ProQR®

EXPANDING THE AXIOMER™ RNA EDITING OPPORTUNITY BEYOND AX-0810

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Agenda

Agenda

Welcome & Agenda

Sarah Kiely

Opening Remarks

Daniel A. de Boer

Platform and Pipeline Programs

Cristina Lopez Lopez
Gerard Platenburg

Corporate Outlook

Dennis Hom

Q&A

Daniel A. de Boer
Cristina Lopez Lopez
Gerard Platenburg
Dennis Hom

Speakers

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Founder & CEO

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Chief Medical Officer

Dennis Hom
Chief Financial Officer

Gerard Platenburg
Chief Scientific Officer

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 and Phase 1b of the 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 the Phase 1b cohort 1 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.

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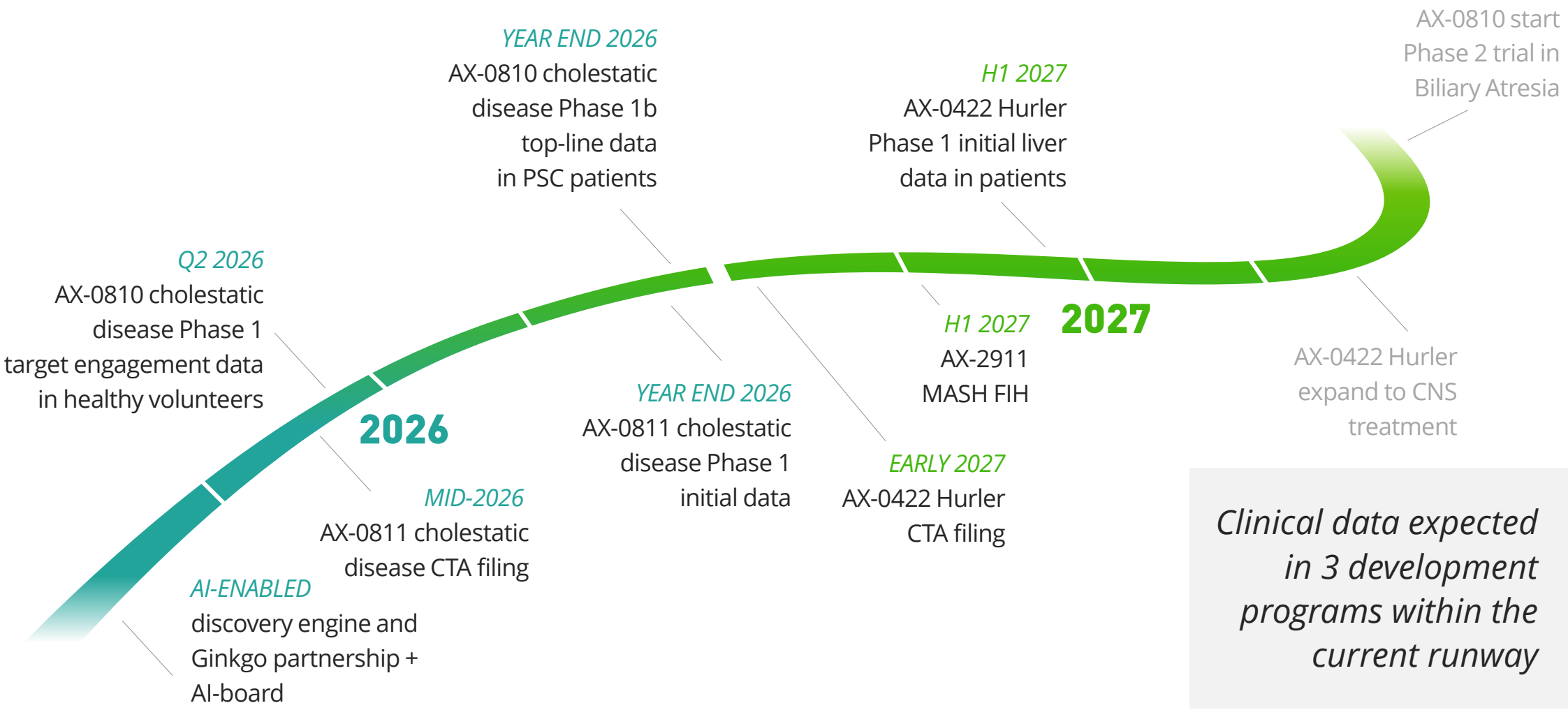
Strategic Overview

Presenter: Daniel A. de Boer

Multiple clinical catalysts within the runway

Core focus on cholestatic development, with value creating pipeline beyond



Clinical data expected in 3 development programs within the current runway

Pipeline Programs

Presenters: Cristina Lopez Lopez & Gerard Platenburg

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[1,2]

BILE ACID TOXICITY

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

NTCP MODULATION STRATEGY

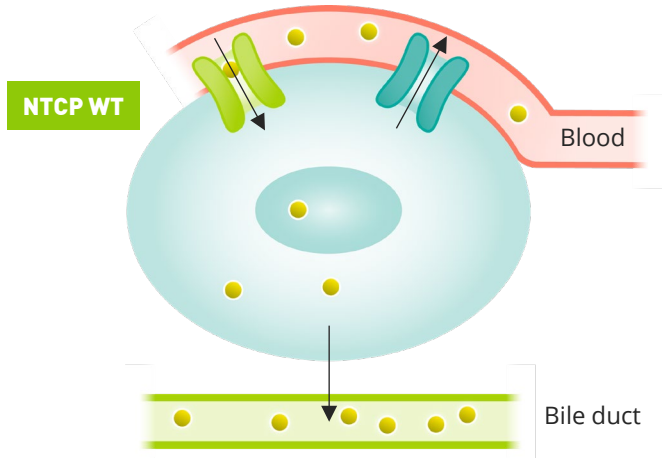
- Human genetics supports NTCP modulation as hepato-protective mechanism to reduce bile acid reuptake and protect liver

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

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

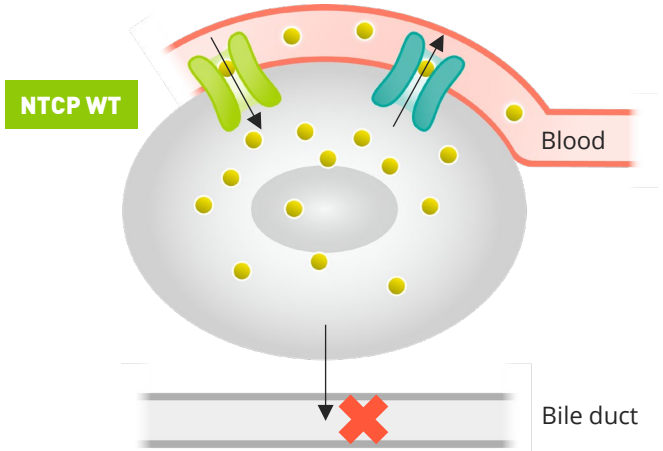
HEALTHY LIVER

Normal bile acids homeostasis in hepatocytes



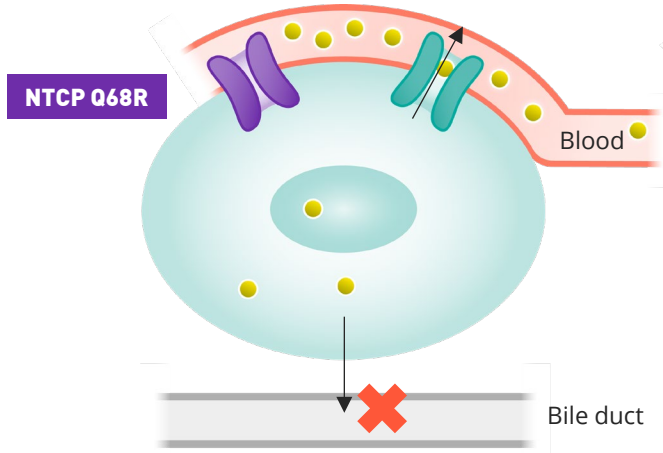
LIVER WITH CHOLESTATIC DISEASE

High concentration of bile acids in hepatocytes



AX-0810 STRATEGY FOR DISEASED LIVER

AX-0810 restore bile acids homeostasis in the hepatocytes

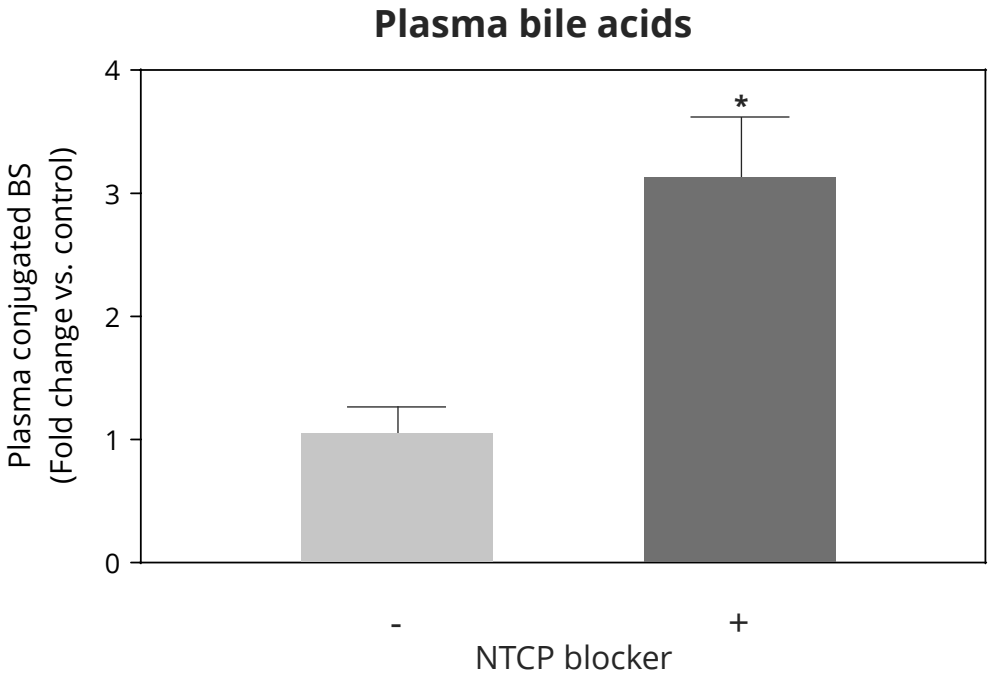


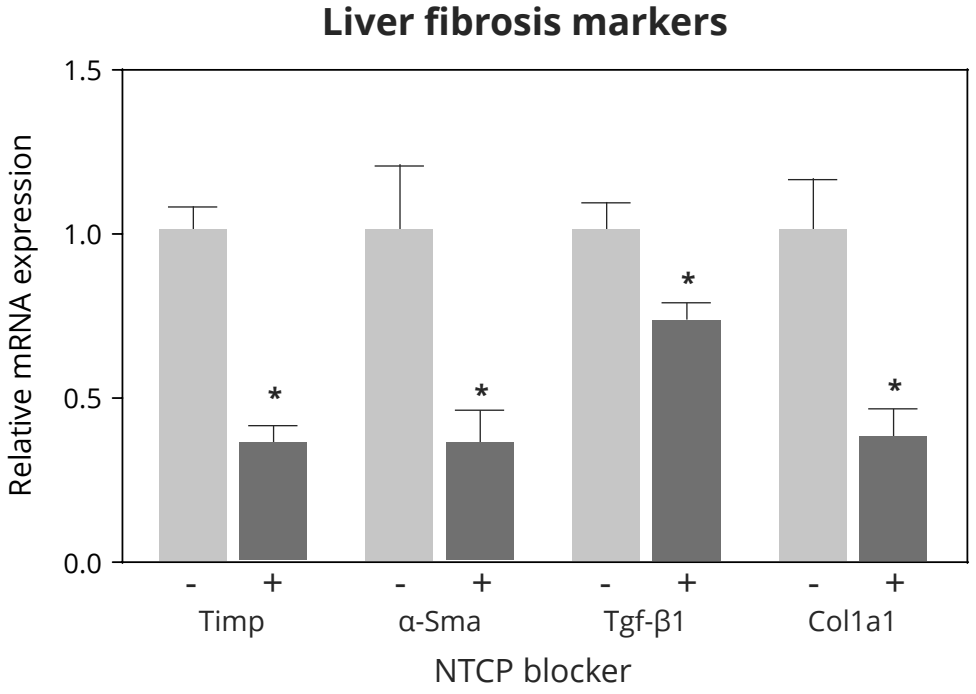
↓ *hepatocyte toxicity*

↓ *inflammation/ fibrosis*

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





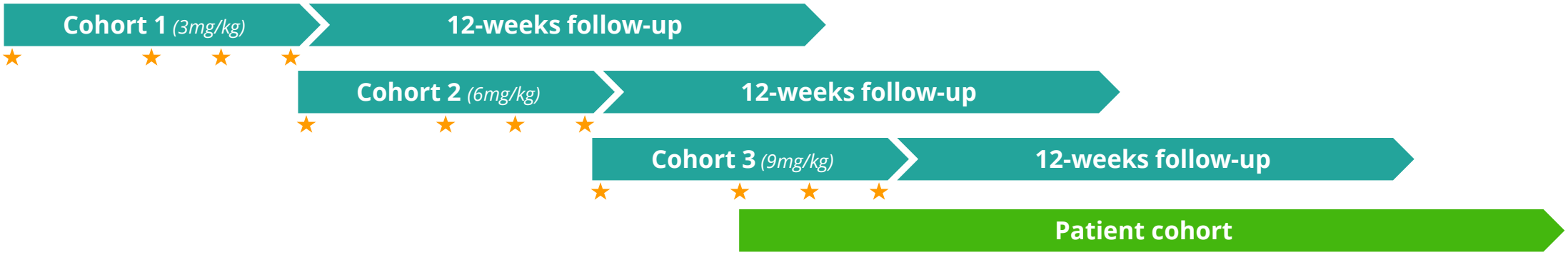
NTCP channel blocking **increases plasma bile acids concentrations,** up to 3-fold in cholestatic disease mouse model

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.

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

Multiple ascending dose (MAD) N=33 (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	POPULATION	SYMPTOMS	PROGRESSION	STANDARD OF CARE	SIGNIFICANT UNMET NEED
Pediatric: in the first weeks of life	*Approximately 20,000 patients worldwide*	*Jaundice, poor weight gain, pale stool, dark urine*	*Rapid progression to cirrhosis and portal hypertension early in life*	*Kasai procedure as first-line therapy*	*No approved pharmacological treatments; 60-80% require liver transplant despite Kasai*

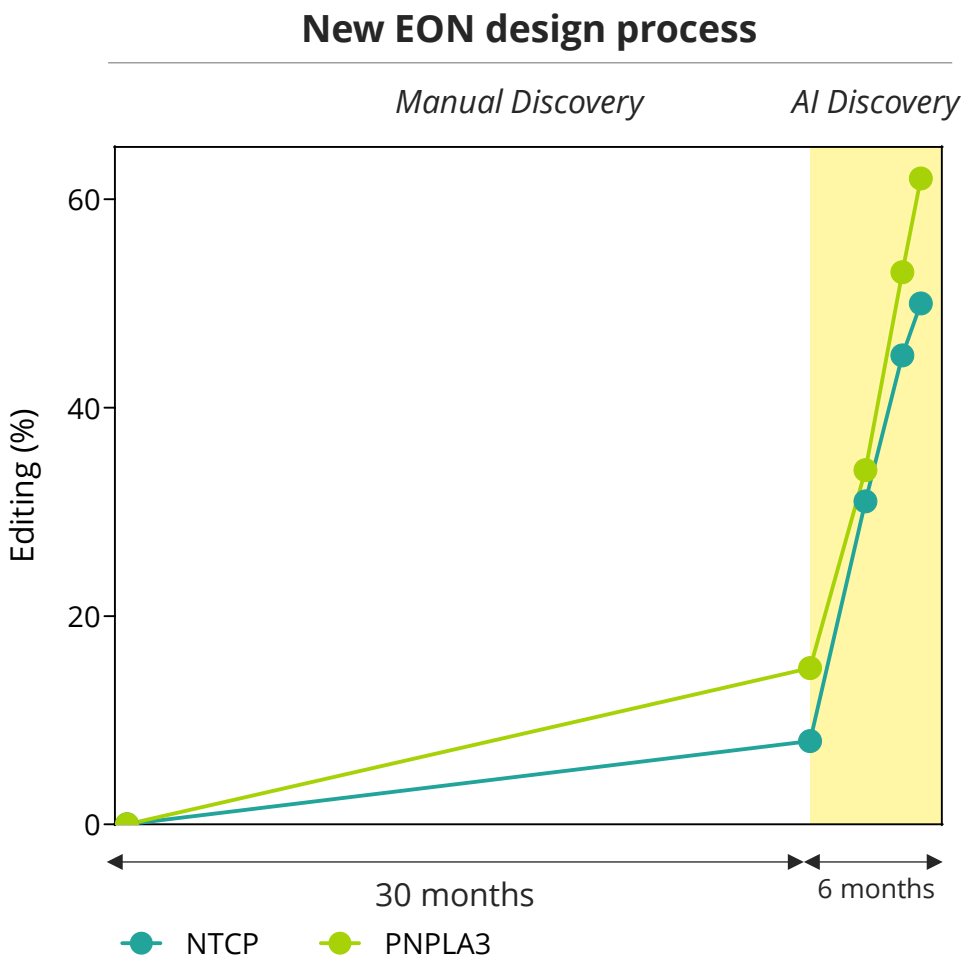
Adike A, et al. Expert Rev Gastroenterol Hepatol. 2018 Oct;12(10):1025-1032; Verkade HJ, et al. J Hepatol. 2016 Sep;65(3):631-42; Sundaram SS, et al. Liver Transpl. 2017 Jan;23(1):96-109; Raghu VK, et al. Liver Transpl. 2021 May;27(5):711-718; NORD, 2019, Japanese Biliary Atresia Society. Japanese Biliary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

Biliary atresia as primary indication for AX-0810

BILIARY ATRESIA				
SEVERITY AND UNMET NEED	**BIOLOGICAL RATIONALE**	**CLINICAL DE-RISKING**	**CENTRALIZED CARE**	**REGULATORY PATHWAY**
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

AI-guided EON design accelerates discovery

~90% faster discovery and up to 6× improvement in EON performance



Trained on 12+ years of

PROPRIETARY AXIOMER DATA

Trained on experimentally-validated editing outcomes of numerous EONS and targets

AI enables discovery of

BETTER-PERFORMING EONs

Models trained on our in-house data generate EONs with higher editing efficiency and greater sequence diversity

Robotics-enabled HTS

ACCELERATES DESIGN-TEST CYCLES

Enabling rapid iteration per target and amplifying AI-driven learning through continuous model improvement

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

~3x higher editing efficiency

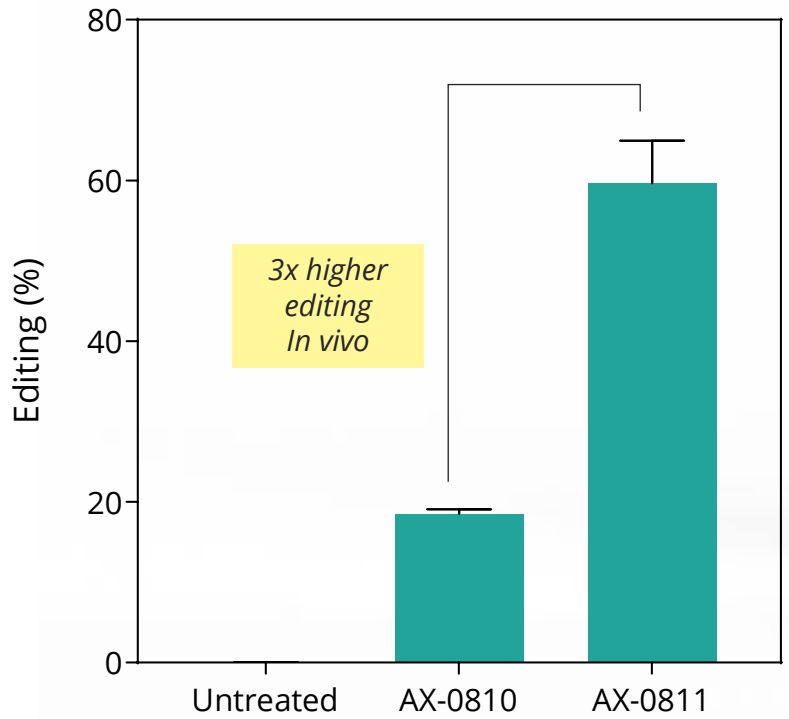
- Improved efficacy and dosing convenience over AX-0810

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



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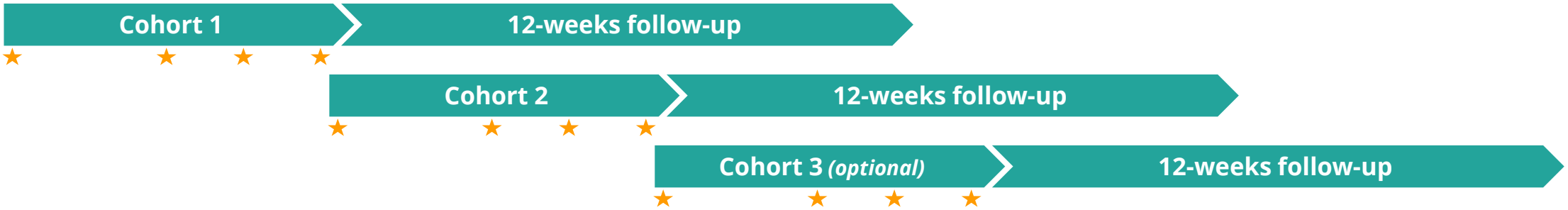

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CTA enabling activities ongoing

- 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

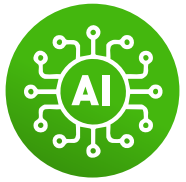
AX-0810

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[1]
- 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: glycosaminogylcans; 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

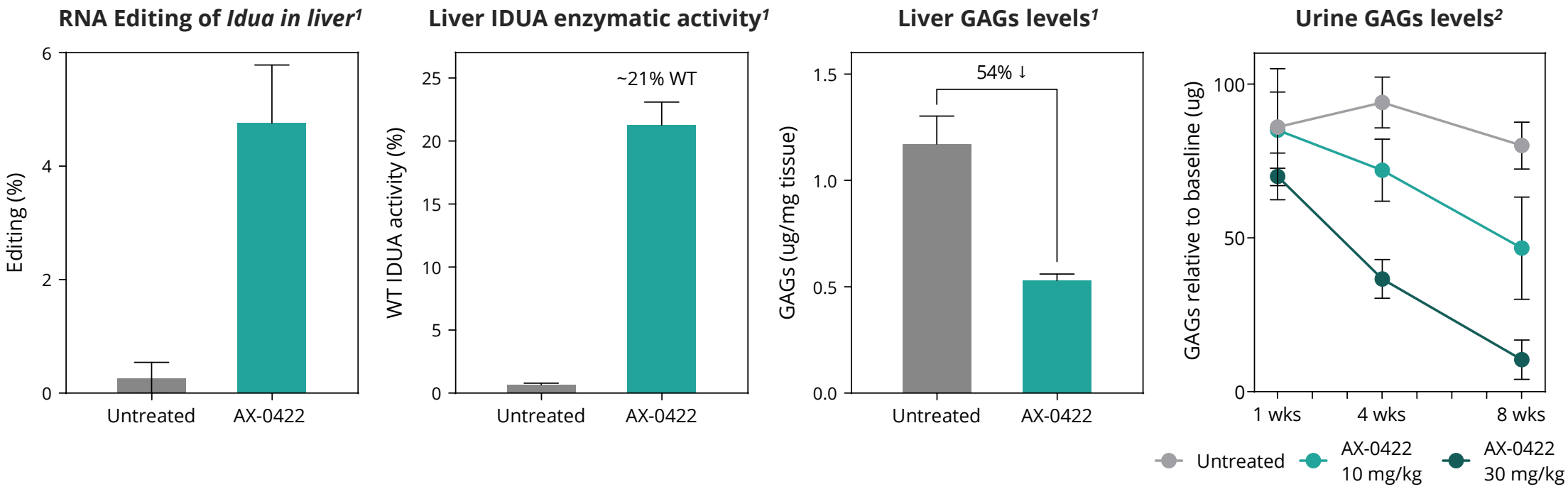
Severity →

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

A restoration of 1-15% of normal IDUA enzymatic function[2] can improve phenotype

[1]Oussoren E, et al. Mol Genet Metab. 2013 Aug;109(4):377-81; [2]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



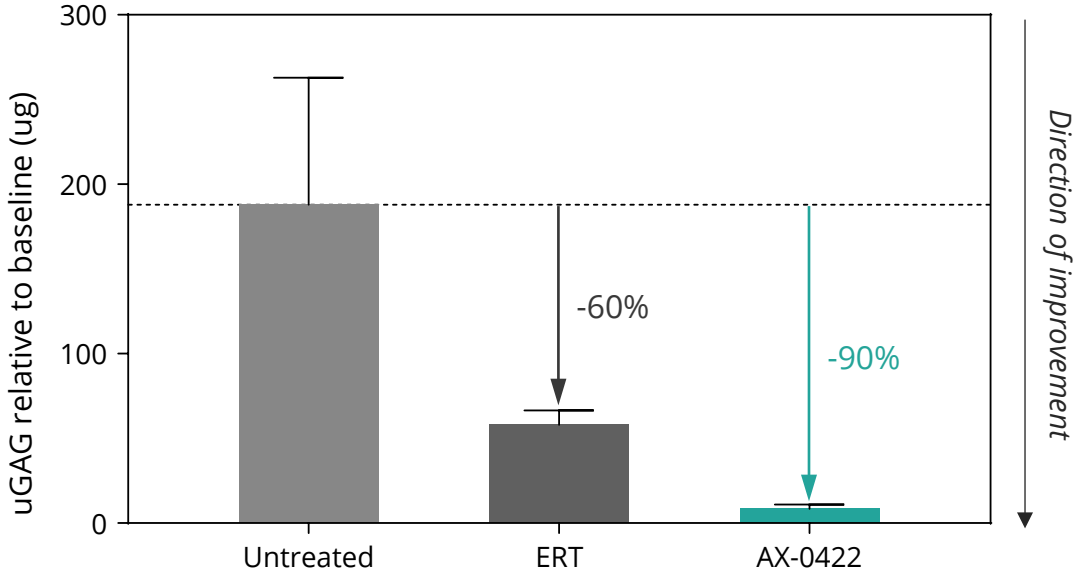
Following SC delivery, targeted editing of the W402X mutation restores ~21% IDUA activity, driving substantial liver GAG reduction and dose-dependent normalization of urinary GAGs - **supporting potential for disease-modifying benefit**

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

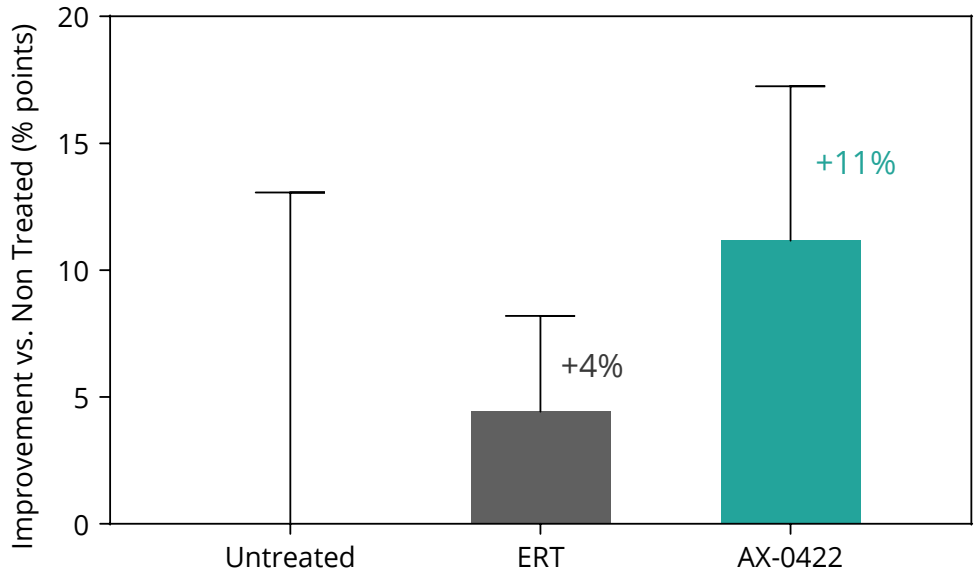
AX-0422 shows differentiated activity vs standard of care in *Idua* mouse model

Greater biomarker reduction and functional improvement vs ERT

Urine GAGs levels at 8 weeks[1]



Hang Test at 10 weeks[1]



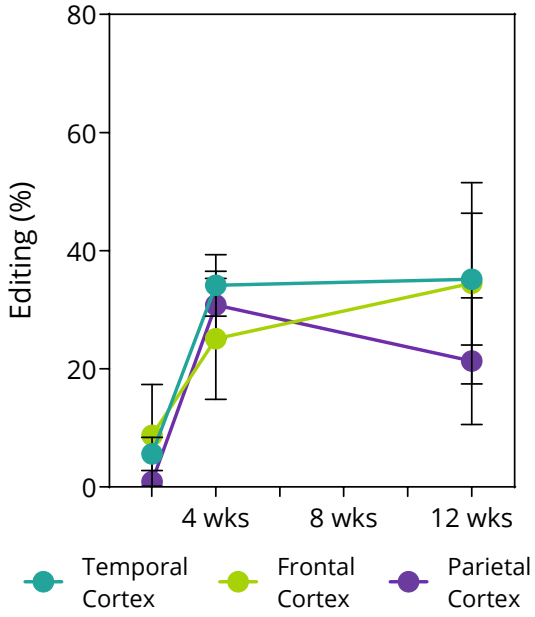
AX-0422 delivers reduction in urinary GAGs compared to ERT, approaching biomarker normalization

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

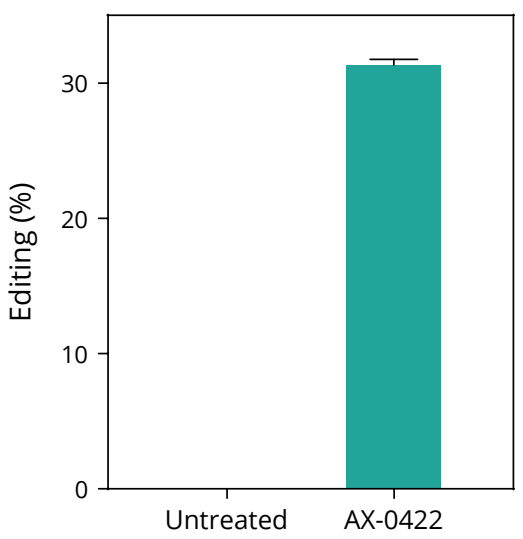
[1]*Idua-W392X mice, AX-0422 surrogate treatment: SC, 30 mg/kg, ERT (Laronidase) treatment: IV, 0.58 mg/kg, Q1W until 4 wks, n=6, mean, SEM*

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

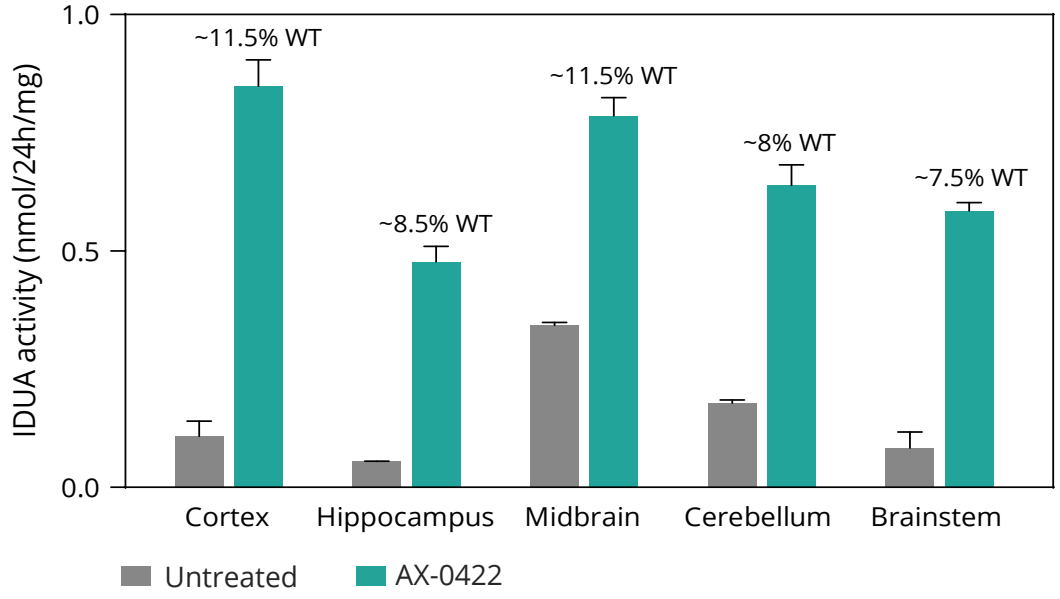
Sustained RNA editing of ACTB in cortex of NHP[2]



RNA Editing of *Idua* in cortex of Idua-W392X mice[1]



IDUA enzymatic activity in the brain of *Idua*-W392X mice[1] (% 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

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

AX-0422 positioned to redefine the standard of care in Hurler Syndrome

Positioned to deliver systemic and neurological benefit through a single, targeted mechanism

DIFFERENTIATED APPROACH

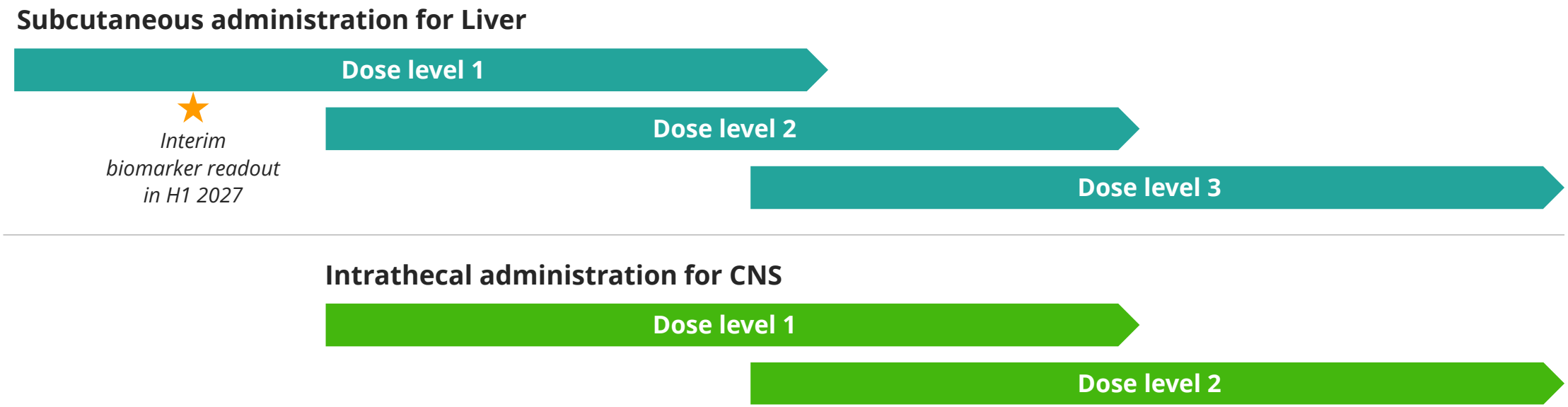
- Impact liver and neurological driven symptoms
- Convenient, infrequent dosing potential
- Avoids limitations of SoC

HIGH AXIOMER PLATFORM POTENTIAL

- RNA editing restores endogenous enzyme production
- Preclinical data show relevant enzyme restoration, biomarker and functional improvement

AX-0422 preliminary clinical development

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



- 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[1] highlight the significant unmet medical need, particularly in lean MASH patients

PNPLA3 I148M

Patatin-like phospholipase domain-containing[3] variant

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

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

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

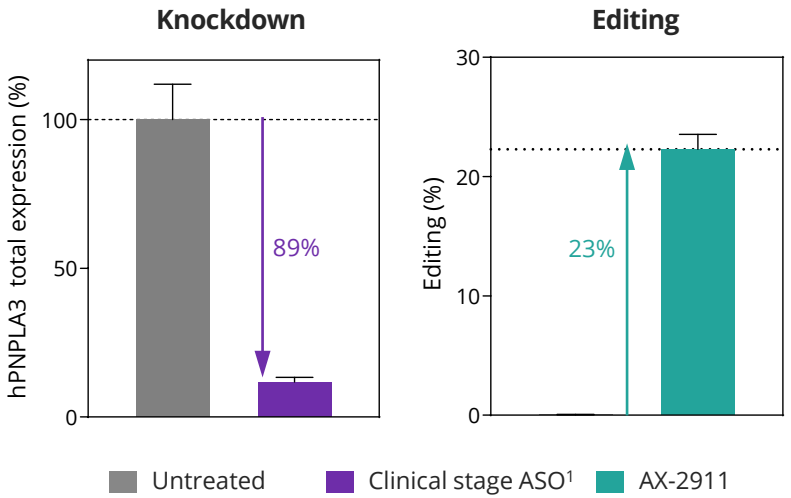
Editing has functional advantage over knockdown

AX-2911 substantially reduces liver fat vs clinical-stage ASO[2]

mRNA

hPNPLA3 I148M humanized mouse liver model[1]

dPCR (Qiagen), AVG±SEM



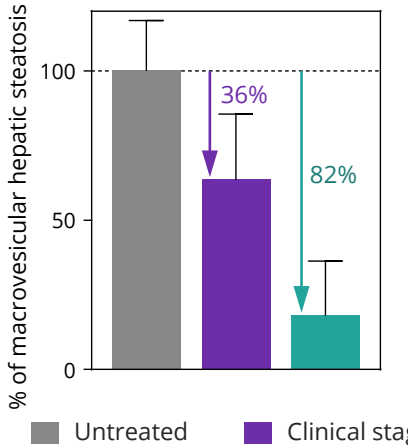
Clinical-stage ASO[2]: **~89%** mRNA reduction via knockdown of *hPNPLA3*

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

LIVER FUNCTION *(steatosis)*

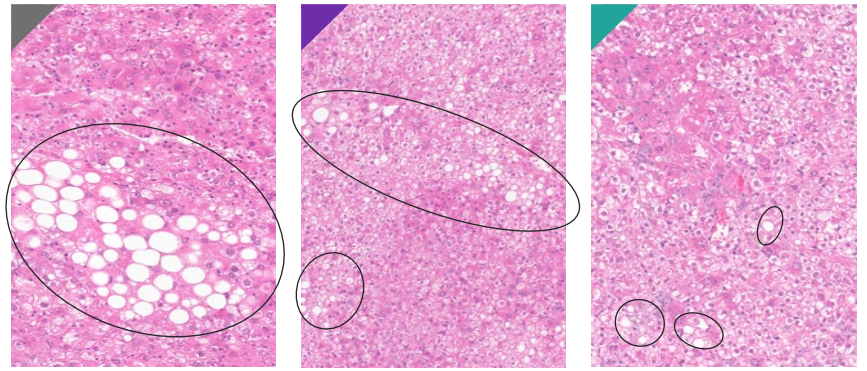
Macrovesicular steatotic incidence scoring[1] (%)

AVG±SEM



Liver sections of steatosis mouse model treated with ASO[2] or AX-2911[1]

PNPLA3 I148M humanized FRG mouse, WD 4W+4W



82% reduction of macrovesicular lipid droplets

Untreated

Clinical-stage ASO[2]

AX-2911

[1]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; [2]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

ProQR development pipeline and milestones

	TARGET	AXIOMER APPLICATION	DISCOVERY	NON-CLINICAL	CLINICAL	MILESTONES	ESTIMATED POPULATION
DEVELOPMENT PIPELINE							
AX-0810 *for Cholestatic diseases*	NTCP	*Modulate*				Target engagement data 1H 2026	~100K patients
AX-0811 *for Cholestatic diseases*	NTCP	*Modulate*				Target engagement data in 2026	
AX-0422 *for Hurler Syndrome*	IDUA	*Correct*				CTA filing early 2027; Clinical biomarkers in H1 2027	~500-1000 patients
AX-2911 *for MASH*	PNPLA3	*Correct*				FIH H1 2027	~8M patients
AX-2402 *for Rett syndrome*	MECP2 R270X	*Correct*					RETT SYNDROME RESEARCH TRUST ~5K
PARTNERED PIPELINE							
10 undisclosed targets (option to expand to 15)			*Progress undisclosed*				Lilly

ProQR®

IT'S IN OUR RNA