Synlogic

DESIGNED FOR LIFE

SYNB1618
Phase 1/2a Clinical Trial
Topline Data from PKU Patient Cohorts
July 15th, 2019
SYNB1618 Potential to Address Unmet Need Across Patient Groups

- **Initial Focus**
  - **Uncontrolled Adults**
  - **Partially Controlled Adults** (Adults on Kuvan and/or low-Phe Diet)
  - **Pediatric Patients** (controlled / partially controlled) (Pediatric patients on Kuvan and / or low-Phe diet)

- **Phe** concentration levels:
  - **360 μmol /L**
  - **Natural protein**
SYNB1618 Phase 1/2a Study Design

Part 1: Healthy Volunteers
- Single Ascending Dose (SAD)
  - 6 cohorts, N = 24
- Multiple Ascending Dose (MAD)
  - TID x 7 days
  - 4 cohorts, N = 32

Part 2: PKU Patients
- Single Dose (SD)
  - N = 4
- Multiple Dose (MD)
  - TID x 7 days
  - N = 10

PKU Clinical Trial Design
- Randomized, double-blind placebo-controlled study at multiple sites in the US
- Primary outcome: establish safety/tolerability following single and multiple doses in HV and PKU patients
- Secondary outcome: SYNB1618 kinetics in feces
- Exploratory: change from baseline in plasma and urinary biomarkers of Phe metabolism

Presented in September 2018

New Data
SYNB1618 Activity Biomarkers Indicate Significant Phe Consumption
Similar activity in HVs and PKU Patients

Urine HA and D5 HA

Dose of Cells (CFU)

HA=hippurate, D5-HA= labeled HA, CFB=change from baseline, CFP=change from placebo HV=healthy volunteer PKU=phenylketonuria patient

NS not significant
**p<0.01
***p<0.001
****p<0.0001
p values based on comparison to respective placebo group
Modeling: Potential For Phe Reduction in PKU Patients

Ranges represent
- Low: PAL mechanism only (conservative)
- High: PAL + LAAD activity (estimates maximum with both pathways)
Upcoming Milestones and Path Forward

Established new solid formulation and manufacturing process

Completed EPO1 interactions with FDA to align on program plans (clinical, manufacturing, toxicology)

Completed Phase 1/2a study (healthy volunteers and PKU patients)

Initiate bridging study with solid formulation in Q3 2019

Phase 2 study in PKU patients to assess Phe lowering to start in 1H 2020