
e therapeutics
Non-Confidential
Company Overview

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Forward looking statement

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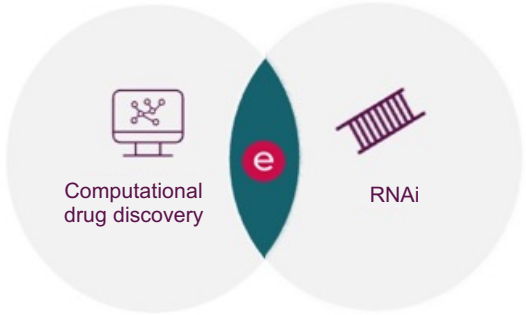
Company Overview

Driving innovation at the intersection of AI and precision medicine

Our mission:

Integrating computational power and biology to discover life-transforming medicines



Network biology pioneers. Unparalleled ability to model human biology and interrogate its complexity

Reproducible 100-1000x higher hit rate

Computational platform validated experimentally and through partnerships

Proprietary RNA interference platform

37 FTE
Multi-disciplinary team

>300M
Data points

siRNA
Gene silencing platform

Experienced Leadership

Ali Mortazavi
Chief Executive Officer

Alan Whitmore
Chief Scientific Officer

Alison Gallafent
Head of IP

Jonny Wray
Chief Technology Officer

Stephanie Maley
Chief People Officer

Laura Roca-Alonso
Chief Business Officer

Michael Bretherton
Acting Interim Chief Financial Officer

Board of Directors

Ali Mortazavi
Chief Executive Officer

Professor Trevor Jones CBE
Non-Executive Chairman

Michael Bretherton
Non-executive Director
CEO Sarossa Plc

Scientific Advisory Board

Dr Paul Burke
Chair, Former CTO, Pfizer

Professor John Mattick
Former CEO, Genomics England
Professor RNA Biology, UNSW Sydney

Dr Bill Harte
Chief Translational Officer
Case Western Reserve University

Business Model

Adaptable, hybrid business model to maximise the impact of our technologies

Enabling ETX *in silico* Discovery Engine

Discovery

Discovery Collaborations
Monetising Computational Platform

Galápagos · MSD · iTEOS THERAPEUTICS · novo nordisk® · C4XD

- ✓ Small molecule discovery
- ✓ Target ID
- ✓ Mechanistic insights
- ✓ Genetic support

In-house RNAi

Proprietary RNAi Pipeline
Building long-term value

- ✓ Liver centric
- ✓ Complex diseases and systems biology approaches on rare diseases
- ✓ Unexplored target genes

Strategic RNAi

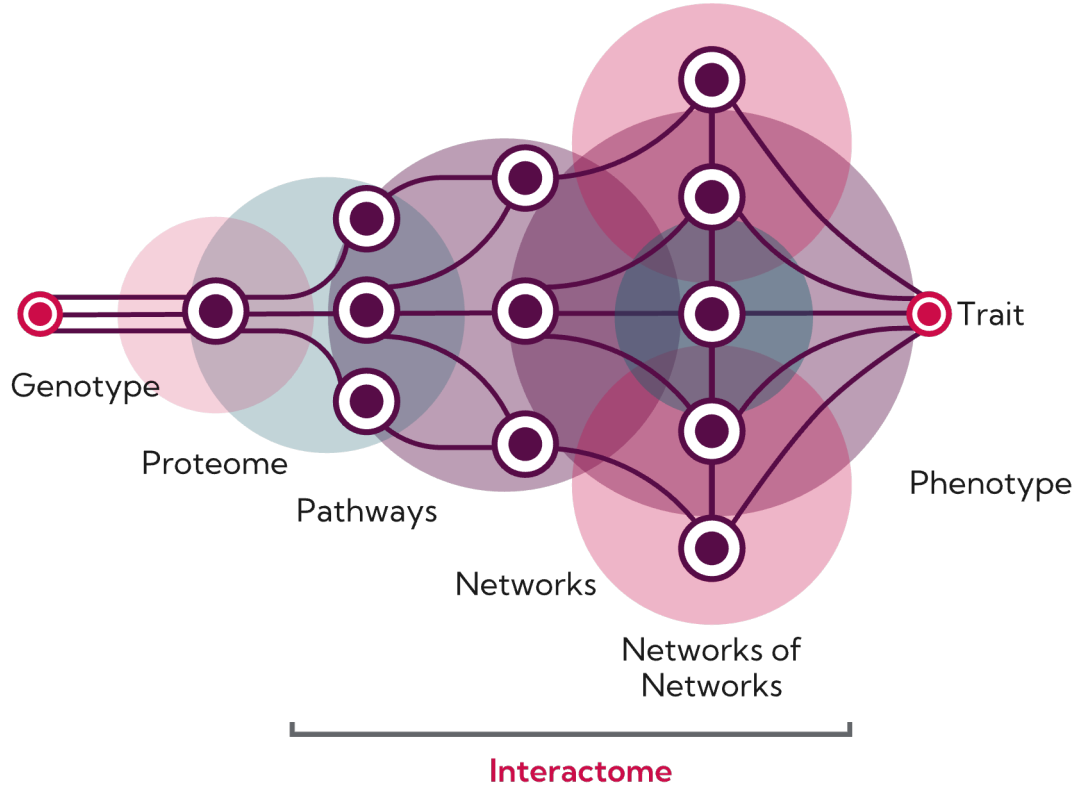
Strategic RNAi Partnerships
Rapid generation of differentiated candidates

- ✓ Leveraging ETX computational platform
- ✓ Proprietary hepatocyte knowledge graph
- ✓ Novel targets
- ✓ Proprietary GalNAc-siRNA gene silencing technology

Biological Complexity Remains the Biggest Challenge

Oversimplification of the genotype-phenotype relationship contributes to drug failures

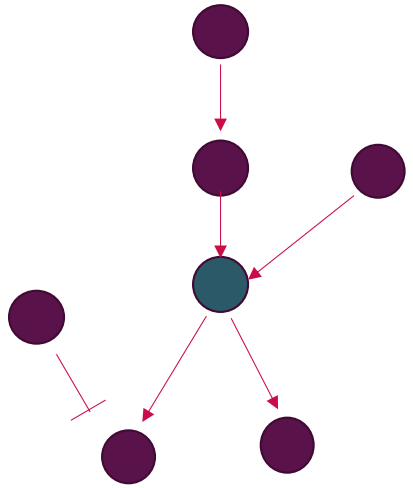
- Phenotype is an emergent property of molecular networks
- Molecular networks impart functional robustness to phenotype
- Networks are the mechanistic bridge between genotype and phenotype



Our way of Understanding and Modelling Biology

Capturing human complexity is key to the discovery of high-confidence drug candidates

Pathway models are too simplistic



Complexity captured

ETX proprietary metrics identify non-obvious as well as known mechanisms and targets. Our models enable superior *in silico* hypothesis generation and testing

Computational biology platform: ETX *in silico* Discovery Engine

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

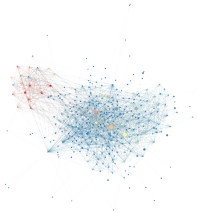
Influenza virus replication

Lipid metabolism

Tryptophan catabolism

Telomerase signaling

Endocytosis



Fibroblast activation

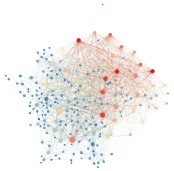
Angiogenic signaling

Neuronal autophagy

Tunneling nanotube regulation

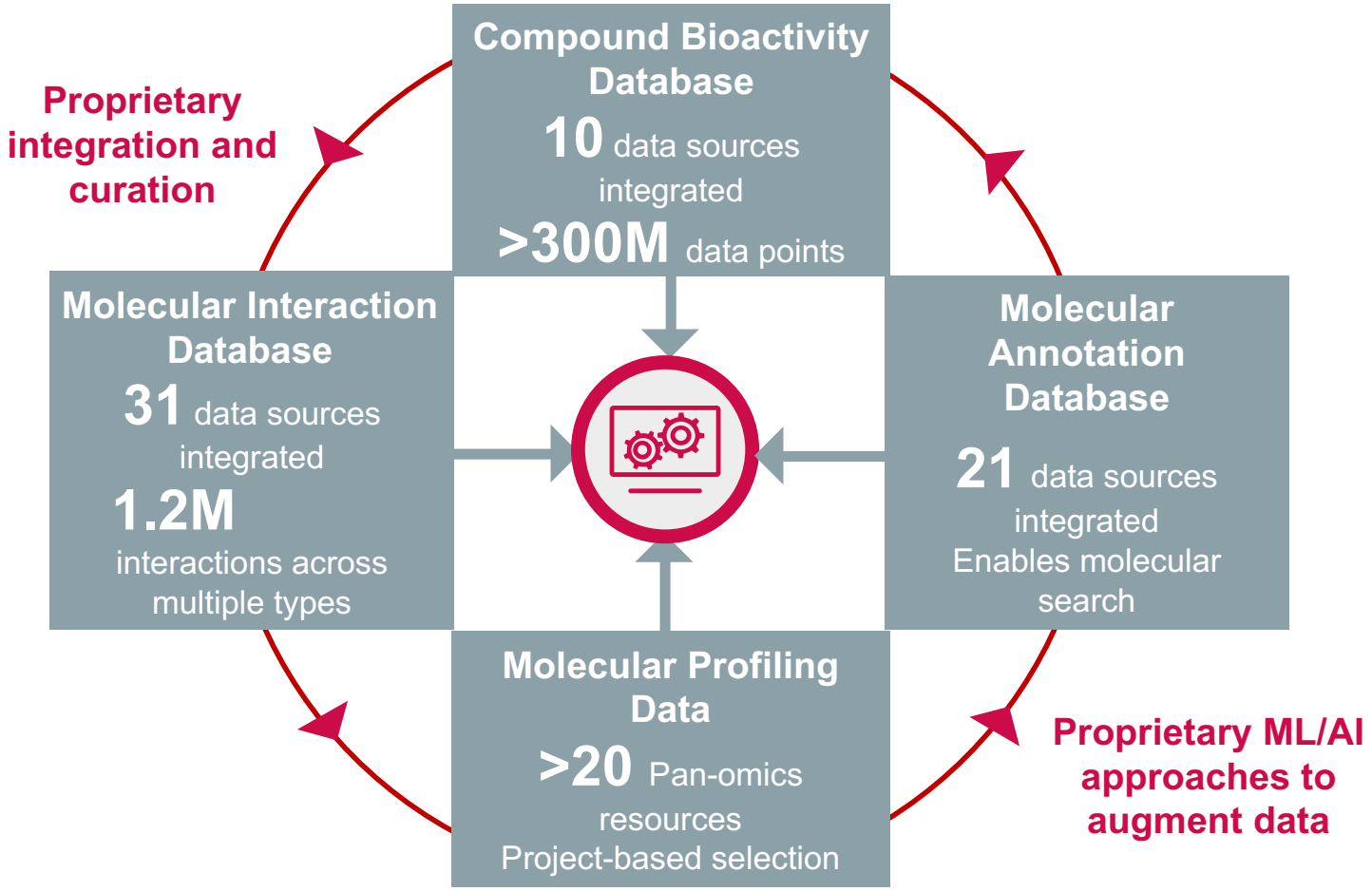
Insulin resistance

Axonal degeneration



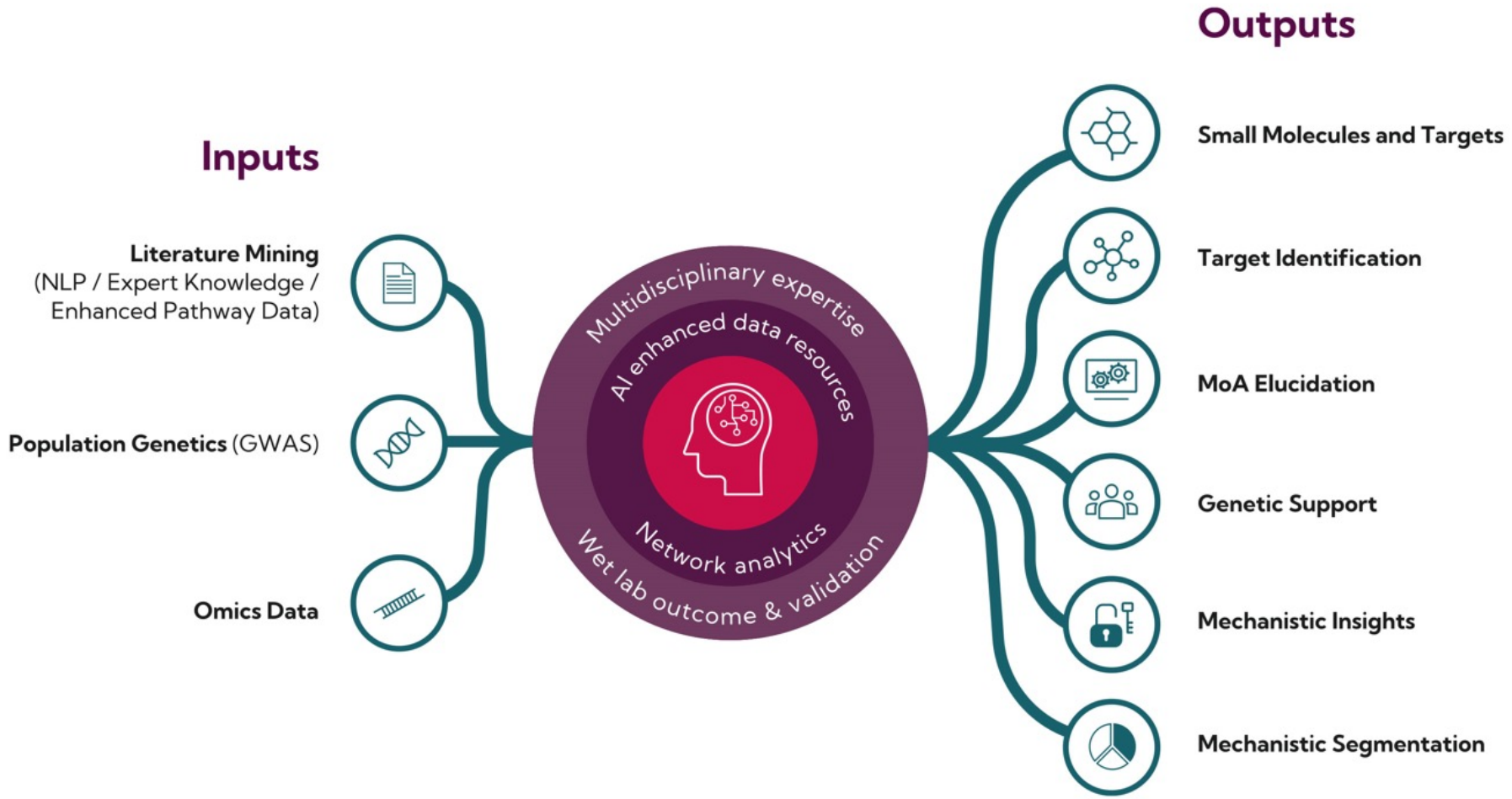
Immune checkpoint signaling

Solid data foundations to enable unparalleled disease biology modelling and better drug discovery

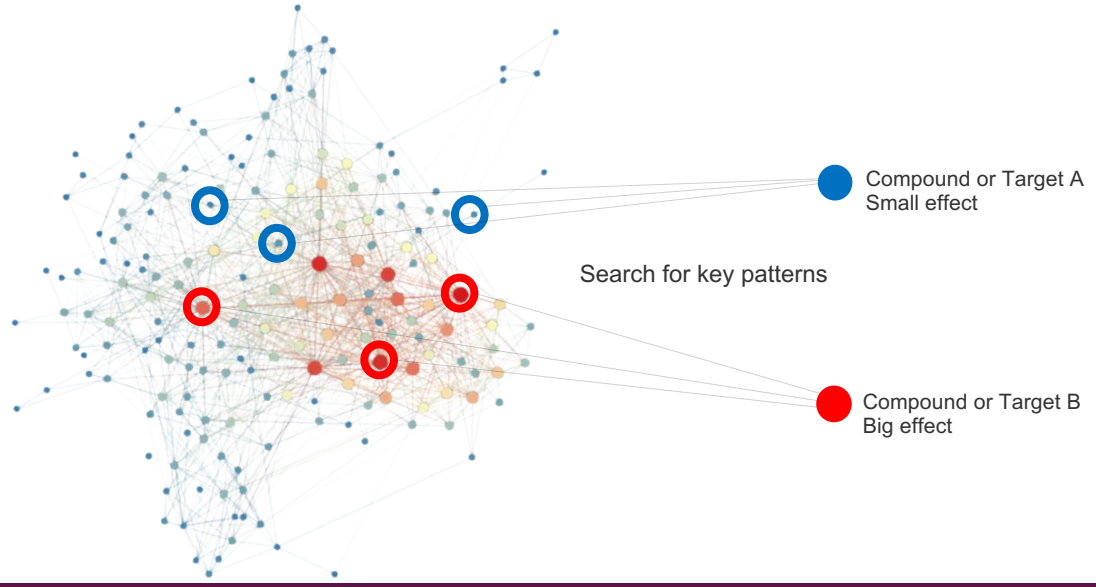


ETX *in silico* Discovery Engine – Inputs & Outputs

Modular computational platform with multiple applications

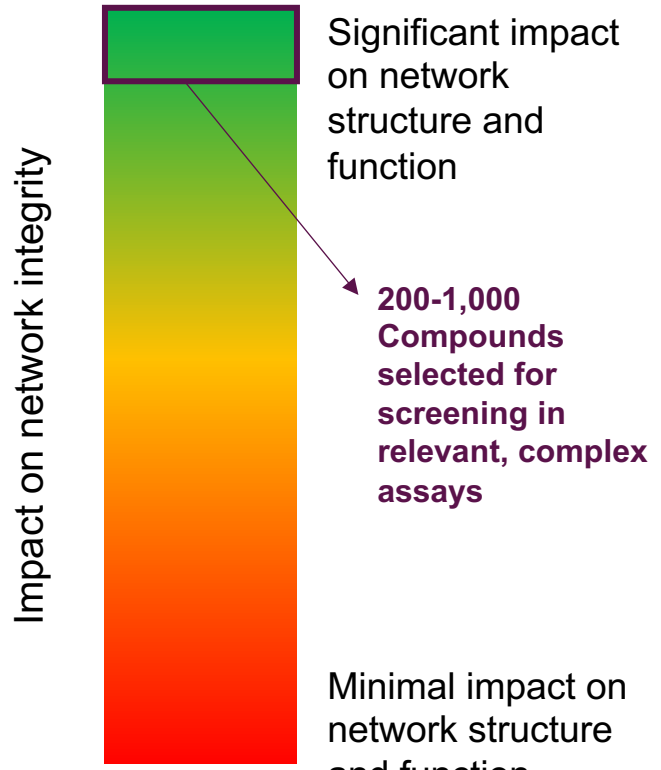


Network Disruption – Assessing Compound/Target Impact

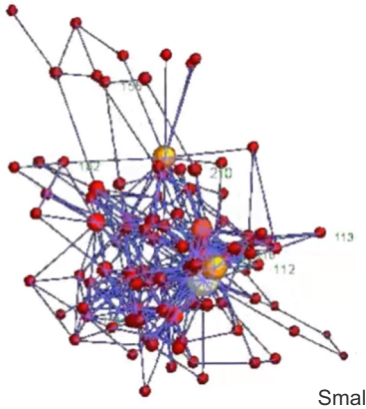


Compound ranking

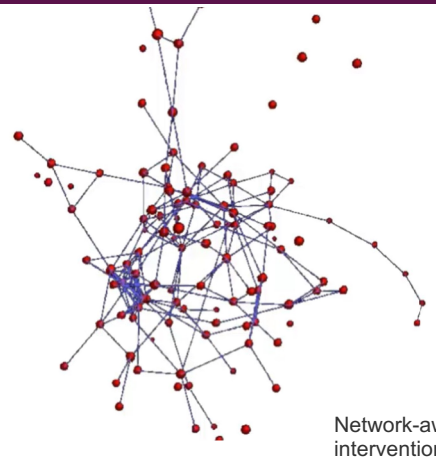
15M compound
AI-enhanced annotated database



***In silico* testing of therapeutic interventions – modelling biological effects**



Small effect



Network-aware intervention; large effect

Biology First, Higher Hit Rates

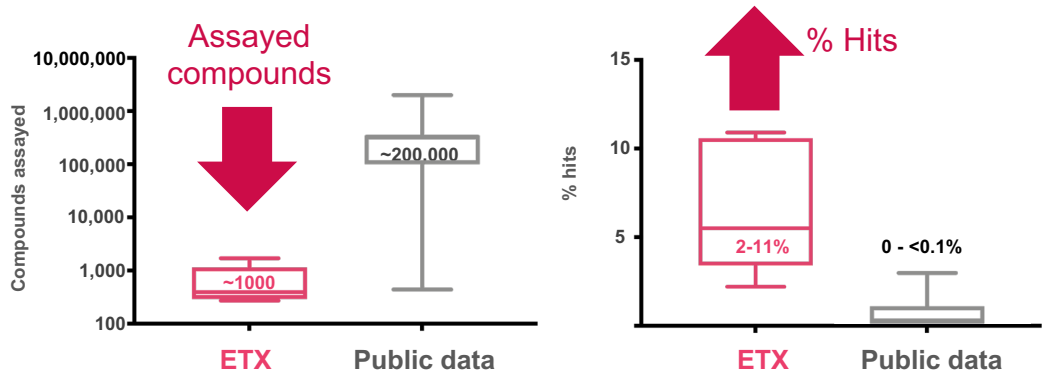
Network models are constructed and interrogated using ETX proprietary computational methods to provide insights into complex diseases and transform drug discovery

	Disease agnostic projects	% 'Hits' confirmed in experimental phenotypic screens
e-therapeutics	Telomerase signalling	4.3%
	Hedgehog pathway	5.5%
	TNFα release	7.3%
	Influenza replication	2.2%
	Tryptophan catabolism	11%
	SIRS	11%
	Axonal degeneration	3.4%
	Reversal of T-cell exhaustion	5%
partners	Type 2 Diabetes	-
	CNS	-
	Idiopathic pulmonary fibrosis	-

Applicable across diverse biology and therapeutic areas

High Bar 'Hit' Confirmed activity <10μM in multiple cell-based assays

No cytotoxicity | Structural QC | Initial FTO Good chemotypic diversity



Our hit rates are 100-1000x higher than industry standards

- Need to **test fewer compounds** to find high quality hits
- **Improves translatability** by enabling use of highly relevant phenotypic assays that better represent human disease at the screening stage
- **Our hits are not 'blind'** – we use our AI-enhanced bioactivity data, network models and other AI-approaches alongside structural information in **target deconvolution**

Target ID from population genomics and other omics data

GAINs: Genome Associated Interaction Networks

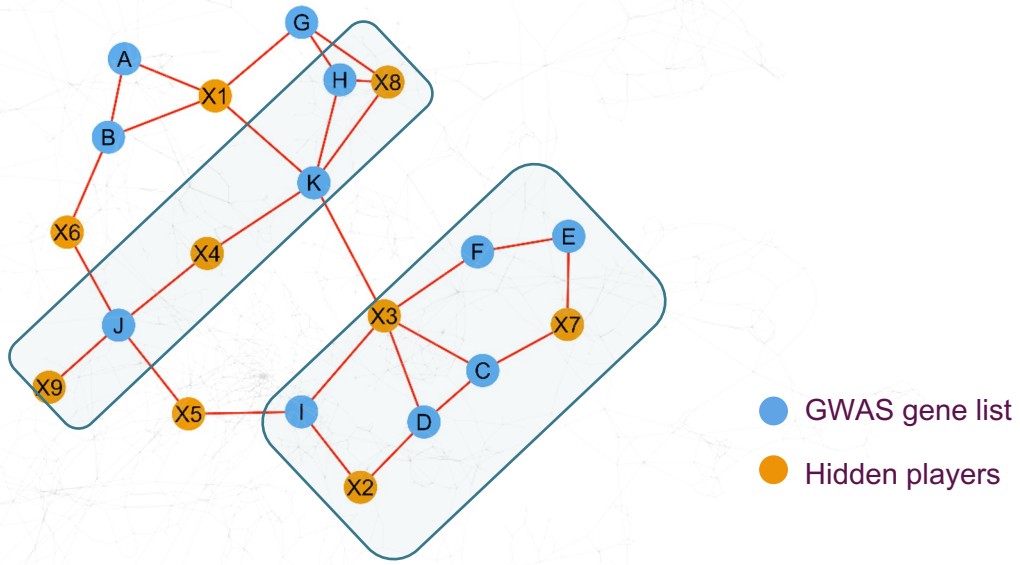
Scope to identify novel targets beyond genetic variant lists

Analytics identify & group pathways that are:

- Important for the structure of the network
- Selective for the network
- Selective for the SNPs-genes
- Are not identifiable from the SNPs alone
- Close in ‘network space’
- Likely to contribute to a common process

Proprietary approaches developed to deal with noise, error and bias

Network construction reveals the wider molecular context of the disease-associated proteins



Network-aware functional annotation

The Convergence of two Cutting-edge Platforms: Populating our in-house RNAi Pipeline

ETX GalNAc-siRNA Platform Development

Equivalent performance to leading platforms demonstrated

New proprietary RNAi platform technology for liver gene silencing. Key advantages:

- Enables ETX to selectively silence any gene in **hepatocytes**

- GalNAc conjugation enables **hepatocyte specificity** and **infrequent, subcutaneous administration**
- **Accelerated generation** of new clinical **candidates** relative to other modalities

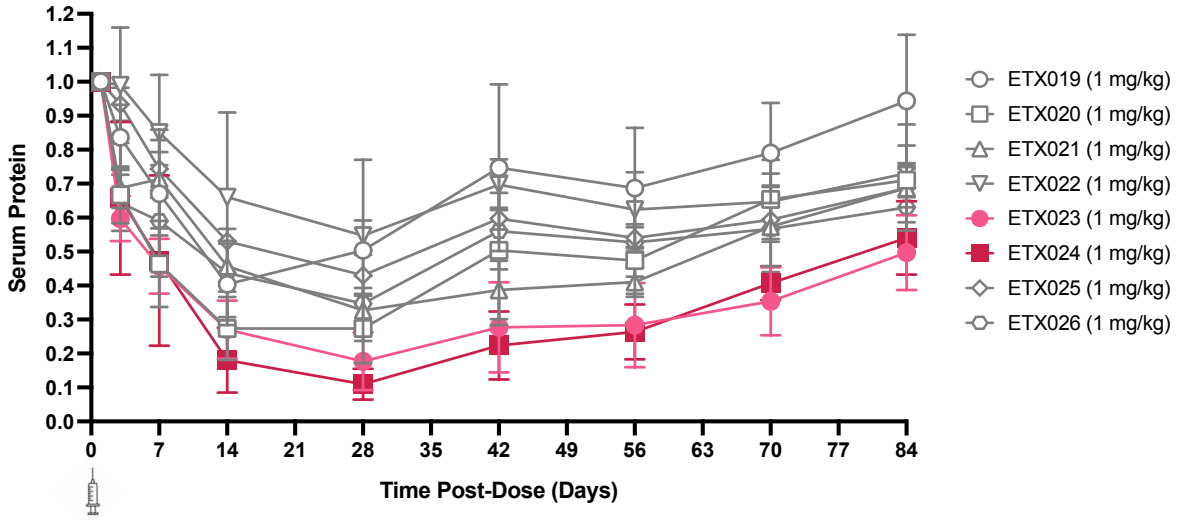
Key Aspects:

- Robust IP position – **11 patent applications filed**
- **Extensive characterisation** completed: 8 different construct designs tested across 3 target genes
- **High hurdle** for performance and safety **benchmarking**
- Significant in-house **molecular design know-how**
- Leveraging our **computational target ID capabilities (key differentiator)**. In-house pipeline upcoming

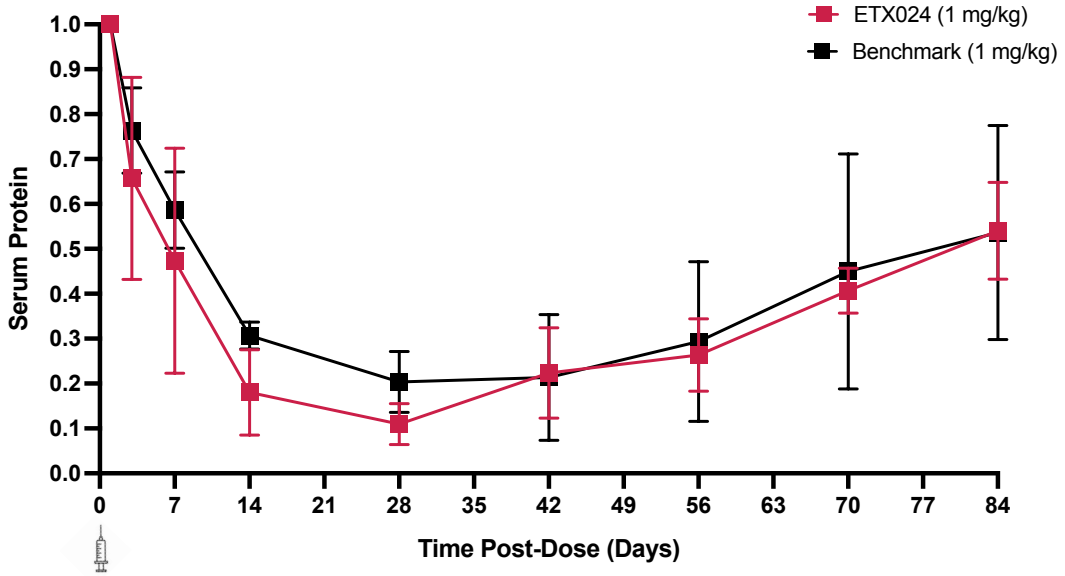
ETX GalNAc-siRNA Platform Performance: Headline Non-Human Primate (NHP) Results

Summary NHP target Y knock-down data (serum protein)

Different ETX constructs tested – **Target Y**



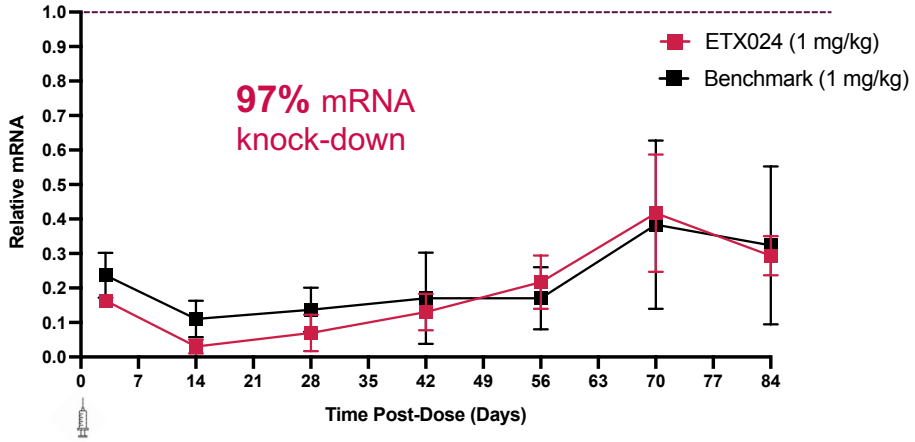
Competitive depth and duration of target knock-down

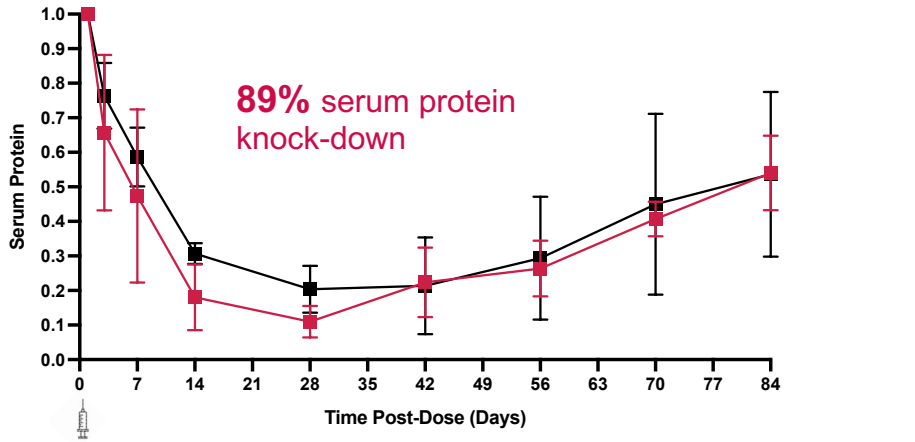


Cynomolgus monkeys, n=3

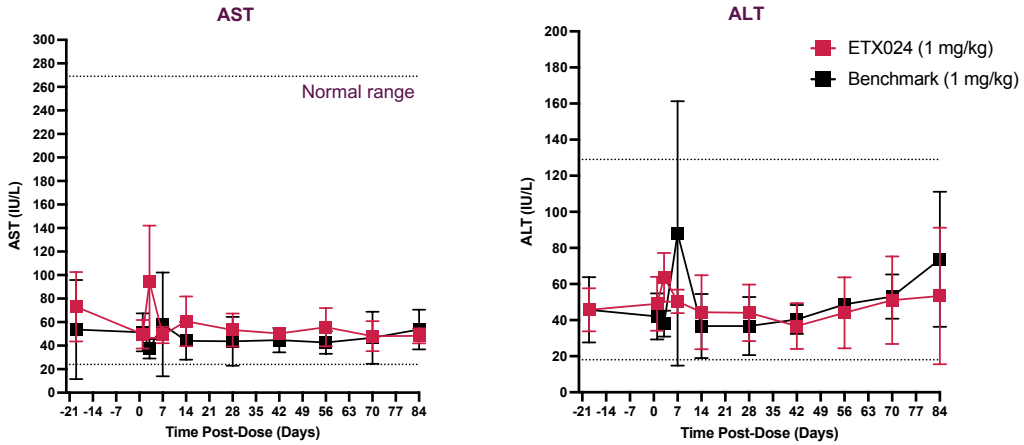
ETX lead Construct Design Performance and Safety (NHP)

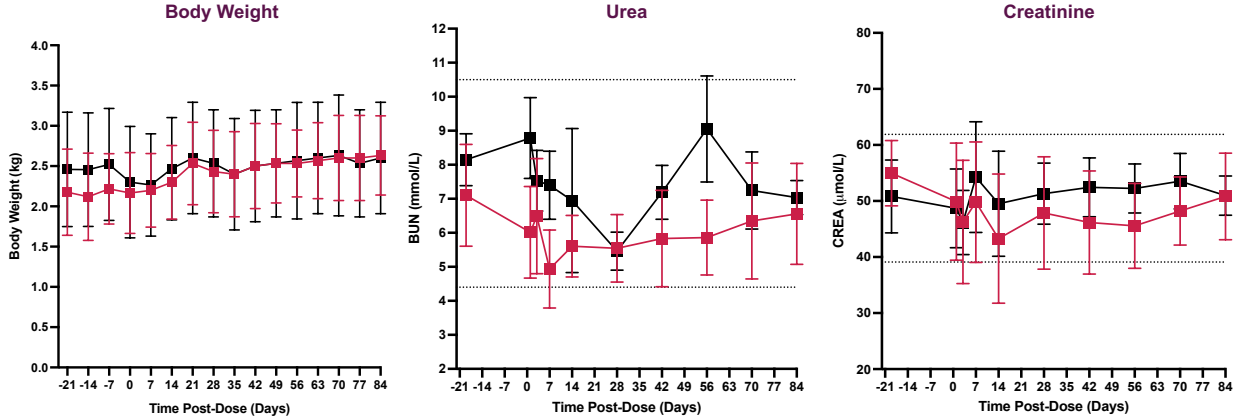
Target Y liver mRNA and serum protein levels show deep and sustainable knock-down for 3 months





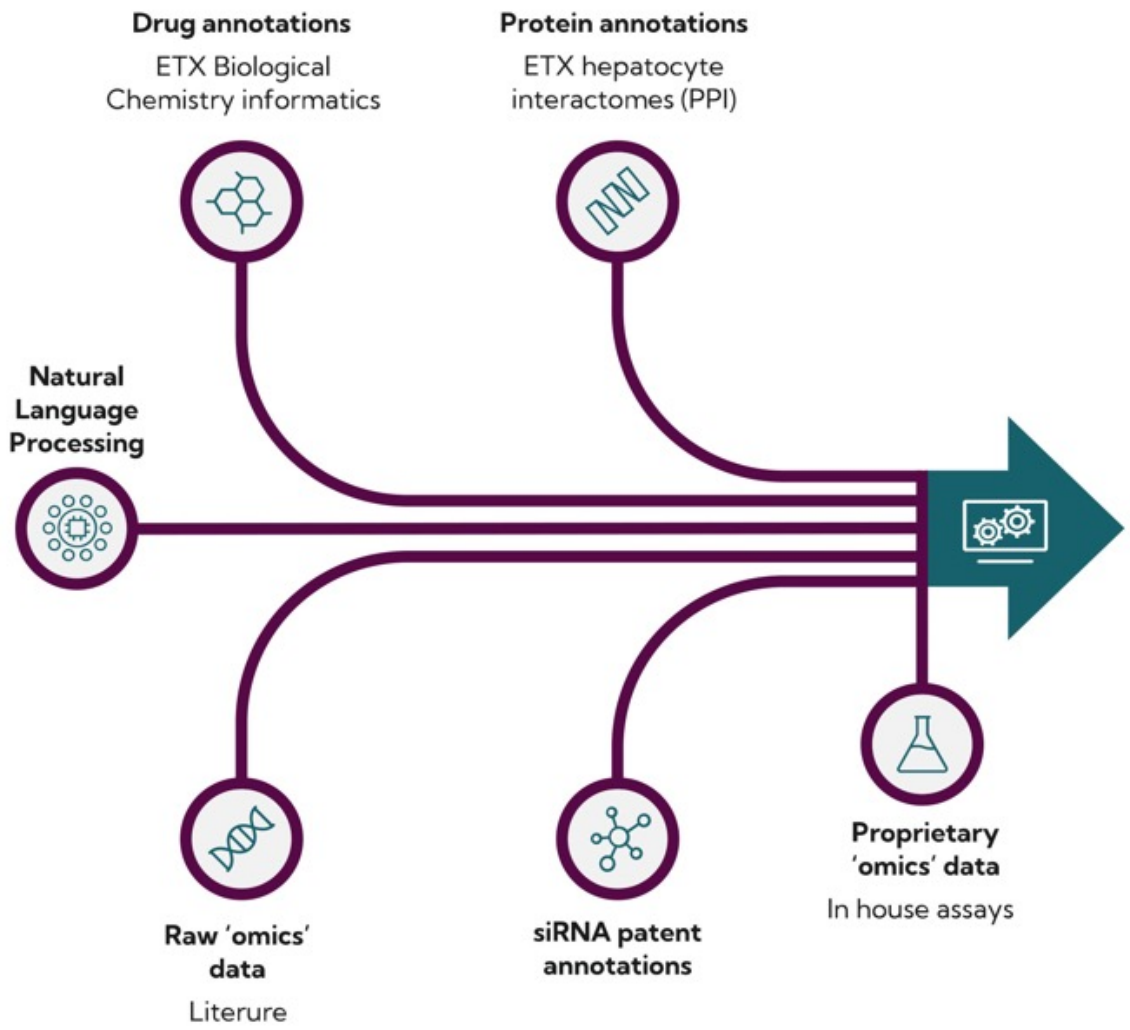
Well tolerated in non-human primates





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

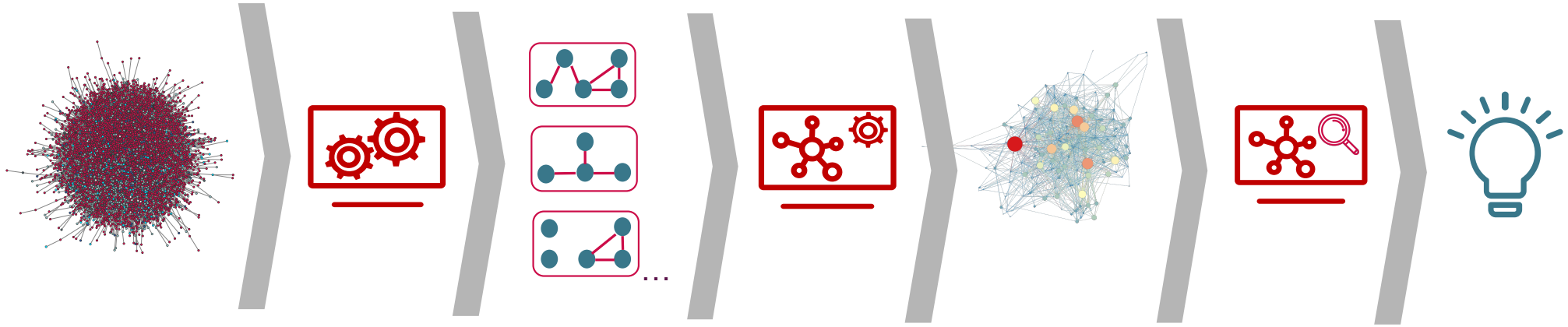
Hepatocyte-specific* Data Strategy and Knowledge Graph



ETX Hepatocyte Knowledge Graph

* Reproducible in other cell types

Hepatocyte Target Identification



Target identification is a key limitation in the field and the competitive landscape is highly overlapping.

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

Recent progress and Next Steps

Computational Platform:

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

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 and rapidly generate drug candidates to prosecute target ideas**

Next Steps:

- Generate **proprietary omics** 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

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