
therapeutics
Computing the Future of Medicine™
Interim results for six months ended 31 July 2023

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Forward looking statement

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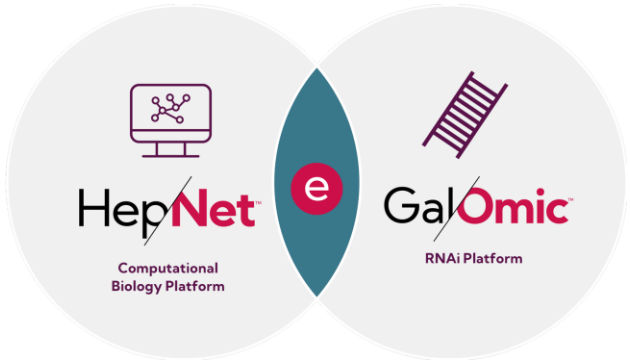
Company Overview

Driving innovation at the intersection of AI and precision medicine

Our mission:

Integrating computational power and biology to discover life-transforming medicines



Cash and cash equivalents
£24.8m 2022: £21.8m

Revenue
£0.2m 2022: £0.3m

R&D spend
£5.3m 2022: £3.1m

Operating loss
£7.0m 2022: £4.6m

Loss after tax
£5.6m 2022: £3.8m

R&D tax credit receivable
£2.5m 2022: £2.2m

Interim results for six months ended 31 July 2023

Multi-disciplinary team (exc NED)
34 FTE 2022: 38

Share Price (25/10/23)
10.7p

Shares outstanding (25/10/23)
583.8m

Market cap (25/10/23)
£62.5m

London
Company HQ

Boston

Our Approach

Integrating computational power and biology to discover life-transforming medicines

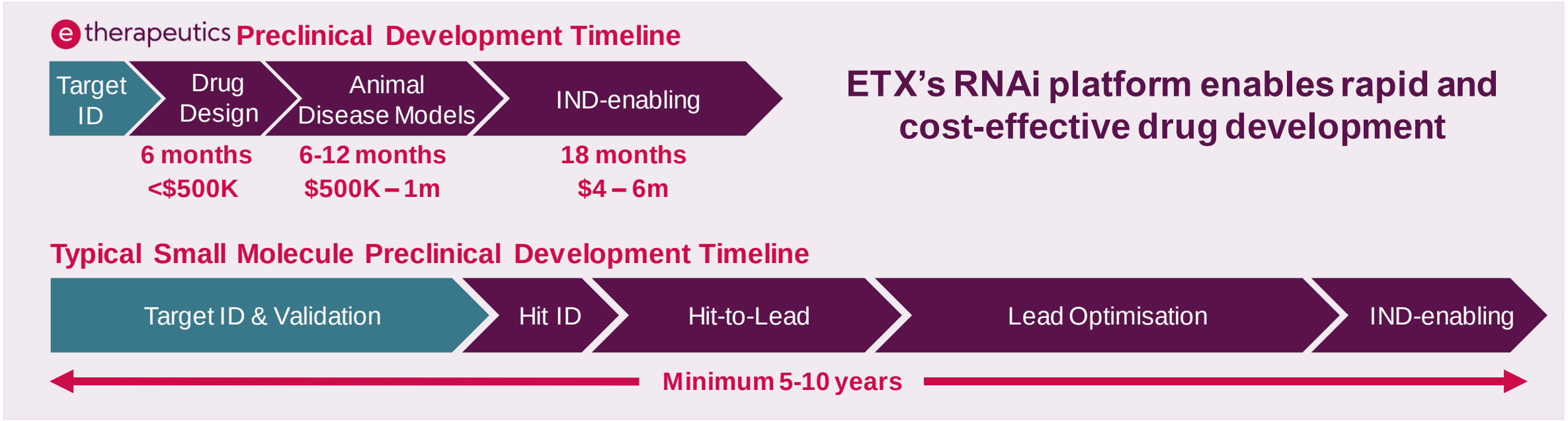
World-class hepatocyte data resource with sophisticated network biology analytics for target ID and ability to automate early stages of preclinical development

Proprietary chemistry platform for potent and durable hepatocyte-specific mRNA knockdown of novel targets identified by HepNet™

In-house pipeline of GalOmic™ RNAi therapies across broad range of indications, with lead assets in cardiometabolic disease and haemophilia

Traditional Approaches to Drug Development are Too Slow and Too Expensive

- Typical small molecule preclinical development takes **a minimum of 5-10 years.**
- Enabled by computation and use of the RNAi modality, we can go from from gene target selection to disease model experiments in **6 months**, costing **less than $500,000** and **IND ready in 3 years.**
- This means we can rapidly develop multiple life-transforming RNAi medicines for the people that need them.



HepNet™


HepNet™
Computational Biology Platform
GalOmic™
RNAi Platform
Therapeutic Pipeline

HepNet™

Our world-class hepatocyte-specific computational biology platform

HepNet™ is our proprietary computational biology platform, built on the world's most comprehensive hepatocyte-specific knowledgebase.

It enables:

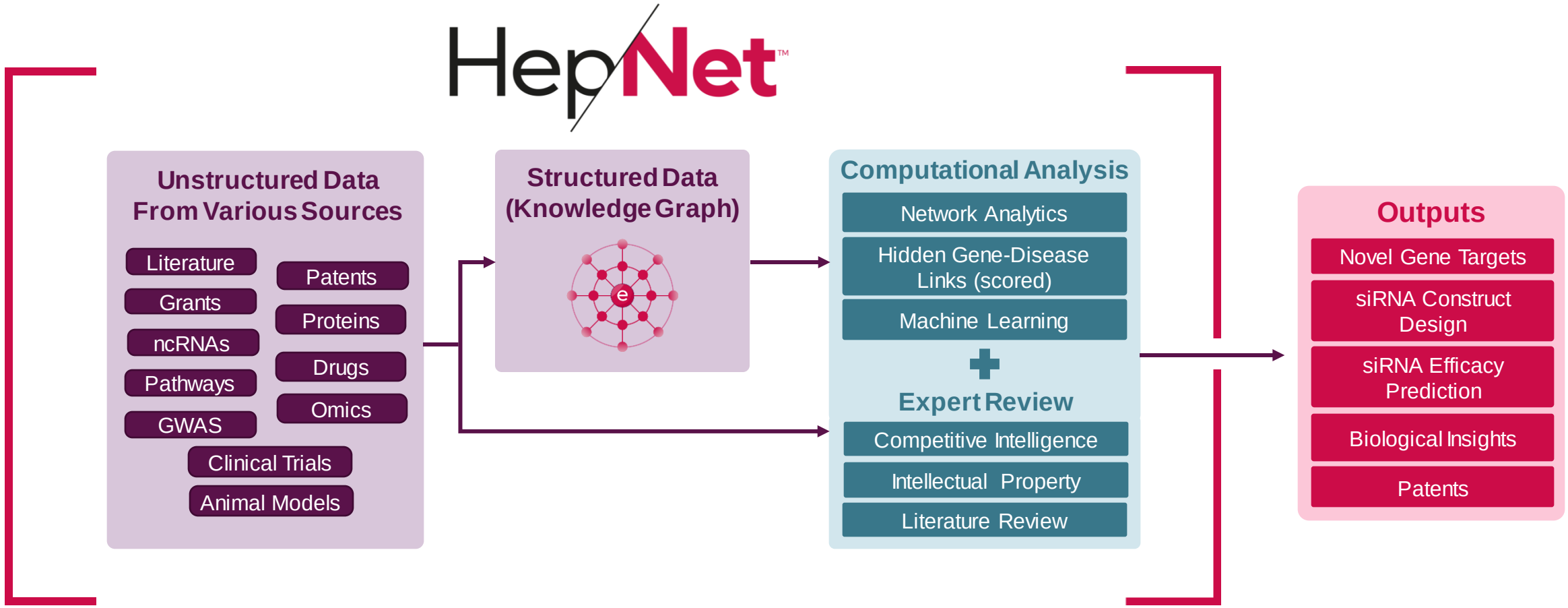
- Identification of novel targets for a wide range of diseases through sophisticated network analytics that account for the true complexity of biology
- Increased speed of execution by automating drug discovery and design processes
- Mining of 100s of integrated data sources to distil new mechanistic knowledge of hepatocyte biology

ETX data and knowledge covers…

- **12,091** expressed genes
- **1039** secreted proteins
- **461** proteins secreted to blood
- **700** biological processes

HepNet™

Our world-class hepatocyte-specific computational biology platform



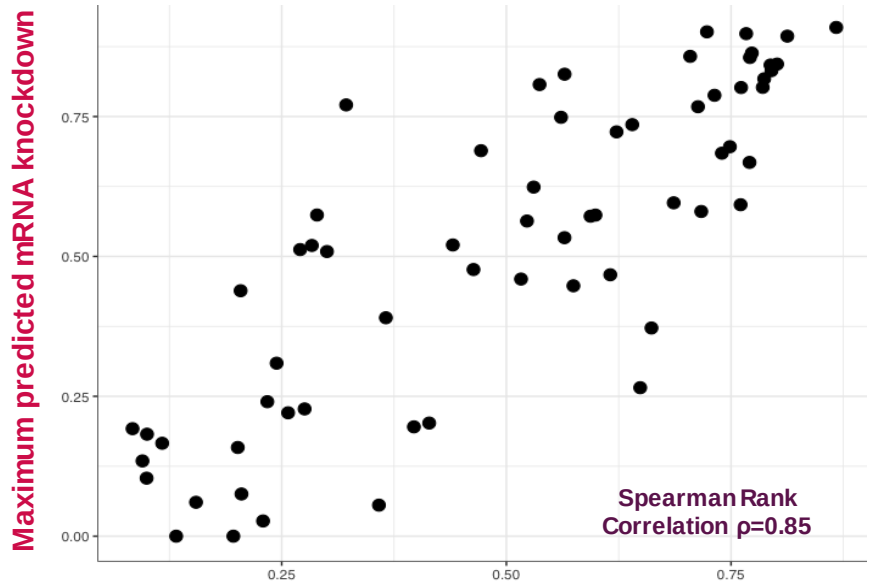
HepNet™ increases automation and provides us with the ability to identify novel targets and rapidly design siRNA constructs.

siRNA Efficacy Prediction

Using machine learning to predict siRNA efficacy and bypass *in vitro* screening

- Highly accurate model trained on proprietary, high-quality training datasets
- Trained model demonstrates high prediction accuracy, performance is superior to widely used algorithms (BioPredSi, ThermoComposition21)
- Enables identification of lead siRNA sequences *in silico,* minimising number of sequences that require screening
- We are now exploring further enhancement of predictions using large language models (LLMs) trained on mRNA sequences

Predicted vs measured siRNA efficacy (Validation Dataset)



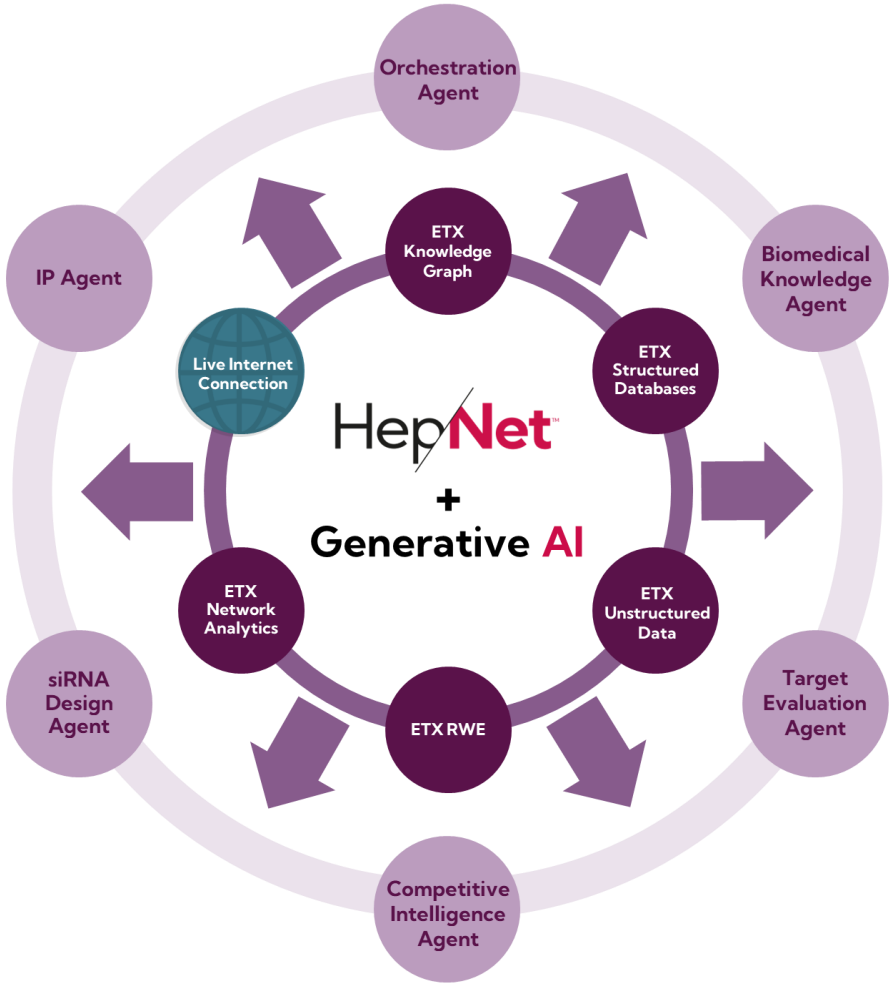
	Pre-AI Approach	Post-AI Approach
Number of siRNA screened	Up to 400	<10
Time to lead identification (potential clinical candidate)	6 months	1 month
Cost of screening	$500,000	$50,000

HepNet™'s siRNA efficacy prediction already reduces preclinical development timelines and costs, with potential to enable bypassing of *in vitro* screening

Enhancing Computation with LLMs

Transforming HepNet™ into a dynamic knowledge resource

- We are fully embracing the latest advances in generative AI and LLMs through integration with HepNet™ and creation of specialist LLM agents
- LLM agents trained on specific data such as scientific papers, mRNA sequences, hepatocyte-specific data, patents etc. will support target ID, target-indication evaluation and drug design
- This will enhance our ability to understand, reason, and infer from vast amounts of data, increasing automation and speed of ETX processes



GalOmic™

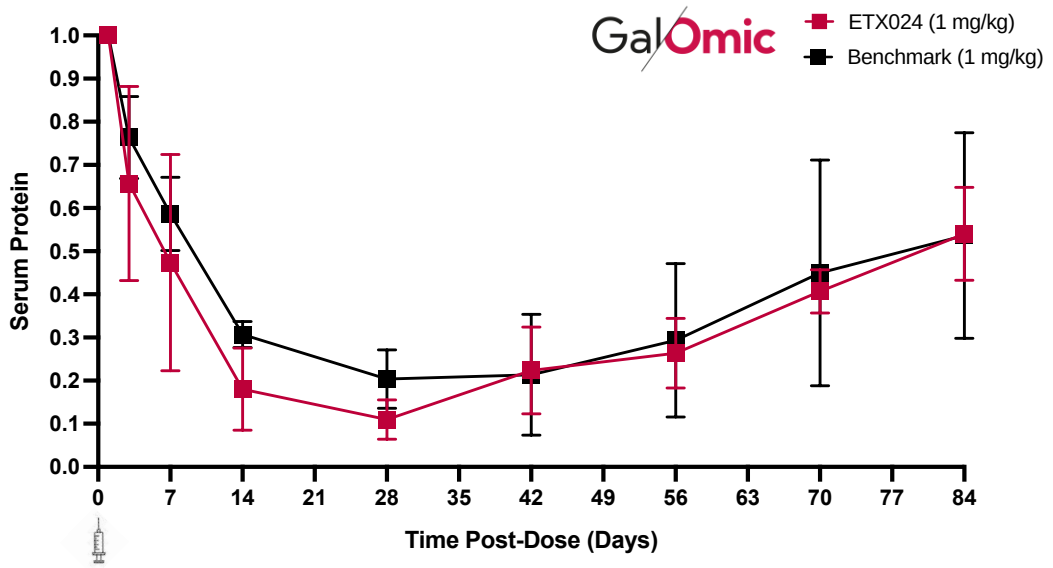

HepNet
Computational Biology Platform
GalOmic
RNAi Platform
Therapeutic Pipeline

GalOmic™

Our proprietary RNA interference chemistry platform

- GalOmic™ enables generation of GalNAc-siRNA drug candidates for hepatocyte-specific gene silencing via RNAi of any target gene identified by HepNet™
- Benchmarking data demonstrates at least equivalent knockdown compared to market leads across multiple genes
- Data from in-house pipeline further highlights potent and durable silencing profile of GalOmic™ siRNA constructs, supporting infrequent, subcutaneous dosing
- Platform is protected by IP covering conjugate design and chemical modifications, including modification patterns

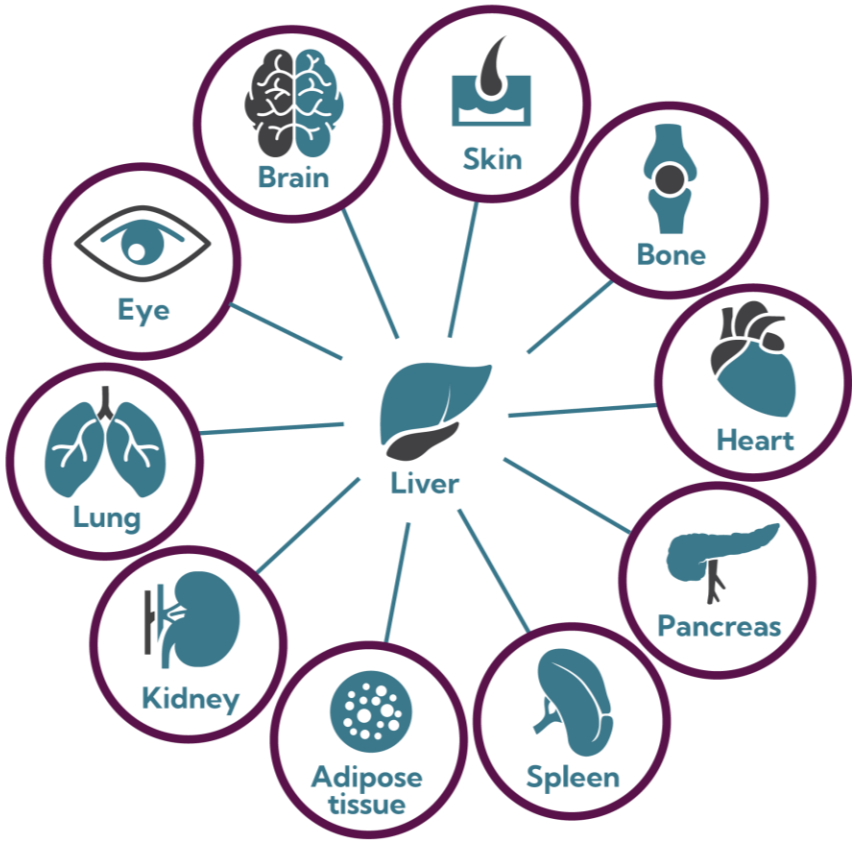
Typical performance profile of our RNAi platform in non-human primate



siRNA - small-interfering RNA | **RNAi** - RNA interference

GalOmic™

Hepatocyte targeting unlocks wide variety of therapeutic possibilities



Hepatocyte-associated Disease Areas

- Cardiovascular
- Metabolic
- Diabetes
- Haematology
- Obesity
- NASH
- Renal
- Rare
- & More

Hepatocytes are highly influential cells, allowing us to develop GalOmic™ RNAi medicines for a broad range of diseases

Therapeutic Pipeline

ETX-291: A HepNet™ Identified Target for Cardiovascular Disease Risk

Pursuing a novel target with human validation and mechanism of action beyond LDL-C modulation

HepNet™ predicted link between the target and metabolic disease risk

Human genetic evidence links target to reduced cardiovascular disease risk in otherwise healthy individuals

Target Product Profile:

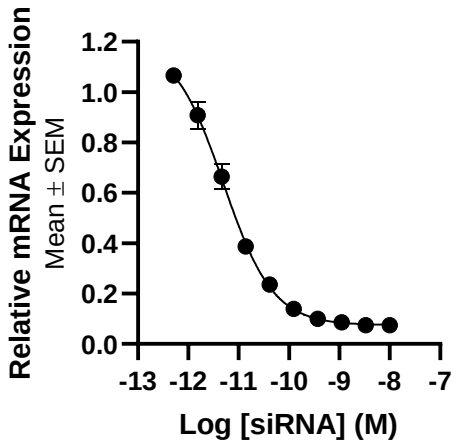
- **Meaningful CVD risk reduction** independent of statins and PCSK9s
- **Holistic treatment potential** for metabolic co-morbidities by modulating insulin sensitivity, promising applicability beyond LDL-C modulation
- Ease of use: **long-acting**, aiming for quarterly+ duration of action
- Using ETX's **GalOmic™ GalNAc-siRNA** technology for highly specific liver targeting

ETX-291 is a Potent siRNA Utilising ETX's GalOmic™ Chemistry

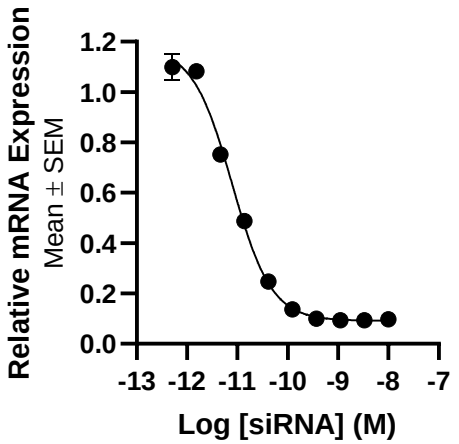
Lead siRNA identified *in vitro* and tested in healthy mice

ETX-291 mRNA Knockdown *in vitro*

Huh7

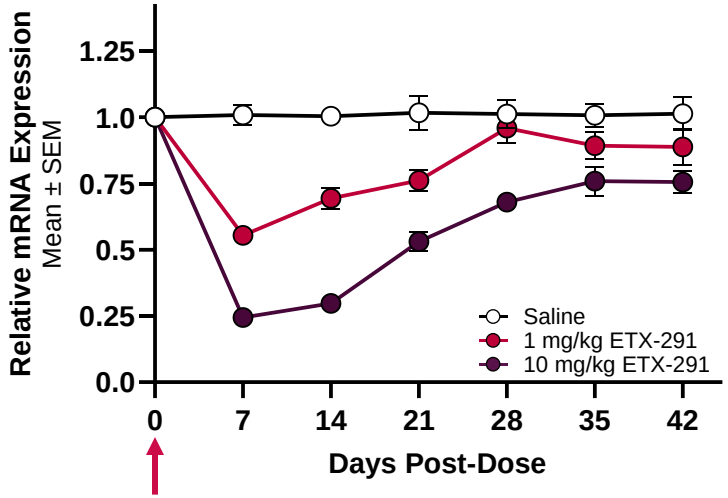


Primary Human Hepatocytes

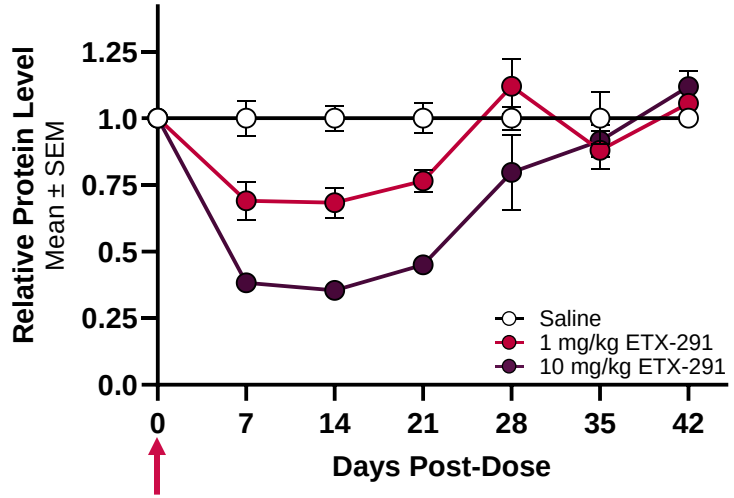


ETX-291 Knockdown in Healthy Mice

mRNA Levels by RT-qPCR



Protein Levels by LC-MS



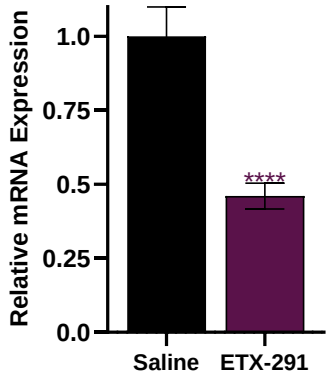
Constructs used in *in vivo* murine models demonstrate deep and sustained mRNA and protein knockdown, with a duration of action that supports quarterly subcutaneous dosing in humans

mRNA – messenger RNA | siRNA – small interfering RNA | **RT-qPCR** – Real-Time Quantitative Reverse Transcription PCR | **LC-MS** – Liquid Chromatography-Mass Spectrometry

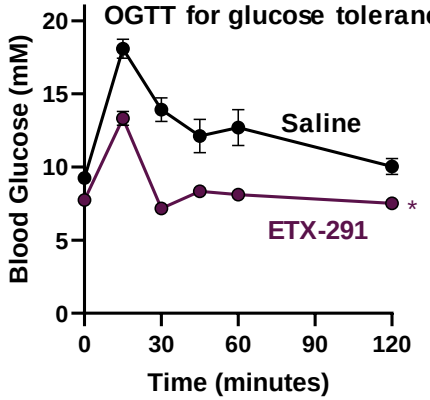
Pleiotropic Effects of ETX-291 on Key Cardiometabolic Risk Factors

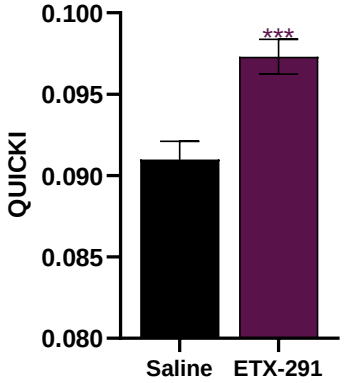
Results from a 12-week study in an ApoE*3L.CETP mouse model of metabolic syndrome

Reduced target mRNA expression



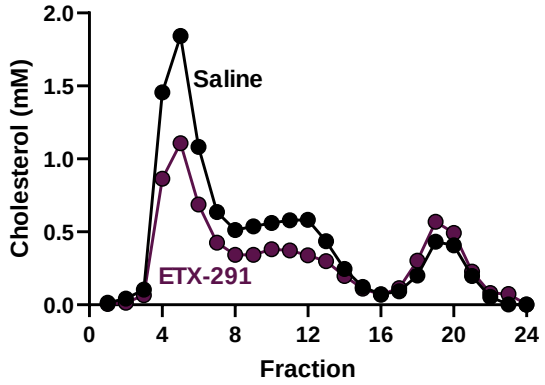
Improved glucose tolerance and insulin sensitivity



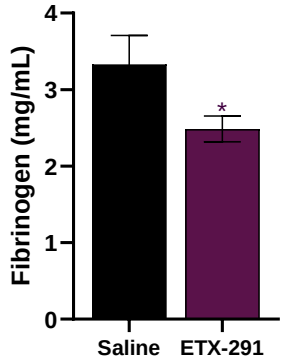


Increased QUICKI index demonstrates improved insulin resistance

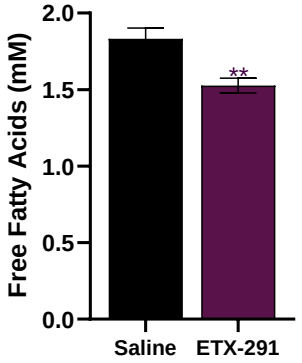
Reduced plasma cholesterol



Reduced fibrinogen



Reduced FFA



Treatment with ETX-291 provides a holistic treatment potential for cardiometabolic diseases beyond LDL-C modulation

12-week study with weekly subcutaneous 10 mg/kg dose of ETX-291. Error bars: mean ± SEM

** p < 0.05, ** p < 0.01, *** p < 0.001, **** p < 0.0001*

ETX-148: A HepNet™ Identified Pan-Haemophilia Target

Pursuing a novel pan-haemophilia rebalancing agent with good joint protection and leading safety profile

HepNet™ established link between the target and haemophilia through haemostasis network analysis

Human genetic evidence suggests reduced target expression not linked to increased risk of thrombosis unlike other rebalancing agents

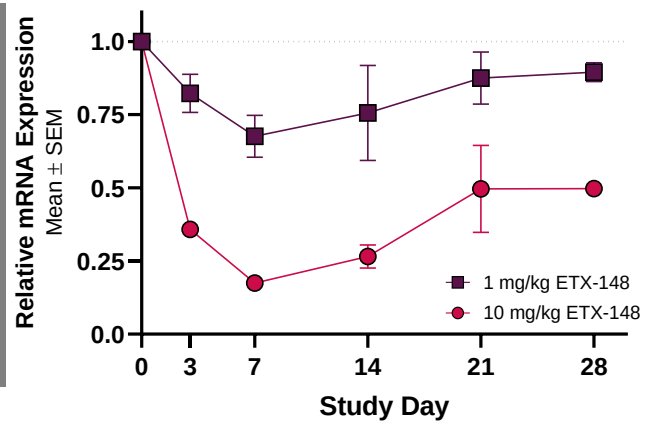
Target Product Profile

- **Combining good joint protection** and a **long duration of action** (aiming for quarterly+ duration)
- **Safe** in combination **with Factor replacement** (for emergency use)
- **Patient-friendly** subcutaneous administration
- Using ETX's proprietary **GalOmic™ GalNAc-siRNA** technology

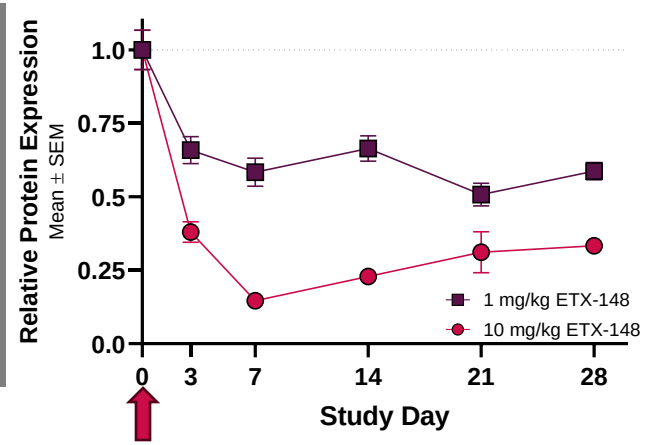
ETX-148 is a Potent siRNA That Demonstrates Joint Protective Effects in a Haemophilia A Haemarthrosis Mouse Model

ETX-148 Knockdown in Healthy Mice

mRNA Levels by RT-qPCR

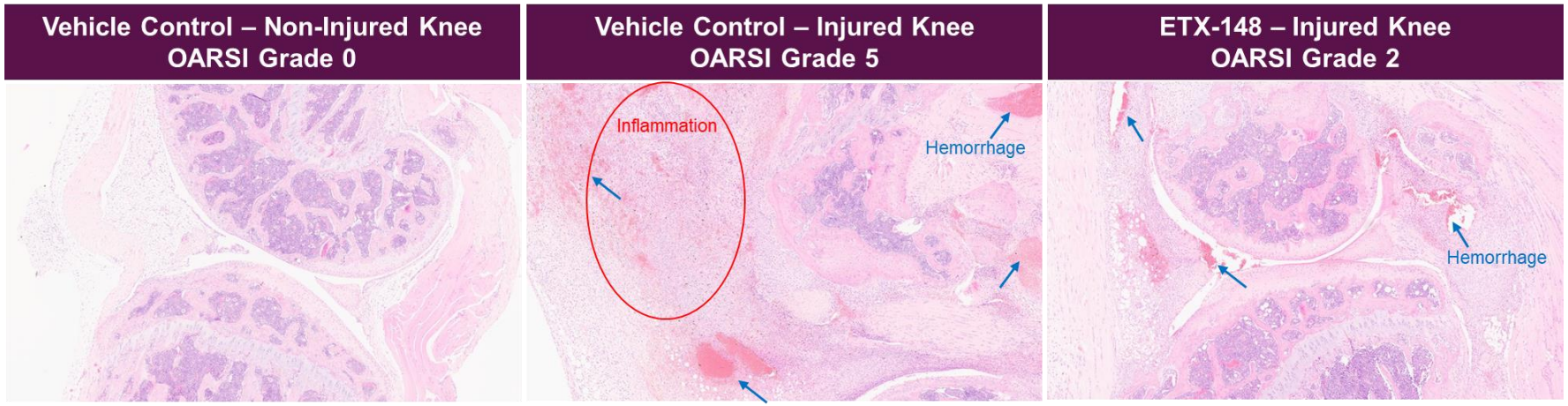


Protein Levels by LC-MS



Data normalised to saline-treated mice on Study Day 0

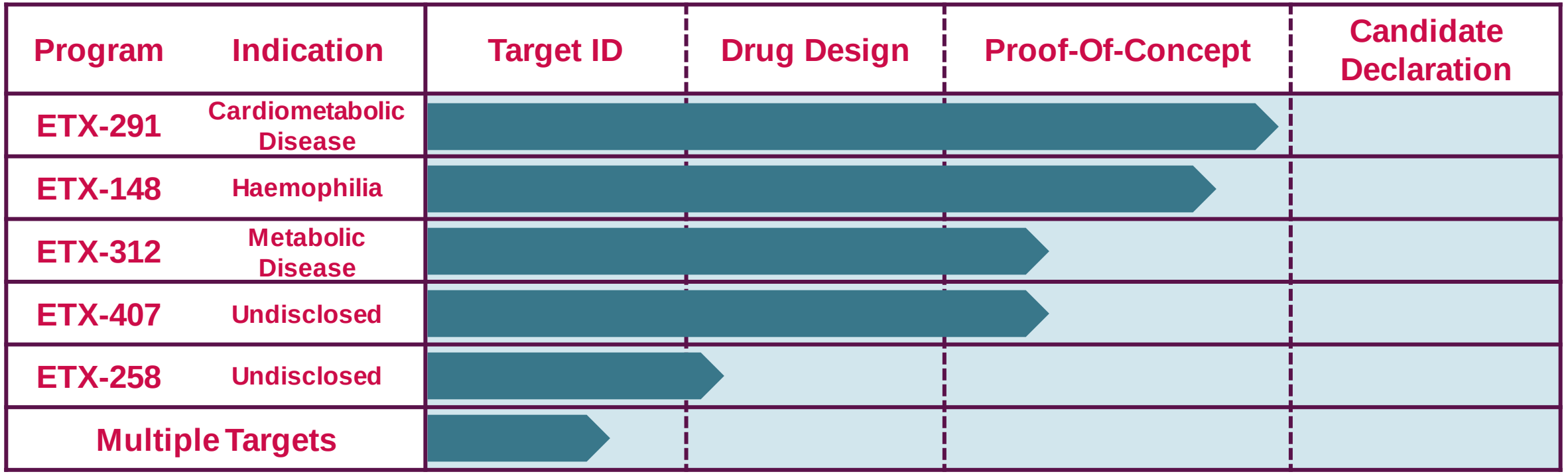
A Haemarthrosis Study in Haemophilia A Mice



- Administration of ETX-148 resulted in improved haemarthrosis knee joint pathology, reduced inflammation, and resulted in smaller areas of haemorrhage
- Additional studies have demonstrated safe administration of ETX-148 in combination with Factor Replacement in Haemophilia A mice (not shown)

Therapeutic Pipeline

Broad pipeline of GalOmic™ constructs targeting novel genes, guided by insights from HepNet™



Outlook

Outlook

Continuing to build on the strong foundation of HepNet™ and GalOmic™

Key H1 2024 Progress	Looking Ahead
Generated positive proof-of-concept data for lead GalOmic RNAi assets, ETX-291 and ETX-148	Complete data packages for lead assets by YE2024
Expansion of our GalOmic™ therapeutic pipeline	Complete data package for at least one additional GalOmic™ asset by YE2024, progress further assets into preclinical development
Increased pool of novel targets identified and assessed *in silico* by HepNet™	Continue growth of target pool, expansion into new therapeutic areas
Validated our siRNA design and straight to *in vivo* siRNA efficacy prediction	Further enhance AI-driven *in vivo* siRNA efficacy prediction with cutting-edge technology to accelerate drug design
Continued development and integration of Generative AI and LLMs into HepNet™	Begin development of novel platform based on LLM technology
Filed additional patent applications protecting our targets, chemistry, and therapeutics	Continue to generate novel IP and protect our inventions

therapeutics

Appendix

Leadership

Ali Mortazavi
Chief Executive Officer

Alan Whitmore
Chief Scientific Officer

Alison Gallafent
Chief Intellectual Property Officer

Timothy Bretherton
Chief Financial Officer

Laura Roca-Alonso
Chief Operating & Business Officer

Board of Directors

Ali Mortazavi
Chief Executive Officer

Professor Trevor Jones CBE
Non-Executive Chairman

Michael Bretherton
Non-executive Director
CEO Sarossa Plc

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Professor RNA Biology, UNSW Sydney

Dr Bill Harte
Chief Translational Officer
Case Western Reserve University