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Transforming Medicine Through Synthetic Biology

Synpheny-1 Phase 2 Top-Line Results

October 18, 2022

Forward Looking Statements

This press release 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" 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 SYNB1618, SYNB1934, SYNB1353 and SYNB8802 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.

Speakers

Aoife Brennan, MB ChB
President & CEO

Molly Harper
Chief Business Officer

Caroline Kurtz, PhD.
Chief Development Officer

Opening Remarks

Dr. Aoife Brennan
President & CEO

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PKU remains a profound burden

Phase 2 top-line data confirm transformative potential of SYNB1934

Expect to initiate Phase 3 with SYNB1934 in H1 2023

The Opportunity & Positioning for PKU

Molly Harper
Chief Business Officer

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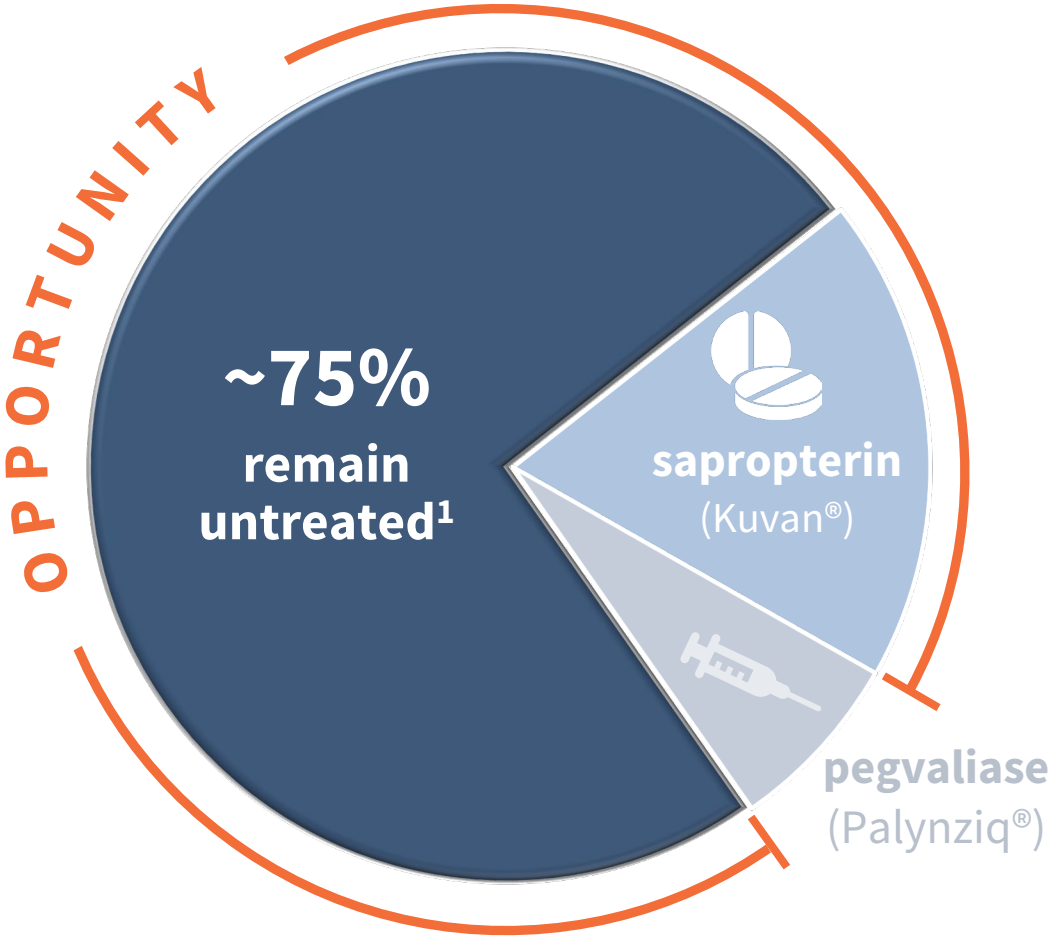
PKU: Universally Diagnosed, Underserved

Underserved Population



Attractive Market Opportunity

- ✓ 17,000 in the US;[1] >150,000 globally[2]
- ✓ Kuvan® achieved $500mm/yr with ~15% share[3]
- ✓ Palynziq®: $300mm for 2022 with ~10% share[3]

What Good Looks Like

Target threshold for plasma Phe reduction **-20%**

Per clinician, KOL input[4]

Regulatory precedent for response target[5]

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1. US Data estimate NPKUA; 2. Hillert et al *AJHG* 2020 3.Pre-genericization; Patient numbers for sapropterin, pegvaliase derived from Biomarin financials and disclosures 4. Synlogic Market Research 2021 5. Palynziq U.S. Prescribing Information

Designed to Fit with PKU Patients

Patient Presentation, SYNB1618 & SYNB1934

- ✓ Potential clinical positioning: as ***both*** **monotherapy** ***and*** **adjunctive* treatment options**
- ✓ **Lack of systemic absorption**
- ✓ Convenient, **oral administration**

synlogic * to sapropterin (Kuvan®)

Synpheny-1 Phase 2 Top-Line Results

Caroline Kurtz, PhD.
Chief Development Officer

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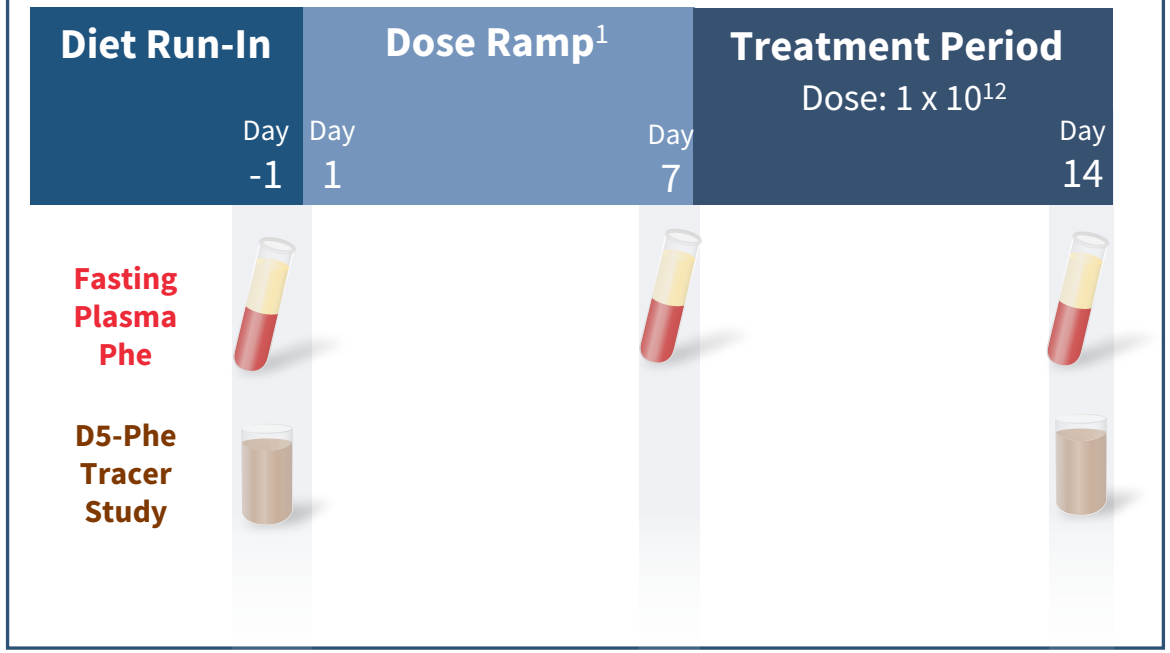
Phase 2 Synpheny-1 in Patients with PKU

Study Design

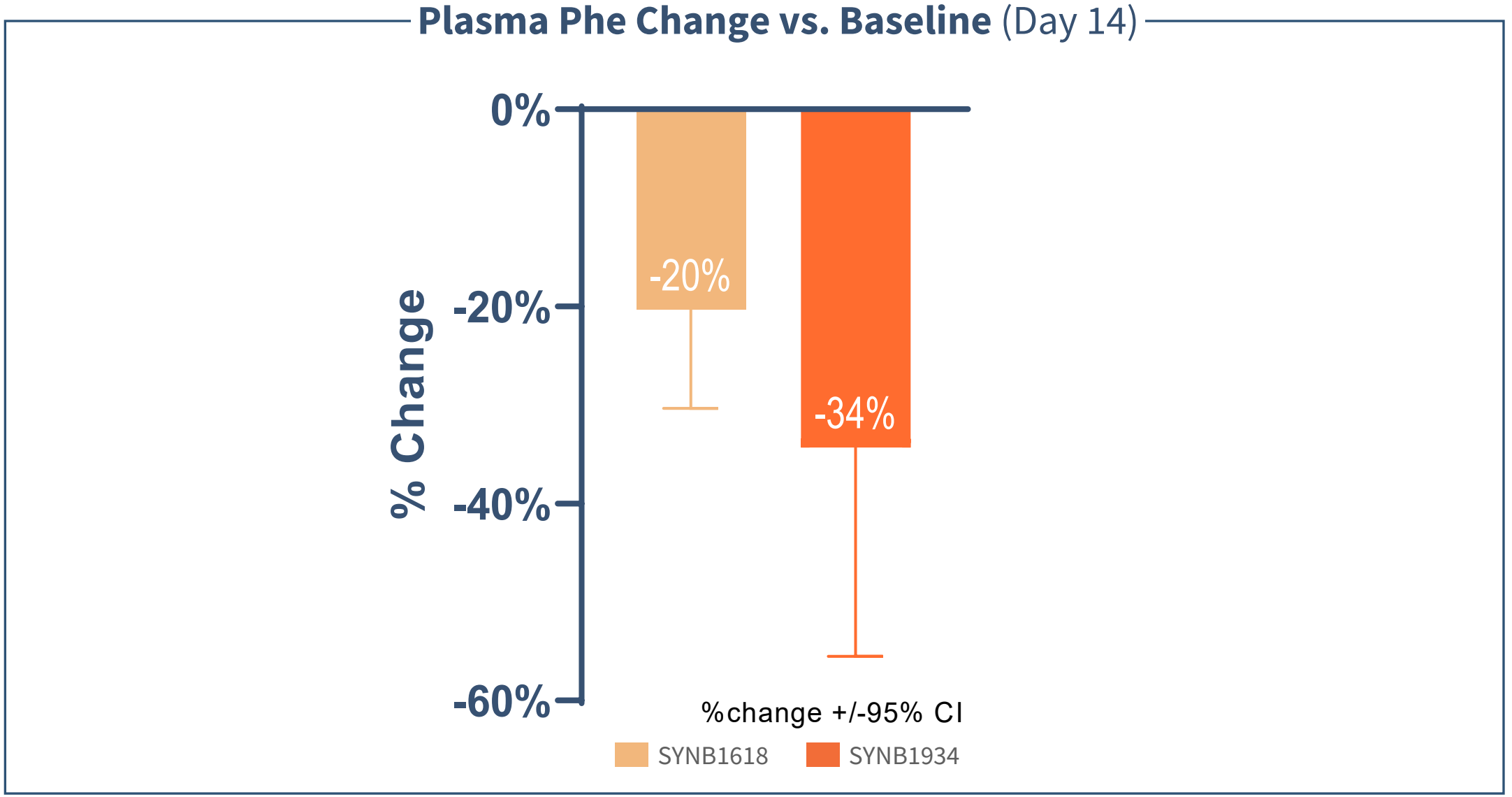


1. SYNB1618: Days 1-3: $1x10^{11}$, Days 4-6: $3x10^{11}$; SYNB1934: Days 1-3: $3x10^{11}$, Days 4-6: $6x10^{11}$
2. Baseline Phe values per data for n=5

Disposition & Demographics

- Enrolled **20 adults** with PKU (SYNB1618 =11, SYNB1934 = 9)
- All had **Phe > 600 µM** at screening, despite diet and/or sapropterin (Kuvan®), with mean of 1,041 µM and 987 µM for SYNB1618 and SYNB1934, respectively[2]
- Baseline characteristics were evenly distributed across arms, with a representative mix by age, gender, Phe levels, and baseline treatment

Robust Mean Reductions in Plasma Phe ("All Comers"*)



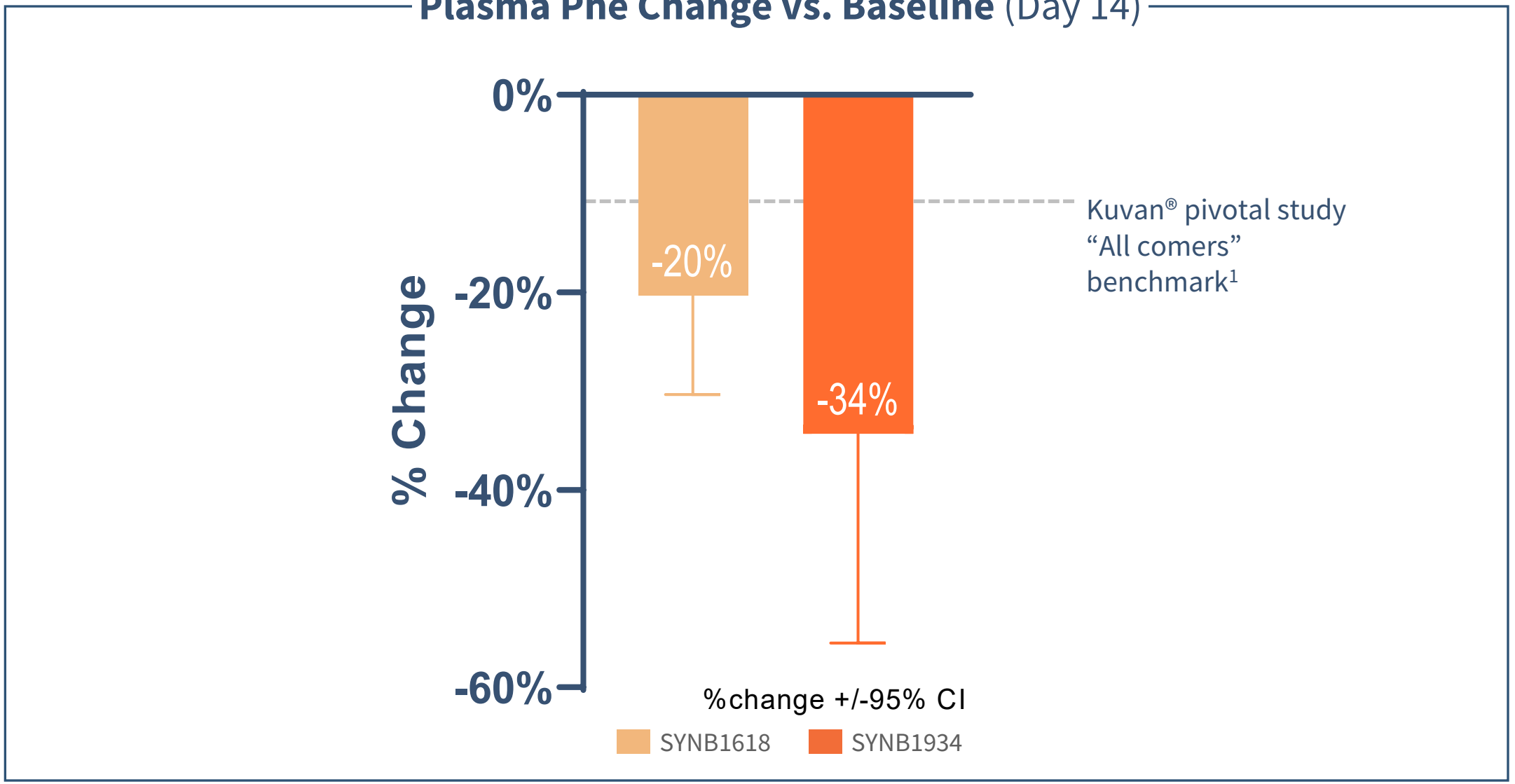
* Defined as those that completed dosing

Note: The 95% confidence interval did not cross zero for either strain

Data are LS mean +/- 95% CI

SYNB1618 n=10; SYNB1934 n=5

Robust Mean Reductions in Plasma Phe ("All Comers"*)



* Defined as those that completed dosing
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1. FDA Statistical Review & Evaluation of sapropterin dihydrochloride 2007, p 9.

Data are LS mean +/- 95% CI
SYNB1618 n=10; SYNB1934 n=5

Responder Data Show Clinical Significance of Phe Lowering

SYNB1618

6/10 achieved at least 20% Phe lowering[1]

Range among responders[2]
-20% to -61%

SYNB1934

3/5 achieved at least 20% Phe lowering[1]

Range among responders[2]
-29% to -80%

1. Responder definition: ≥20% reduction vs. baseline in plasma Phe levels achieved on Day 7 or Day 14
2. Maximum Phe reduction by patient, Day 7 or Day 14

Results Across All Participants Support Strength of Profile

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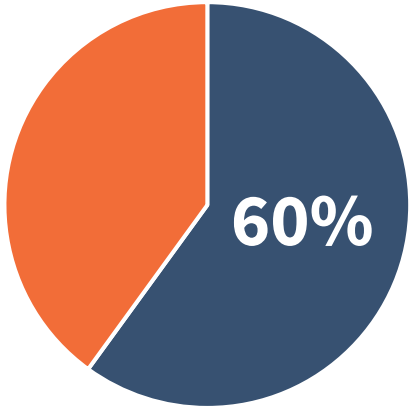
LIVING IN HARMONY WITH PKU

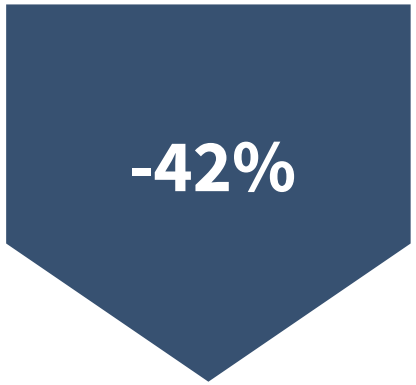
Data Based on Integrated Analysis with Arms 1 & 2 (n=15)

Responders



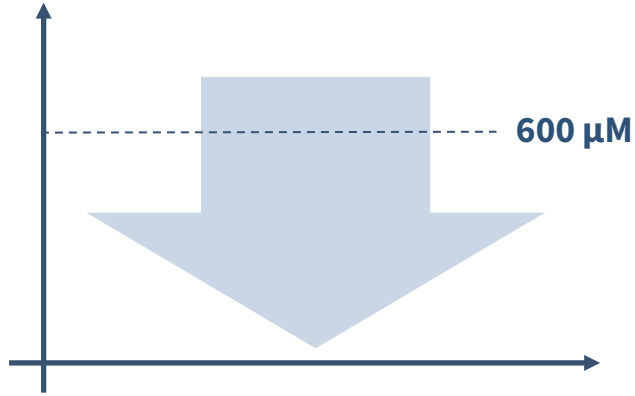
60% (9/15) achieved at least 20% Phe lowering*

Response



42% mean Phe lowering in responders (n=9 responders)

Threshold Lowering



7/9 of the responders achieved Phe levels ≤600 µM

* Responder definition: ≥20% reduction vs. baseline in plasma Phe levels achieved on Day 7 or Day 14

SYNB1618 n=10; SYNB1934 n=5

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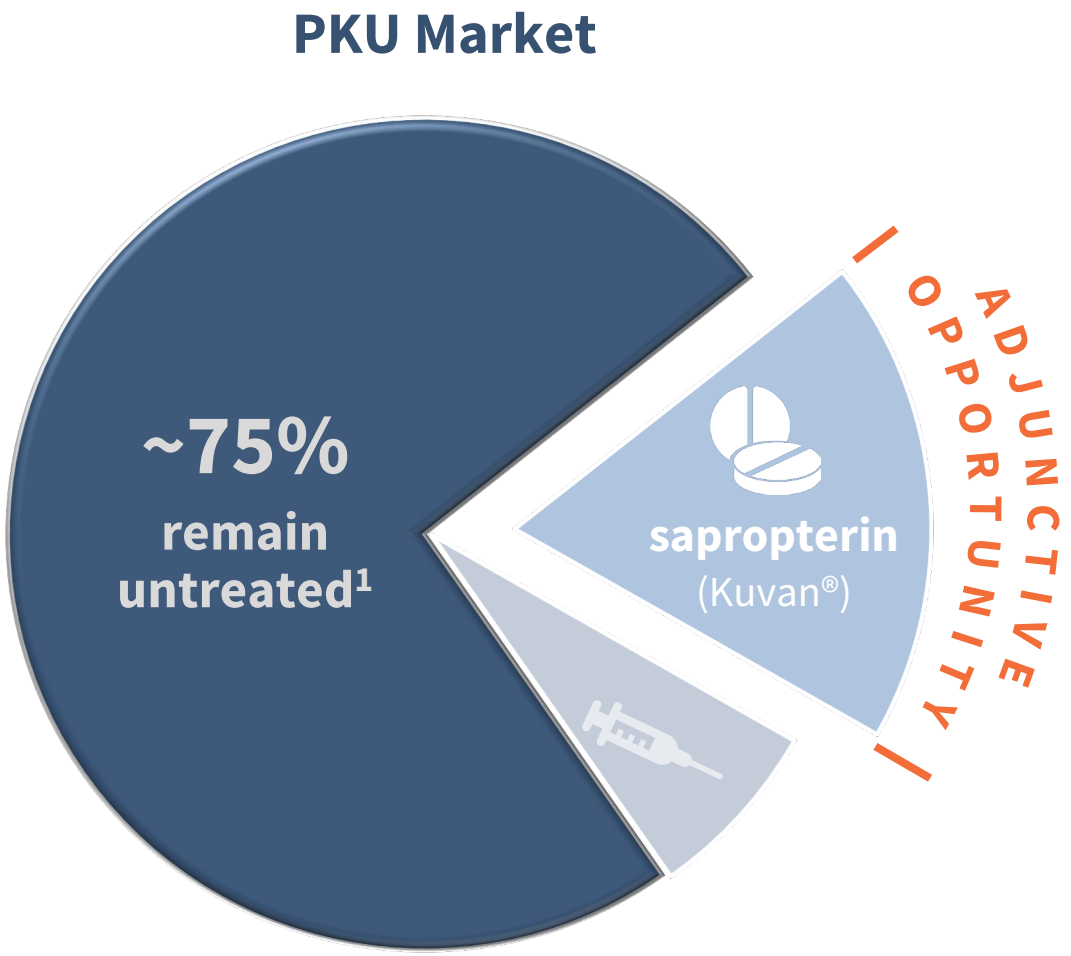
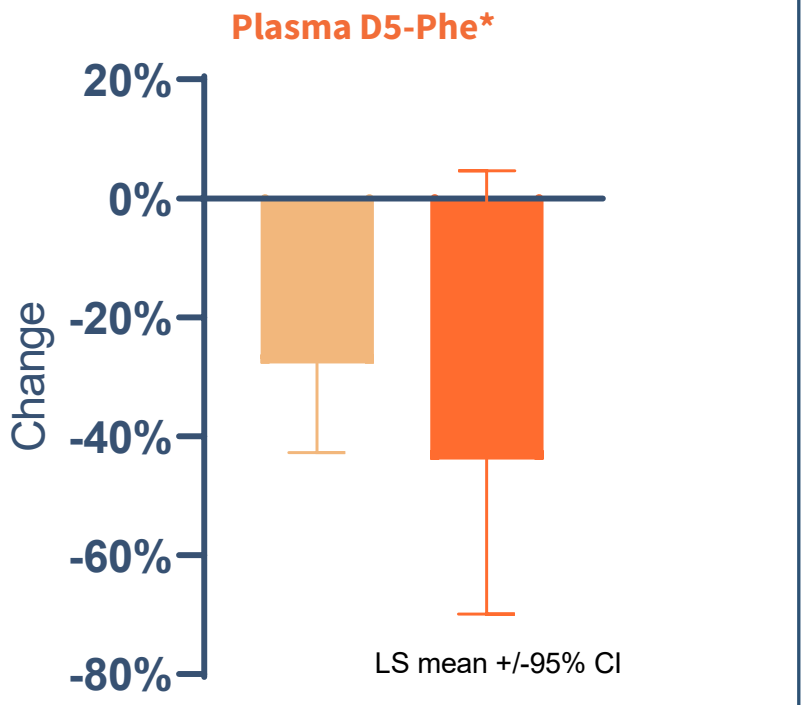
Data Confirm Potential as Adjunctive Treatment Option



- Data included patients who received study drugs as an adjunct to ongoing treatment with sapropterin (Kuvan®)
- Adjunctive data for patients for both strains were consistent with broader findings
  - Phe reductions were 26% and 80%
  - In line with expectations given independent mechanism
- This experience confirms potential as an adjunctive treatment option

Biomarkers Confirm Phe Metabolism in GI Tract by Both Strains

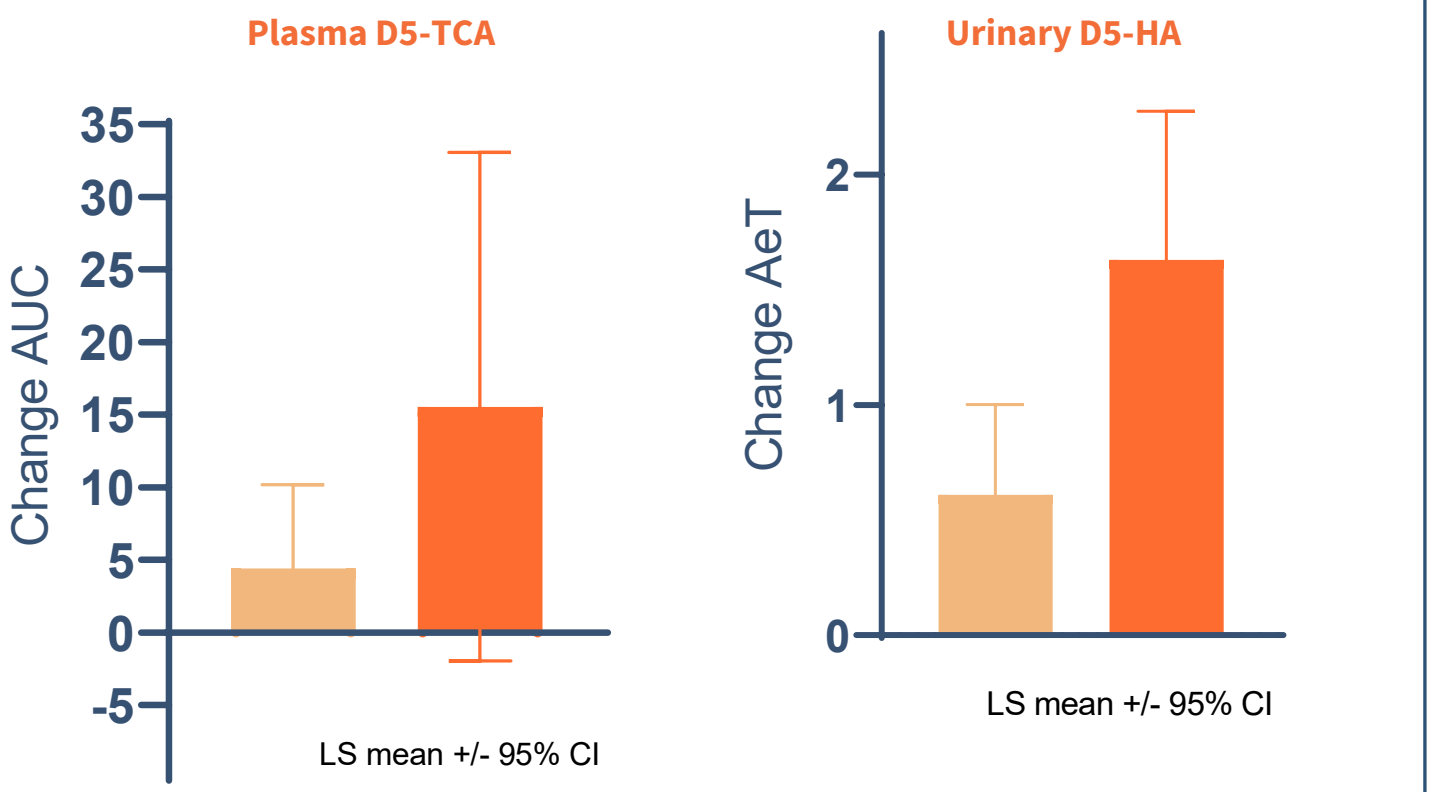
Inhibition of Phe Absorption



* Primary Endpoint

Data are LS mean +/- 95% CI; SYNB1618 n=10; SYNB1934 n=5

Biomarkers of Strain Activity in GI Tract



TCA = trans-cinnamic acid; HA = hippuric acid, AUC=area under the curve, AeT=total amount excreted

SYNB1618 SYNB1934

Safety & Tolerability – Summary of Top-Line Findings

Favorable profile, consistent with program findings to date

Adverse events were all **mild to moderate**, predominantly GI in nature, and similar across SYNB1618 and SYNB1934.

- 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.

There were **no serious adverse events** (SAEs)

Expected Phase 3 plans incorporate these learnings through (1) Starting with a low dose and (2) A slower ramp, with more time at each dose prior to advancing

Phase 2 Top-Line Results Support Potential to Transform PKU

The **vast majority of PKU patients need a medical treatment** to lower Phe, with 75% untreated

- **Clinically meaningful Phe reduction:** SYNB1934 “All-comers” mean Phe reduction of -34%
- **Strong response:** 60% achieved clinical response across both strains, with -42% Phe lowering among responders
- **Potential for adjunctive therapy:** Additional Phe-lowering when provided to Kuvan-treated patients confirms potential for adjunctive use
- **Favorable safety profile:** Across Phase 2, all adverse events were mild or moderate in severity and were predominantly gastrointestinal (GI) in nature. There were no serious adverse events (SAEs).

With >230 patients dosed across 4 clinical trials, PKU Program advances to Ph. 3 with SYNB1934

Potential as 1st orally-administered biotherapeutic for both monotherapy and adjunctive treatment in PKU

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Conclusions

Dr. Aoife Brennan
President & CEO

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PKU Program Has Clear Path to Phase 3

H2 2021

- ✓ **SYNB1618:** POC established
- ✓ **SYNB1934:** Greater potency confirmed in Phase 1
- ✓ **Committed to Ph. 3** based on strength of POC

H2 2022

- ✓ **SYNB1618:** Completed Ph. 2
- ✓ **SYNB1934:** Generated data in PKU patients
- ✓ **Monotherapy and adjunctive** potential positioning confirmed

H1 2023*

Ph. 3 initiation with SYNB1934

- Single, registrational study
- Primary endpoint: plasma Phe reduction (vs. placebo) in responder population[1]
- Low dose to start, slower ramp, and flexible titration to optimize tolerability

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1. 20% reduction vs. baseline in plasma Phe was used as the responder definition for Palynziq (pegvaliase injection), the most recent PKU approval by the EMA and FDA, per Palynziq USPI

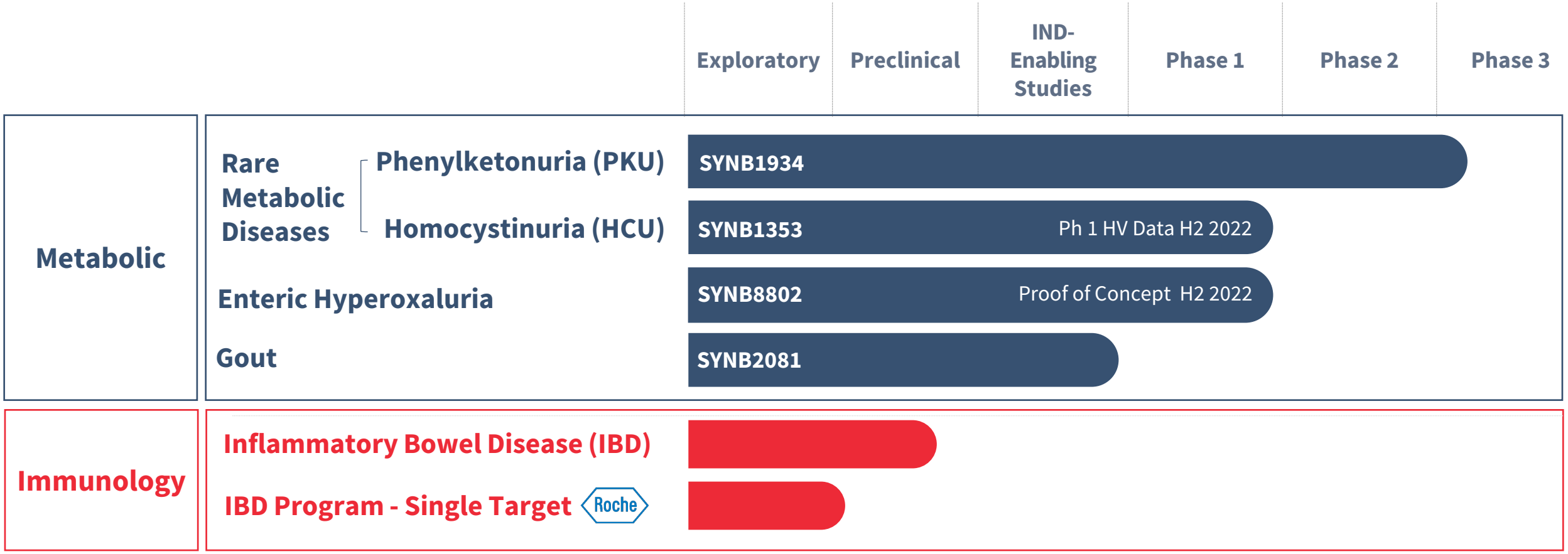
* Anticipated timing and study design

PKU remains a profound burden

Phase 2 top-line data confirm transformative potential of SYNB1934

Expect to initiate Phase 3 with SYNB1934 in H1 2023

Advancing a New Class of Biotherapeutics



HV = Healthy Volunteers

Available For Questions

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Thank You