Introduction to Beam's Clinical Development Program for GSD1a

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Our vision is to provide life-long cures for individuals suffering from serious diseases

To achieve our vision, we have created a strong values-driven organization focused on people, advancing cutting-edge science, and developing a new class of precision genetic medicines

Two locations

Research Triangle, NC

Cambridge, MA

Base editing has potential to treat disease

Hematology, genetic disease, and more in the future

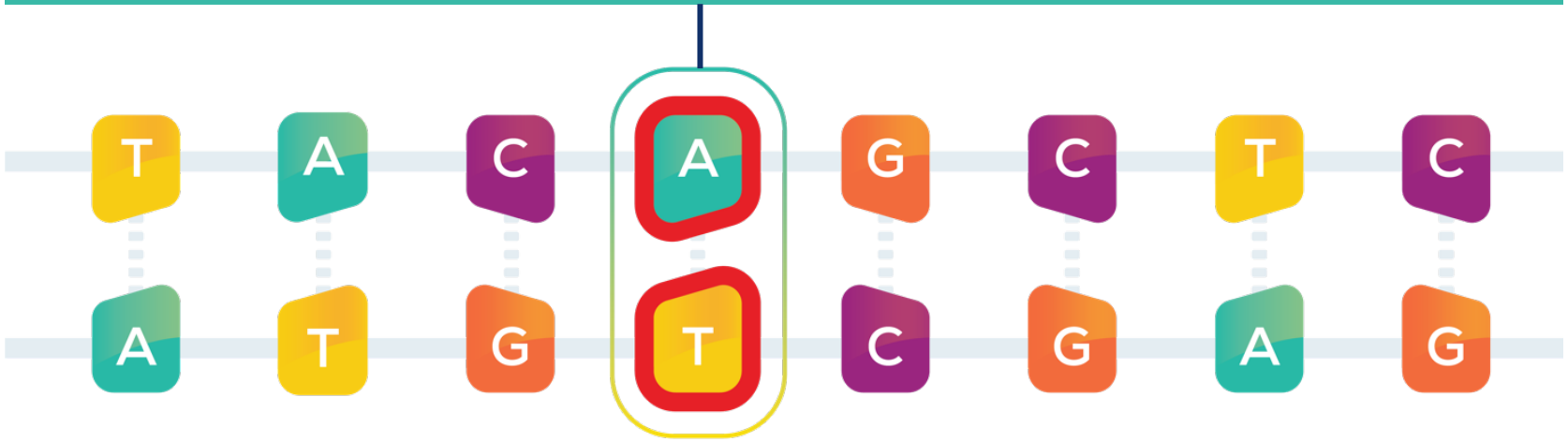
Three programs in clinic

- Glycogen Storage Disease Type Ia
- Alpha-1
- Sickle cell disease

MA, Massachusetts; NC, North Carolina

In our genetic code, spelling matters, and a single base change can result in disease

A single spelling error in the code—known as a **point mutation**—can lead to serious illness just as a single misspelled letter in a word can lead to an entirely different meaning: list or lost, batter or better.

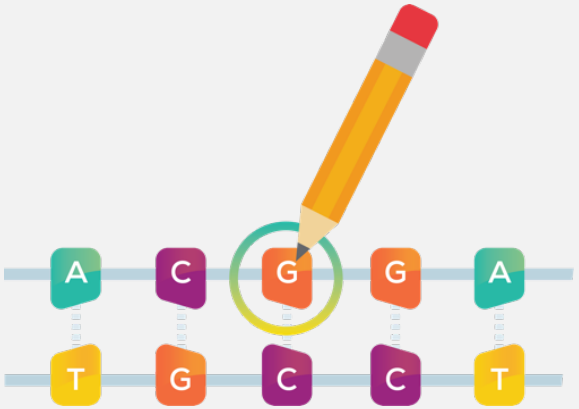


Sickle cell disease, glycogen storage disease type Ia, and alpha-1 antitrypsin deficiency are all serious diseases with high unmet needs that are caused by point mutations.

Base editing provides a unique opportunity to address serious disease with precision, working like a “pencil and eraser” on the genome

Many existing gene editing approaches are like ‘scissors’ that cut the genome. Base editors are like ‘pencils’ that enable erasing and rewriting one letter of the genome at a time.”

Giuseppe Ciaramella
President



an **adenine (A)** to **guanine (G)**

or

cytosine (C) to **thymine (T)**

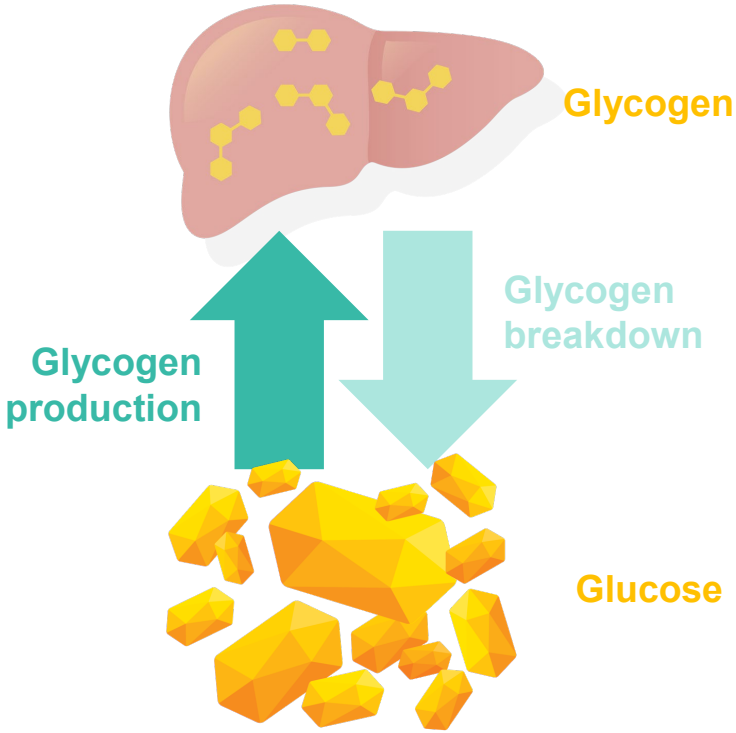
Glycogen storage disease type Ia (GSD1a) can be caused by a single point mutation

- A DNA change (or variant) called R83C* is one of the more common mutations in the *G6PC* gene encoding glucose-6-phosphatase (G6Pase), leading to a severe deficiency of this enzyme
- Animal studies suggest that only ~11% enzyme activity is sufficient for restoring metabolic profile

*c.247C>T (p.Arg83Cys)

Normal G6Pase

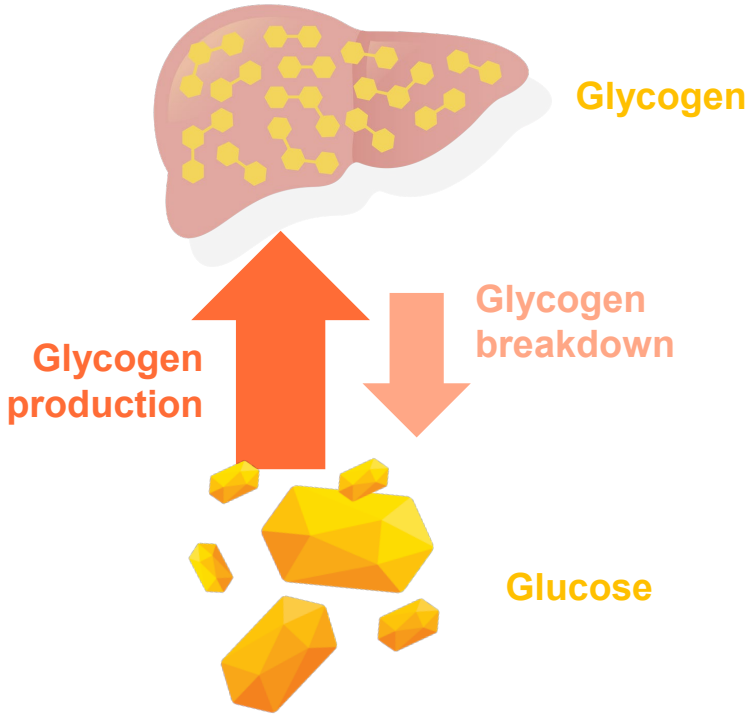
Normal levels of glycogen in liver



Healthy

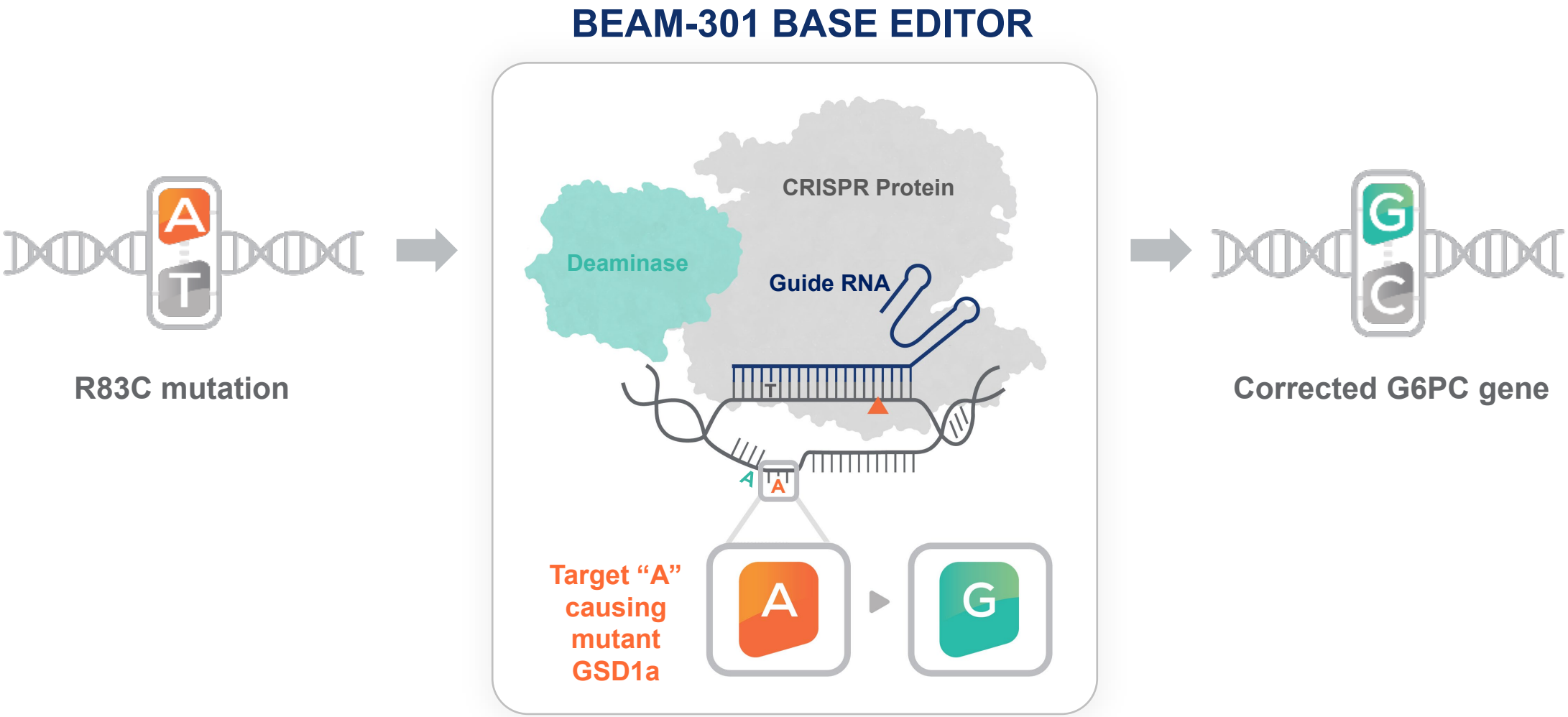
Nonfunctional G6Pase

Glycogen storage increased in liver and other organs



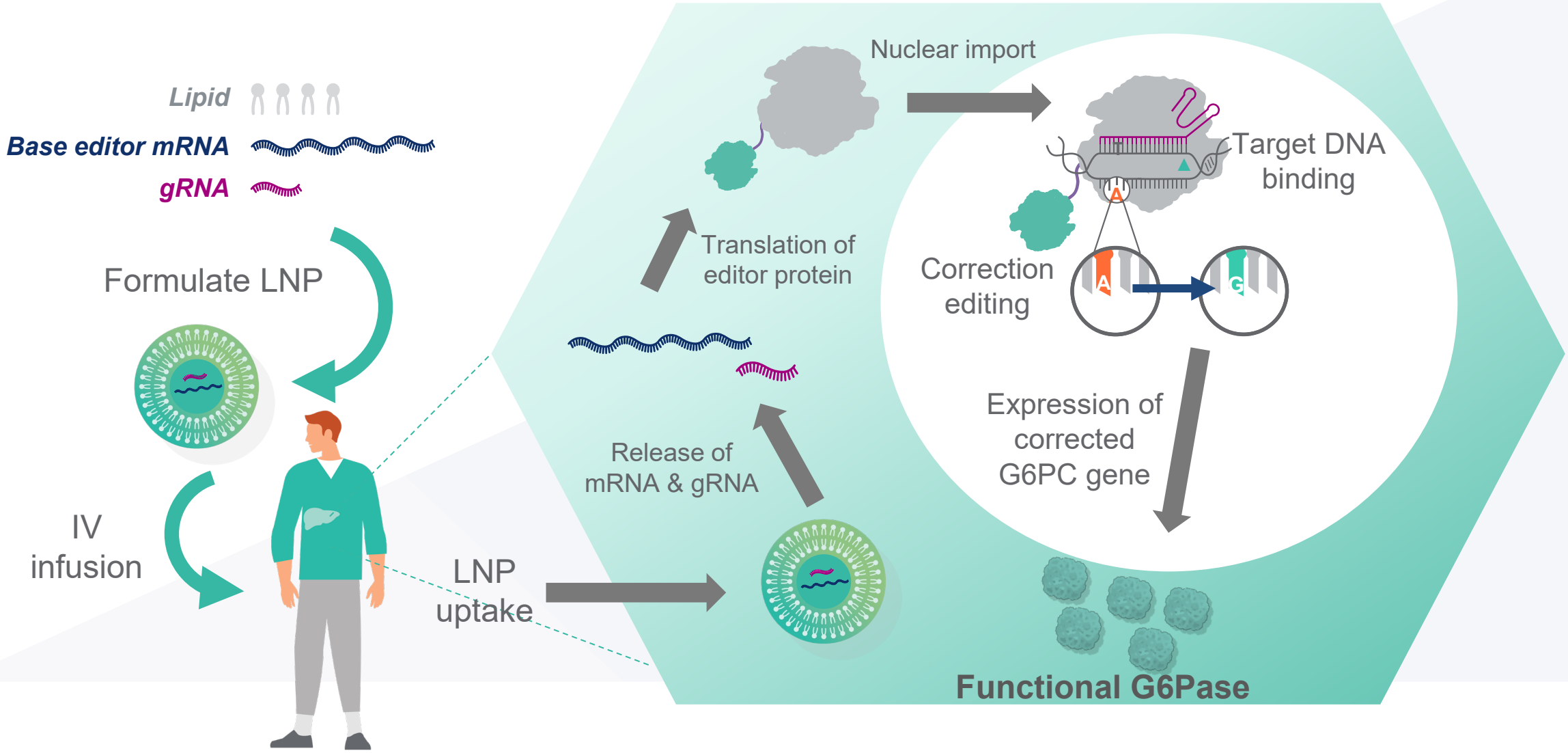
GSD1a

BEAM-301* is an investigational one-time therapy that uses base editing to correct the R83C mutation causing GSD1a



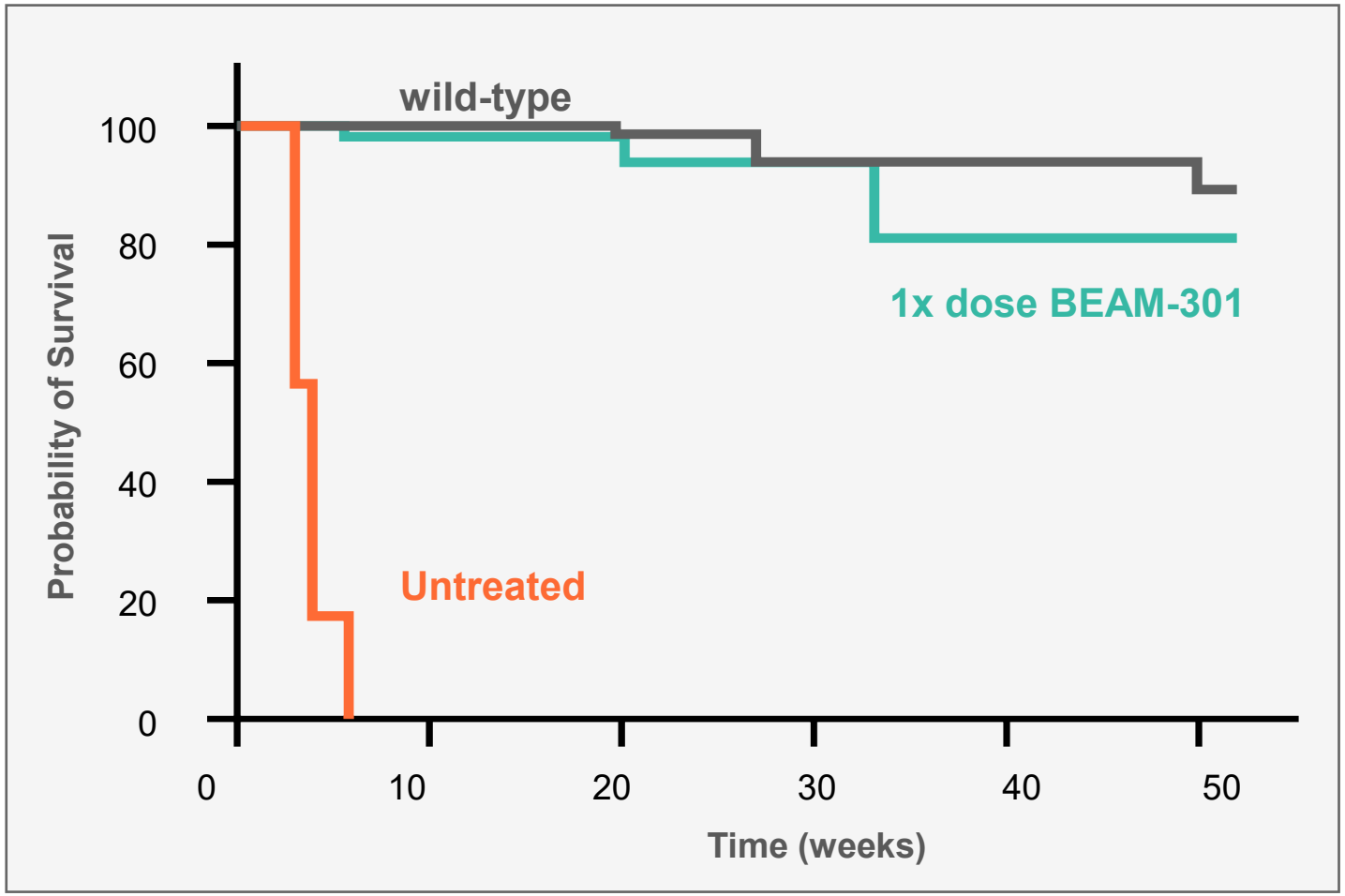
*The safety and efficacy of BEAM-301 has not been established. Clinical trials are ongoing.

BEAM-301 utilizes non-viral, lipid nanoparticle (LNP) delivery to target the liver and correct the A base mutation back to G



Animal Data

BEAM-301: Treatment with a single dose significantly improved long-term survival in GSD1a mouse model

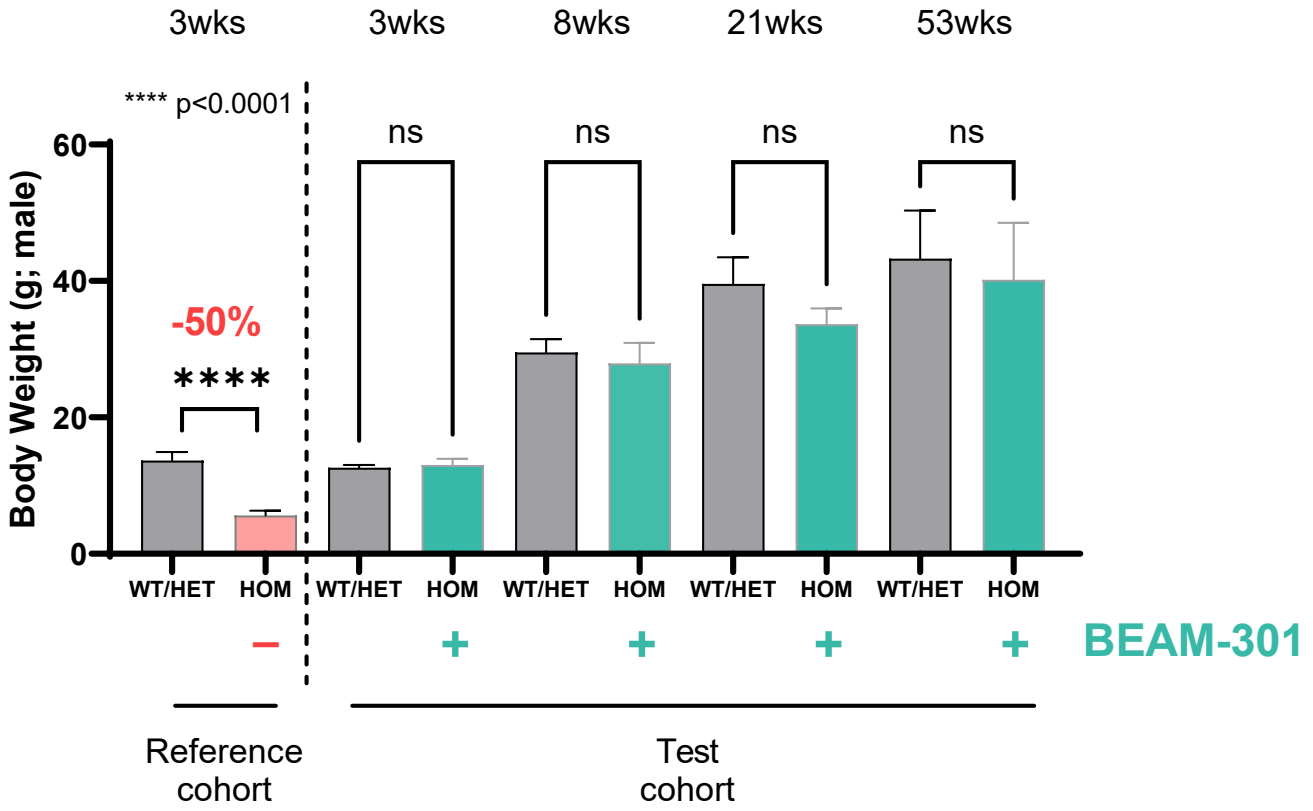


- Preclinical studies of BEAM-301 demonstrated a single dose **significantly improved long-term survival out to a year** in GSD1a mice with R83C
- Untreated GSD1a R83C mice die within weeks of birth

ESGCT, 2023

Normal body weight was maintained over a year after a single dose of BEAM-301

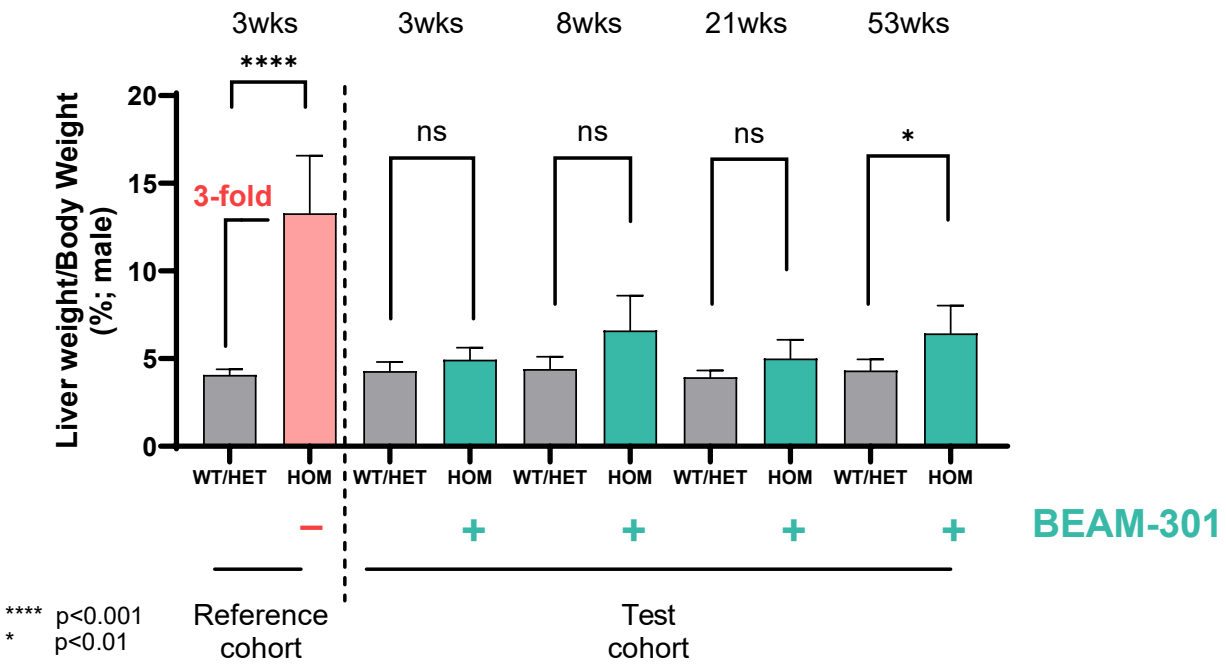
Reference cohorts: Untreated

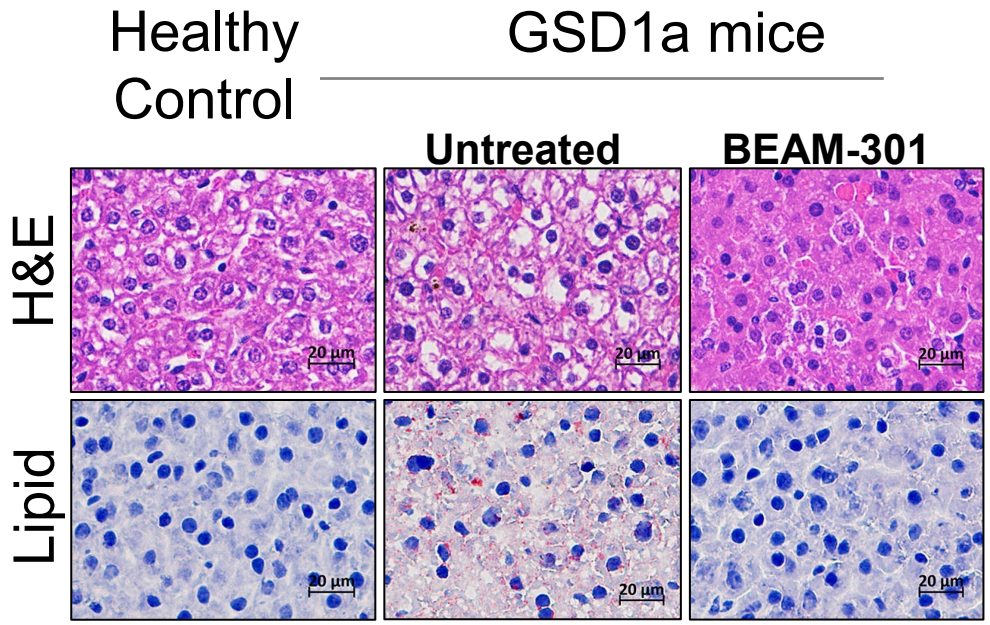


- Untreated GSD1a mice exhibited significant growth impairment relative to control littermates
- Single-dose of BEAM-301 **recovered normal gain in body weight** in the short-term and to at least one year

ESGCT, 2023

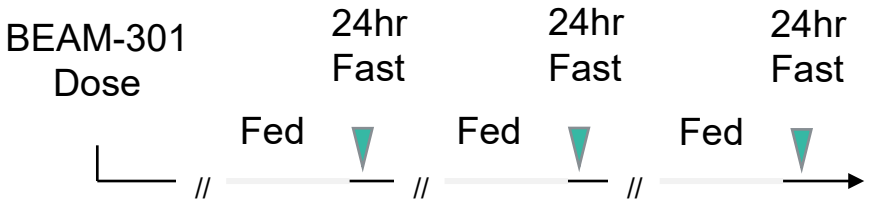
Normal liver size was maintained over a year after a single dose of BEAM-301

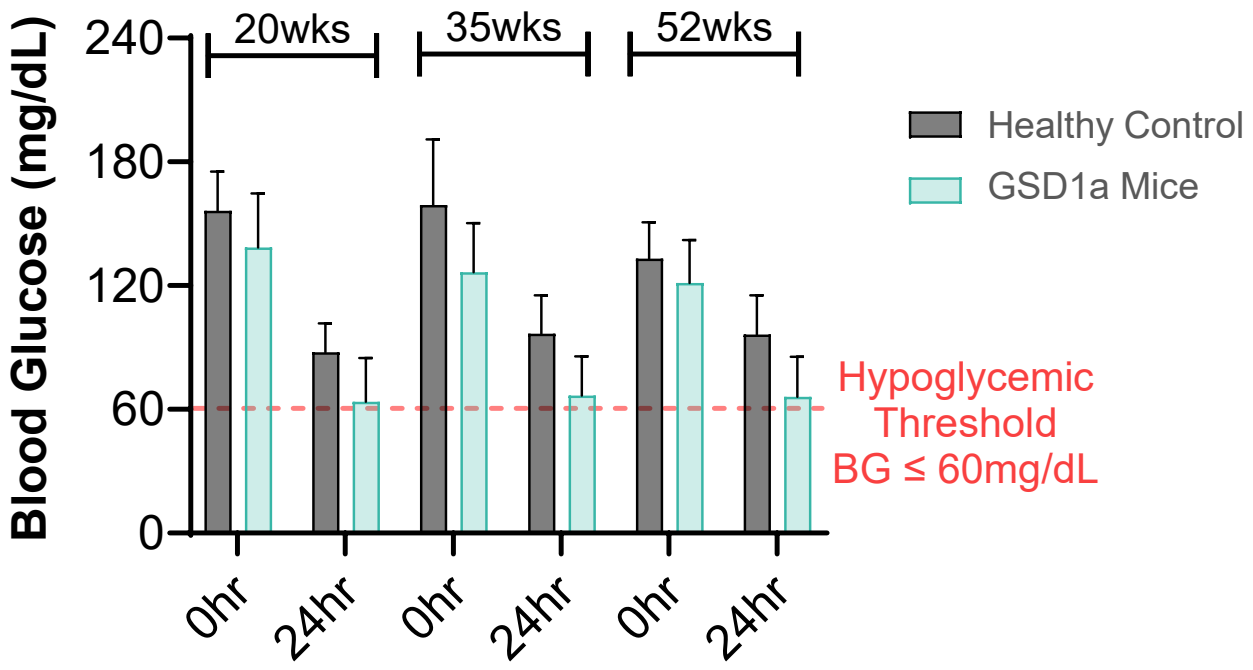




- Liver size was 3-fold larger than normal in untreated GSD1a mice (elevated glycogen, lipids) Glucose-supplemented untreated GSD1a mice exhibited enlarged livers, hepatocyte size, and elevated lipids
- BEAM-301 treatment was associated with **reduction in liver size and lipid deposition**

GSD1a mice survived multiple 24hr fasting challenges through 1yr post BEAM-301 dose

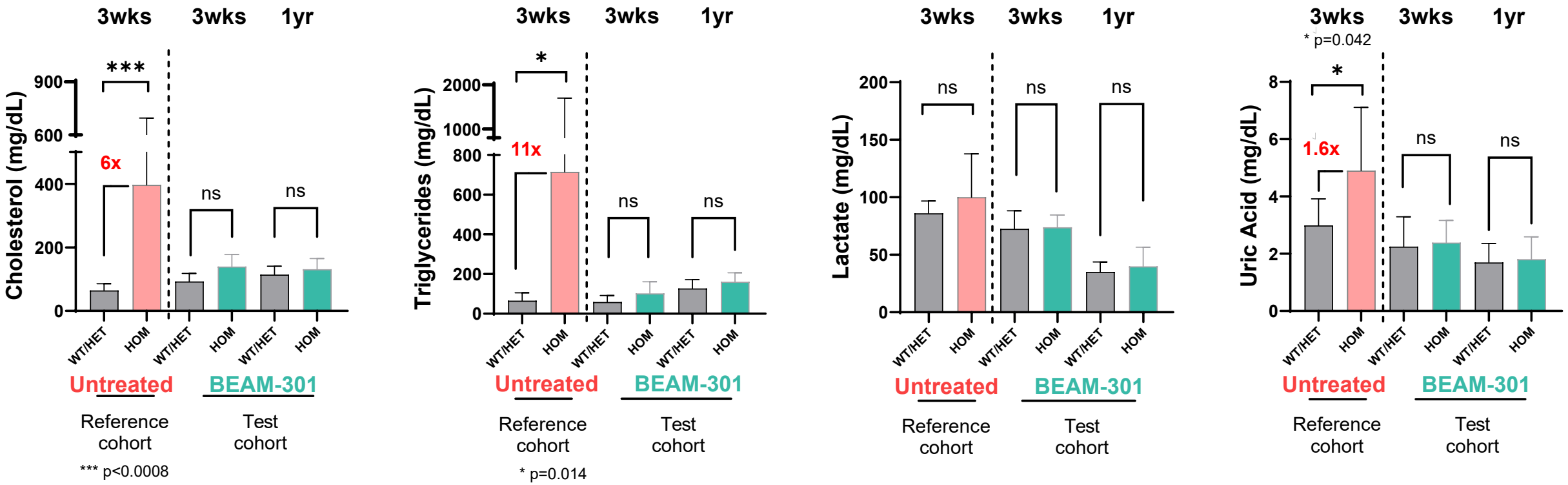




- Blood glucose levels were **maintained above hypoglycemic threshold** for multiple fasting challenges
- Untreated GSD1a mice did not survive beyond 6wks and exhibited hypoglycemic seizures. Therefore, they were not able to survive a fasting challenge

ESGCT, 2023

Normal serum metabolites were maintained at 1 year post BEAM-301

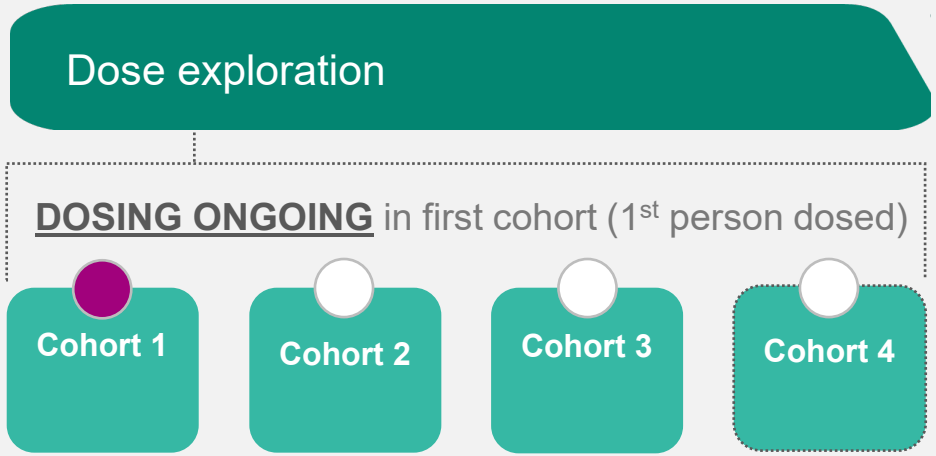


- Untreated GSD1a mice exhibited predominantly elevated serum metabolites at 3wks of age
- GSD1a mice administered BEAM-301 exhibited **normal secondary serum metabolites, maintained through at least 1yr** (including mice with single-digit base-editing rates)

BEAM-301 Study

Beam THERAPEUTICS

The Phase 1/2 study aims to evaluate the safety and efficacy of BEAM-301 in people with GSD1a and at least one R83C variant



KEY OBJECTIVES & ENDPOINTS

- Safety and efficacy (time to hypoglycemia, starch supplementation dose, serum glucose and other metabolic parameters) of BEAM-301 to confirm optimal biologic dose

KEY INCLUSION/ EXCLUSION CRITERIA*

Inclusion

- Age 18 or older years of age
- Diagnosis of GSDIa (1 or 2 copies of the R83C variant)
- History of at least 1 episode of hypoglycemia <60 mg/dL within the 2 years prior

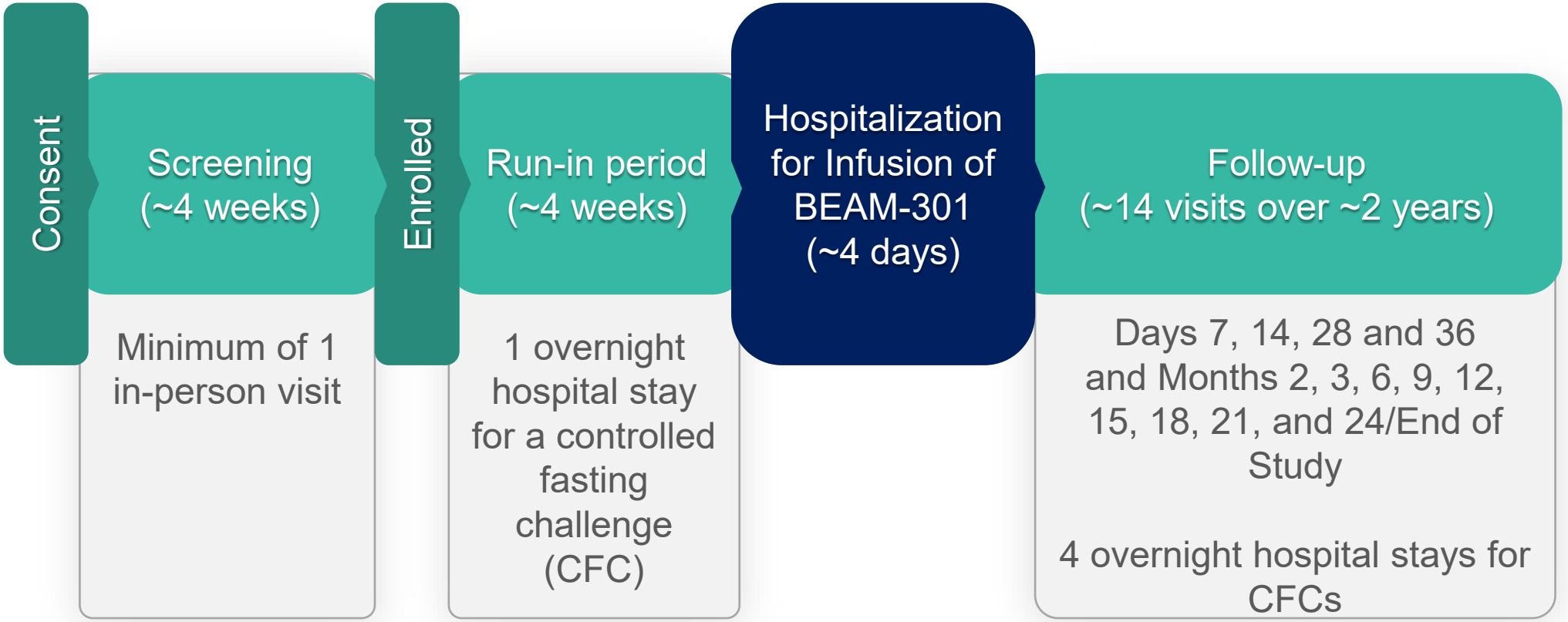
Exclusion

- Presence of liver adenoma >5 cm in size based on liver MRI or liver ultrasound performed at screening or within 6 months prior to screening
- Presence of liver adenoma >3 cm and ≤5 cm with a documented annual growth rate of ≥0.5 cm per year
- Previous treatment with any cell-, gene-, or viral vector-derived therapy

Clinicaltrials.gov (NCT06735755)

*list is not exhaustive

The Phase 1/2 study is open for enrollment with 3 sites in CT, TX, and CA



Email clinicalinfo@beamtx.com for additional information about the BEAM-301 study

We thank the patients, caregivers, researchers, advocacy groups, healthcare professionals, and study sites that have contributed to the BEAM-301 study

https://www.youtube.com/watch?v=SKFO86jthIY

https://www.youtube.com/watch?v=XFDVGkPqeEM