Amanda, Lives with PKU

synlogic

Focused on potentially ***transformative biopharmaceuticals*** *for* ***rare metabolic diseases***

Sidoti Micro-Cap Virtual Conference
January 17, 2024

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.

SYBX: Clinically Validated, Phase 3 Program Underway

3 catalysts in next 18 months** present potential for **significant value creation

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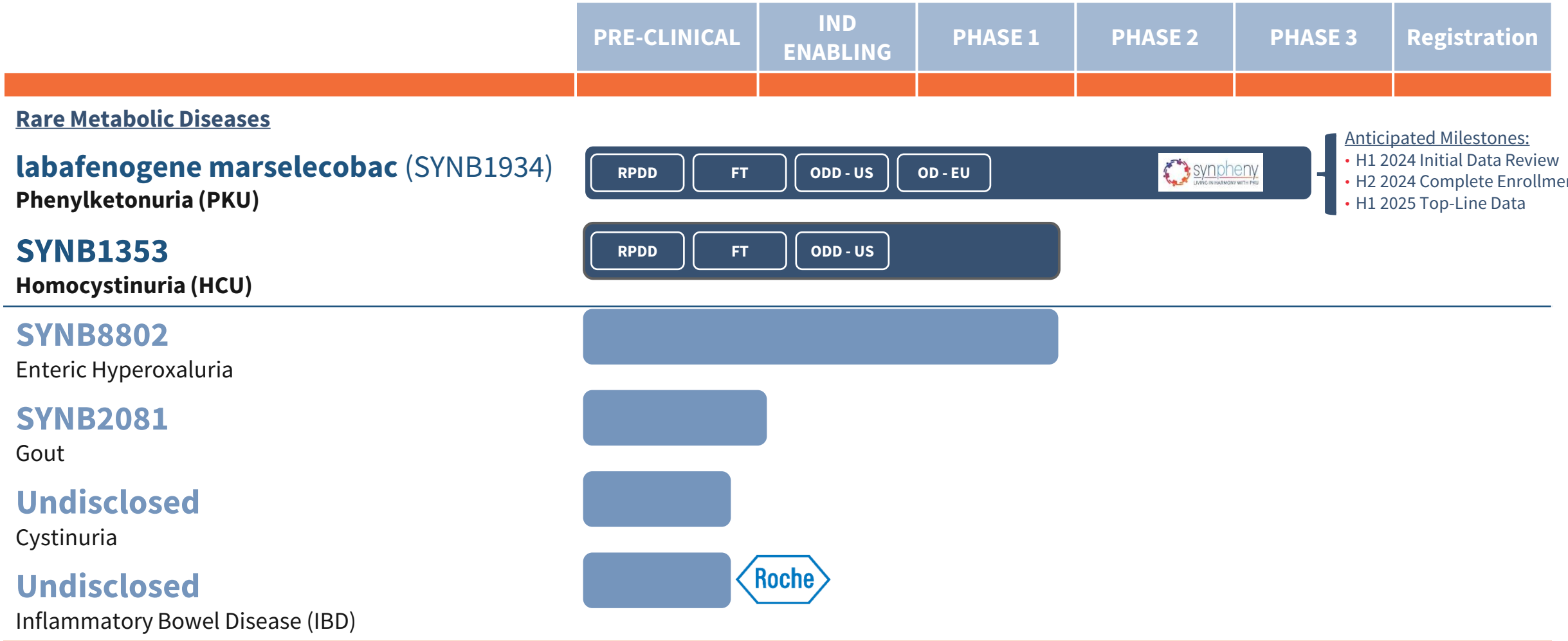
Deep clinical **pipeline of rare disease assets** produced by proprietary platform

3 Milestones for Phase 3 study within 18 months

- **H1 2024:** Review of initial data to expand patient eligibility to 12 to 17 year olds
- **H2 2024:** Full study enrollment
- **H1 2025:** Top-line data

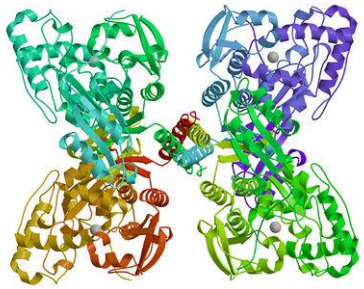
October $21mm **financing extends cash runway** into H1 2025

High-Potential Pipeline, Focused on Rare Metabolic Diseases



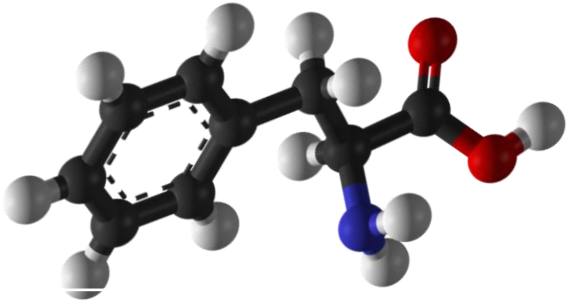
RPDD = Rare Pediatric Disease Designation granted by FDA | FT = Fast Track granted by FDA | ODD – US = Orphan Drug Designation granted by FDA | OD – EU = Orphan Designation granted by EMA

PKU: A Disease So Devastating it Transformed Medicine



Phenylalanine Hydroxylase (PAH)

Enzyme that is ***defective in PKU*** *due to genetic mutations, impairing metabolism of phenylalanine (Phe)*



Phenylalanine (Phe)

Amino acid found in ***all natural sources of protein****, can be* ***neurotoxic at high levels***

The Power of Phenylalanine (Phe) Control

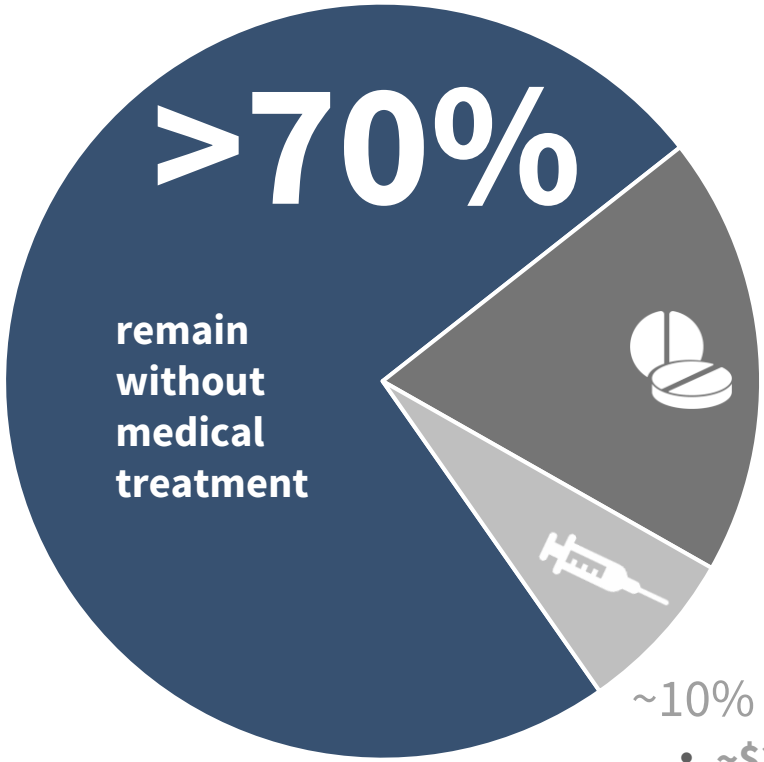
The importance of Phe control in PKU led to newborn screening

Today, the ***majority of adults remain with uncontrolled Phe*** *levels, due to difficulty of Phe-restrictive diets (e.g. 4-6 g protein/day)*

1. Wolf & Adams. Int J Neonatal Screen. 2020 Sep; 6(3): 59.

Majority of Patients Remain Without Medical Option

Estimated Share by Treatment Status of PKU Patients, US: (n=17,000)[1]



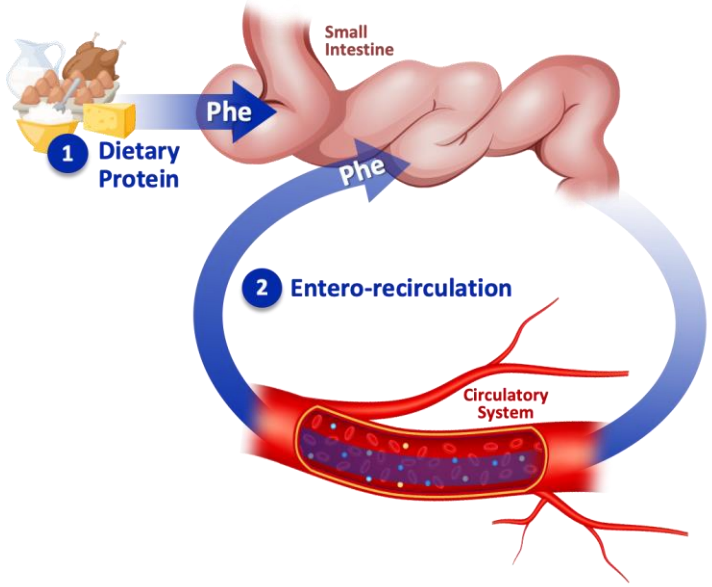
~20% Sapropterin (Kuvan)[2]
- ~$500 million annual revenue[2]
- **Adjunctive treatment opportunity**

~10% **Palynziq®** (pegvaliase injection)[2]
- **~$300 million annual revenue[2]**

1. National PKU Alliance (NPKUA) "About PKU" 2. Patient numbers, revenue for sapropterin, pegvaliase derived from BioMarin financials and disclosures; 3. Hillert et al. *American Journal of Human Genetics* (2020).
4. Synpheny-1 Phase 2 Study Results, Society for Inherited Metabolic Diseases 2023, Slide 10 & pivotal Synpheny-3 design, per clinicaltrials.gov 5. USPIs for Kuvan, Palynziq

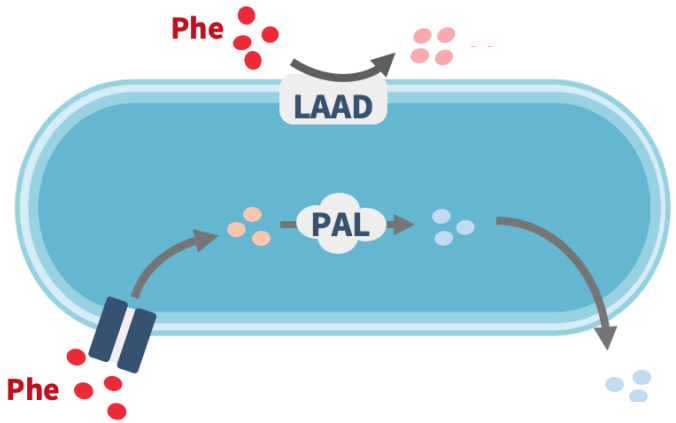
labafenogene marselecobac (SYNB1934): Targeted Design

Targeting Phe from Two Sources



labafenogene marselecobac (SYNB1934)

Engineered enzymes metabolize Phe, in a patient-friendly presentation



Engineered Enzymes Consume Phe[2]

Within a well-studied probiotic

Optimized Product Profile [3]

- ✓ **Convenient, orally-administered**
- ✓ **Efficacy**: ↓ Phe, ↑ Phe tolerance
- ✓ For **monotherapy and adjunctive** use
- ✓ **Non-systemic** absorption, **reversible**

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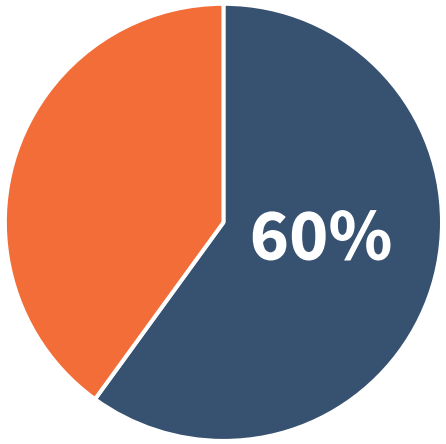
TCA = trans-cinnamic acid; HA = hippuric acid,- both are metabolic byproducts specific to Phe metabolism by PAL

1. Chang et al. *Artif. Cells Blood Substit. Immobil. Biotechnol.* 23, 1–21 (1991). 2. Adolfsen, et al. *Nature Communications* (2021). 3. Per study design for Synpheny-3, as described on clinicaltrials.gov

Phase 2 Confirmed Proof of Concept in PKU Patients

Results for SYNB1934 from Synpheny-1, Phase 2 published in *Nature Metabolism*

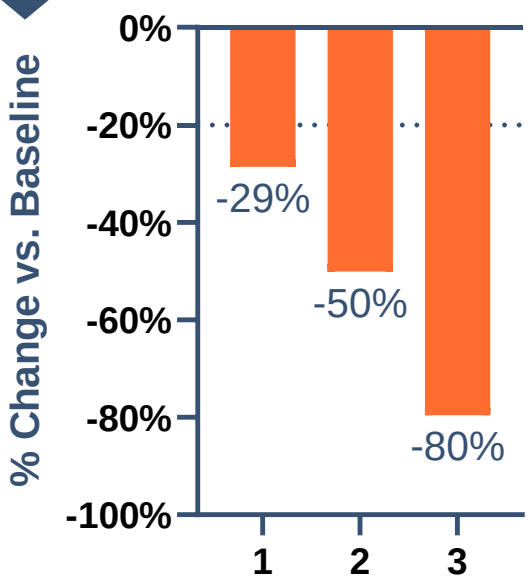
Response Rate



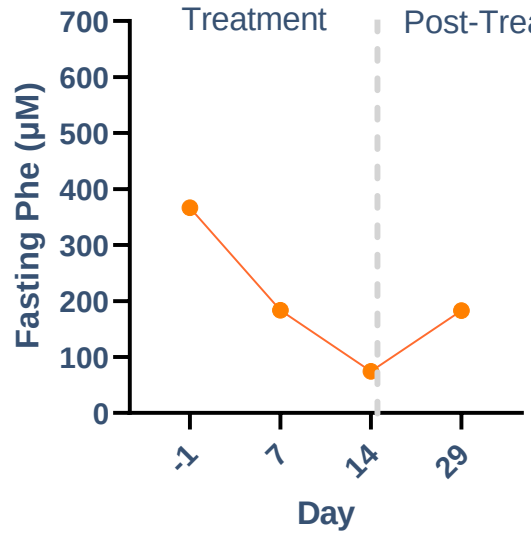
60% (3/5) achieved at least 20% Phe lowering*

Phe Reduction*

-53% Mean



Combination with Kuvan® (sapropterin)



-80%

*In responders based on pre-determined responder definition of -20% change in Phe vs. baseline

Source: Vockley, et al *Nature Metabolism.* 2023

Safety & Tolerability Across Program: Consistent, Favorable

- ✓ **No serious adverse events** (SAEs) across the PKU program to date (n=240 through Ph 2))[1]

- ✓ All adverse events have been **mild to moderate**, **transient, reversible**, predominantly GI in nature, and consistent with those described in the dosing of probiotics
  - In the Phase 2 study arm with SYNB1934 (n=9), 2 patients discontinued treatment due to GI-related AEs[2, 3]

- ✓ Synpheny-3, the **pivotal study for SYNB1934 is designed to optimize patient experience** via:
  1. Optimized palatability
  2. A low starting dose
  3. An extended dose escalation period, of 9-15 weeks for each patient

1. 240 = Phase 1 with SYNB1618 (liquid formulation): 56 HVs and 14 PKU pts + Phase 1 with SYNB1618 (solid form): 88 HVs; + Phase 1 with SYNB1934: 62 HVs + Synpheny-2 Phase 2: 20 PKU patients
2. Study data was presented at Society for Inherited Metabolic Diseases, 2023
3. Vockley, et al *Nature Metabolism.* 2023

Patient Experience Expected to Benefit from Multiple Measures Introduced in Phase 3

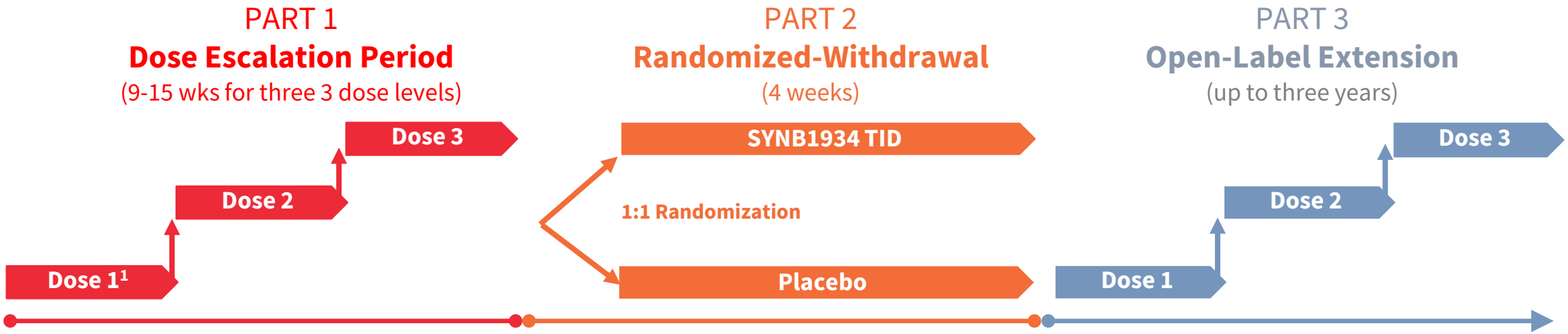
H1 2024 milestone: Independent data monitoring committee (DMC) review of safety, tolerability from Part 1

May expand population: Potential to result in expanding study population to include 12-17 year-olds

Opportunity to assess benefit from new dose regimen, and other measures

	Synpheny-1 (Phase 2)	Synpheny-3 (Phase 3)
Formulation	Peppermint oil, bicarb, sucralose	**Optimized for palatability**: reduced bicarb, peach flavor
Tolerability	Forced dose ramp	**Flexible** individualized titration
	One week to escalated 3 dose levels	**9-15 weeks for dose ramp** (3-5 weeks at each dose level)
	No formal guidance for anti-nausea meds	**Advise to use meds prophylactically** if mild symptoms

Synpheny-3: Global, Pivotal, Phase 3 Study of labafenogene marselecobac (SYNB1934)



Primary endpoint:
Phe vs. placebo (change v baseline)

Results **based on responders** subset[3] (from Part 1)

Synpheny-3 Expected Milestones

- **H1 2024:** Independent DMC review of initial data for potential expansion to 12-17 year olds
- **H2 2024:** Full enrollment completed
- **H1 2025:** Top-line data

1. For ~150 patients ages 18 years and older with Phe >360 µM; 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 $1x10^{12}$; each begins with once/daily and increases frequency to 3x/day, with meals
3. 20% reduction vs. baseline in plasma Phe during Part 1 is responder definition

With Recent Financing, Operations Funded into H1 2025

Balance Sheet (unaudited)	30 September 2023	31 December 2022
Cash, Cash Equivalents, and Marketable Securities	$33.4M	$77.6M

(in thousands, except share and per share data)

Financial Performance (unaudited)	Three Months Ended September 30		Nine Months Ended September 30	
	2023	2022	2023	2022
Revenue	$ 393	$ 678	$ 602	$ 1,074
R&D Expenses	$ 9,616	$ 14,610	$ 33,831	$ 38,405
G&A Expenses	$ 3,400	$ 4,402	$ 11,291	$ 12,785
Net loss	$ (12,078)	$ (17,912)	$ (42,748)	$ (49,451)
Net loss per share - basic and diluted*	$ (2.57)	$ (3.73)	$ (9.17)	$ (10.29)
*Weighted Average Shares Outstanding**	4.7M	4.8M	4.7M	4.8M

$21.0 million financing in October and $2.5 million earned from Roche collaboration in November add to September 30, 2023 cash balance, extending cash runway into H1 2025

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

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Thank You

