**Introduction**

- Oxalate is an end-product of human metabolism and is present in a variety of common foods, including green vegetables, nuts, grains, fruits and chocolate.
- Enteric hyperoxaluria (EH) is a metabolic disorder commonly observed in patients with underlying GI disease related to fat malabsorption, such as IBD, or surgical interventions such as Roux-en-Y.
- Chronic EH is associated with recurrent kidney stones, nephrocalcinosis, and chronic kidney disease, which can lead to kidney failure and the need for kidney transplantation.
- Untreated EH can progress to systemic oxalosis, a condition in which oxalate accumulates in joints, bones, eyes, heart, and other organs.
- SYNB8802 is an engineered probiotic, derived from *Escherichia coli* Nissle and designed to degrade oxalate.

**Synopsis**

**Dose**

SYNB8802 is an engineered bacterial therapeutic capable of consuming oxalate in the gut and lowering urinary oxalate and may be as a potential treatment for EH.

- Oral administration of SYNB8802 leads to significantly decreased UOx excretion in non-human primates.
- Mathematical modeling using in vitro and in vivo preclinical data predicts clinically meaningful lowering of UOx excretion in EH patients.
- SYNB8802, was safe and well-tolerated in a Ph I study in healthy volunteers (HV).
- SYNB8802 led to a consistent and significant dose-related reduction of UOx and fecal oxalate in HVs on a high oxalate diet, confirming strain ability to access dietary oxalate from within the gut.

**Results**

**SYNB8802 lowers UOx in vivo in preclinical models of acute Hyperoxaluria**

- SYNB8802 lowered UOx in healthy volunteers (HV).
- SYNB8802 was safe and well-tolerated in healthy volunteers.

**Conclusion**

Dose-related reduction of urinary and fecal oxalate at well-tolerated doses

- SYNB8802 showed dose-related reduction of UOx and was generally well-tolerated in healthy volunteers. No serious or systemic adverse events were observed. Most frequent AEs mild or moderate, transient, and GI-related. A dose-ramp improved tolerability.