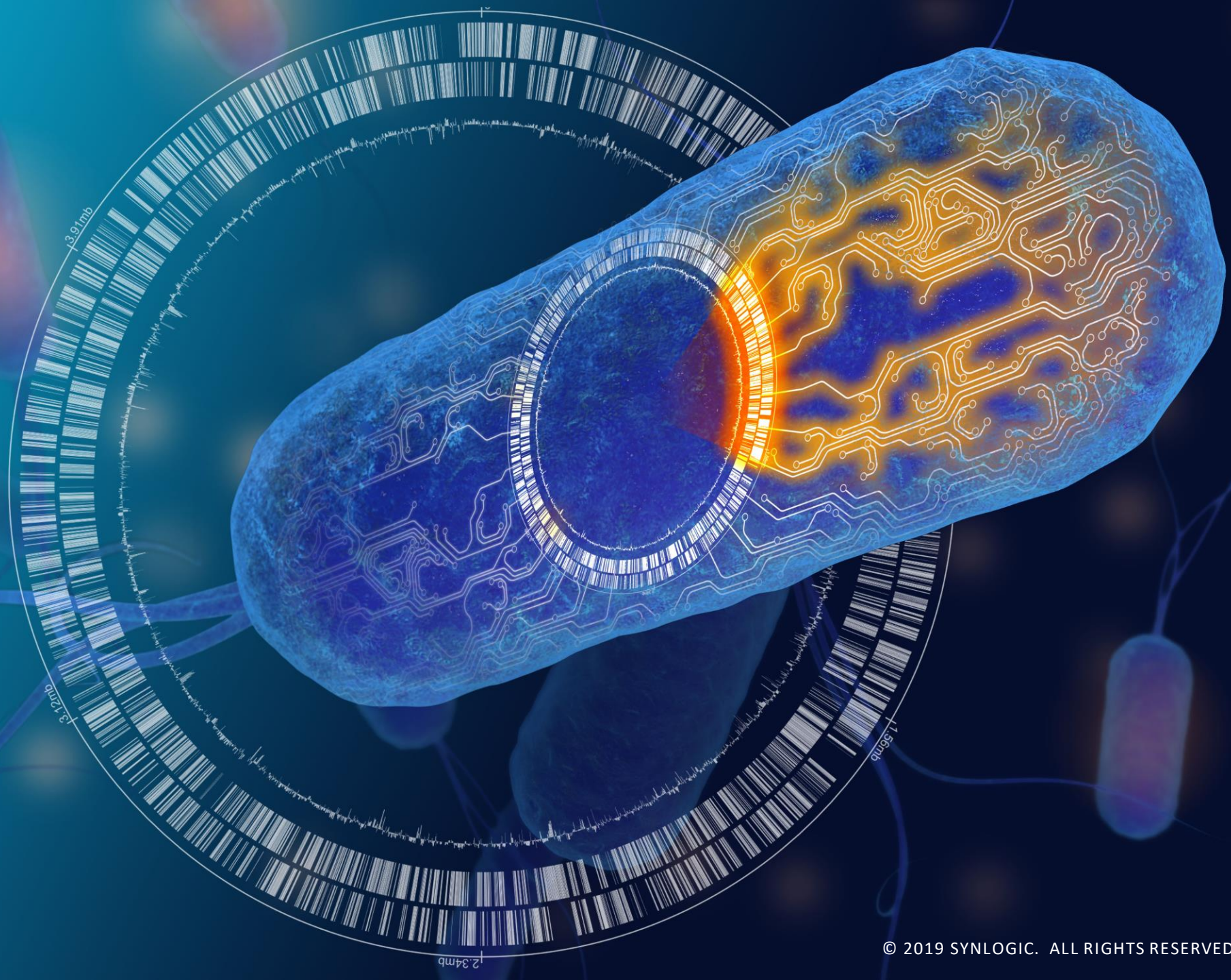
Synlogic

DESIGNED FOR LIFE



June 2019
Corporate Presentation

synlogic

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 Annual Report on Form 10-K filed with the SEC on May 9, 2019. 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 Designed For Life

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

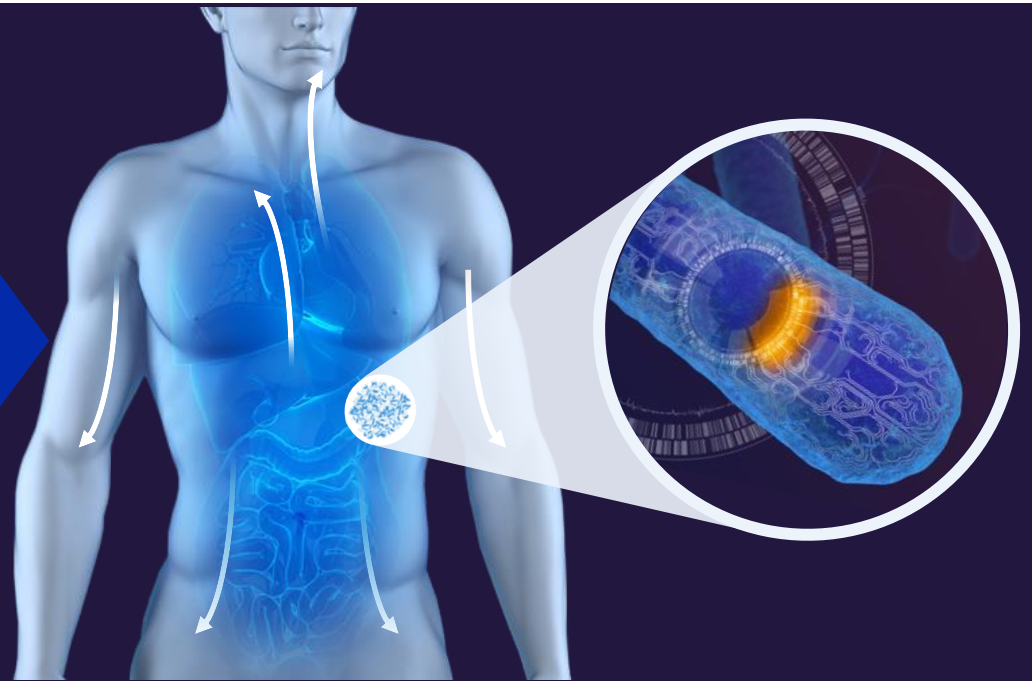
BIOTIC

- 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

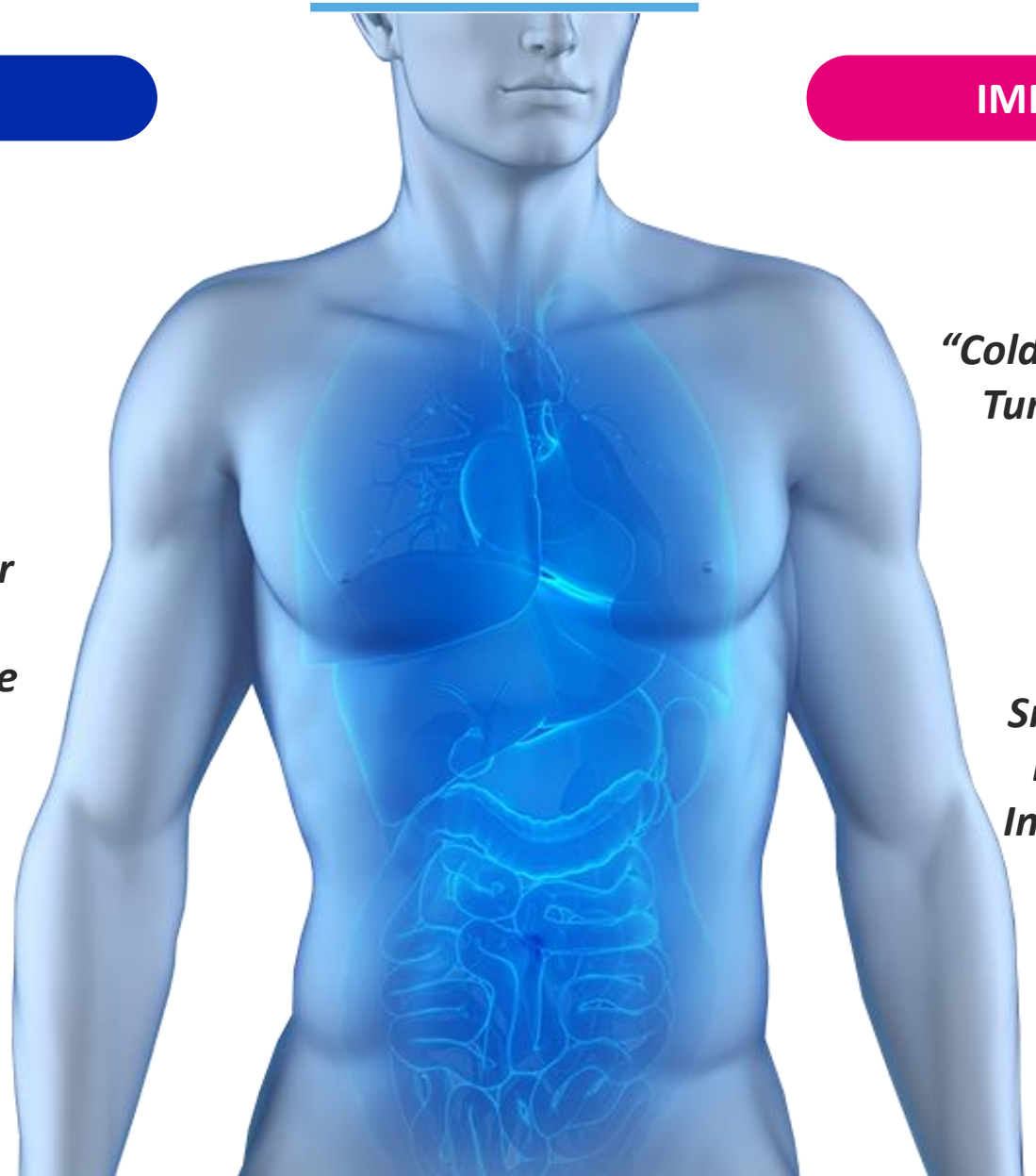
Initial Applications Designed to Target Different Sites of Action in Metabolic and Immunomodulatory Diseases

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

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Platform Collaboration to Accelerate Development of Synlogic's Synthetic Biotic Medicines

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- Provides access to Ginkgo's industrial scale, high-throughput strain optimization and screening
- Enables screening and identification of higher quality optimized candidates, increasing potential for success
- Delivers novel tools for increased candidate potency
- Includes equity investment at a premium, extending runway through multiple milestones

Builds off validated pilot program initiated in 2017

Platform Collaboration to Accelerate Development of Synlogic's Synthetic Biotic Medicines

GINKGO BIOWORKS
THE ORGANISM COMPANY

- Industry leader in the construction and editing of microbial strains and organisms
- Leaders in non-therapeutic commercial applications of synthetic biology
- Comprehensive database of microbial genome sequences and unparalleled automated foundry

Rapid prototyping and screening enables efficient iteration through 1000's of microbial strains

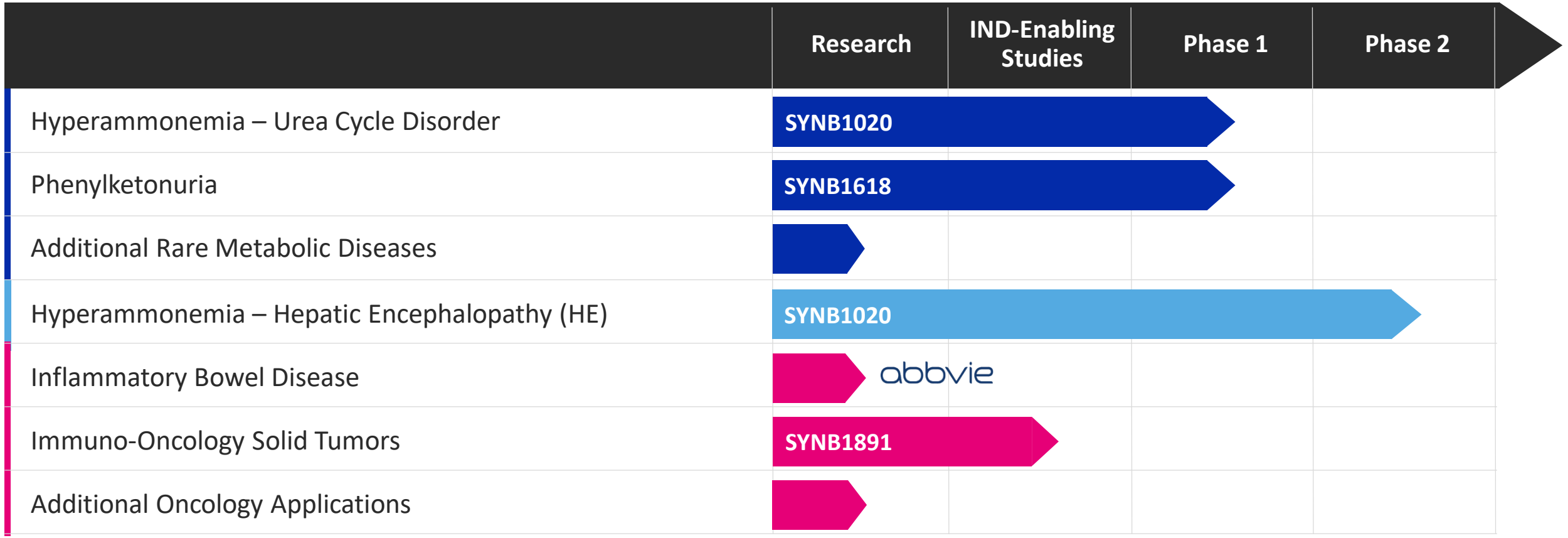
Top-tier platform companies and collaborations

JOYN BIO
motif
BAYER
Roche
CRONOS GROUP

High-quality investor base

Viking
CASCADE INVESTMENT GROUP, INC.
Y
GENERAL ATLANTIC
SENATOR

Investing in Development of a Robust Pipeline for a Range of Diseases



Rare Metabolic Diseases

Broad Metabolic Disease

Immunomodulation

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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:

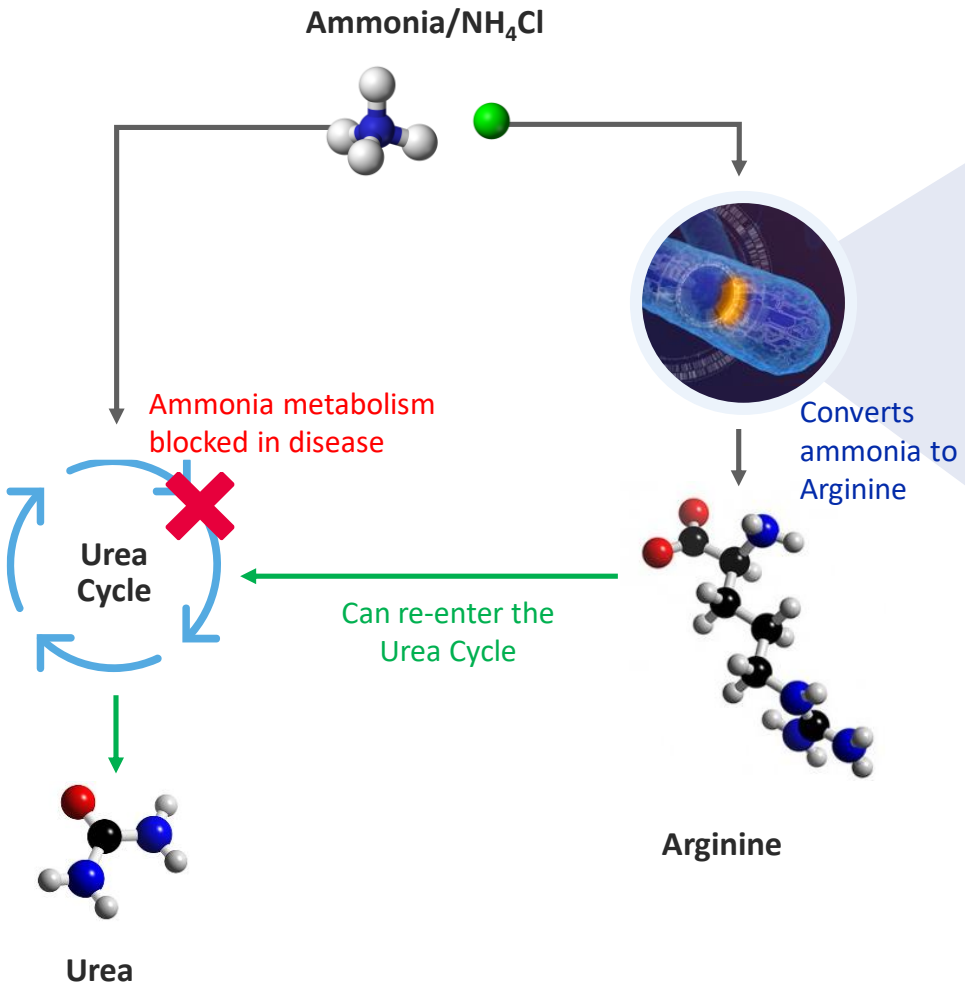
- Ammonia scavengers: Buphenyl® (sodium phenylbutyrate), Ravicti® (glycerol phenylbuterate)
- Low protein diet with amino acid supplements

Target Profile to Address Unmet Need:

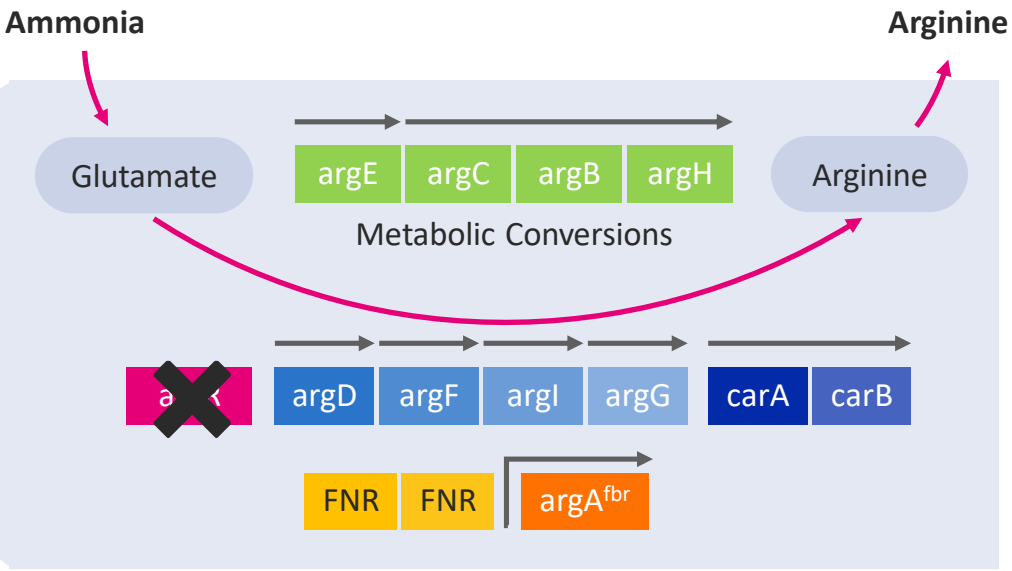
- Maintain blood ammonia in normal range, avoid crisis
- Protein liberalization: 50-100% more per day
- Oral administration

SYNB1020 Mechanism of Action:

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



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



- Under normal conditions, the **urea cycle metabolizes ammonia into urea**
- In UCD and HE, ammonia is not efficiently metabolized via urea cycle. **SYNB1020 provides an alternative mechanism**

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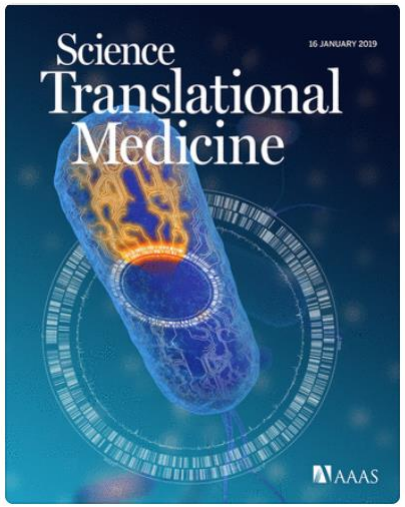
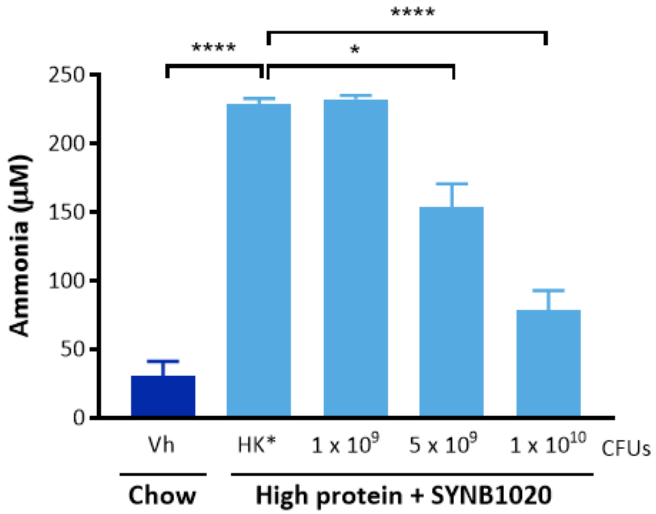
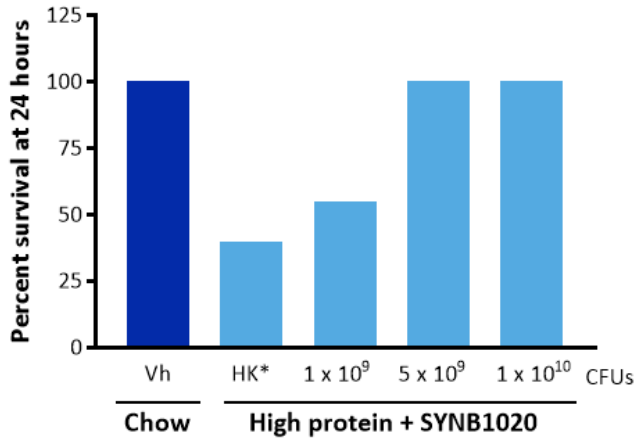
SYNB1020 data recently published in *Science Translational Medicine*

In vivo data in mouse models and healthy volunteers demonstrate mechanism of action

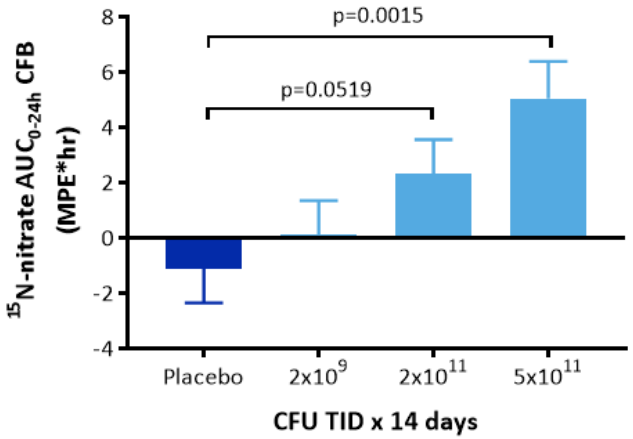


MOUSE MODEL

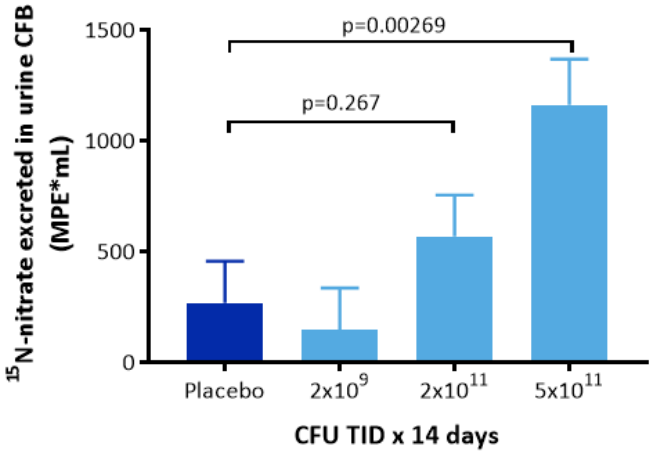




PLASMA NITRATE



URINARY NITRATE



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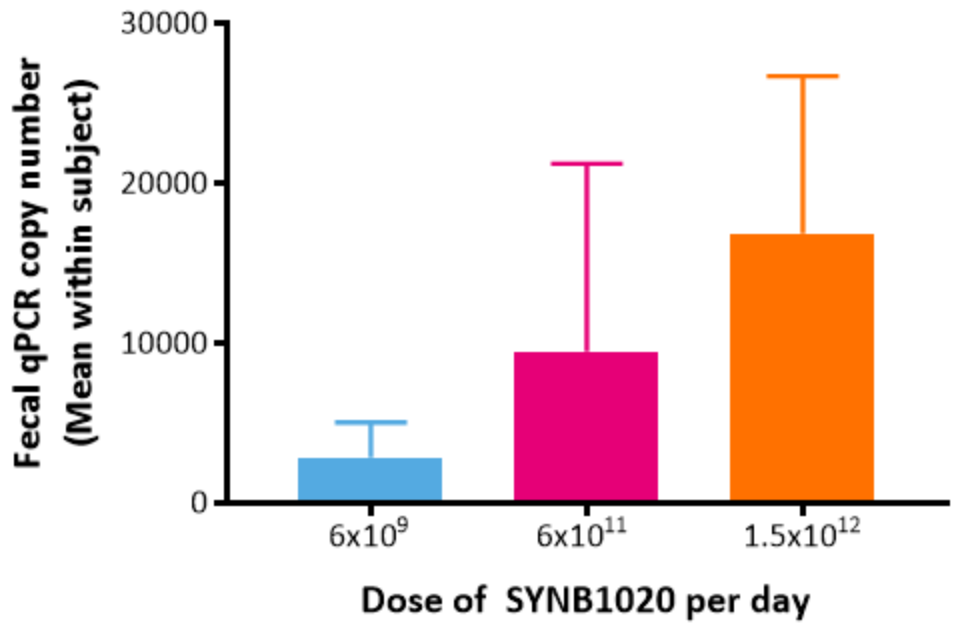
SYNB1020 Clinical Data in Healthy Volunteers

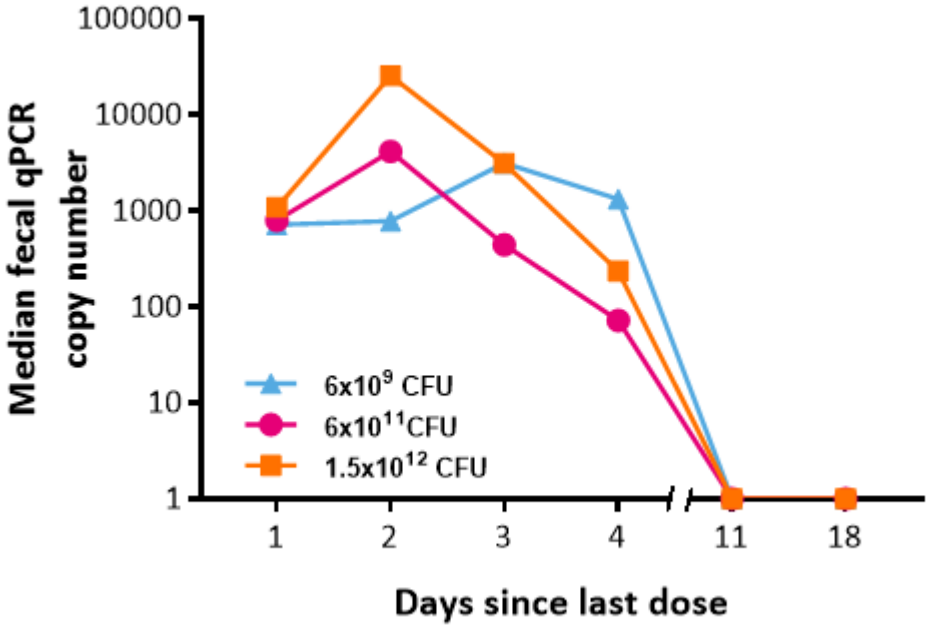
Dose-dependent Increase in SYNB1020 in Feces, Clearance on Cessation of Dosing

DOSE-DEPENDENT INCREASE IN FECES



Dosing period = 14 days
Samples collected daily

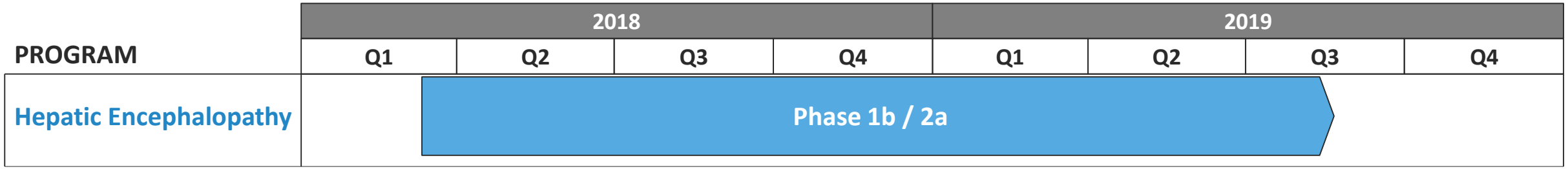
CLEARANCE



Dosing period = 14 days

SYNB1020 Clinical Development

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



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

Urea Cycle Disorders

(Plans to continue development in UCD dependent on data from Ph 1b/2a HE study)

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[1] *MELD score: scoring system model for end-stage liver disease*

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 μmol / L
- If left untreated, symptoms include cognitive impairment, convulsions, behavioral problems, skin rash

Patients:

- 16,500 diagnosed in US, similar in EU5

Treatment:

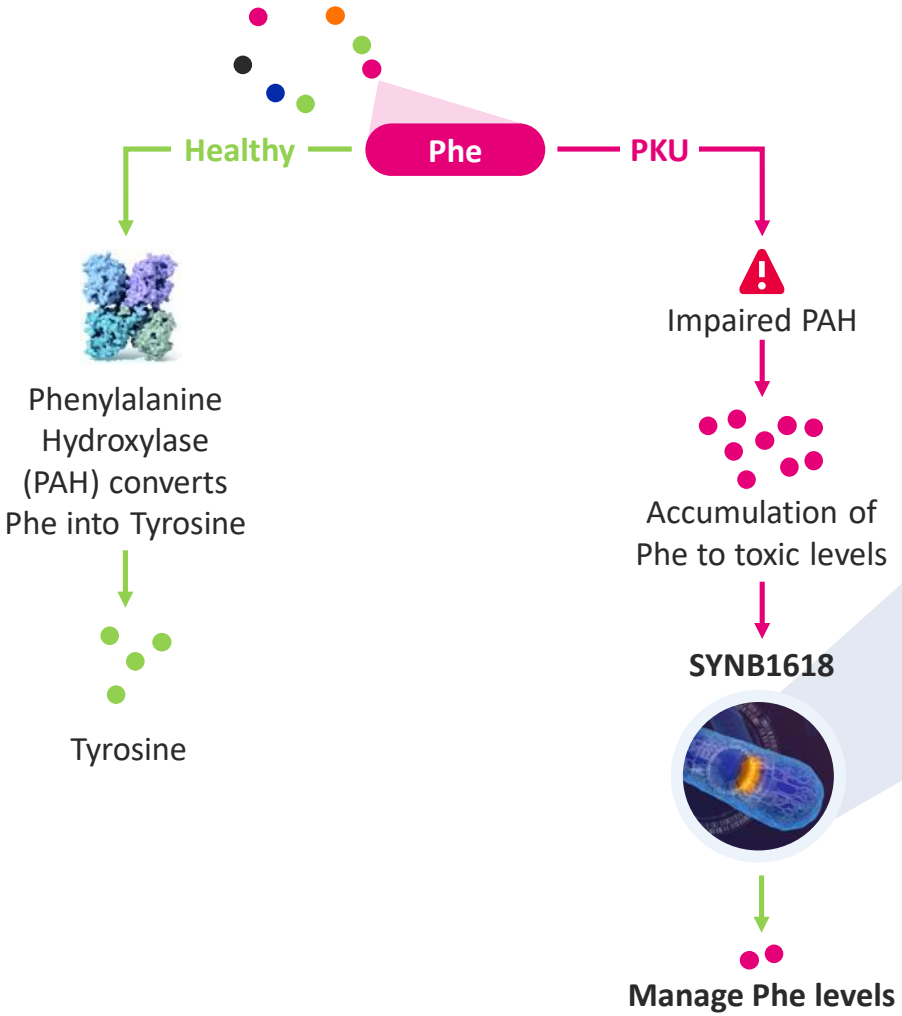
- Phenylalanine is found in all proteins therefore low protein diet is followed (no meat, dairy, nuts, eggs)
- KUVAN® (sapropterin dihydrochloride): PAH cofactor. 20-40% of patients are responders
- Palynziq™ (pegvaliase-pqpz): injectable, pegylated, bacterial enzyme (phenylalanine ammonia-lyase or PAL)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



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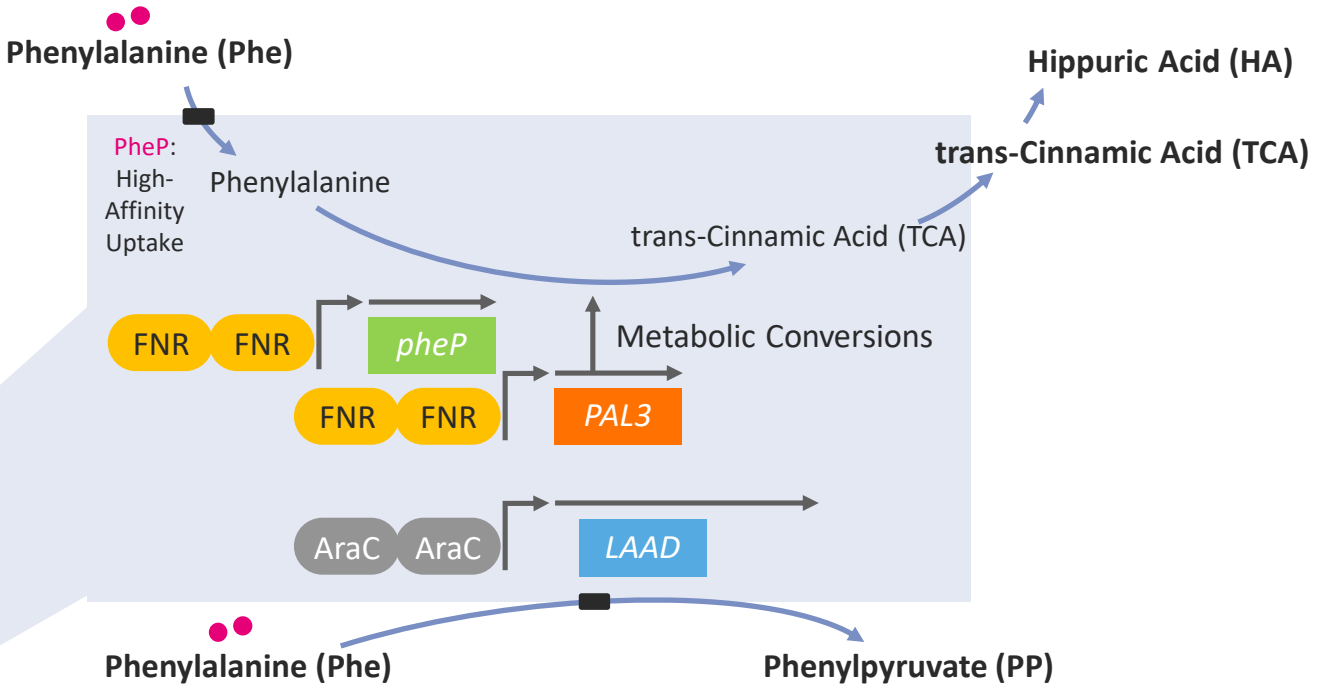


When Phe is not efficiently metabolized (PKU) **SYNB1618** provides an alternative mechanism

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

SYNB1618 Preclinical Characterization

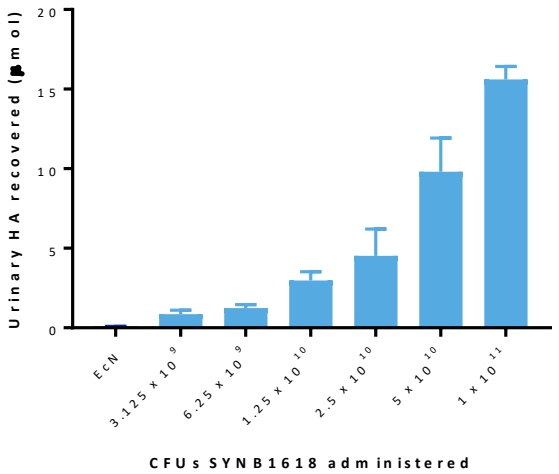
Biomarkers Demonstrate Activity of SYNB1618 in Mouse Model of PKU and Healthy NHPs

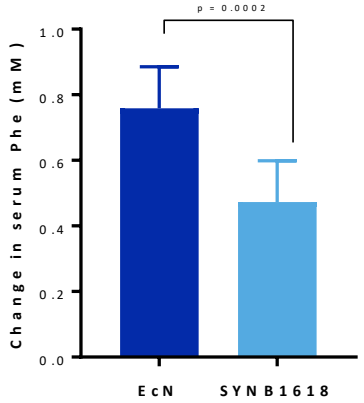
nature biotechnology

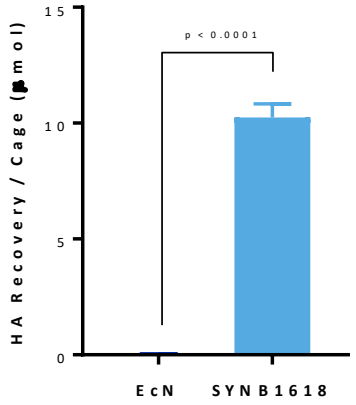
Development of synthetic live bacterial therapeutic for the human metabolic disease phenylketonuria

Vincent M Isabella et al, Synlogic, Inc.

IN VIVO EFFICACY IN (PKU) PAH$^{enu2/enu2}$ MOUSE

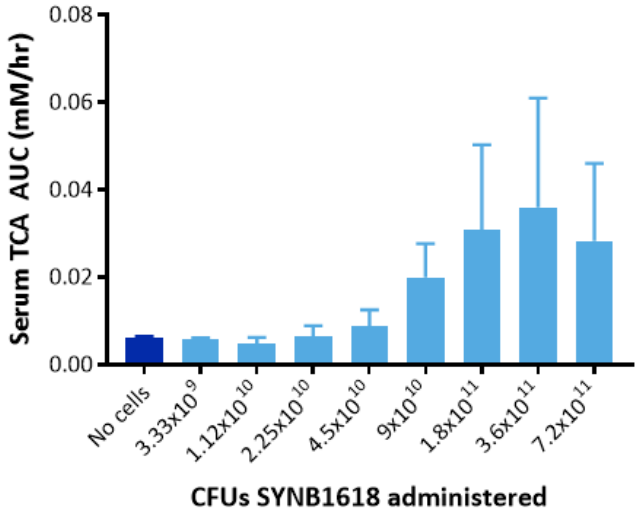


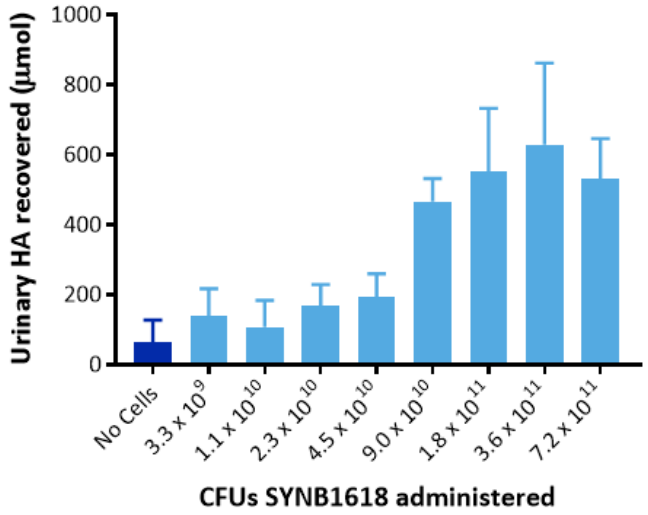




Nat. Biotechnol. 2018 Oct;36(9):857-864

DOSE RESPONSE IN HEALTHY NHPs





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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

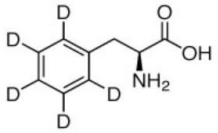
- ✓ There were no treatment-related serious adverse events, no systemic toxicity or infections
- ✓ Treatment-emergent adverse events were either mild or moderate in severity, and reversible. Most adverse events were GI-related
- ✓ Single dose MTD was defined as $2x10^{11}$ CFU. Doses above this level 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 $7x10^{10}$ CFU was identified for the second part of the study in PKU patients

SYNB1618 in the Clinic: Activity

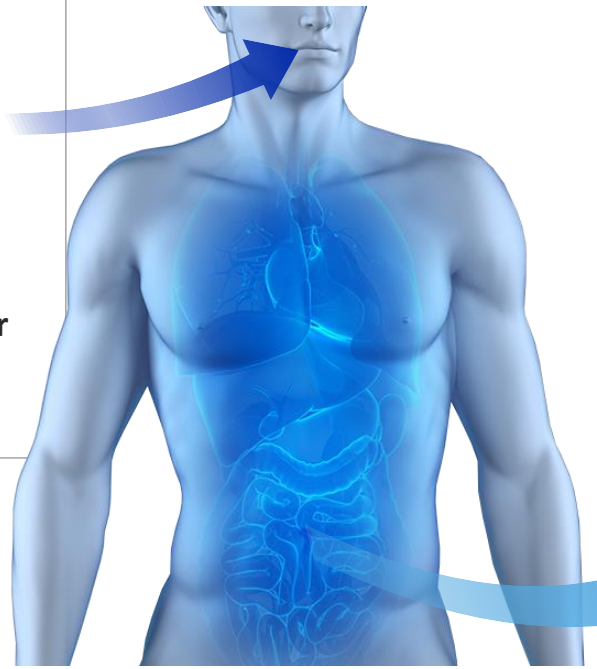
Statistically Significant Dose-dependent Activity of SYNB1618 in Healthy Volunteers

Protein shake / meal



D5-Phe

SYNB1618 or placebo



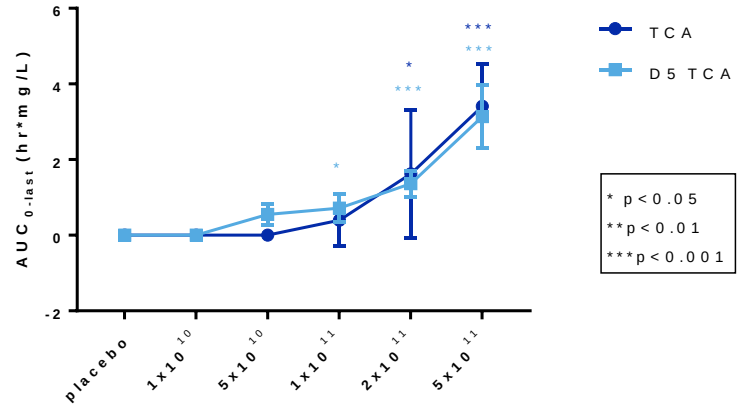
Measure over 6hrs:

Plasma:

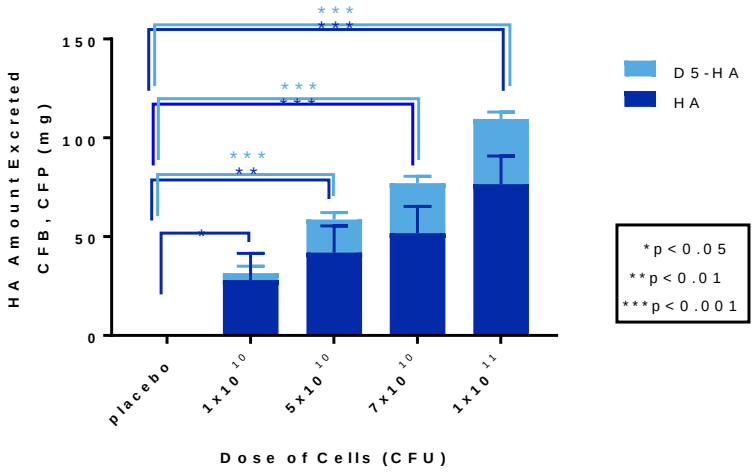
- **Phe/D5-Phe**
- **TCA/D5-TCA**

Urine: HA/D5-HA

TCA AUC SINGLE DOSE RESPONSE



MAD URINARY HA AND D5-HA

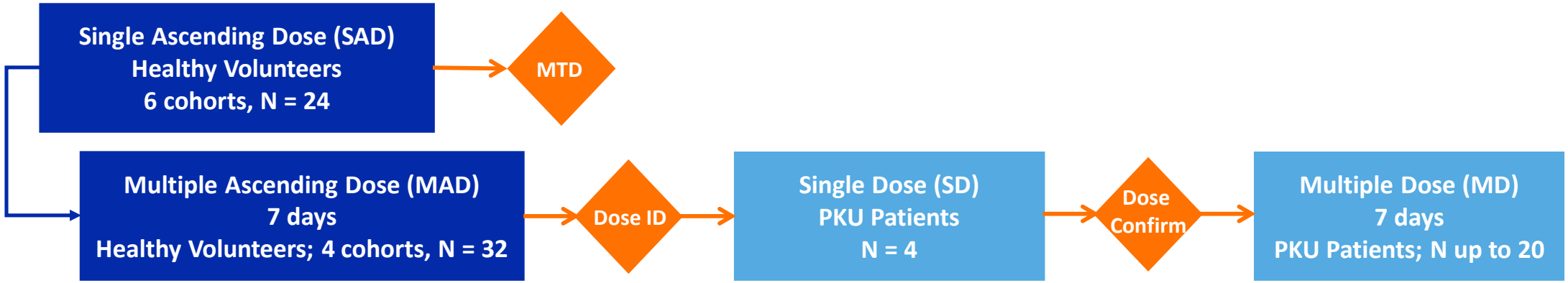


Key: HA: Hippurate, D5-HA: labeled HA, CFB: change from baseline, CFP: change from placebo

SYNB1618 Clinical Development

Phase 1/2a in Healthy Volunteers with Patient Cohort

PROGRAM	2018 Q1	2018 Q2	2018 Q3	2018 Q4	2019 Q1	2019 Q2	2019 Q3	2019 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

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Immuno-Oncology

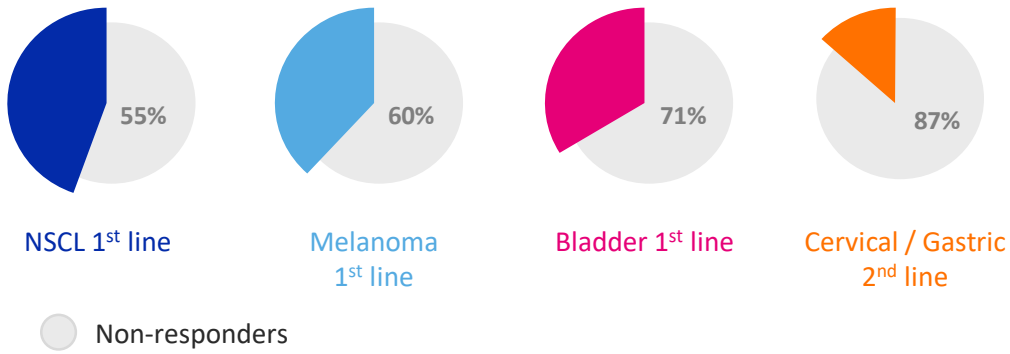
Synlogic Vision for Immuno-Oncology

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

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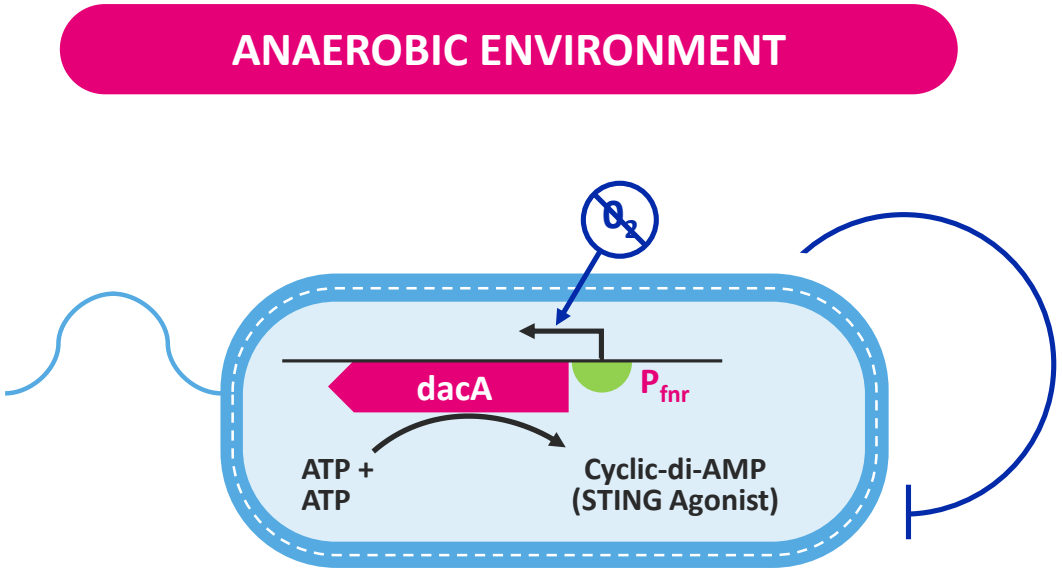
Dual Innate Immune Activator: Synthetic Biotic Medicine Producing STING Agonist (SYNB1891)

- 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_{fnr}) to produce c-di-AMP (CDA)
- Dual biosafety feature via auxotrophies – no proliferation in tumor, systemic circulation or environment
- Learnings inform future combinations



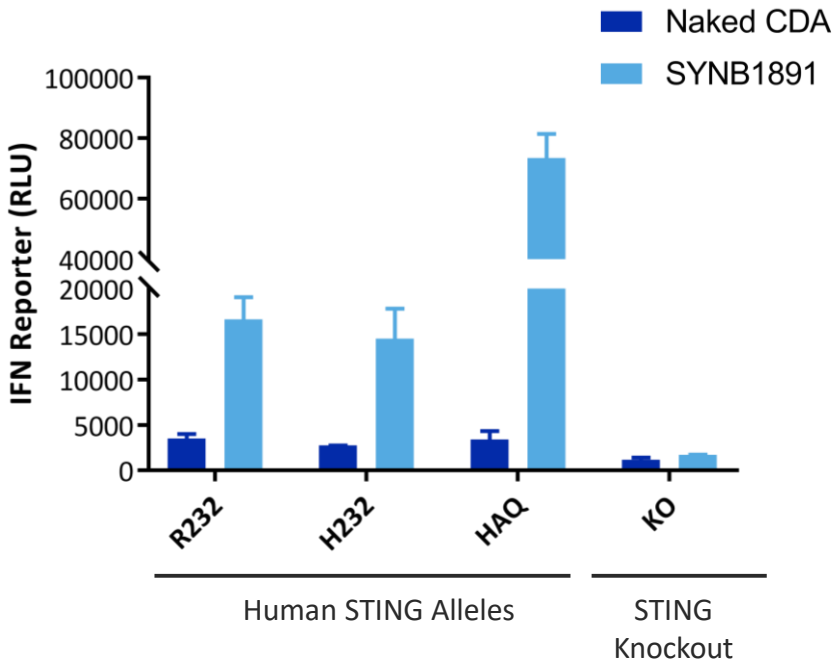
Auxotrophies

- Diaminopimelic acid (DAP)
- Thymidine

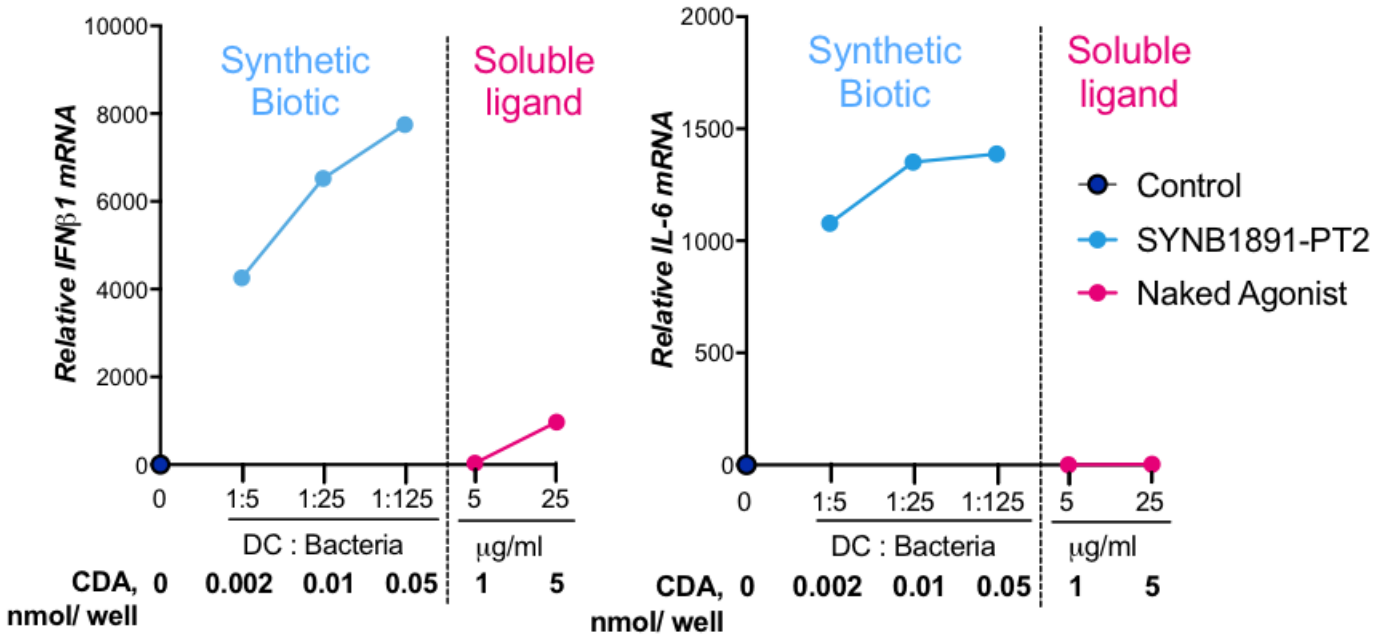
SYNB1891 *In Vitro* Characterization

Interferon Production Across Multiple Human STING Alleles – Activity Greater than Naked STING Agonist

REPORTER HUMAN MONOCYTIC LINE



HUMAN PRIMARY DENDRITIC CELLS



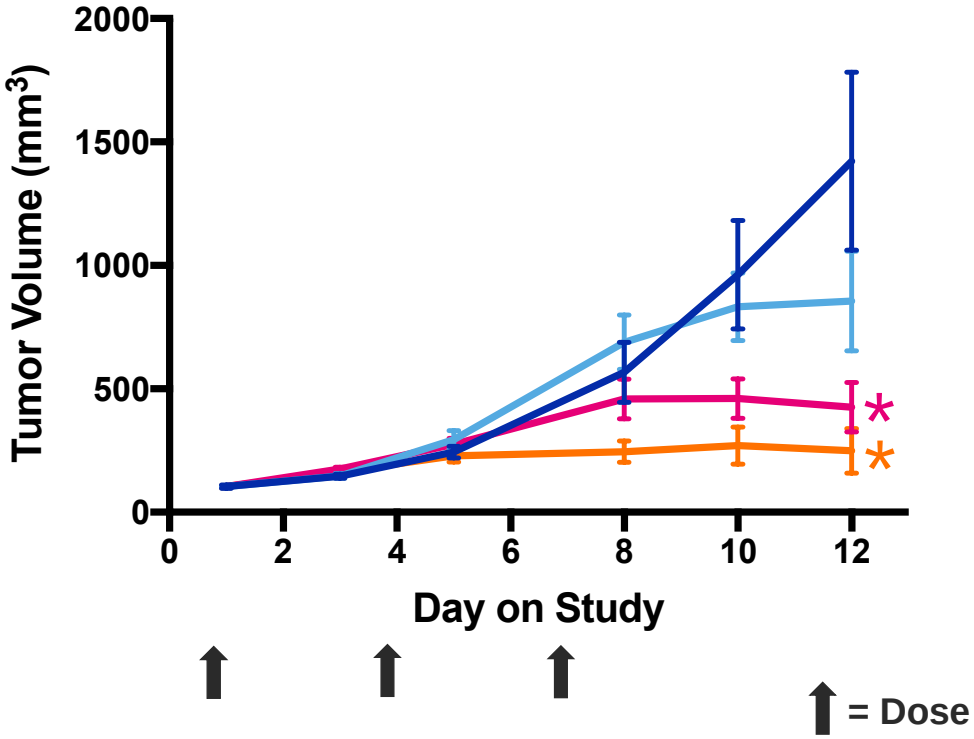
SYNB1891 *In Vivo* Characterization

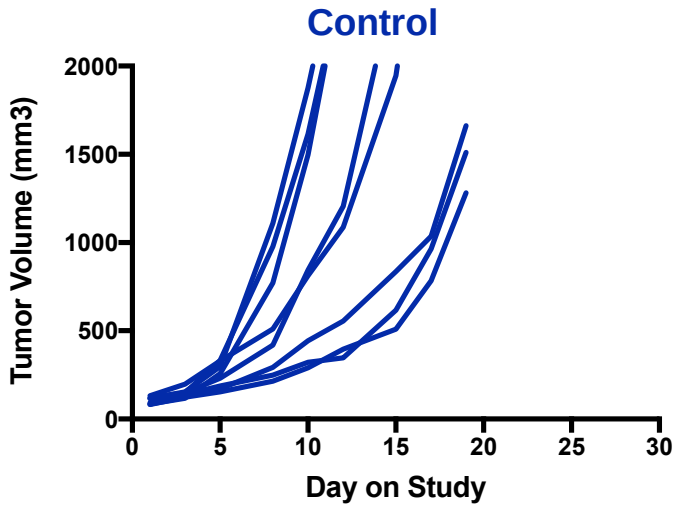
Dose-dependent Anti-tumor Activity of SYNB1891 Prototype Strain (PT1) as a Single Agent

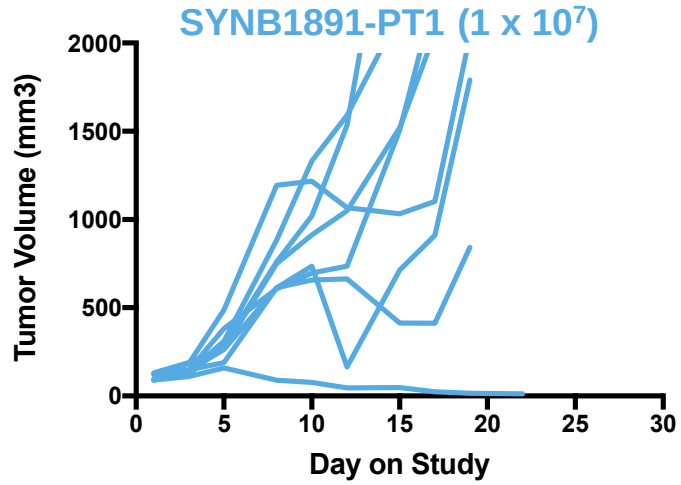
A20 tumors ~100 mm^3, randomize groups

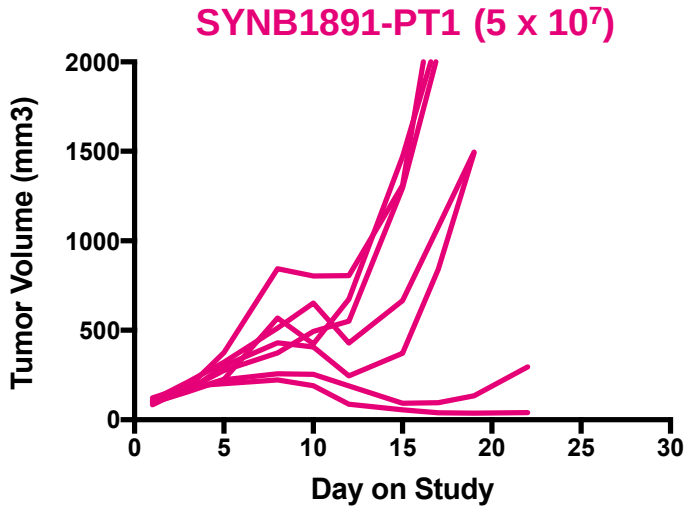
10^7, $5x10^7$ or 10^8 CFU, i.t. (SYNB1891-PT1)

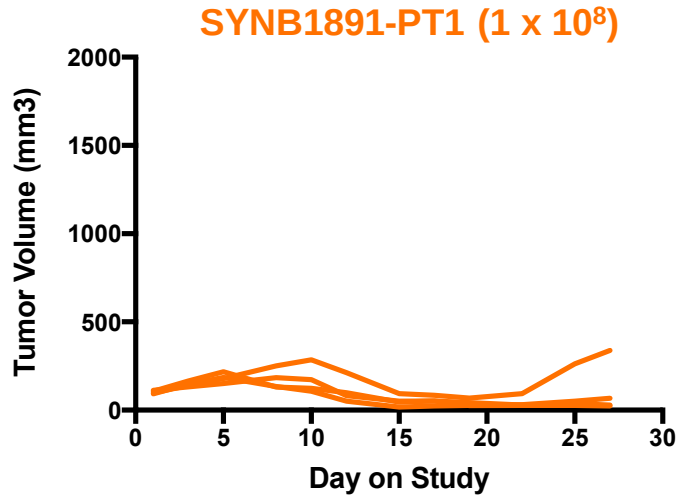
d1 d4 d7 d18











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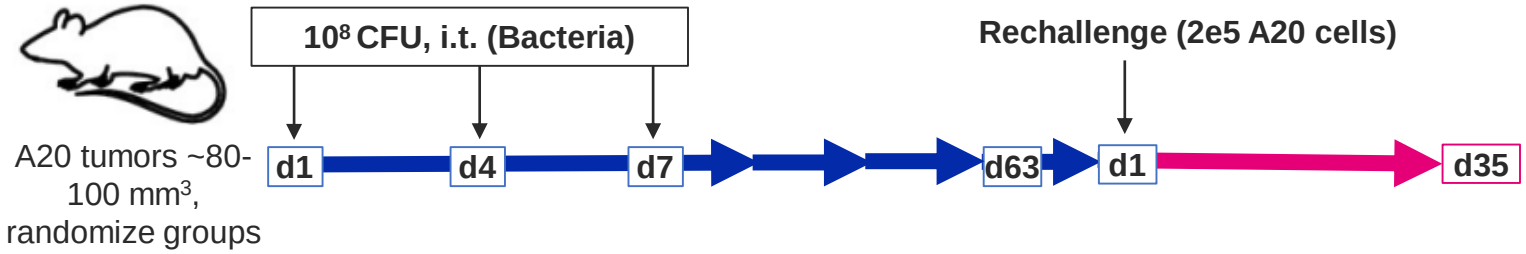
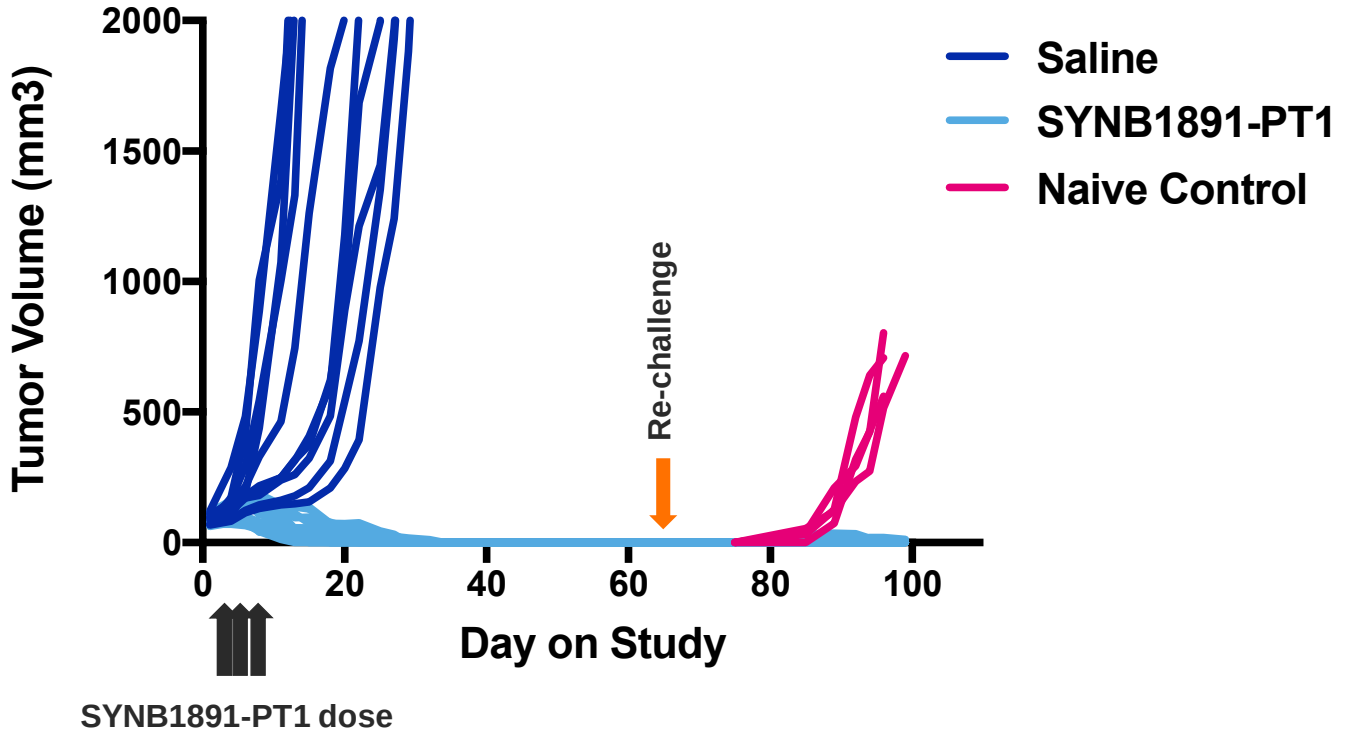
SYNB1891 *In Vivo* Characterization

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





Dual Innate Immune Activator SYNB1891

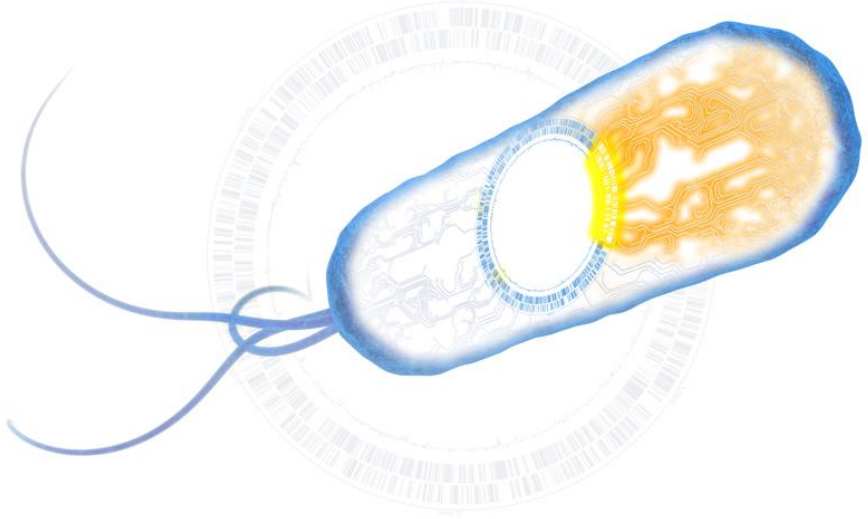
Designed to Locally Inflame the TME and Systemically Drive Tumor Antigen-Specific Immunity

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
- Clinical trial material manufactured
- 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



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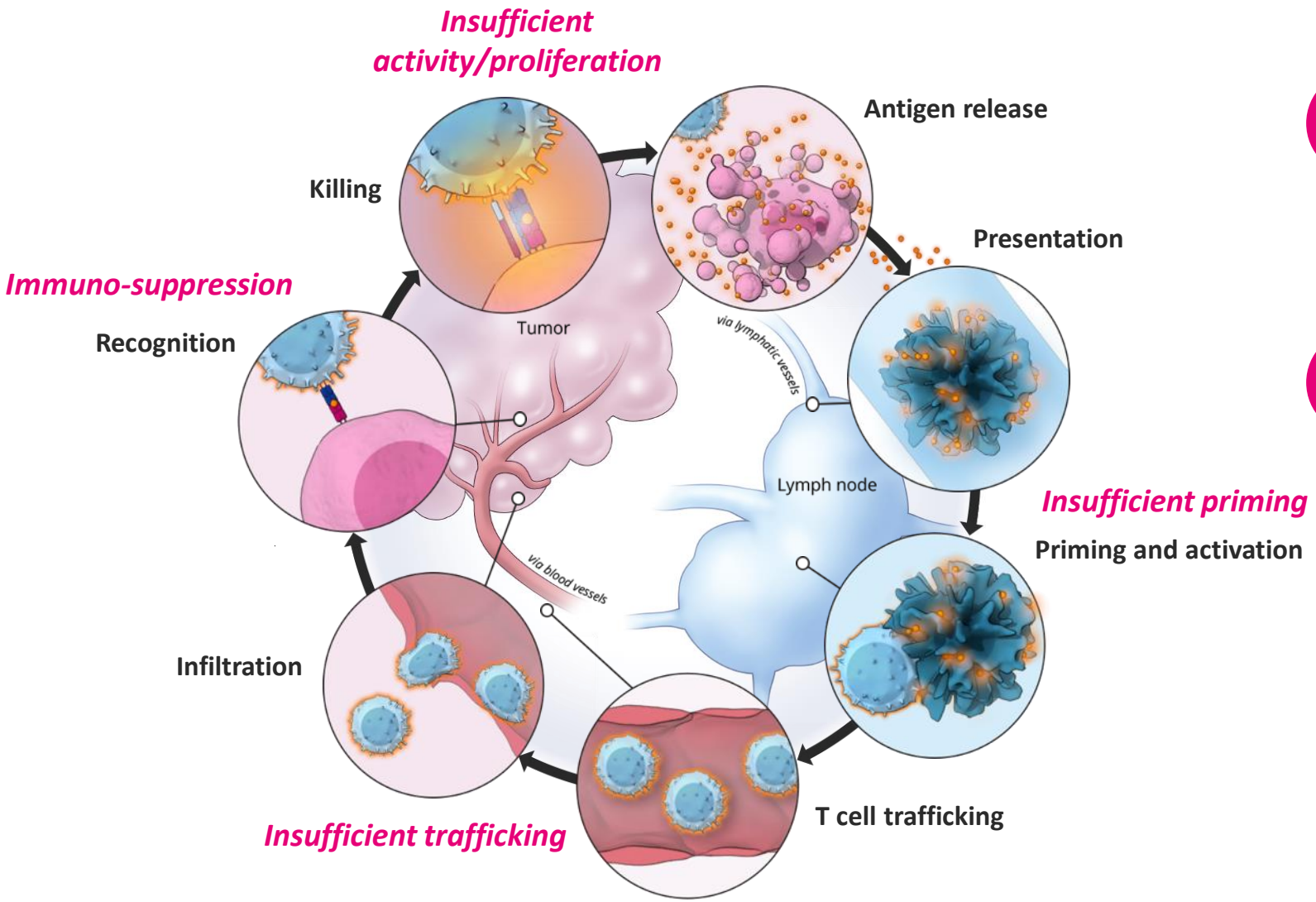
A Tumor Can Evade Multiple Critical Aspects of the Cancer-Immunity Cycle



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 Inflame the tumor microenvironment (TME)

Systemically Drive Tumor-Antigen Specific Immunity

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

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Adapted from Chen, Melman; Immunity 2013

Additional Synthetic Biotic Effectors

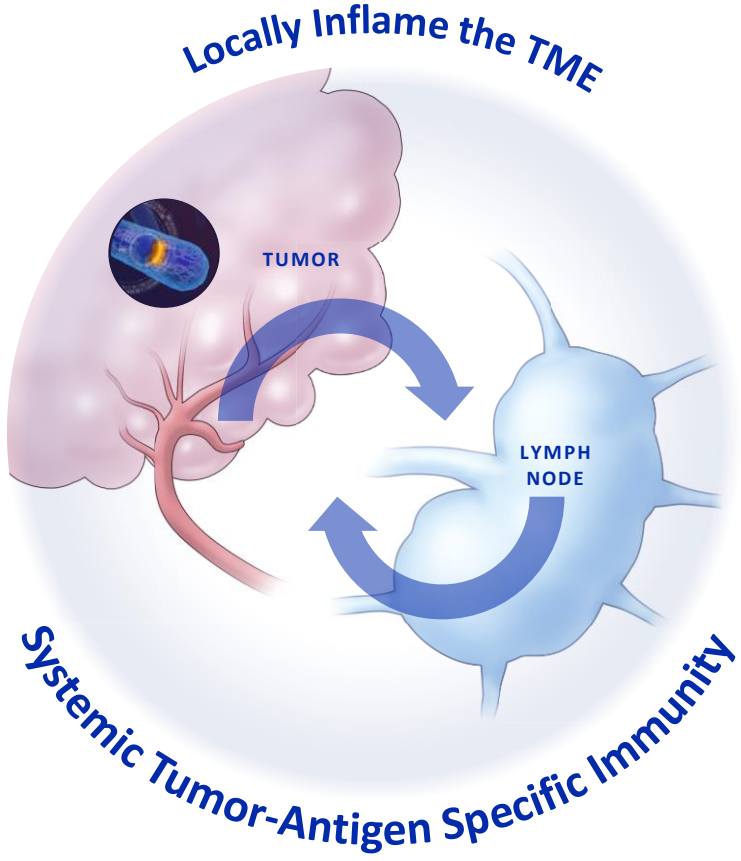
VISION: Rational Design to Locally Inflame the TME AND Systemically Drive Tumor-Antigen Specific Immunity

RELIEVE IMMUNOSUPRESSION

- Kyn Consumption
- Ade Consumption
- αPD-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→5FU
- STING
- αCD40 scFv/CD40L
- TNFα
- IFNγ
- αCD47 ScFv / Sirpα
- GM-CSF

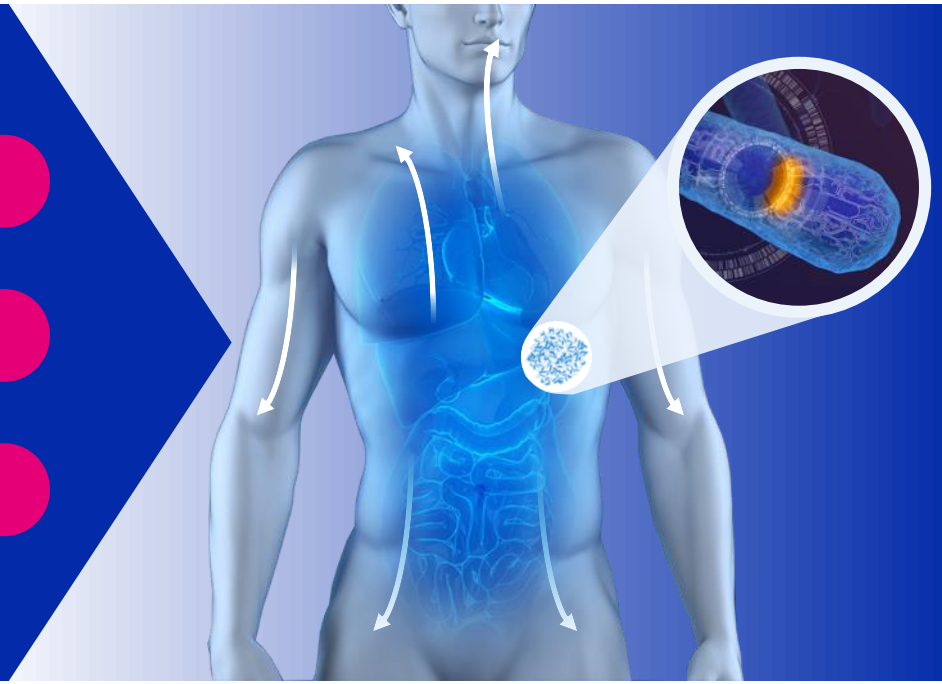
Broad Ambitions in Immuno-Oncology

Vision: Expand and Exceed the Effect of Cancer Immunotherapies

SYNB1891

DISCOVERY PORTFOLIO

INTRATUMORAL



COMBINATIONS

HARNESS THE MICROBIOME

ORAL

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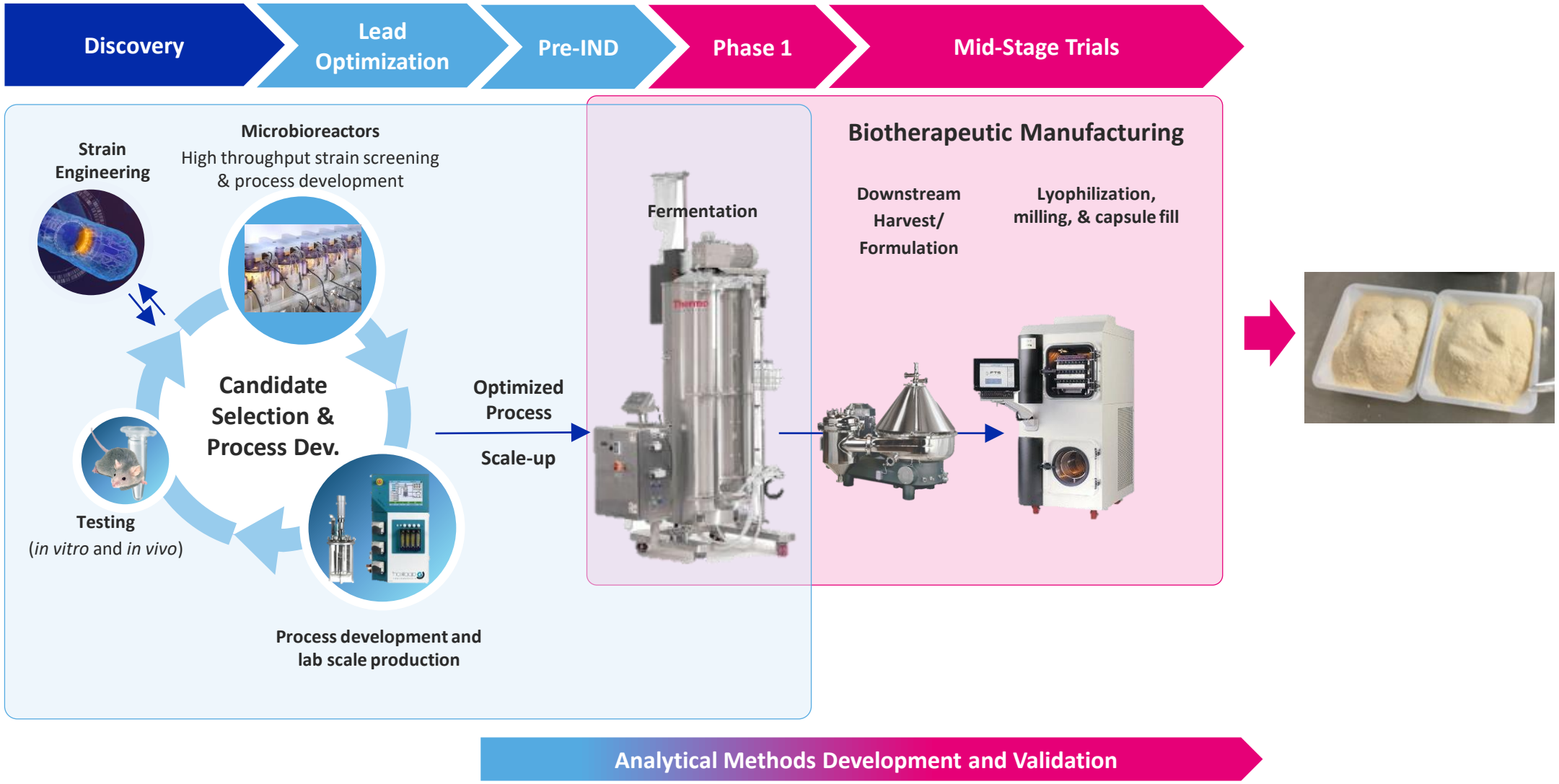
Synlogic Internal GMP Manufacturing Capabilities

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

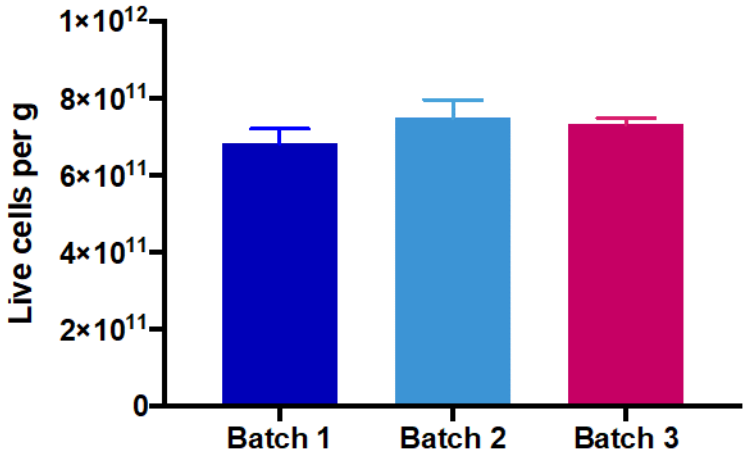


Demonstrated Progress in Development of Lyophilized SYNB1618

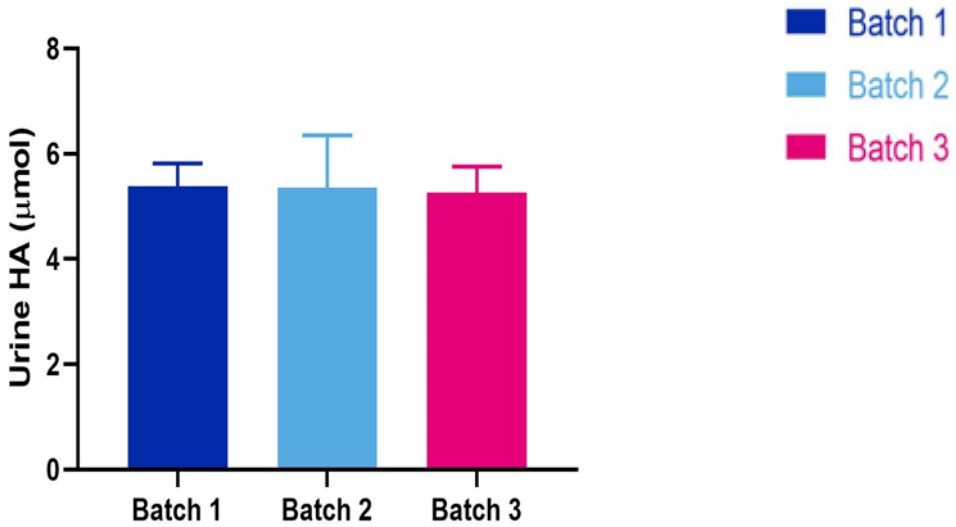
- Improved fermentation process enables production of a solid formulation of SYNB1618 with minimal impact on cell viability or activity
- Lyophilized SYNB1618 is similarly active to frozen liquid in terms of consumption of Phe or production of TCA/HA i*n vitro* and *in vivo*
- New solid process material is expected to have improved quality attributes including less free protein and reduced viscosity
- Process is robust and reproducible at 30 L production scale
- Lyophilized SYNB1618 is stable for >90 days at 2-8 °C and >30 days at room temperature
- Suite build-out complete and ready to manufacture cGMP lyophilized SYNB1618

Batch to Batch Consistency of SYNB1618 Solid Formulation

Viability



Activity in WT mice



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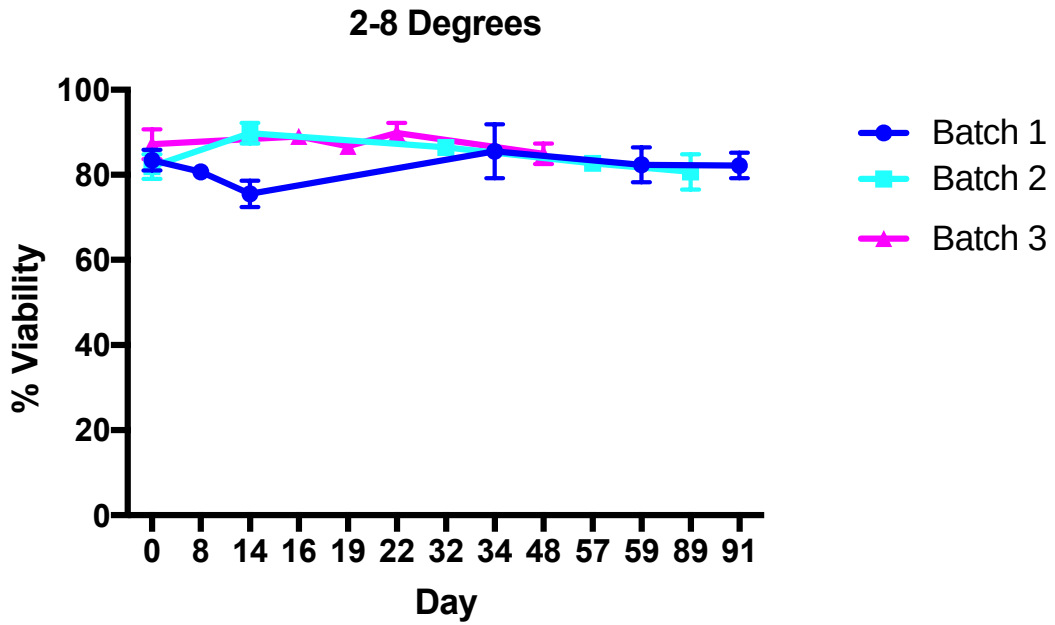
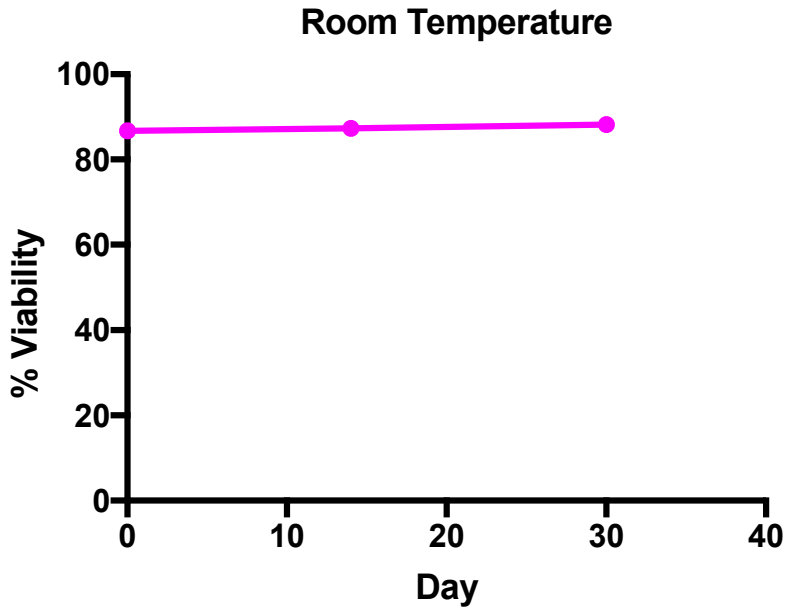
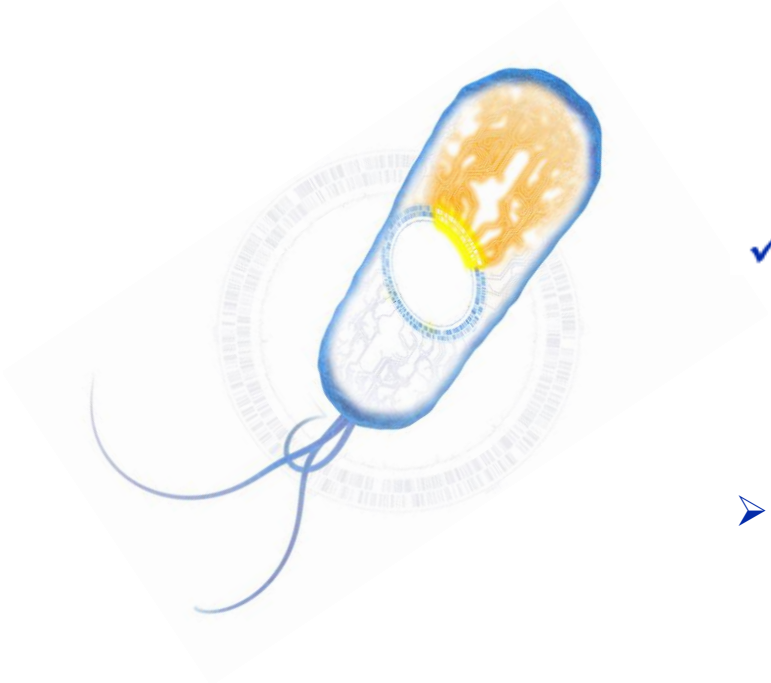
Stability of SYNB1618 Solid Formulation





2019 Progress and Milestones



SYNB1618 in PKU

- ➢ Complete ongoing study in patients
- ➢ Data expected 3Q2019 (safety, tolerability and biomarkers)

SYNB1020 in Hyperammonemia

- ✓ Preclin. and HV clin. data published in *Sci. Transl. Med.*
- ➢ Complete ongoing study in patients with cirrhosis
- ➢ Data expected 3Q2019 (safety, tolerability and ammonia-lowering)
- ➢ With ammonia-lowering data define development plan

SYNB1891 in Immuno-Oncology

- ➢ IND submission 2H2019
- ✓ Clinical trial material manufactured

- ✓ Advance **AbbVie collaboration**
- ➢ Advance **preclinical pipeline**

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Synthetic Biotic™ Medicines Designed For Life

Harnessing nature and technology
to create LIVING medicines
designed to significantly
improve patients' LIVES

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