ProQR®

DEVELOPING RNA-EDITING MEDICINES

for patients in need

Nasdaq: PRQR

November 2025

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 CTA authorized

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

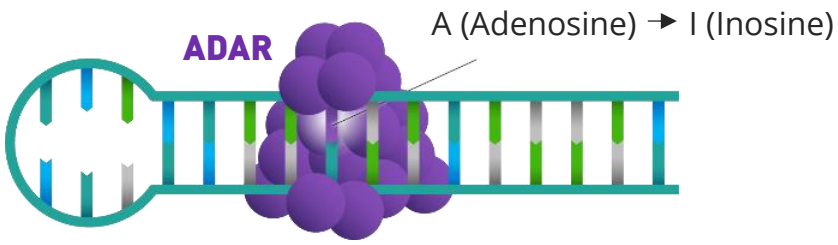
RUNWAY INTO MID 2027

Funding the clinical readout of multiple programs

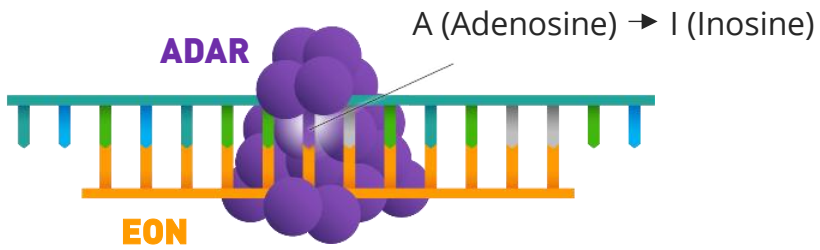
€ 106.9 million cash and cash equivalents as of end of Q3 2025

How Axiomer™ edits RNA

NATURAL ADAR EDITING



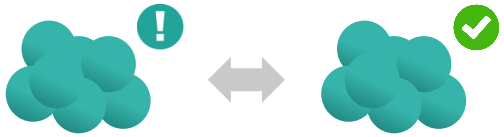
EDITING OLIGONUCLEOTIDE *(EON)-directed* EDITING



MODULATE

Modify protein function

CORRECT



Correct disease-causing mutations

PROTECT

Introduce protective variants

Pipeline horizons

Near term, next, and beyond

Near term

AX-0810 IN THE CLINIC

Axiomer entering first-in-human (FIH) trial with AX-0810 targeting NTCP in **cholestatic disease;** CTA authorized – Phase 1 trial beginning to establish safety, PK, and target engagement

Next

AX-2402 RAPIDLY ADVANCING

Leading RNA editing CNS capability and first neuro pipeline program, AX-2402 for **Rett syndrome**, advancing rapidly – positioning ProQR at the forefront of neurological RNA editing medicines

Beyond

BROADER EXPANSION

Continued advancement of our platform, including earlier programs AX-1412 for **CVD** and AX-2911 for **MASH**, broadening the portfolio

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.

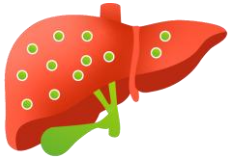
Learnings from human genetics and literature demonstrate that **modulation of the NTCP channel** responsible for majority of bile acids re-uptake in liver cells could lead to **hepato-protective effects**.

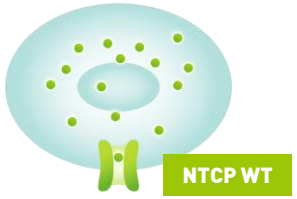
NTCP, sodium taurocholate co-transporting polypeptide. References: [1]Trivedi PJ, et al. Clin Gastroenterol Hepatol. 2022 Aug;20(8):1687-1700.e4; [2]Schreiber RA, et al. J Clin Med. 2022 Feb 14;11(4):999

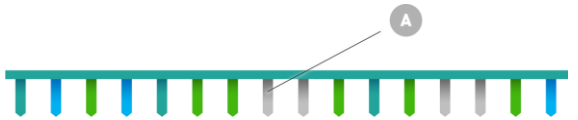
AX-0810: first-in-class RNA editing therapy targeting NTCP for cholestatic diseases

LIVER WITH CHOLESTATIC DISEASE

High concentration of bile acids in hepatocytes

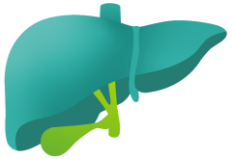


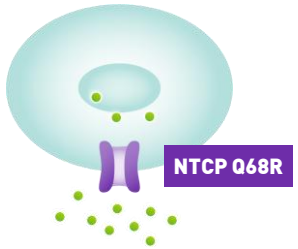


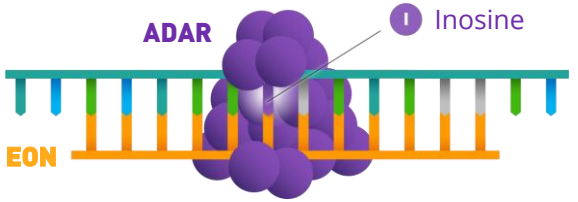


AX-0810 STRATEGY FOR DISEASED LIVER

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]

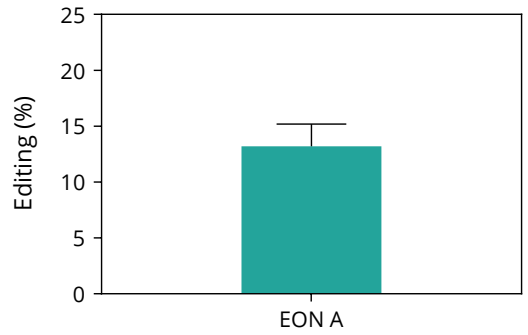
Bulevirtide (Hepcludex) is a daily SC injected NTCP inhibitor approved for Hepatitis D. NTCP channel is a known transporter for bile acids and hepatitis virus from bloodstream to the liver.
[1]Ho RH, et al. J Biol Chem. 2004 Feb 20;279(8):7213-22; [2]Vaz FM, et al. Hepatology. 2015 Jan;61(1):260-7; [3]Schneider 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 | **Plasma total bile acids**

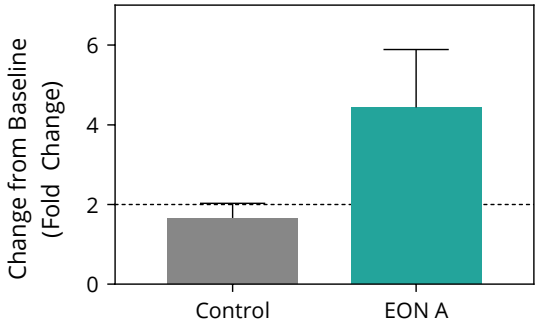
NTCP RNA Editing in Humanized Mice

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



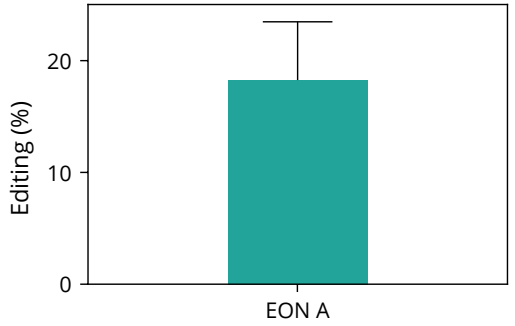
Plasma TBA in Humanized Mice

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



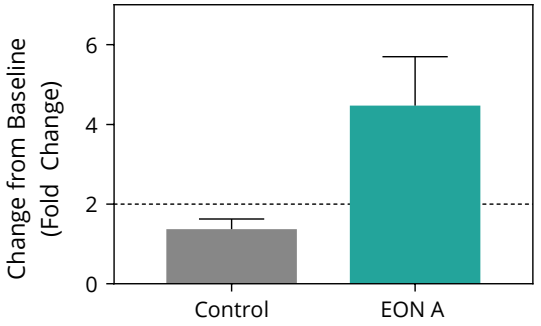
NTCP RNA Editing in NHP

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



Plasma TBA in NHP

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

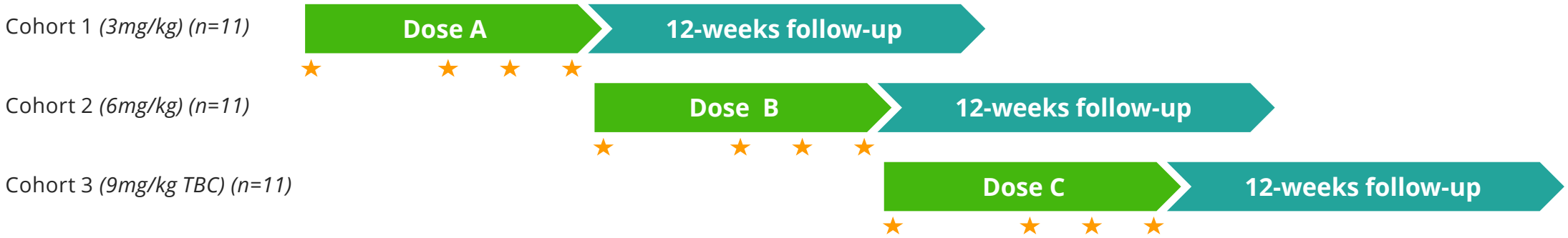


- EON A results in consistent editing data in humanized mouse model and NHP *in vivo* with approx. 15% editing reaching expected NTCP modulation
- Reaching >2-fold changes in biomarkers - expected impact on plasma bile acids levels following NTCP EON treatment

CTA approved for first-in-human (FIH) trial

Safety, tolerability, PK, and biomarker-based target engagement of AX-0810 in healthy volunteers

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

CTA approved and open

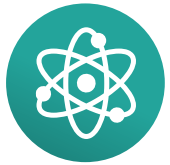
- Cohort 1 safety, tolerability, PK towards year end
- Target engagement data on all cohorts in H1 2026

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.

Clinically relevant biomarker strategy to inform future development

From target engagement to pharmacodynamics biomarkers

TARGET ENGAGEMENT



DISEASE RELEVANCE

MECHANISTIC PHARMACODYNAMIC

Total bile acids (TBAs) levels

Assess effect on bile acids transporter activity

Bile acids profile

Confirm NTCP specificity

Conjugated bile acids clearance (TUDCA)

Differentiate effect between doses to inform dosing regimen in disease population

NTCP, sodium taurocholate co-transporting polypeptide; TUDCA, Tauroursodeoxycholic acid.

Learnings from the FIH translating into the disease population

Healthy volunteers	Disease population
Plasma TBA from normal to ↑ with AX-0810	**Plasma TBA** From ↑ in cholestasis to ↑↑↑ with AX-0810
Plasma conjugated bile acids from normal to ↑ with AX-0810	**Plasma conjugated bile acids** from normal to ↑ with AX-0810
TUDCA challenge from normal clearance to ↓ with AX-0810	**TUDCA challenge** from ↓ clearance to ↓↓ with AX-0810
	Disease endpoints: ↓ ***Liver enzymes***
	Disease endpoints: ↓ ***Cholestasis markers***
	Disease endpoints: ↓ ***Fibrosis markers***

FIH, First in Human; TBA, Total Bile Acids.

AX-2402 RNA editing therapy targeting MECP2 for Rett Syndrome

RETT SYNDROME RESEARCH TRUST

Rett Syndrome is a **devastating and progressive neurodevelopmental disorder** caused by variants in the transcription factor Methyl CpG binding protein 2 (*MECP2*). There is a **high unmet need for a disease modifying therapy**.

Nonsense variants lead to **severe phenotypes.** They represent more than one third **of Rett Syndrome** cases and are projected to affect **20,000 individuals** in US and EU.[1,2]

Rett Syndrome is **not a neurodegenerative disorder** and restoring levels of the MECP2 protein has shown to **reverse symptoms** in mice.[3]

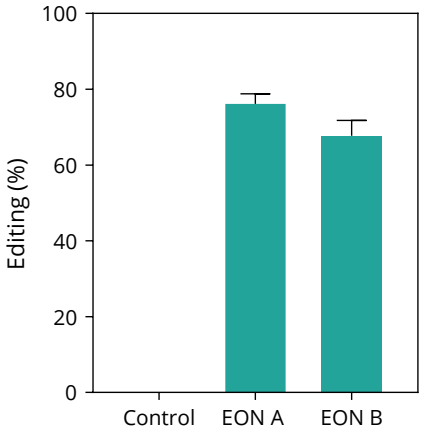
Axiomer has the potential to **restore the precise level of MECP2 protein regulatory function,** which is lacking in Rett Syndrome, and become a disease modifying therapy.

Rett Syndrome Research Trust partnership includes $9.2 M in funding; collaboration established in January 2024, expanded in December 2024

[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.

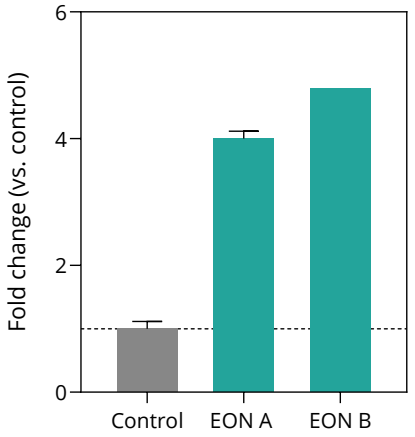
Editing increases mRNA levels and restores protein expression; Broad editing distribution in CNS

R270X MECP2 editing



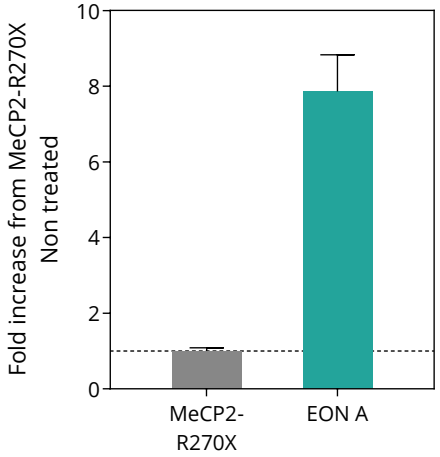
Up to 80 % editing of R270X MECP2 in patient fibroblasts

MECP2 RNA levels



Increased MECP2 RNA levels due to PTC recoding and NMD inhibition

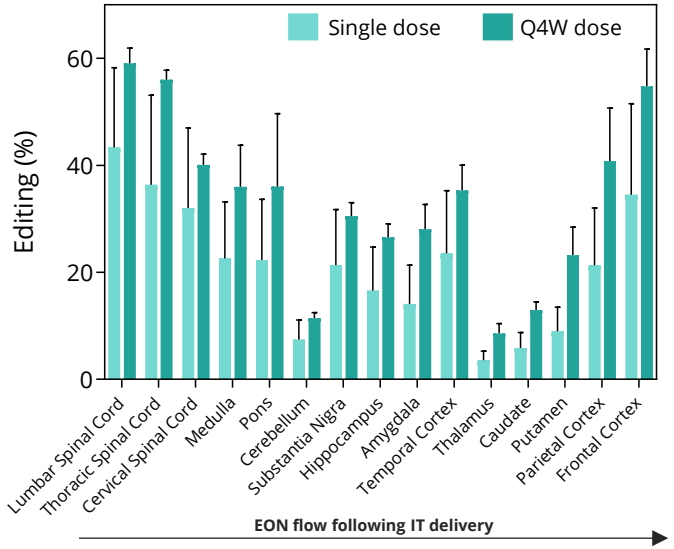
R270W MECP2 protein levels



Increased R270W MECP2 protein levels

RNA editing in NHP *in vivo*

IT administration, ACTB, 10.6mg, single dose (SD)/Q4W, N=2-3, 12 weeks, ddPCR, mean±SEM



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

EON, Editing oligonucleotide; NT, Non-treated; TF, transfection, Conditions panel on the left and middle: 100 nM EON, transfection, 48h, N=2, mean±SEM.
Conditions panel on the right: MeCP2-R270X-NanoLuc activity; 100 nM EON, transfection, 48h, N=8, mean±SEM.

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 cardiovascular disease**.

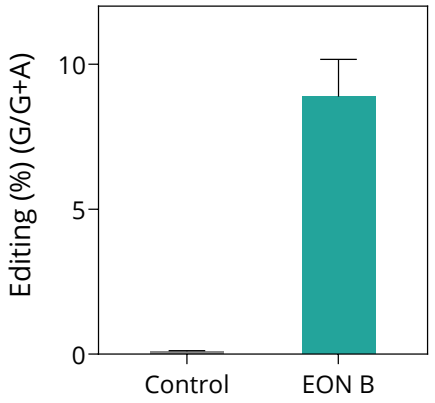
AX-1412 may become a **stand-alone cardiovascular therapy** that may also work **synergistically with standard of care** to further reduce risk of CVDs.

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

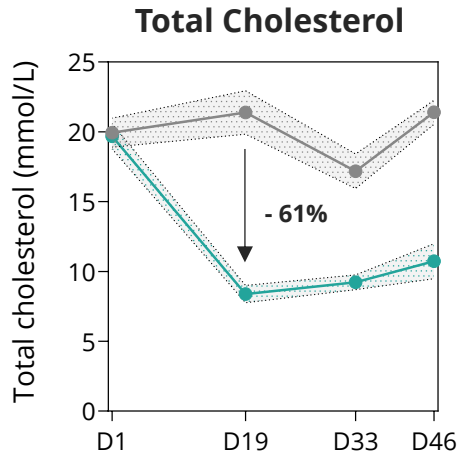
EON-mediated editing of B4GALT1 leads to meaningful effect on key biomakers in E3L.CETP Mice

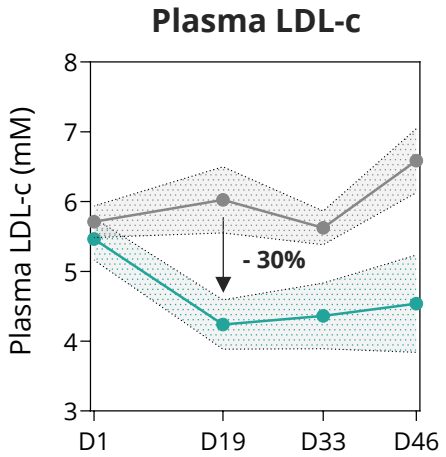
B4GALT1 editing and biomarkers in E3L.CETP mice

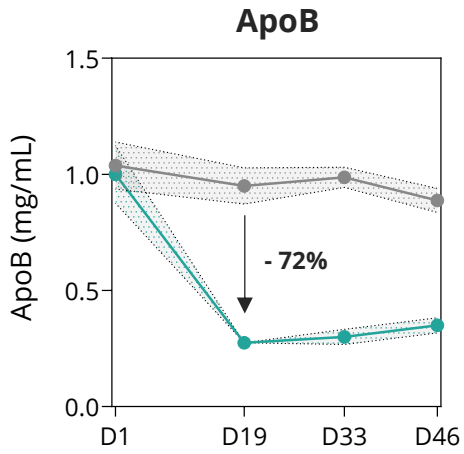
(N=10, 2mg/kg, LNP formulation, IV Q1W, D46, ddPCR)

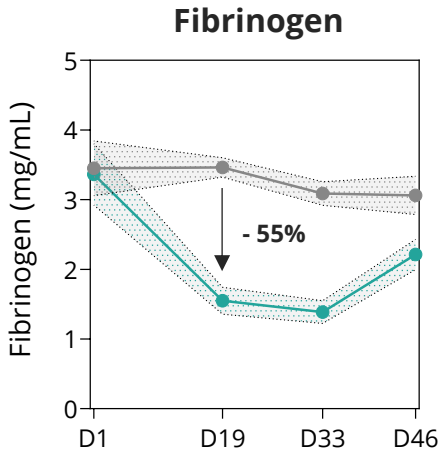


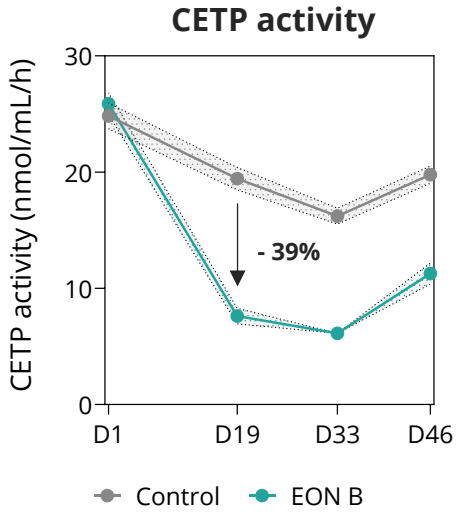
Treatment with EON B led to a reduction in total cholesterol, ApoB, and LDL-c confirming this therapeutic approach to address cardiovascular diseases











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

MASH and subsequent stages of liver disease **are very prevalent and still on the rise worldwide**. MASH individuals have a high unmet medical needs due to the **progressive** nature of the disease (cirrhosis and hepatocellular carcinoma) and **limited therapeutic options** available[1]

PNPLA3 (patatin-like phospholipase domain-containing 3) I148M is a variant **commonly reported** in the MASH population worldwide (20-60% of the patients) and is known as **associated risk factor**.[2,3] Approximately 8 million individuals in US and EU are homozygous for the 148M variant.

Axiomer EONs have the potential to change the Methionine into a Valine bringing the **PNPLA3 protein back to a WT-like functional conformation**.

[1]Sandireddy R, et al. Front Cell Dev Biol. 2024 Jul 16;12:1433857; [2]Romeo S, et al. Nat Genet. 2008 Dec;40(12):1461-5; [3]Salari N, et al. BMC Endocr Disord. 2021 Jun 19;21(1):125.

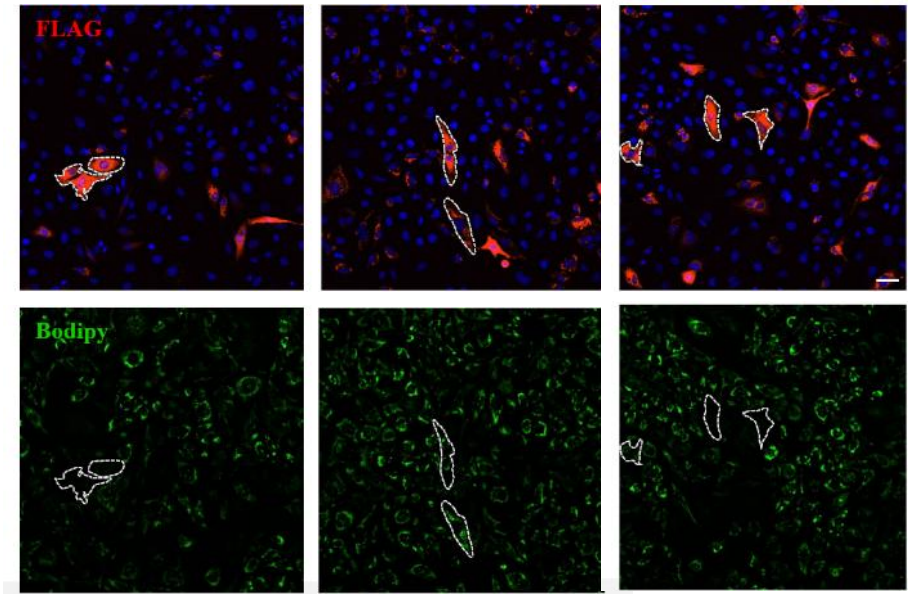
Axiomer™ creates a PNPLA3 protein with WT-like functionality

148I and 148V reports equivalence in lipid droplet sizes

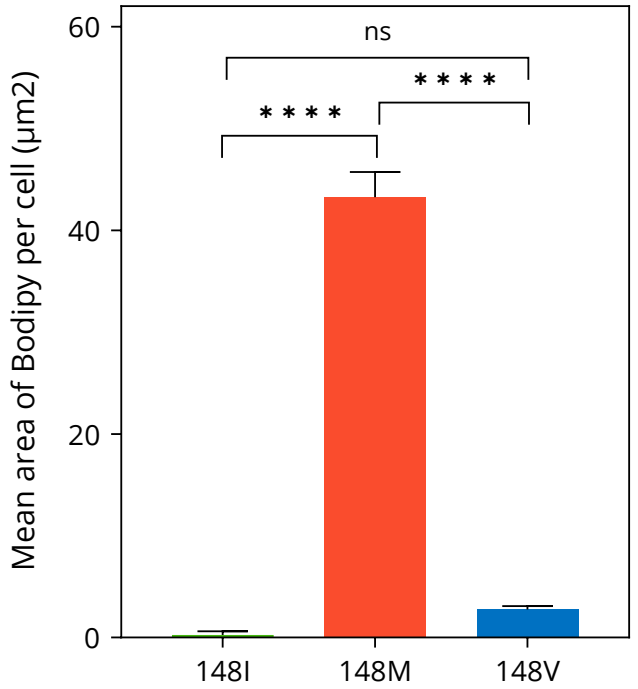
PNPLA3 148I
(WT)
Isoleucine (ATC)

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

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



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

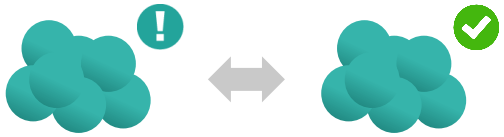


- The wild-type 148I shows smaller lipid droplets, reflecting normal lipid metabolism
- The 148M variant induces significantly larger lipid droplets, consistent with its pathogenic role in lipid metabolism disorders
- The corrected variant 148V results in wild-type like droplet sizes, suggesting a corrective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

Pipeline leverages the promise of RNA editing

Demonstrating applications to modulate, correct and protect



MODULATE	CORRECT		PROTECT
AX-0810 *NTCP for cholestatic diseases*	**AX-2402** *MECP2 program for Rett syndrome*	**AX-2911** *PNPLA3 program for MASH*	**AX-1412** *B4GALT1 program for cardiovascular diseases*
Preliminary safety and PK data towards end of 2025 Target engagement in H1 2026	*Multiple additional Rett programs*		

Partnered pipeline *10 undisclosed targets (option to expand to 15)*

B4GALT1, Beta-1,4-galactosyltransferase 1; MECP2, Methyl CpG binding protein 2; NTCP, sodium taurocholate co-transporting polypeptide; PNPLA3, Patatin-like phospholipase domain-containing 3.

ProQR®

IT'S IN OUR RNA