e therapeutics

Digital Drug Discovery

Computational Biology Platform
Novel Mechanisms, Targets & Drug Candidates

25th February 2021

Non-Confidential Overview

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Forward looking statement

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About us

Oxford, UK-based, AIM listed

Network-driven computational drug discovery platform

RNAi technology platform

Commercial collaborations with top-tier pharma companies

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Our in-Silico Laboratory

We Construct
in-silico Models of Biological Functions

We Identify
Novel Targets and Mechanisms

We Design
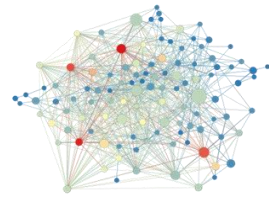Novel Small Molecules and RNAi Therapeutics
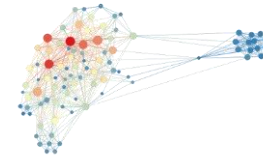
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Network Biology

Network models of biological functions

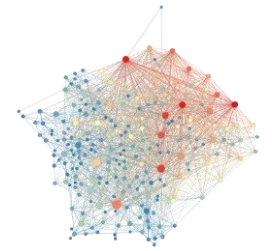Biological functions are controlled by networks of genes and proteins

Insulin resistance

Sars-Cov2-hyperinflammation
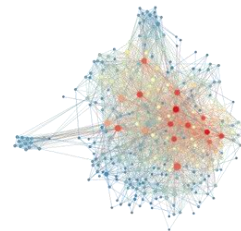

Sars-Cov2-protein production
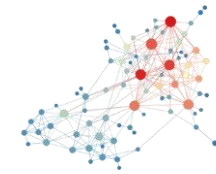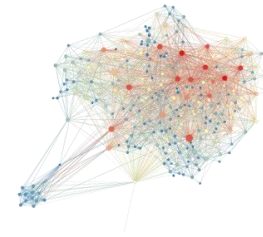

Axonal degeneration

Immune checkpoint signaling
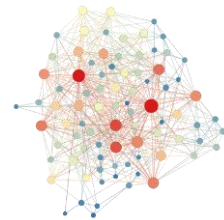

Axonal outgrowth

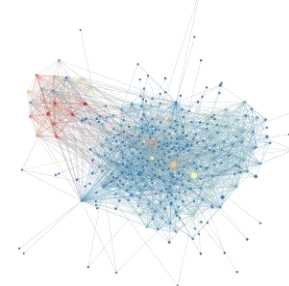Influenza virus replication

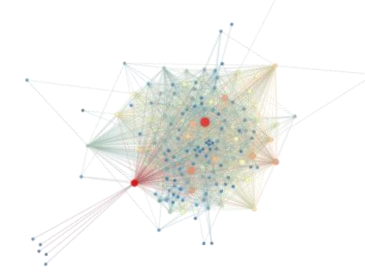Lipid metabolism

Tryptophan catabolism

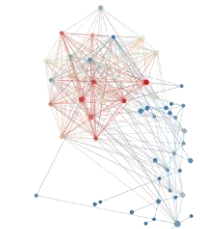Telomerase signaling
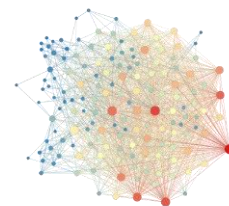

Tunneling nanotube regulation

Endocytosis

Fibroblast activation

Angiogenic signaling
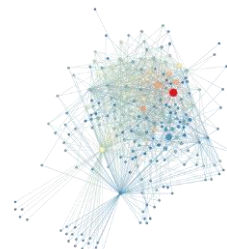

Neuronal autophagy

Immunoreceptor ligand expression

TNFa signaling regulation

Millions of network models have been generated to date

Drug Discovery Platform

Network Biology Platform

Multidisciplinary domain expertise

Proprietary & AI enhanced data resources
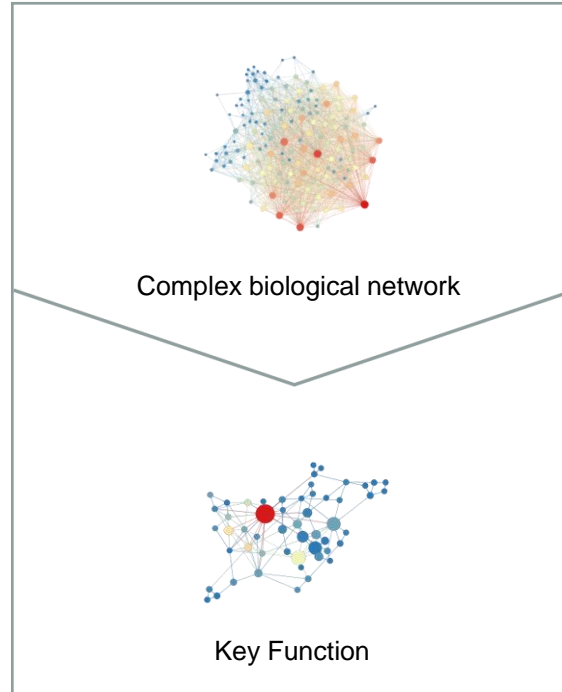
Proprietary cutting-edge network analytics

Wet lab outcomes

Dealing with Biological Complexity

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In-Silico Laboratory Outputs

Network models produce effective wet lab outcomes

Get Mechanistic Insights

Complex biological network

Key Function

Find Compounds

Active Compounds
15 million AI-enhanced signatures
Hit Rates 100-1000x improvement

Target Deconvolution
Novelty

Find Key Proteins

Novel Targets
Wet Lab Validation

Get Genetic Insights

Alzheimer's
Cancer
ALS
Stroke
Parkinson's
Diabetes
….

Complex Risk Drivers

Find Key Functions

Novel Mechanisms
Genetic Validation
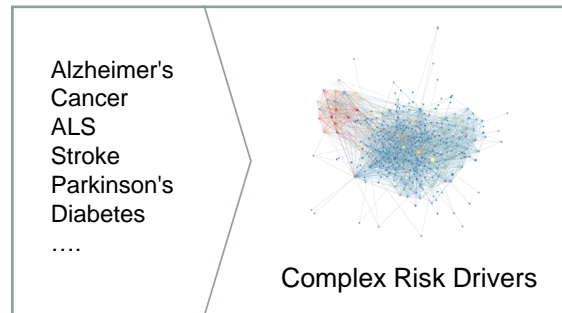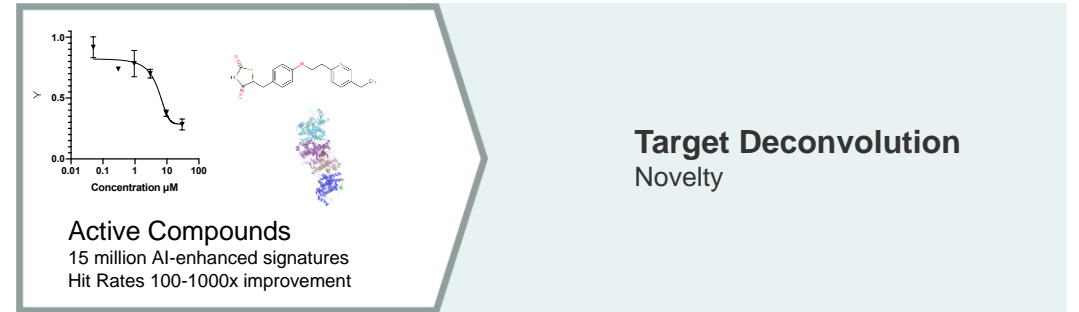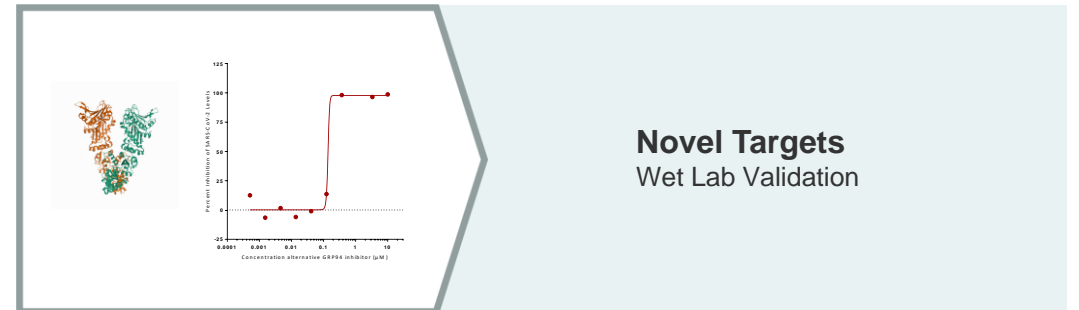
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Validated Platform

Demonstrating advantages over blind screening for small molecule discovery

	Project	% 'Hits' in parallel 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	novo nordisk Type 2 Diabetes	—
	MSD CNS	—
	Galápagos 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

NDD Guided vs. Other Phenotypic Screening*
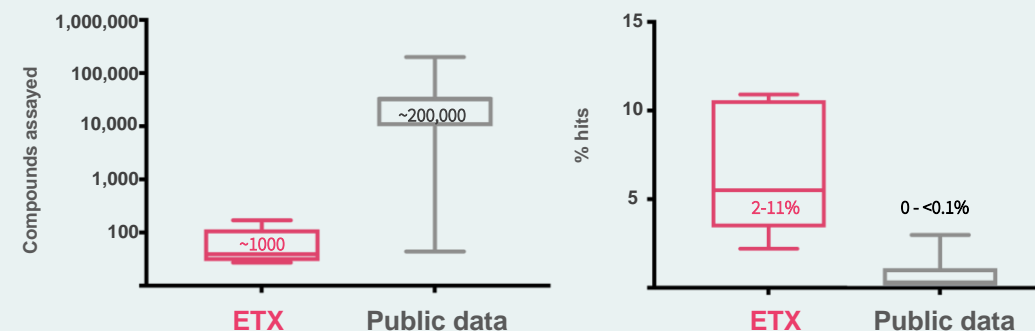
Our hit rates are 100-1000x higher than industry standards

◆ 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 have information on their potential MoA

Source: * based on 15 publications

RNAi Platform

Comparison mRNA Vaccines and RNAi Therapeutic Mechanism

COVID-19 mRNA vaccine sequences in a lipid envelope

The vaccine provides patient's cells with the mRNA to create millions of copies of the SARS-CoV-2 spike protein, which triggers an immune response

siRNA conjugated to a GalNAc ligand for hepatocyte targeting

GalNAc-siRNA mediates mRNA degradation, leading to inhibition of synthesis of the corresponding protein

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RNAi in Liver

Unique Drug Like Properties

Highly specific – one cell type, one target mRNA

Long duration of action – one subcutaneous injection
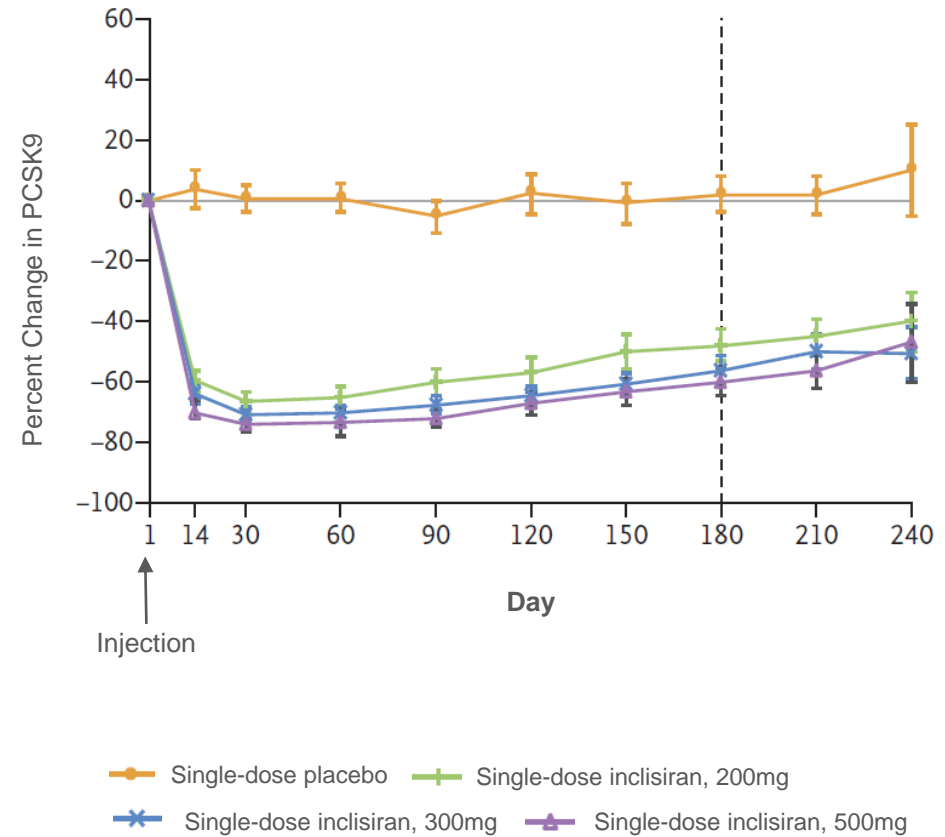
Multi billion dollar drug platform opportunity
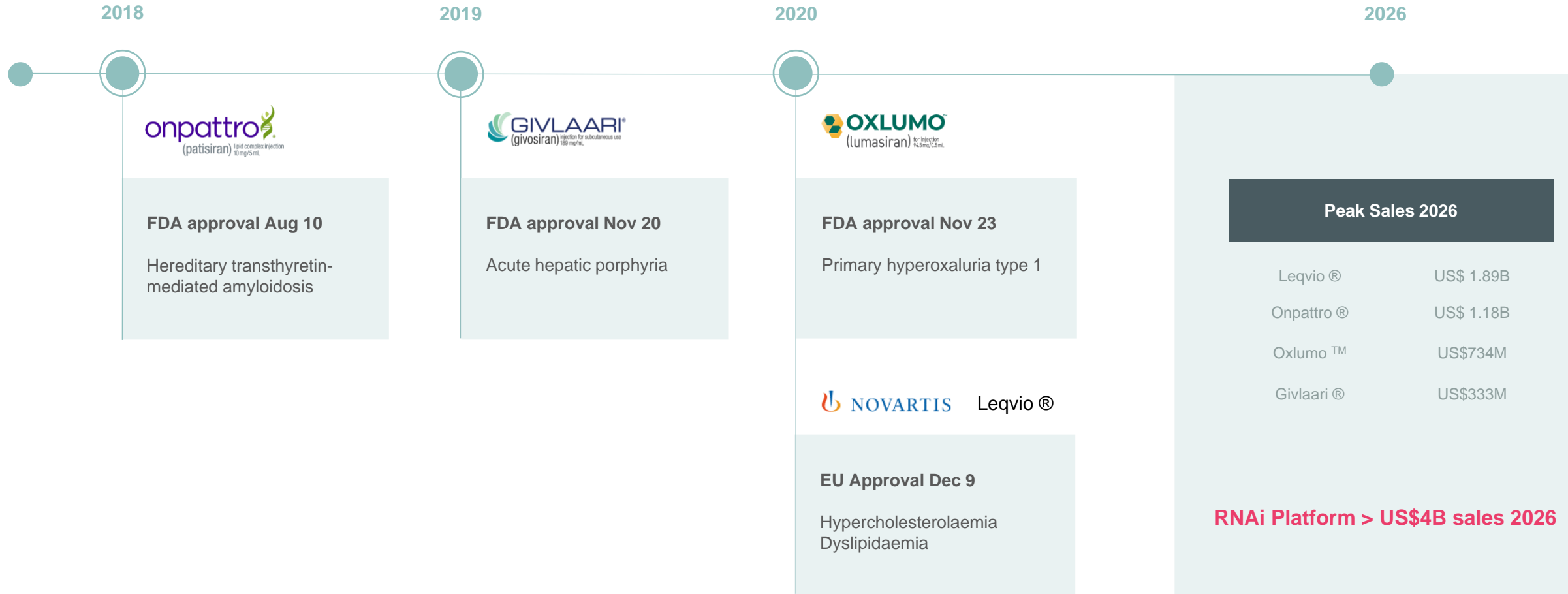
Clinically validated technology

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

Data from Phase 2 ORION-1 trial in patients with high cardiovascular risk and elevated LDL-C

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Clinically Validated RNAi Platform

Validated Platform Transitioning from Rare to Complex Disease

2018

2019

2020

2026

onpattro
(patisiran) lipid complex injection
10 mg/5 mL

FDA approval Aug 10

Hereditary transthyretin-mediated amyloidosis

GIVLAARI®
(givosiran) injection for subcutaneous use
189 mg/mL

FDA approval Nov 20

Acute hepatic porphyria

OXLUMO™
(lumasiran) for injection
94.5 mg/0.5 mL

FDA approval Nov 23

Primary hyperoxaluria type 1

NOVARTIS   Leqvio ®

EU Approval Dec 9

Hypercholesterolaemia
Dyslipidaemia

Peak Sales 2026

Leqvio ®	US$ 1.89B
Onpattro ®	US$ 1.18B
Oxlumo ™	US$734M
Givlaari ®	US$333M

RNAi Platform > US$4B sales 2026

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RNAi Deals are Commanding Significant Financials

Deals highlighting up-front payments for exclusive rights for predominantly pre-clinical targets

Overall value of deals in 000's
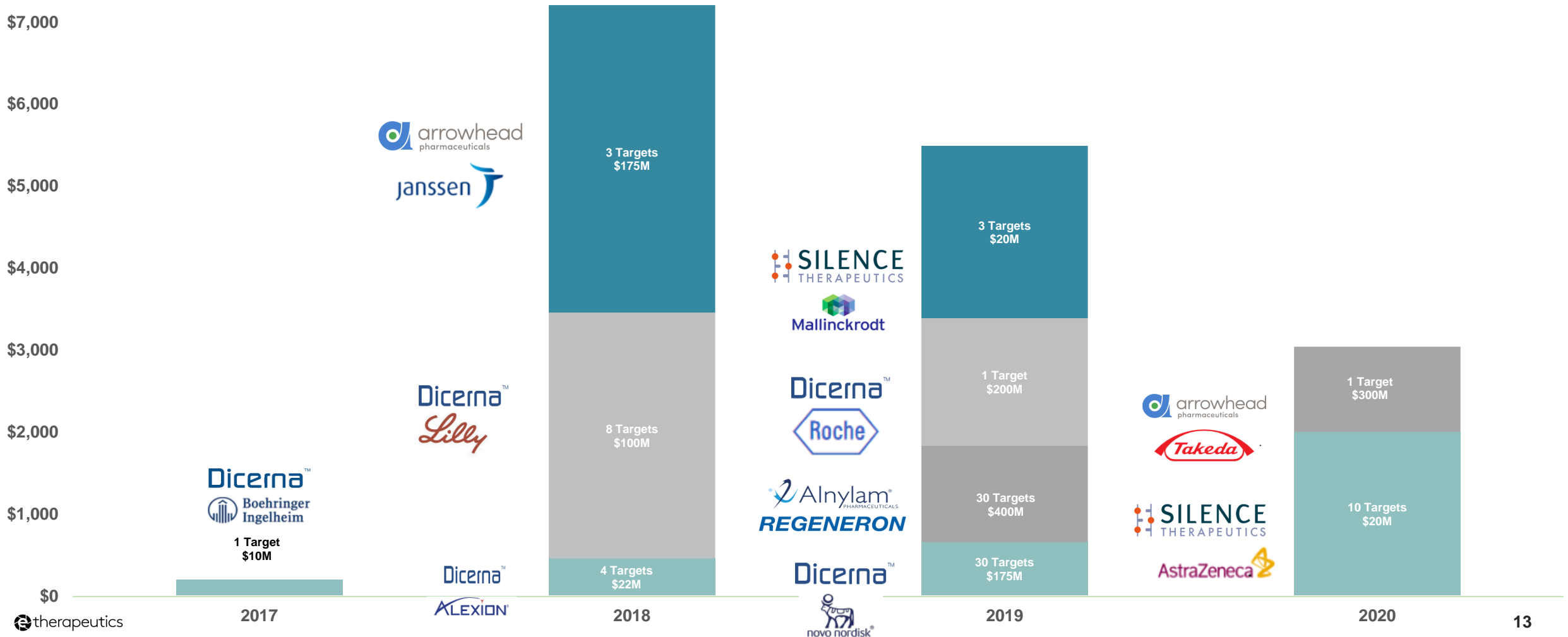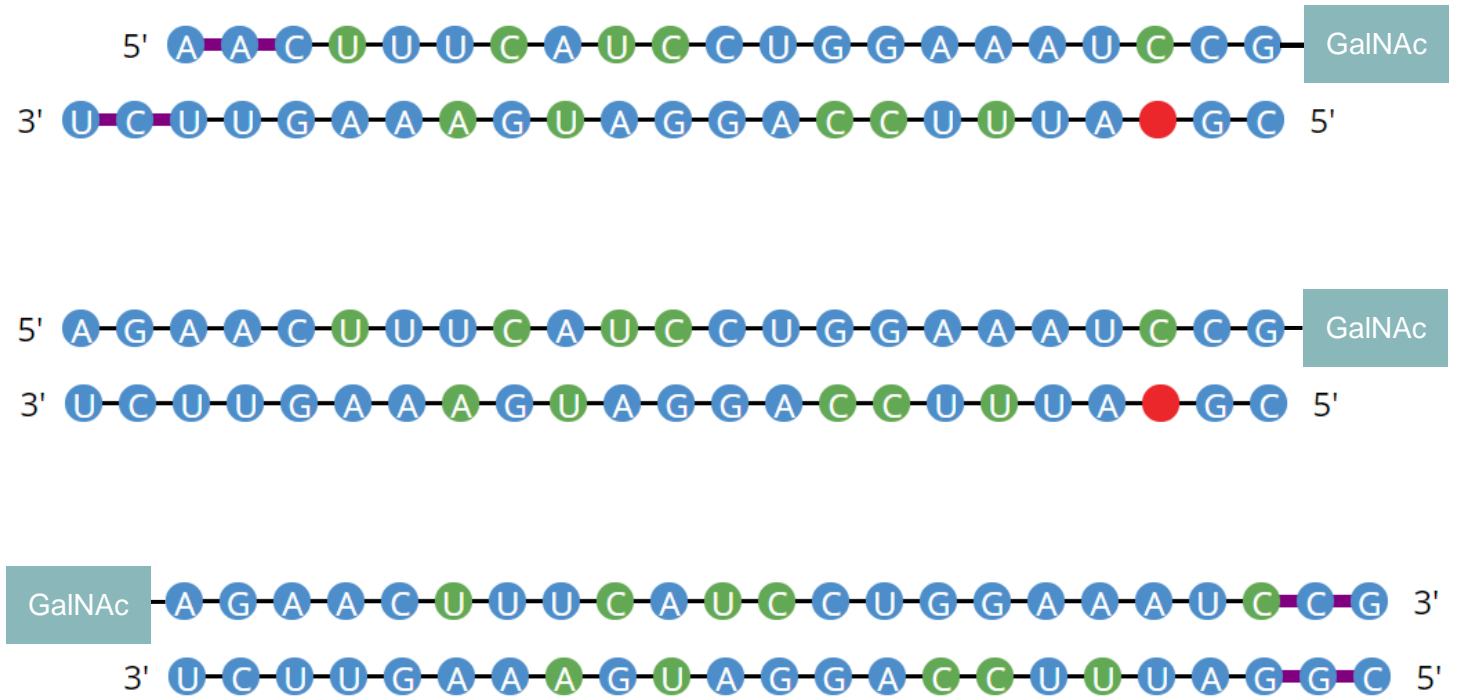
ETX RNAi Platform

Strong IP position

Novel GalNAc linker with patent filed

Position specific stabilization chemistry

Preclinical timelines significantly faster

Initial Chemical Designs

Stabilization chemistry

- 🟢 2'-OMe
- 🔵 2'-F
- 🟣 PS linkage
- 🔴 Other modification

Hepatocyte Delivery System

GalNAc   *N*-acetylgalactosamine

Liver Presents Large Opportunities for RNA Therapies

~10K proteins expressed in liver hepatocytes

~1K are secreted to influence other organs*

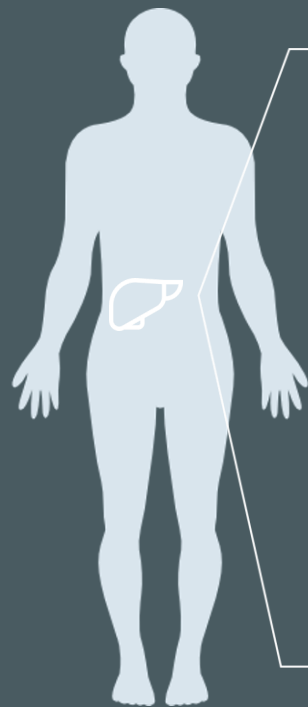To date only 1% liver-expressed genes targeted using RNA therapeutics

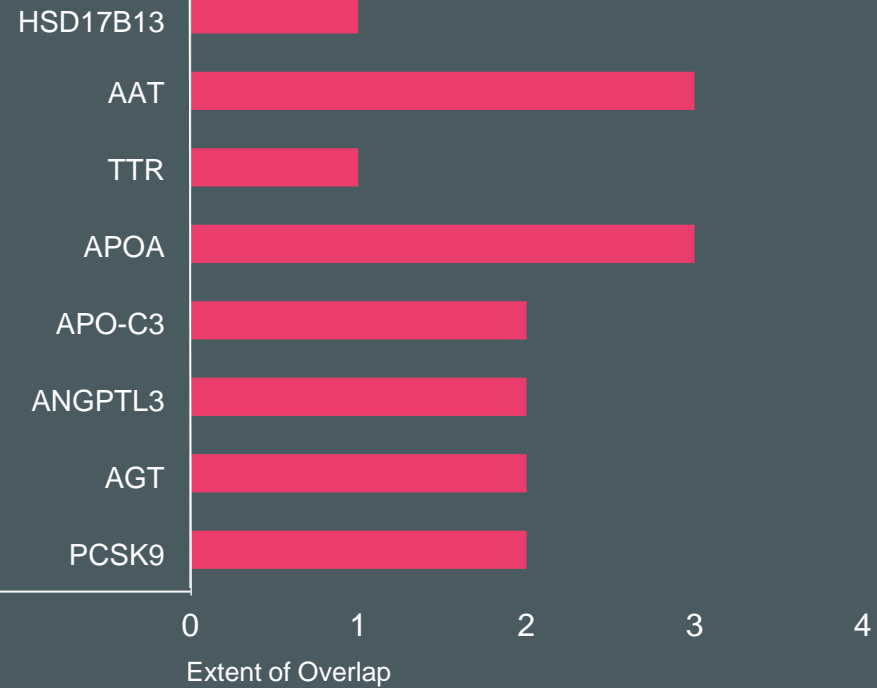Many therapeutic opportunities in the liver yet to be identified by competitors

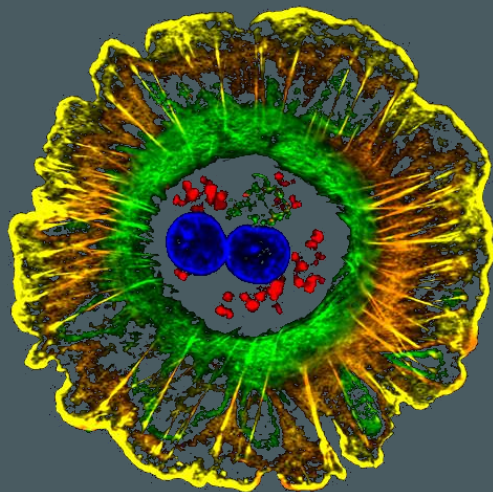# Liver-Expressed Genes Targeted by RNAi Therapeutics

Liver Focused Informatics Team

Most complete network map of hepatocyte biology **Proprietary to ETX**

Leading experts in **hepatocyte biology**

Generation and AI-supported curation of **proprietary experimental data** in human primary hepatocytes

Network-driven Target ID tailored to GalNAc siRNA

Focusing Network Science & AI on Hepatocytes

- ◆ Functional interpretation of genetic data

- ◆ Network Biology Platform AI/Machine Learning

- ◆ Disease Biology expertise

- ◆ Proprietary hepatocyte-specific interactome & molecular profiling data

- ◆ Primary Human Hepatocyte assays

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Building Collaborations

Type 2 diabetes, fibrosis and neurodegeneration

Maximising platform value through creative deal structures

Positioning ETX as global leader in Network Biology

Multi-year research collaborations

Actively pursuing **new collaborations** in addition to ongoing business development.
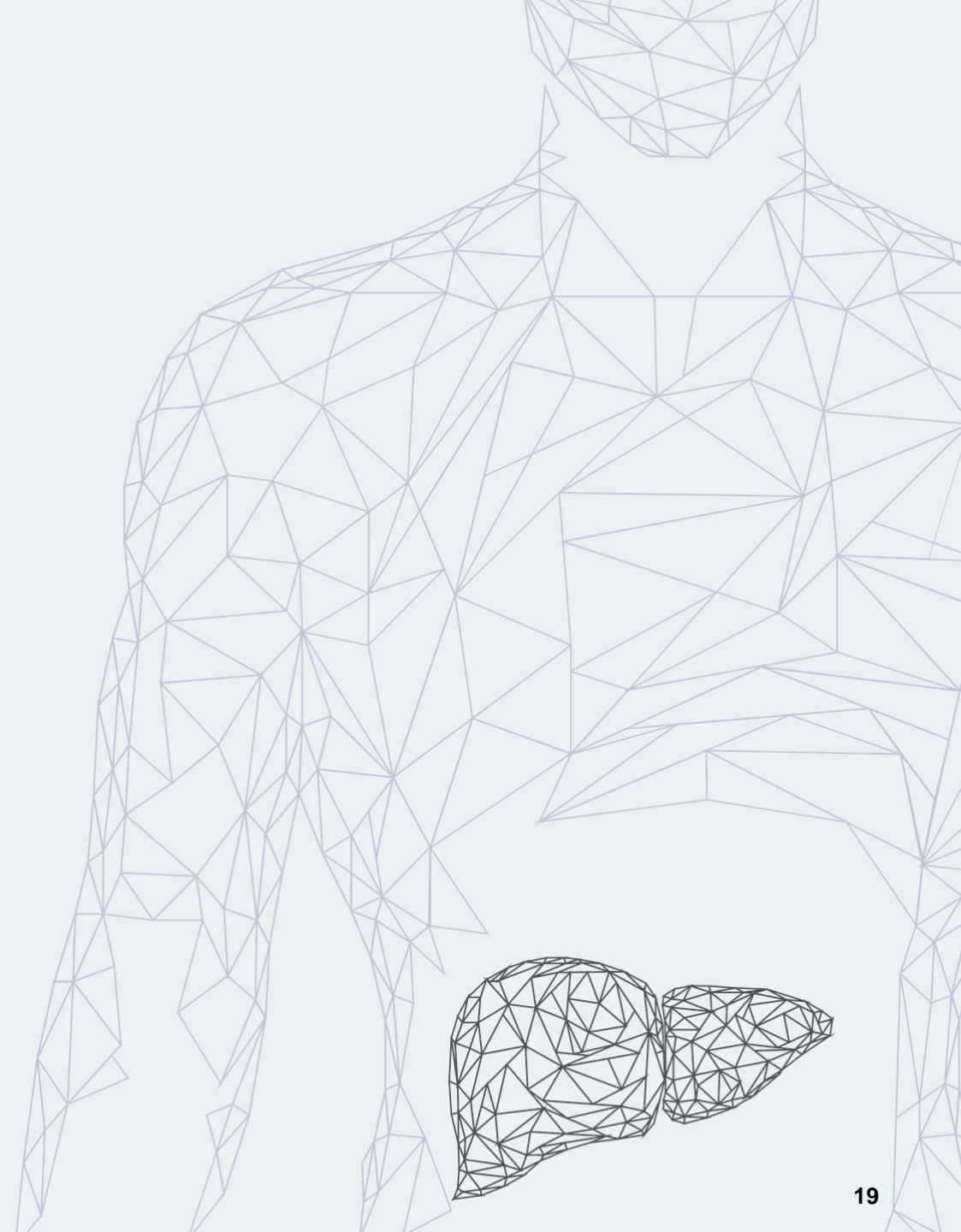
Current and Future Plans

Expand our computational platform collaborations

Establish world leading hepatocyte expertise

Generate novel hepatocyte-expressed targets

Commence RNAi platform partnerships

Experienced Management Team and Scientific Board

Board of Directors

Ali Mortazavi
Executive Chairman

Professor Trevor Jones CBE
Non-executive director

Michael Bretherton
Non-executive director
CEO Sarossa Plc

Scientific Advisory Board

Dr Paul Burke
Chair, Former CTO Pfizer

Dr Bill Harte
Chief Translational Officer
Case Western Reserve University

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

Ali Mortazavi
CEO, Executive Chairman

Alan Whitmore
Chief Scientific Officer

Jonny Wray
Chief Technology Officer

Colin Stubberfield
Chief Research Officer

Laura Roca-Alonso
Chief Business Officer

Stephanie Maley
Chief People Officer

Sarah Clare
Director Finance

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