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A Randomized, Placebo-Controlled, Phase 2/3 Study of Glycolate Oxidase (GO) Inhibitor BBP-711 in Children and Adults with Primary Hyperoxaluria Type 1

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[1]Cantero Therapeutics, a BridgeBio company

european society for paediatric nephrology

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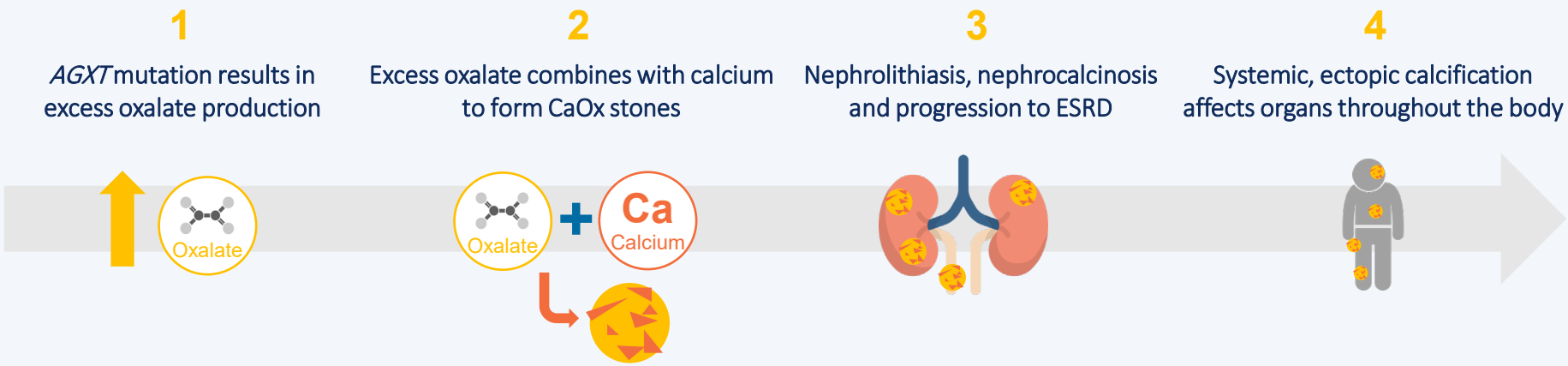
Disclosures

- Employee and stockholder of BridgeBio
- The investigational agent discussed in this presentation has not been approved by the EMA or any other regulatory authority

PH1 is a severe genetic disorder characterized by overproduction of oxalate

Primary hyperoxaluria type 1 (PH1) disease pathway

Onset often occurs in early childhood with delayed diagnosis



Genetic prevalence

5k

US & EU

BBP-711 therapeutic approach

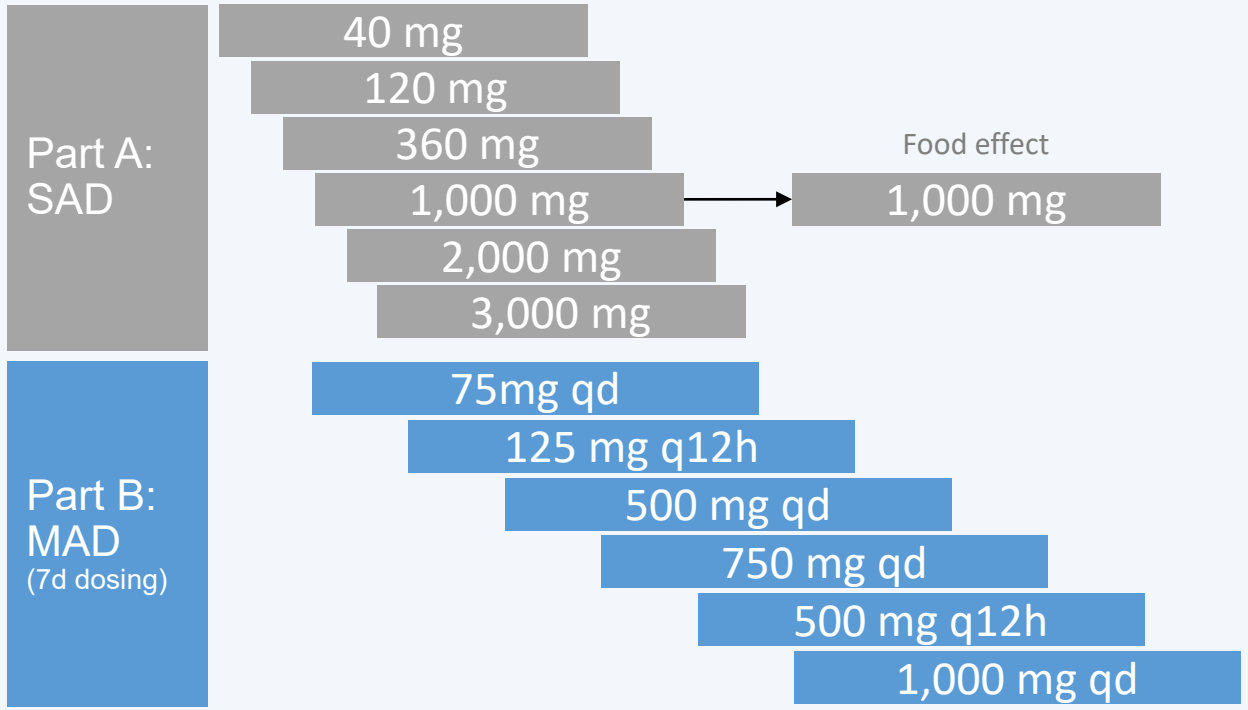
BBP-711 is an investigational oral small molecule **GO inhibitor** designed to reduce oxalate production

Source: Lieske et al., 2005; Cochat & Rumsby, 2013; Hopp et al., 2015

BBP-711 was tested in a Phase 1 study with 92 healthy volunteers

Randomized, double-blind, pbo-controlled SAD/MAD study in healthy adult volunteers

- **Healthy adult volunteers**
- **6 cohorts / part**
- **Up to 8 subjects per cohort**
- **3:1 randomization with 1:1 sentinel dosing**



Key endpoints

- **Safety and tolerability**
- **Pharmacokinetic profile**
- **Change in plasma glycolate**

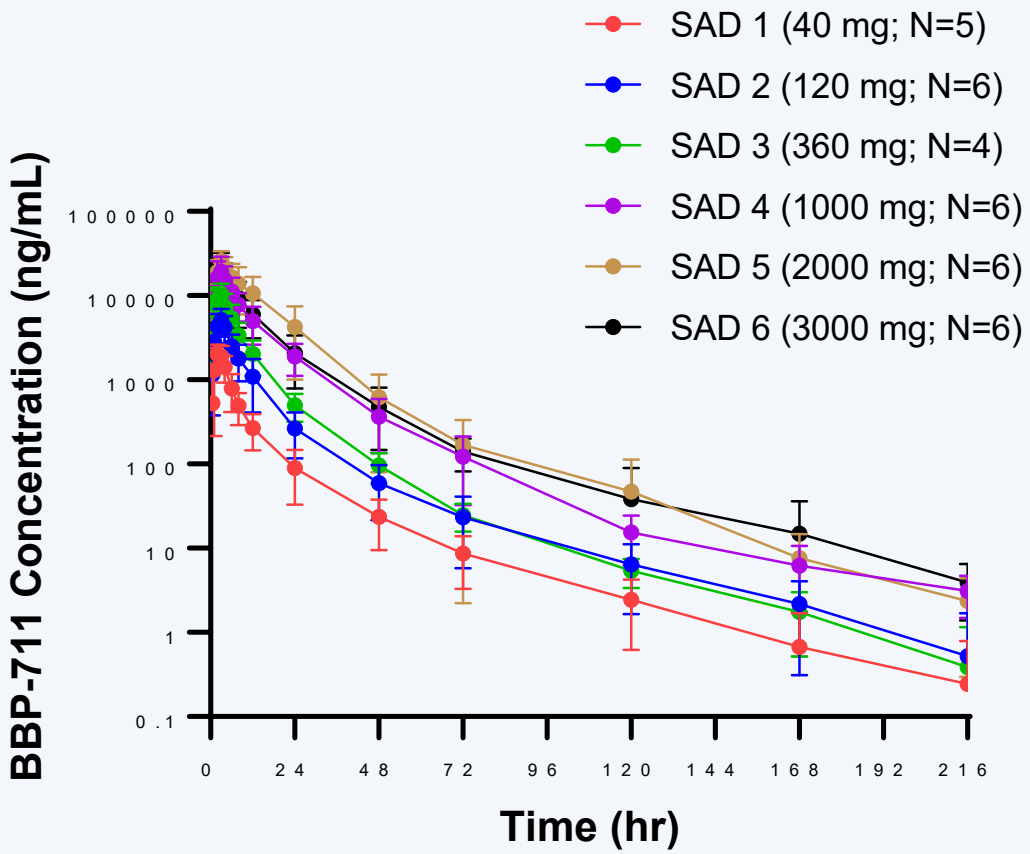
BBP-711 was well tolerated up to 3g as a single dose & 1g per day for 7 days

Safety summary in healthy volunteers – preliminary data

- No SAEs, All TEAEs were mild to moderate in severity
- Single doses (40 mg to 3000 mg) administered to 33 subjects
  - 5 of 33 (15%) experienced 15 TEAEs
- Multiple doses (75 mg to 1000 mg) administered to 35 subjects
  - 12 of 35 (34%) experienced 31 TEAEs
- TEAEs occurring more than once
  - Back pain (n=3; SAD 40 mg and 1000 mg and MAD 500 mg Q12H)
  - Headache (n=3; SAD 40 mg, MAD 75 mg, and 500 mg Q12H)
  - Muscle spasm (n=2; MAD 1000 mg)
  - Pain in extremity (n=2; SAD 40 mg and 1000 mg)
- No changes in clinical laboratory, ECG, or vital signs were observed

Pharmacokinetics of BBP-711 are supportive of once-daily dosing

Pharmacokinetic summary in healthy volunteers – preliminary data

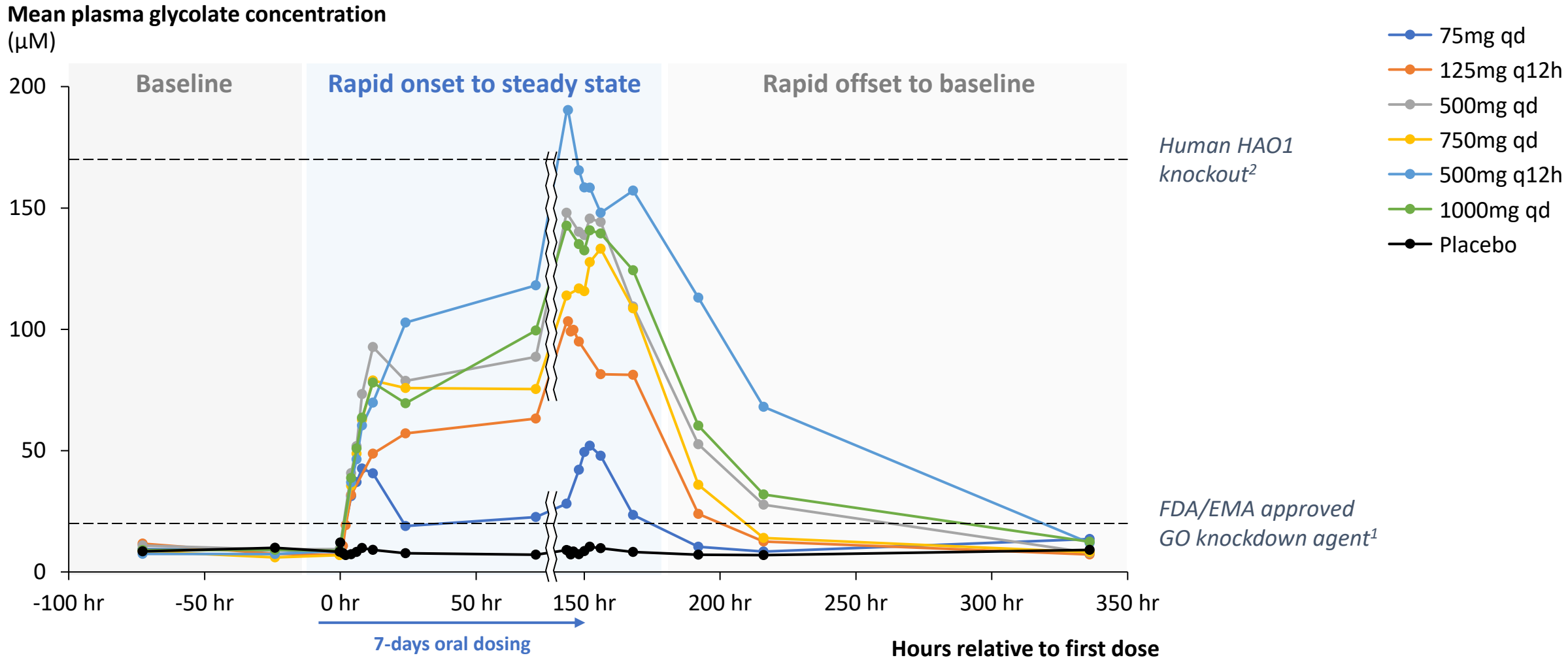


	$t_{1/2}$ (hr)	t_{max} (hr)	C_{max} (ng/mL)	AUC_{last} (hr*ng/mL)
SAD1	25 (48%)	1.9 (41%)	2,040 (27%)	13,900 (50%)
SAD2	22 (72%)	2.3 (21%)	5,020 (38%)	41,000 (45%)
SAD3	26 (39%)	2.3 (59%)	10,500 (27%)	83,200 (41%)
SAD4	28 (38%)	2.5 (47%)	17,200 (62%)	184,000 (51%)
SAD5	23 (29%)	2.9 (42%)	25,600 (29%)	312,000 (60%)
SAD6	34 (47%)	2.9 (22%)	22,500 (40%)	226,000 (39%)

Geometric mean (geometric CV%)
Accumulation ratios with QD MAD dosing (7-d dosing) were < 2

BBP-711 inhibited GO within 2 hours with increased plasma glycolate concentrations

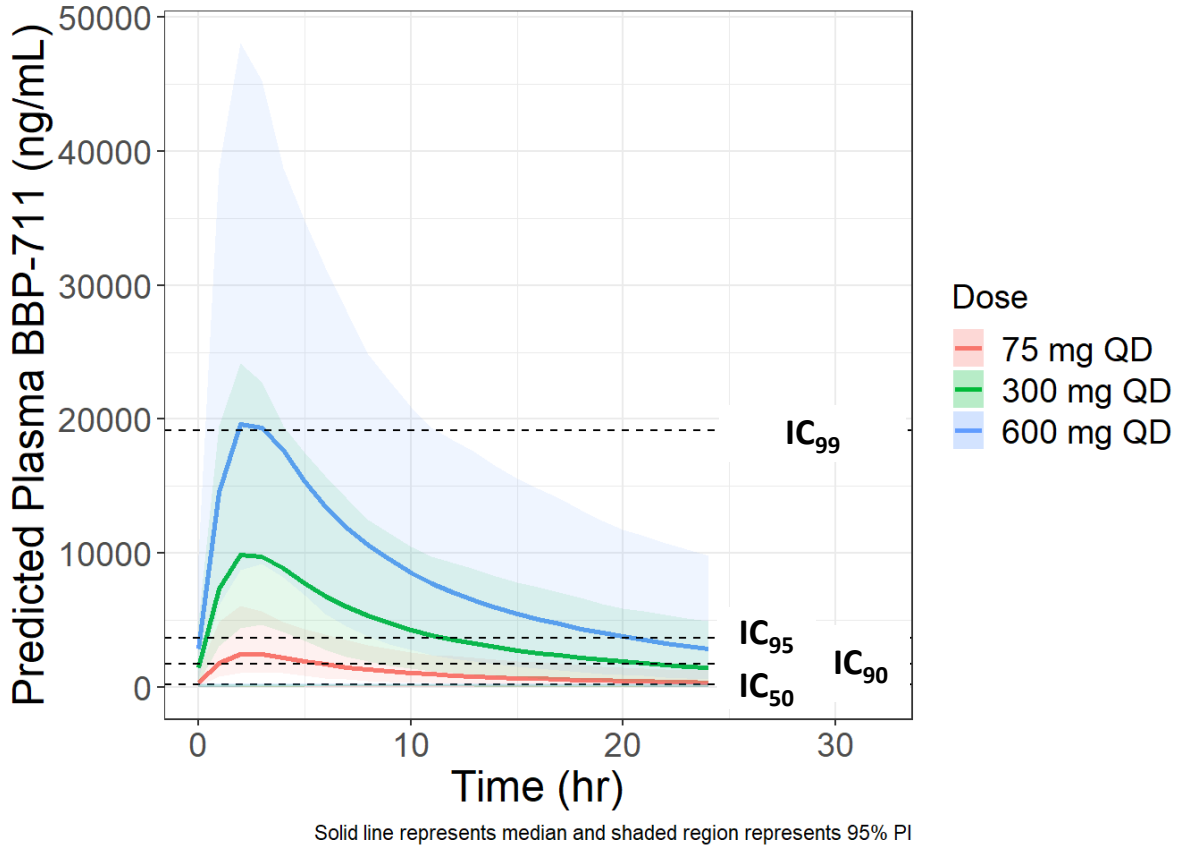
Pharmacodynamic summary in healthy volunteers – multiple dose cohorts – preliminary data

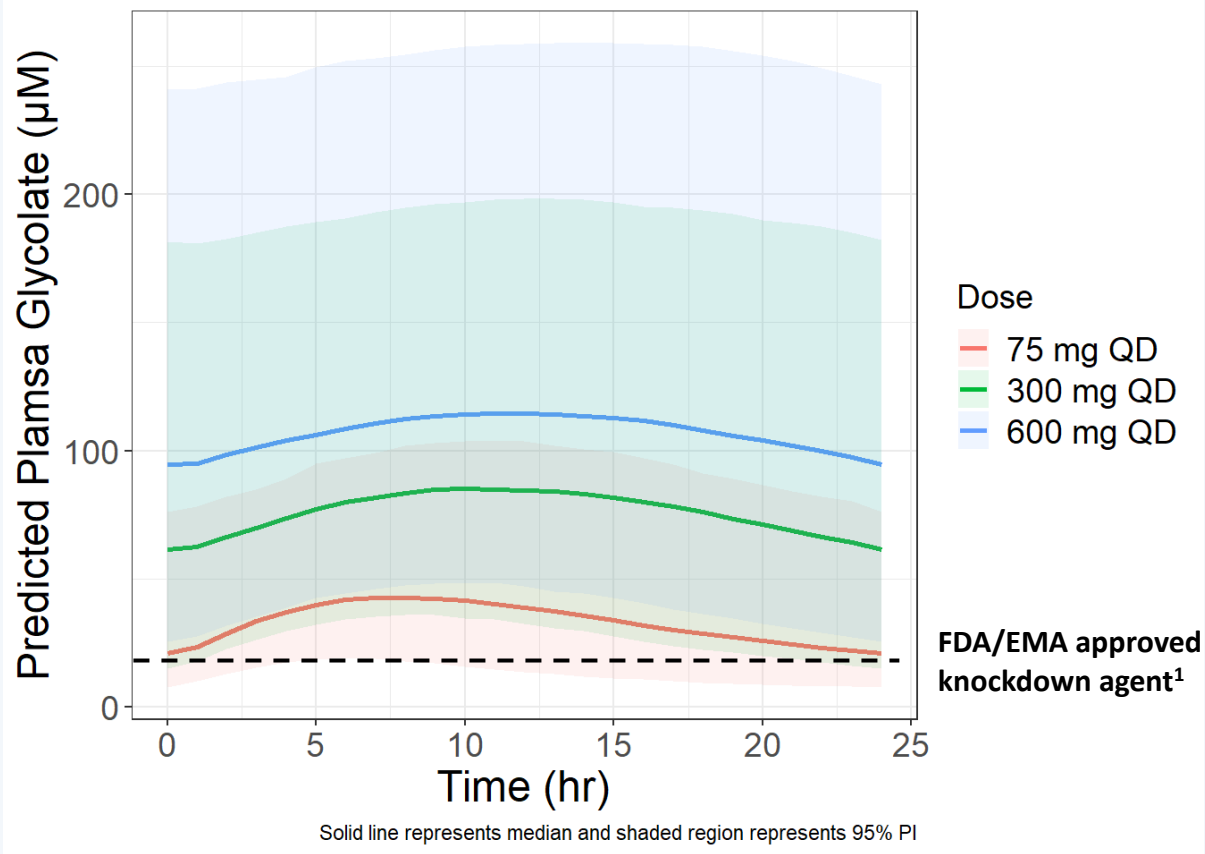


Note: *HAO1* = hydroxyacid oxidase 1, the gene encoding GO; Error bars not shown for visual clarity
Source: [1]Frishberg 2021 (3 mg/kg dose); [2]McGregor 2020

Doses selected for a Phase 2/3 study to target the IC_{50}, IC_{90}, and IC_{95}

PK-PD modeling for Phase 2/3 dose selection





Source: [1]Frishberg 2021 (3 mg/kg dose)

Global, operationally seamless Phase 2/3 study in PH1

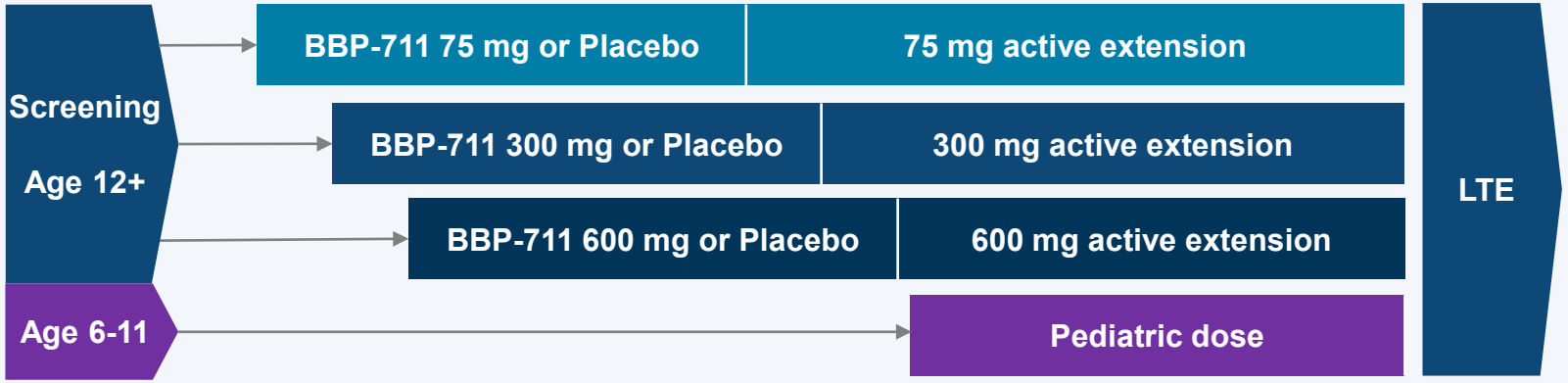
Study of Adult and Pediatric PH1 by REducing oxalate synthesis

SAPPH1RE

Part A: Dose-finding: Sequential Group, Randomized, Single-Blind, Placebo-controlled

Objective

To select a safe dose for Part B



Primary endpoint

AE/SAE incidence

Percent reduction from baseline in 24-hr uOxalate excretion

Note: Final study design pending alignment with regulatory agencies

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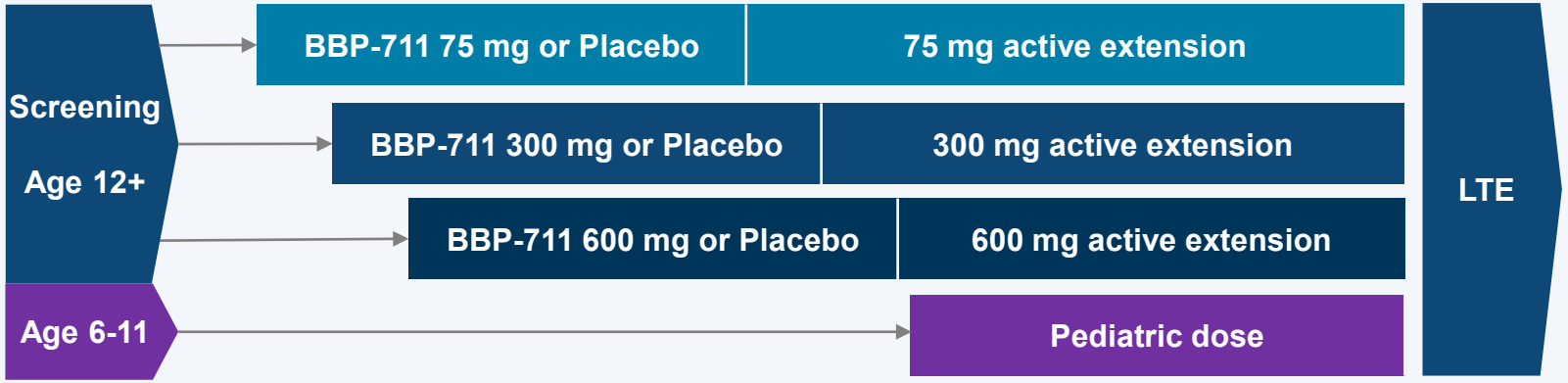


Primary endpoint

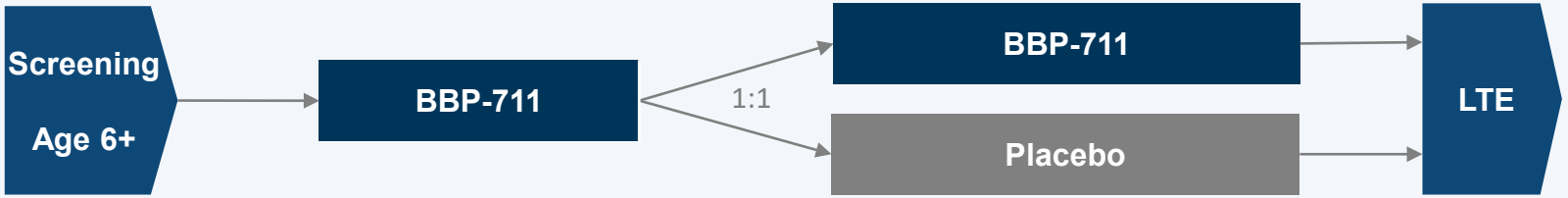
AE/SAE incidence

Percent reduction from baseline in 24-hr uOxalate excretion

Part B: Randomized Withdrawal: Double-Blind, Placebo-controlled

Objective

To establish the efficacy and safety of BBP-711 for the treatment of PH1



Primary endpoint

Proportion of participants with response in 24-hr uOxalate reduction*

Note: Final study design pending alignment with regulatory agencies

* Response defined as achieving normalization of urinary oxalate excretion or a ≥ 50% reduction in 24-hr uOxalate excretion from baseline

PH1 patients aged 6 and above with mild to moderate chronic kidney disease

SAPPH1RE

Key inclusion criteria

- ≥ 6 years old
- Confirmation of AGXT gene mutation
- uOxalate excretion > 0.7 mmol/1.73m^2 per 24hr
- eGFR ≥ 30 mL/min/1.73 m^2
- pOxalate < 20 µmol/L
- If taking pyridoxine, participant must be stable for 3 months prior to screening

Key exclusion criteria

- Participants who have received a liver transplant
- Participants who are receiving renal replacement therapy
- Participants treated with lumasiran within 9 months of screening
- Participants treated with experimental RNAi agents (e.g., nedosiran) within 9 months of screening
- Female participants that are pregnant, planning to be pregnant, or breastfeeding

Note: Final study design pending alignment with regulatory agencies

Additional studies are planned to address all patients with PH1

Cantero PH1 Clinical Program

Initiating 2H 2022		
SAPPH1RE	**SAPPH1RE-2**	**SAPPH1RE-3**
PH1 patients that are 6 years of age and older with intact renal function	**PH1 patients that are less than 6 years of age with intact renal function**	**PH1 patients with impaired renal function (eGFR < 30 mL/min/1.73m^2)**
Phase 2/3 Study	**Open label Phase 3**	**Open label Phase 3**

Summary

- **BBP-711, an oral small molecule glycolate oxidase inhibitor, is being developed for PH1 and other hyperoxaluria disorders**
  - BBP-711 has completed a Phase 1 study in healthy volunteers
  - BBP-711 was well tolerated up to evaluated single doses of 3g and multiple doses of 1g
  - PK data supports once daily administration of BBP-711 and rapid onset of action
  - PD data (plasma glycolate) suggests BBP-711 **rapidly** and **maximally** inhibits GO
  - PK-PD modeling suggests BBP-711 inhibits GO up to ~97% and doses of 75 mg, 300 mg, and 600 mg were chosen for evaluation in the Phase 2/3 study
- **A Phase 2/3 study in PH1 patients aged 6 and above with intact renal function is anticipated to start by end of year**
  - Global site selection in progress
  - Follow on Phase 3 studies are being planned to evaluate younger patients and those with impaired renal function