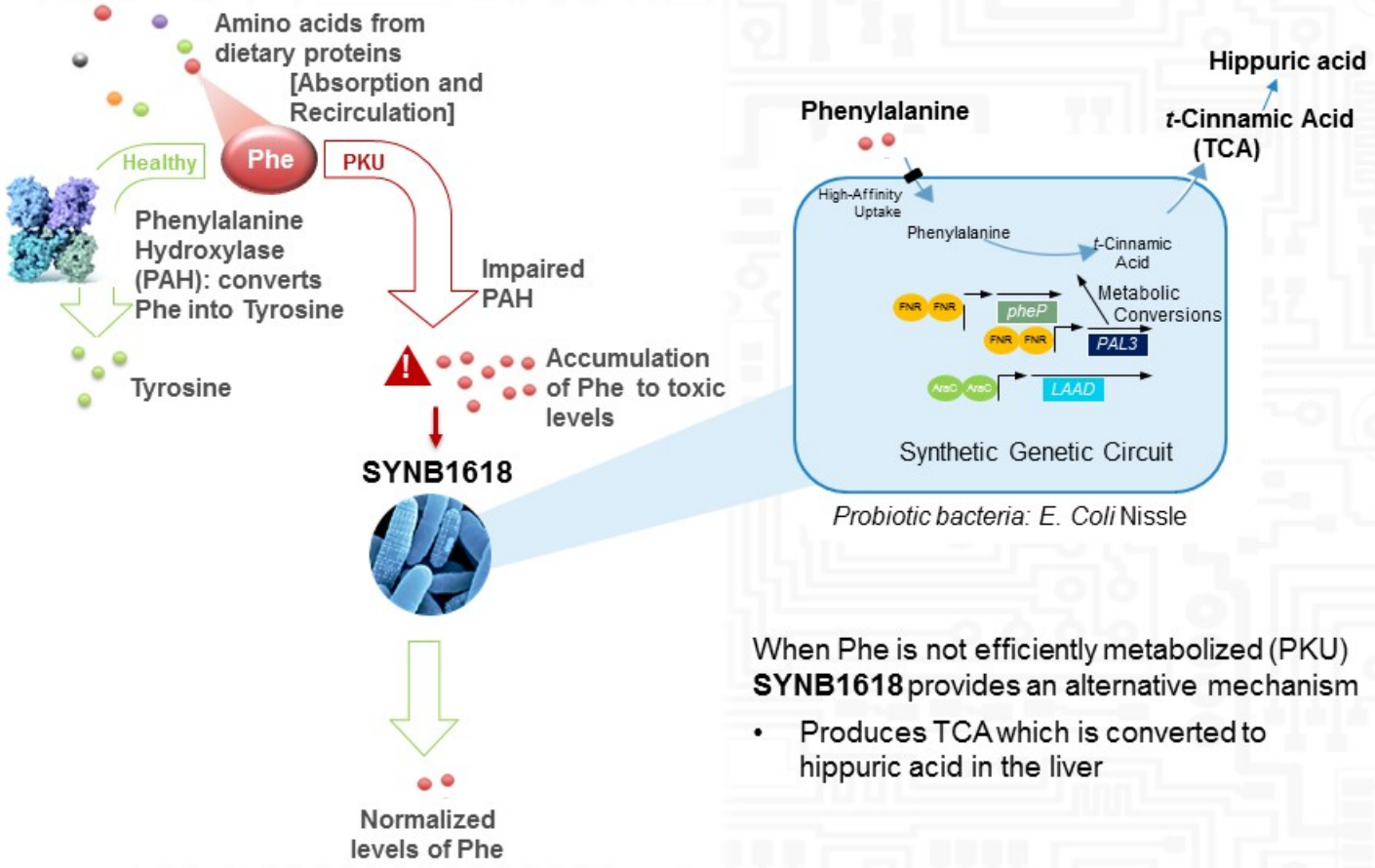
Facilitating Normalization of Plasma Phe Levels

- **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, musty body odor
- **Treatment:**
  - Low protein diet (no meat, dairy, nuts, eggs)
  - Kuvan: PAH cofactor. 20-40% of patients

- **Target Profile to Address Unmet Need:**
  - Normalize Phe: less than half manage to target (120 - 360 mmol / L, source: NPKUA)
  - Increase protein intake to >25g (vs 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

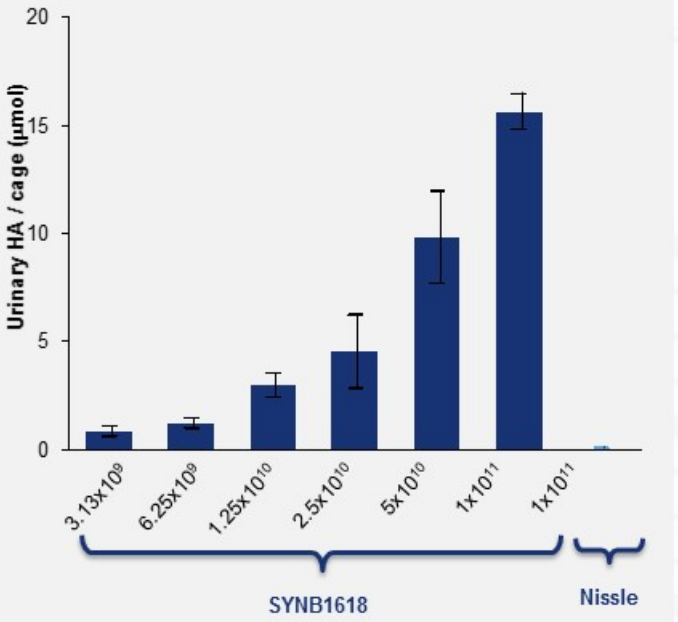
- Produces TCA which is converted to hippuric acid in the liver

SYNB1618 Preclinical Characterization in Mice:

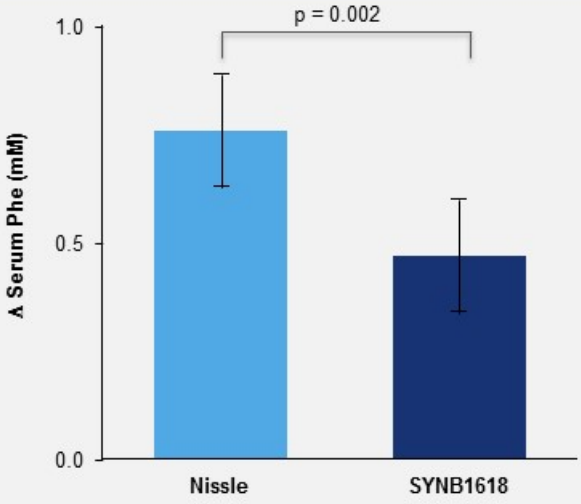
Efficient Phe Degradation and Hippuric Acid Excretion

Following SQ Phe administration to PKU mouse in the presence of SYNB1618

Dose-responsive urinary hippuric acid production in *Pah^{enu2}*



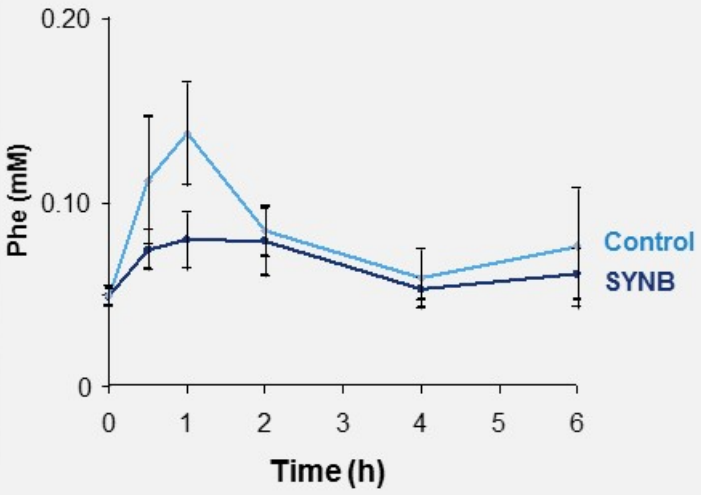
Reduced plasma Phe in *Pah^{enu2}* mice



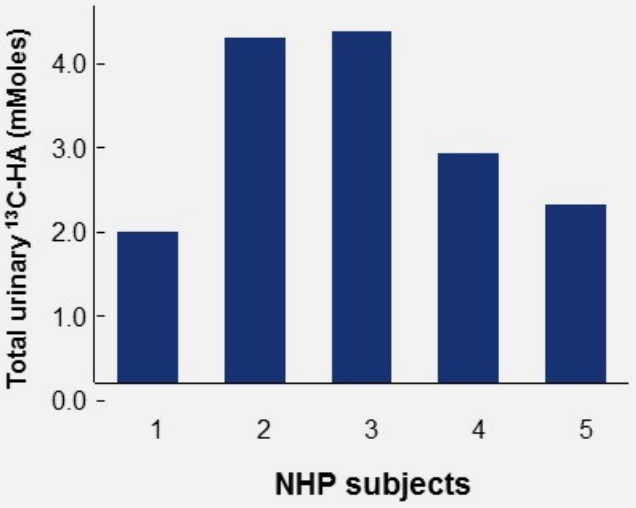
SYNB1618 Preclinical Characterization in Healthy NHPs:

Proof of Mechanism - Metabolizes Phe Whether Administered Orally or Systemically

Phe (oral administration) metabolism with a Synthetic Biotic medicine



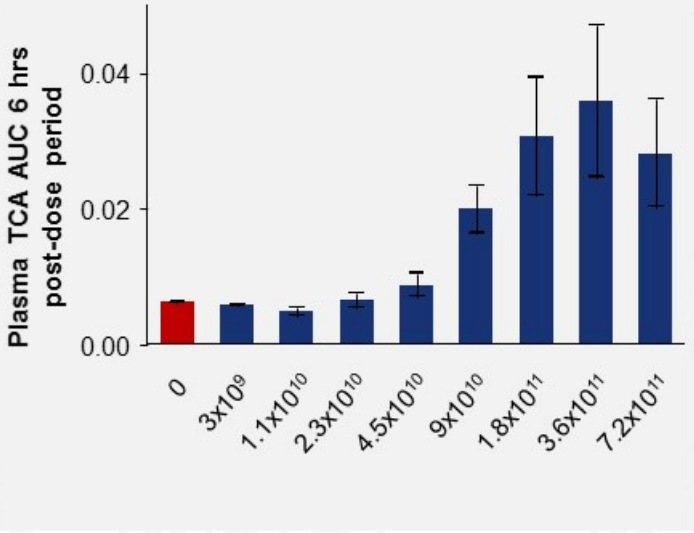
^{13}C Phe (systemically administered) metabolism to ^{13}C HA with Synthetic Biotic medicine



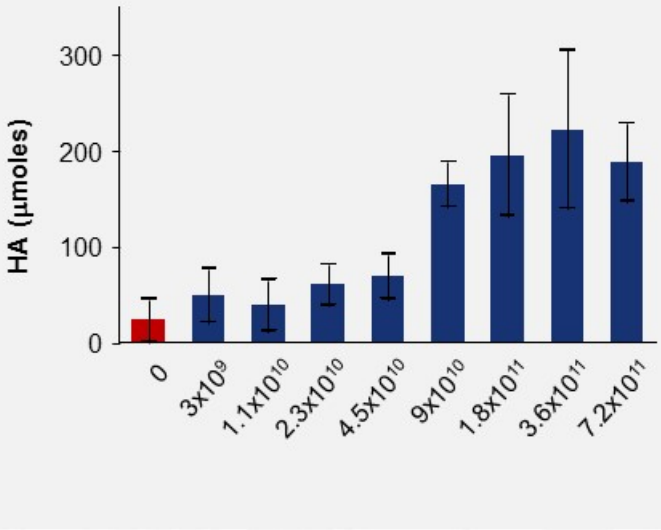
SYNB1618 Preclinical Characterization in Healthy NHPs:

Phe Metabolism is Dose Responsive

Dose dependent conversion of Phe to plasma TCA



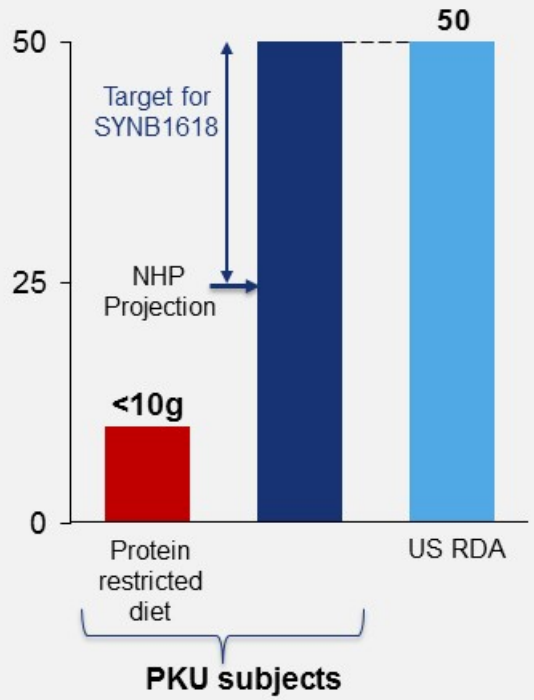
Dose dependent excretion of urinary HA



SYNB1618 Preclinical Characterization in Healthy NHPs:

Phe Metabolism is Clinically Relevant

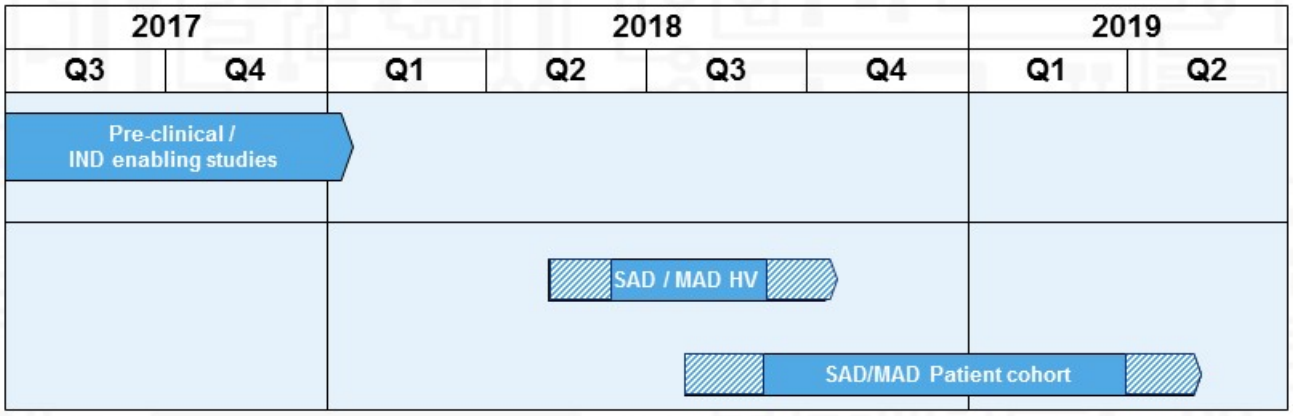
Dietary protein (g) recommended levels



- PKU patients: restricted to <10g protein/day
- Extrapolation from highest dose in NHPs:
  - Supports a minimum of 25g of dietary protein intake in humans
  - ~50% of daily recommended protein intake (US RDA) or 2.5x increase in protein intake
- Clinical target for SYNB1618 up to US RDA

SYNB1618 in the Clinic:

Phase 1 SAD/MAD in Healthy Volunteers with Patient Cohort



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

SYNB1020 and SYNB1618:
What We Have Learned

Preclinical

- ✓ **Established mechanism of action** (MoA) for ammonia and phenylalanine lowering in plasma
- ✓ **Correlated MoA with efficacy and survival**
- ✓ Identified biomarkers
- ✓ Demonstrated **dose-dependent changes** in systemic metabolite levels based on activity in the gut
- ✓ In *ex-vivo* human GI models demonstrated survival, resident time and potency
- ✓ Completed preclinical / tox program for 2 biotics

Clinical

- ✓ Completed Phase I study in **52 healthy volunteers for SYNB1020**
- ✓ Safety: **safe and well-tolerated**; nausea and vomiting is dose-limiting toxicity
- ✓ Efficacy:
  - **Dose responsive effect on systemic metabolite** through programmed mechanism which is active in the gut
  - Bacteria are active *in vivo*, can survive transit through the GI tract, and be metabolically active in feces
- ✓ Clearance: bacteria behave in a consistent and predictable way; clearance within 2 weeks following completion of dosing in all subjects

Regulatory

- ✓ Successful Regulatory interactions:
  - **Established a development path**: requirements for preclinical and clinical testing and manufacturing of a live biotherapeutic

Manufacturing

- ✓ Operationalized manufacturing for a human trial with an LBP
- ✓ Developed process to manufacture 3,000 – 5,000 doses of active drug

Manufacture of Drug Substance and Drug Product

From Flask to Fermenter to the Clinic

Discovery and Preclinical

Strain engineering

- Fast - >40 in 3 years
- Switch technology enables productive biomass

***In vitro* testing**

- Small scale manufacture- ambr® 15
- In-house testing of:
  - Strength – CFUs
  - Potency – micro well plate assays

Tox and *In vivo* lots

- 3,000 dose lots
- CMO currently producing
- In-house in 2018

Drug Substance

Clinical supplies

- Standard process for consistent biomass and potency
- Phase 1 scale 150-200L fermentation ambr® 250
- CMO producing lead program supplies

Commercial supplies

- Probiotics at massive scale, lyophilized
- Prebiotic formulation for energetics, survival, and switches
- Under evaluation: Large scale CMOs, lyophilization, spray dry

Drug Product

Clinical supplies

- Liquid/oral formulation
- Under development
  - Solid oral
  - Injectable for intratumoral

Commercial supplies

- Probiotics are solid oral
- Solid dose CMO capabilities under evaluation
- Evaluating: Capsules, sachet, enteric coating

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

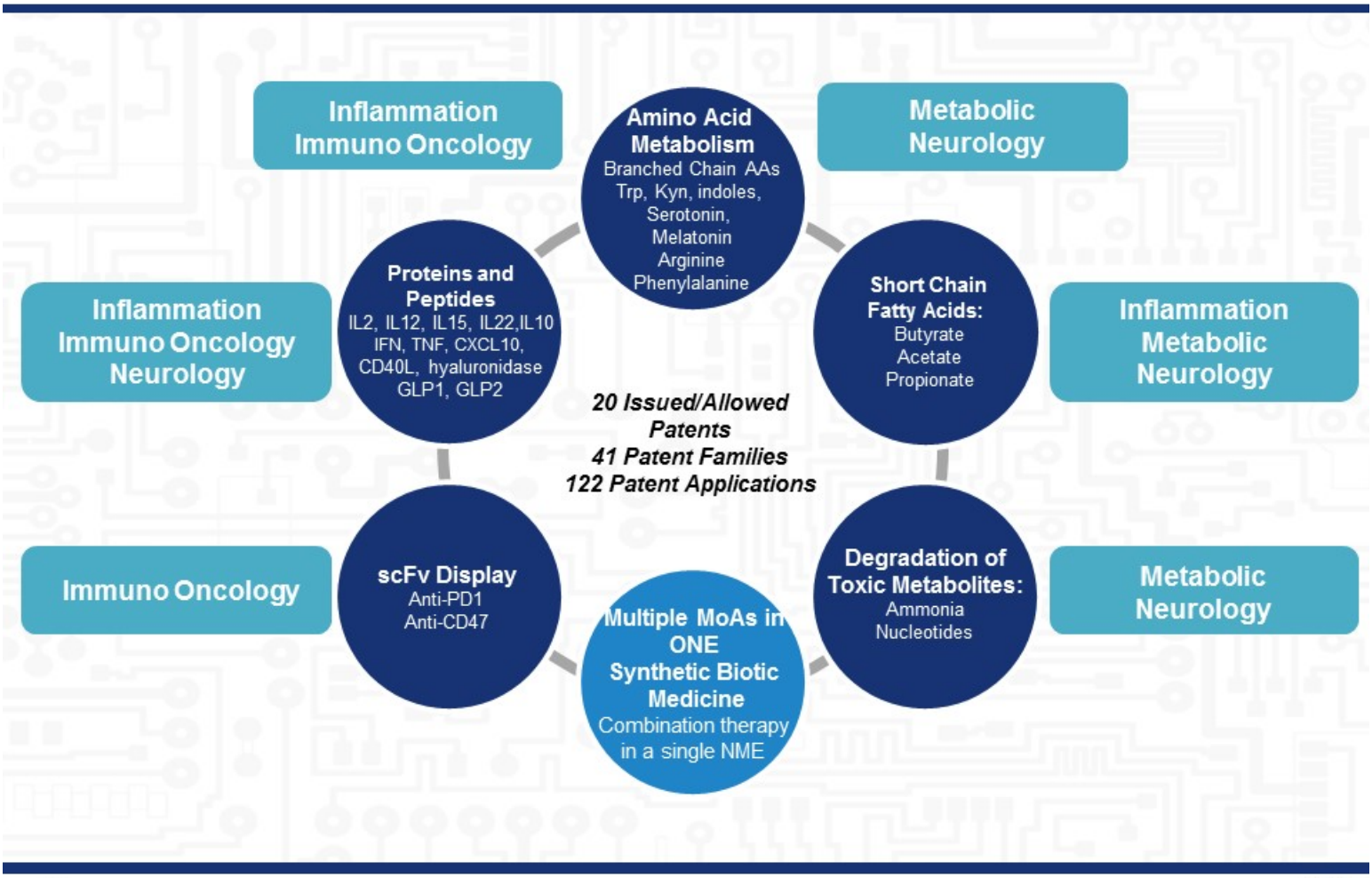
Develop Reliable Manufacturing

GMP manufacturing:

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

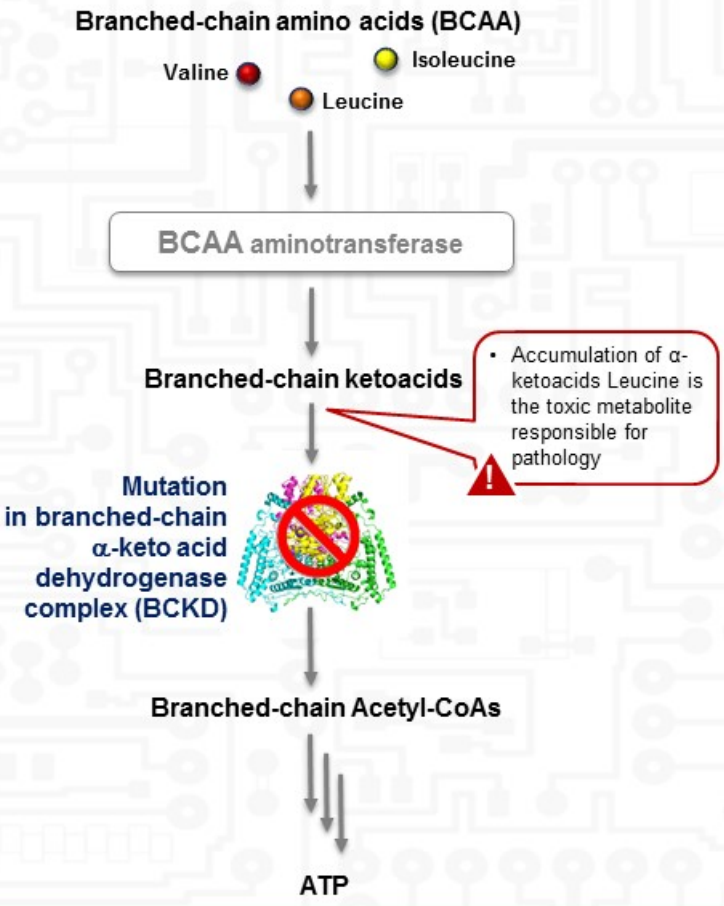
Synthetic Biotic Medicines:

Applicability Beyond Rare Disease Across Multiple Pathways



SYN-MSUD for Maple Syrup Urine Disease (MSUD):

Degradation of toxic branched-chain amino acids



Genetic Aminoacidopathy

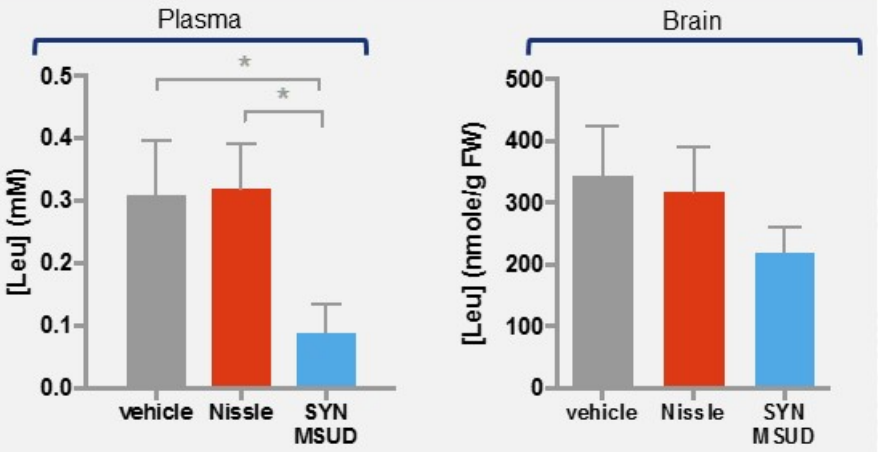
- Enzyme defect in catabolic pathway of branched-chain amino acids (BCAAs)

- **Incidence:** 1:185,000; higher in certain population e.g Mennonites 1:176
  - Diagnosis via newborn screening program
  - Symptoms: lethargy, hypotonia, seizures, hypoglycemia, ketoacidosis, pancreatitis, coma, neurological decline
- **Treatment:**
  - No therapeutic options
  - Long term dietary management: restriction of BCAAs

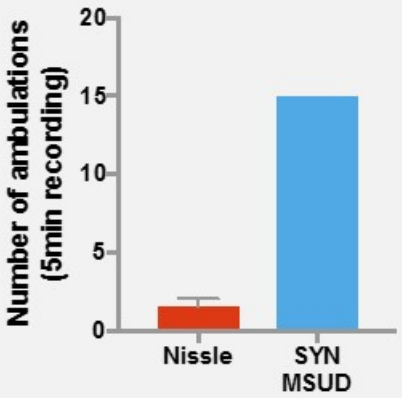
- **Target Profile to Address Unmet Need:**
  - Maintain target leucine levels
  - Prevention of acute episodes

SYN-MSUD *In Vivo*:
Lowers Plasma and Brain *Leu* Levels

- Plasma Leu significantly reduced on Day 3
- Trend for Leu lowering in the brain



Protective effect on iMSUD animals fed high-protein chow

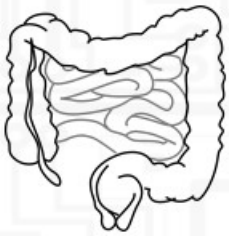


GINKGO BIOWORKS

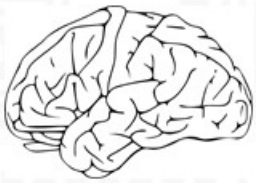
synlogic

Engineered Probiotics to Modulate Cross-talk between the Gut and the Liver or Brain

Metabolite production, consumption, transformation



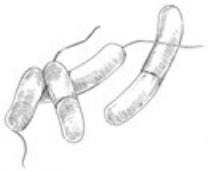
Neurotransmitter or hormone production/consumption, Toxin consumption, Neuroprotectant production



Bianconi et al., Atlas of Human Biology 2013
Sender et al, PLoS Biology 2016

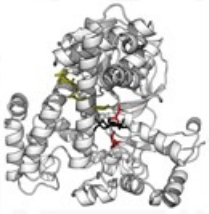
Unprecedented Engine for Rational Drug Development of Living Medicines

Chassis → **Pathway** → **Preclinical** → **Translation** → **Delivery**

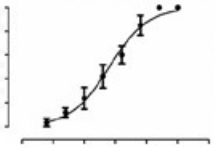


- Engineerability
- Effectiveness
- Safety

- Understand disease pathology
- Identify mechanisms to restore health
- Design
  - Bioinformatics
  - Pathway enumeration
  - In silico design
  - Systems-level characterization



- High Throughput Strain Engineering
  - Enzyme optimization
  - Pathway balancing
  - Industrial scale gene synthesis
- Automated and Parallel Testing
  - Mutli-dimensional analytics
  - Integrated manufacturability
  - Predictive translational

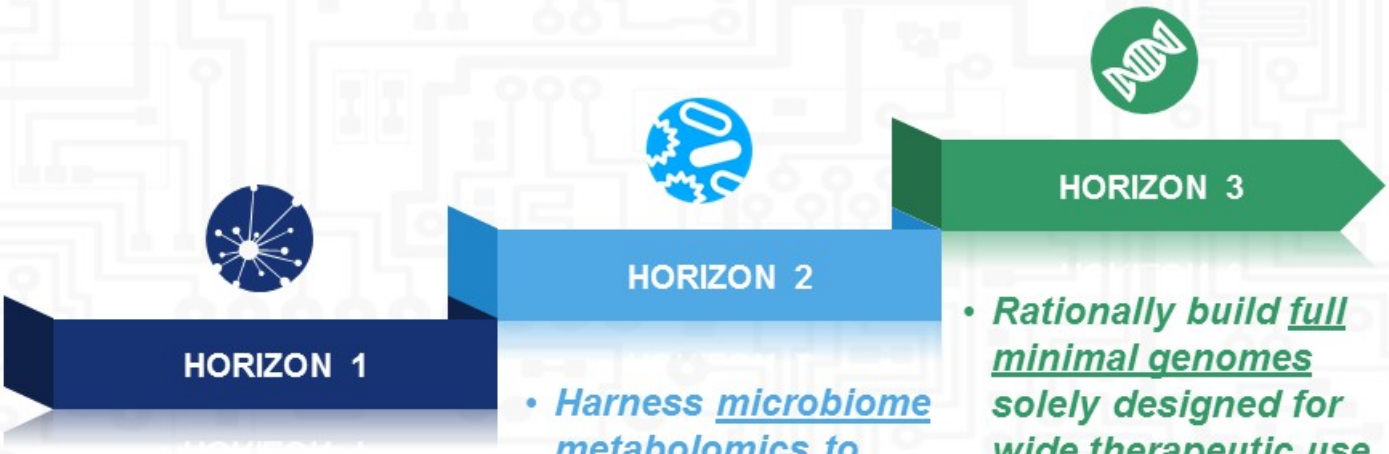


- Pharmacology, modeling
  - Dose
  - Toxicity
  - Bioavailability
  - Potency
  - Residence Time
  - Conversion Efficiency

- Manufacturability
- Drug Substance and Drug Product Manufacturing:

Synlogic Mission: To Re-define Medicine through Synthetic Biology

Bringing Minimal Therapeutic Genomes to Oncology



- ***Test simple synthetic biology concepts in the local tumor microenvironment***

- ***Harness microbiome metabolomics to widen response to cancer immunotherapies***

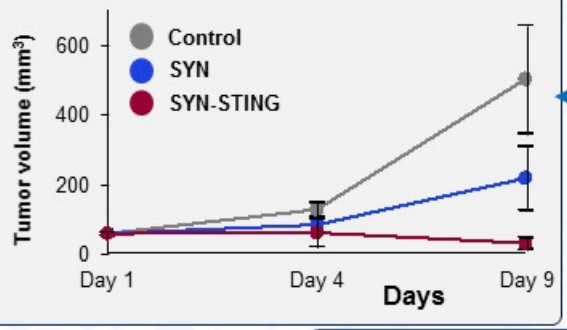
- ***Rationally build full minimal genomes solely designed for wide therapeutic use in cancer***

Synlogic Vision for Immuno-Oncology: One Drug, 2 Mechanistic Modules to Turn Cold Tumors to Hot, Driving High Response Rates and Abscopal Effect

Immune Initiator: Antigen Release, Activation & Priming

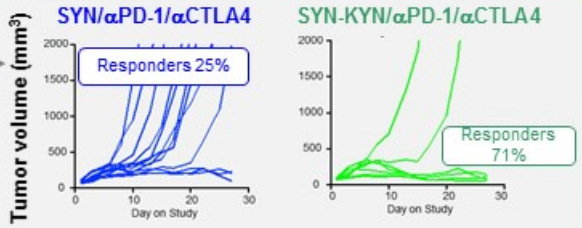
Immune Sustainer: Immune Augmentation & T Cell Expansion

SYN-STING activates innate cytokines and adaptive T-cell response to drive tumor regression



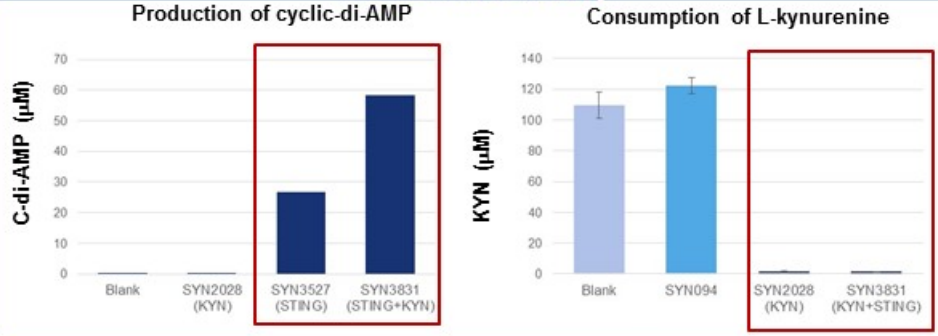
SYNB0828: Lead IO Program

SYN-Kyn with PD-1/CTLA4 reprograms tumor microenvironment to drive tumor necrosis and antigen release



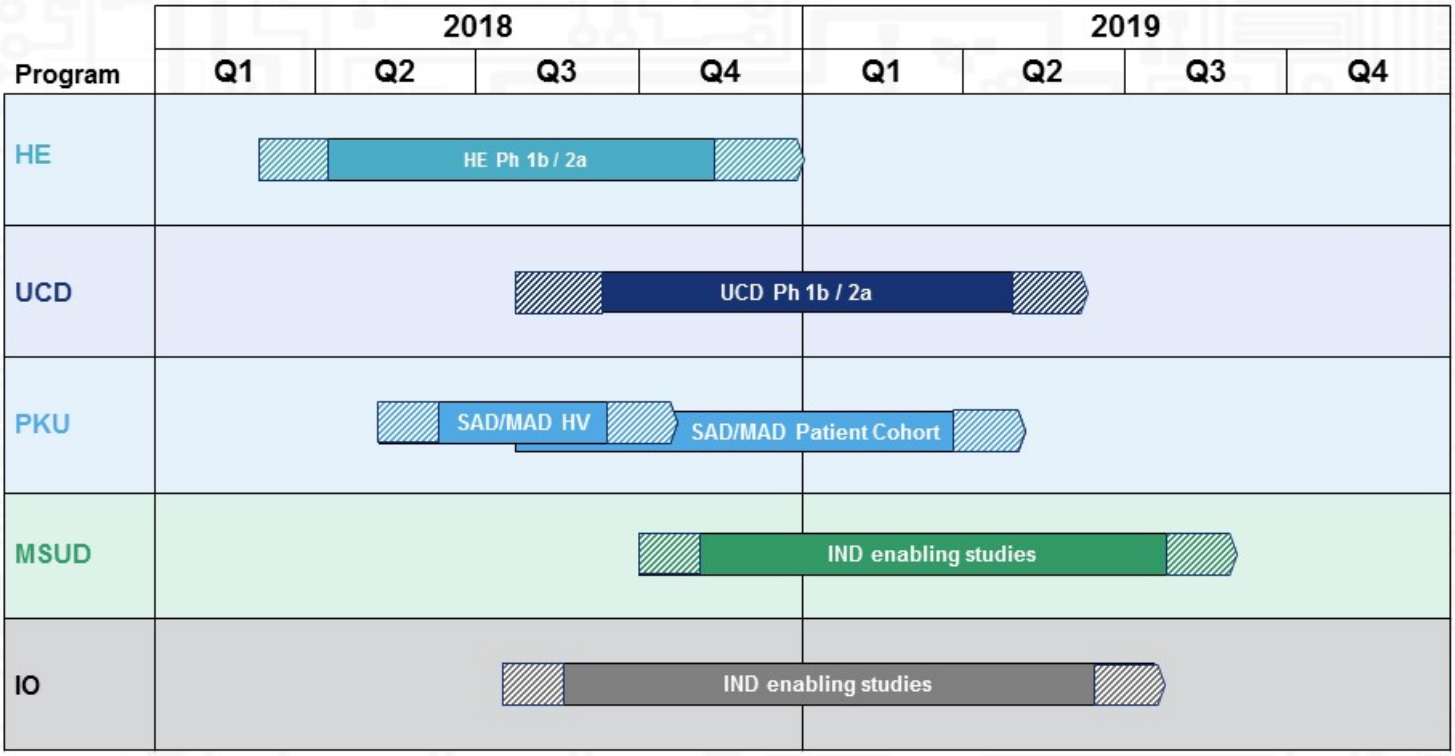
Control: Responders 0%

Combination of initiator & sustainer circuit in one strain to enhance activity



Synlogic Development Pipeline:

Programs' Timelines Summary



Synlogic:
Significant Delivery in 2017 …. Primed to Deliver in 2018

2017 Accomplishments

Significant pipeline progress:

- SYNB1020: UCD / HE
  - ✓ Phase 1 completion
  - ✓ Fast track designation
- SYNB1618: PKU
  - ✓ Orphan status
  - ✓ IND on track for Q1 ’18

Corporate:

- ✓ Public listing on NASDAQ
- ✓ 1st milestone in AbbVie collaboration in IBD
- ✓ Strategic collaboration with Gingko Bioworks
- ✓ Organization growth: hiring into key roles to support clinical and manufacturing functions

2018 Goals

Programs:

- SYNB1020: UCD / HE
  - ❑ Phase 1 results presentation at medical conferences: Q1 ’18
  - ❑ Initiate Phase 1b / 2a in HE in Q1 ’18
  - ❑ Initiate Phase 1b / 2a in UCD mid ’18
- SYNB 1618: PKU
  - ❑ Phase 1 SAD / MAD study in HV and PKU patients in H1 ’18
- Early pipeline: new indications (including IO) data presentation at major meetings

Corporate:

- Advance existing collaborations
- Expand platform reach through new partnerships

Synlogic Overview

Novel Therapeutic Class

- Leader of **therapeutic synthetic biology,** genetically reprogram probiotics for transformative impact on disease treatment
- Simple, robust and rapid process for the discovery, development and manufacturing of drug candidates
- Key differentiation: potency, pharmacology/dose responses, reproducible manufacturing

Robust Pipeline with Orphan Drug Programs

- **SYNB1020** for Hyperammonemia including Urea Cycle Disorder (UCD) & Hepatic Encephalopathy (HE). Healthy volunteer study completed November 2017: Safe and well tolerated, positive Proof of Mechanism
- **SYNB1618** for Phenylketonuria (PKU); Positive PoM in NHPs. 2018 IND and clinical study

Broad Platform - Multiple Product Opportunities

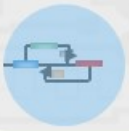
- **Immuno Oncology**: Non pathogenic bacterial chasis "armed" synthetically with effector functions that activate/expand immune response for tumor regression and memory response
- Inflammatory Bowel Disease (**IBD**) partnered with **Abbvie**
- **Liver Diseases and CNS diseases**: direct exposure to Liver/plasma of designed metabolites

Dominant Synthetic Biotic IP Portfolio
As of Jan 2018

- 20 Issued/Allowed Patents
- 41 Patent Families
- 122 Pending Patent Applications

Strong Balance Sheet

- $96.6M in cash as of 3Q 2017
- Investors include: Aju IB Investment, Ally Bridge Group, Atlas Venture, Deerfield Management, New Enterprise Associates (NEA), OrbiMed, Perceptive Advisors, Rock Springs Capital



Highly Experienced Management Team

- JC Gutierrez-Ramos, CEO
- Aoife Brennan, CMO
- Todd Shegog, CFO
- Andrew Gengos, COO
- Paul Miller, CSO
- Dean Falb, CTO
- Richard Schwartz, SVP Manufacturing
- Caroline Kurtz, VP Translational Science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Synlogic Management Team:

From Funding of Platform to Clinic in Less than Three Years

JC Gutierrez-Ramos, CEO
- Group SVP Biotherapeutics, Pfizer
- SVP, Head Immunoinflammation Center for Drug Discovery, GSK
- CSO & Site Head, Amgen Mountain View

Aoife Brennan, CMO
- VP, Rare Disease Innovation Unit, Biogen
- Medical Director, Tolerx

Todd Shegog, CFO
- SVP & CFO, Forum Pharmaceuticals
- SVP & CFO, Millennium Pharmaceuticals

Paul Miller, CSO
- VP, Infection iScience, AstraZeneca
- VP, Antibacterials Research Unit, Pfizer

Adam Thomas, CHRO
- VP, Head of Human Resources for R&D, Shire
- Head of HR for Research, Development & Engineering, S.C. Johnson Co

Dean Falb, CTO
- Entrepreneur in Residence, Atlas Venture
- VP, R&D, Stryker Regenerative Medicine

Caroline Kurtz, SVP, Translational Science
- Vice President, GCC Platform Lead, Ironwood Pharmaceuticals
- Director, Infectious Diseases, Genzyme

Dick Schwartz, SVP, Manufacturing
- Chief, Vaccine Production Program Lab, NIH
- Senior Director, Process & Manufacturing Sciences, MedImmune

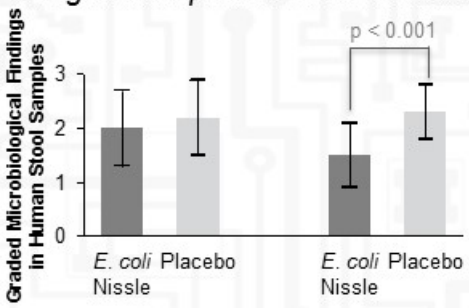
Andrew Gengos, COO & Head of Corp. Dev.
- President and CEO ImmunoCellular Therapeutics
- President & CEO Neuraltus Pharmaceuticals
- VP, Strategy & Corp. Development Amgen,
- VP, CFO & CBO Dynavax Technologies

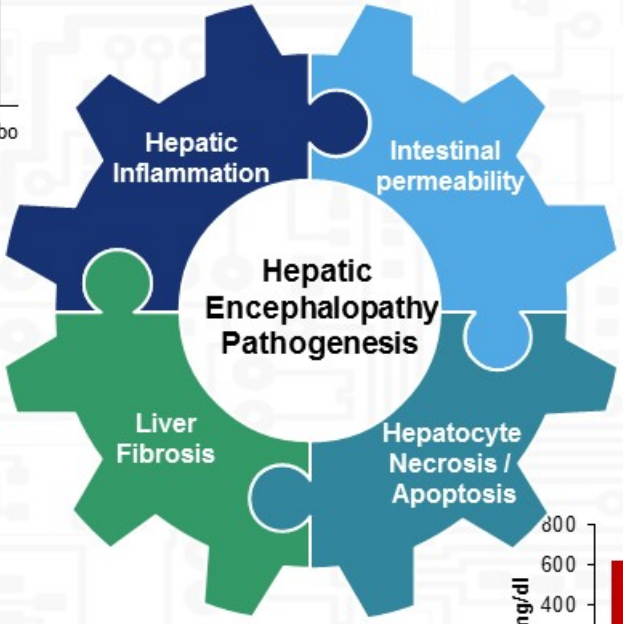
Maiken Keson-Brooks, General Counsel
- SVP, General Counsel, uniQure
- SVP, General Counsel, Forum Pharmaceuticals

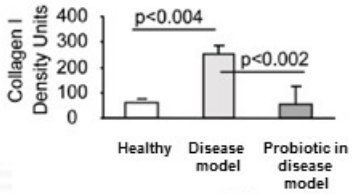
SYNB1020 for Treatment of Liver Disease:

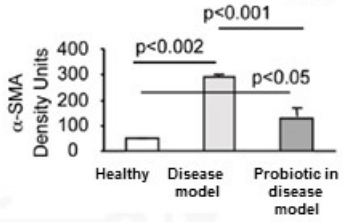
Potential Mechanisms of Action

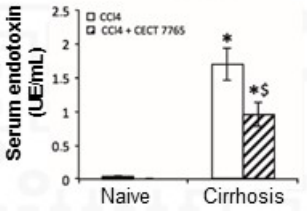
Engineered probiotic bacteria have the potential beyond ammonia control in hepatic encephalopathy

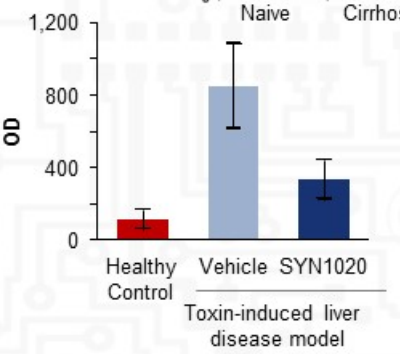


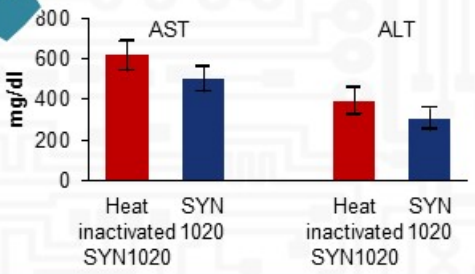












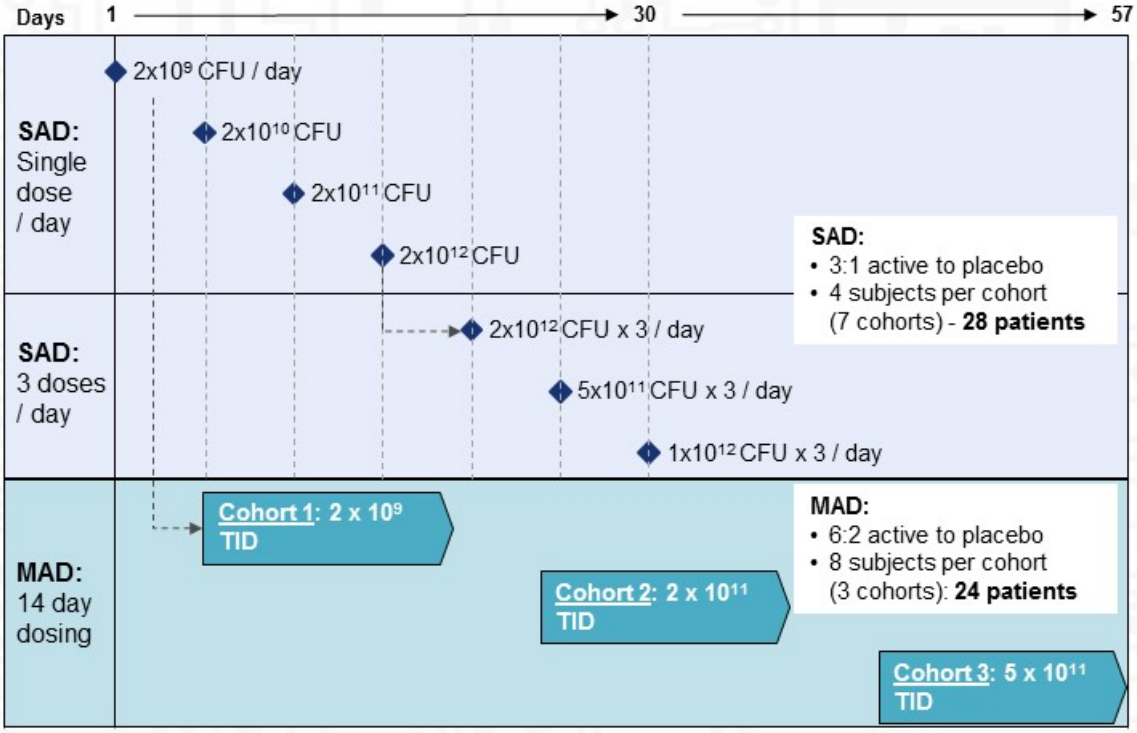
SYNB1020 for Hyperammonemia:
Strong Preclinical Package Informs Clinical Strategy

	Animal Data	Human Data
Potency	• *In vitro* – Ammonia consumption – Arginine production: nitrate precursor	
Exposure	• Survival past stomach and small intestine: – In mouse models of disease – In simulated human gut (Prodigest)	• Dose exposure relationship • Functional activity following transit through the gut
Biomarker	• *In vivo* – Unlabeled / wild-type mouse: increase in arginine and arginine metabolites – Mouse and NHP: tracer data	• Plasma and Urinary Nitrate (tracer data)
Efficacy	• Efficacy in animal model of UCD and liver disease – Ammonia lowering and survival in UCD – Ammonia lowering in liver disease	• Patient studies planned in 2018

SYNB1020 Phase 1 SAD / MAD Study:

Phase I Study - Safe and Well-Tolerated in Healthy Volunteers

A randomized, double-blind, placebo-controlled study to assess the safety, tolerability, and pharmacodynamics of SYNB1020 in healthy volunteers



Met primary and secondary objectives

- Safe and well tolerated: no SAEs, AEs mild to moderate nausea and vomiting at highest doses tested
- Well tolerated in MAD up to $1.5x10^{12}$ CFU for 14 days
- SYNB1020 cleared from system within 11 days

SYNB1020:
Toxicology Package and Regulatory Path

Preclinical and Clinical Safety & Toxicology

Preclinical:

- No toxicity at highest feasible dose in two species
- No evidence of distribution outside the GI tract

Clinical:

- Well tolerated in MAD up to 1.5 x 10^{12} CFU for 14 days
  - Mild nausea and vomiting at higher dose
  - 52 healthy volunteers dosed orally with either SYNB1020 or placebo
  - SAD-28 subjects in 7 cohorts
  - MAD-24 subjects in 3 cohorts
- SYNB1020 cleared from system within expected timeframe

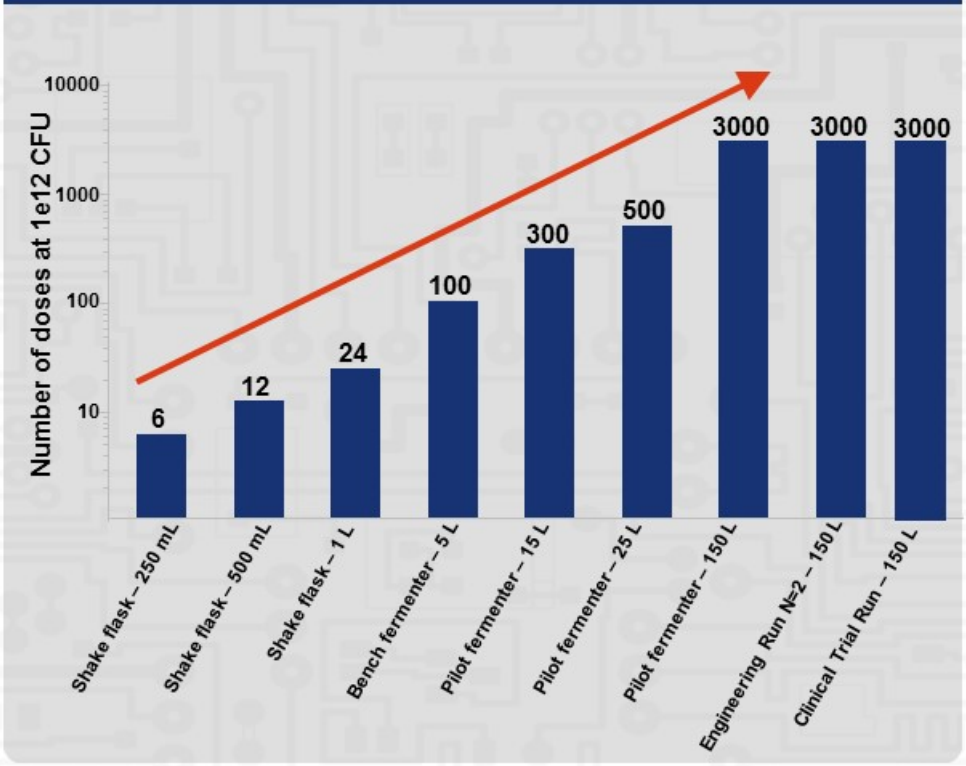
Regulatory

- Orphan Drug Designation (UCD, PKU)
- Fast Track Designation (UCD)
- Feedback from FDA Office of Vaccines Research and Review (CBER)
  - No Recombinant DNA Advisory Committee (RAC) required
  - Lowering of blood ammonia level is an approvable end-point (UCD)

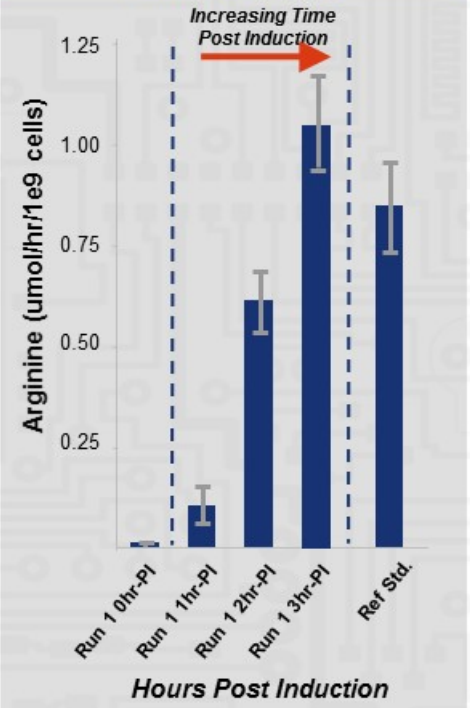
CMO Manufacture - From Flask to Industrial Fermenter:

Well-Controlled Process at 150L

Successful Scale-up to Biomass for Clinical Scale



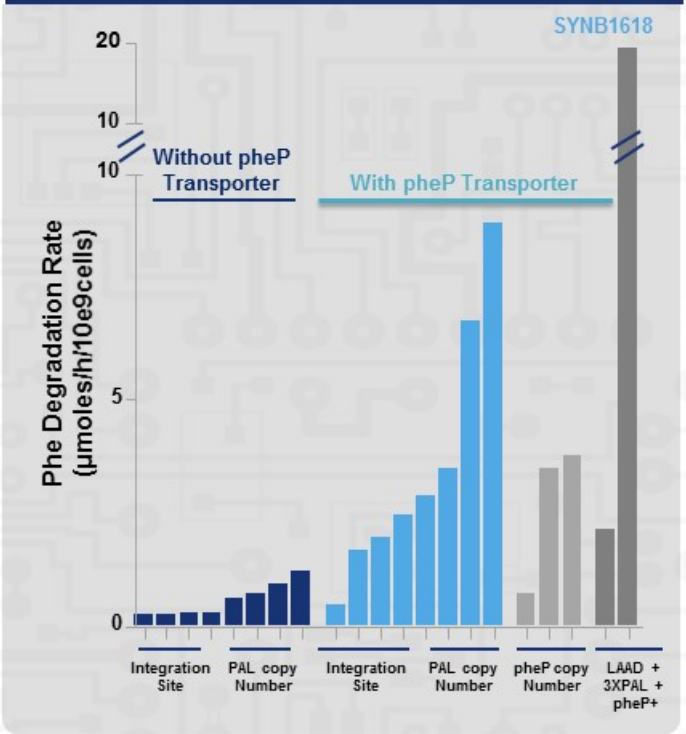
Control of Activity During Manufacturing



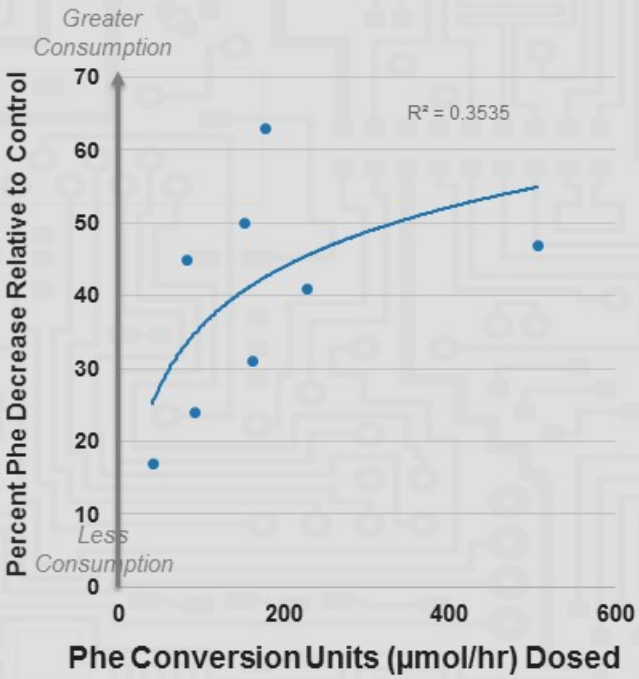
PKU Design and Preclinical Characterization:

Efficient Phe Degradation *In Vitro* and *In Vivo*

Lead Optimization *in vitro*



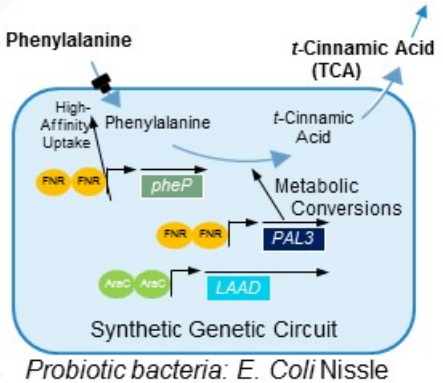
Dose response for Blood Phe *in vivo*



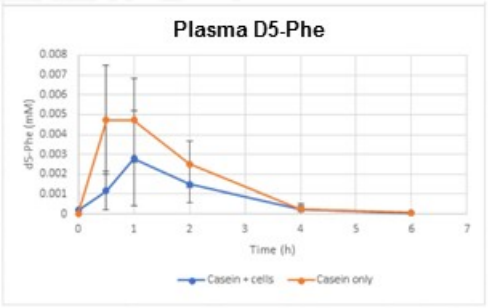
SYN1618 Preclinical Characterization:
Casein Study in NHPs

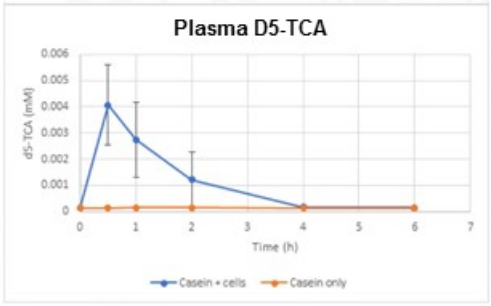
NHP challenge studies:

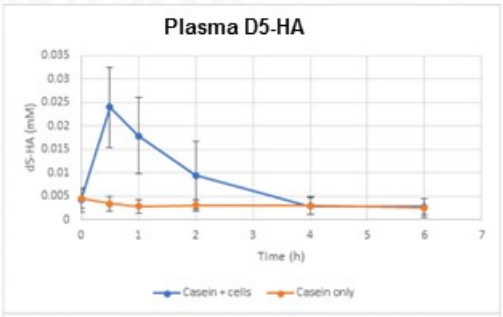
- Oral D5-Phe
- SQ D5-Phe
- Oral dipeptides and tripeptides with D5-Phe
- Casein containing D5-Phe



Probiotic bacteria: E. Coli Nissle







Synthetic Biotic Medicines:
Designed for Clinical Performance

100s-1000s
GI metabolites and conversions

100s
proteins/peptides that affect metabolic or immunomodulatory diseases from the gut

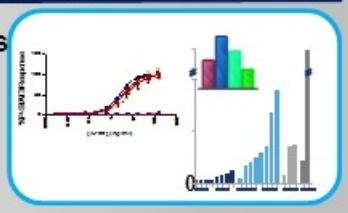
PROGRAMMED TO SENSE AND RESPOND

- *In silico* design, pathway modeling
- Enzyme selection, optimization
- **10+** Switches for GI sensing
- Promoters for signal optimization
- Systems profiling of cell metabolism

Over 40
strains engineered with *in vitro* activity

ENGINEERED FOR EFFICACY AND SAFETY

- **9** landing pads for combinations
- **15** Proteins secreted
- **10** Secretion strategies
- Ribosome binding sites



Over 15
progressed to *in vivo* activity

BUILT TO TRANSLATE ACTIVITY & DOSE

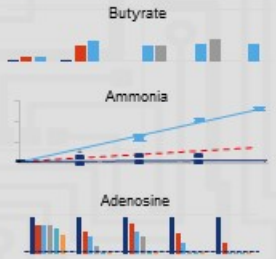
- Biomarkers by design
- *Ex vivo* GI model
- Auxotrophies
- Integrated manuf. feasibility
- Platform formulation strategy
- Local delivery

2
with dose dependent effect on systemic biomarker in primates

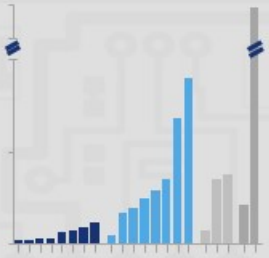
Synthetic Biotic Platform:

Rational Drug Discovery and Development

Rapid Lead Generation

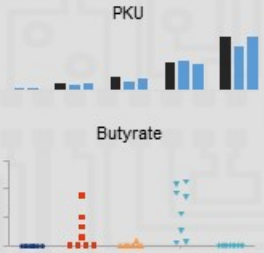


Rational and Efficient Lead Optimization

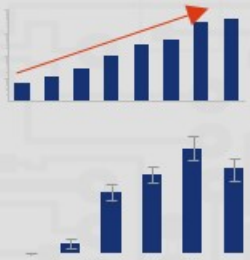


Dose Response

PK/PD Based on Unique Biomarkers

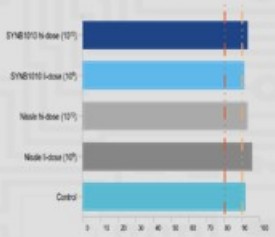


Predictable and Controlled Scale Up for Drug Substance



Drug Product Feasibility

Safety and Toxicology Resemble Probiotics



Regulatory Path

FDA

Orphan Drug Designation

Fast Track Designation


synlogic