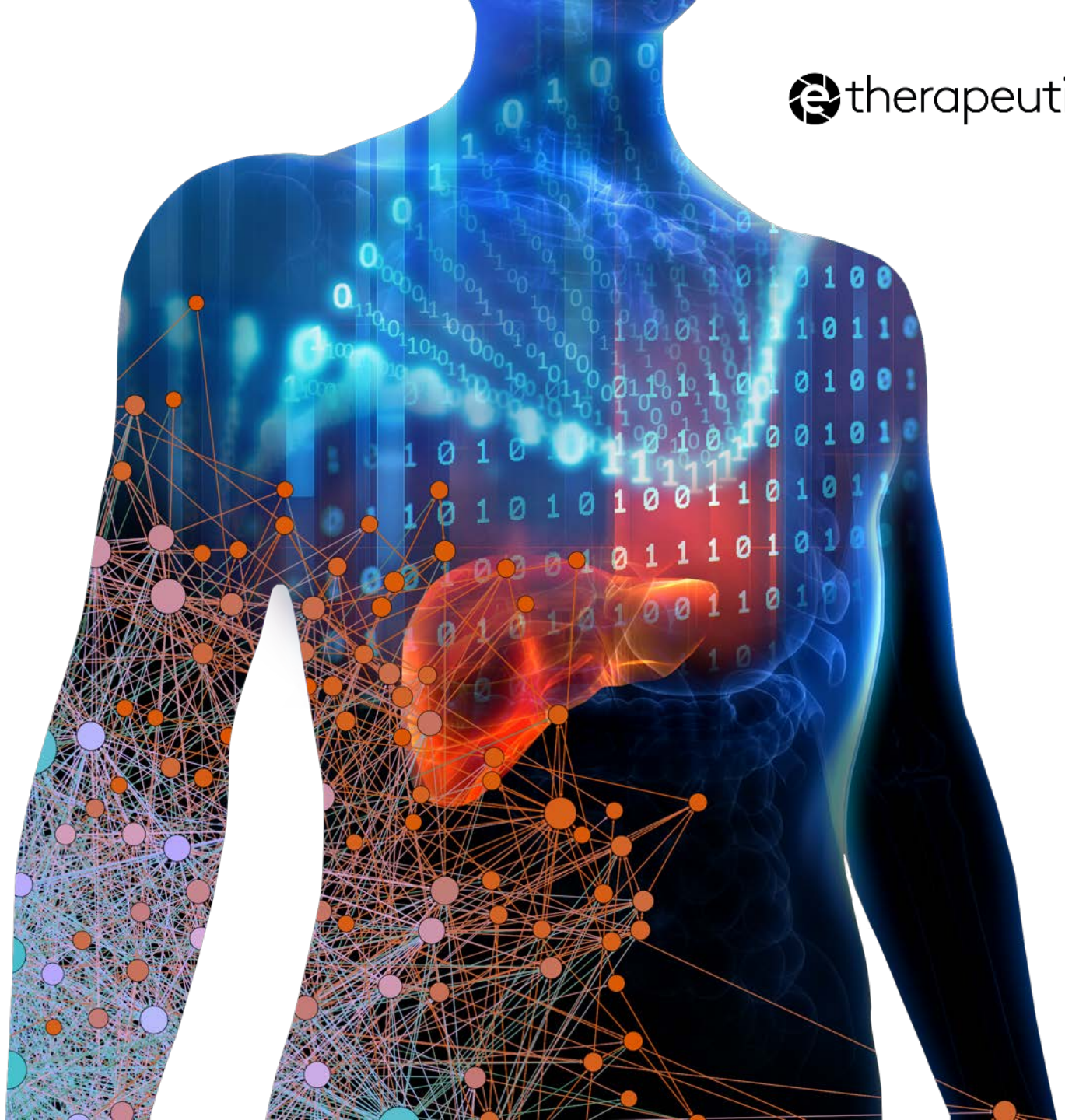
Computational Drug Discovery

From Machine to Man



Investor presentation
May 2021

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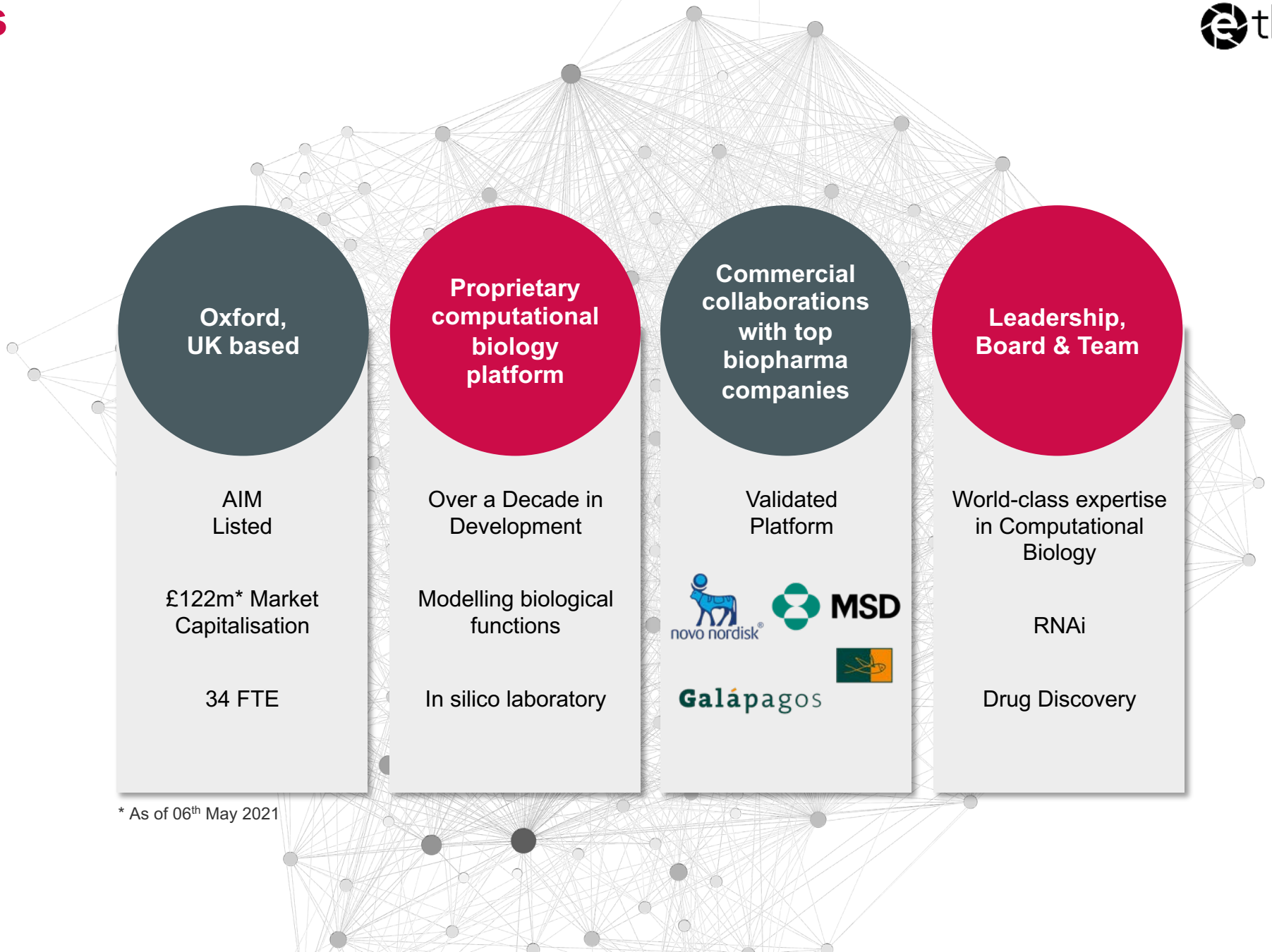
therapeutics

I could actually end this post right here by stating one simple, predominant reason why the science of drug discovery is so tortuous: **it's because biology is complex.**

Why Drugs are Expensive, Scientific American, 2014
Ashutosh Jogalekar

About us



* As of 06th May 2021

Business model

In-house Pipeline

RNAi

Leverage Computational platform	High specificity, long duration of action	Scope for early-stage BD transactions

Partnering

Our partners to date

Monetise Computational platform	Disease area and modality agnostic	Small molecules, novel target ID

ETX *in silico* discovery engine

How do we understand biology better?

ETX *in silico* laboratory

We create network models of biological processes

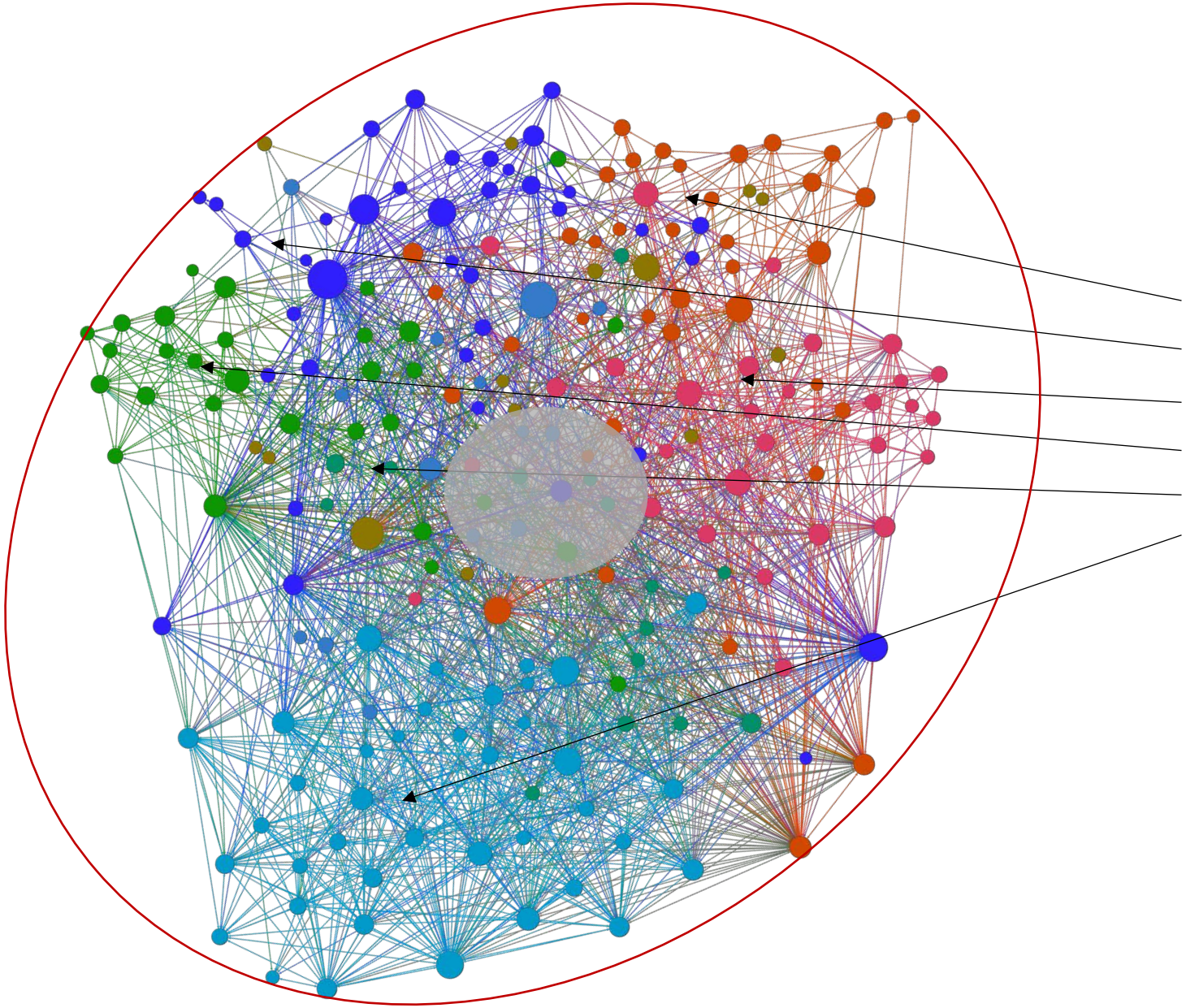
Proprietary data sets

ML/AI & Network Algorithms

Computational biologists

in silico Discovery Engine

ETX network maps of cellular function



Cellular functions

Represented as network models

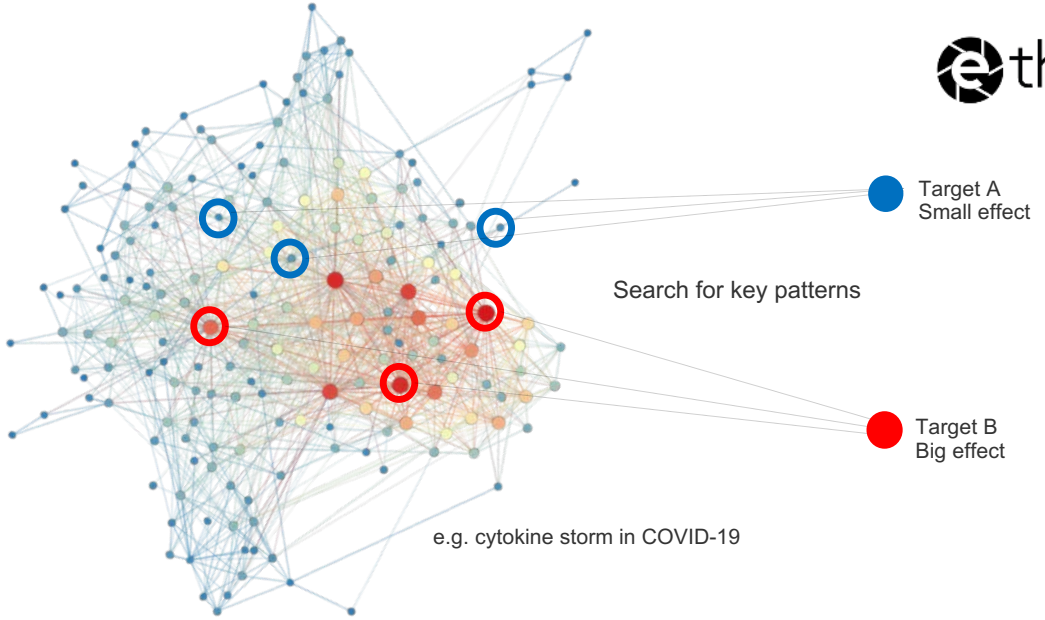
We study these processes and how they interact in the context of disease

- Trophic signaling
- Endocytosis
- Proteostasis
- Oxidative phosphorylation
- Exocytosis
- ER chaperone regulation
- Etc…

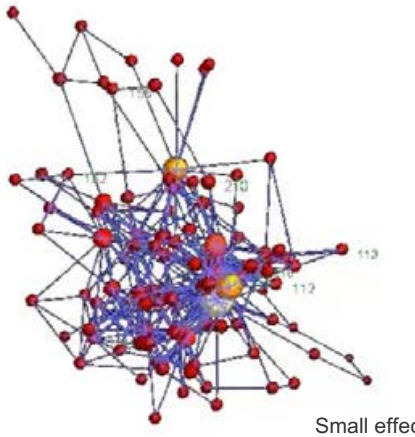
This enables us to propose rational therapeutic interventions

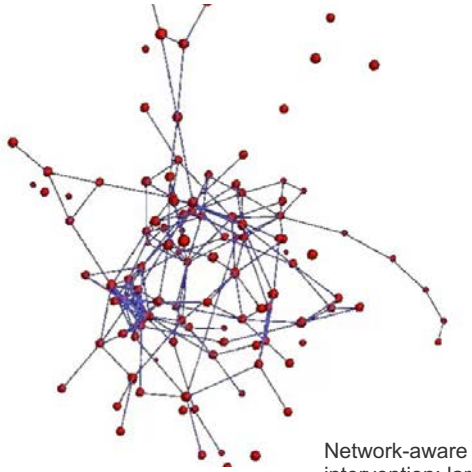
Network biology

- 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**

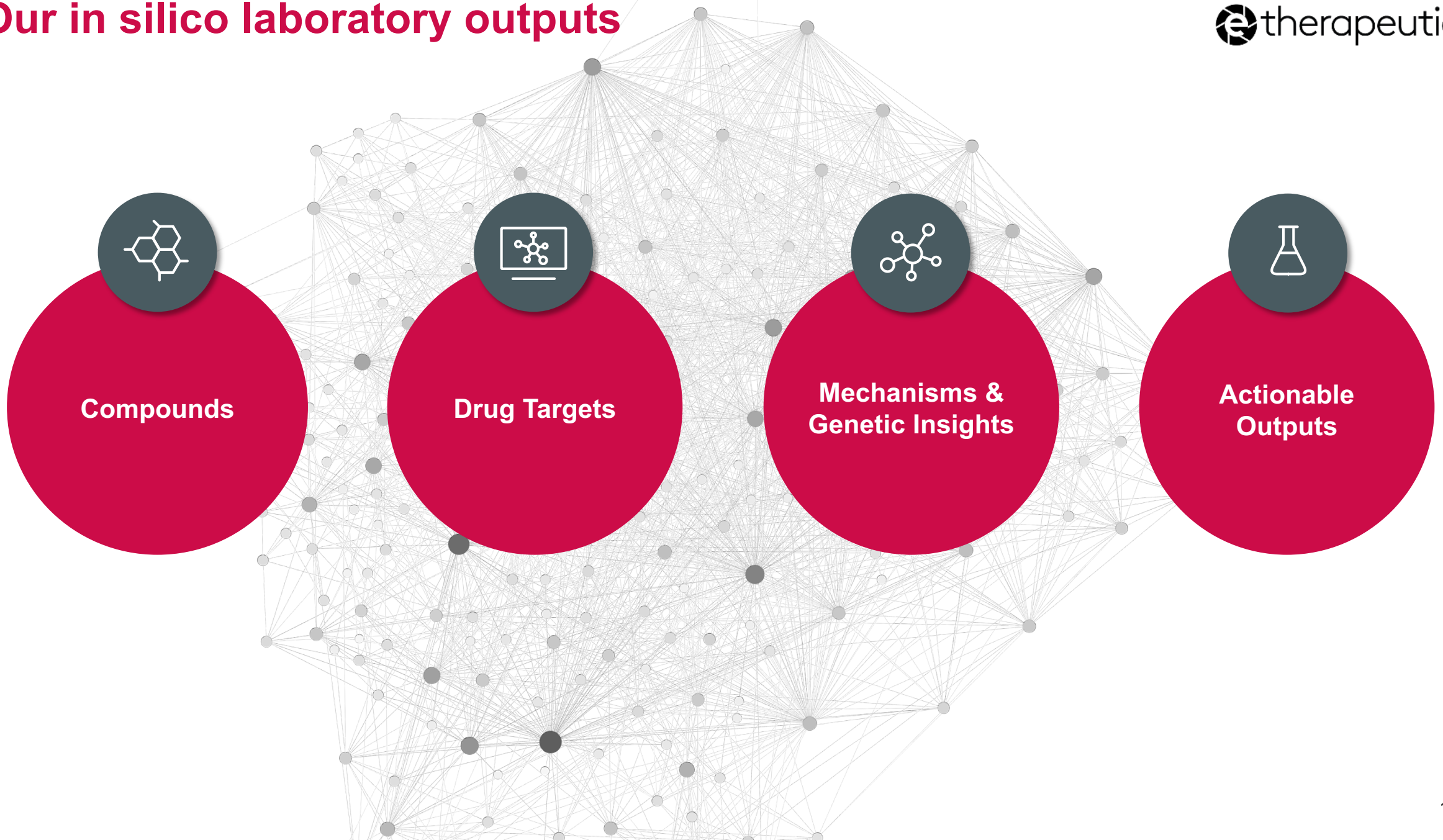


***In silico* testing of therapeutic interventions – modelling biological effects**


Small effect

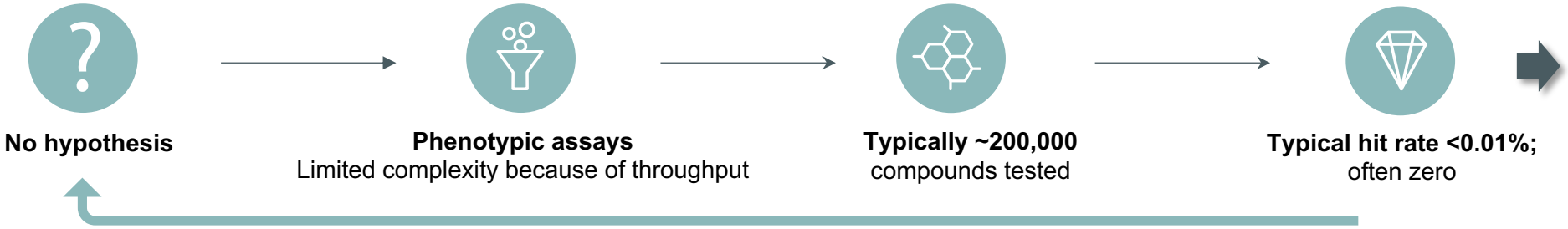

Network-aware intervention; large effect

Our in silico laboratory outputs



ETX in silico discovery engine

Traditional Approach: Blind Phenotypic Screening

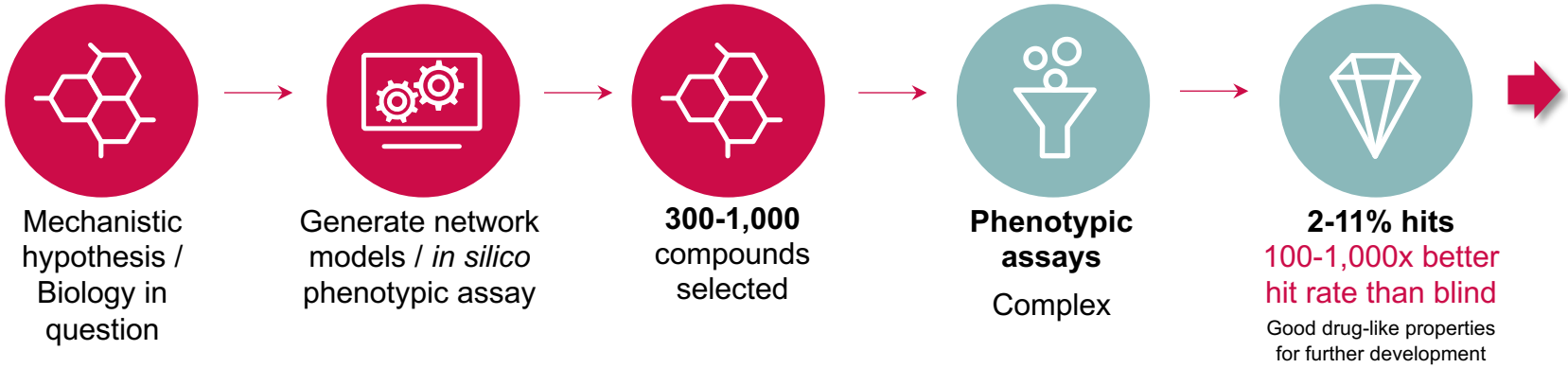


Mechanism unknown

- Very challenging target deconvolution
- Less translatable assays

Fail late / fail expensive

e-therapeutics: Computational Biology Platform Guided Phenotypic Screening



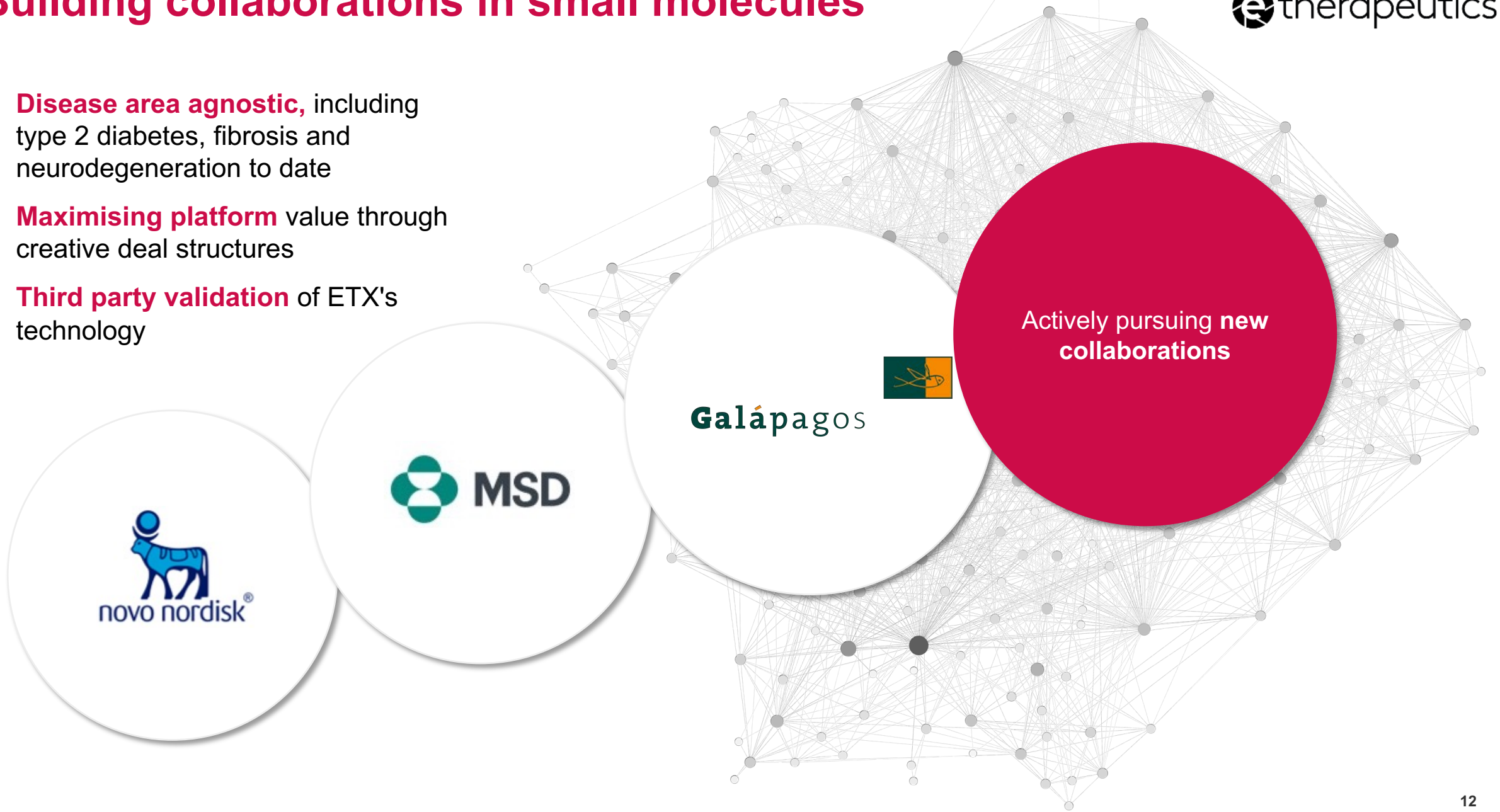
Mechanism identified

- Straightforward target deconvolution
- Enables complex translatable assays

Fail early / fail cheap

Building collaborations in small molecules

- **Disease area agnostic,** including type 2 diabetes, fibrosis and neurodegeneration to date
- **Maximising platform** value through creative deal structures
- **Third party validation** of ETX's technology



RNAi Drug Platform

In-house pipeline

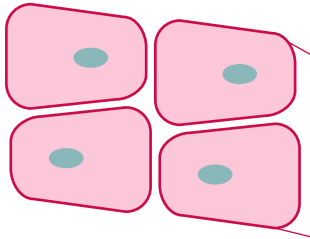
ETX RNAi drug platform

siRNA – Short Interfering RNA

Platform Properties

- Platform developed in 2020
- Robust IP position, novel GalNAc linker patent application filed
- Significant in-house molecular design know-how

Liver presents large opportunities

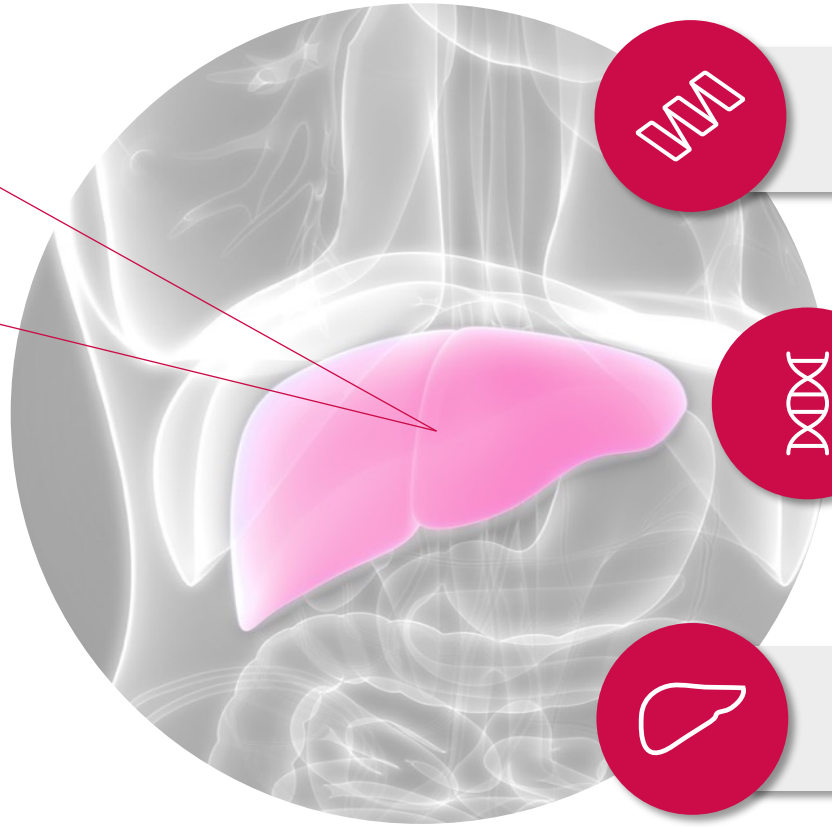


70%

of liver cells are Hepatocytes
– play pivotal role in metabolism and protein synthesis

Secrete proteins / signals that influence cells in other organs

Detect proteins / signals from other cells / organs that influence hepatocyte function



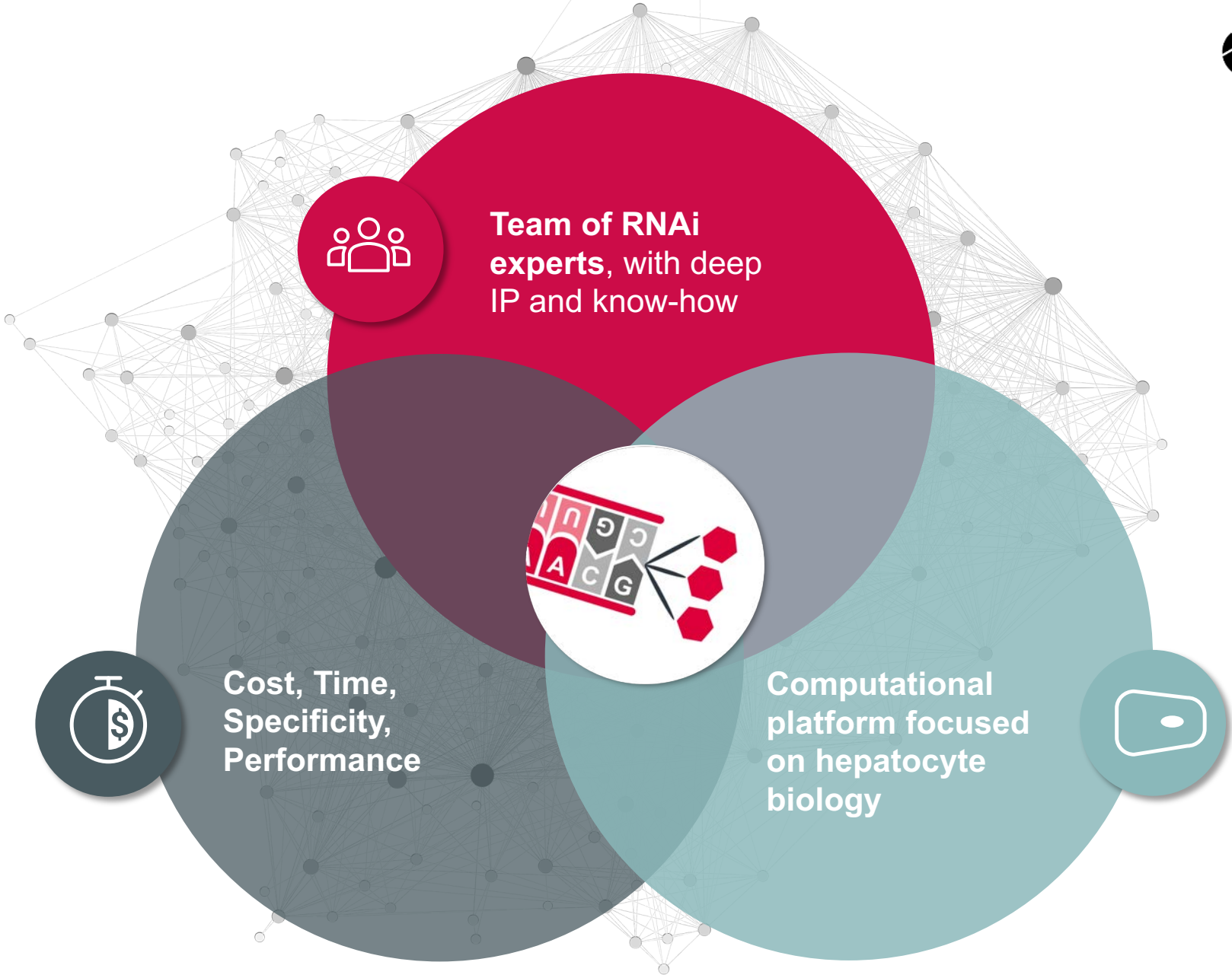
~10K proteins expressed in liver hepatocytes
~1K are secreted to influence other organs*

To date only 1% liver-expressed genes targeted using RNAi therapeutics

Secreted hepatocyte targets allow for the pursuit of indications **beyond liver disease**

*doi: https://www.mdpi.com/2072-6643/11/8/1795. Source: The Human Protein Atlas

Why RNAi?


Team of RNAi experts, with deep IP and know-how
Cost, Time, Specificity, Performance
Computational platform focused on hepatocyte biology

RNAi platform advantages

Time & Cost

Drug design

Traditional
Small molecules

c.Cost
$4m
c.4 years

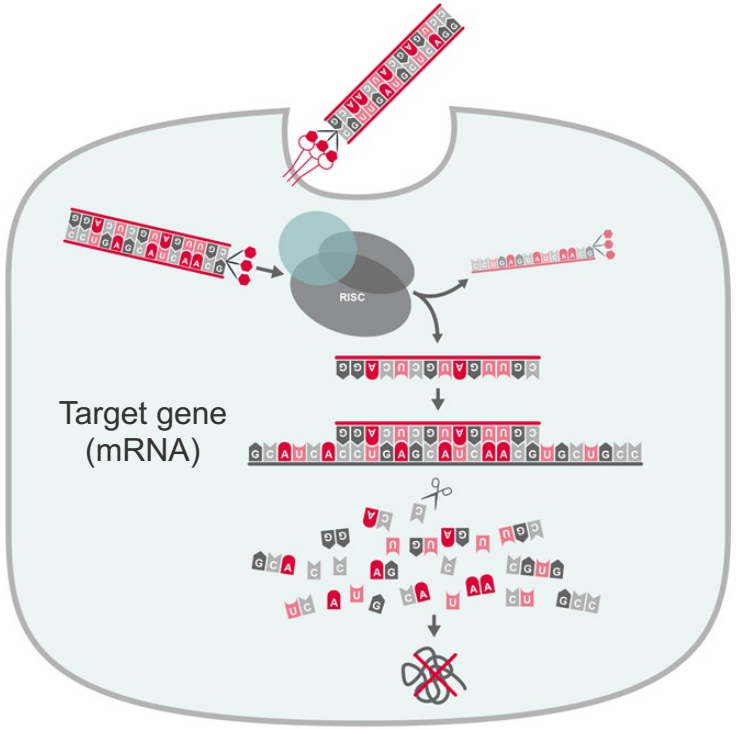
e-therapeutics
siRNA

Cost
$500K
5-6 months

Cost of development phase reduced drastically with RNAi

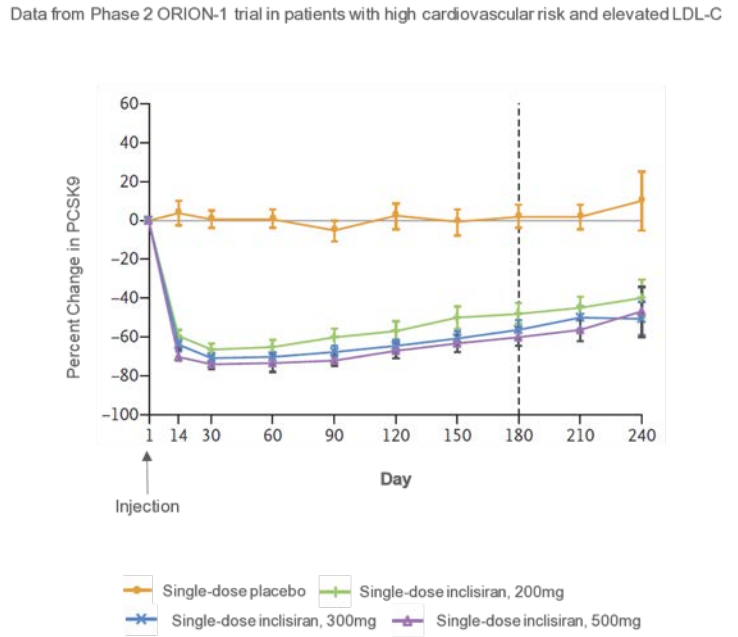
Specificity

Hepatocytes and target gene



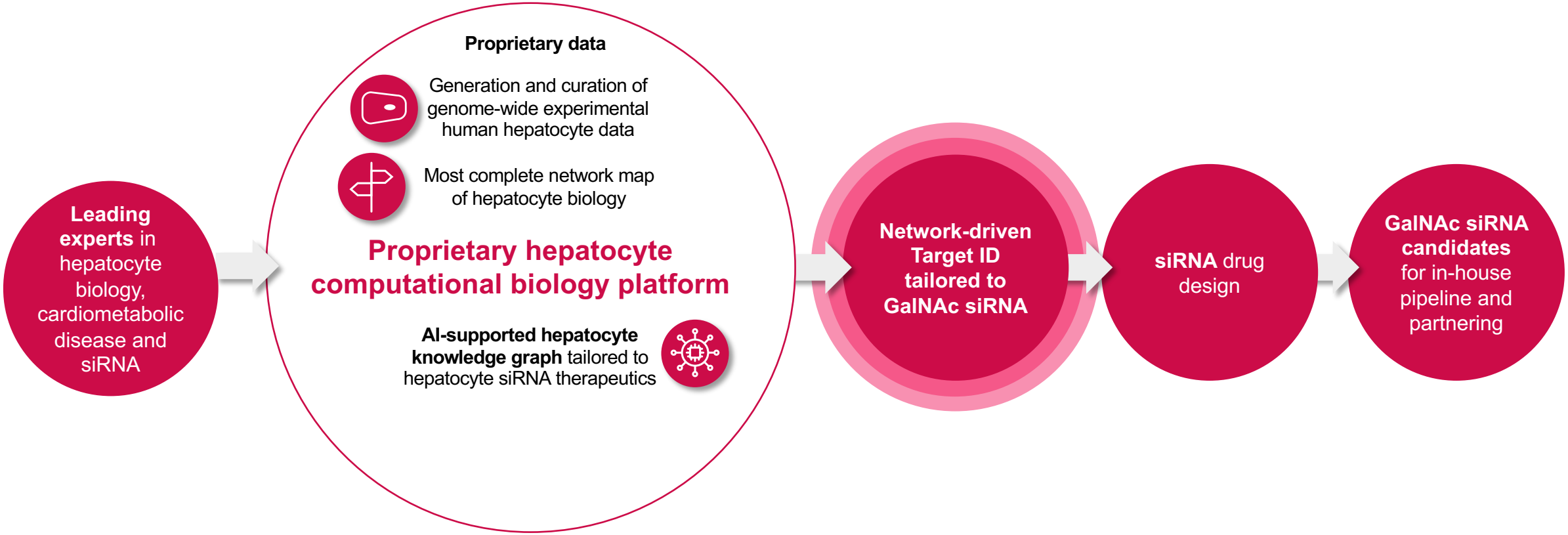
Performance

Changes in PCSK9 Levels with a single dose regimen of Inclisiran vs. placebo

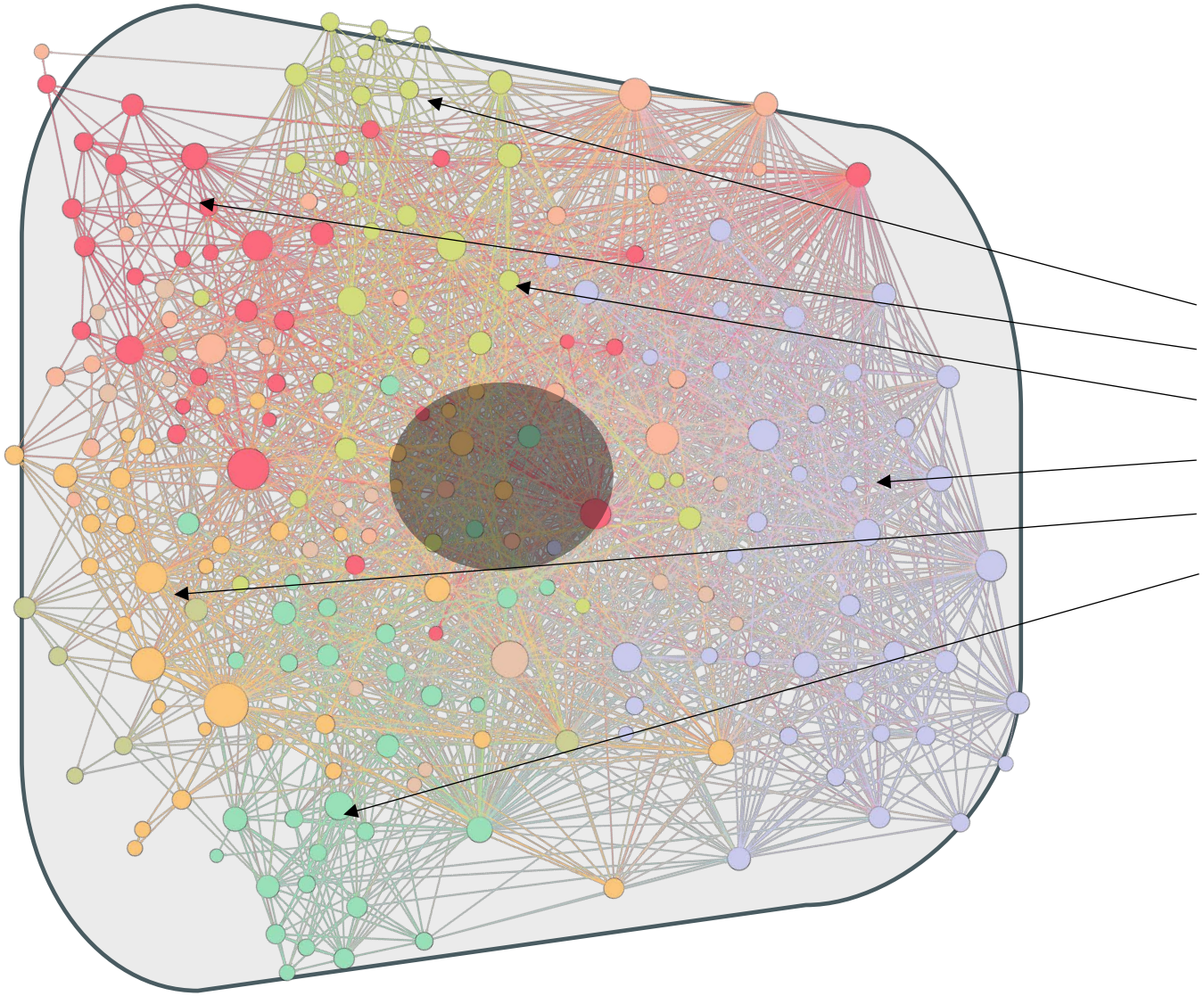


Hepatocyte target team

Zooming into hepatocytes



Proprietary ETX hepatocyte network map



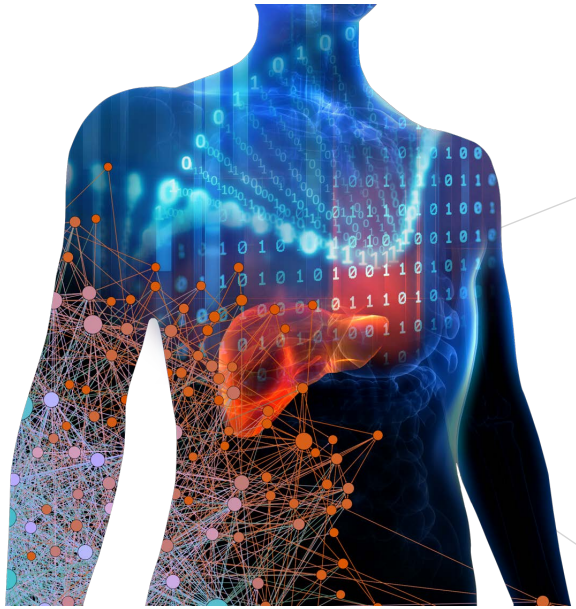
Hepatocyte biological functions

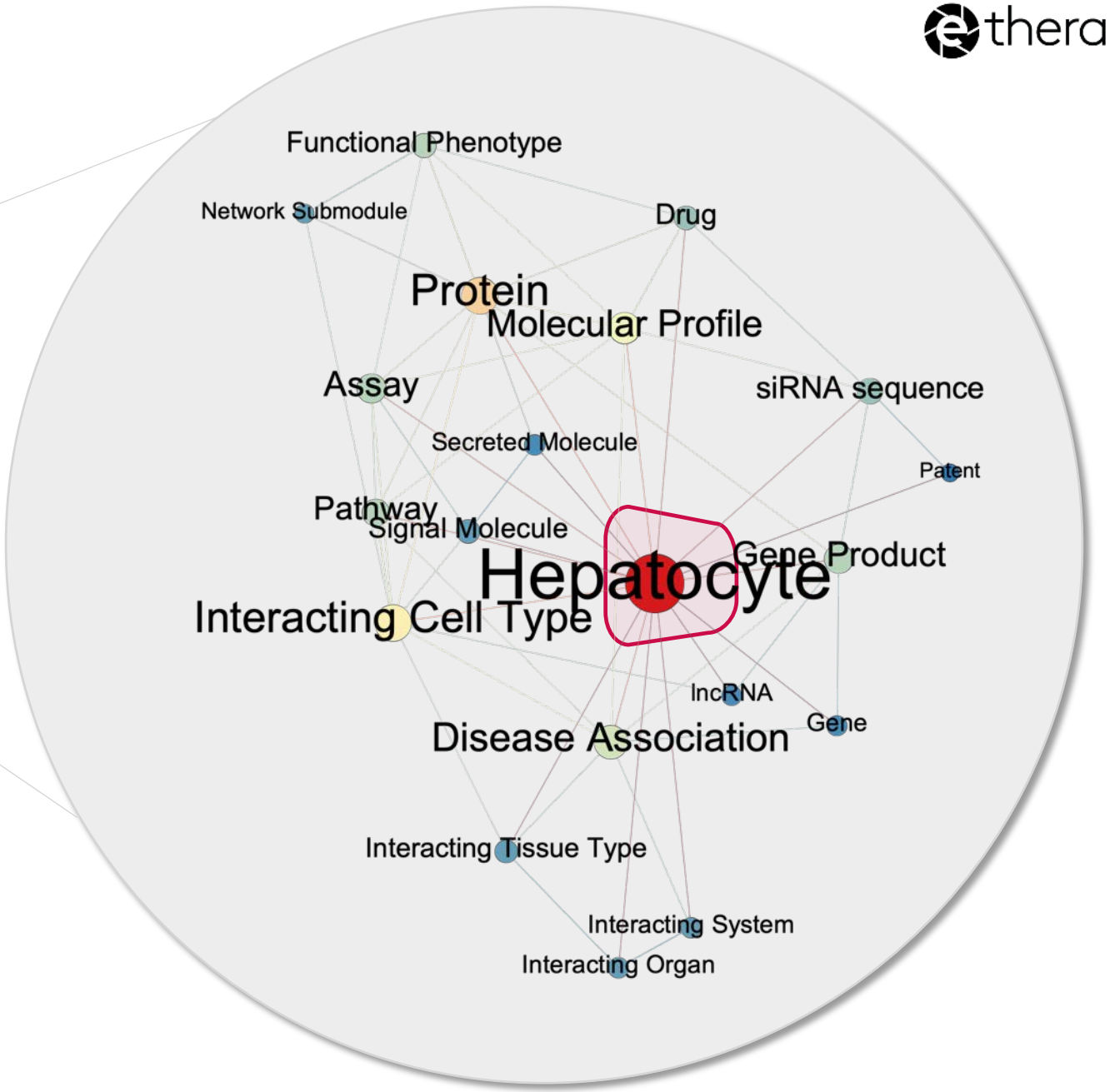
Represented as network models

- Insulin signaling
- Glucagon signaling
- Lipid metabolism
- Xenobiotic metabolism
- Glucose production
- Clotting factor synthesis & secretion
- Etc…

The hepatocyte atlas

Proprietary knowledgebase





- Proprietary NLP mined literature knowledge
- Proprietary experimental data
- Public data sources
- Proprietary data enhancement
- Prediction of missing relationships
- Network Biology
- Genetic Data

RNAi – Significant early stage financials

RNAi Platforms

Platform/Preclinical Deal	Phase I	Phase 2	Phase 3	Approved			
Dicerna / Alexion 2018 4 targets **$22M + $105M milestones per target**	Dicerna / Roche 2019 1 asset (HBV) **$200M upfront** **$1.47B milestones**	arrowhead / Takeda 2020 1 asset (AAT) **$300M upfront** **$740M milestones**	Novartis / The Medicines Company 2020 **1 asset (PCSK9)** **$9.7B acquisition**	onpattro (patisiran) **FDA approval** **Aug 10, 2018** Hereditary transthyretin-mediated amyloidosis	GIVLAARI (givosiran) **FDA approval** **Nov 20, 2019** Acute hepatic porphyria	OXLUMO (lumasiran) **FDA approval** **Nov 23, 2020** Primary hyperoxaluria type 1	Novartis Leqvio ® **EU Approval** **Dec 9, 2020** Hypercholesterolaemia Dyslipidaemia
Silence Therapeutics / Mallinckrodt 2019 **3 targets** **$20M upfront**							
Dicerna / novo nordisk 2019 30 targets **$175M + $357.5M milestones per target**							
arrowhead / Janssen 2018 3 targets **$1.9B option, milestones**		arrowhead / Janssen 2018 1 asset (HBV) **$175M upfront** **$1.6B milestones**					
Alnylam / Regeneron 2019 **$400M + $200M milestones**							
Dicerna / Lilly 2018 10+ targets **$100M + $350M milestones per target**							
				> US$4B sales 2026			
				US$1.18B	**US$333M**	**US$734M**	**US$ 1.89B**

Source: Alnylam Q4 & full year financial results Feb 11, 2021; GlobalData consensus Q4 2020; Alnylam royalty 2026 forecast US$233M.

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Alan Whitmore
Chief Scientific Officer

Jonny Wray
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Chief Research Officer

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