Integrating Computational Power and Biology to Discover Life-transforming Medicines

December 2021

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Forward looking statement

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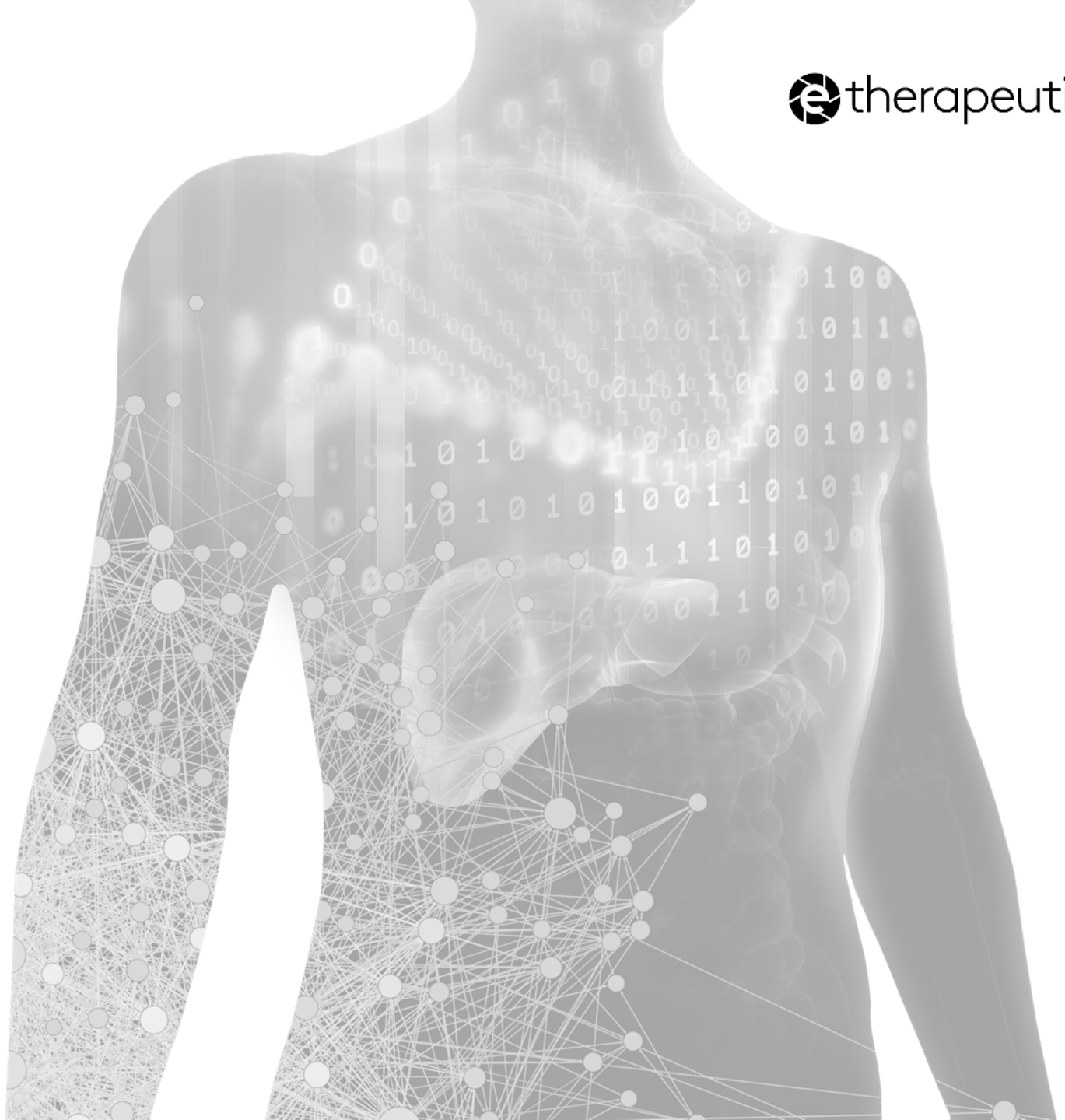
Company Overview

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
- **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

Computational Biology Platform: ETX *in silico* Discovery Engine



Network & Systems Biology – Core ETX Expertise

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

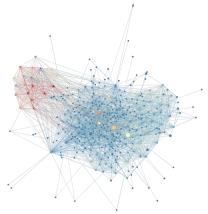

Influenza virus replication

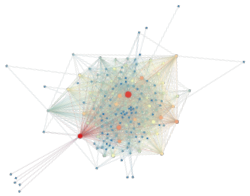

Lipid metabolism

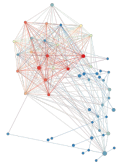

Tryptophan catabolism

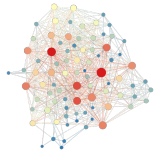

Telomerase signaling


Endocytosis


Fibroblast activation

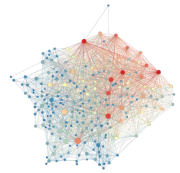

Angiogenic signaling


Neuronal autophagy

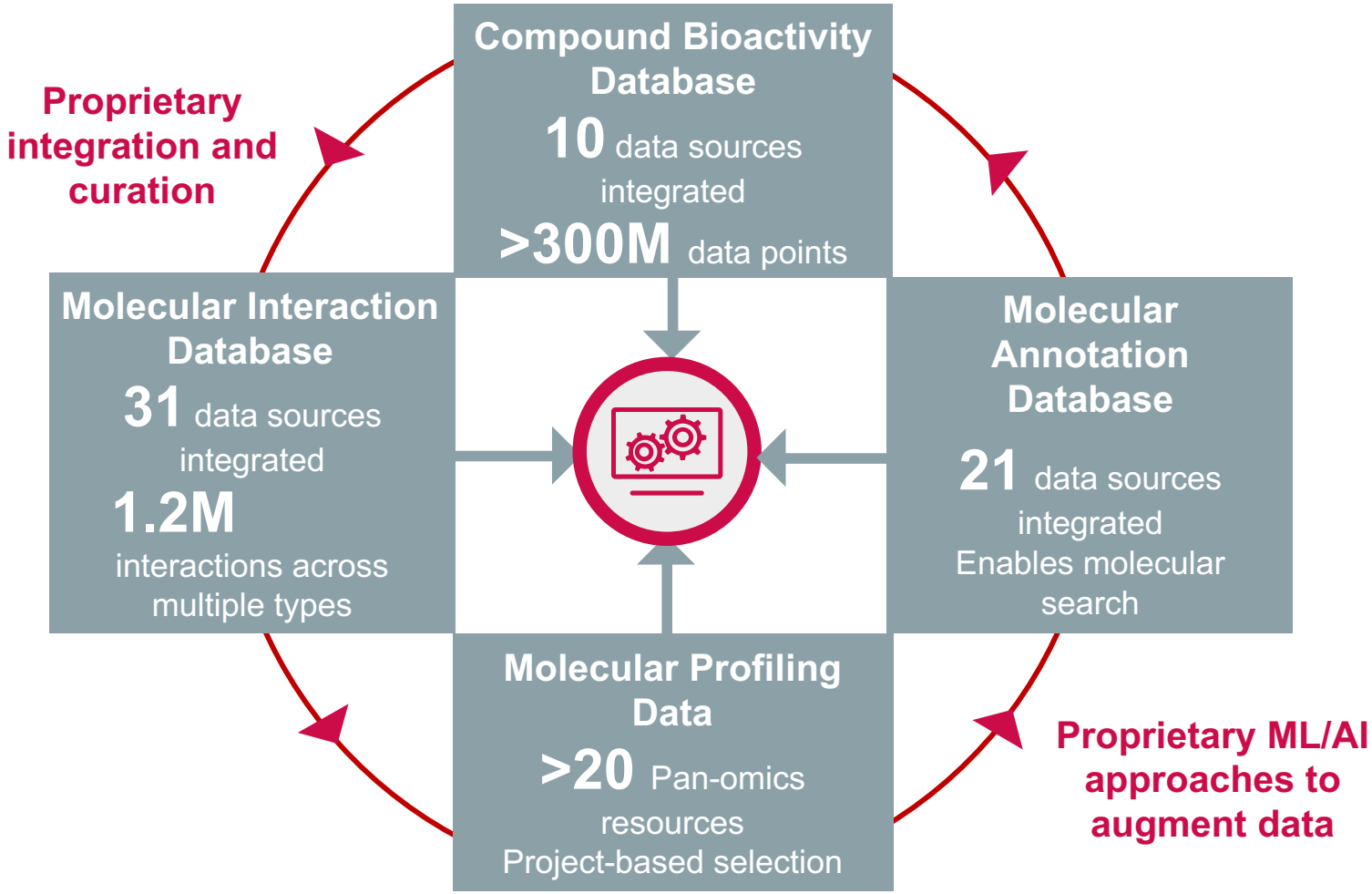

Tunneling nanotube regulation


Insulin resistance


Axonal degeneration

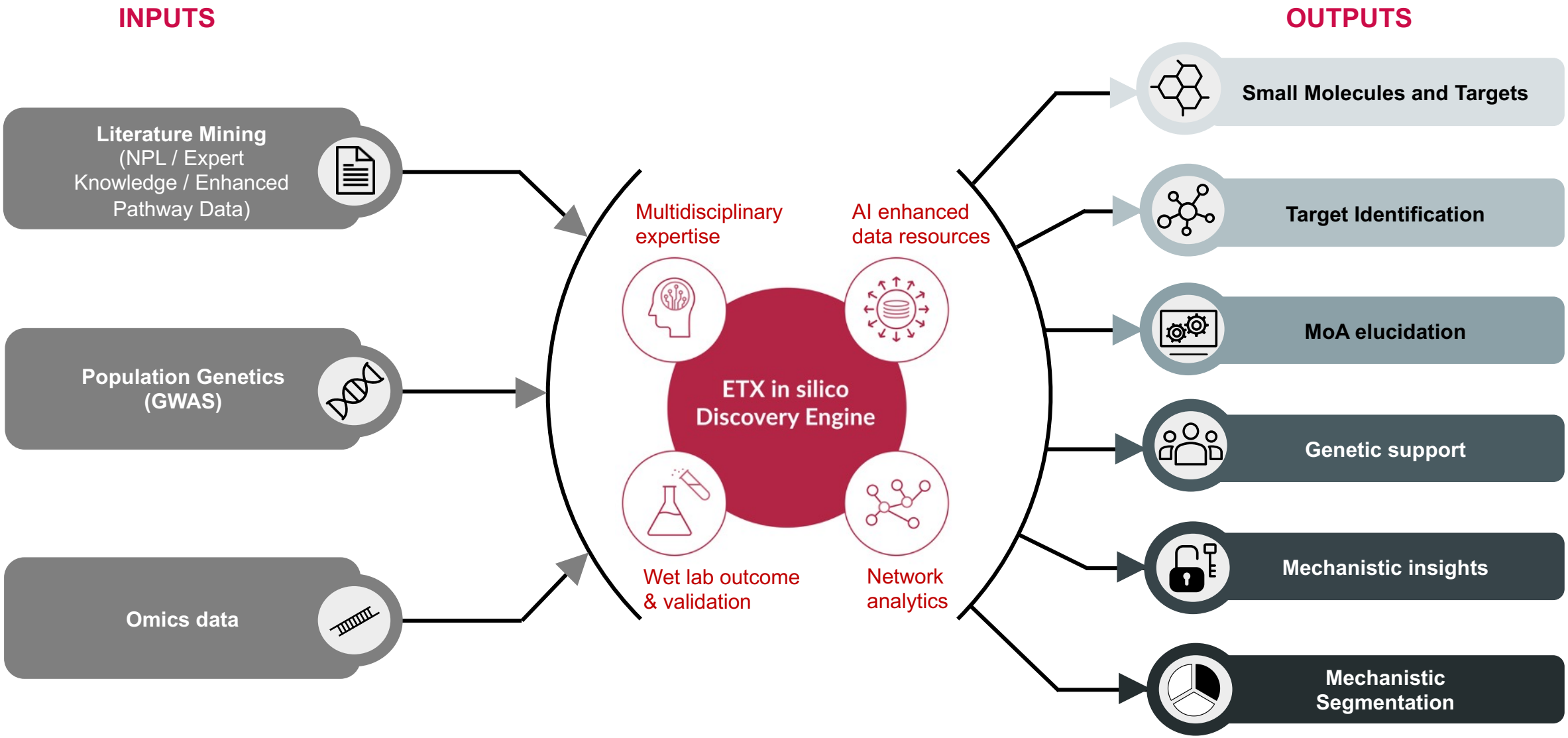

Immune checkpoint signaling

Solid data Foundations to Enable Unparalleled Disease Biology Modelling and Better Drug Discovery

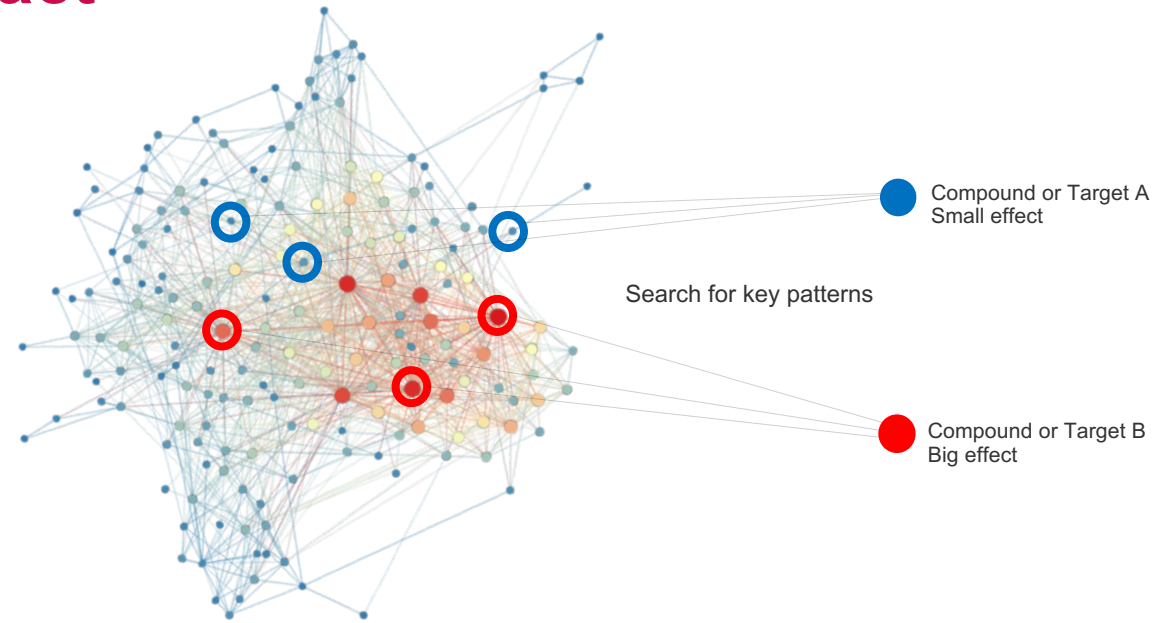


ETX *in silico* Discovery Engine – Inputs & Outputs

therapeutics

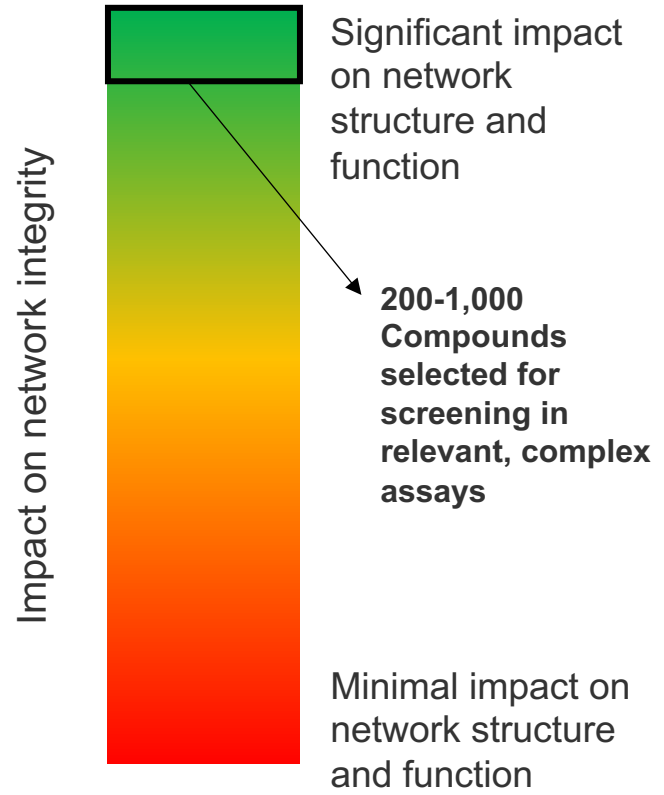


Network Disruption – Assessing Compound and Target Impact

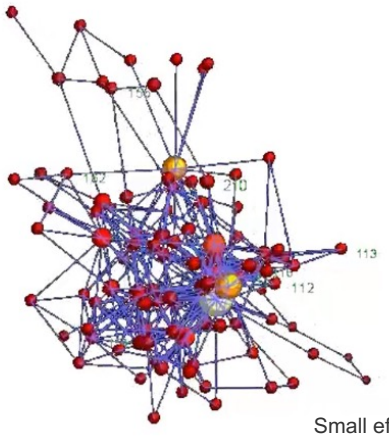


Compound ranking

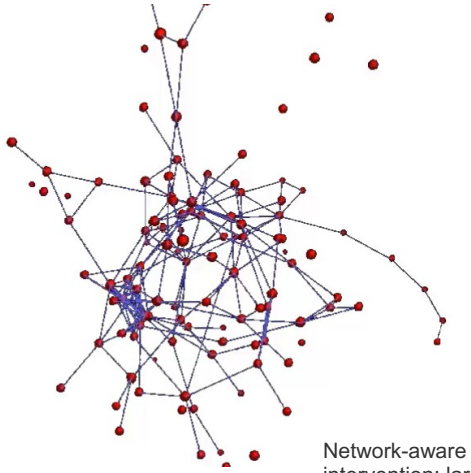
15M compound
AI-enhanced annotated database



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



Small effect



Network-aware intervention; large effect

Our *in silico* Laboratory Yields Higher Hit Rates

Demonstrating advantages over blind screening for small molecule discovery

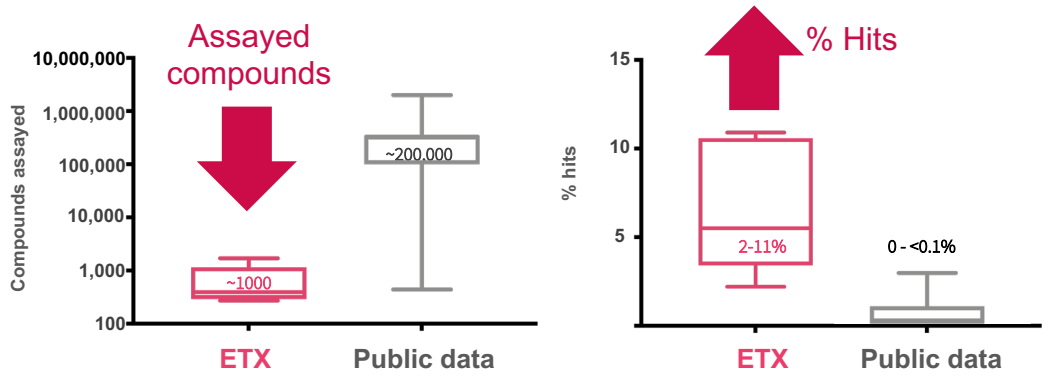
	Disease agnostic projects	% 'Hits' confirmed in experimental phenotypic screens
e-therapeutics	Telomerase signalling	4.3%
	Hedgehog pathway	5.5%
	TNFα release	7.3%
	Influenza replication	2.2%
	Tryptophan catabolism	11%
	SIRS	11%
	Axonal degeneration	3.4%
	Reversal of T-cell exhaustion	5%
partners	Type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

NDD Guided vs. Other Phenotypic Screening*



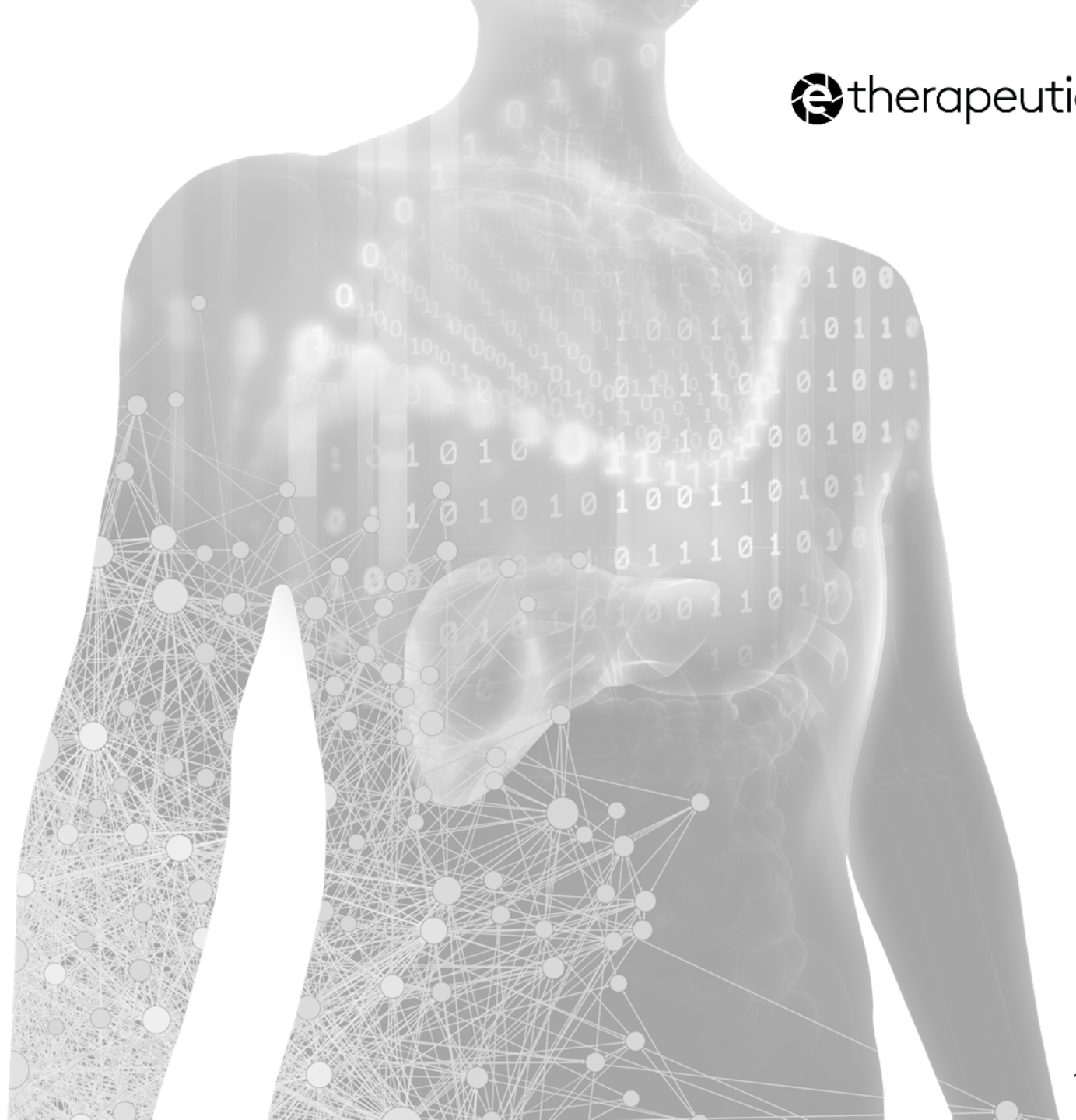
Our hit rates are 100-1000x higher than industry standards

- 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**

Source: * based on 15 publications

The Convergence of two Cutting-edge Platforms

Development of a World-leading Proprietary RNAi technology

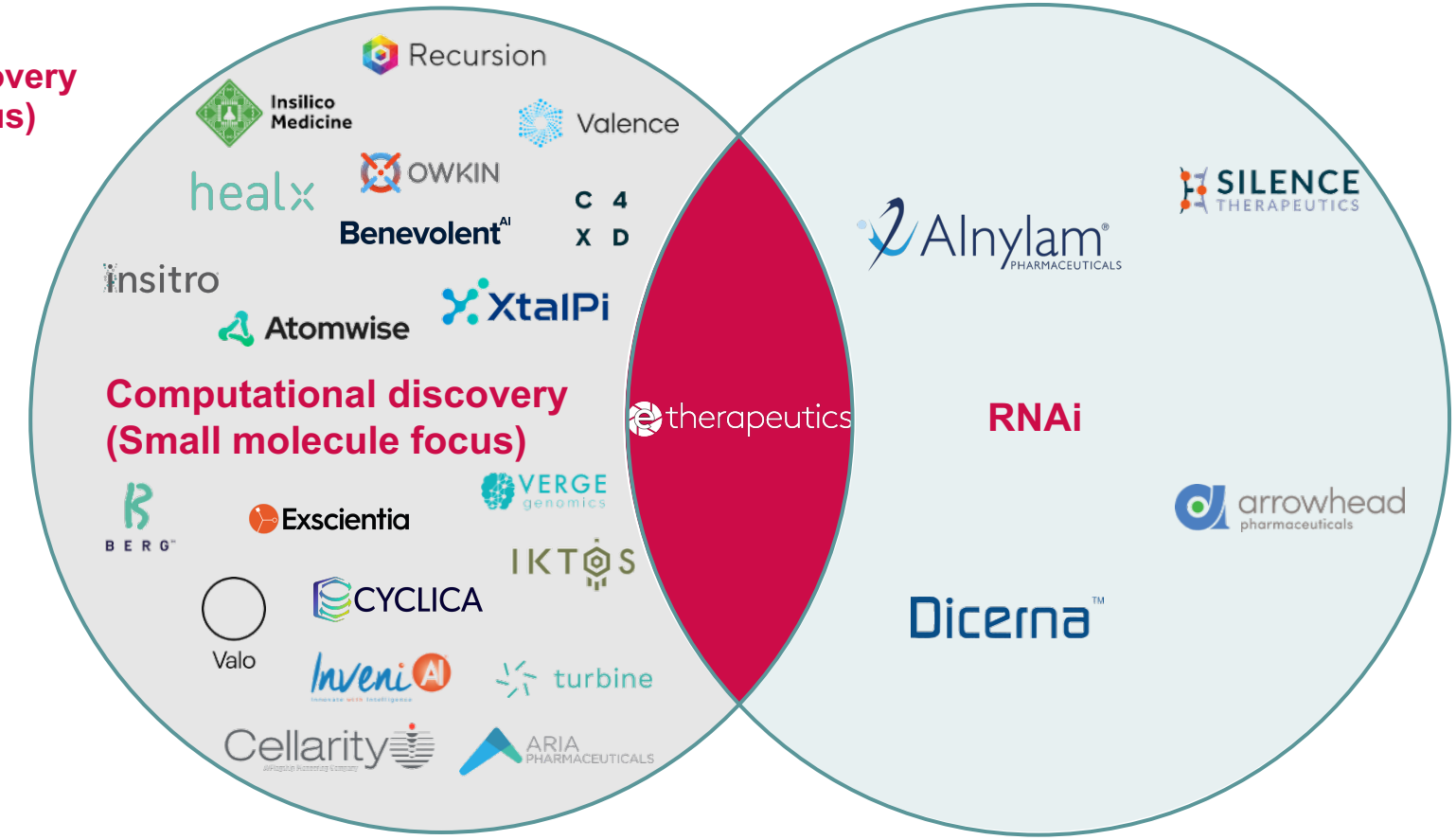


Competitive Landscape – Differentiated Positioning

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

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

Benchmarking Studies – ETX GalNAc-siRNA Platform Characterisation Completed

Experimental plan (Design Oct 2020, Start Feb 2021)

- **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

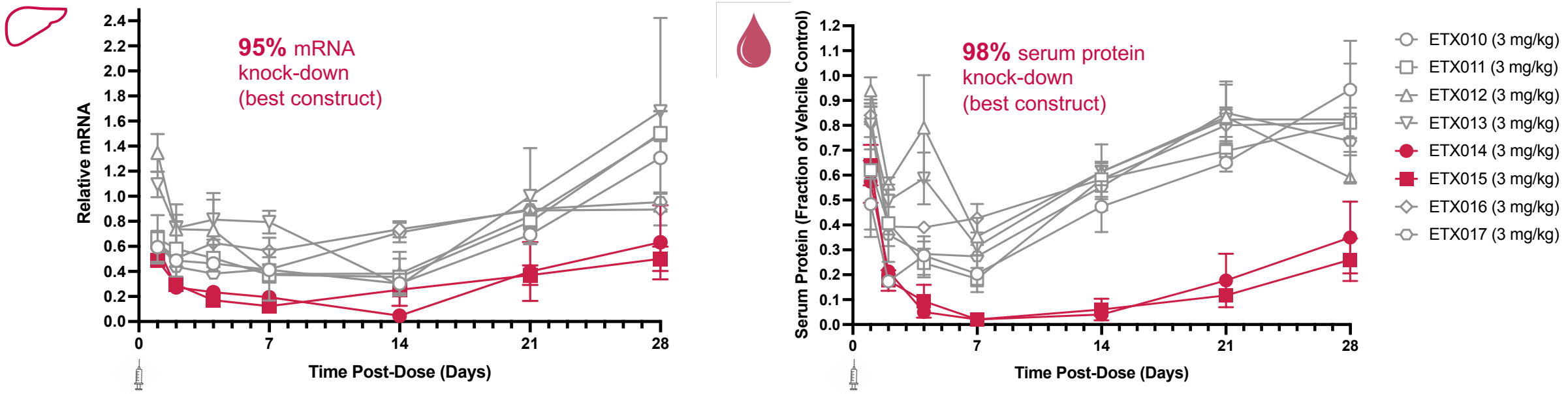
Results (October 2021)

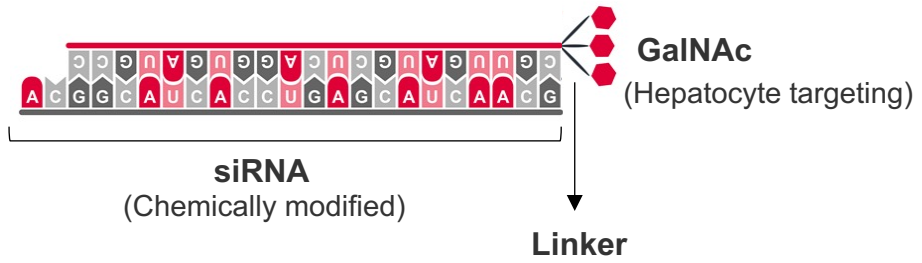
- ✓ **Data package:** *In vitro* and *in vivo* experiments completed. Characterisation datasets generated *(See next slides for headline results)*
- ✓ **Lead designs:** Most potent designs consistently identified
- ✓ **11 patent applications filed**
- ✓ **Competitive depth and duration of target gene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



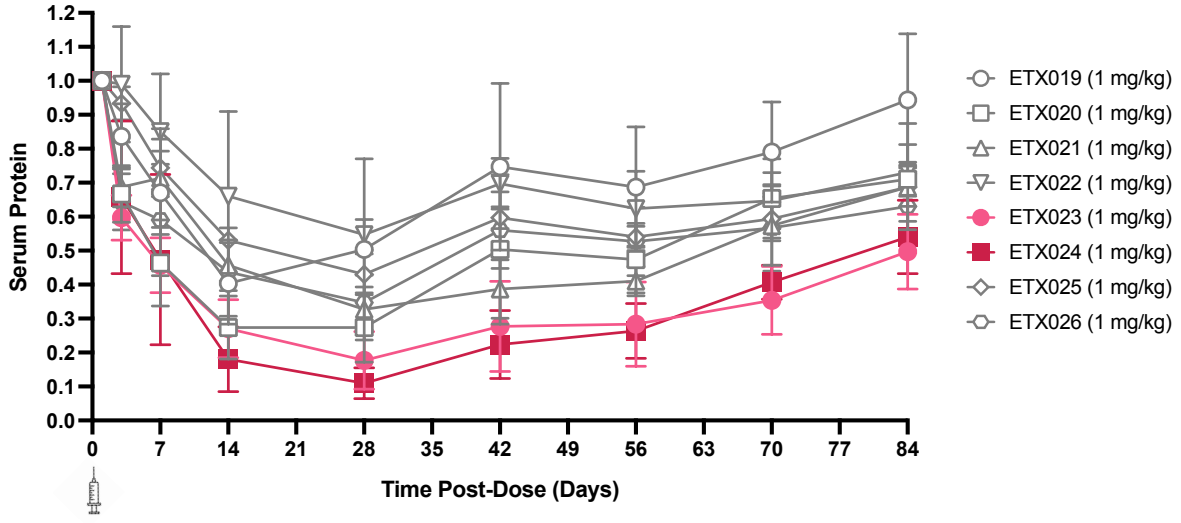


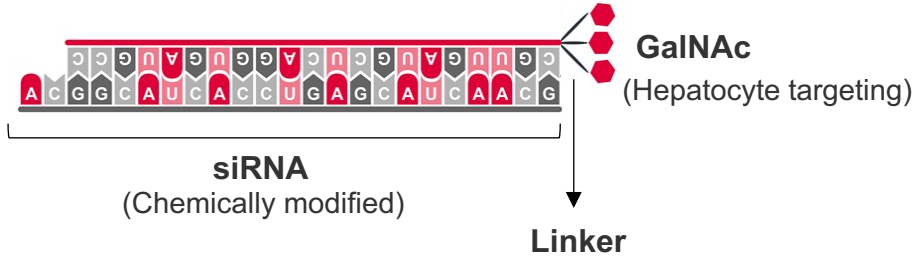
n=3, C57BL/6 mice

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

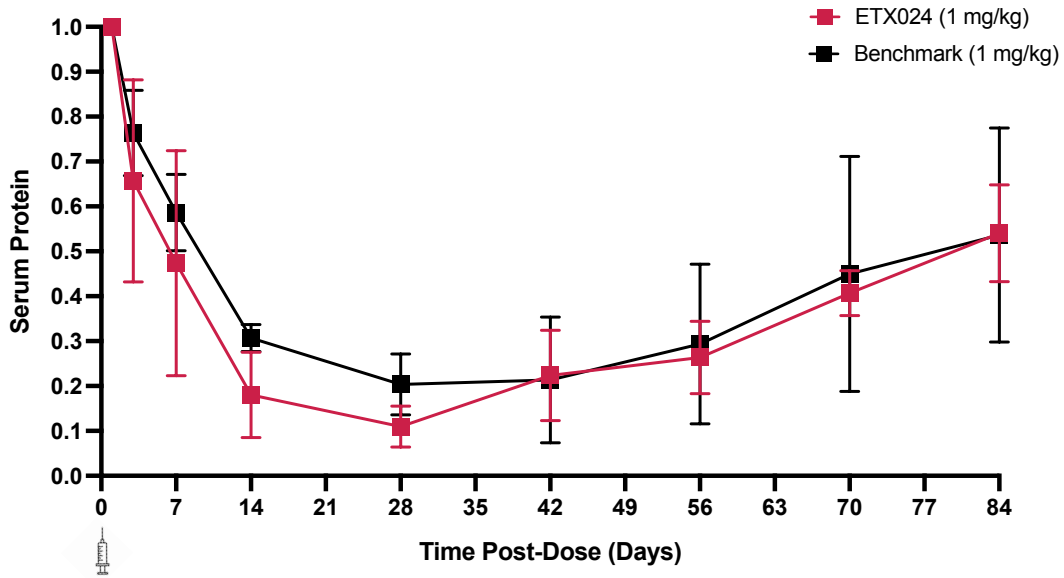
Summary non-human primate target Y knock-down data (serum protein):

Different ETX constructs tested – **Target Y**





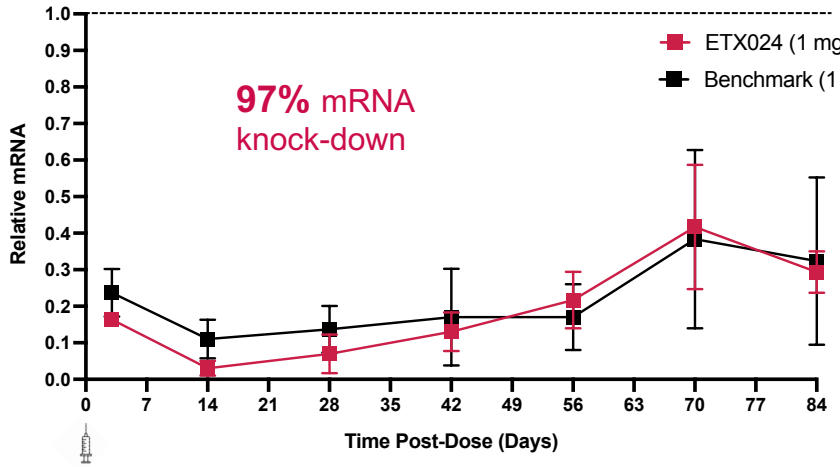
Competitive depth and duration of target knock-down

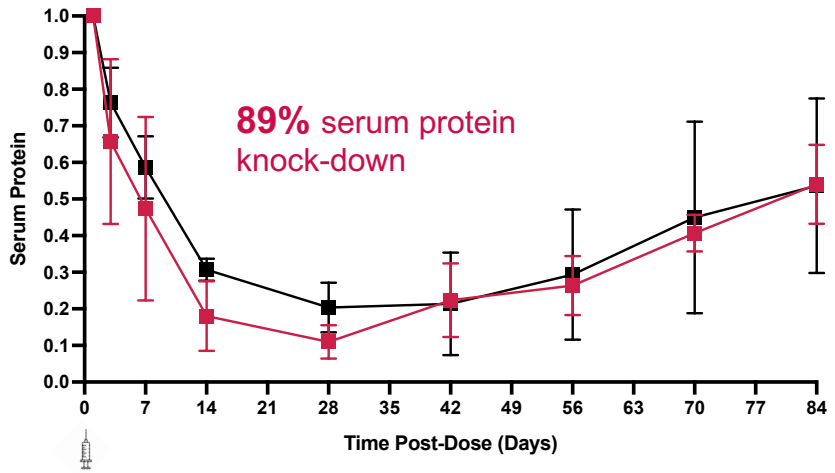


Cynomolgus monkeys, n=3

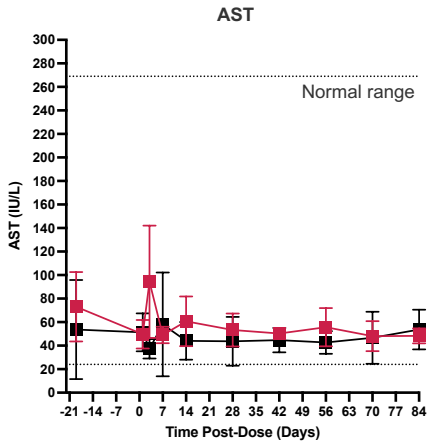
ETX lead Construct Design Performance and Safety (NHP)

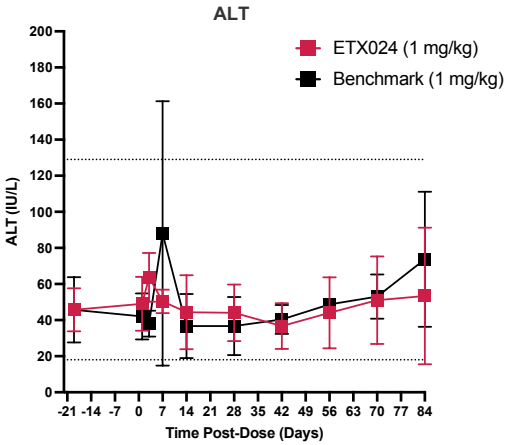
Target Y liver mRNA and serum protein levels show deep and sustainable knock-down for 3 months in non-human primates

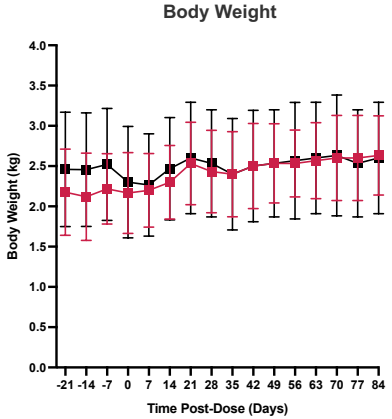


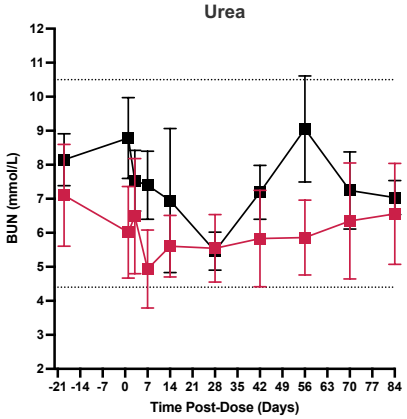


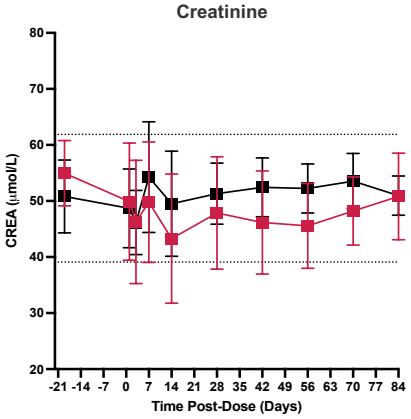
Well tolerated in non-human primates











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

Hepatocyte-specific* Data Strategy and Knowledge Graph

etherapeutics

In silico

Drug annotations
ETX Biological Chemistry Informatics

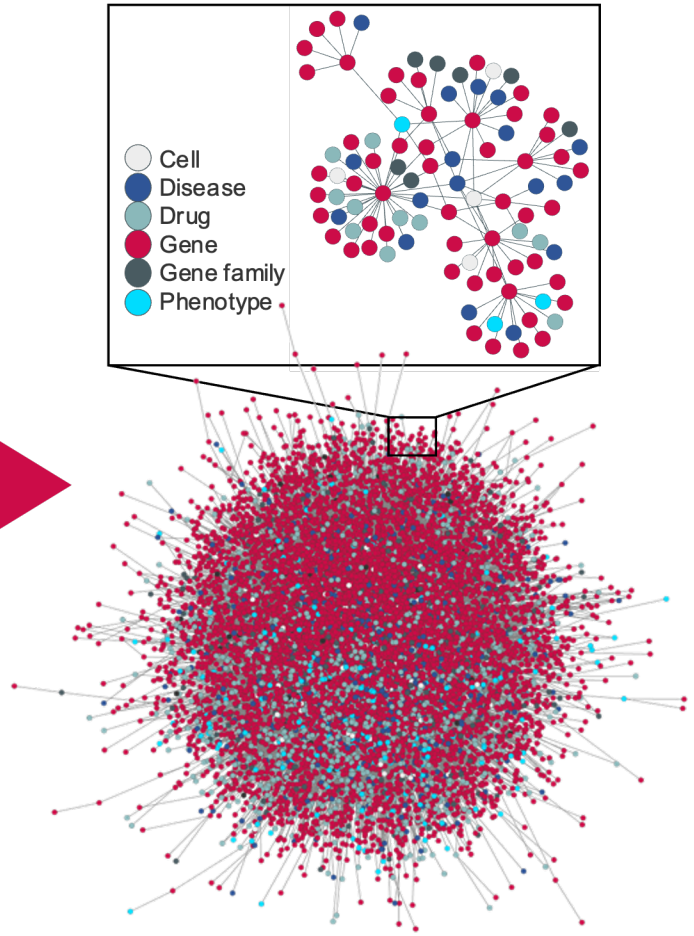
Protein annotations
ETX hepatocyte interactomes (PPI)

Natural Language Processing
258,000 text sources

Raw 'omics' data
Literature

siRNA patent annotations

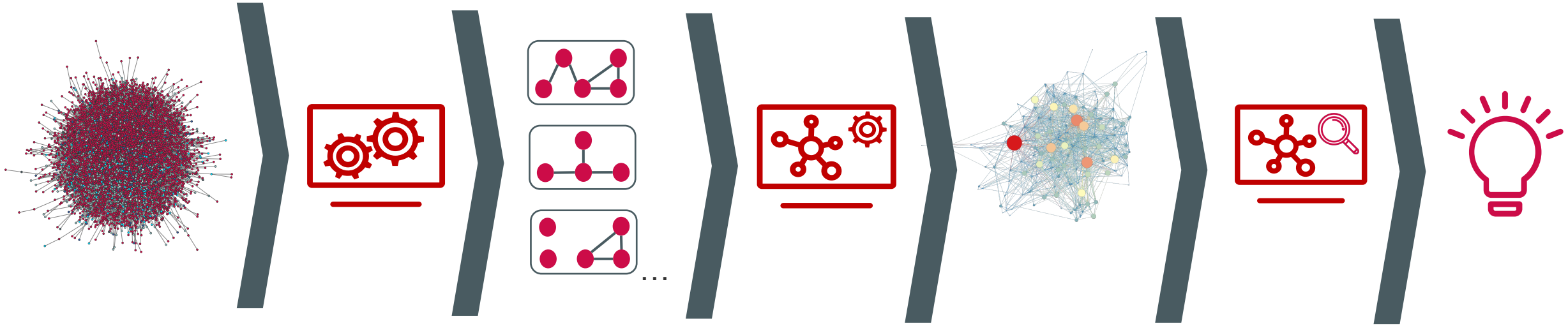
Proprietary 'omics' data
In house assays
H1 2022



ETX Hepatocyte Knowledge Graph
24,700 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

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**

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