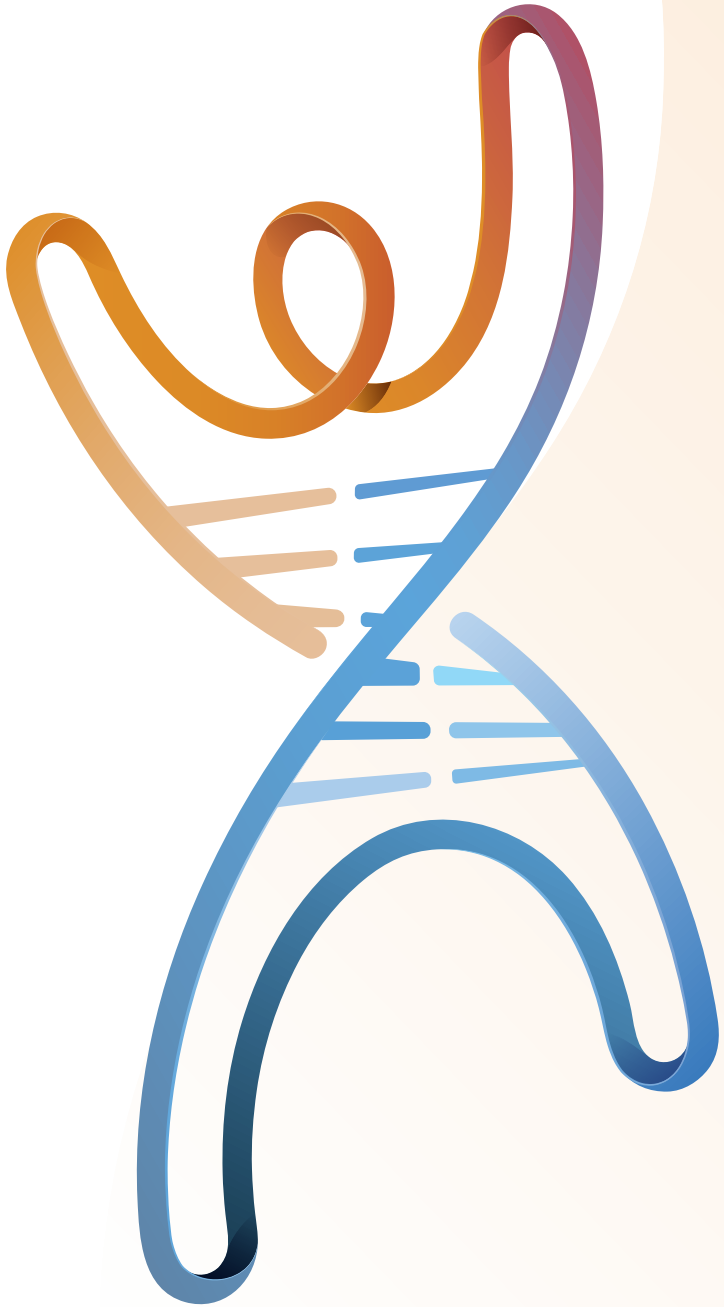
ABO-101, a novel gene editing therapy for primary hyperoxaluria type 1, is efficacious and well tolerated in NHPs and results in high fidelity editing in primary hepatocytes

Arbor Biotechnologies, Inc.

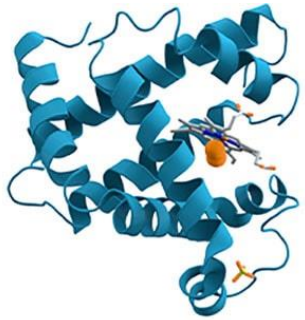


Presented at the American Society of Gene and Cell Therapy (ASGCT) annual meeting on May 13, 2025

Proprietary AI/ML-driven discovery engine has yielded an expansive portfolio of differentiated genomic editors

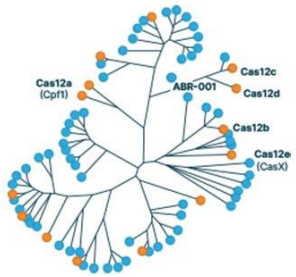
AI/ML discovery pipeline has generated a suite of proprietary nucleases enabling therapeutic application

Discover:
Source from Nature



>3 billion unique protein sequences

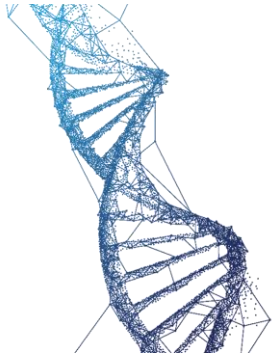
Search:
New Discoveries with Novel Properties



- Nuclease Family in Literature
- Arbor Discovered Nuclease Family

>10 proprietary gene editors
200 nuclease families
30,000 unique nucleases
>93% of human genome

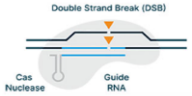
Optimize:
Screening and AI/ML



Up to 30x improvement in wt editing efficiency

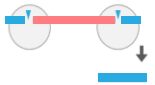
Apply:
Toolbox of Proprietary Editors

Knockdown+



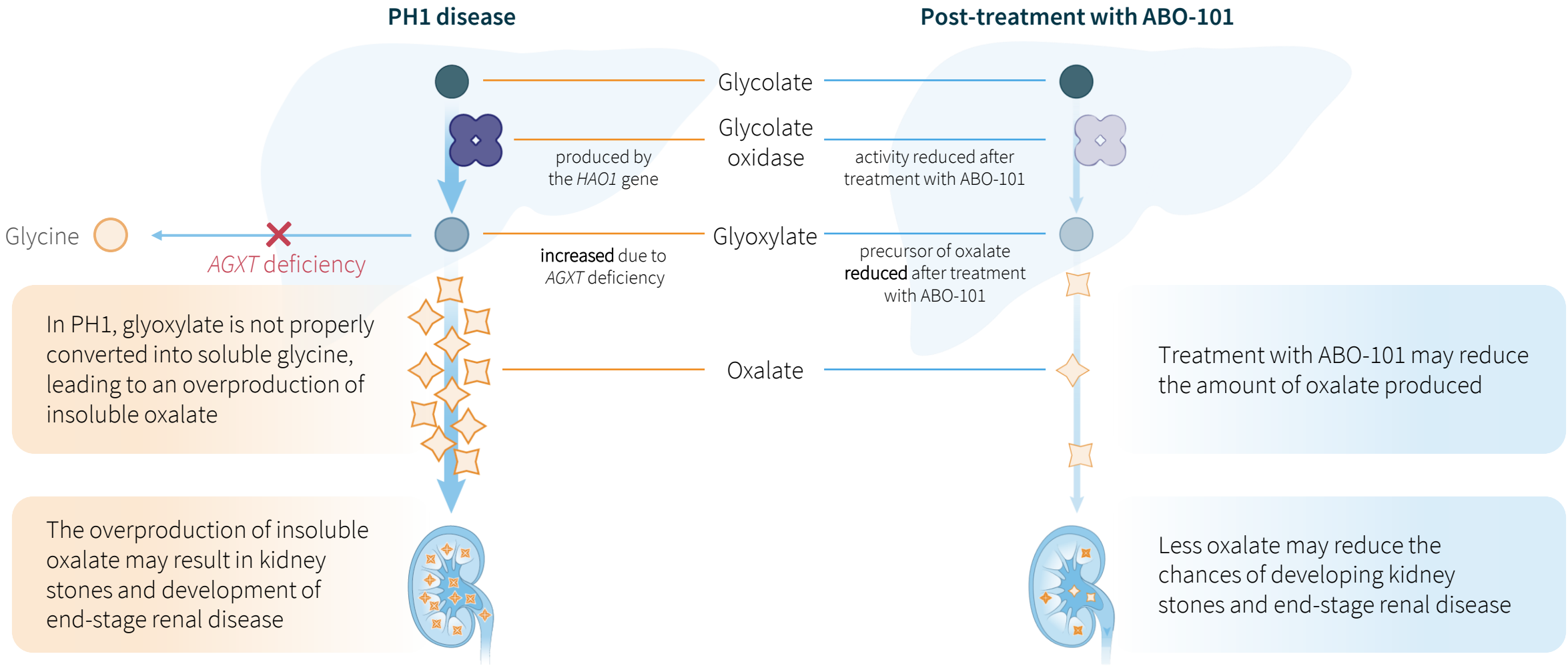
Precision (RT) Editing

Nuclease Excision



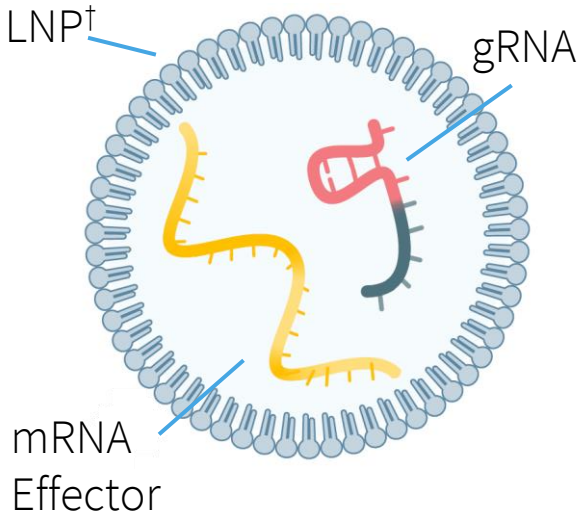
Whole Gene Insertion

ABO-101 targets *HAO1* in the liver



AGXT, alanine-glyoxylate aminotransferase ; *HAO1*, hydroxyacid oxidase 1; PH1, primary hyperoxaluria type 1.

Multiple model systems used for the optimization and characterization of the ABO-101 clinical candidate



Model systems:

Human Cell Lines

Purpose:

- Nuclease & guide selection
- Off-target screening & validation

Murine Models*

Purpose:

- Proof of biology in disease model
- Germline studies
- Pharmacology PK/PD

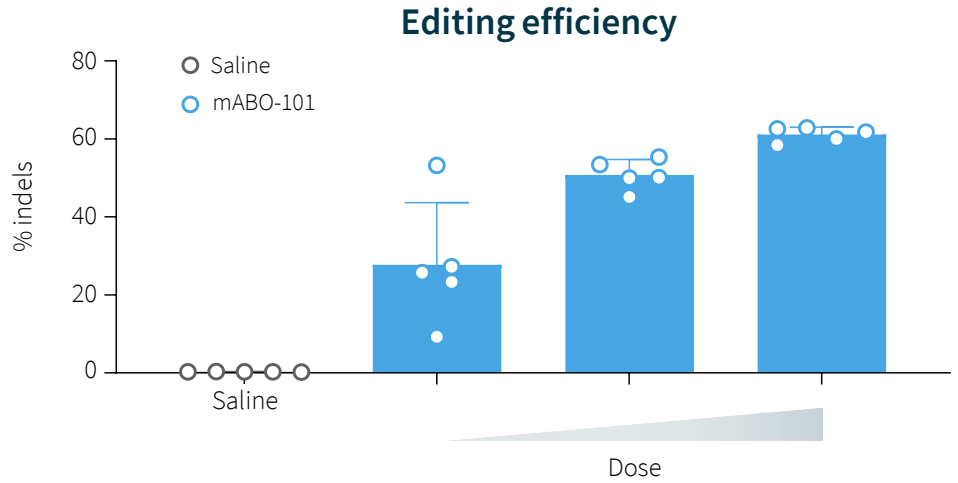
NHPs

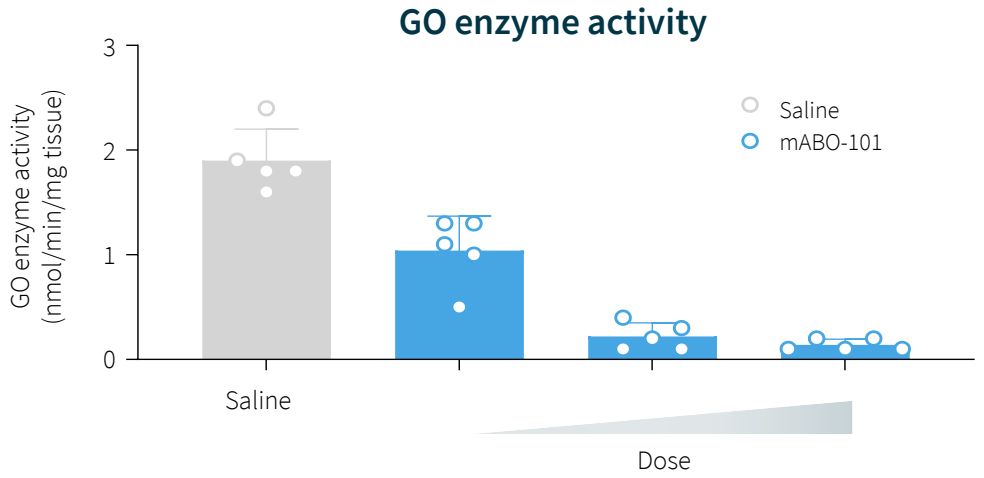
Purpose:

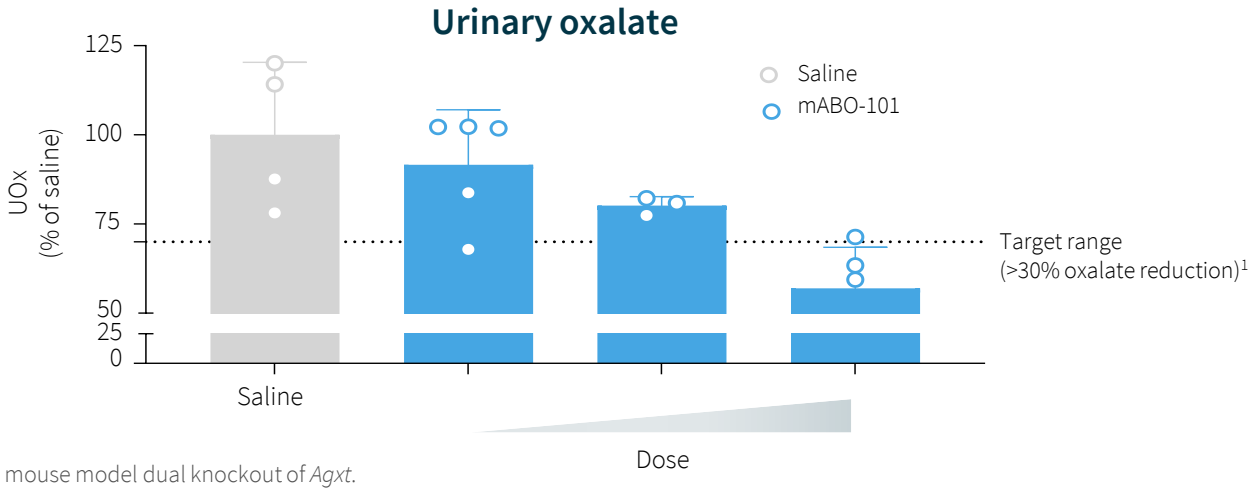
- Final LNP configuration testing
- Safety studies
- Human translation (perfect homology to clinical candidate)

*mABO-101 is a surrogate compound designed to specifically target mouse *Hao1*
†LNP licensed from Acuitas

PH1 mouse model: mABO-101 demonstrates reduced GO enzyme activity and oxalate levels







mABO-101 editing correlates with reduction of UOx

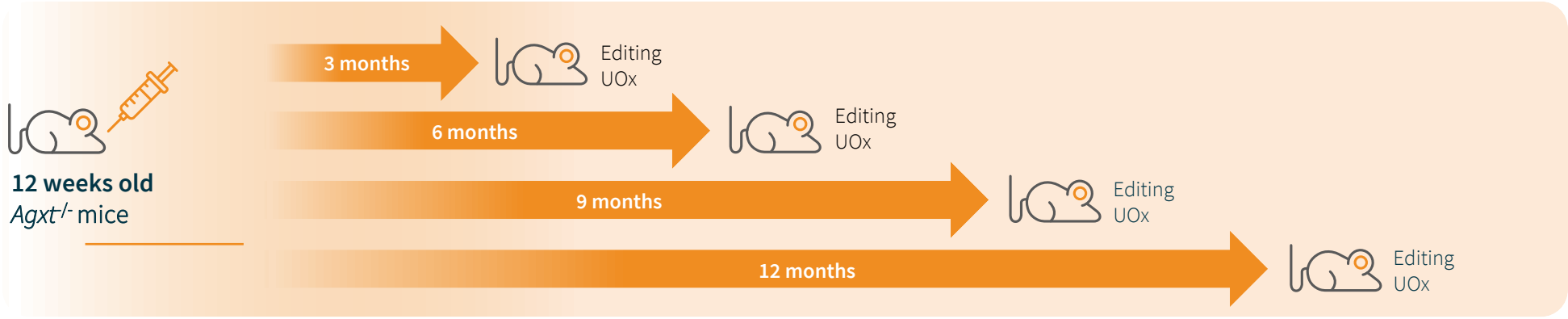
- ✓ Dose-dependent liver *Hao1* editing
- ✓ Ablation of liver GO enzyme activity
- ✓ >40% reduction of UOx

PH1 mouse model dual knockout of *Agxt*.

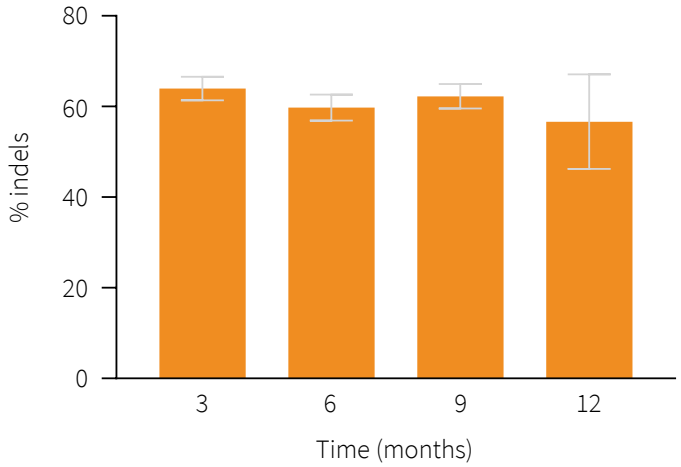
Agxt, alanine--glyoxylate aminotransferase; GO, glycolate oxidase; *Hao1*, hydroxyacid oxidase 1; indels, insertions-deletions; KO, knockout; mABO-101, mouse surrogate ABO-101; UOx, urinary oxalate.

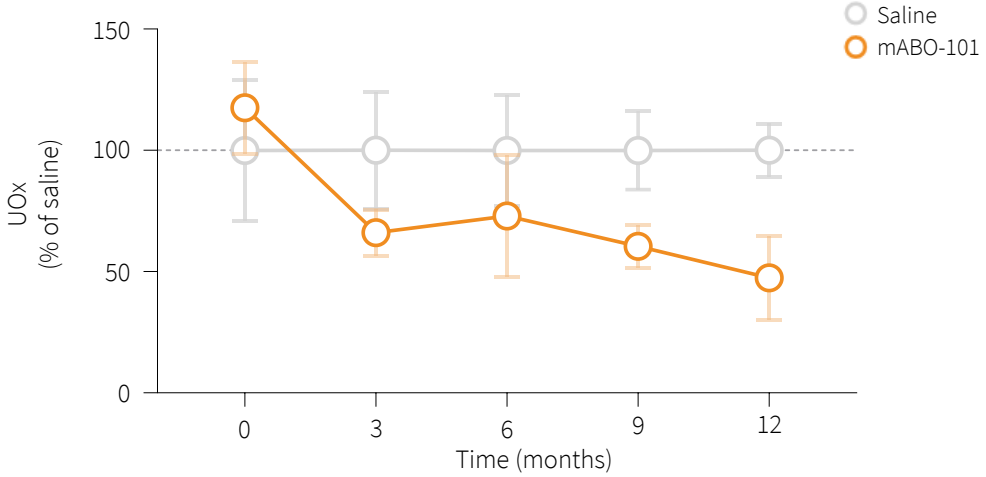
1. Leumann E, Hoppe B. *Nephrol Dial Transplant.* 1999;14(11):2556–2558.

PH1 mouse model: Hepatic *Hao1* indels and UOx reduction persist for 12 months in PH1 mice



Long-term maintenance of editing (left) and oxalate reduction (right) in *Agxt* $^{-/-}$ PH1 mouse model





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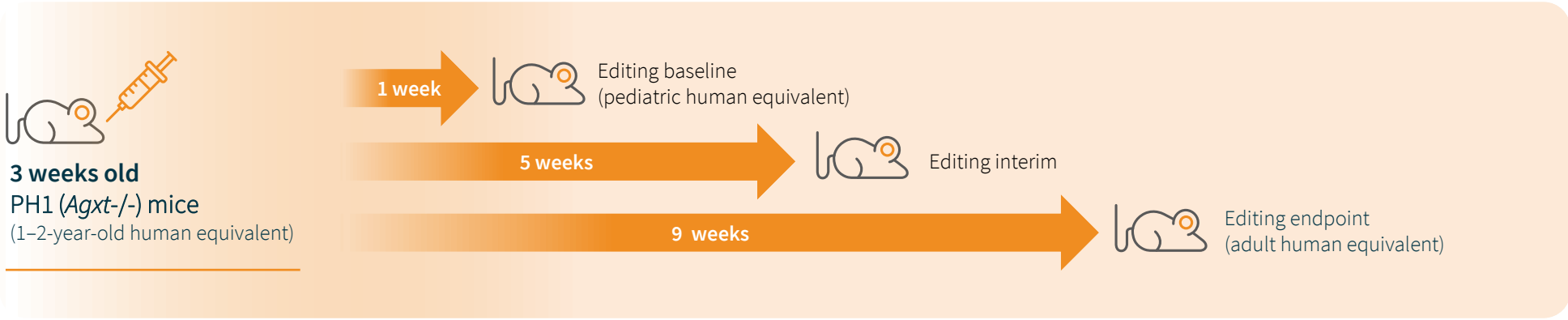
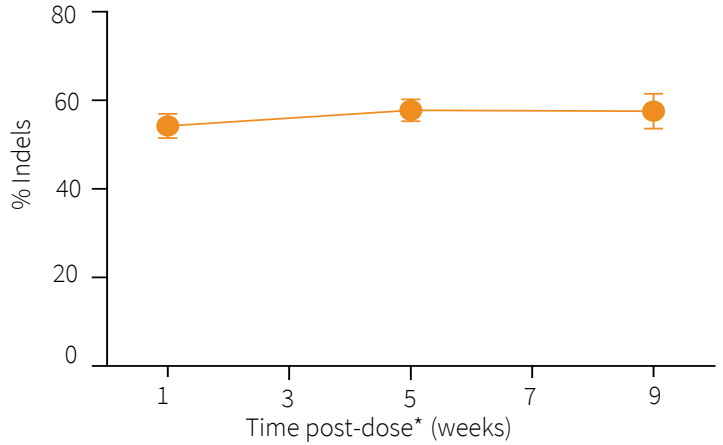
Agxt, alanine--glyoxylate aminotransferase; *Hao1*, hydroxyacid oxidase 1; indels, insertions-deletions; mABO-101, mouse surrogate ABO-101; PH1, primary hyperoxaluria type 1; UOx, urinary oxalate.

PH1 mouse model: ABO-101 administration to juvenile PH1 mice durably reduces urinary oxalate into adulthood

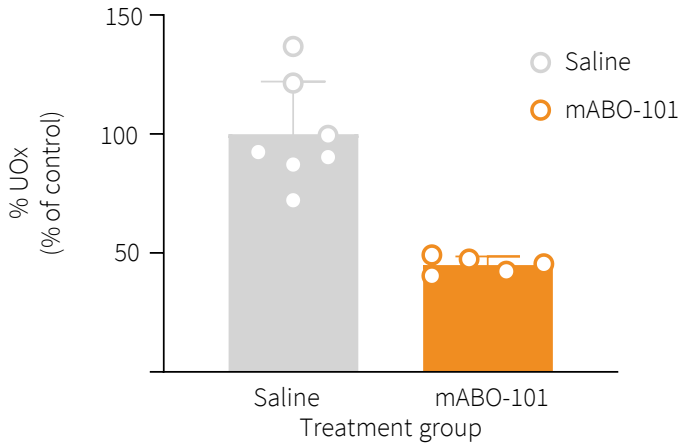


A single dose of mABO-101 in juvenile mice resulted in durable editing (left) prevented disease onset into adulthood in PH1 mice (right)

Liver editing



Urinary oxalate



PH1 mouse model dual knockout of *Agxt*. *Indel timepoints correspond to 4, 8, and 12 weeks old.
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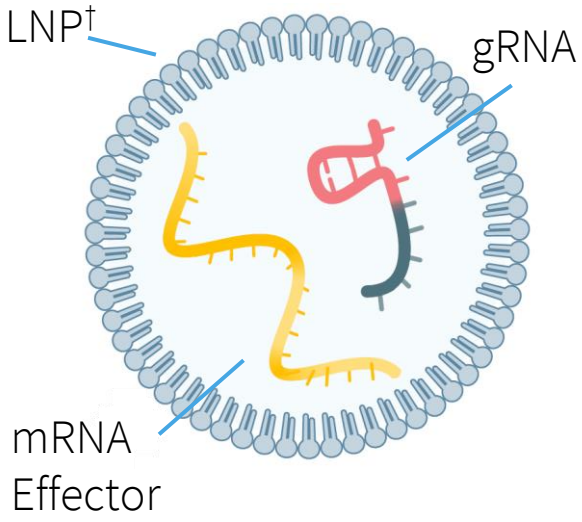

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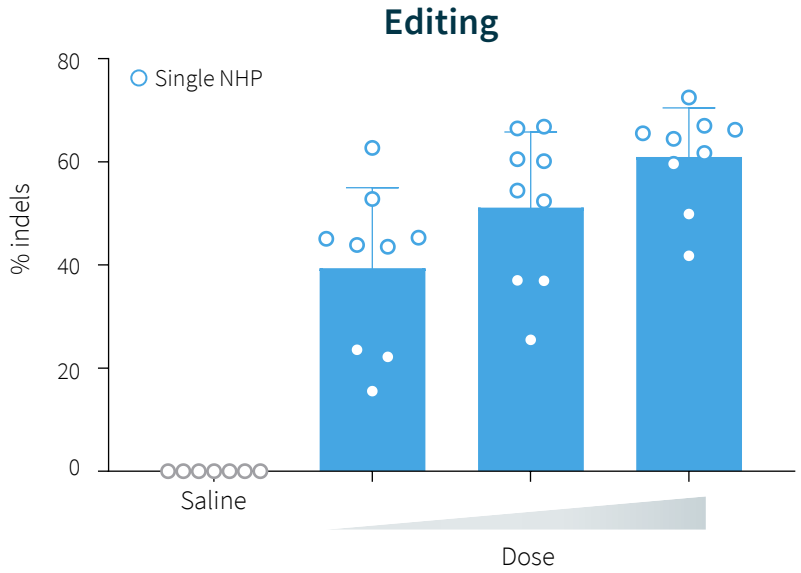
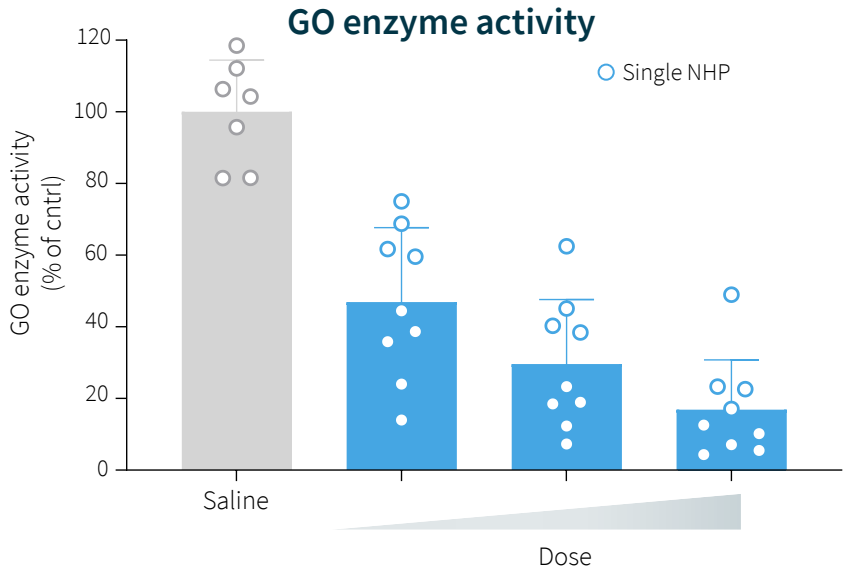
NHP: ABO-101 demonstrates robust editing and GO enzyme activity reduction



Robust editing levels exceeding 55%



Greater than 75% reduction in GO protein activity

Tolerability

NHPs were normal, bright, alert, and reactive throughout the entire in-life period and experienced no adverse clinical signs or symptoms at all dose levels

7 DAYS

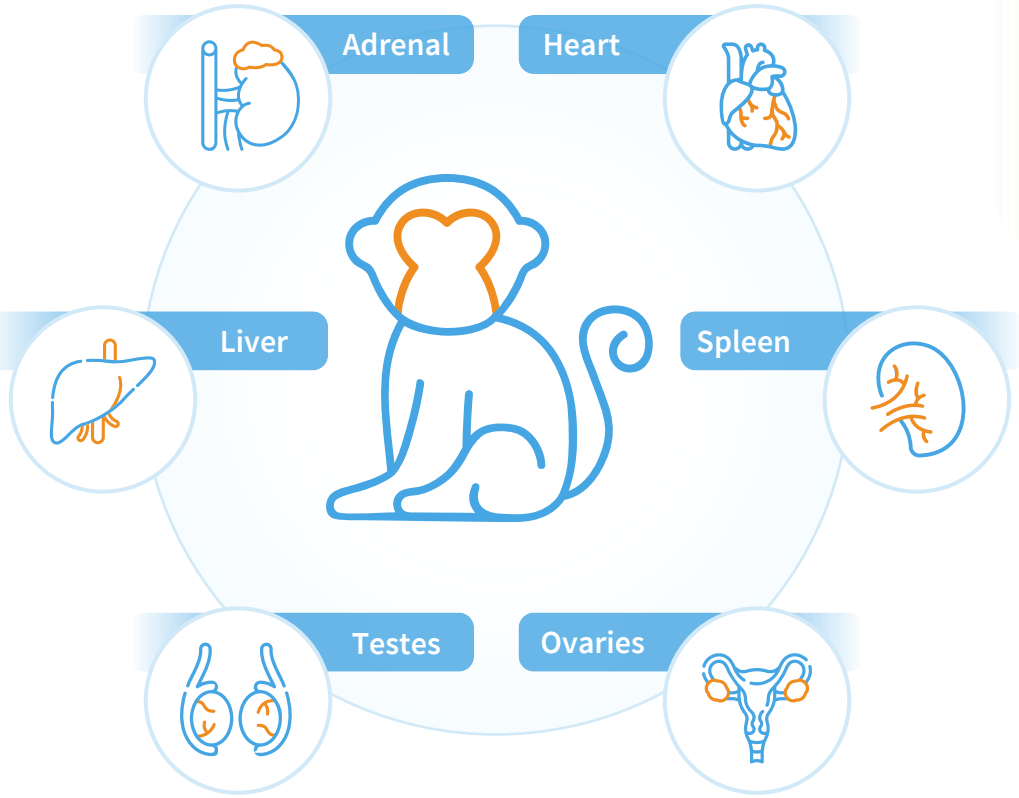
Transient elevation of LFTs occurred in a dose-dependent manner and largely resolved within 7 days

No coagulopathy or histopathological liver injury observed

ABO-101 is efficacious and tolerable in NHPs at multiple dose levels

FC, fold change; GO, glycolate oxidase; indel, insertion-deletion; LFT, liver function test; NHP, non-human primate.

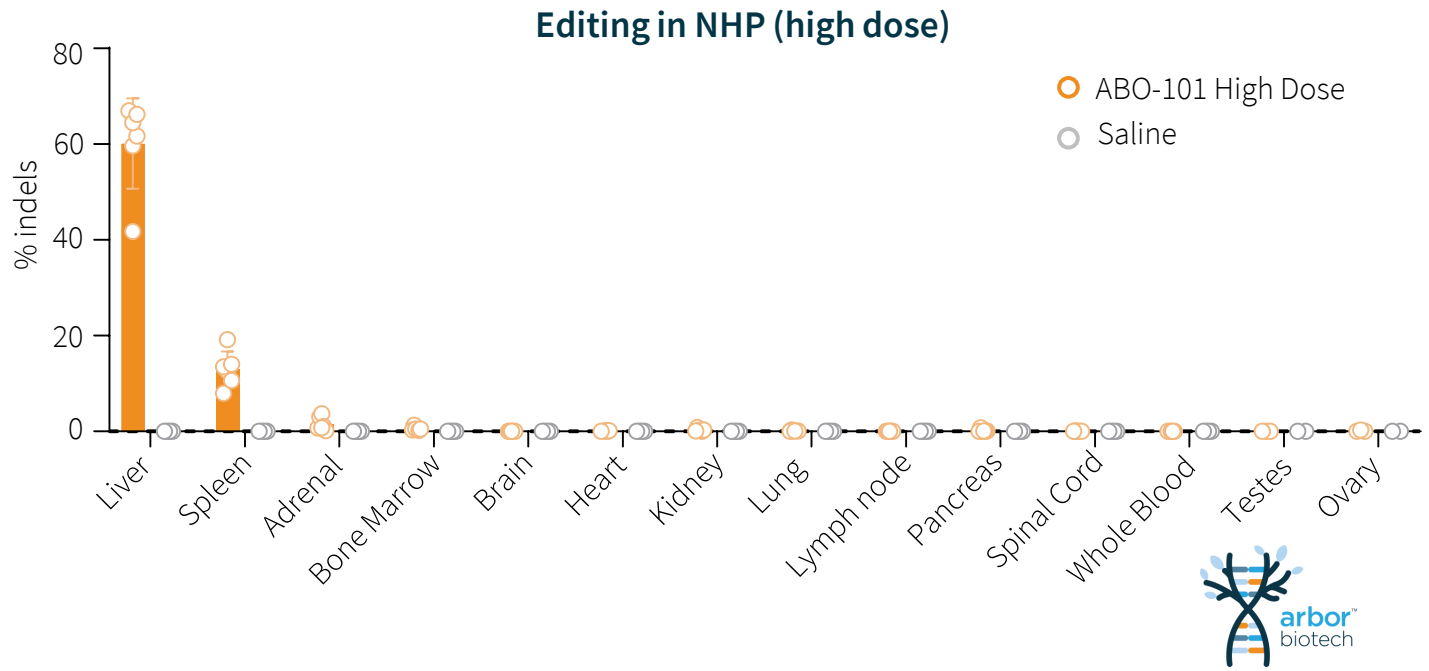
Editing and tolerability in NHPs: No clinical findings were observed with ABO-101, and editing was dominant in the liver



A comprehensive list of tissues was examined by an experienced pathologist:

- There were no ABO-101-related macroscopic findings, organ weight changes, or microscopic findings
- Transient elevation of LFTs occurred in a dose-dependent manner and largely resolved within 7 days

A select list of tissues evaluated for non-target tissue editing:



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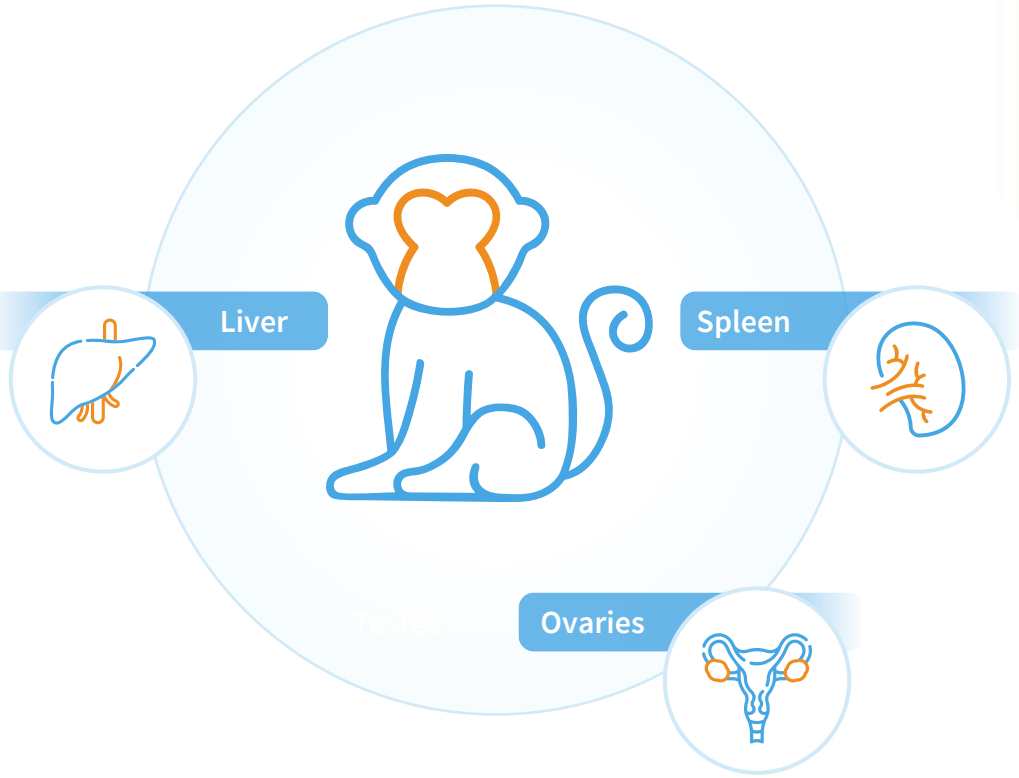

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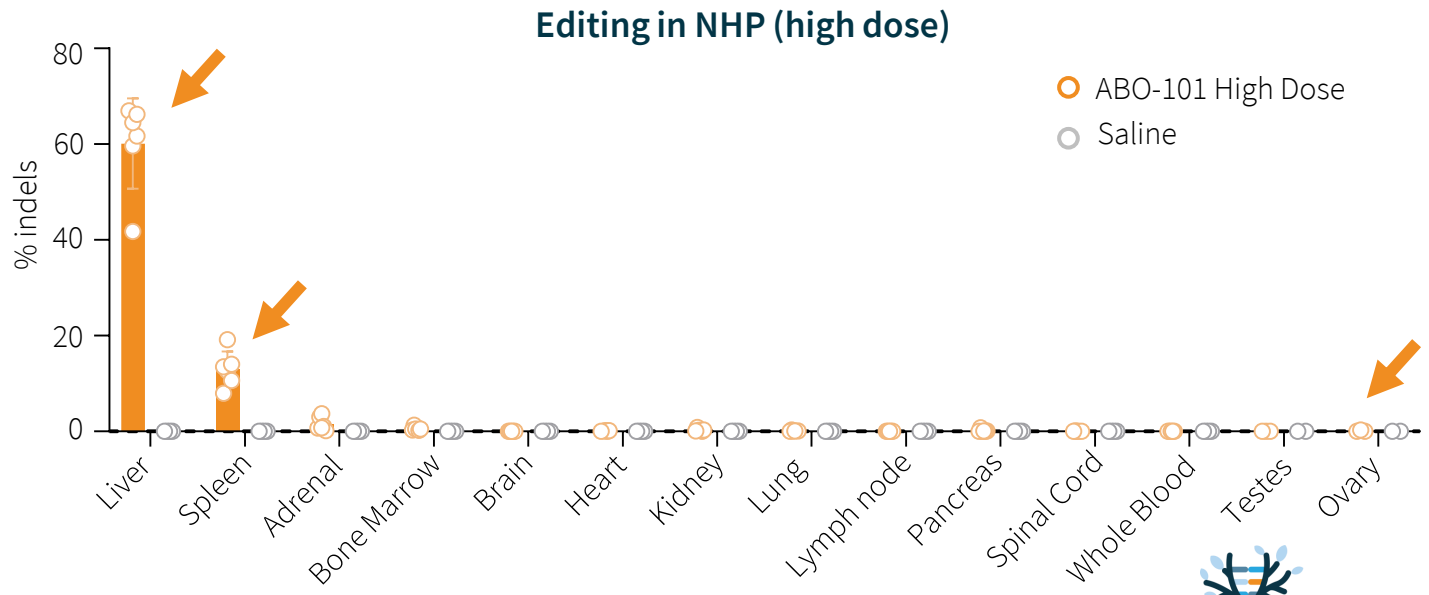


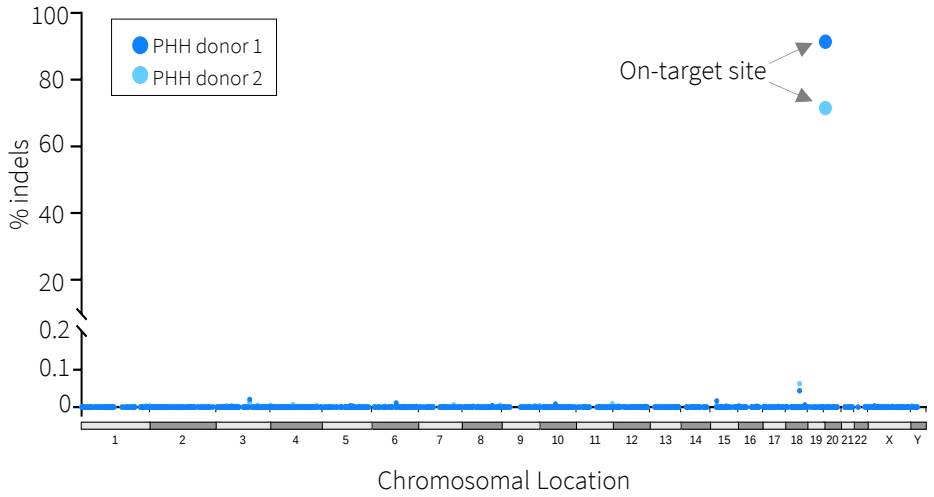
Additional studies to assess off-target and non-target tissue editing outcomes

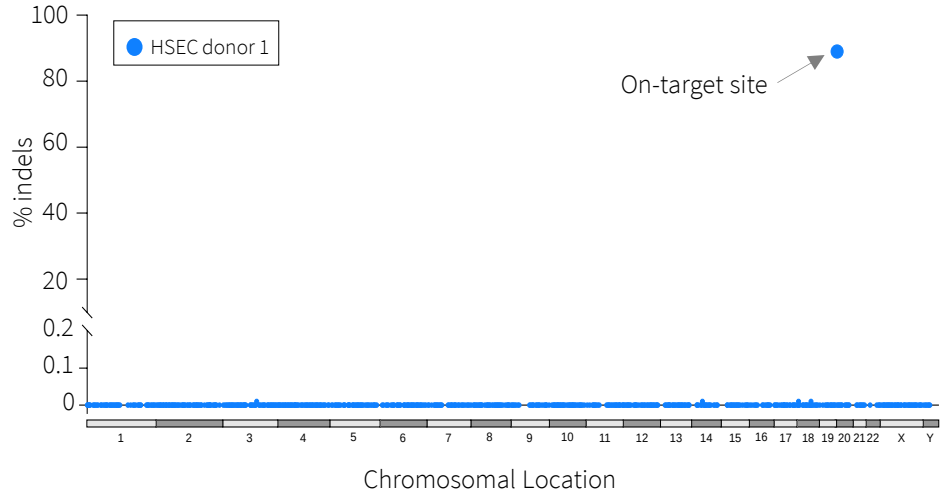
ABO-101 is specific and chromosomal structure is maintained

Genotoxicity

No observed structural variants and no observed off-target editing >0.1% at 1,541 sites in primary human hepatocytes treated with supersaturating doses of ABO-101 in vitro

Assessment of indels at >1,500 potential off-target sites





At supersaturating doses (1.5x ec90) in primary hepatocytes, 3 low-level potential off-targets were observed which we assess as low risk given their level (<0.07%) and location (non-coding regions).

Optical genome mapping and long range sequencing were used to assess the chromosomal structure. No treatment related structural variants at the genome level were observed in ABO-101 treated primary hepatocytes.

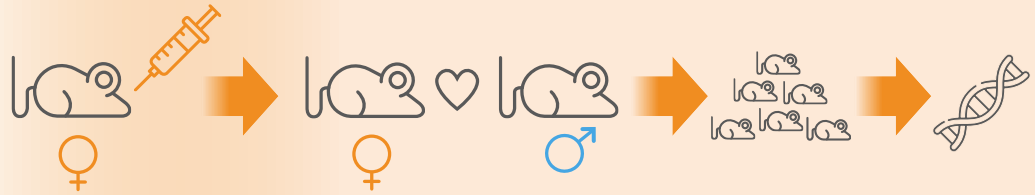
PHH, primary human hepatocytes. HSEC: human splenic endothelial cells.

Editing is not passed down to offspring after administration of supersaturating doses of ABO-101

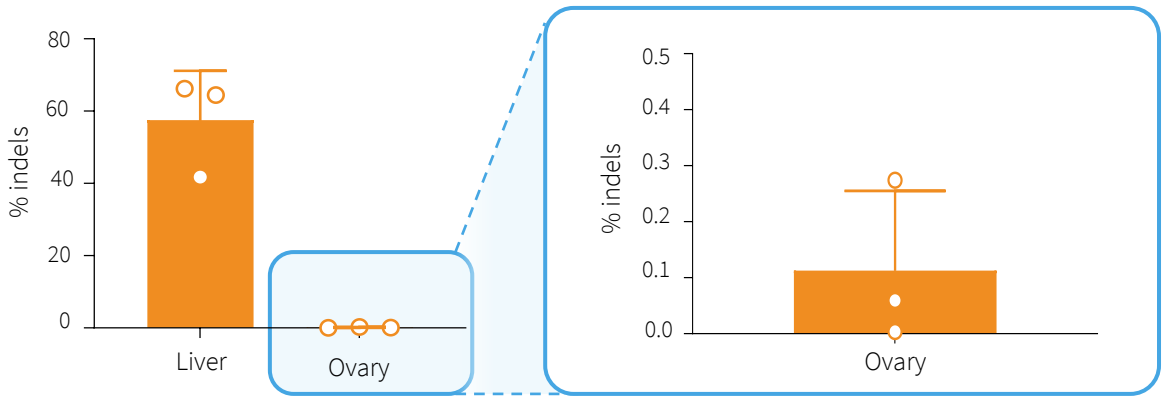
NHP biodistribution

Biodistribution of editing in NHPs shows extremely low levels of editing (<0.2% avg at high dose) in whole ovary tissue

Mouse progeny study design



Liver and Ovary Tissue in NHP



Test condition	mABO-101
Liver indels of mothers	>55% (majority of hepatocytes)
Total offspring analyzed	>500 pups
Total offspring with *Hao1* indel	0

Hao1, hydroxyacid oxidase 1; indels, insertions-deletions; mABO-101, mouse surrogate ABO-101; NHP, non-human primate.

Conclusions

- mABO-101 demonstrated efficient in vivo editing of *Hao1* in the *Agxt* KO mouse model of PH1 with corresponding reduction of urinary oxalate by >40%
- Single administration of mABO-101 shows durable editing and long-lasting reduction of oxalate when administered to juvenile mice and out to 1 year post-dose in the *Agxt* KO mouse model of PH1
- Efficacy and tolerability of ABO-101 is seen in NHPs with efficient editing, reduced GO enzyme activity and no clinical signs or adverse events
- ABO-101 exhibits ability to target *HAO1* with high specificity
- Progeny studies demonstrate that editing is not passed down through the germline
- Presented data, together with additional IND-enabling studies, were accepted by the FDA and MHRA to support continued development of ABO-101 in a Phase 1/2 Study

Open-label Phase 1/2 study of ABO-101: FDA approved, planned Global Study

redephine

FIH dose escalation in adults → Establish Recommended Dose (RD) → Adult Expansion & Peds at RD

Key eligibility criteria:

- Genetic PH1 diagnosis
- siRNA naïve or last dose ≥24 months prior
- eGFR ≥30 mL/min/1.73 m^2
- Hyperoxaluria ≥1.5x ULN: mean of two 24-hour UOx ≥0.7 mmol/24 hour/1.73 m^2
- Weight ≤90 kg

Part A*
Ages ≥18 to ≤64 years

- Adult, high
- Adult, mid
- Adult, low

Initial UOx will be used to establish the RD

Part B
Ages ≥6 to <18 years;
Sentinel patient ≥12 to <18 years

- Pediatric, RD

Long-term follow-up to monitor safety for ~13 years

Key primary objectives and endpoints

Evaluate safety and tolerability

- Incidence and severity of treatment-emergent and serious adverse events

Secondary objectives and select endpoints

Evaluate pharmacokinetics, pharmacodynamics, and signals of early efficacy

- Percent change (or AUC of percent change – Part C) in 24-hour UOx from baseline to Month 6
- Changes in eGFR from baseline to Months 12 and 24

Now enrolling, visit clinicaltrials.gov (NCT 06839235) or arbor.bio/clinical-trial/ to learn more

*Additional doses may be added, and dose expansion may occur in selected cohorts.
† eGFR, estimated glomerular filtration rate; siRNA, small interfering RNA; UOx, urinary oxalate; FIH, first in human study