Transforming Medicine Through Synthetic Biology

Corporate Presentation

July 2023
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 press release regarding strategy, future operations, clinical development plans, 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 press release, the words "may," "could," "should," "anticipate," "believe," "look forward," "estimate," "expect," "intend," "on track," "plan," "predict," "prepare" and similar expressions and their variants, as they relate to Synlogic, may identify forward-looking statements. Examples of forward-looking statements include, but are not limited to, statements regarding the potential of Synlogic's approach to Synthetic Biotics to develop therapeutics to address a wide range of diseases including: inborn errors of metabolism and inflammatory and immune disorders; our expectations about sufficiency of our existing cash balance; the future clinical development of Synthetic Biotics; the approach Synlogic is taking to discover and develop novel therapeutics using synthetic biology; and the expected timing of Synlogic's clinical trials of labafenogene marselecobac (SYNB1934), SYNB1353, SYNB8802 and SYNB2081 and availability of clinical trial data. Actual results could differ materially from those contained in any forward-looking statements as a result of various factors, including: the uncertainties inherent in the clinical and preclinical development process; the ability of Synlogic to protect its intellectual property rights; and legislative, regulatory, political and economic developments, as well as those risks identified under the heading "Risk Factors" in Synlogic's filings with the U.S. Securities and Exchange Commission. The forward-looking statements contained in this press release reflect Synlogic's current views with respect to future events. Synlogic anticipates that subsequent events and developments will cause its views to change. However, while Synlogic may elect to update these forward-looking statements in the future, Synlogic specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Synlogic's view as of any date subsequent to the date hereof.
Our Mission

To treat *diseases underserved* by other modalities by *researching, developing and commercializing* a new class of medicines through the application of *synthetic biology* to therapeutics.
Synlogic: Now in Phase 3, with A Clinical Pipeline that Reflects Validated Synthetic Biotic Product Platform

Clinical stage pipeline of oral, non-systemic, novel biotherapeutics

- Late-stage programs focused on rare, metabolic disorders
- Lead drug candidate for PKU, labafenogene marselecobac, initiated Phase 3 June 2023; four current clinical programs, ~400 individuals dosed to date

Reproducible, productive product platform based on synthetic biology

- **Synthetic Biotic platform**: drug candidates based on genetically engineered probiotics targeting validated, disease-specific metabolites:

- **Differentiated drug candidates**: GI-restricted, non-colonizing, reversible via GI clearance

- **Integrated internal capabilities**: development, manufacturing and discovery
## Advancing a New Class of Biotherapeutics

**Late-Stage Drug Candidates Focused on Rare Metabolic Diseases, PKU & HCU**

<table>
<thead>
<tr>
<th>Drug Candidate</th>
<th>Disease</th>
<th>Pre-Clinical</th>
<th>IND Enabling</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Registration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>labafenogene marselecobac (SYNB1934)</strong></td>
<td>Phenylketonuria (PKU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RPDD, US-OD, EU-OD</td>
</tr>
<tr>
<td><strong>SYNB1353</strong></td>
<td>Homocystinuria (HCU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RPDD, US-OD, FT</td>
</tr>
<tr>
<td><strong>SYNB8802</strong></td>
<td>Enteric Hyperoxaluria</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>SYNB2081</strong></td>
<td>Gout</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Undisclosed</strong></td>
<td>Cystinuria</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Undisclosed</strong></td>
<td>Inflammatory Bowel Disease (IBD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Roche</td>
</tr>
</tbody>
</table>

*RPDD = Rare Pediatric Disease Designation granted by FDA | EU-OD = Orphan Designation granted by EMA | US-OD = Orphan Drug Designation granted by FDA | FT = Fast Track granted by FDA*
PKU, HCU Programs Benefit from Precedents and Synergies
Prior Approvals Provide De-Risked Paths Forward; Both Present Commercially Compelling Markets

<table>
<thead>
<tr>
<th>Candidate</th>
<th>Disease</th>
<th>Clinical/Regulatory Endpoint¹</th>
<th>Est. U.S. Prevalence</th>
<th>Potential Peak Global Revenue</th>
<th>Clinical Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>labafenogene marselecobac</td>
<td>Phenylketonuria</td>
<td>Phenylalanine (Phe)</td>
<td>~17,000</td>
<td>&gt;$1B²</td>
<td>Phase 3</td>
</tr>
<tr>
<td>(SYNB1934)</td>
<td>(PKU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SYNB1353</td>
<td>Homocystinuria</td>
<td>Total Homocysteine (tHcy)</td>
<td>~2,500</td>
<td>&gt;$500mm²</td>
<td>Advancing to Phase 2</td>
</tr>
<tr>
<td></td>
<td>(HCU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Synergies Facilitate Development & Commercialization:

- Shared network of metabolic clinicians, PIs, clinics
- Connected patients, with common lived experience of restrictive diets, required medical formula, and residual neurocognitive challenges

¹ For PKU: Kuvan, Palynziq both approved based on phenylalanine (Phe) change vs. PBO; For HCU: Cystadane approved based on change in total homocysteine (tHcy)
² Assumes indicated for pediatric through adult
labafenogene marselecobac  
(SYNB1934)

*Potential as first and only oral, non-systemic biotherapeutic available as both monotherapy and adjunctive medical treatment for PKU*

**Currently being evaluated in Synpheny-3, pivotal Phase 3 study**
- Rare Pediatric Disease Designation (FDA)
- Orphan Drug Designation (FDA)
- Orphan Designation (EMA)
The Lifelong Burden of PKU Includes Both the Extreme Diet, and Neurocognitive Challenges of Uncontrolled Phe

PKU is caused by defects in PAH enzyme responsible for metabolizing Phe, amino acid in dietary protein

Built-up, Phe becomes neurotoxic, risking intellectual disabilities, deficits in mental processing, social engagement, emotional problems1,2,3

PKU burdens include neurocognitive symptoms and lifelong diet requirements of:
- Restricted protein (e.g. 4-6 g/day)
- Low protein/Low-Phe foods (e.g. pasta)
- Supplemental amino acid medical formula

Reflecting adherence challenges of diet, ~80% of patients’ Phe levels > goals in a major US center studied
PKU Presents a Large Rare Disease Market, Across Geographies

<table>
<thead>
<tr>
<th>Country/Territory</th>
<th>Estimated Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU</td>
<td>~1:10,000 (~25,000 patients)</td>
</tr>
<tr>
<td>Turkey</td>
<td>~1:6,000 (~14,000 patients)</td>
</tr>
<tr>
<td>China</td>
<td>~1:17,000 (~80,000 patients)</td>
</tr>
<tr>
<td>Japan</td>
<td>~1:125,000 (~1,000 patients)</td>
</tr>
<tr>
<td>US</td>
<td>~1:16,000 (~17,000 patients)</td>
</tr>
</tbody>
</table>

- PKU is the most prevalent inborn error of metabolism for which there is no cure
- Widespread newborn screening for PKU diagnoses patients, and connects families to clinics, starting in infancy
- Specific mutations affect degree of PAH enzyme functionality, disease prevalence and severity
- Diagnosis, monitoring and treatment decisions based on plasma Phe levels (vs. genetic testing)

1. Hillert et al. Ajv The Genetic Landscape and Epidemiology of Phenylketonuria, AJHG 2020
PKU Patients and Clinicians are Connected, Facilitating Clinical Development & Commercialization

Concentrated Sites of Care

- Care for patients with inborn errors of metabolism like PKU is provided through a well-defined network of metabolic clinics
- After diagnosis during infancy, patients and families are connected to local and national organizations, for support and education

PKU clinicians represent a focused potential prescriber universe, including in the US:
- ~150 metabolic dietitians
- ~1,000 medical geneticist physicians

Precedents de-risk the PKU opportunity: previously approved medicines (Kuvan, Palynziq) providing pathways for:
- Clinical: Single registrational study with primary analysis conducted on subset of pre-defined responders
- Regulatory: Full (vs. accelerated) approval based on Phe reduction vs. placebo as endpoint
- Reimbursement: Payer coverage typically requires alignment with study population, and demonstration of benefit per pivotal study

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Reimbursement for PKU Medicines in the US is Straightforward

- **Access**: Through pharmacy benefit, typically at specialty tier, per each payer’s medical policy for that product

- **Reimbursement**: Prior Authorization requirements typically follow product labeling, requiring:
  - Physician attestation
  - Clinical notes and lab values
  - Demonstration of response in Phe reduction for re-authorization

- **Distribution**: Through specialty pharmacy(ies) contracted with manufacturer

### Analog Pricing: Rare Metabolic Disease Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Annual Price (Adult, US)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbaglu (carglumic acid)</td>
<td>Hyperammonemia due to NAGS deficiency</td>
<td>~$600,000</td>
</tr>
<tr>
<td>Ravicti (glycerol phenylbutyrate)</td>
<td>Urea cycle disorders (UCDs)</td>
<td>~$700,000</td>
</tr>
<tr>
<td>Orfadin (nitisinone)²</td>
<td>Hereditary tyrosinemia type 1 (HT-1)</td>
<td>~$325,000</td>
</tr>
<tr>
<td>Lumizyme (alglucosidase alfa)</td>
<td>Pompe disease</td>
<td>~$600,000</td>
</tr>
<tr>
<td>Palynziq (pegvaliase injection)</td>
<td>PKU</td>
<td>~$200,000</td>
</tr>
<tr>
<td>Kuvan (sapropterin)²</td>
<td>PKU</td>
<td>~$200,000</td>
</tr>
</tbody>
</table>

1. Synlogic US payer market research, United Healthcare and other medical policies for Palynziq, Kuvan
2. pre-gener icization
Current Treatment Limitations Leave Need for New Approach

>70% of PKU patients remain without medical treatment

**“Classical” PKU**

Typically more severe phenotype

**Sapropterin (Kuvan,® biopterin class)**
- ~$500mm/year revenue pre-genericization
- Limited to the BH4-responsive patient segment
- **Adjunctive medical treatment opportunity**

**PKU Patients, US (n=17,000)**

1. NPKUA, patient numbers for sapropterin, pegvaliase derived from Biomarin financials and disclosures; 2. USPIs for Kuvan, Palynziq 3. Synlogic Market Research 2021

*Responsive to BH4 (tetrahydrobiopterin) = molecule that the body produces to act as a cofactor with PAH, the enzyme that is impaired in PKU. Sapropterin is a synthetic form of BH4.*
labafenogene marselecobac (SYNB1934): Designed to Consume Phe, Meet Patient Needs

The small intestine provides a reservoir for targeting Phe, from two sources

**Targeting Dietary & Circulating Phe in the GI Tract**

**Optimized for Patient Experience**

Probiotic E. Coli *Nissle*, engineered to produce Phe-consuming enzymes: Phe ammonia lyase (PAL) and L-amino acid deaminase (LAAD)

- Oral administration (presentation familiar to PKU community)
- Non-systemic, reversible
- Studied as both monotherapy and adjunctive medical treatment

1. Phase 2 and Phase 3 study designs accept patients taking pterins (Kuvan/sapropterin and sepiapterin) at baseline
## Synlogic’s PKU Program Advanced to Phase 3 in 2Q 2023

<table>
<thead>
<tr>
<th>Stage</th>
<th>Modality</th>
<th>Company/Program</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ph 3 Complete</strong></td>
<td>Biopterin</td>
<td>PTC/PTC923</td>
</tr>
<tr>
<td><strong>Ph 3 Study Ongoing</strong></td>
<td><strong>Synthetic Biotic</strong></td>
<td><strong>Synlogic / labafenogene marselecobac</strong> (SYNB1934)</td>
</tr>
<tr>
<td>Ph 1</td>
<td>Gene Editing</td>
<td>Homology/HMI-103</td>
</tr>
<tr>
<td></td>
<td>Allosteric inhibitor of SLC6A19</td>
<td>Jnana/JNT-517</td>
</tr>
<tr>
<td></td>
<td>Oral enzyme</td>
<td>Codexis/CDX-6114</td>
</tr>
<tr>
<td></td>
<td>Gene Therapy</td>
<td>Homology/HMI102 (Paused enrollment Aug 2022)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Biomarin/BMN 307 (Clinical Hold since Sept 2021)</td>
</tr>
<tr>
<td>Preclinical</td>
<td>Systemic mRNA for PAH</td>
<td>Moderna/mRNA-3283</td>
</tr>
<tr>
<td></td>
<td>PAH stabilizer (oral)</td>
<td>Agios/NA</td>
</tr>
<tr>
<td></td>
<td>Gene Therapy</td>
<td>Sangamo/ST101</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOM-Biotech/SOM1311</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Generation Bio/NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>American Gene Tech/NA</td>
</tr>
</tbody>
</table>

Source: Company websites and filings, last updated March 2023
Phase 2 Study Design Provided Proof of Concept

**Synpheny-1 Phase 2 Design**

<table>
<thead>
<tr>
<th>Diet Run-In</th>
<th>Dose Ramp</th>
<th>Treatment Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day -1</td>
<td>Day 1</td>
<td>Day 14</td>
</tr>
</tbody>
</table>

**Disposition, Demographics Reflected Target PKU Population**

- 20 adults with PKU (SYNB1618 = 11, labafenogene marselecobac (SYNB1934) = 9)
- Phe > 600 μM at screening, despite diet and/or sapropterin (Kuvan®); mean 1,041 μM and 987 μM for SYNB1618 and SYNB1934, respectively²
- Baseline characteristics evenly distributed, with a representative mix by age, gender, Phe levels, and baseline treatment

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1. SYNB1618: Days 1-3: 1x10¹¹, Days 4-6: 3x10¹¹; SYNB1934: Days 1-3: 3x10¹¹, Days 4-6: 6x10¹¹
2. Baseline Phe values per data for n=5
Phase 2 Data Demonstrated Potential Phe Reduction with labafenogene marselecbac (SYNB1934)

Response Rate

60% (3/5) achieved at least 20% Phe lowering*

-53% Mean*

Phe Reduction

% Change vs. Baseline

0%  -20%  -40%  -60%  -80%  -100%

1  2  3

-29%  -50%  -80%

Combination with Kuvan® (sapropterin)

Fasting Phe (μM)

Day

0  100  200  300  400  500  600  700

Treatment  Post-Treatment

-80%

* n = 3 responders; (-20% vs baseline)
Favorable Safety & Tolerability Profile Across PKU Program

✓ No serious adverse events (SAEs)

✓ Adverse events all mild to moderate, predominantly GI in nature, and consistent with those described in the dosing of probiotics
  • Across both arms, 3 patients discontinued due to GI-related AEs. One patient withdrew consent at the baseline visit and one reported facial flushing which was attributed to a potential allergic reaction

✓ The study design for the labafenogene marselecohac (SYNB1934) Phase 3 incorporates these learnings through
  1. Low starting dose
  2. An extended, slower dose ramp, with more time at each dose prior to advancing
Synpheny-3: Global, Pivotal, Phase 3 Study of labafenogene marselecobac (SYNB1934)

Three-Part Design Reflects Input from Regulators, Clinicians and Patient Community

**PART 1**
**Dose Escalation Period**
(9-15 weeks)

- Open-label, extended dose ramp (weeks per dose) enables individualized titration
- Informs responder population for Part 2
- To enroll ~150 patients with Phe >360 µM
- For patients currently without medical treatment or those on pterins;
- Study participants may follow their usual diet while participating in the trial

**PART 2**
**Randomized-Withdrawal**
(4 weeks)

- Placebo-controlled primary analysis: change in plasma Phe for labafenogene marselecobac vs. placebo during withdrawal among responders (from Part 1)
- All patients eligible to roll into OLE. Dose re-established, as in dose escalation period
- Change in Phe tolerance (i.e. dietary liberalization)

**PART 3**
**Open-Label Extension**
(up to three years)

- Placebo-controlled primary analysis: change in plasma Phe for labafenogene marselecobac vs. placebo during withdrawal among responders (from Part 1)
- All patients eligible to roll into OLE. Dose re-established, as in dose escalation period
- Change in Phe tolerance (i.e. dietary liberalization)

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1. For patients ages 18 years and older; an initial subset of data from patients in Part 1 will be used to assess the opportunity to lower the age of enrollment to 12
2. Dose levels for ramp are: 3x10^{11}, 6x10^{11} and 1x10^{11}; each begins with once/daily and increases frequency to three times daily, with meals
3. 20% reduction vs. baseline in plasma Phe during Part 1 is responder definition
Transformative Potential in PKU with labafenogene marselecobac

- **Large orphan disease population: majority remain without treatment** due to limitations of today’s options
  - Commercially validated by currently approved medications, but safety/efficacy leaves need for new approaches)
  - Diagnosed, connected patients and concentrated sites of care facilitate clinical development and commercial launch

- **Phase 3 initiated; prior regulatory approvals de-risk path forward**
  - Two prior FDA approvals with full approval (not accelerated) based on biomarker in single registrational study

- **Compelling expected product profile** meets patient needs
  - Orally-administered, powder/sachet presentation consistent with standard of care medical formula
  - Non-systemic; Reversible, non-colonizing; favorable safety and tolerability profile with no SAEs, and
  - Efficacy as monotherapy or adjunct to biopterins (-53% average Phe reduction in responders; -29 - -80% range)

- **Pursuing broad US and Ex-US patent protection** (e.g., composition of matter patent exclusivity to 2041)
  - Composition of matter directed to the engineered bacterium and its drug formulation; coverage will continue to grow
  - Methods of treatment and administration & manufacturing methods

$\text{Potential as 1}^\text{st} \text{ and only orally-administered biotherapeutic for both monotherapy and adjunctive treatment in PKU}$

>$1B \text{ revenue opportunity globally}$
SYNB1353 for Homocystinuria (HCU)

- Rare Pediatric Disease Designation (FDA)
- Orphan Drug Designation (FDA)
- Fast Track Designation (FDA)
HCU: Multi-System Burden, Acute Risks due to Uncontrolled Homocysteine

Life-Threatening Risks, Multi-System Complications

- Central Nervous System: Developmental delays, intellectual disabilities, psychosocial challenges
- Ophthalmological System: Lens dislocation
- Circulatory System: Thromboembolism, resulting in stroke
- Skeletal System: Reduction of bone mass, scoliosis and osteoporosis

~5,000
Est. prevalence for CBS or “Classical” HCU, US & Europe:


“I think about my HCU patients like potential time bombs due to their risk of acute events” - HCU KOL

Methionine: Key Mediator and Precursor to Homocysteine

- Methionine (Met): Crucial precursor; Met-restricted diet is 1st line Tx to lower tHcy
- Homocysteine (Hcy): Caused by mutations in Cystathionine β-synthase (CBS) enzyme
- Lowering total homocysteine (tHcy) levels is the goal of HCU treatment
- Methionine (Met) -> Cystathionine -> Cysteine

SYNB1353: New Approach to Lowering tHcy through Methionine

Current Options Leave Majority of HCU Patients Behind

- **Total homocystinuria (tHcy):** HCU treatment target ("lower is better")\(^1\,^2\)
  - Guidelines: -20% for clinical response, <100 μmol/L if possible\(^1\)
  - Normal (healthy) range: 5-15 μmol/L
  - In HCU, levels can be >200 μmol/L
  - Regulatory precedent for approval (per Cystadane\(^\circledR\))

- **Current HCU treatments are limited**
  1. Low-Met diet (low in natural protein),
  2. Supplemental formula (Met-free L-AA mixture)
  3. Betaine (Cystadane\(^\circledR\))

Majority of HCU patients are far above goals, despite current options\(^4\)

SYNB1353: Consumes Met to Lower Plasma tHcy

- Designed to **metabolize methionine** (Met) via the methionine decarboxylase (MetDC) pathway, preventing conversion into Hcy
- Converts Met to 3-methylthiopropylamine (3-MTP); YjeH gene deleted to prevent release of Met from cell
- Orally administered (powder in sachet), non-systemic absorption

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### SYNBI353: Designed for Safety, Efficacy, and Convenience

Product Presentation and Expected Profile to Enable Use Across Age Spectrum in PKU

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>Enzyme Replacement Therapy (ERT)</th>
<th>Synthetic Biotic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Manufacturer</strong></td>
<td><strong>Drug/Status</strong></td>
<td><strong>SYNB1353</strong></td>
</tr>
<tr>
<td><strong>Traverce</strong></td>
<td>Pegtitinase (TVT-058)</td>
<td>Synlogic</td>
</tr>
<tr>
<td><strong>Therapeutic</strong></td>
<td><strong>Phase 1/2</strong></td>
<td><strong>Phase 1, Proof of Mechanism</strong></td>
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<tr>
<td><strong>AGLE-177</strong></td>
<td>Paused Ph 1/2*</td>
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<tr>
<td><strong>Synlogic</strong></td>
<td>Pegtarvillase (TVT-058)</td>
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</tr>
<tr>
<td><strong>Synlogic</strong></td>
<td><strong>Phase 1, Proof of Mechanism</strong></td>
<td></td>
</tr>
</tbody>
</table>

| Dosing & Administration$^1, 2, 3, 4$ | 1.5 mg/kg biweekly lyophilized Injection | Up to 1.35 mg/kg weekly Injection |

| Safety Considerations | ERT mechanism associated with potential for allergic/immunological challenges | Non-systemic, Transient/reversible, mild GI-related side effect |

| Potentially Applicable Patient Population$^1, 2, 3$ |  |  |

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*Patients developed anti-drug antibodies at 1.35 mg/kg dose, Aeglea BioTherapeutics Press Release (12 April 2023); **>12 in UK/Australia only, >18 in US https://www.aeglea.com/clinical-trials/
SYNB1353 Phase 1 Study Demonstrated Proof-of-Mechanism in Healthy Volunteers

- Phase 1 study used healthy volunteer dietary model for (methionine meal challenge) to assess SYNB1353 ability to affect plasma Met levels

- November 2022: proof of mechanism achieved in HVs using a meal challenge by data showing:
  - Lowering plasma methionine and
  - Producing strain-specific biomarker (3MTP-glycine)

- Previously presented mechanistic modeling data suggests that SYNB1353 may lower plasma Hcy by up to 58% and may increase protein intake and in HCU patients\(^1\)

- Based on this proof of mechanism, SYNB1353 will advance to a Phase 2 proof of concept study in patients with HCU

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**Significant Change in Plasma Met**

**Confirmed SYNB1353 Activity as Intended**

<table>
<thead>
<tr>
<th></th>
<th>LS mean change, 95% CI</th>
<th>Formulation: placebo n=8, 1x10(^{12}) form 1 n=6, 1x10(^{12}) form 2 n=5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-26% (^*) p &lt; 0.05</td>
<td><strong>SYNB1353</strong> 1 x 10(^{12}) cells</td>
</tr>
</tbody>
</table>

\(^1\) Sondheimer et al., SIMD 2023
SYNB1353 was generally well-tolerated in healthy volunteers.

There were no serious adverse events (SAEs)

Adverse events (AEs) were all mild to moderate, transient, and predominantly GI in nature
  • One subject discontinued dosing due to an adverse event

Frequency and severity of GI-related AEs were similar in the active and control group
  • 7 of 22 SYNB1353 compared to 3 of 8 placebo subjects had at least 1 GI-related AE

All subjects completing the 28-day analysis cleared SYNB1353 in feces
SYNB1353 for HCU: Potential for Differentiated Convenience & Safety Across the Full Age Spectrum

- HCU is a rare metabolic disease caused by an inborn error of metabolism with well-recognized need for new treatment options
  - Burden includes life-threatening acute risks of ischemic stroke and chronic, multi-system complications
  - Large majority of patients with severely elevated total homocysteine levels, in need of new treatment options

- Commonalities and synergies with PKU, facilitating clinical, regulatory and commercial paths
  - Precedent in HCU for regulatory approval based on biomarker endpoint (total homocysteine or tHcy)
  - Shared sites of care, investigator and clinician community with PKU; connected patient communities

- Differentiated target product profile offers potential for patient convenience, safety tHcy lowering across the full age spectrum of PKU
  - Engineered probiotic designed to consume methionine, a precursor to homocysteine, in the GI tract
  - Orally-administered, non-systemically absorbed powder – easily mixed with water or juice
  - Mechanism and safety profile expected to support use across the full age spectrum

- Based on positive proof of mechanism, will advance to Phase 2 proof of concept study in HCU patients
Additional Pipeline Programs
**Additional Clinical Candidates Target Validated Metabolites**

All Programs Benefit from Cross-Platform Synergies in Discovery, Development, & CMC

<table>
<thead>
<tr>
<th>Program</th>
<th>Enteric Hyperoxaluria</th>
<th>Gout</th>
<th>Cystinuria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Candidate</strong></td>
<td>SYNB8802</td>
<td>SYNB2081</td>
<td>Undisclosed</td>
</tr>
<tr>
<td><strong>Target Metabolite within the GI Tract</strong></td>
<td>Dietary oxalate</td>
<td>Uric acid</td>
<td>Methionine</td>
</tr>
<tr>
<td><strong>Clinical Biomarker</strong></td>
<td>Urinary oxalate</td>
<td>Plasma uric acid</td>
<td>Urinary cystine concentration</td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Clinical proof of concept established</td>
<td>IND enabling studies ongoing</td>
<td>Preclinical</td>
</tr>
<tr>
<td><strong>Shared chassis of Synthetic Biotic</strong></td>
<td><img src="Image" alt="Shared Chassis Diagram" /></td>
<td><img src="Image" alt="Shared Chassis Diagram" /></td>
<td><img src="Image" alt="Shared Chassis Diagram" /></td>
</tr>
</tbody>
</table>
Industry-Leading Partners Reflect Synlogic Expertise, Progress to Date

- Established June 2021
- Research collaboration for discovery of novel Synthetic Biotic addressing novel single target for the treatment of inflammatory bowel disease (IBD)
- Roche has exclusive option to enter a licensing and collaboration agreement for further development and commercialization
- Synlogic achieved prespecified research milestones and payments in Q3 2021 and Q3 2022

- Established 2019
- Five-year, $30 million strategic research collaboration
- Accelerates expansion and development of Synlogic’s pipeline, based on Synlogic’s product engine and Ginkgo’s discovery capabilities
- Synlogic retains exclusive marketing rights
- Results to date include:
  - SYNB1353 for HCU
  - SYNB2081 for gout
Corporate
Leadership Strength Brings Depth Across Biopharma
# Financial Results for First Quarter 2023

## Summary Results

### Balance Sheet (unaudited)

<table>
<thead>
<tr>
<th></th>
<th>31 March 2023</th>
<th>31 December 2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash, Cash Equivalents,</td>
<td>$57.4M</td>
<td>$77.6M</td>
</tr>
<tr>
<td>and Marketable Securities</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Financial Performance (unaudited)

<table>
<thead>
<tr>
<th></th>
<th>Three Months Ended</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>31 March 2023</td>
</tr>
<tr>
<td>Revenue</td>
<td>$0.2M</td>
</tr>
<tr>
<td>R&amp;D Expenses</td>
<td>$12.5M</td>
</tr>
<tr>
<td>G&amp;A Expenses</td>
<td>$4.0M</td>
</tr>
<tr>
<td>Net Loss</td>
<td>$(15.6M)</td>
</tr>
<tr>
<td>Net Loss per share – basic and diluted*</td>
<td>$(0.23)</td>
</tr>
<tr>
<td>Weighted Average Shares Outstanding*</td>
<td>69.1M</td>
</tr>
</tbody>
</table>

*Weighted average shares used in computing net loss per shares – basic and diluted
Thank You