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.
Harnessing nature and technology to create LIVING medicines designed to significantly improve patients’ LIVES
Synthetic Biotic™ Medicines
A Novel Class of Engineered Living Medicines

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

- 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

**IMMUNOMODULATION**
- Immuno-Oncology
- "Cold" Solid Tumors
- Inflammatory and Autoimmune

*Small or Large Intestine*
Platform Collaboration to Accelerate Development of Synlogic’s Synthetic Biotic Medicines

• 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

- 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

High-quality investor base
### Investing in Development of a Robust Pipeline for a Range of Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperammonemia – Urea Cycle Disorder</td>
<td>SYNB1020</td>
</tr>
<tr>
<td>Phenylketonuria</td>
<td>SYNB1618</td>
</tr>
<tr>
<td>Additional Rare Metabolic Diseases</td>
<td></td>
</tr>
<tr>
<td>Hyperammonemia – Hepatic Encephalopathy (HE)</td>
<td>SYNB1020</td>
</tr>
<tr>
<td>Inflammatory Bowel Disease</td>
<td></td>
</tr>
<tr>
<td>Immuno-Oncology Solid Tumors</td>
<td>SYNB1891</td>
</tr>
<tr>
<td>Additional Oncology Applications</td>
<td></td>
</tr>
</tbody>
</table>

**Phase 1**

**Phase 2**

**Rare Metabolic Diseases**

**Broad Metabolic Disease**

**Immunomodulation**
SYNB1020 for Hyperammonemia Indications
Characterized by Systemic Ammonia Accumulation

**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

**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

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

• 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**
SYNB1020 data recently published in *Science Translational Medicine*

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

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

Healthy Phenylalanine (Phe) - PKU

Phenylalanine Hydroxylase (PAH) converts Phe into Tyrosine

Tyrosine

Impaired PAH

Accumulation of Phe to toxic levels

SYNB1618

Manage Phe levels

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

Phenylalanine (Phe)

Phenylalanine

FNR

FNR

pheP

PAL3

trans-Cinnamic Acid (TCA)

Phenylalanine (Phe)

Phenylpyruvate (PP)

Metabolic Conversions

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

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

DOSE RESPONSE IN HEALTHY NHPs

SYNB1618 in the Clinic: Safety

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

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

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

- 56 healthy volunteers
- Received at least one dose of SYNB1618 or placebo
- Adults
  - Age range: 18-62 yrs old
SYNB1618 in the Clinic: Activity
Statistically Significant Dose-dependent Activity of SYNB1618 in Healthy Volunteers

Measure over 6hrs:
Plasma:
• Phe/D5-Phe
• TCA/D5-TCA
Urine: HA/D5-HA

Key: HA: Hippurate, D5-HA: labeled HA, CFB: change from baseline, CFP: change from placebo
## SYN1618 Clinical Development

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

<table>
<thead>
<tr>
<th>PROGRAM</th>
<th>2018</th>
<th>2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAD / MAD Healthy Volunteers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD / MD PKU Patients</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 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: SYN1618 kinetics in feces
- Exploratory: change from baseline in plasma and urinary biomarkers
Immuno-Oncology
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

- NSCL 1st line: 55%
- Melanoma 1st line: 60%
- Bladder 1st line: 71%
- Cervical / Gastric 2nd line: 87%

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

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

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
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
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

Human STING Alleles

STING Knockout

Naked CDA
SYNB1891

Naked CDA
SYNB1891

Synthetic Biotic
Soluble ligand

Synthetic Biotic
Soluble ligand

Control
SYNB1891-PT2
Naked Agonist

© 2019 SYNLOGIC. ALL RIGHTS RESERVED. | 23
SYNB1891 In Vivo Characterization

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

A20 tumors ~100 mm³, randomize groups

10⁷, 5x10⁷ or 10⁸ CFU, i.t. (SYNB1891-PT1)

Control

SYNB1891-PT1 (1 x 10⁷)

SYNB1891-PT1 (5 x 10⁷)

SYNB1891-PT1 (1 x 10⁸)
SYNB1891 *In Vivo* Characterization

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

A20 tumors ~80-100 mm³, randomize groups

10⁸ CFU, i.t. (Bacteria)

Rechallenge (2e5 A20 cells)

SYNB1891-PT1 dose

Tumor Volume (mm³)

Saline

SYNB1891-PT1

Naive Control

Day on Study

SYNB1891-PT1 dose

© 2019 SYNLOGIC. ALL RIGHTS RESERVED.
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
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

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→SFU
- STING
- αCD40 scFv/CD40L
- TNFα
- IFNγ
- αCD47 ScFv / Sirpα
- GM-CSF

Locally Inflame the TME
Systemic Tumor-Antigen Specific Immunity

Synlogic
Broad Ambitions in Immuno-Oncology

Vision: Expand and Exceed the Effect of Cancer Immunotherapies

SYNB1891

DISCOVERY PORTFOLIO

INTRATUMORAL

COMBINATIONS

HARNESS THE MICROBIOME

ORAL
Synlogic Internal GMP Manufacturing Capabilities

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

- **Discover**
  - Strain Engineering
  - Microbioreactors
- **Lead Optimization**
  - Candidate Selection & Process Dev.
- **Pre-IND**
  - Testing (in vitro and in vivo)
  - Process development and lab scale production
- **Phase 1**
  - Optimized Process Scale-up
- **Mid-Stage Trials**
  - Biotherapeutic Manufacturing
  - Downstream Harvest/Formulation
  - Lyophilization, milling, & capsule fill

**Analytical Methods Development and Validation**
Demonstrated Progress in Development of Lyophilized SYN1618

• Improved fermentation process enables production of a solid formulation of SYN1618 with minimal impact on cell viability or activity

• Lyophilized SYN1618 is similarly active to frozen liquid in terms of consumption of Phe or production of TCA/HA in 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 SYN1618 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 SYN1618
Batch to Batch Consistency of SYNB1618 Solid Formulation

Viability

Activity in WT mice

- **Batch 1**
- **Batch 2**
- **Batch 3**
Stability of SYNB1618 Solid Formulation

2-8 Degrees

- Batch 1
- Batch 2
- Batch 3

Room Temperature

% Viability vs. Day for different batches and conditions.
2019 Progress and Milestones

SYNB1618 in PKU
- Complete ongoing study in patients
- Data expected 3Q2019 (safety, tolerability and biomarkers)

SYNB1020 in Hyperammonemia
- 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
Harnessing nature and technology to create LIVING medicines designed to significantly improve patients’ LIVES.

Synthetic Biotic™ Medicines Designed For Life