Synlogic Provides Corporate Update and Outlook for 2024

January 4, 2024

- Data review from pivotal Synpheny-3 study in PKU expected in H1 2024, with potential to expand study population to patients aged 12-17 years of age -

- Top-line, Phase 3 data in PKU expected in H1 2025 -

CAMBRIDGE, Mass., Jan. 04, 2024 (GLOBE NEWSWIRE) -- Synlogic, Inc. (Nasdaq: SYBX), a clinical-stage biotechnology company advancing novel, oral, non-systemically absorbed biotherapeutics to transform the care of serious diseases, today summarized accomplishments for 2023 and anticipated key milestones for 2024.

"We are pleased with the important corporate progress we achieved in 2023 - highlighted by the initiation of our global pivotal Synpheny-3 study evaluating our potentially transformative treatment option for PKU," said Aoife Brennan, M.B. Ch.B., Synlogic President and Chief Executive Officer. "We expect 2024 to be similarly momentous, with the achievement of key milestones, including the upcoming Data Monitoring Committee review of initial study data. This review could enable the expansion of the study into younger PKU patients, specifically the adolescents who remain in tremendous need of new medical options to control Phe levels."

2023 Program & Corporate Milestones

Labafenogene marselecobac (SYNB1934), a potential treatment for PKU:

- Initiation of Synpheny-3, a global, pivotal Phase 3 study evaluating the efficacy and safety of labafenogene marselecobac (SYNB1934) as a potential treatment for PKU
- Positive results from Synpheny-1 Phase 2 study in patients with PKU presented at the Society for Inherited Metabolic Disorders (SIMD) 44th Annual Meeting, and at the 37th E.S. PKU Conference 2023, and published in *Nature Metabolism*
- Received multiple significant regulatory designations:
  - Rare Pediatric Disease Designation (RPDD) by the U.S. Food and Drug Administration (FDA)
  - Fast Track Designation from the FDA
  - Orphan drug designation (ODD) from the FDA
  - Positive Opinion on Orphan Designation from the European Medicines Agency (EMA)
  - Selection by the International Nonproprietary Names (INN) Expert Committee of the World Health Organization (WHO-INN) of "labafenogene marselecobac" for the nonproprietary name of SYNB1934
- Granted U.S. Patent (U.S. Pat. No. 11,766,463), specifically covering the mutant PAL enzyme expressed by labafenogene marselecobac and extending patent term exclusivity to 2041

SYNB1353, a potential treatment for homocystinuria (HCU):

- Proof of mechanism results from a Phase 1 clinical study demonstrating that consuming methionine (Met), a precursor to homocysteine, in the GI tract lowers plasma Met levels in a dietary model of HCU, and preclinical evidence that showed blunting plasma levels of labeled total homocysteine (tHCy) in a mouse model, were both presented at the Society for Inherited Metabolic Disorders (SIMD) 44th Annual Meeting
- Data showing a further increase in methionine degradation activity by SYNB1353 due to fermentation process improvements were presented at the International Conference on Microbiome Engineering 2023

Corporate

- Closed $21.0 million underwritten public offering, extending the Company's cash runway into the first half of 2025
- Earned $2.5 million milestone payment for the achievement of prespecified success criteria under the research collaboration agreement with Roche for the discovery of a novel Synthetic Biotic for the treatment of inflammatory bowel disease (IBD)
- Entered into an approximately $1 million subcontract under an Air Force Research Laboratory (AFRL) prime contract to develop a manufacturing process to support development of a potential live probiotic product

Anticipated Milestones

- **H1 2024:** Data monitoring committee (DMC) review of initial subset of Synpheny-3 data, potentially supporting study expansion to include 12- to 17 year-olds
- **H2 2024:** Completion of Synpheny-3 full study enrollment

- **H1 2025:** Top-line data for Synpheny-3

Synpheny-3 Trial Design

Synpheny-3 is a randomized, placebo-controlled, global, pivotal Phase 3 clinical trial designed to evaluate the efficacy and safety of SYNB1934 as a treatment for PKU. The trial's primary endpoint is the change in phenylalanine (Phe) levels from baseline for SYNB1934 compared to placebo, in a subset of patients who are considered responders (defined as >20% reduction in Phe).

The trial consists of three parts: Part 1, an open-label dose escalation period, during which patients titrate through up to three dose levels, with at least three weeks per dose; Part 2, a four-week randomized withdrawal period used for the pivotal analysis; and Part 3, an open-label extension which includes an evaluation of Phe tolerance, or dietary liberalization.

The trial expects to enroll approximately 150 patients with plasma Phe levels at baseline of >360 µM. Study participants may follow their usual diet while participating in the trial and may be taking sapropterin.

Synpheny-3 currently includes patients ages 18 years and older. A DMC review is planned to evaluate an initial subset of data from Part 1 to assess lowering the age of enrollment to 12 years of age. The focus of this review is expected to be safety, tolerability and experience across the range of doses during Part 1 for 20-30 patients.

More information on the Synpheny-3 study is available at www.clinicaltrials.gov, identifier NCT05764239 and also by visiting pkuresearchstudy.com.

About Synlogic

Synlogic advances novel, oral, non-systemically absorbed biotherapeutics to transform the care of serious diseases in need of new treatment options. The Company's late-stage clinical pipeline is focused on rare metabolic diseases, led by labafenogene marselecobac (SYNB1934), currently being studied as a potential treatment for phenylketonuria (PKU) in Synpheny-3, a global, pivotal Phase 3 study. Additional product candidates address diseases including homocystinuria (HCU), enteric hyperoxaluria, gout, and cystinuria. This pipeline is fueled by the Synthetic Biotic platform, which applies precision genetic engineering to well-characterized probiotics. This enables Synlogic to create GI-restricted, oral medicines designed to consume or modify disease-specific metabolites – an approach well suited for PKU and HCU, both inborn errors of metabolism, as well as other disorders in which the disease–specific metabolites transit through the GI tract, providing validated targets for these Synthetic Biotics. Research activities include a partnership with Roche focused on inflammatory bowel disease (IBD), and a collaboration with Ginkgo Bioworks in synthetic biology, which has contributed to two pipeline programs to date. For more information, please visit https://www.synlogictx.com or follow us on Twitter, LinkedIn, Facebook, Instagram, and YouTube.

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," "focused on," "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 labafenogene marselecobac (previously known as 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.

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