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Transforming Medicine through Synthetic Biology

Corporate Presentation

July 2022

Our Mission

Bringing the transformative power of synthetic biology to medicine.

Synlogic's Commitment

We're committed to partnership with the PKU Community to develop therapies which help you have more control over your PKU and your life.

Almost 17,000 people in the US struggle with PKU. The disease affects the whole family.

Maintaining a strict lifelong diet can be difficult and frustrating, and spikes in phenylalanine (Phe) levels can lead to trouble concentrating, depression, and other challenges.

Synlogic has developed novel technology which may offer a new potential therapy: a modified probiotic designed to consume Phe in the gut.

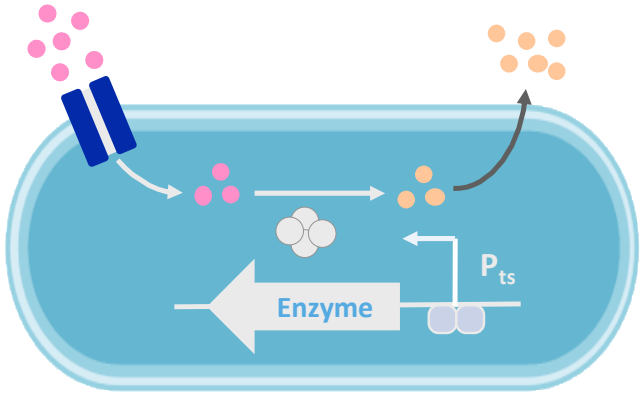
In two previously completed studies, our study treatment has shown the potential for clinically meaningful Phe reduction in a safe and well-tolerated way.

A New Paradigm of Biotherapeutics

Reproducible, Proprietary Product Engine Based on Synthetic Biology

Synthetic Biotics

Programable, precision **genetic engineering** + Well-characterized **probiotic *chassis***

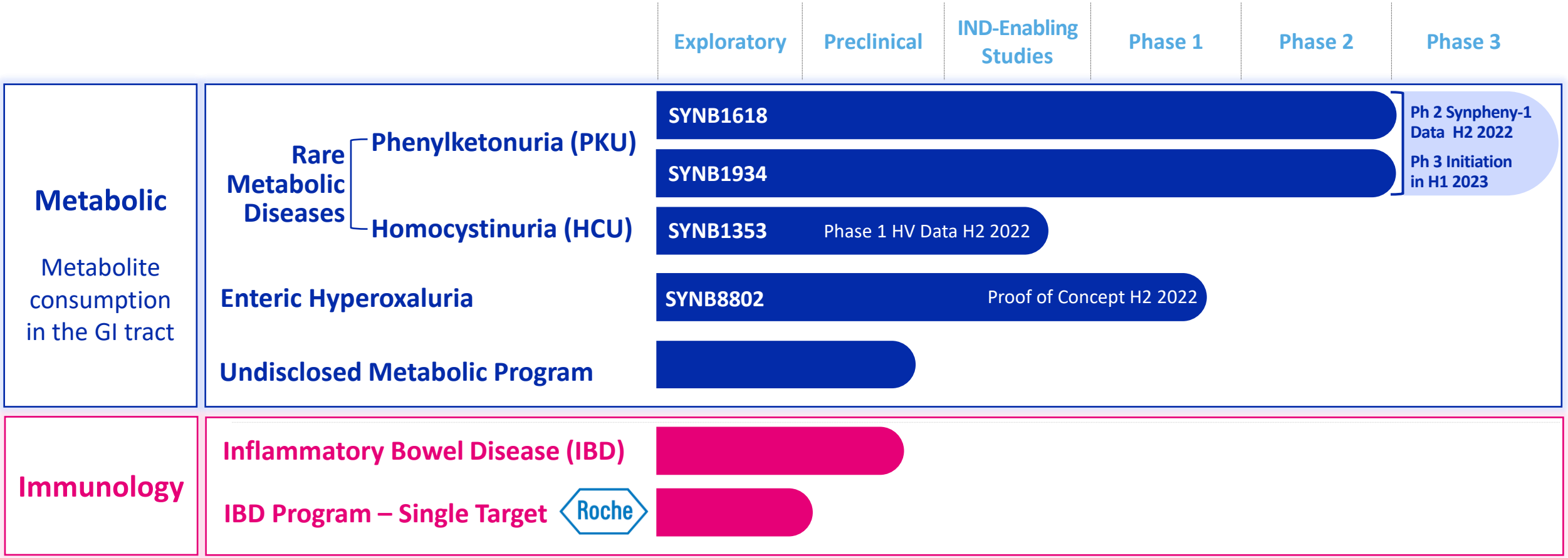


Differentiated Drug Candidates

- Target metabolites from **validated biological pathways**
- **Orally-administered** convenience
- Probiotic *chassis* that **avoids systemic absorption** (restricted to GI tract)
- Non-colonizing, non-integrating, and **reversible** via rapid GI clearance
- Addressing **rare and common,** metabolic and immunological diseases diseases

GI = gastrointestinal

Pipeline Targets Metabolic, Immunological Diseases



GI = Gastrointestinal; HV = Healthy Volunteers

PKU Can Be Devastating for Patients and Families

*"Adding **10g of protein** per day would be a **game changer for my family**"*

— Parent of PKU Patient

*"If my boys could **just eat a slice of normal bread** or a serving of regular pasta it would be huge"*

— Parent of PKU Patient

*People think this isn't too bad, I look okay. But this is **a lifelong burden.** It's a challenge to think straight, to plan my day.*

— Adult PKU Patient

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PKU = phenylketonuria; PAH = phenylalanine hydroxylase; 1. Bilder, et al. 2017; 2. Levy, et al. 2020; 3. Gentile, et al. 2010

Phase 2 Synpheny-1 Study Design in Patients with PKU

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SynPheny-1 Trial Design

Diet Run-In	Treatment Period (monotherapy & adjunctive to sapropterin)	Wash-Out

	Dose Ramp	$1e^{12}$ TID	$2e^{12}$ QD
Arm 1: SYNB1618			
Arm 2: SYNB1934			

Days	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29

Trial Endpoints:

D5-Phe Tracer Study

Fasting Plasma Phe

Biomarker Study

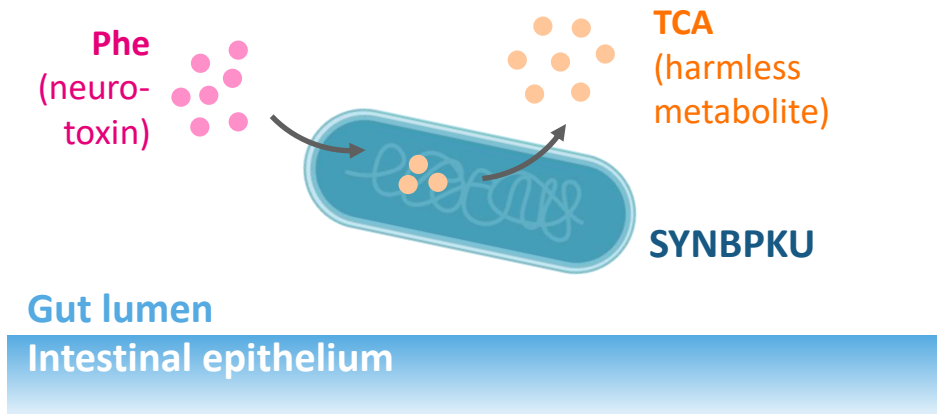
Safety and Tolerability
(AE collection)

- ✓ Phase 1 HV data confirmed greater potency for SYNB1934 vs. SYNB1618 in healthy volunteers, **2nd arm with SYNB1934** to Phase 2 to assess activity in PKU patients
- ✓ Study amended to include treatment as **monotherapy and adjunctive treatment**

1. Endpoints: % Change from baseline in D5 Phe: 24h AUC evaluated, d-1, 14 (at 2e12 dose); Fasting Phe: Evaluated in AM pre-dose on Days -1, 7, 14, 29; Biomarkers (TCA, HA): Evaluated d1, 7, 15; Safety & tolerability: AEs collected throughout treatment and at Day 29

Synlogic's Approach: Targeted to Meet Needs in PKU

Intuitive Design



- **Consumes Phe in GI** tract -> converts to harmless metabolite (TCA) -> **reduces Phe levels in plasma** via enterorecirculation
- **Avoids systemic absorption** and associated adverse events

Transformative Profile

Efficacy

- SYNB1618 **achieved target mean Phe change in Phase 2 interim analysis** of -20%[1]
  - Compares to -10% in Kuvan Ph 3 (mean ITT)[2]
- SYNB1934 Ph 1 data confirmed greater potency[1]

Favorable safety profile, no treatment-related SAEs to-date

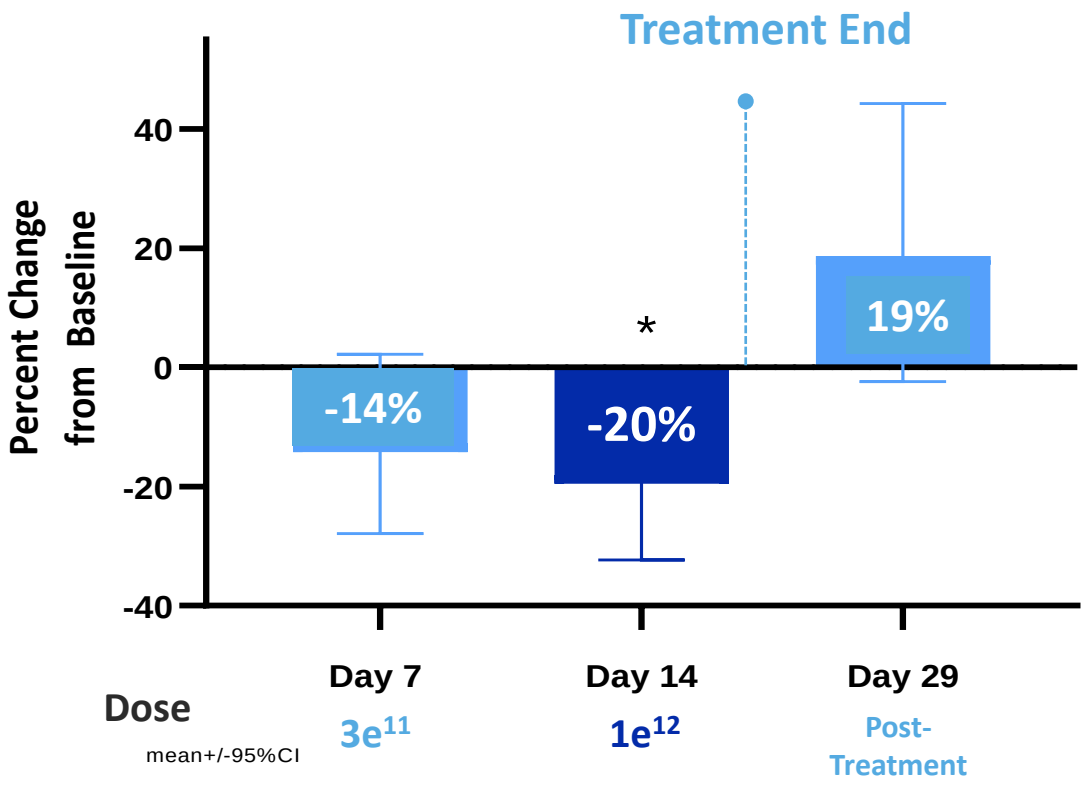
Convenience: Oral administration

Monotherapy or Adjunct

TCA = trans-cinnamic acid. ITT= Intent to Treat; 1. Synlogic PKU Program Update, September 20, 20211.
2. FDA Statistical Review & Evaluation of sapropterin dihydrochloride 2007 3. Synlogic HCP & Payer US Market Research 4Q 2021

Proof of Concept in PKU Patients Achieved in Phase 2 Interim Analysis

Phe Reduction: Intent-to-Treat
(ITT or "All Comers", N=8)



Clinically Meaningful Efficacy

- **Mean Reduction Met Target:** % change is ~2x that of sapropterin's pivotal study

50% response rate (4 of 8)

- **Response Rate Favorable:** Four of eight patients in analysis achieved the pre-specified responder definition (>20% reduction) in plasma Phe

- **Additional Biomarkers Support Effect:** A labeled Phe challenge and other biomarker assessments confirm Phe-lowering effect of drug candidate

ITT = Intent to Treat population
*Result is statistically significant because the 95% CI does not cross zero.; p<0.05

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Phase 2 Synpheny-1 Interim Analysis with SYNB1618

Safety Findings

- **No Serious Adverse Events (SAEs)** or systemic safety issues identified
- Tolerability profile in Phase 2 interim analysis **consistent with experience** in healthy volunteers
- **Most adverse events were mild-to-moderate** and GI in nature
- One discontinuation in Phase 2 interim analysis (anxiety due to PKU)

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GI = Gastrointesinal; 1. Synlogic PKU Program Update, September 20, 2021

Get Involved!

For more information on study participation…

Check out our Study Website at…

PKUResearchStudy.com

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Find us on ClinicalTrials.gov

ct.gov #: NCT04534842

Protocol: SYNB1618-CP-003

