ProQR®

DEVELOPING RNA-EDITING MEDICINES

for patients in need

Nasdaq: PRQR

January 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 planned Phase 1 clinical study of AX-0810 in NTCP for cholestatic diseases, including the planned trial design, implementation and initiation in the Netherlands, and our ability to recruit for and complete a Phase 1 clinical trial for AX-0810 in healthy volunteers; 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 Q4 2025, and clinical updates across multiple programs in 2025; 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; 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.

Axiomer™ advancing
to value inflection

EON-GUIDED ADAR RNA EDITING, INVENTED BY PROQR

Now translating Axiomer in clinic

Foundational IP estate securing long-term leadership in the field

DIFFERENTIATED PIPELINE FOR RANGE OF HIGH UNMET NEEDS

AX-0810 Phase 1 trial continuing dosing following initial saftey/PK

ProQR leading neurological application of RNA editing; robust and durable efficiency across regions of CNS

HIGH IMPACT STRATEGIC PARTNERSHIPS

With Eli Lilly, Rett Syndrome Research Trust

Accelerating development and creating meaningful value for patients

OVER A DECADE OF RNA THERAPY LEADERSHIP

With experienced team and further strengthened management to drive the future of ProQR

RUNWAY INTO MID 2027

Funding the clinical readout of multiple programs

€ 106.9 million cash and cash equivalents as of end of Q3 2025

ProQR development pipeline

	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[1] patients
AX-2402 *for Rett syndrome*	MECP2 R270X	*Correct*				✓ Candidate selected	~5K patients
AX-2911 *for MASH*	PNPLA3	*Correct*				✓ Candidate selected	~8M patients
AX-1412 *for Cardiovascular disease*	B4GALT1	*Protect*					~200M[2] patients
DISCOVERY PIPELINE							
Multiple programs in liver and CNS							
PARTNERED PIPELINE							
10 targets (option to expand to 15)	Undisclosed		*Progress undisclosed*				Lilly

[1]Approximately 100K people affected with Primary Sclerosing Cholangitis and Biliary Atresia in US and EU5. [2]Approximately 200 million people suffer from too high a level of cholesterol in US and EU5; SLC10A1 is the gene that encodes for NTCP protein; CVD: Cardiovascular Diseases, NASH: Nonalcoholic steatohepatitis, | References: Trivedi PJ, et al. Clin Gastroenterol Hepatol. 2022 Aug;20(8):1687-1700.e4; Schreiber RA, et al. J Clin Med. 2022 Feb 14;11(4):999; Tsao CW, et al. Circulation. 2022;145(8):e153–e639. World Health Organization, World Gastroenterology Organization

ProQR corporate outlook
for 2026

AX-0810 (NTCP, CHOLESTATIC DISEASE)

Report target engagement data from AX-0810 Phase 1 trial in healthy volunteers in first half of 2026; Initiate patient cohort in the AX-0810 Phase 1 trial following the healthy volunteer cohorts

AX-2402 (MECP2 R270X, RETT SYNDROME)

Advance development activities for first-in-human trial to start in first half of 2027

EARLIER STAGE PROGRAMS AND PLATFORM

Disclose additional preclinical data across earlier-stage programs, highlighting continued productivity and versatility of the Axiomer platform

LILLY COLLABORATION

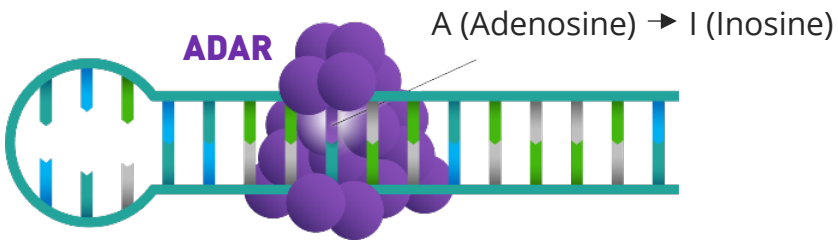
Continue to execute on partnership with Eli Lilly, with potential data updates and milestone income from the ongoing collaboration

FINANCIAL STRENGTH

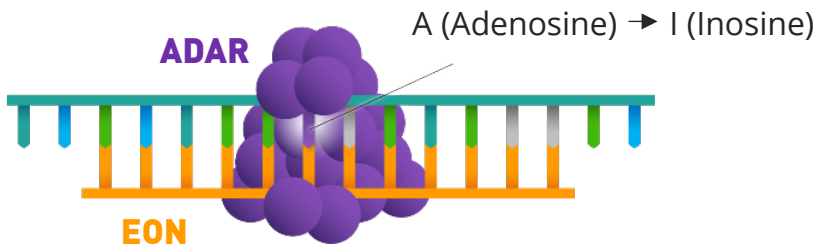
Continue to strengthen balance sheet and evaluate potential partnerships to maximize platform value

How Axiomer™ edits RNA

NATURAL ADAR EDITING



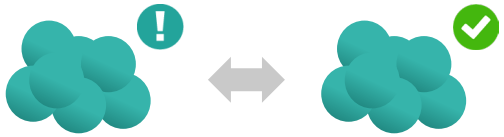
EDITING OLIGONUCLEOTIDE *(EON)-directed* EDITING



MODULATE

Modify protein function

CORRECT



Correct disease-causing mutations

PROTECT

Introduce protective variants

Addressing unmet need in cholestatic diseases through NTCP modulation

Cholestatic diseases have high unmet medical need, especially **Primary Sclerosing Cholangitis** affecting adults (~80,000 patients) and Congenital **Biliary Atresia** affecting pediatrics early in life (~20,000 patients). Both conditions have no approved therapies and may require liver transplantation.[1,2]

Patients **accumulate bile acids** in liver leading to fibrosis and ultimately liver failure.

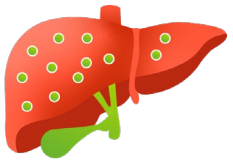
Learnings from human genetics and literature demonstrate that **modulation of the NTCP channel** responsible for majority of bile acids re-uptake in liver cells could lead to **hepato-protective effects**.

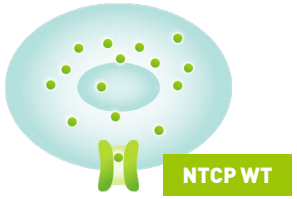
NTCP, sodium taurocholate co-transporting polypeptide. References: [1]Trivedi PJ, et al. Clin Gastroenterol Hepatol. 2022 Aug;20(8):1687-1700.e4; [2]Schreiber RA, et al. J Clin Med. 2022 Feb 14;11(4):999

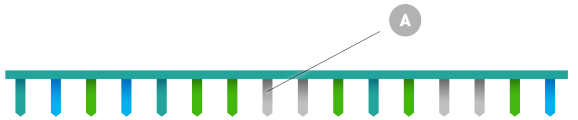
AX-0810: first-in-class RNA editing therapy targeting NTCP for cholestatic diseases

LIVER WITH CHOLESTATIC DISEASE

High concentration of bile acids in hepatocytes

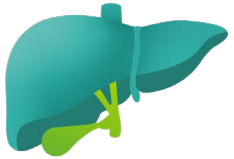


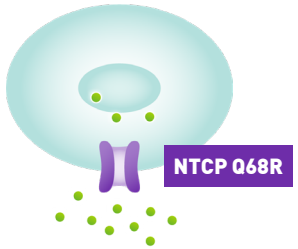


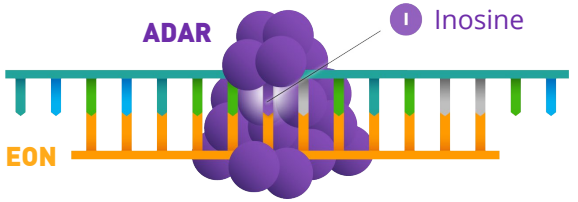


AX-0810 STRATEGY FOR DISEASED LIVER

AX-0810 modifies the NTCP channel to limit bile acids uptake while preserving all other functions of the channel







- AX-0810 makes an A-to-I edit that mimics a variant to enable lower bile acids concentration in hepatocytes
- AX-0810 is designed to be a disease-modifying treatment

Therapeutic goals

- Reduce inflammation and fibrosis from bile acids toxicity
- Alleviate symptoms in PSC and BA
- Prevent or delay cirrhosis, organ failure, and transplant

ADAR, Adenosine Deaminase Acting on RNA; BA, Biliary atresia; EON, Editing Oligonucleotide; NTCP, sodium taurocholate co-transporting polypeptide; PSC, Primary Sclerosing Cholangitis; WT, Wild Type.

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[1-3]

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[4-5]

IN CLINIC

Clinical PoC with bulevirtide in Ph3 Hepatitis D trial, for which liver improvement occur in patients, even without virologic response[6-8]

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.

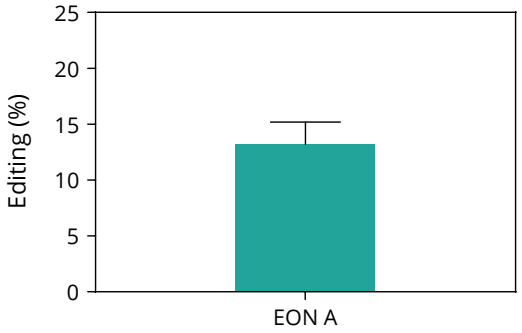
[1]Ho RH, et al. J Biol Chem. 2004 Feb 20;279(8):7213-22; [2]Vaz FM, et al. Hepatology. 2015 Jan;61(1):260-7; [3]Schneider AL, et al. Clin Res Hepatol Gastroenterol. 2022 Mar;46(3):101824; [4]Slijepcevic D, et al. Hepatology. 2018 Sep;68(3):1057-1069; [5]Salhab A, et al. Gut. 2022 Jul;71(7):1373-1385; [6]Wedemeyer H, et al. N Engl J Med. 2023 Jul 6;389(1):22-32; [7]Wedemeyer H, J Hepatol. 2024 Oct;81(4):621-629.; [8]Dietz-Fricke C, JHEP Rep. 2023 Mar 15;5(4):100686.

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

EDITING EFFICIENCY

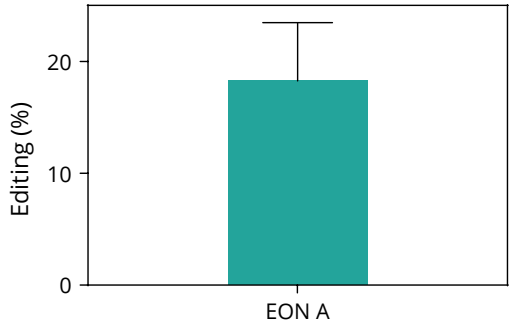
NTCP RNA Editing in Humanized Mice

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



NTCP RNA Editing in NHP

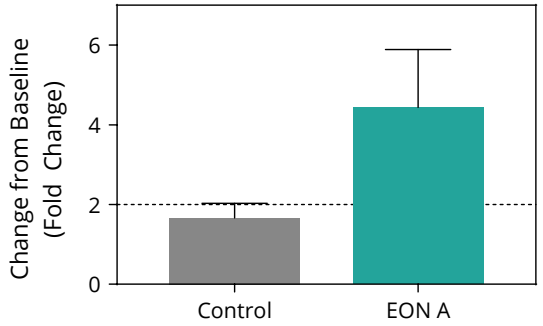
(N=1, 1-4mg/kg, 4 doses, LNP formulation, IV, up to D46, ddPCR)



PLASMA TOTAL BILE ACIDS

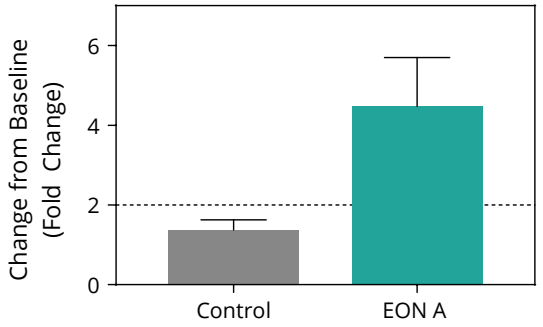
Plasma TBA in Humanized Mice

(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)

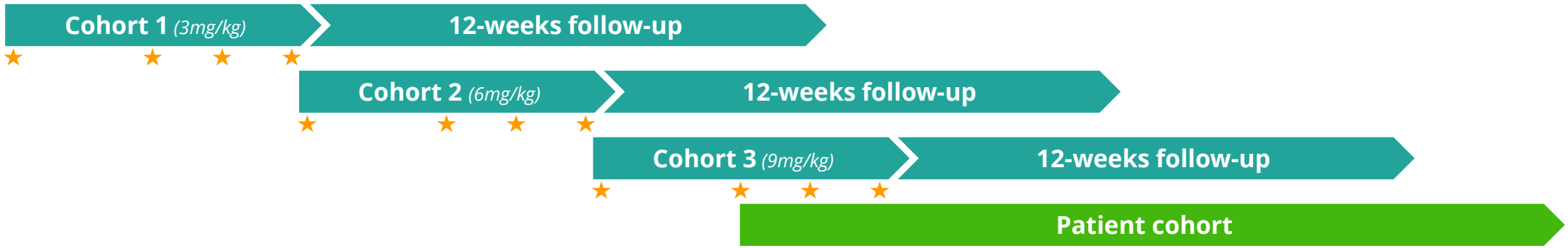


- EON A results in consistent editing data in humanized mouse model and NHP *in vivo* with approx. 15% editing reaching expected NTCP modulation
- Reaching >2-fold changes in biomarkers - expected impact on plasma bile acids levels following NTCP EON treatment

AX-0810 first-in-human (FIH) Phase 1 trial

Dosing healthy volunteers to assess safety, tolerability, PK, and biomarker-based target engagement of AX-0810

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
- Phase 1 enrollment and dosing in healthy volunteers ongoing

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).

AX-2402 RNA editing therapy targeting MECP2 for Rett Syndrome

Rett Syndrome is a **severe neuro-developmental** disorder caused by variants in the transcription factor Methyl CpG binding protein 2 (MECP2) with high unmet need for a disease modifying therapy.

Nonsense variants lead to **severe phenotypes and affect ~1/3** of **patients** (**~20,000 individuals** in US/EU.[1,2])

Rett Syndrome is not a neuro-degenerative disorder. Restoring MECP2 protein levels **reversed** symptoms in mice.[3]

AX-2402 aims to restore the **normal level of MECP2 protein**, enabling disease modification

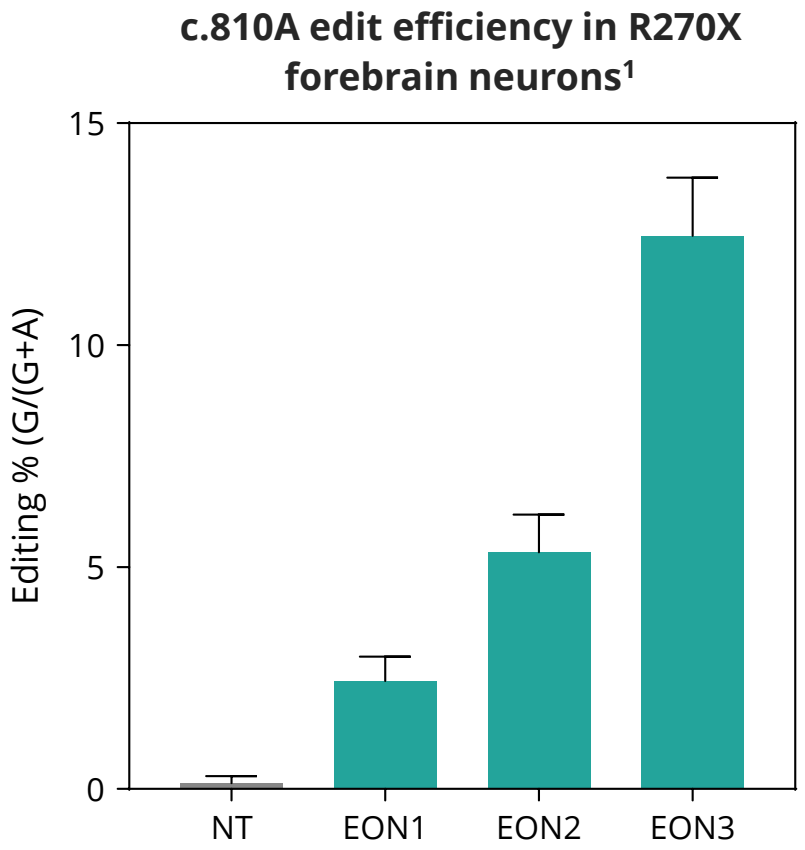
Development candidate selected; first-in-human trial planned **H1 2027**

$9.2M partnership with Rett Syndrome Research Trust

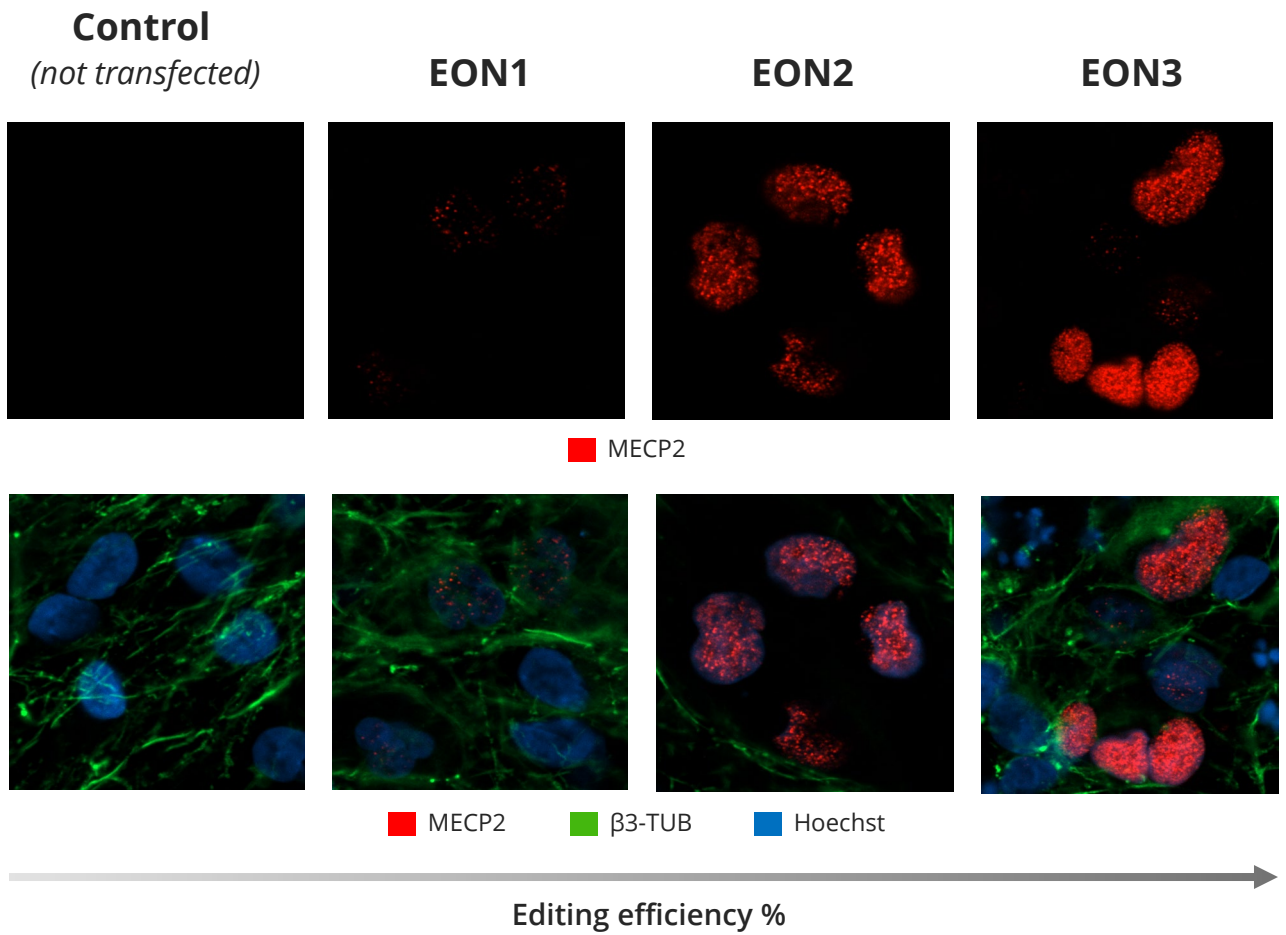
[1]Krishnaraj R, et al. Hum Mutat. 2017 Aug;38(8):922-93; [2]RSRT 2023 conference; [3]Guy J, et al. Science. 2007 Feb 23;315(5815):1143-7.

AX-2402 restores MECP2 protein in Rett neurons

Higher RNA editing efficiency shows greater MECP2 protein restoration in hiPSC-derived neurons of Rett Syndrome patients

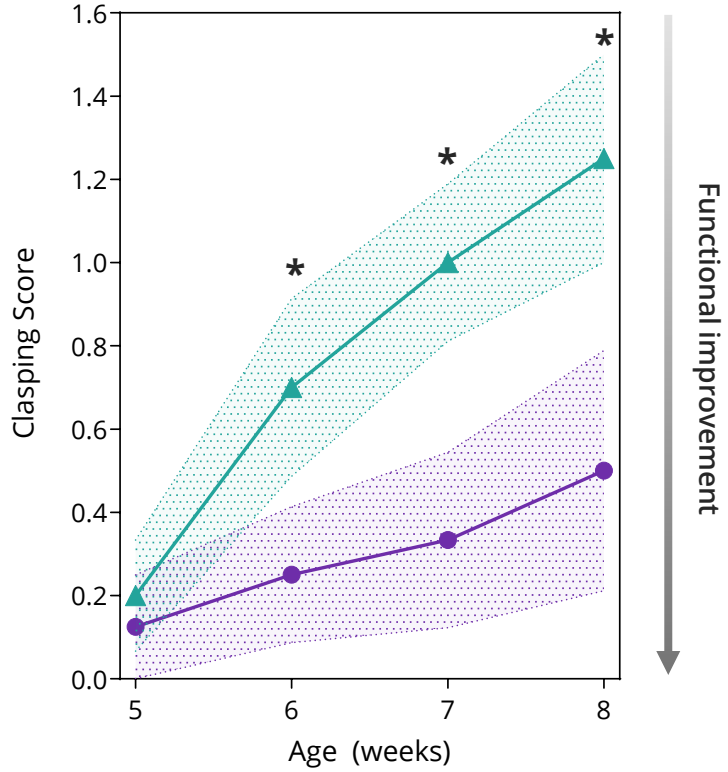


[1]*TF (RNAimax), 100nM, 11d, N=3, Avg +/-SD*



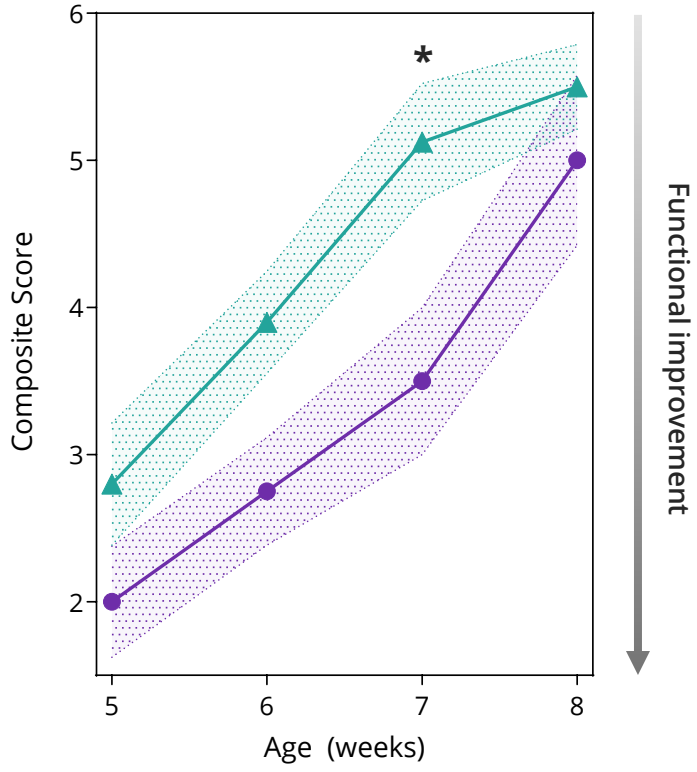
AX-2402 reverses disease in a severe Rett mouse model

Hindlimb clasping score
(Mean ± SEM)



AX-2402 improves motor deficits[2] sustained through 8 weeks post-dosing

Composite Bird score
(Mean ± SEM)



AX-2402 improves neurological disease severity[1] with effects sustained through 7 weeks post-dosing

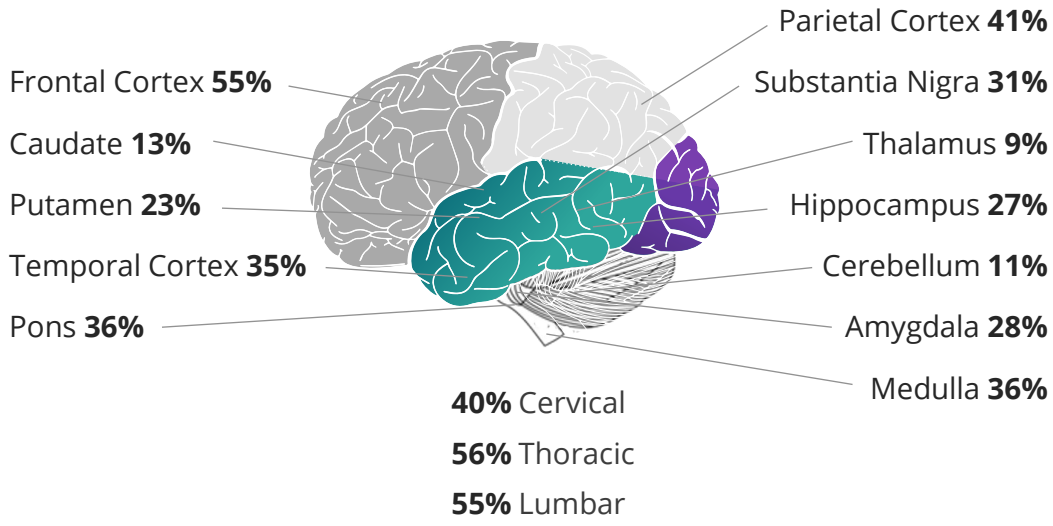
Vehicle EON

[1]As measured by the Bird score, a composite neurological severity score in Rett models evaluating motor function, gait, clasping, breathing, and overall condition. [2]As measured by the hindlimb clasping score , a behavioral measure of neurological impairment in Rett mouse models, where reduced clasping reflects improved motor function. Graphs represent mixed-effects model (repeated measures) + Tukey's posthoc test (* p<0.05)

EON IT injection drives durable, widespread RNA editing across the CNS in NHP

RNA editing in NHP *in vivo*

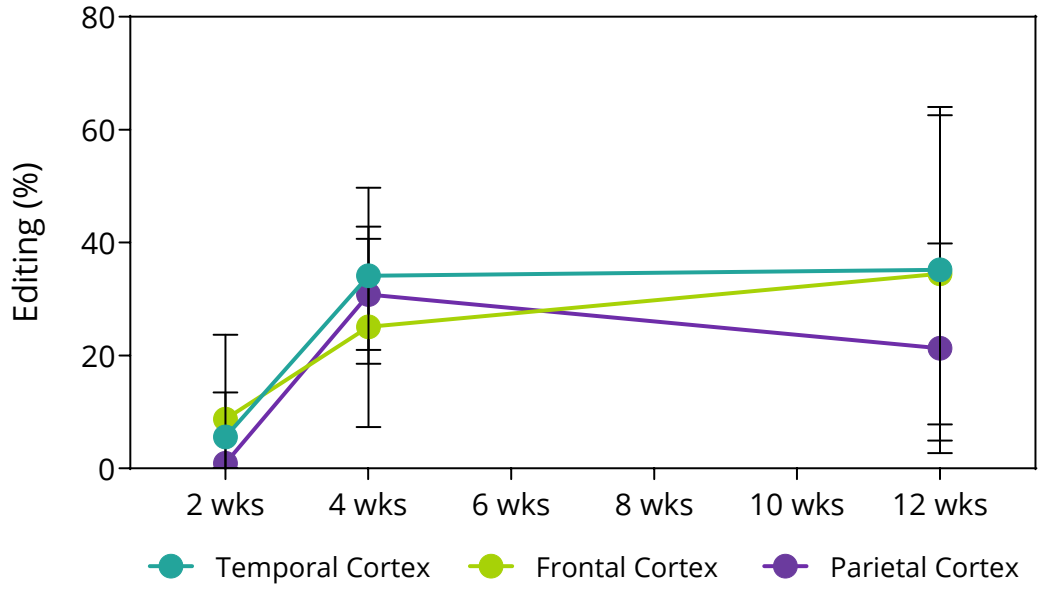
IT administration, ACTB, 10.6mg, Q4W, N=2-3, 12 weeks, ddPCR, mean±SEM



Stable and durable editing efficiency in both superficial and deep brain regions

RNA editing of ACTB in NHP - Cortex

IT administration, 10.6mg EON, single dose, n=3, up to 12 weeks, ddPCR, mean, SD



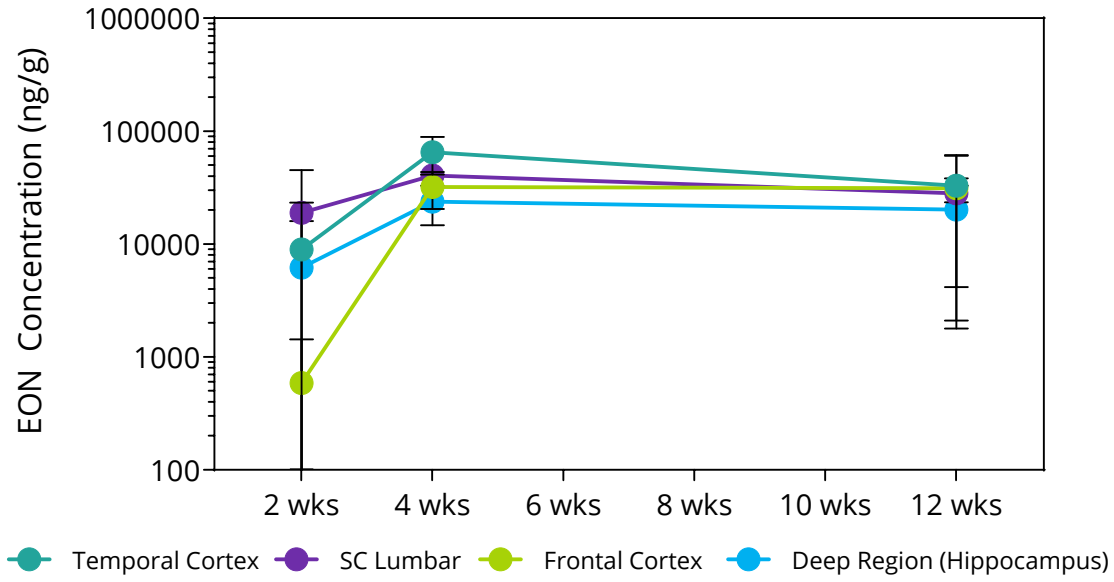
Axiomer EONs lead to robust and sustained editing up to 12 weeks, following single dose

ACTB: Actin beta ; EON: Editing Oligonucleotide; IT: Intrathecal; NHP: Non-Human Primate; SC: Spinal Cord; SD: Standard Deviation

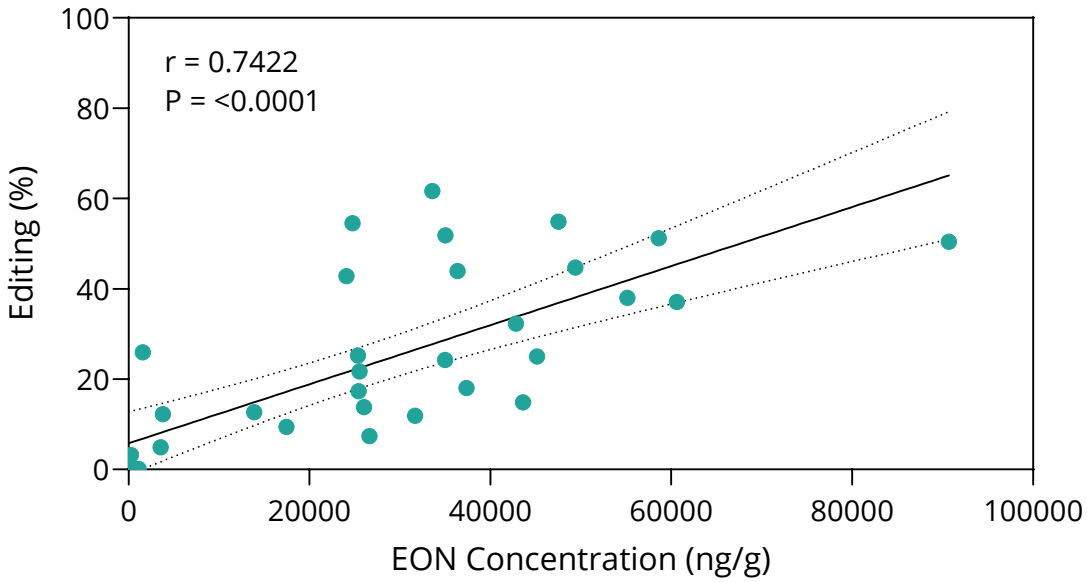
Sustained EON concentration associated with consistent editing efficiency

ACTB EON concentration in NHP (ng/g)

IT administration, 10.6mg EON, single dose, n=3, up to 12 weeks, ddPCR, mean, SD



ACTB RNA editing and concentration relationship in NHP *IT administration, 10.6mg EON, single dose, n=3, 2-week, 4-week and 12-week, ddPCR*



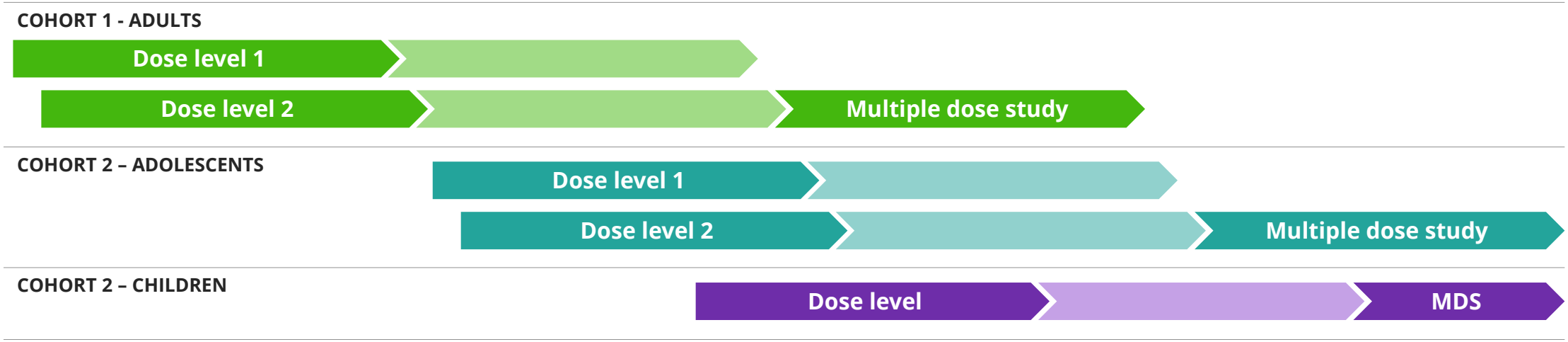
EON concentrations measured across different brain regions consistently peaked at Week 4. Sustained exposure observed up to 12 weeks post-dosing supporting infrequent dosing regimen

Higher intracellular EON concentrations resulted in greater editing efficiency

ACTB: Actin beta ; EON: Editing Oligonucleotide; IT: Intrathecal; NHP: Non-Human Primate; SC: Spinal Cord; SD: Standard Deviation; Peason correlation

AX-2402 preliminary Phase 1/2 design

A First-in-Human, Phase 1/2 study to assess safety, tolerability, and pharmacokinetics of AX-2402 in female patients with Rett syndrome



- Primary objective: safety, tolerability
- Secondary: PK (CNS and circulation)
- Exploratory PD and clinical measures: Developmental milestones, EEG/EP, biosensor data, ECG, seizure frequency, RSBQ, CGI-I, Motor Behavior Assessment

- Financially supported by up to $9.2M funding provided by Rett Syndrome Research Trust
- Development candidate selection announced January 2026
- Advancing development activities for first-in-human trial to start in first half 2027

CNS=-central nervous system; EEG= electro-encephalogram; RSBQ= Rettt Syndrome Behavioral Questionnaire; CGI-I= Clinical Global Impression of Improvement

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

MASH is **highly prevalent and increasing worldwide**. MASH individuals have a **high unmet medical** need due to disease progression into cirrhosis, HCC, and liver-related mortality with **limited therapeutic options** available.[1] Emerging evidence shows that NAFLD patients with the I147M variant are **less responsive** to GLP-1 agonists[2].

PNPLA3 (patatin-like phospholipase domain-containing 3) **I148M** is the **strongest known genetic risk** factor of steatosis, MASH and fibrosis, being present in **~39–47% of MASLD patients**[3].

Homozygous carriers are approx. **8 million individuals** in US+EU and show **+73% higher liver fat**[4], **3.5× higher risk of NASH/MASH**[4], faster fibrosis progression and increased liver-related **mortality and HCC**[5].

Axiomer EONs recode the PNPLA3 I148M variant (Met→Val), restoring WT-like protein function. AX-2911 is designed to **correct the primary genetic driver of MASH**, unlike current therapies that target downstream metabolic or inflammatory pathways.

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

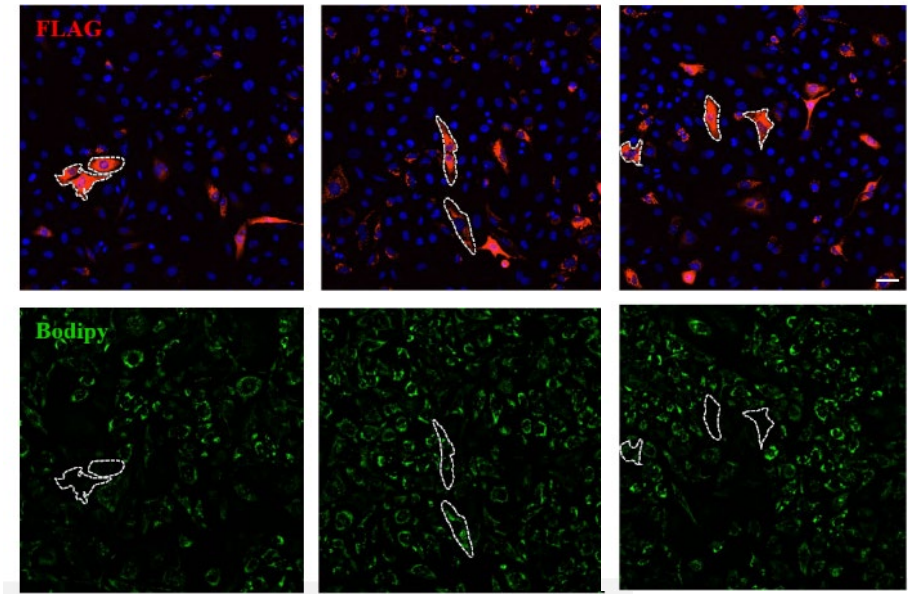
AX-2911 to restore WT-like PNPLA3 function

148I and 148V show comparable lipid droplet sizes

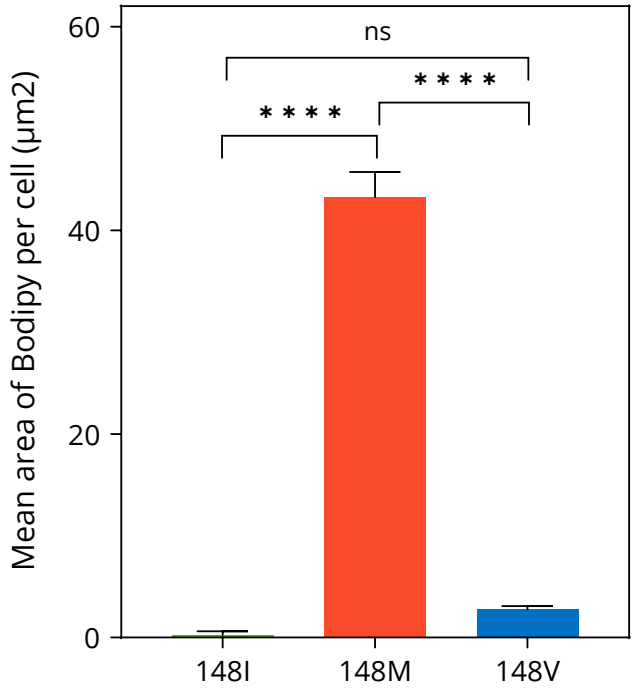
PNPLA3 148I
(WT)
Isoleucine (ATC)

PNPLA3 148M
(Mutant)
*Methionine (**A**TG)*

PNPLA3 148V
(Axiomer variant)
*Valine (**G**TG)*



Hoechst (nuclei), Bodipy (Lipids) and M2 anti-flag (PNPLA3)



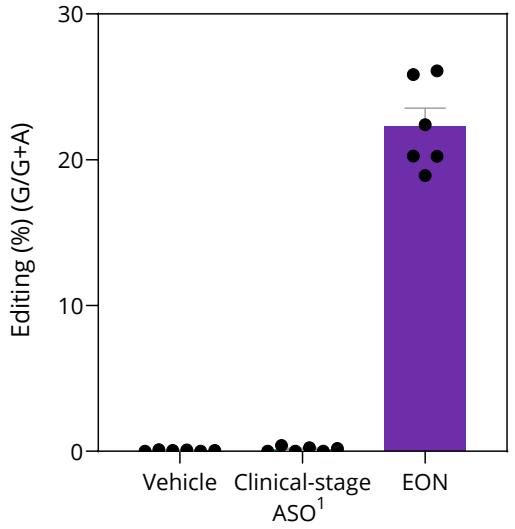
- WT 148I PNPLA3 shows smaller lipid droplets, reflecting normal lipid metabolism.
- 148M PNPLA3 shows significantly larger lipid droplets, consistent with its pathogenic role in lipid metabolism disorders.
- The corrected variant 148V results in wild-type-like droplet sizes, suggesting a similar effect on lipid accumulation to 148I.

Treatment conditions: HeLa cells, plasmid, transfection, 250uM linoleic acids, 24h, cell lipase activity by IF One-way ANOVA, ****, P<0.0001; Mean, SEM.

AX-2911 substantially reduces liver fat in a mouse steatosis model comparing to a clinical-stage ASO1

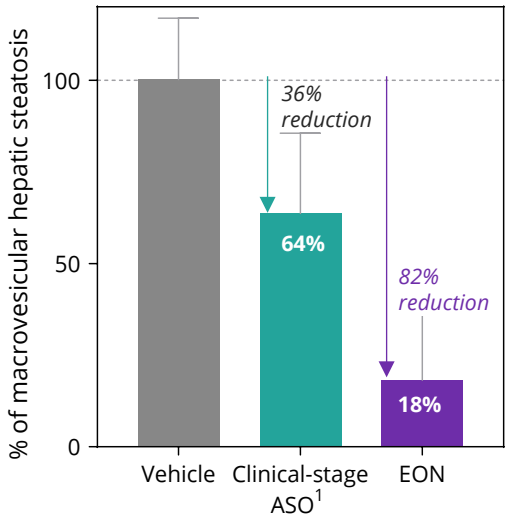
Editing of hPNPLA3 I148M in mouse livers engrafted with human hepatocytes

dPCR(Qiagen), AVG±SEM



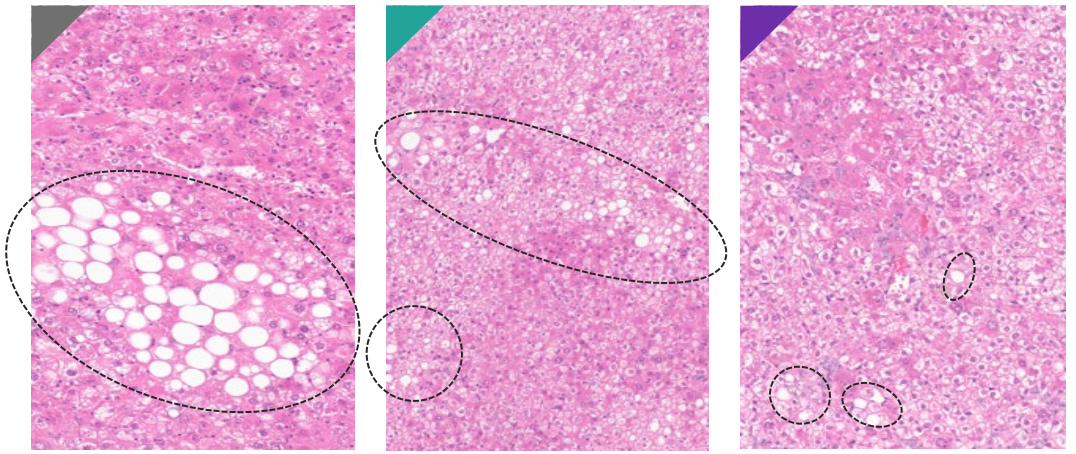
Macrovascular steatotic incidence scoring

AVG±SEM



Liver sections of steatosis mouse model treated with ASO or AX-2911

PNPLA3 148M Humanized FRG mouse fed on western diet (4W+4W)



EON treatment achieves 23% editing of PNPLA3 in humanized mouse livers

EON treatment reduces liver fat content by 82% in humanized mouse steatosis model

Vehicle

Clinical-stage ASO[1] treatment after 28 days

EON treatment after 28 days

[1]Clinical candidate AZ AZD2693

AX-1412 RNA editing therapy targeting B4GALT1 for cardiovascular diseases

Leading causes of death in the world
~18 million people die from CVDs every year (**32% of all global deaths**) Despite therapies, the unmet medical need remains.

AX-1412 is designed to provide people with a protective genetic variant of B4GALT1 that is associated with **36%**[1] **reduction in the risk of cardio-vascular disease**.

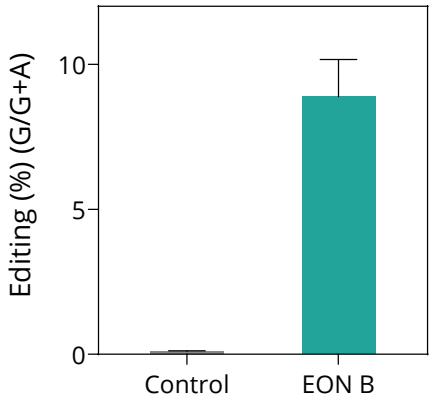
AX-1412 may become a **stand-alone cardio-vascular therapy** that may also work **synergistically with standard of care** to further reduce risk of CVDs.

[1]Montasser ME, et al. Science. 2021 Dec 3;374(6572):1221-1227

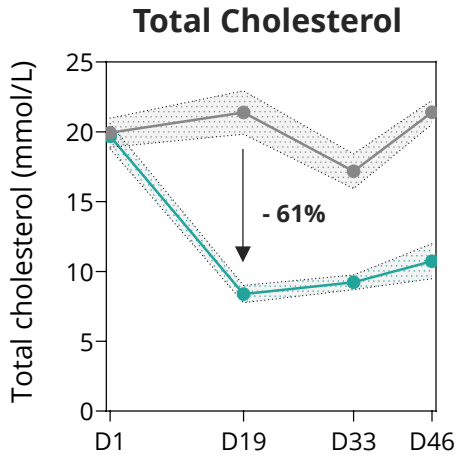
AX-1412 improves multiple cardiovascular risk biomarkers in E3L.CETP mice

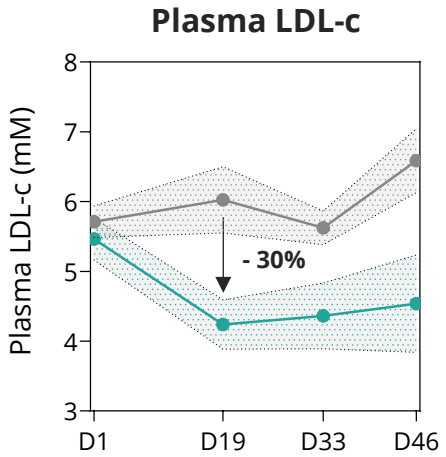
B4GALT1 editing in E3L.CETP mice and biomarker changes

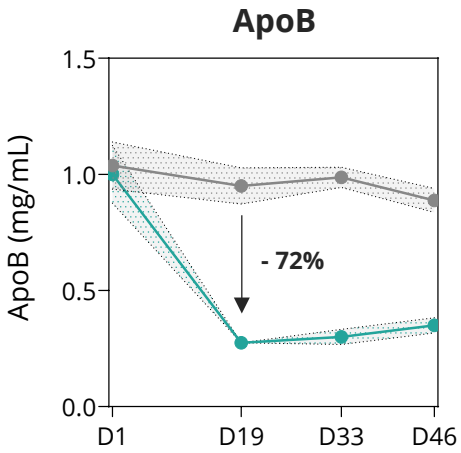
(N=10, 2mg/kg, LNP formulation, IV Q1W, D46, ddPCR)

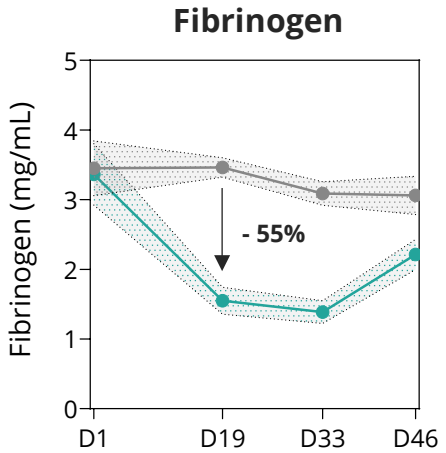


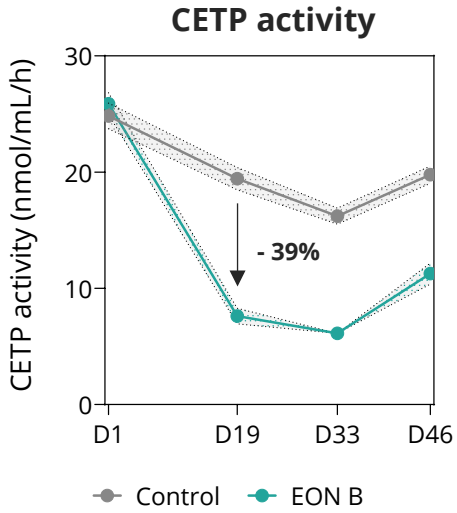
AX-1412 reduced total cholesterol, ApoB, and LDL-c, supporting its potential as a cardiovascular risk-modifying therapy.











ProQR corporate outlook
for 2026

AX-0810 (NTCP, CHOLESTATIC DISEASE)

Report target engagement data from AX-0810 Phase 1 trial in healthy volunteers in first half of 2026; Initiate patient cohort in the AX-0810 Phase 1 trial following the healthy volunteer cohorts

AX-2402 (MECP2 R270X, RETT SYNDROME)

Advance development activities for first-in-human trial to start in first half of 2027

EARLIER STAGE PROGRAMS AND PLATFORM

Disclose additional preclinical data across earlier-stage programs, highlighting continued productivity and versatility of the Axiomer platform

LILLY COLLABORATION

Continue to execute on partnership with Eli Lilly, with potential data updates and milestone income from the ongoing collaboration

FINANCIAL STRENGTH

Continue to strengthen balance sheet and evaluate potential partnerships to maximize platform value

ProQR®

IT'S IN OUR RNA