Computing The Future of Medicine™

Non-Confidential

February 2024

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Forward looking statement

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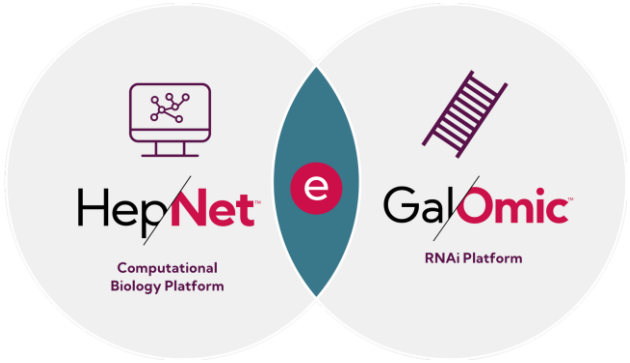
Company Overview

Driving innovation at the intersection of AI and precision medicine

Our mission:

Integrating computational power and biology to discover life-transforming medicines



*Full year results ended **31 January 2023***

Cash and cash equivalents
£31.7m H1 FY24: £24.8m

R&D spend
£7.2m H1 FY24: £5.3m

Operating loss
£10.2m H1 FY24: £7.0m

R&D tax credit receivable
£1.5m H1 FY24: £2.5m

Multi-disciplinary team
38 FTE H1 FY24: 34

Market cap (31/01/24)
£105.9m

London
Company HQ

Boston

GalOmic™

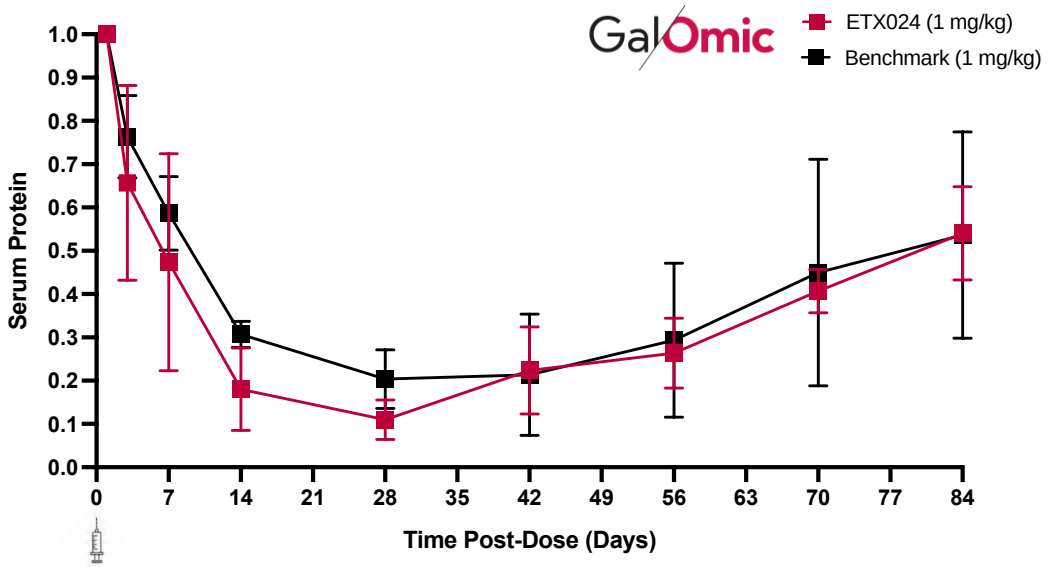
GalOmic™ RNAi Platform For Selective and Effective Gene Silencing

Proprietary RNAi chemistry platform enabling rapid generation of hepatocyte-targeting potent siRNAs

GalOmic™ GalNAc-siRNAs

- Specific knockdown of target genes in hepatocytes
- Long duration of action, usually supporting quarterly+ administration in humans
- RNAi is a commercial stage modality, with exceptional safety and tolerability profile
- Protected by robust IP portfolio
- Ability to generate lead candidates in 6 months

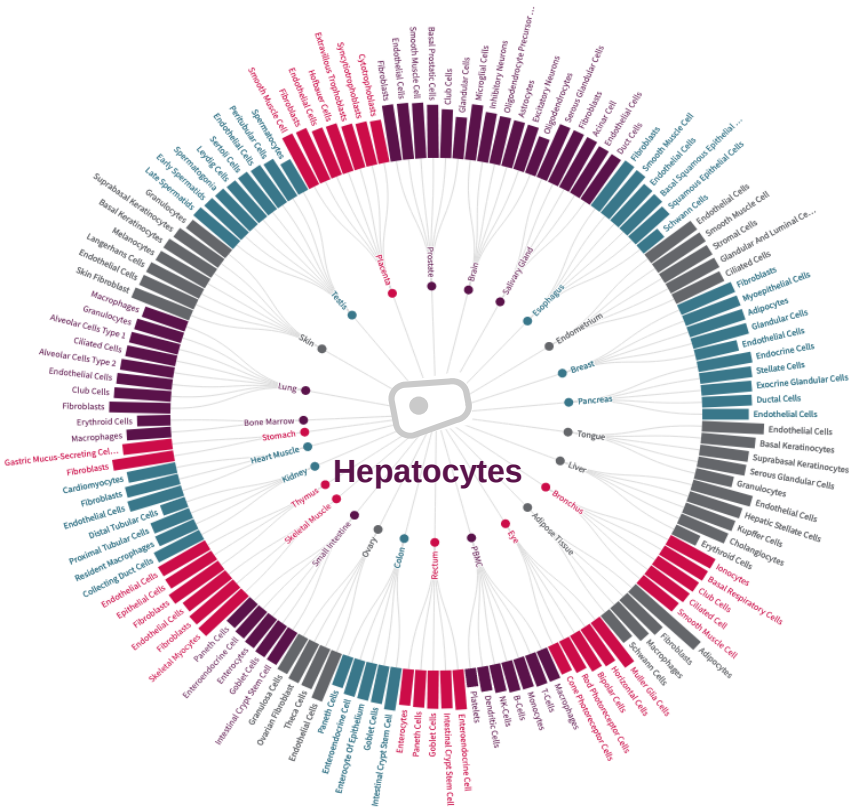
Typical performance profile of GalOmic™ constructs in non-human primate

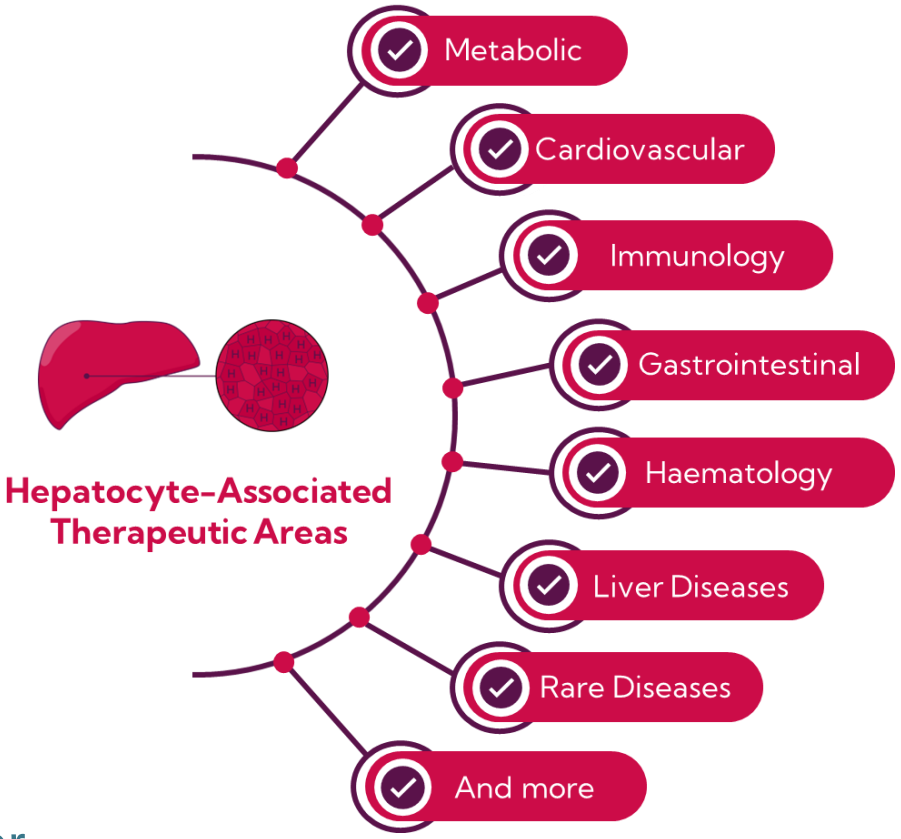


GalNAc - N-acetylgalactosamine | **siRNA** - small-interfering RNA

Hepatocytes Drive Processes Underlying Numerous Disease Areas

Hepatocytes influence a wide variety of cell types and tissues beyond the liver





Hepatocytes have a **high level of influence** over other cell types, which we capture in our computational models

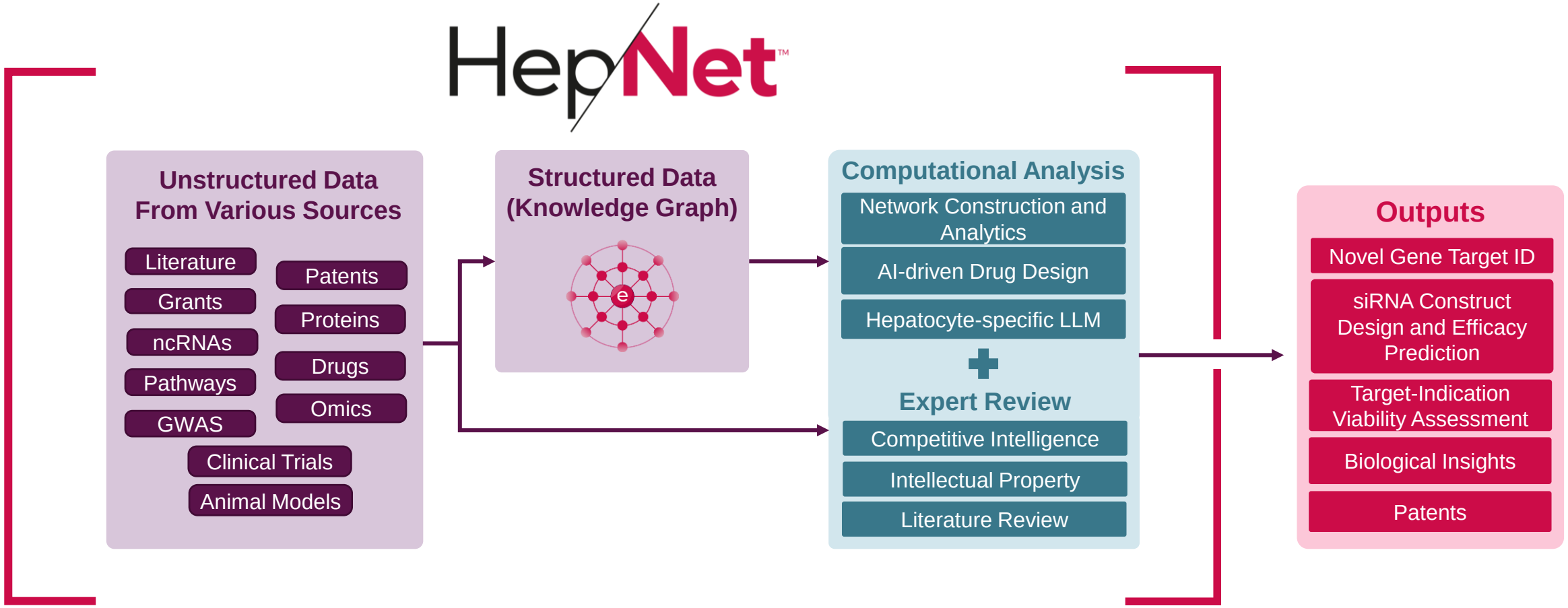
Traditional Approaches to Drug Development are Too Slow and Too Expensive

- 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™

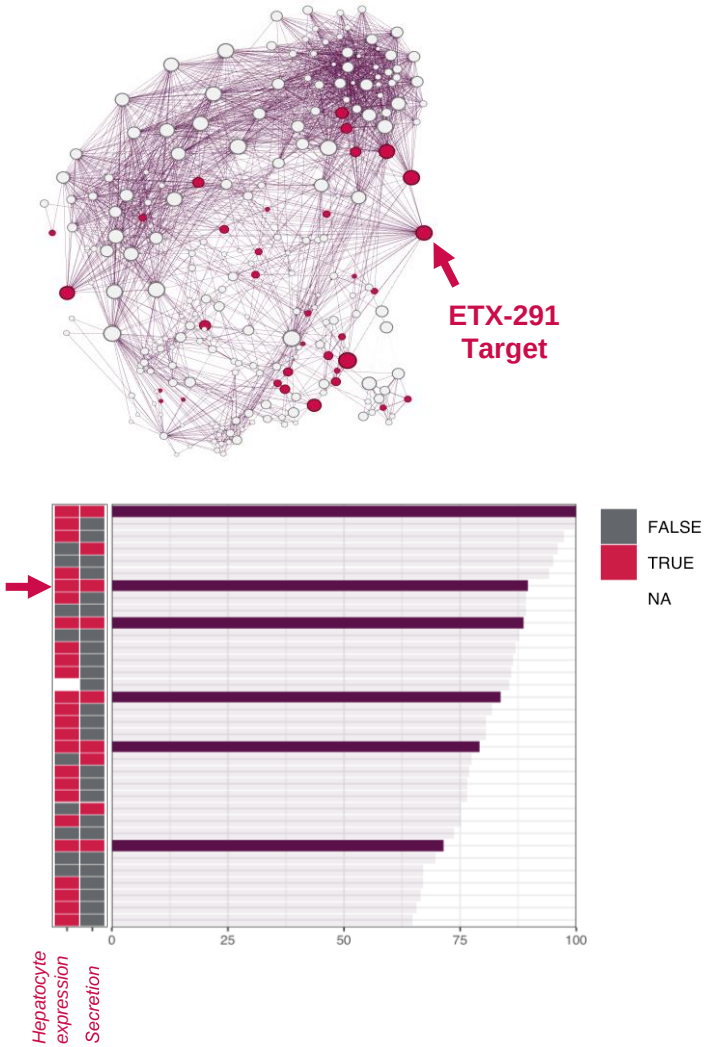
Our world-class hepatocyte-specific computational biology platform



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

Network Construction and Analysis for Target ID

Computational identification of ETX-291's target gene



HepNet™ predicts link between target and metabolic disease risk:

- Identification of key process from network analysis of metabolic GWAS data (diabetes risk)
- Building a process-specific network model
- Identification of target using proprietary network analysis
- Top proteins ranked using our Key Protein Analysis (KPA) approach - triage of top decile led to identification of an RNAi target selected for evaluation

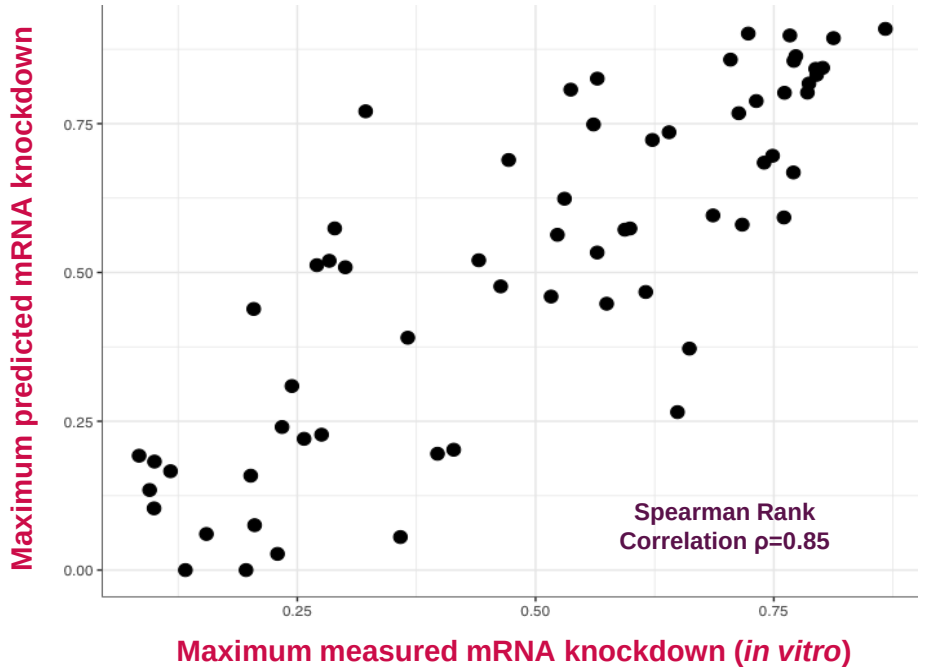
AI-Driven Drug Design

Using AI to predict siRNA efficacy and bypass *in vitro* screening

- Model trained on proprietary, high-quality training datasets, including siRNAs with GalOmic modification patterns
- Trained model has high prediction accuracy, enabling identification of lead siRNA sequences *in silico* and minimising number of sequences screened *in vitro*

In development: further enhancement of predictions using large language models (LLMs) trained on mRNA sequences. This includes prediction of secondary and tertiary structures

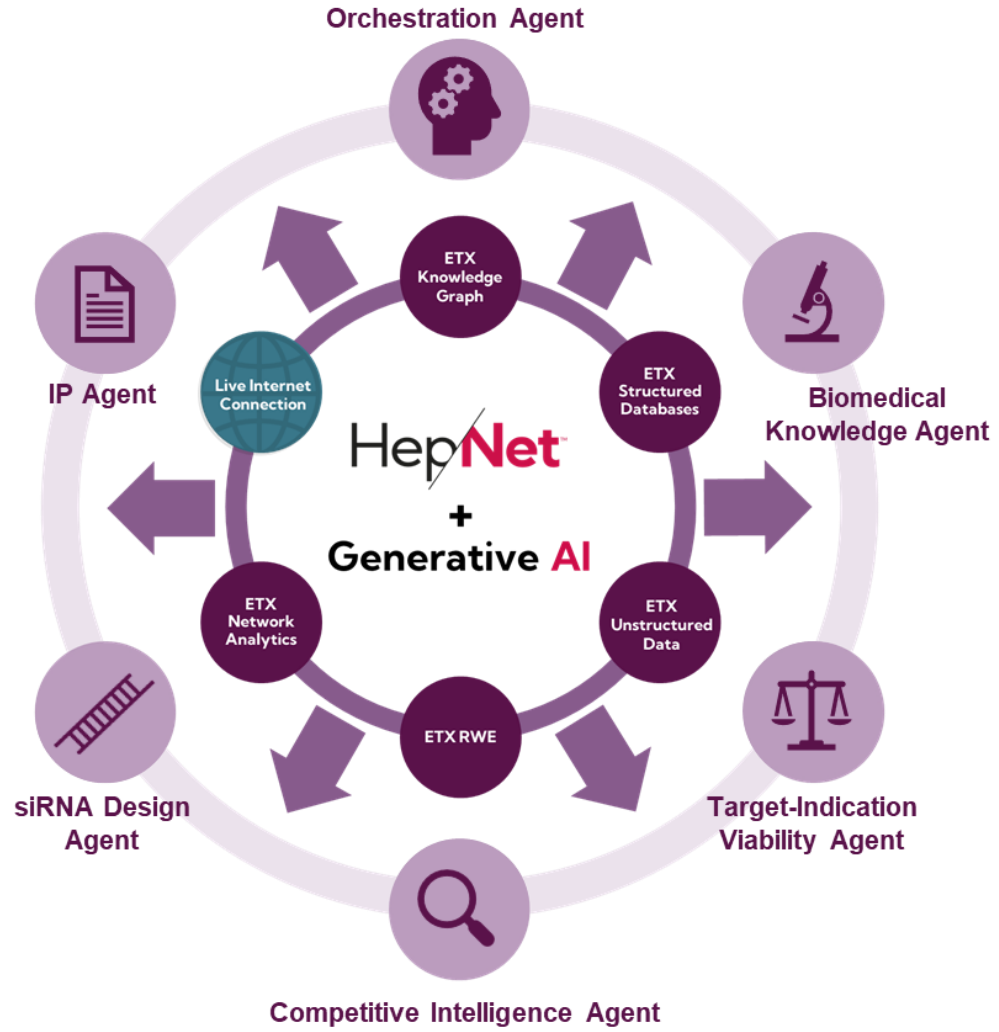
Predicted vs measured siRNA efficacy (Validation Dataset)



Creating a Hepatocyte-Specific Large Language Model Ecosystem

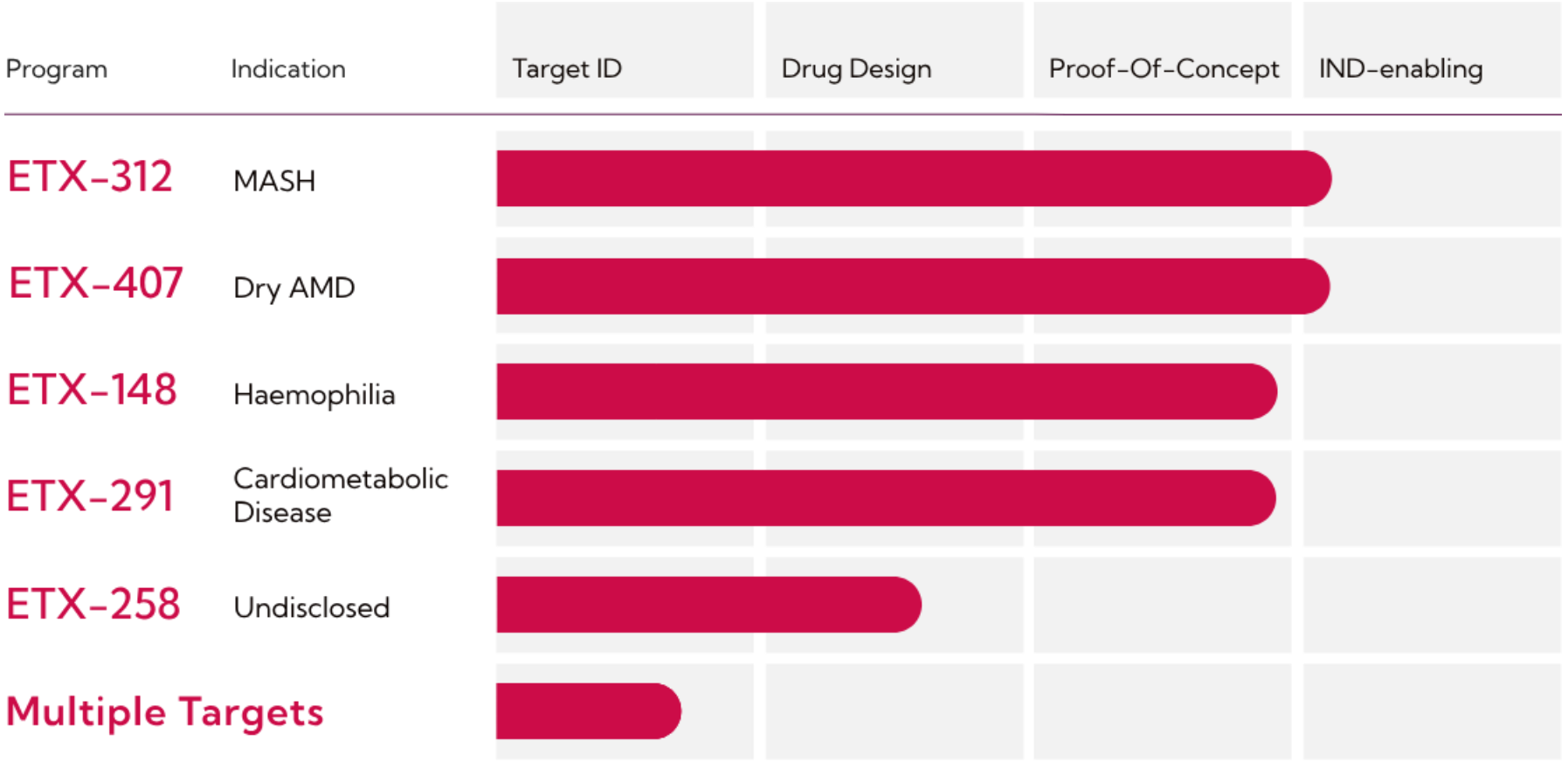
Transforming HepNet™ into a dynamic knowledge resource through creation of specialist LLM agents

- **LLM agents** trained on specific data will support a variety of ETX's drug development processes including target ID, target-indication viability assessment, 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



Therapeutic Pipeline

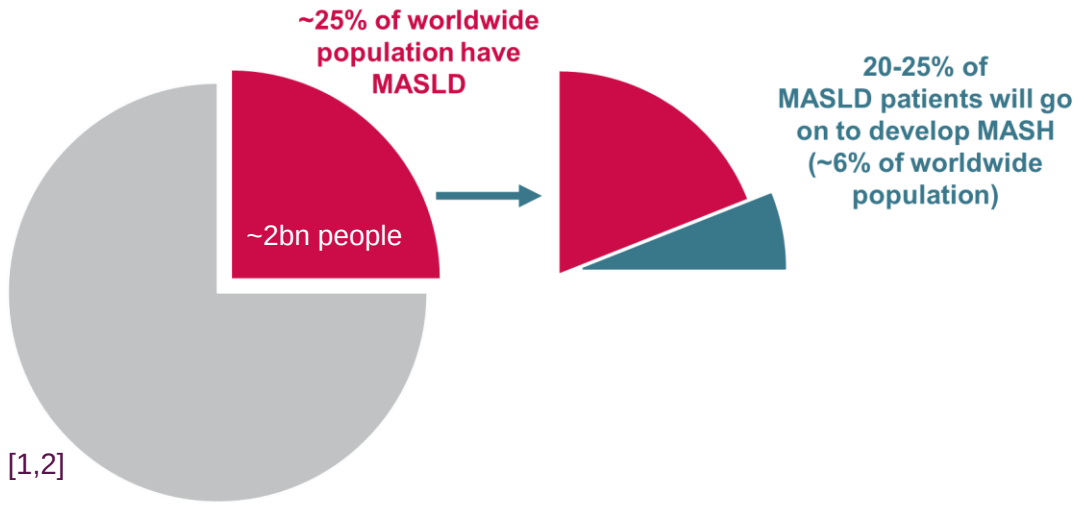
Therapeutic Pipeline



Our candidates pursue novel, highly differentiated targets in a variety of therapeutic areas

ETX-312 for the Treatment of MASH

A safe and effective GalOmic siRNA treatment for a prevalent disease with high unmet need



Currently no FDA approved therapies for treatment of MASH

Target Product Profile

- Reduced Steatohepatitis
- No Worsening of Fibrosis
- Improvement of MASH Biomarkers
- Low Treatment Burden
- Safe

**MASH -* *metabolic dysfunction-associated steatohepatitis is now the replacement term for NASH*

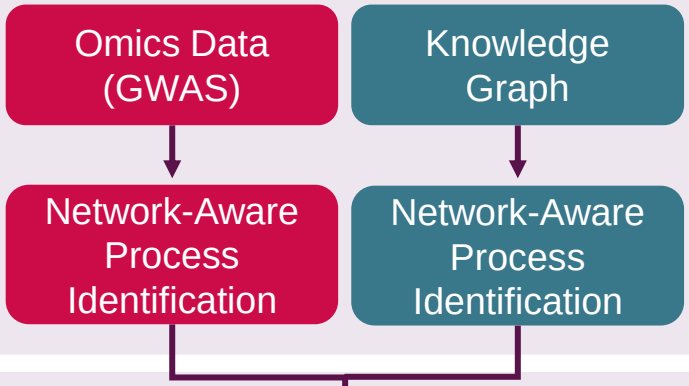
[1] Younossi, Zobair M.*; Koenig, Aaron B.; Abdelatif, Dinan; Fazel, Yousef; Henry, Linda; Wymer, Mark. Global epidemiology of nonalcoholic fatty liver disease—Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology 64(1):p 73-84, July 2016. | DOI: 10.1002/hep.28431

[2] Bellentani S. The epidemiology of non-alcoholic fatty liver disease. Liver Int. 2017 Jan;37 Suppl 1:81-84. doi: 10.1111/liv.13299. PMID: 28052624.

ETX-312 Computational Target Identification

HepNet data foundation and analytical functionality deployed for target ID

1



Independent network analysis of two data sources, **Meta-GWAS Data** and **Knowledge Graph**, identified the **same key biological process in MASH**

2

Networks of this **key biological process** in context of MASH constructed using **proprietary ETX interactome**

3

Targets ranked based on key characteristics including expression profile, modality fit, and strategic fit – **ETX-312 target selected**

ETX-312 Construct Design, Selection, and Performance

Efficacy of all possible constructs ranked *in silico* using AI model trained on GalOmic siRNA chemistry

In Silico

AI-driven design of siRNA constructs

↓

siRNA selection criteria applied

↓

Efficacy prediction using **HepNet AI model** trained on siRNAs with **GalOmic modification patterns**

↓

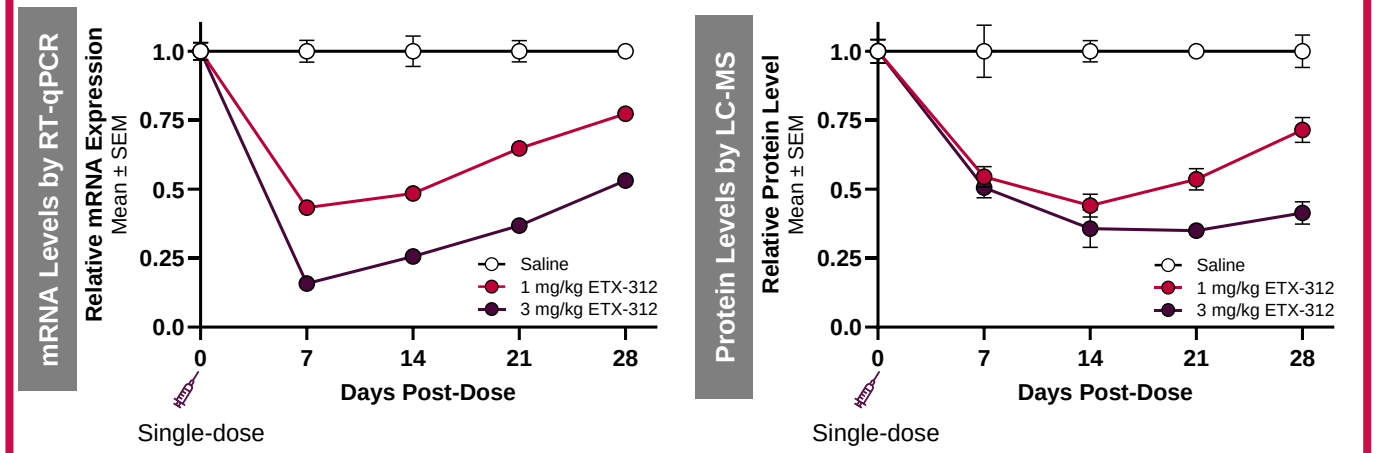
Wet Lab

siRNAs screened *in vitro* and *in vivo*

↓

Most potent siRNA selected as **ETX-312 lead construct**

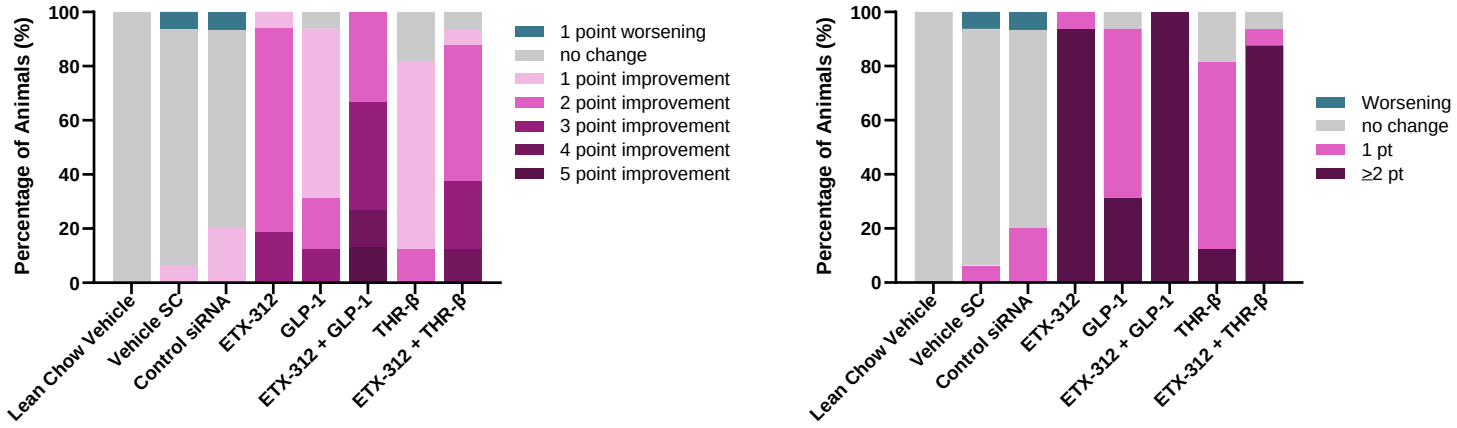
ETX-312 Knockdown in Healthy Mice



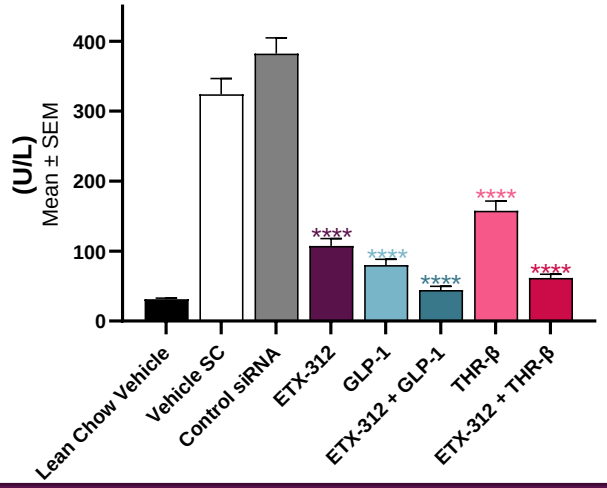
ETX-312 demonstrates potent and durable target knockdown in healthy mice

ETX-312 Demonstrates Significant Therapeutic Benefit in the Gubra DIO-MASH Mouse Model

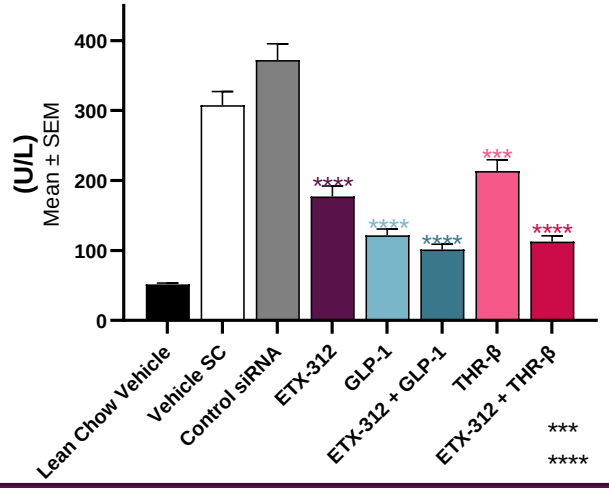
NAFLD Activity Score



Plasma ALT



Plasma AST



*** $p \leq 0.001$
**** $p < 0.0001$

- ETX-312 **dramatically improved the NAFLD Activity Score** alone or in combination with either a GLP-1 or THR-β agonist
- ETX-312 treatment **improves liver function**
- **Significant reduction in ALT and AST levels** was observed with ETX-312 treatment alone or in combination

ETX-312 clinical candidate nominated and proceeding to IND-enabling studies

ETX-407 for the Treatment of Dry AMD

Providing an effective alternative to invasive intravitreal injections

288 million people worldwide projected to have AMD by 2040 [1]

No. 1 cause of blindness in adults aged 60 yrs and older [2]

- Dry AMD **severely impacts vision and daily life** for millions – 16% of patients progress to legal blindness within two years of diagnosis. [3]
- All approved treatments for dry AMD are **intravitreally injected** – urgent need for **lower burden treatment**

Target Product Profile

- **Human Genetic Validation**
- **Precision Medicine Approach**
- **Effective Target Inhibition**
- **Low Treatment Burden**
- **Safe**

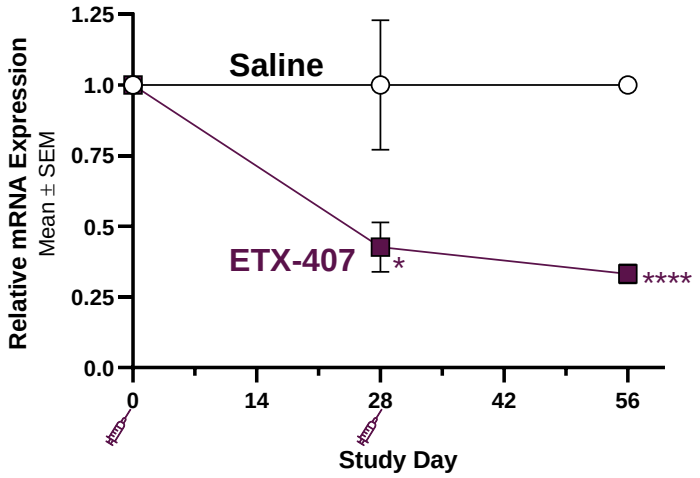
[1] Wong, W.L. et al. (2014) “Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis,” The Lancet Global Health, 2(2), pp. e106–e116. Available at: https://doi.org/10.1016/s2214-109x(13)70145-1.
[2] VISION 2020 Global Initiative for the Elimination of Avoidable Blindness: Action plan 2006-2011. World Health Organization, 2007. World Health Organization report called: “Global data on visual impairment 2010” (WHO/NMH/PBD/12.01)
[3] Chakravarthy U, et al. (2018) Ophthalmology, 125(6):842-849.

ETX-407 Lead Candidate Selected Based on NHP Study Results

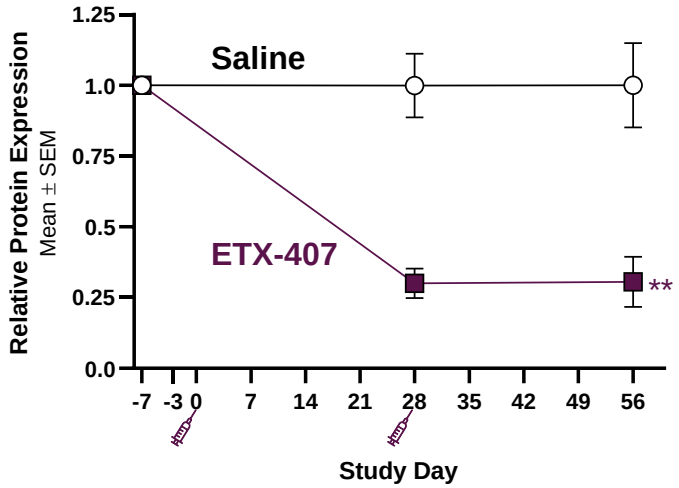
ETX-407 demonstrates the applicability of ETX's hepatocyte-targeting GalOmic platform in indications affecting distal organs

ETX-407 constructs were tested *in vivo* in *Cynomolgus macaques*

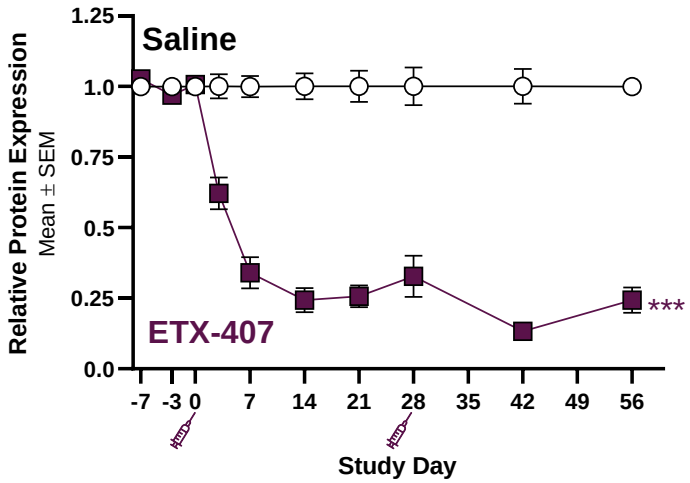
Hepatic mRNA



Hepatic Protein



Plasma Protein



- ETX-407 effectively reduces target mRNA and protein in the liver following 1and 2 doses (3mg/kg)
- Deep knockdown of circulating, as well as ocular, protein levels confirmed

ETX-407 clinical candidate nominated and proceeding to IND-enabling studies

* $p \leq 0.05$
** $p \leq 0.01$
*** $p \leq 0.001$
**** $p < 0.0001$

Continued Progress on All Pipeline Assets

ETX-148 and ETX-291 PoC datasets generated in disease models support our therapeutic hypotheses

ETX-148 for the treatment of Haemophilia

Addressing the **key unmet need of haemarthrosis** with a safe approach and low treatment burden

- **Joint bleed protection** demonstrated in haemophilia models (A and B)
- **No thrombosis risk** seen, supporting both monotherapy and combination with factor therapies where needed

ETX-291 for the treatment of Cardiometabolic Disease

Meaningfully **lowering cardiometabolic disease risk** with a safe approach and low treatment burden

- Genetic support of target points at **pleiotropic applications and benefit**
- Confirmed **impact on various disease drivers**, including: improved insulin sensitivity, glucose homeostasis, lipoprotein levels, fibrinogen and free fatty acids

Summary

Where TechBio meets genetic medicine

Tangible progress on our mission of *Computing the Future of Medicine*:

- Proprietary, enabling **technology platforms** in AI (HepNet™) and RNAi (GalOmic™)
- Maturing pipeline of **highly differentiated GalOmic RNAi assets** across a variety of therapeutic areas with high unmet need
  - ETX-407 in dry AMD and ETX-312 in MASH progressing to **IND enabling** studies
  - Complete **proof-of-concept** datasets in cardiometabolic disease (ETX-291) and haemophilia (ETX-148), supporting target product profiles
  - ETX-258 progressing in an undisclosed indications
- **Externally validated** computational methods based on network biology, with an additional success **milestone** in iTeos collaboration recently achieved
- A cash position of **c.£20.1m**

etherapeutics

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