



# DEVELOPING RNA-EDITING MEDICINES

*for patients in need*

Nasdaq: PRQR

May 2026



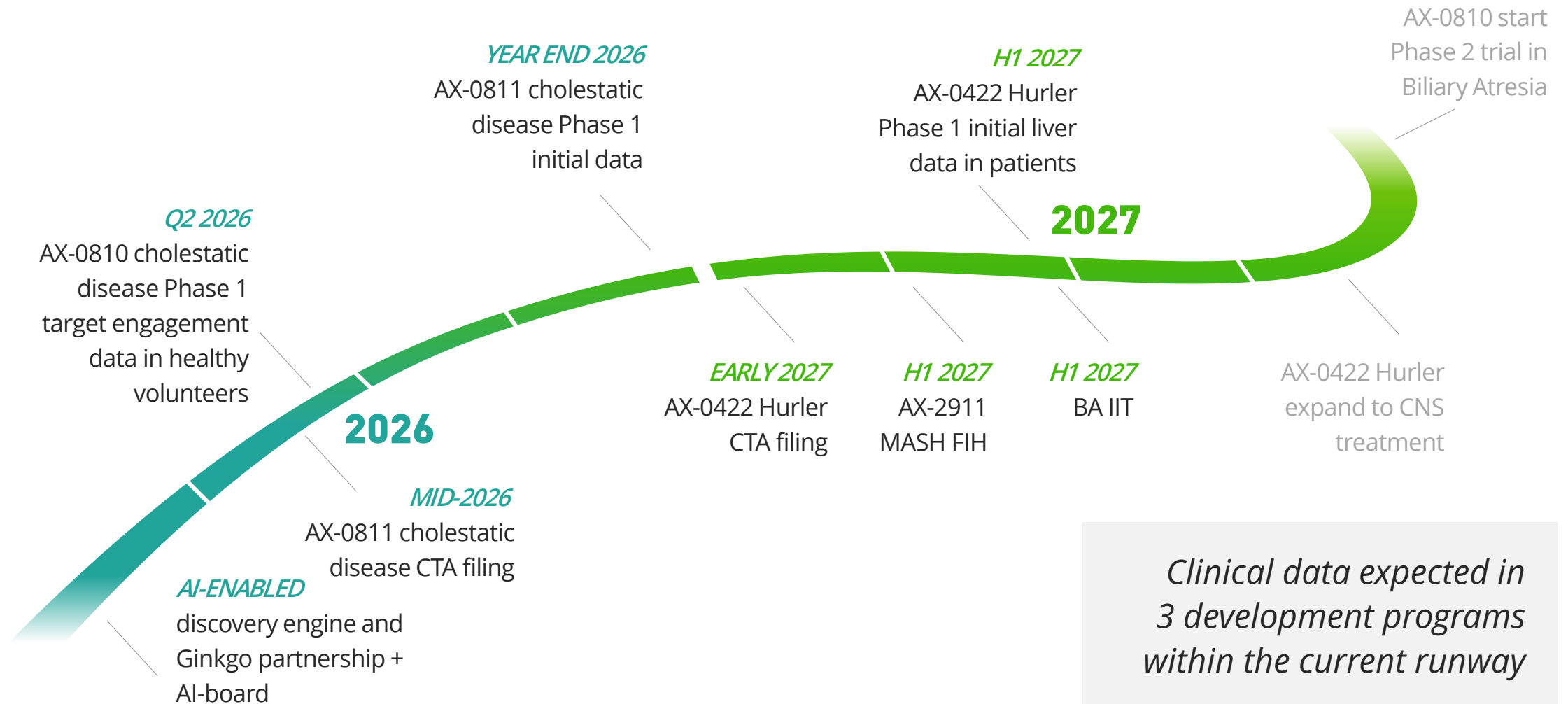
# Forward-looking statements

This presentation contains forward-looking statements. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as “continue,” “anticipate,” “believe,” “could,” “estimate,” “expect,” “goal,” “intend,” “look forward to”, “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” and similar expressions. Such forward-looking statements include, but are not limited to, statements regarding our business, technology, strategy, preclinical and clinical model data; our initial pipeline targets and the upcoming strategic priorities and milestones related thereto, the continued advancement of our lead development pipeline programs, including approved, ongoing and planned clinical trials; expectations regarding the ongoing Phase 1 clinical trial of AX-0810 in NTCP for cholestatic diseases, including the planned trial design, and our ability to recruit for and complete a Phase 1 clinical trial for AX-0810, biliary atresia as our primary indication for AX-0810, the timing of top-line data readout for Phase 1 clinical trial and the initiation of Phase 2 trial; expectations regarding the safety and therapeutic benefits of AX-0810, including the planned dosing levels and their efficacy; the anticipated timing of initial Phase 1 clinical data for our lead program, AX-0810, in H1 2026; our new pipeline targets, including the planned Phase 1 clinical trial of AX-0811 in NTCP for cholestatic diseases, our ability to recruit for and complete a Phase 1 clinical trial for AX-0811, an anticipated CTA filing and data readout for AX-0811 pending regulatory clearance, expectations regarding the efficacy, clinical development timeline, and expected trial designs and development of AX-0422 and AX-2911, including the potential CTA filings and data readout pending regulatory clearance; clinical updates across multiple programs in 2026 and 2027; the therapeutic potential and development timeline regarding AX-0810, AX-0811, AX-0422, AX-2911 and AX-2402; the continued development and advancement of our Axiomer™ platform; the therapeutic potential of our Axiomer RNA editing oligonucleotides and product candidates; the timing, progress and results of our preclinical studies and other development activities, including the release of data related thereto; our patent estate, including our anticipated strength and our continued investment in it; our AI strategy and expectations regarding AI’s ability to accelerate Axiomer discovery; our partnership with Ginkgo; and the potential of our technologies and product candidates. Forward-looking statements are based on management’s beliefs and assumptions

and on information available to management only as of the date of this presentation. Our actual results could differ materially from those expressed or implied by these forward-looking statements for many reasons, including, without limitation, the risks, uncertainties and other factors in our filings made with the Securities and Exchange Commission, including certain sections of our most recent annual report filed on Form 20-F. These risks and uncertainties include, among others, the cost, timing and results of preclinical studies and clinical trials and other development activities by us and our collaborative partners whose operations and activities may be slowed or halted shortage and pressure on supply and logistics on the global market, economic sanctions and international tariffs; the likelihood of our preclinical and clinical programs being initiated and executed on timelines provided and reliance on our contract research organizations and predictability of timely enrollment of subjects and patients to advance our clinical trials and maintain their own operations; our reliance on contract manufacturers to supply materials for research and development and the risk of supply interruption from a contract manufacturer; the potential for future data to alter initial and preliminary results of early-stage clinical trials; the unpredictability of the duration and results of the regulatory review of applications or clearances that are necessary to initiate and continue to advance and progress our clinical programs; the ability to secure, maintain and realize the intended benefits of collaborations with partners, including the collaboration with Lilly; the possible impairment of, inability to obtain, and costs to obtain intellectual property rights; possible safety or efficacy concerns that could emerge as new data are generated in research and development; general business, operational, financial and accounting risks, and risks related to litigation and disputes with third parties; and risks related to macroeconomic conditions and market volatility resulting from global economic developments, geopolitical events and conflicts, high inflation, rising interest rates, tariffs and potential for significant changes in U.S. policies and regulatory environment. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements, and we assume no obligation to update these forward-looking statements, even if new information becomes available in the future, except as required by law.

# Multiple clinical catalysts within the runway

Core focus on cholestatic development, with value creating pipeline beyond



# Axiomer™ RNA editing

*From platform to multi-asset clinical pipeline*



## CLINICAL VALIDATION

AX-0810 (NTCP) target engagement data expected Q2 2026

First validation of Axiomer in humans

Biliary atresia selected as initial indication for AX-0810 in Phase 2



## PIPELINE EXPANSION

AX-0811 next generation NTCP program resulting from AI-enabled discovery

AX-0422 for Hurler syndrome (IDUA) liver + CNS opportunity with CTA filing in early 2027

AX-2911 for MASH (PNPLA3) advancing to FIH IIT in China H1 2027



## HIGH IMPACT PARTNERSHIP

Collaboration with Eli Lilly for multiple RNA editing targets, supporting the scalability of Axiomer

Ongoing execution across partnership



## CONTINUING TO ADVANCE AXIOMER PLATFORM

ProQR AI-enabled discovery

Autonomous high-throughput screening capability with Ginkgo Bioworks





## RUNWAY INTO MID 2027

Multiple clinical catalysts

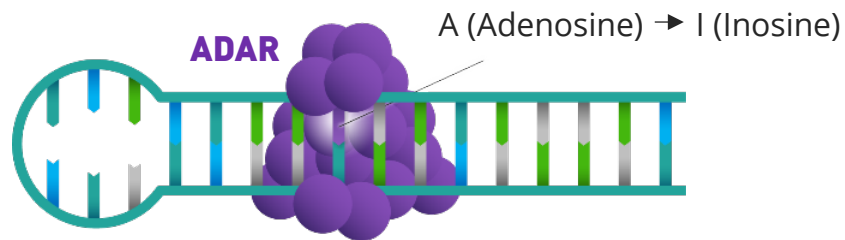
**€ 81.1** million cash and cash equivalents as of end of Q1 2026

# ProQR development pipeline and milestones

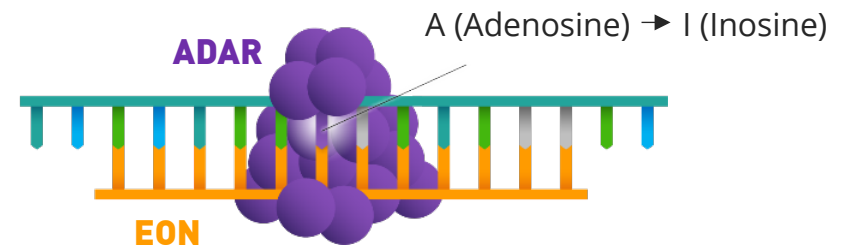
	TARGET	AXIOMER APPLICATION	DISCOVERY	NON-CLINICAL	CLINICAL	MILESTONES	ESTIMATED POPULATION
<b>DEVELOPMENT PIPELINE</b>							
<b>AX-0810</b> <i>for Cholestatic diseases</i>	NTCP	<i>Modulate</i>				Target engagement data Q2 2026	~100K patients
<b>AX-0811</b> <i>for Cholestatic diseases</i>	NTCP	<i>Modulate</i>				Target engagement data in 2026	
<b>AX-0422</b> <i>for Hurler Syndrome</i>	IDUA	<i>Correct</i>				CTA filing early 2027; Clinical biomarkers in H1 2027	~500-1000 patients
<b>AX-2911</b> <i>for MASH</i>	PNPLA3	<i>Correct</i>				FIH H1 2027	~8M patients
<b>AX-2402</b> <i>for Rett syndrome</i>	MECP2 R270X	<i>Correct</i>					 ~5K
<b>PARTNERED PIPELINE</b>							
10 undisclosed targets (option to expand to 15)			<i>Progress undisclosed</i>				

# How Axiomer™ edits RNA

## NATURAL ADAR EDITING



## EDITING OLIGONUCLEOTIDE (EON)-directed EDITING



## MODULATE



*Modify protein function*

## CORRECT



*Correct disease-causing mutations*

## PROTECT



*Introduce protective variants*

# Addressing unmet need in cholestatic diseases through NTCP modulation



## CHOLESTATIC DISEASE

- Biliary Atresia affects pediatrics early in life (~20,000 patients worldwide)
- Primary Sclerosing Cholangitis affects adults (~80,000 US+EU)
- No approved therapies and may require liver transplantation<sup>1,2</sup>



## BILE ACID TOXICITY

- Bile acid accumulation drives liver injury, leading to fibrosis and liver failure



## NTCP MODULATION STRATEGY

- Human genetics supports NTCP modulation as hepato-protective mechanism to reduce bile acid reuptake and protect liver



NTCP, sodium taurocholate co-transporting polypeptide. References: <sup>1</sup>Trivedi PJ, et al. Clin Gastroenterol Hepatol. 2022 Aug;20(8):1687-1700.e4; <sup>2</sup>Schreiber RA, et al. J Clin Med. 2022 Feb 14;11(4):999

# NTCP modulation approach broadly validated

Reducing liver bile acids toxic overload via NTCP modulation is a key driver for hepatoprotective effects



## HUMAN GENETICS

Healthy population discovered with NTCP variants that reduces bile acids uptake into liver<sup>1-3</sup>



## IN VITRO

NTCP variant leads to an 8-fold decrease of bile acids re-uptake *in vitro*



## IN VIVO

NTCP modulation demonstrated activity in mouse cholestatic disease model, with 2- to 3-fold change in conjugated bile acids<sup>4-5</sup>



## IN CLINIC

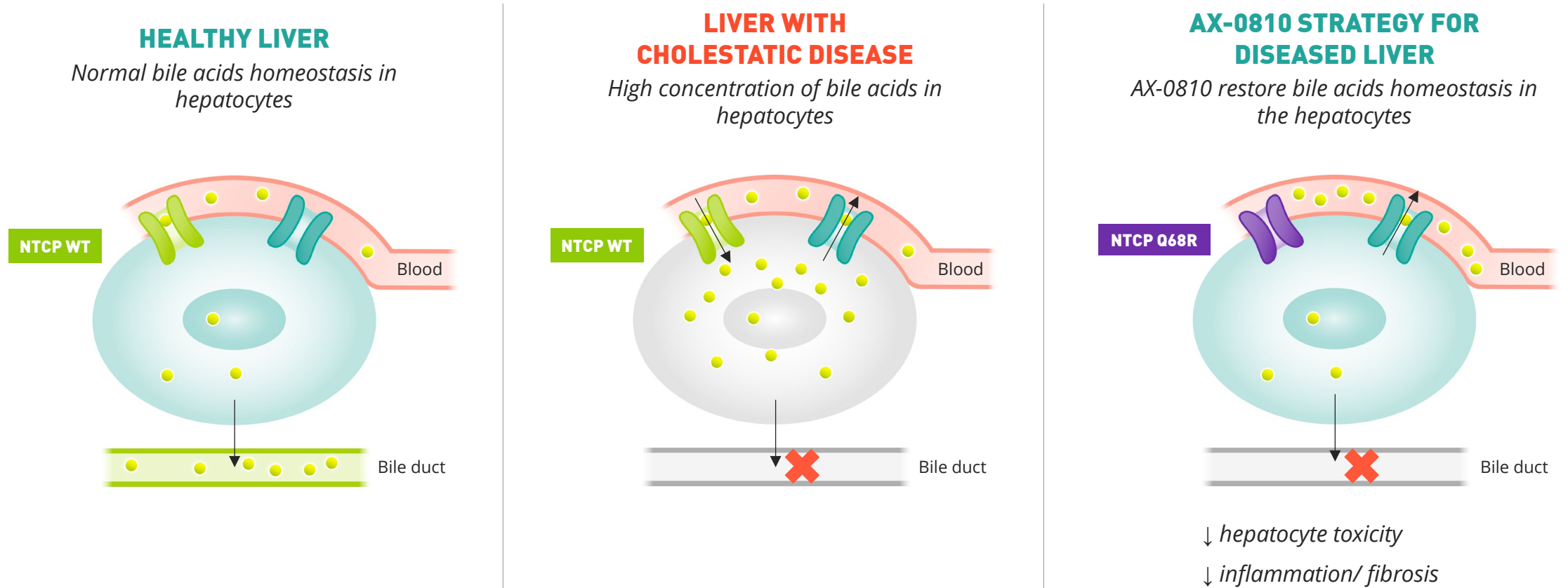
Clinical PoC with bulevirtide in Ph3 Hepatitis D trial, for which liver improvement occur in patients, even without virologic response<sup>6-8</sup>



Bulevirtide (Hepcludex) is a daily SC injected NTCP inhibitor approved for Hepatitis D. NTCP channel is a known transporter for bile acids and hepatitis virus from bloodstream to the liver.

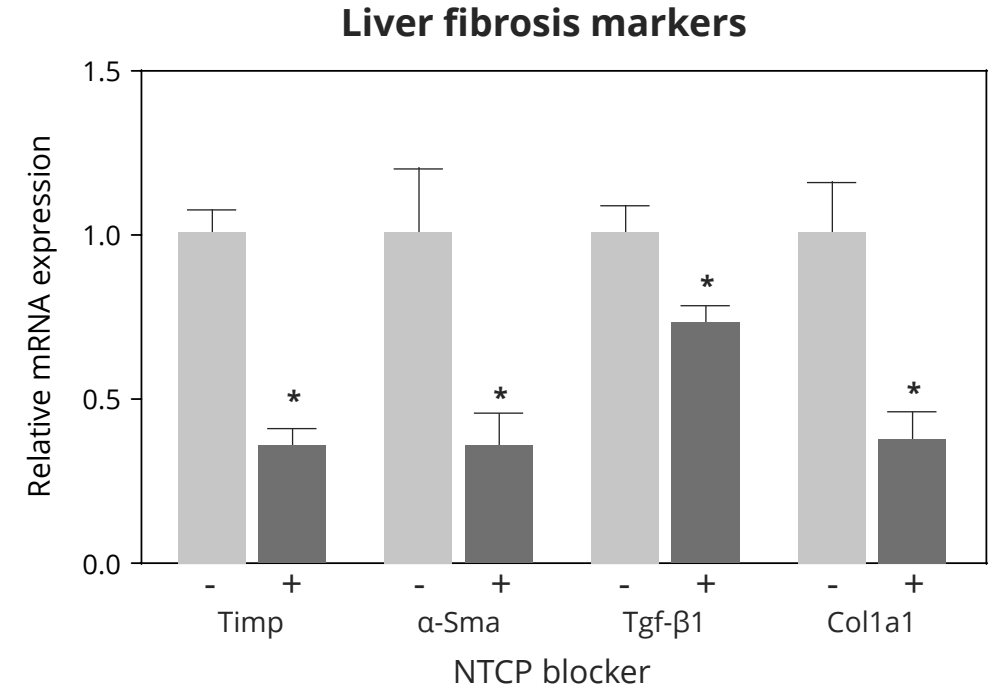
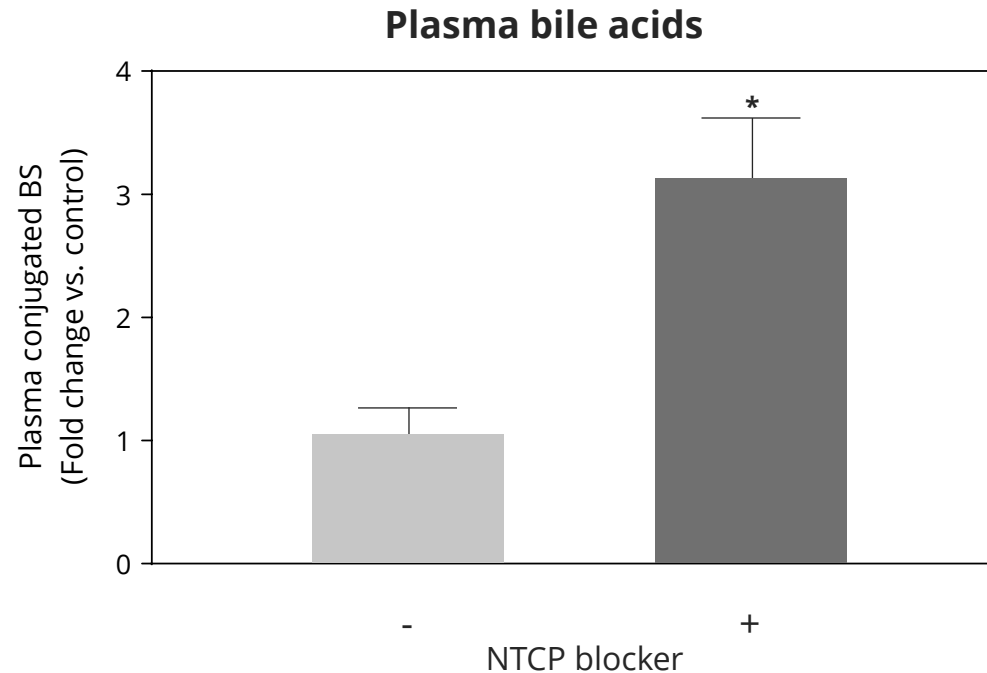
<sup>1</sup>Ho RH, et al. J Biol Chem. 2004 Feb 20;279(8):12713-22; <sup>2</sup>Vaz FM, et al. Hepatology. 2015 Jan;61(1):260-7; <sup>3</sup>Schneider AL, et al. Clin Res Hepatol Gastroenterol. 2022 Mar;46(3):101824; <sup>4</sup>Sljepcevic D, et al. Hepatology. 2018 Sep;68(3):1057-1069; <sup>5</sup>Salhab A, et al. Gut. 2022 Jul;71(7):1373-1385; <sup>6</sup>Wedemeyer H, et al. N Engl J Med. 2023 Jul 6;389(1):22-32; <sup>7</sup>Wedemeyer H, J Hepatol. 2024 Oct;81(4):621-629; <sup>8</sup>Dietz-Fricke C, JHEP Rep. 2023 Mar 15;5(4):100686.

# AX-0810 reduces bile acid accumulation in hepatocytes by modulating NTCP activity



Halilbasic E, et al. J Hepatol. 2013 Jan;58(1):155-68; Nyholm I, et al. J Hepatol. 2025 Aug;83(2):440-452.

# NTCP modulation reduces fibrosis markers and elevates circulating bile acids



NTCP channel blocking **increases plasma bile acids concentrations**, up to 3-fold in cholestatic disease mouse model

**Pro-fibrotic markers show reduced expression** after NTCP channel blocking

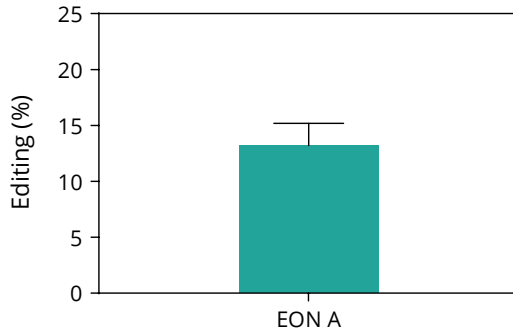
*Bulevirtide (Hepcludex) is a daily SC injected NTCP inhibitor approved for Hepatitis D. Slijepcevic D, et al. Hepatology. 2018 Sep;68(3):1057-1069.*

# EON mediated editing demonstrates consistent editing of NTCP and impact on biomarker *in vivo*

## EDITING EFFICIENCY

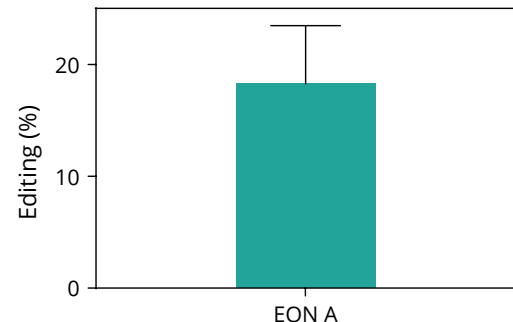
### NTCP RNA Editing in Humanized Mice

(N=4, 20mg/kg, 6 doses, GalNac conjugation, SC, D25, ddPCR)



### NTCP RNA Editing in NHP

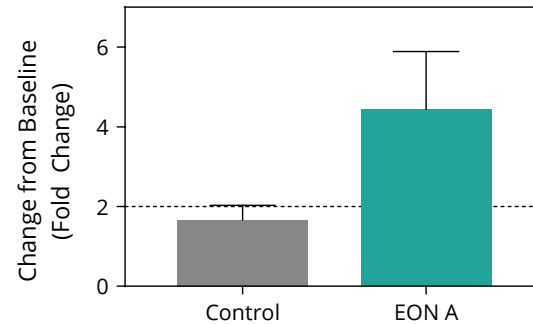
(N=1, 1-4mg/kg, 4 doses, LNP formulation, IV, up to D46, ddPCR)



## PLASMA TOTAL BILE ACIDS

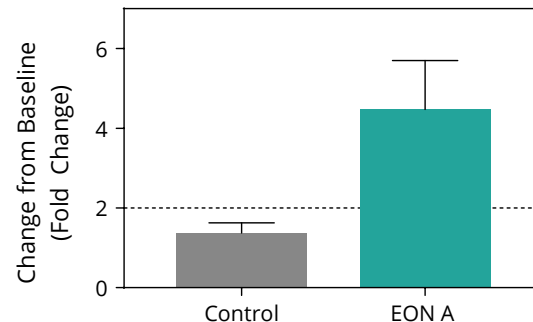
### Plasma TBA in Humanized Mice

(N=4, 20mg/kg, 6 doses, GalNac conjugation, SC, D25)



### Plasma TBA in NHP

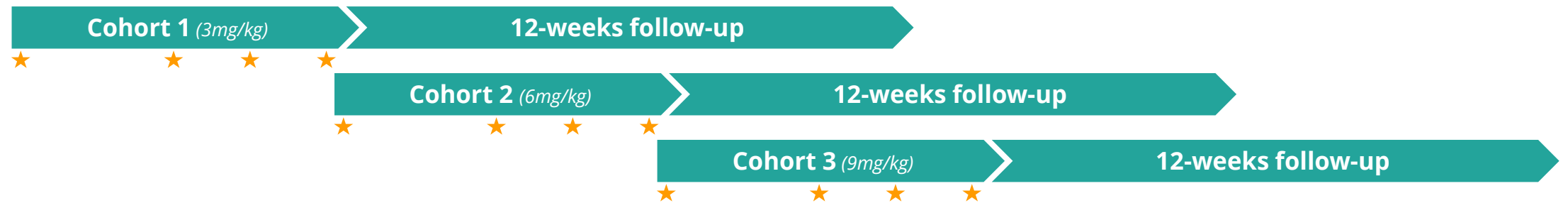
(N=1, 1-4mg/kg, 4 doses, LNP formulation, IV, up to D39)



- EON A results in consistent editing data in humanized mouse model and NHP *in vivo* with approx. 15% editing reaching expected NTCP modulation
- Reaching >2-fold changes in biomarkers - expected impact on plasma bile acids levels following NTCP EON treatment

# Assessing Safety, PK and Target Engagement of AX-0810 in First-in-Human Trial

**Multiple ascending dose (MAD)** N=33 healthy volunteers (24 on treatment, 9 on placebo)



*DMC safety reviews before proceeding to next dose and dose escalation is sequential during the dosing phase*

## Treatment

AX-0810 GalNAc conjugated editing oligonucleotide

## Objectives

- Assess safety, tolerability, and PK of AX-0810
- Confirm target engagement as measured by biomarkers

## Key endpoints

- Change in bile acids levels
- Bile acids profile
- TUDCA challenge
- Liver biomarkers

## Phase 1 progressing

- ✓ Initial AX-0810 data demonstrate no safety signals and pharmacokinetics consistent with non-clinical models
- Target engagement data on track for H1 2026

CTA, Clinical Trial Application; DMC, Data Monitoring Committee; MAD, Multiple Ascending Dose; PK, Pharmacokinetics; TUDCA, Tauroursodeoxycholic acid; AX-0810 CTA has been approved in Europe (October 2025).

# Biliary atresia is a severe pediatric disease

*with no approved therapies*



## DIAGNOSIS

*Pediatric:  
in the first  
weeks of life*



## POPULATION

*Approximately  
20,000  
patients  
worldwide*



## SYMPTOMS

*Jaundice, poor  
weight gain,  
pale stool, dark  
urine*



## PROGRESSION

*Rapid  
progression  
to cirrhosis  
and portal  
hypertension  
early in life*



## STANDARD OF CARE

*Kasai procedure  
as first-line  
therapy*



## SIGNIFICANT UNMET NEED

*No approved  
pharmacological  
treatments;  
60-80% require  
liver transplant  
despite Kasai*

Adike A, et al. Expert Rev Gastroenterol Hepatol. 2018 Oct;12(10):1025-1032; Verkade HJ, et al. J Hepatol. 2016 Sep;65(3):631-42; Sundaram SS, et al. Liver Transpl. 2017 Jan;23(1):96-109; Raghu VK, et al. Liver Transpl. 2021 May;27(5):711-718; NORD, 2019, Japanese Biliary Atresia Society. Japanese Biliary Atresia Registry (JBAR). <https://jbas.net/en/national-registration/>.

# Biliary atresia as primary indication for AX-0810

BILIARY ATRESIA				
<b>SEVERITY AND UNMET NEED</b>	<b>BIOLOGICAL RATIONALE</b>	<b>CLINICAL DE-RISKING</b>	<b>CENTRALIZED CARE</b>	<b>REGULATORY PATHWAY</b>
Leading cause of pediatric liver transplantation and no approved therapies	AX-0810 targets the key driver of liver injury in the disease	No comorbidities and limited confounding factors	Patients concentrated in specialized centers	Pediatric guidance and orphan designation potential

# AX-0811: AI-enabled next-gen RNA editing therapy targeting NTCP for cholestatic diseases

## ~3x higher editing efficiency

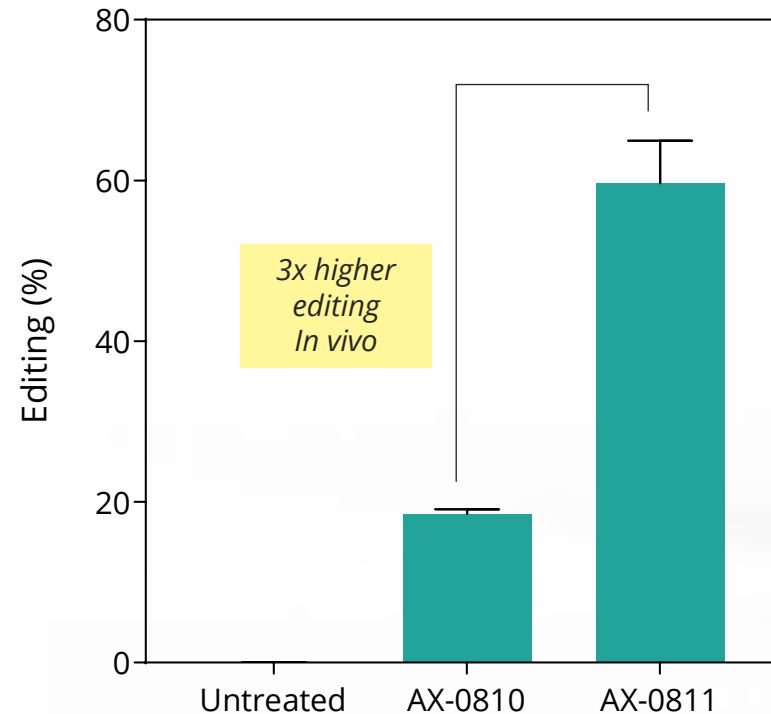
- Improved efficacy and dosing convenience over AX-0810

## Upcoming development milestones

- AX-0811 program advancing rapidly, with CTA filing in mid-2026
- Initial clinical data in healthy volunteers expected before year-end 2026

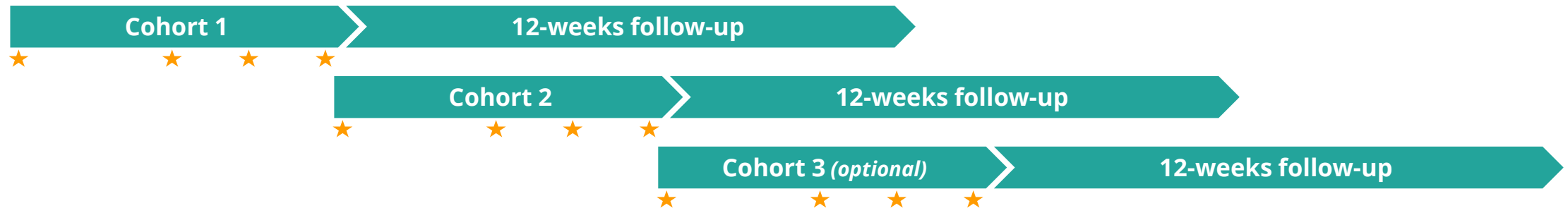
## Editing of *hNTCP* in livers of humanized mice

*SC administration, GalNAc EONs, 30mg/kg, 10 doses, n=3-4, D24, dPCR, Mean, SEM*



# Assessing Safety, PK and Target Engagement of AX-0811 in First-in-Human Trial

**Multiple ascending dose (MAD)** N=33 healthy volunteers (24 on treatment, 9 on placebo)



*DMC safety reviews before proceeding to next dose and dose escalation is sequential during the dosing phase*

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## Objectives

- Assess safety, tolerability, and PK of AX-0811
- Confirm target engagement as measured by biomarkers

## Key endpoints

- Change in bile acids levels
- Bile acids profile
- TUDCA challenge
- Liver biomarkers

## CTA enabling activities

### ongoing

- CTA filing in mid 2026
- Target engagement data expected by year-end 2026

CTA, Clinical Trial Application; DMC, Data Monitoring Committee; MAD, Multiple Ascending Dose; PK, Pharmacokinetics; TUDCA, Tauroursodeoxycholic acid

# ProQR building a leading NTCP franchise in cholestatic disease

## NTCP FRANCHISE

### AX-0810



*Rapid path to patients with **high unmet medical need***

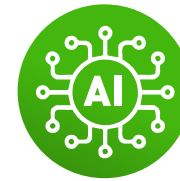


*Establishes clinical validation*



*Awareness amongst **physicians and centers of excellence***

### AX-0811



***AI-discovered next-gen candidate** with enhanced efficiency*



*Optimized Dose and scalability*

# AX-0422 RNA editing therapy

*to address Hurler Syndrome*



## HURLER SYNDROME

- Most severe form of MPS1
- Early onset, multi-symptom disease
- Progressive deterioration, high morbidity
- Current therapies do not address all comorbidities and have limitations



## IDUA DEFICIENCY

- W402X mutation (c. 1293G>A; p.W402X) is present in up to 60% of patients with severe phenotype<sup>1</sup>
- Causes IDUA deficiency, leading to toxic accumulation of GAGs



## CLINICAL DE-RISKING

- AX-0422 corrects the W402X mutation back to WT
- Restores endogenous enzyme production, leading to GAGs clearance
- Potential to impact systemic and CNS disease



GAGs: glycosaminoglycans; MPS1: Mucopolysaccharidosis type I. 1Baldo G, et al, 2018, <https://doi.org/10.1111/cge.13224>

# Increases in IDUA enzymatic activity drive meaningful clinical impact

Severity

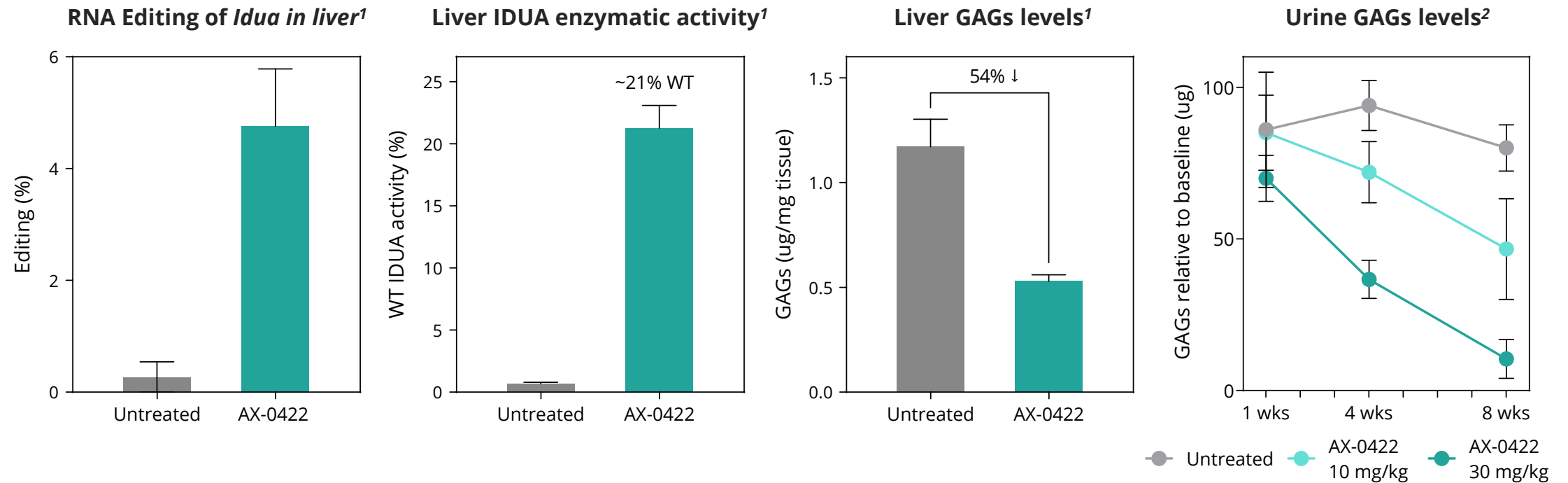


	Scheie	Hurler-Scheie	Hurler
Diagnosis	Teens	Childhood	< 18 months
Life expectancy	Normal	20 yo	10 yo
Enzymatic activity in fibroblasts (% of WT) <sup>1</sup>	<b>0.8%</b>	<b>0.3%</b>	<b>0.2%</b>

A restoration of 1-15% of normal IDUA enzymatic function<sup>2</sup> can improve phenotype

<sup>1</sup>Oussoren E, et al. *Mol Genet Metab.* 2013 Aug;109(4):377-81; <sup>2</sup>Kakkis ED, et al. *N Engl J Med.* 2001 Jan 18;344(3):182-8.

# RNA editing achieves therapeutically meaningful enzyme restoration in *Idua* mouse model



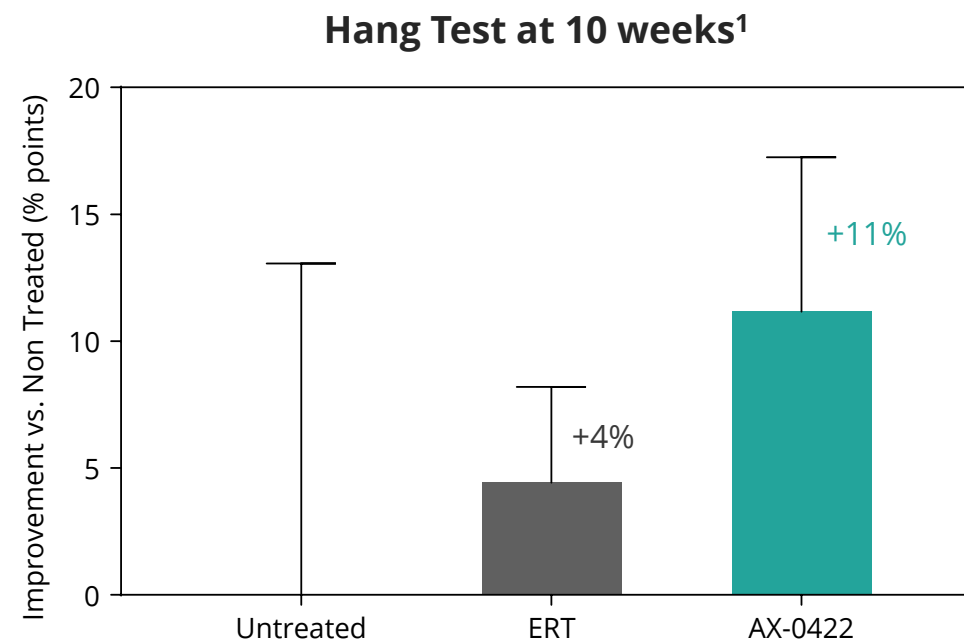
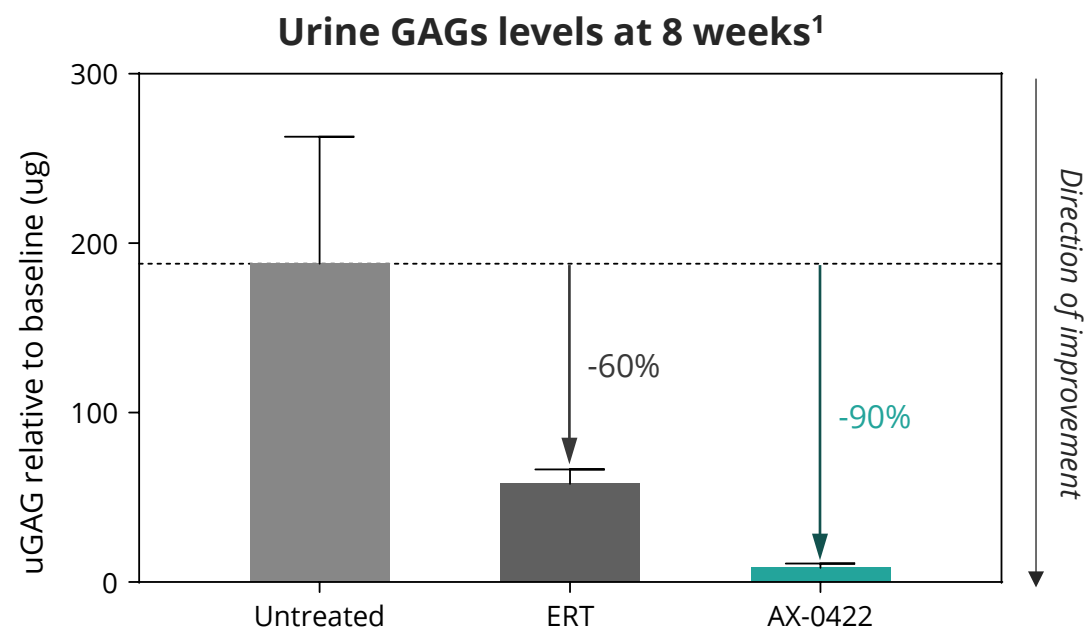
Following SC delivery, targeted editing of the nonsense mutation restores ~21% IDUA activity, driving substantial liver GAG reduction and dose-dependent normalization of urinary GAGs - **supporting potential for disease-modifying benefit**

<sup>1</sup>AX-0422 surrogate treatment of *Idua*-W392X mice, SC, 30 mg/kg, Q1W until 8 wks, data at 8 weeks, n=6, mean, SEM; <sup>2</sup>AX-0422 surrogate treatment of *Idua*-W392X mice, SC, 10 and 30 mg/kg, Q1W until 4 wks, n=4-6, mean, SEM

# AX-0422 shows differentiated activity vs standard of care in Idua mouse model



*Greater biomarker reduction and functional improvement vs ERT*



AX-0422 delivers reduction in urinary GAGs compared to ERT, approaching biomarker normalization

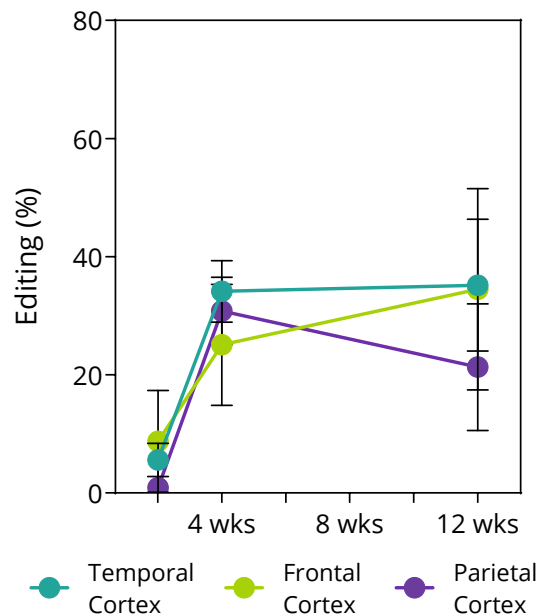
AX-0422 shows improvement in motor skills test compared to ERT

<sup>1</sup>Idua-W392X mice, AX-0422 surrogate treatment: SC, 30 mg/kg, ERT (Laronidase) treatment: IV, 0.58 mg/kg, Q1W until 4 wks, n=6, mean, SEM

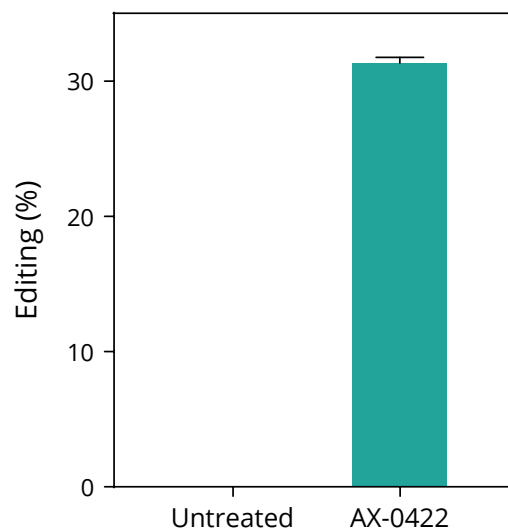
# AX-0422 achieves robust, durable CNS editing with functional enzyme restoration



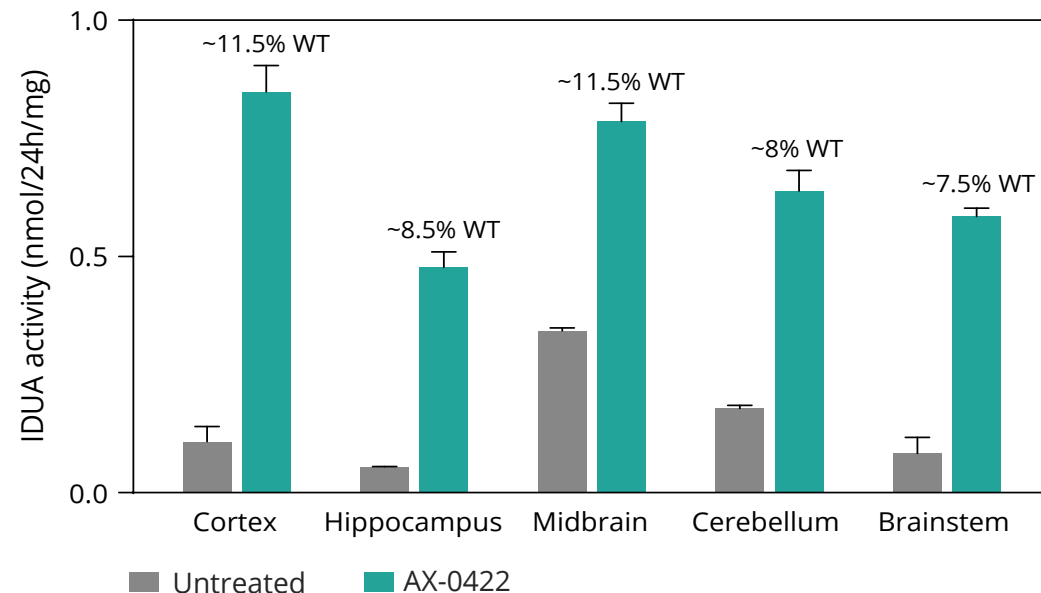
Sustained RNA editing of ACTB in cortex of NHP<sup>2</sup>



RNA Editing of *Idua* in cortex of *Idua*-W392X mice<sup>1</sup>



IDUA enzymatic activity in the brain of *Idua*-W392X mice<sup>1</sup> (% WT recovery)



- Axiomer results in sustained CNS editing of up to 12 weeks (single dose, NHP)
- Following ICV delivery, efficient editing in Hurler disease model leads to broad enzyme restoration across brain regions (~7–12% of WT)
- Levels consistent with disease-modifying potential in Hurler syndrome

<sup>1</sup>AX-0422 surrogate treatment of *Idua*-W392X mice ICV, 250µg, single dose, n=6, 4 weeks, ddPCR, mean, SEM / western blot, mean, SEM; <sup>2</sup>IT administration, 10.6mg AX-0422 surrogate treatment, single dose, n=3, up to 12 weeks, ddPCR, mean, SD

# AX-0422 preliminary clinical development

*A two-step approach with liver delivery followed by CNS delivery*

## Subcutaneous administration for Liver



## Intrathecal administration for CNS



- Primary objective: safety, tolerability
- Secondary: pharmacokinetics
- Exploratory PD and clinical measures: plasma IDUA enzyme activity and protein level; HS and DS levels
- Development candidate selected
- CTA filing in early 2027
- First-in-human trial clinical biomarker data in patients in H1 2027

DS: dermatan sulfate; HS: heparan sulfate

# AX-2911 RNA editing therapy to address metabolic dysfunction-associated steatohepatitis (MASH)



## MASH

- Highly prevalent and increasing worldwide
- Progression to cirrhosis, liver cancer and liver-related mortality
- Limited treatment options<sup>1</sup> highlight the significant unmet medical need, particularly in lean MASH patients



## PNPLA3 I148M

*Patatin-like phospholipase domain-containing<sup>3</sup> variant*

- Strongest genetic risk factor for disease progression
- ~50% of MASH patients<sup>2-4</sup>
- Associated with higher liver fat, NASH risk, and fibrosis progression
- Carriers may show reduced response to GLP-1 agonists<sup>5</sup>



## RESTORING WT-LIKE PNPLA3

- AX-2911 restores PNPLA3 I148M (Met→Val) function
- Targets MASH primary genetic driver, unlike metabolic therapies
- Broad potential, including GLP-1-low response and lean MASH patients



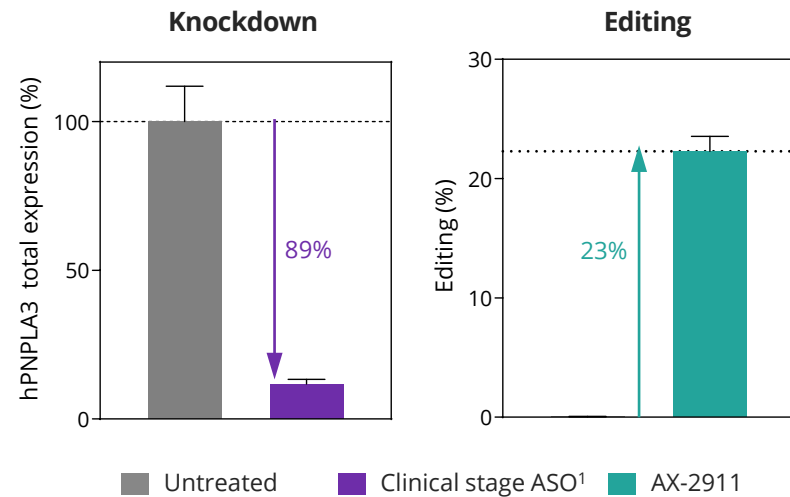
<sup>1</sup>Sandireddy R, et al. Front Cell Dev Biol. 2024 Jul 16;12:1433857; <sup>2</sup>Tsedendorj Yumchinsuren et al., 2025; <sup>3</sup>Sookoian Silvia et al., 2011; <sup>4</sup>Souza Matheus et al., 2024; <sup>5</sup>Chen, Yunzhi et al, 2020

# Editing has functional advantage over knockdown

*AX-2911 substantially reduces liver fat vs clinical-stage ASO<sup>2</sup>*

## mRNA

**hPNPLA3 I148M humanized mouse liver model<sup>1</sup>**  
*dPCR (Qiagen), AVG±SEM*

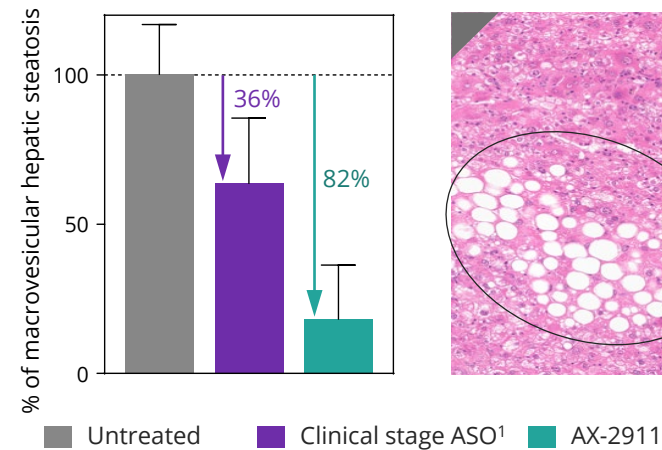


Clinical-stage ASO<sup>2</sup>:  
 ~89% mRNA reduction  
 via knockdown of  
*hPNPLA3*

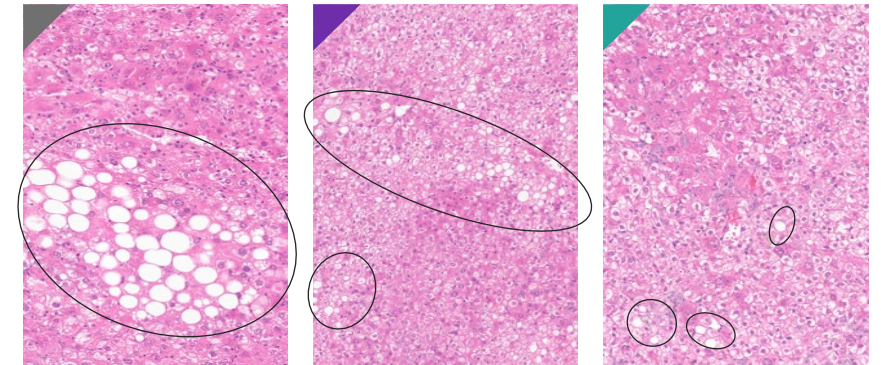
AX-2911 leads to **23%**  
 editing of  
*hPNPLA3* mRNA

## LIVER FUNCTION (steatosis)

**Macrovesicular steatotic  
 incidence scoring<sup>1</sup> (%)**  
*AVG±SEM*



**Liver sections of steatosis mouse model  
 treated with ASO<sup>2</sup> or AX-2911<sup>1</sup>**  
*PNPLA3 I148M humanized FRG mouse, WD 4W+4W*



**82%** reduction of  
 macrovesicular lipid  
 droplets

Untreated

Clinical-stage  
 ASO<sup>2</sup>

AX-2911

<sup>1</sup>N=4-6, 20mg/kg, 14 doses, GalNAc conjugated-AX-2911 or 0.7mg/kg, 14 doses, AZ AZD2693 treatment, SC, readout at day D28; <sup>2</sup>AZ AZD2693 previously evaluated in Phase 2b

# AX-2911 development strategy

*Exploring an Investigator-Initiated Trial (IIT) in China*



## OBJECTIVE

*Generate early proof-of-concept in patients*

*De-risk the program and inform development strategy*



## ACCELERATED APPROACH

*Parallel preparation for global CTA/IND development*



## EXPECTED TIMELINE

*FIH in H1 2027*

*Interim readouts to guide next steps*

# Upcoming milestones

*positioned for value creation*



## **AX-0810**

*Target engagement data in Q2 2026*



## **AX-0811**

*Entering the clinic with initial data expected by year-end 2026*



## **BILIARY ATRESIA**

*Pediatric study (IIT, China) initial data targeted for H1 2027*



## **AX-0422**

*Advancing toward initial patient data in H1 2027*



## **AX-2911**

*Progressing to first-in-human study (IIT, China) in H1 2027*



## **LILLY**

*Lilly collaboration driving potential data updates and milestones*



## **CASH RUNWAY**

*Into mid 2027,  
supporting  
multiple clinical  
catalysts within  
the runway*



**IT'S IN  
OUR RNA**