Integrating computational power and biology to discover life-transforming medicines

Interim results for six months ended 31 July 2021

Successful RNAi Platform Development

October 2021

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Forward looking statement

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Company Overview

Integrating computational power and biology to discover life-transforming medicines

- **Ability to model human biology and interrogate complexity for better and faster drug discovery**
  - Experimentally validated computational platform centered around network biology
  - Increased translatability and improved probability of success
  - Third party validation Galápagos novo nordisk C4XD Top5 Pharma
- **Competitive proprietary RNAi platform developed.** Convergence with computational platform to rapidly identify and prosecute novel targets to unlock further value
- Experienced leadership and growing **multi-disciplinary team**. Currently 34 FTE
- **Scope for future partnerships,** across computational and RNAi platforms
- **Well-funded** following recent £22.5m capital raise

Highlights (incl. post period)

Significantly strengthened cash position to facilitate a number of initiatives, expanding the Company's platform capabilities and acceleration of the development of in-house RNAi pipeline

RNAi platform development

- Successful proprietary **GalNAc-siRNA platform developed** and characterised. Equivalent performance to leading platforms demonstrated
- **11 patent** applications filed to protect innovative GalNAc-siRNA construct designs

Computational platform – zooming into hepatocytes

- **Hepatocyte Knowledge Graph** created and ambitious experimental omics data strategy underway
- Expanded **target identification** focus and creation of tailored computational applications in hepatocytes and RNAi
- Increased **automation and cloud computing**

Collaborations – further validation of our computational platform

- **Galapagos collaboration:** Hit compounds successfully identified and 3 milestone payments received during the period. Collaboration active and hits being further investigated. Scope for further milestones through pre-clinical, clinical and commercial

Corporate

- Successful **£22.5m gross fund raise** from new and existing shareholders
- Commenced trading on **OTCQX Best Market** in the U.S. – important step to broaden shareholder base
- **Board and leadership** changes and significant increase in scientific staff

Financial Summary: Six months ended 31 July 2021

	Six months ended 31 July 2021	Six months ended 31 July 2020
Revenue	£0.5m	£0.04m
Operating loss	£3.5m	£2.7m
Cash and cash equivalents	£31.6m	£15.1m*
R&D	£2.5m	£1.2m

Financial Highlights

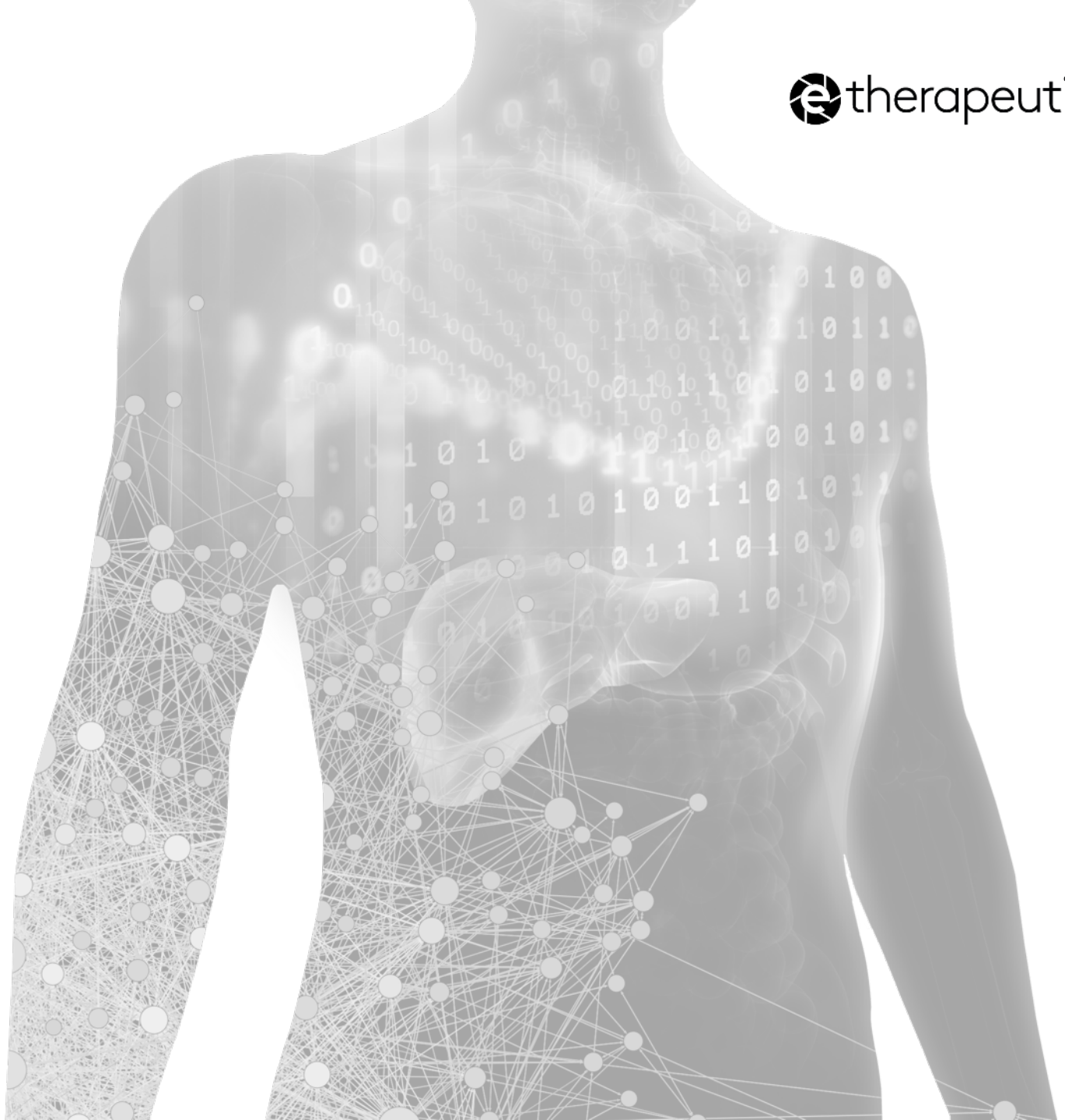
- **Strengthened financial position** following successful fund raise of £22.5m gross
- Continued to carefully manage the underlying cash burn
  - focusing on generating income and achieving external commercial validation with our partners and;
  - investing in a new RNAi platform

Financial Outlook

- Underlying cash burn in H2 expected to be higher than H1
  - further progress R&D activities
  - build administrative infrastructure to support scaling of business

* £13.0m as of 31 January 2021

The Convergence of two Cutting-edge Platforms



Network & systems biology – core expertise of ETX

Network models are constructed and interrogated using ETX proprietary computational methods to provide insights into complex diseases and transform drug discovery

Biological complexity remains the big challenge in drug discovery and development. We strive to address it

- Biological functions are controlled by **networks of genes and proteins**
- Understanding these networks is key to **understanding disease**
- Millions of network models of **disease processes** built to ask therapeutic questions
- Ability to test **millions of interventions** *in silico*
- Computational outputs feed directly into **translatable** laboratory assays


Influenza virus replication


Lipid metabolism

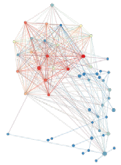

Tryptophan catabolism

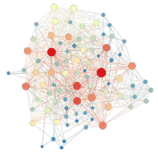

Telomerase signaling


Endocytosis

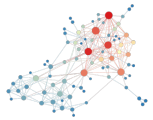

Fibroblast activation

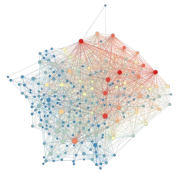

Angiogenic signaling


Neuronal autophagy

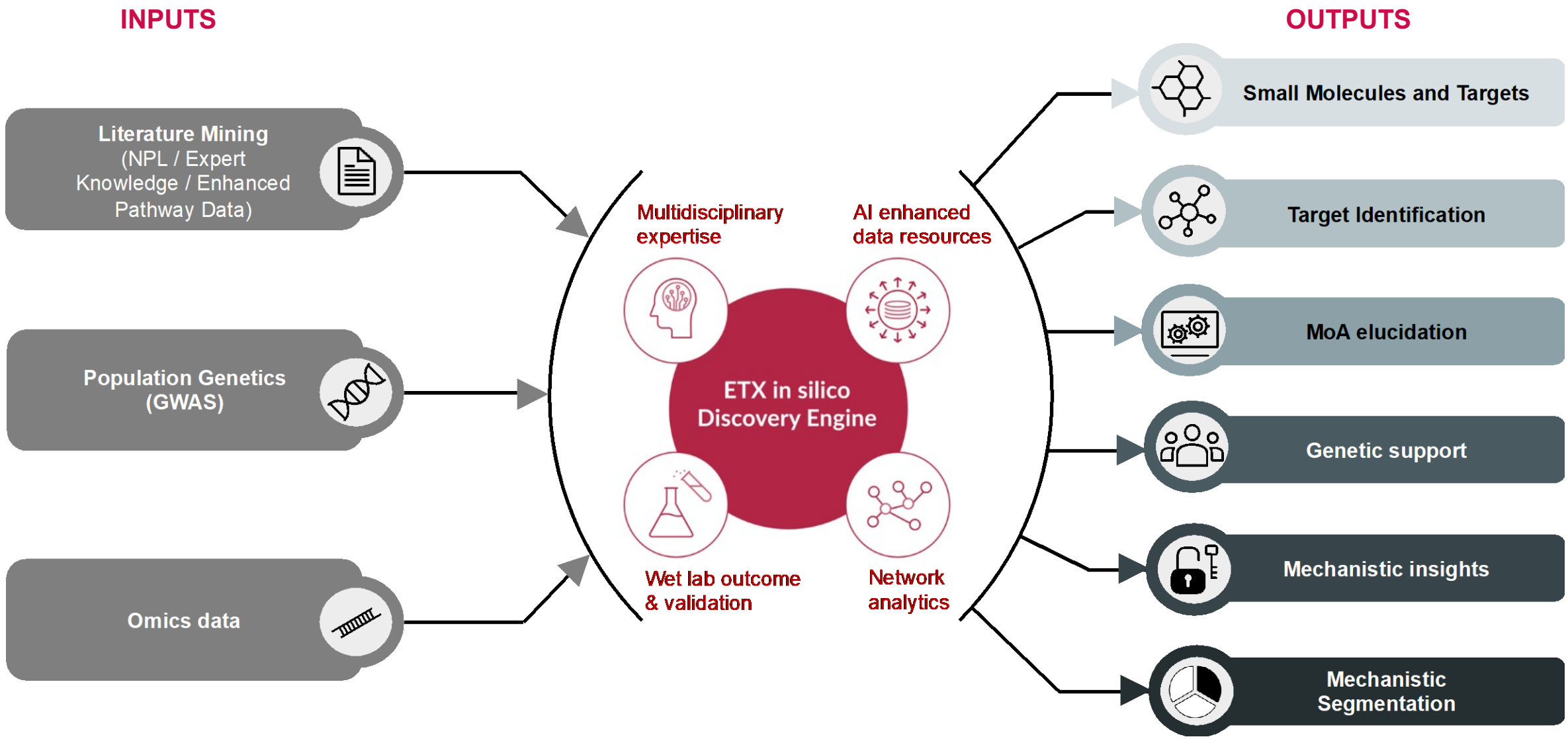

Tunneling nanotube regulation


Insulin resistance


Axonal degeneration


Immune checkpoint signaling

ETX *in silico* Discovery Engine – Inputs & Outputs



Competitive landscape – differentiated positioning

The industry faces two huge difficulties: understanding biology and making good drugs

therapeutics

Computational discovery (small molecule focus)

- Huge effort around solving small molecule chemistry
- Speed asymmetry
- Poorly understood biology

RNAi

- Significantly faster molecular design
- Lack of novel targets
- Poorly understood biology

Drug design times and costs (estimated)

Small molecules: **>$4M**, >4 years

siRNA: **$0.5M**, 6 months

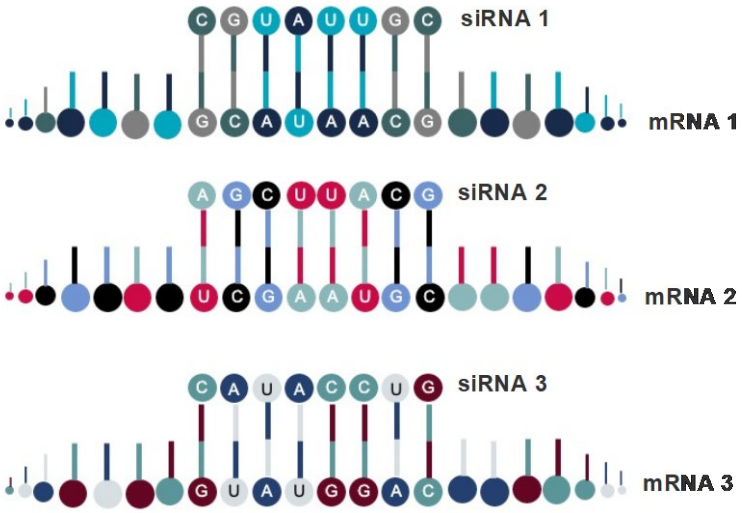
Information RNAi Molecules

Expansion into RNAi, a highly specific and reproducible modality for gene silencing that enables accelerated timelines and lower R&D costs

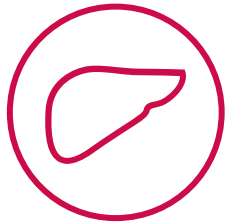
New proprietary RNAi platform technology for liver gene silencing:

- Enables ETX to silence selectively **any of the ~10k genes** in the genome of hepatocytes
- **Ability to quickly prosecute** target gene ideas generated computationally (key differentiator)
- **Rapid design of information molecules** that become drug candidates
- GalNAc conjugation enables **hepatocyte specificity and subcutaneous administration**
- **Accelerated** generation of new candidates relative to other modalities

siRNA design based on genetic code

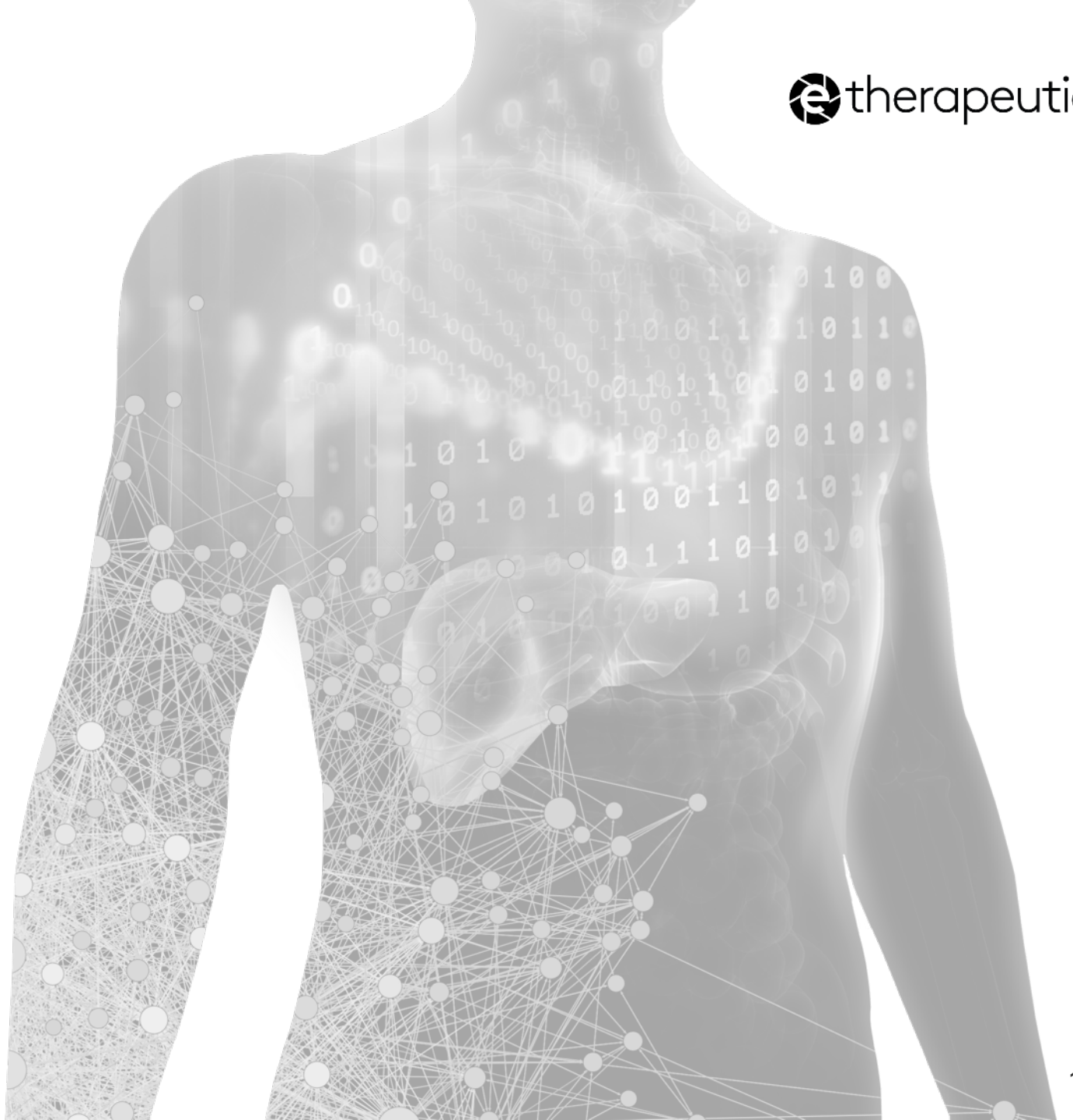


GalNAc conjugation enables specific siRNA delivery to hepatocytes (liver)



GalNAc: N-acetylgalactosamine

Development of a World-leading Proprietary RNAi Platform



Benchmarking Studies – ETX GalNAc-siRNA Platform Characterisation Completed

Experimental plan

- **Construct designs:** 8 oligonucleotide chemistries and different GalNAc linkers tested
- **Target knock-down:** both depth and duration of knock-down evaluated
- **High hurdle:** ETX platform benchmarked against leading peer platforms (including one approved drug and one in registration)
- **Reproducibility:** 3 targets evaluated

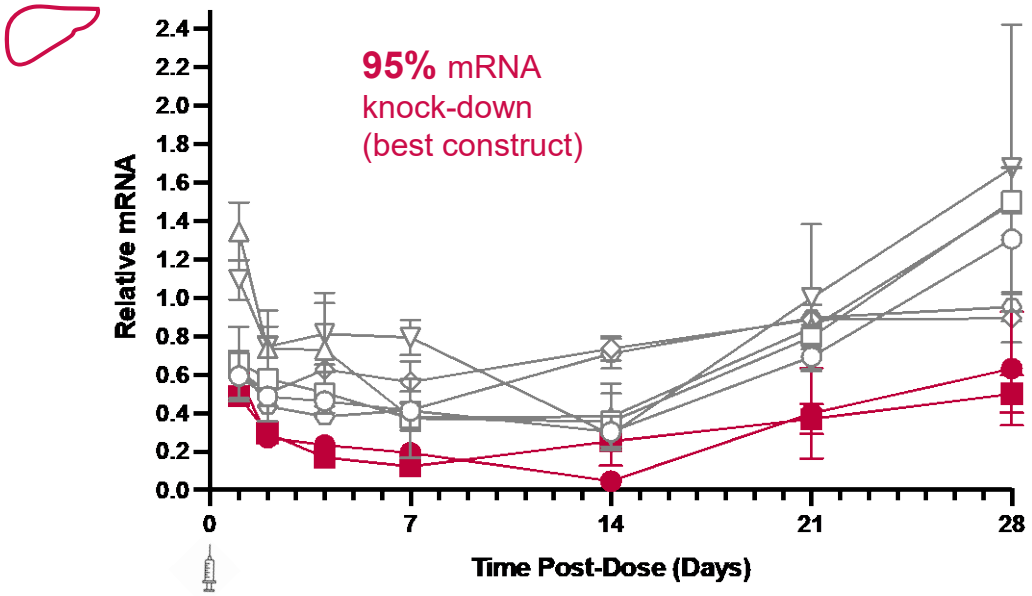
Results

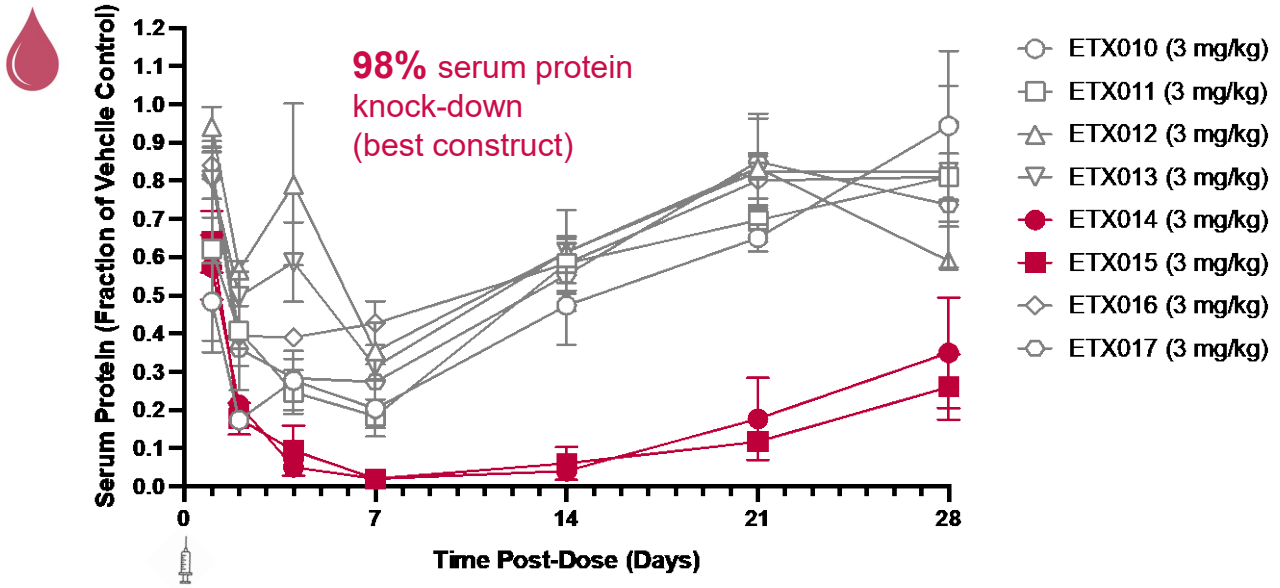
- ✓ **Data package:** *In vitro* and *in vivo* experiments completed. Characterisation datasets generated *(See next slides for headline results)*
- ✓ **Lead designs:** Most potent designs consistently identified
- ✓ **11 patent applications filed**
- ✓ **Competitive depth and duration of target gene knock-down. Equivalent performance to leading platforms**

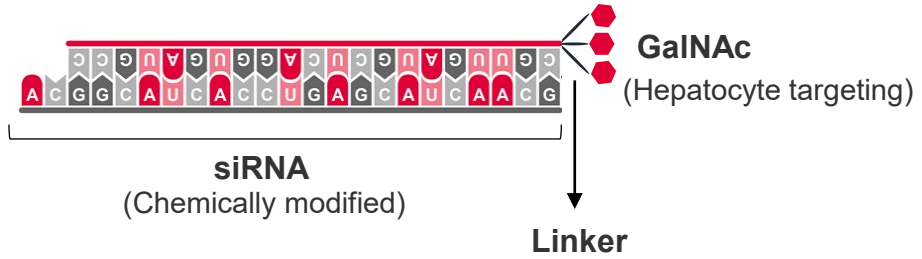
RNAi platform ready to prosecute targets identified in-house

ETX GalNAc-siRNA Platform Performance: Headline Mouse Results

Different ETX constructs tested in mice for **Target X**





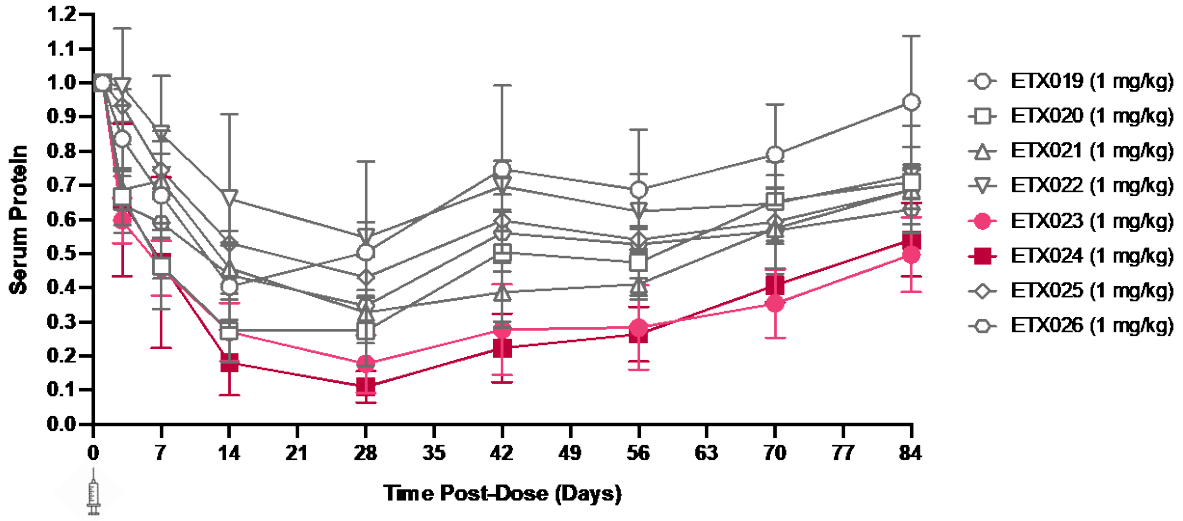


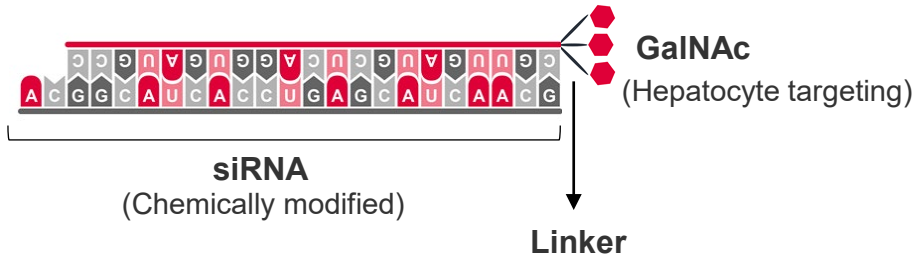
n=3, C57BL/6 mice

ETX GalNAc-siRNA Platform Performance: Headline Non-Human Primate (NHP) Results

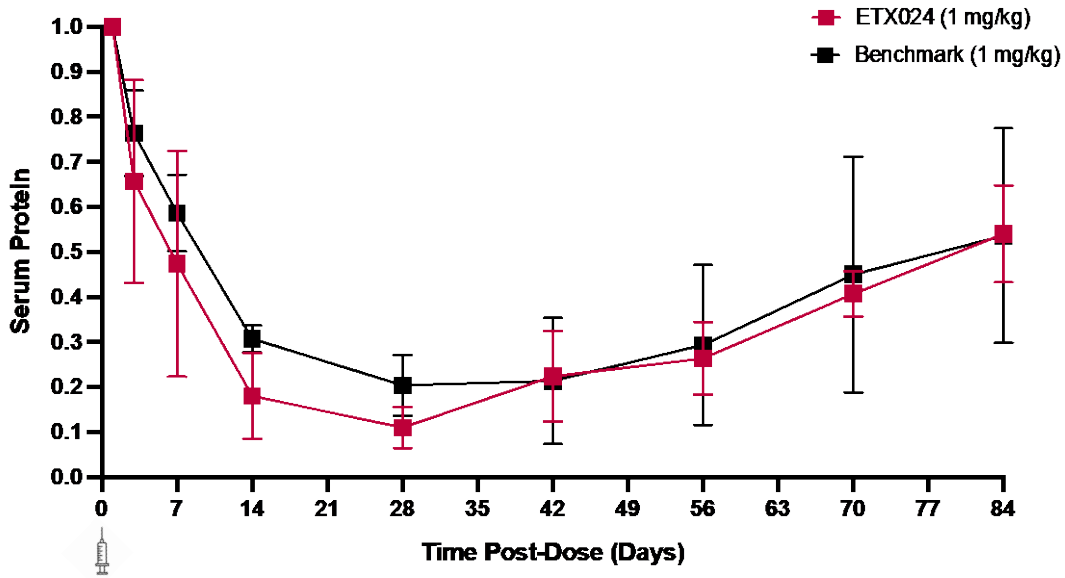
Summary non-human primate target Y knock-down data (serum protein):

Different ETX constructs tested – **Target Y**





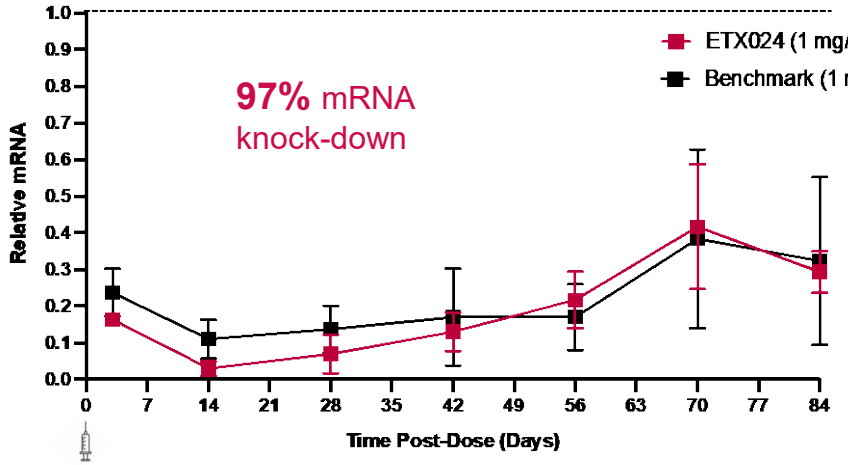
Competitive depth and duration of target knock-down

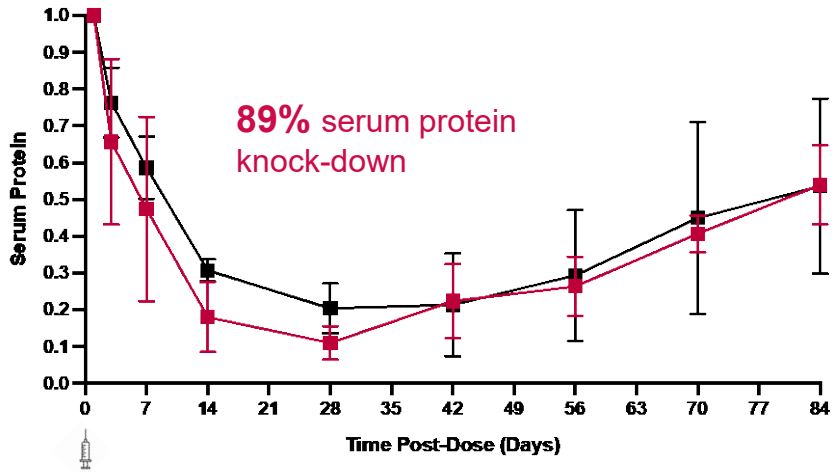


Cynomolgus monkeys, n=3

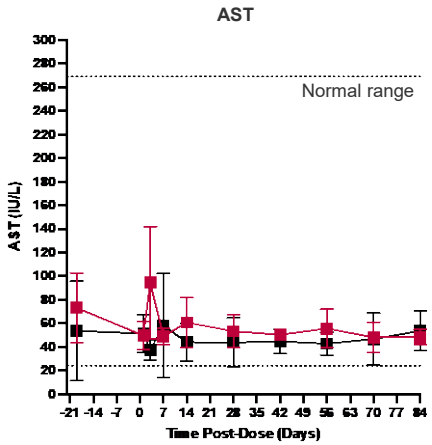
ETX lead Construct Design Performance and Safety (NHP)

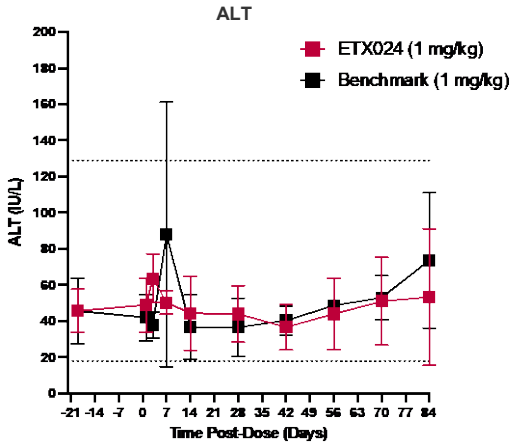
Target Y liver mRNA and serum protein levels show deep and sustainable knock-down for 3 months in non-human primates

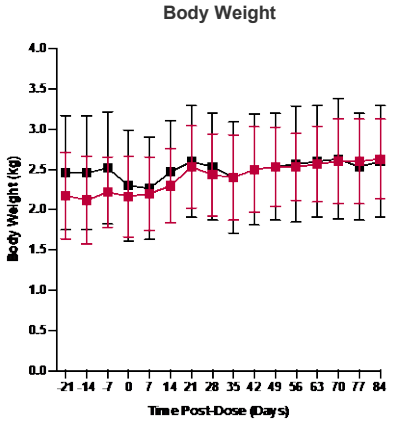


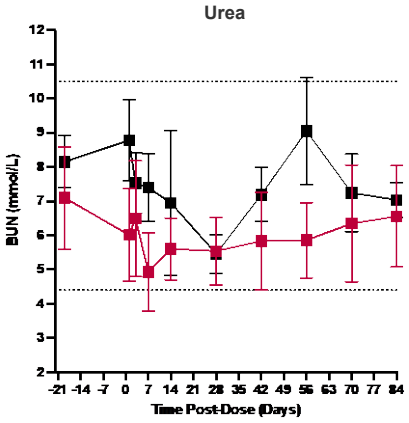


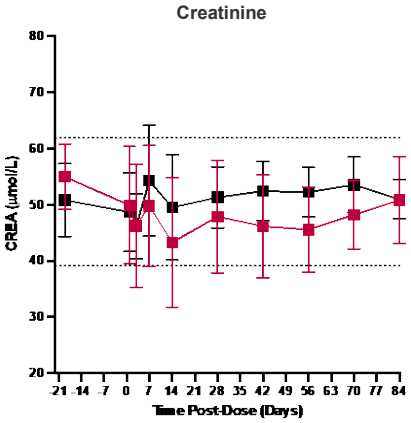
Well tolerated in non-human primates







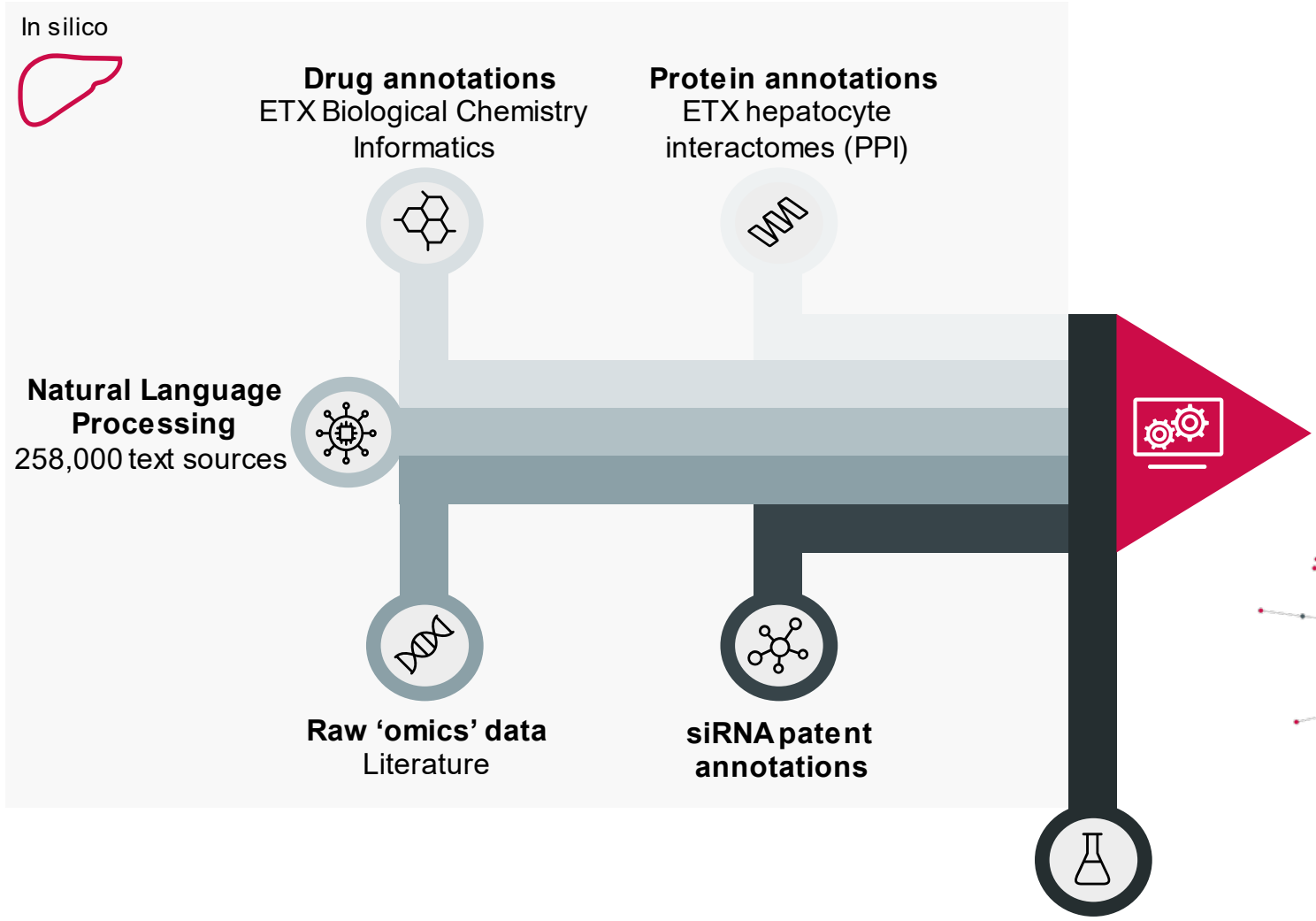


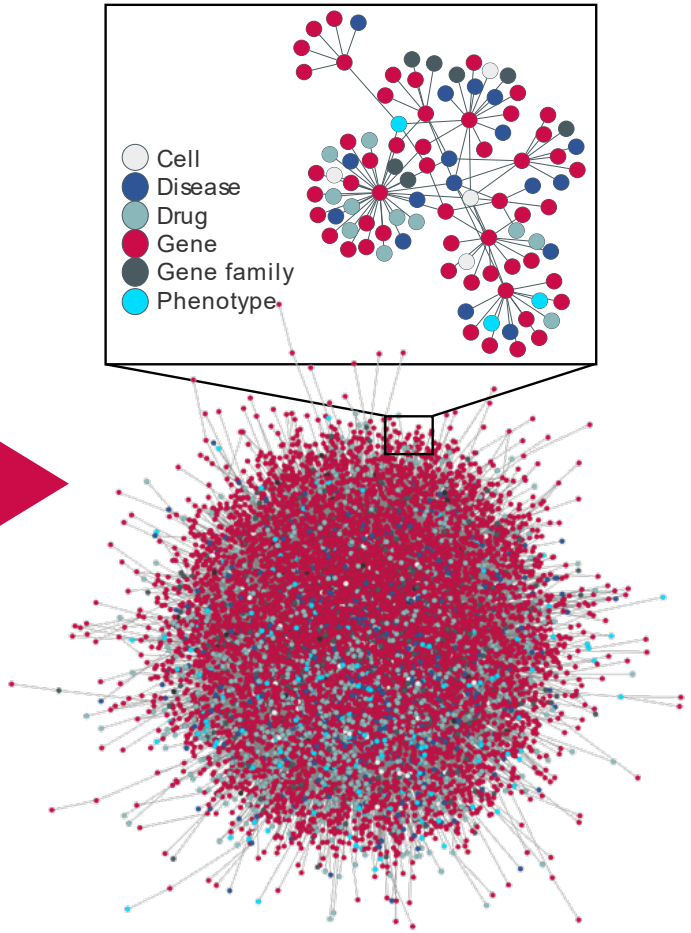


Cynomolgus monkeys, n=3, ALT (alanine aminotransferase), AST (aspartate aminotransferase)

Hepatocyte-specific Computational Platform

Hepatocyte-specific* Data Strategy and Knowledge Graph



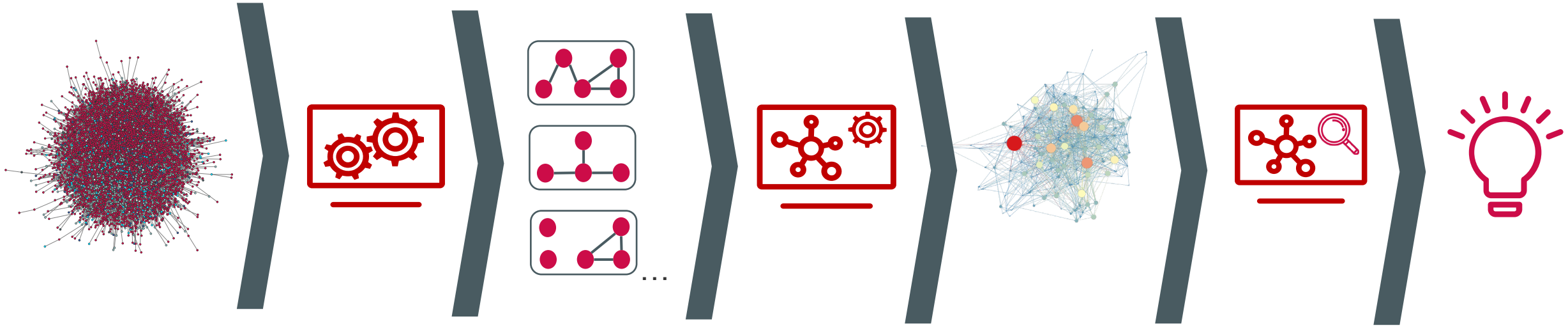


ETX Hepatocyte Knowledge Graph

24,7000 entities (nodes)
96,700 interactions (edges)

* Reproducible in other cell types

Hepatocyte Target Identification



Target identification is the biggest limitation in the field.

We leverage our computational platform to identify targets. We are uniquely positioned to drive novelty, based on a better understanding of disease biology

Value Inflection Points & Business Model

Optionality and near-term opportunities for value realisation

ETX RNAi Platform

ETX Computational Platform & Hepatocyte-specific data

In-house pipeline offers scope for early partnerships

GO!	siRNA drug design	Disease model(s)	IND enabling	Phase 1
Target nomination	5-6 months $500K	18 months c.$500K	18 months c.$1.5m	

Relevant deal examples

Dicerna / novo nordisk
2019
30 targets
$175M + $357.5M milestones per target

VERGE genomics / Lilly
2021
ALS
$25M + $694M
Potential royalties

Alnylam / REGENERON
2019
$400M + $200M milestones

Benevolent AI / AstraZeneca
2019
CKD and IPF
Undisclosed financials

arrowhead pharmaceuticals / AMGEN
2016
1 target (LPa)
$35M upfront
$21.5M equity
$617M milestones

Dicerna / Roche
2019
1 asset (HBV)
$200M upfront
$1.47B milestones

Summary and Next Steps

RNAi:

- Proprietary GalNAc-siRNA platform technology developed and extensively characterised
  - Equivalent level of target gene knock-down and duration of action demonstrated against leading platforms
  - 11 patent applications filed to protect inventions
- **Ability to inhibit any gene in hepatocytes (liver) and rapidly generate drug candidates to prosecute target ideas**

Computational Platform:

- **Galapagos collaboration**: Successfully identified hits (replicated 100-1000x higher hit rate) and received 3 milestone payments in the period. Scope for further upside throughout development and commercial
- Most complete hepatocyte-specific **knowledge graph** created
- Expansion of **target ID** capabilities, including mode of action elucidation and target deconvolution capabilities
- Adaption and application of computational approaches to RNAi discovery
- Continued streamlining via **increased automation and cloud computing**
- Further partnering conversations ongoing

Next Steps:

- Generate **proprietary omics** (experimental) hepatocyte data to feed into knowledge graph
- Continued development of **computational platform** for internal use and further collaborations
- Populate in-house **RNAi pipeline** and initiate partnering discussions
- **R&D Day in 2022**

Experienced Leadership

Karl Keegan
Chief Financial Officer

Ali Mortazavi
Chief
Executive Officer

Alan Whitmore
Chief Scientific Officer

Stephanie Maley
Chief People
Officer

Jonny Wray
Chief Technology
Officer

Alison Gallafent
Head of IP

Laura Roca-Alonso
Chief Business
Officer

Board of Directors

Ali Mortazavi
Chief Executive Officer

Professor Trevor Jones CBE
Non-Executive Chairman

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