AI' Role in Novel Target Discovery for High Unmet Needs Through Multi-Omics Integration

Namshik Han

UNIVERSITY OF CAMBRIDGE

YONSEI UNIVERSITY

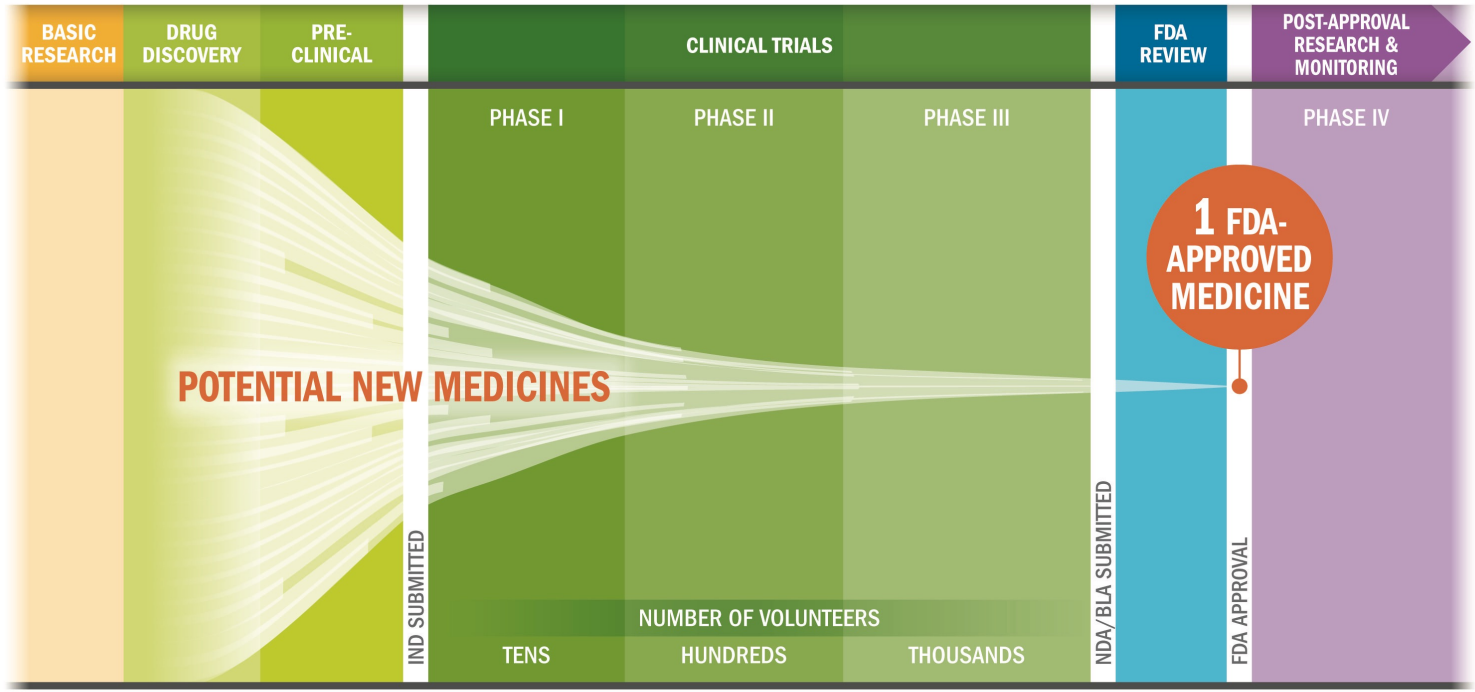
CardiaTec BIO

x4

Challenges in Drug Discovery

THE BIOPHARMACEUTICAL RESEARCH AND DEVELOPMENT PROCESS

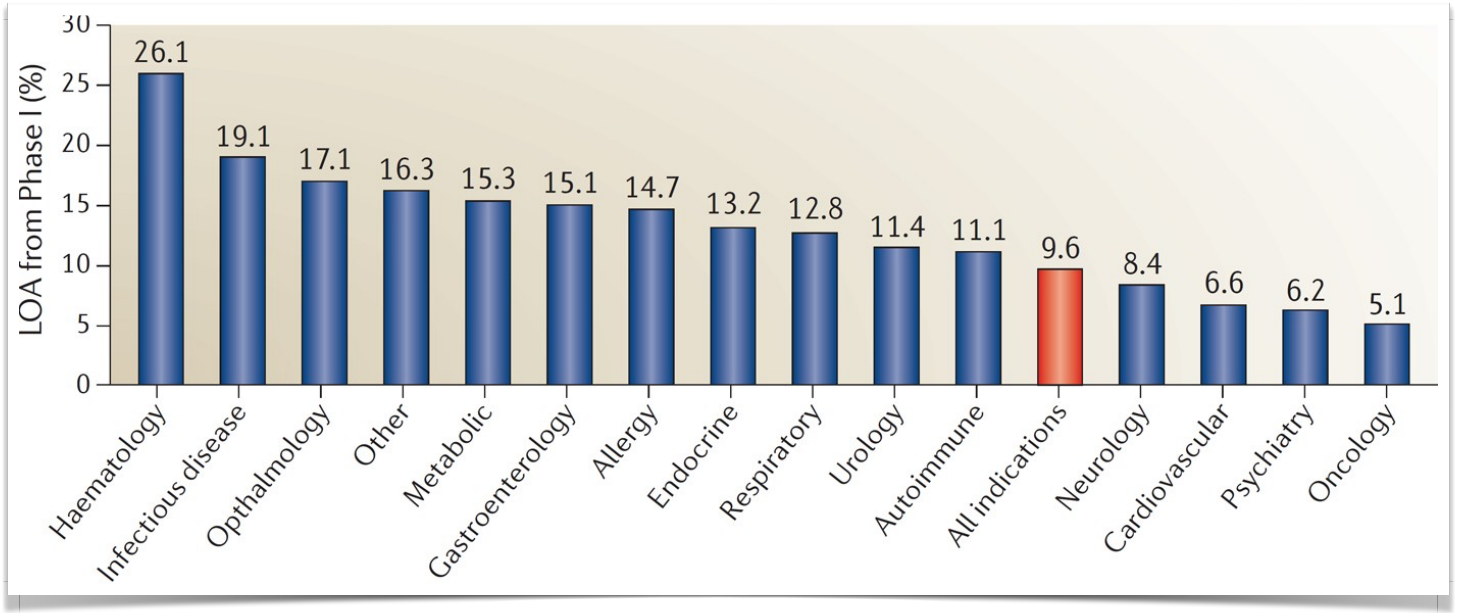
From drug discovery through FDA approval, developing a new medicine takes at least 10 years on average and costs an average of $2.6 billion.* Less than 12% of the candidate medicines that make it into Phase I clinical trials will be approved by the FDA.



Key: IND: Investigational New Drug Application, NDA: New Drug Application, BLA: Biologics License Application

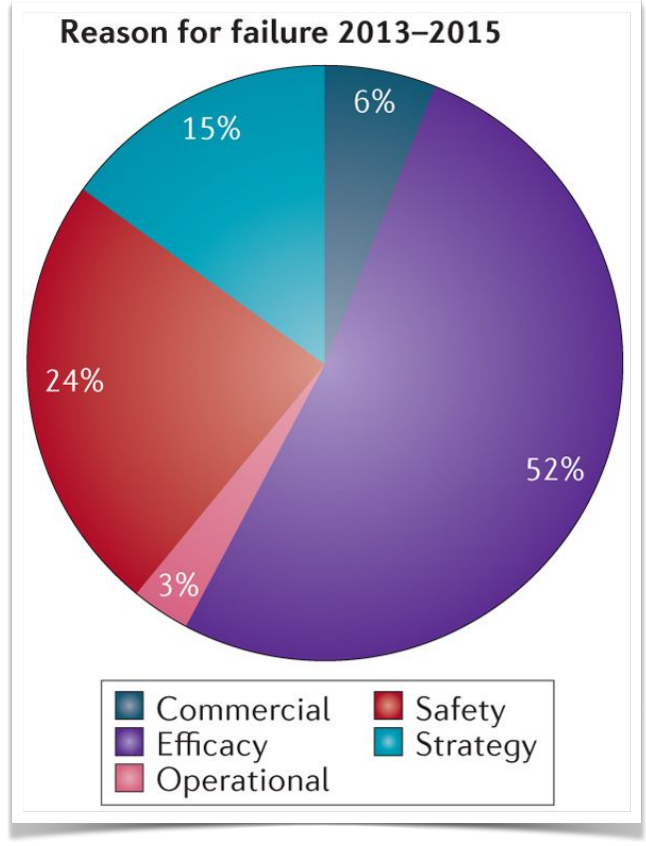
Highest Attrition Rate

Likelihood of approval (LOA) from Phase I



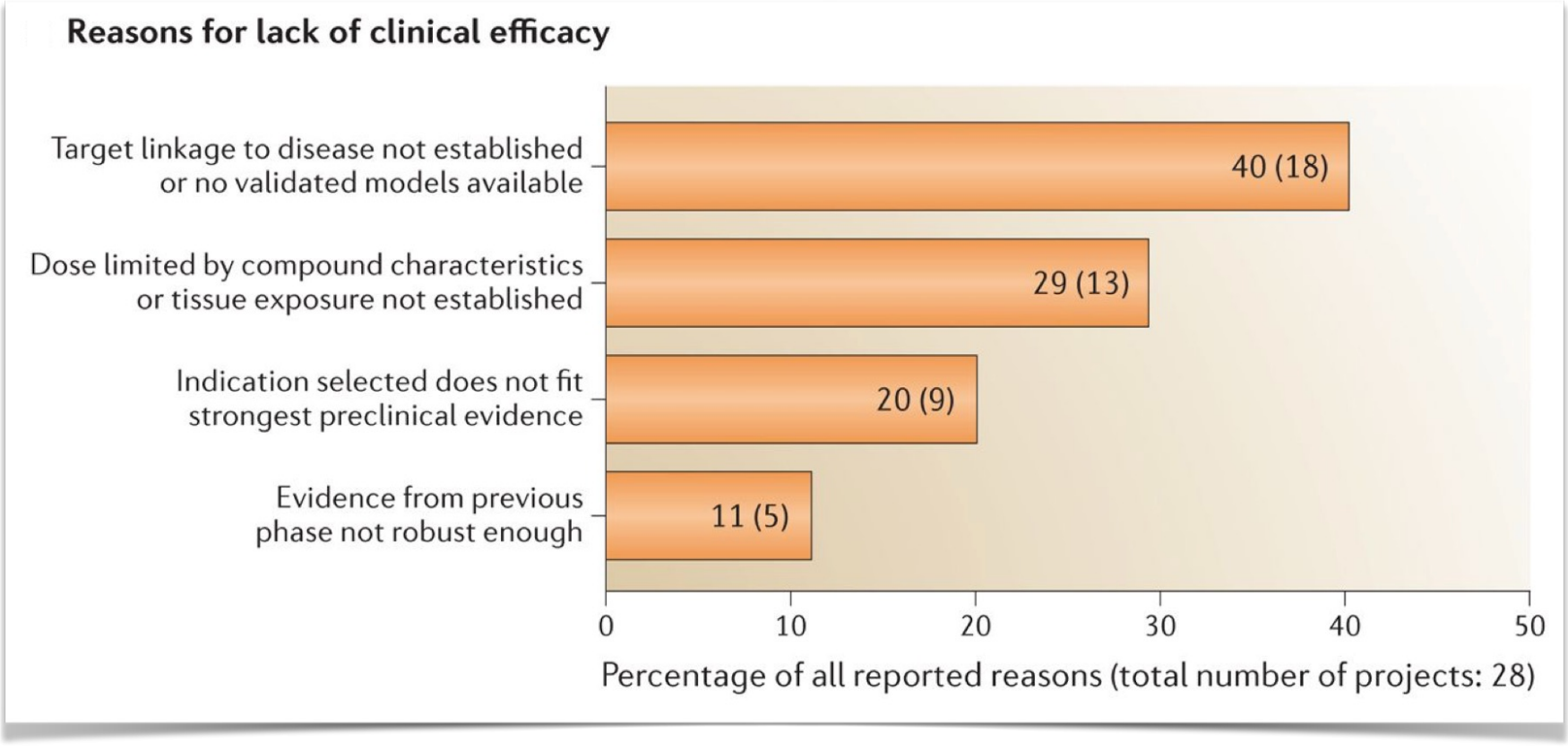
Nature Reviews Drug Discovery v15, 2016

Scientific Reasons



Nature Reviews Drug Discovery v15, 2016

Target-Disease Association



Nature Reviews Drug Discovery v13, 2014

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By Emma Woollacott
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1 August 2017 | Business

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AI-powered drug discovery captures pharma interest

Eric Smalley

Nature Biotechnology **35**, 604–605 (2017) | doi:10.1038/nbt0717-604
Published online 12 July 2017

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Nature Biotechnology, 2017

Technology

Artificial intelligence-created medicine to be used on humans for first time

By Jane Wakefield
Technology reporter

30 January 2020 Share

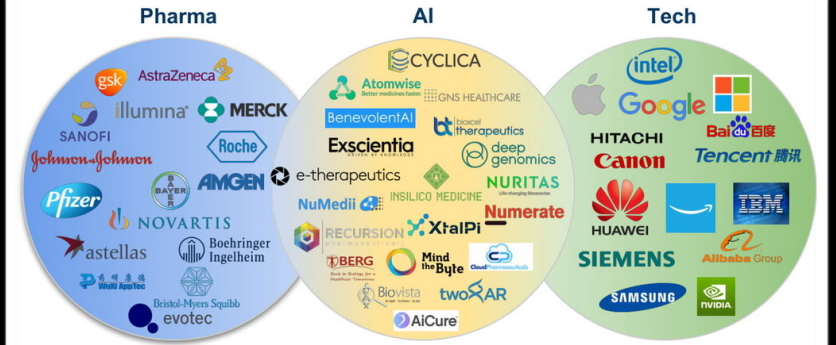
The drug was much quicker to market than ones developed in more traditional ways

A drug molecule "invented" by artificial intelligence (AI) will be used in human trials in a world first for machine learning in medicine.

It was created by British start-up Exscientia and Japanese pharmaceutical firm Sumitomo Dainippon Pharma.

The drug will be used to treat patients who have obsessive-compulsive disorder (OCD).

Typically, drug development takes about five years to get to trial, but the AI drug took just 12 months.



Drug Discovery	Pharma Corporations	Tech Corporations	Advanced R&D in Healthcare
INSILICO MEDICINE, Exscientia, CloudPharmaceuticals	gsk	Tencent 腾讯	XtalPi, Atomwise
CYCLICA, Atomwise, Numerate	MERCK	Alibaba.com	XtalPi
XtalPi, Biovista, IBM Watson	Pfizer	amazon	XtalPi
Exscientia, BERG, RECURSION	SANOFI	Baidu 百度	Atomwise
AiCure, Numerate, NuMedii	Boehringer Ingelheim	Google	XtalPi
Biovista, INSILICO MEDICINE	NOVARTIS	IBM	IBM Watson
Atomwise, CYCLICA	BAYER	NVIDIA	INSILICO MEDICINE
AiCure, GNS HEALTHCARE	Roche	Canon	
BenevolentAI	Johnson&Johnson		
INSILICO MEDICINE	WuXi AppTec	HUAWEI	
BERG	AstraZeneca	intel	

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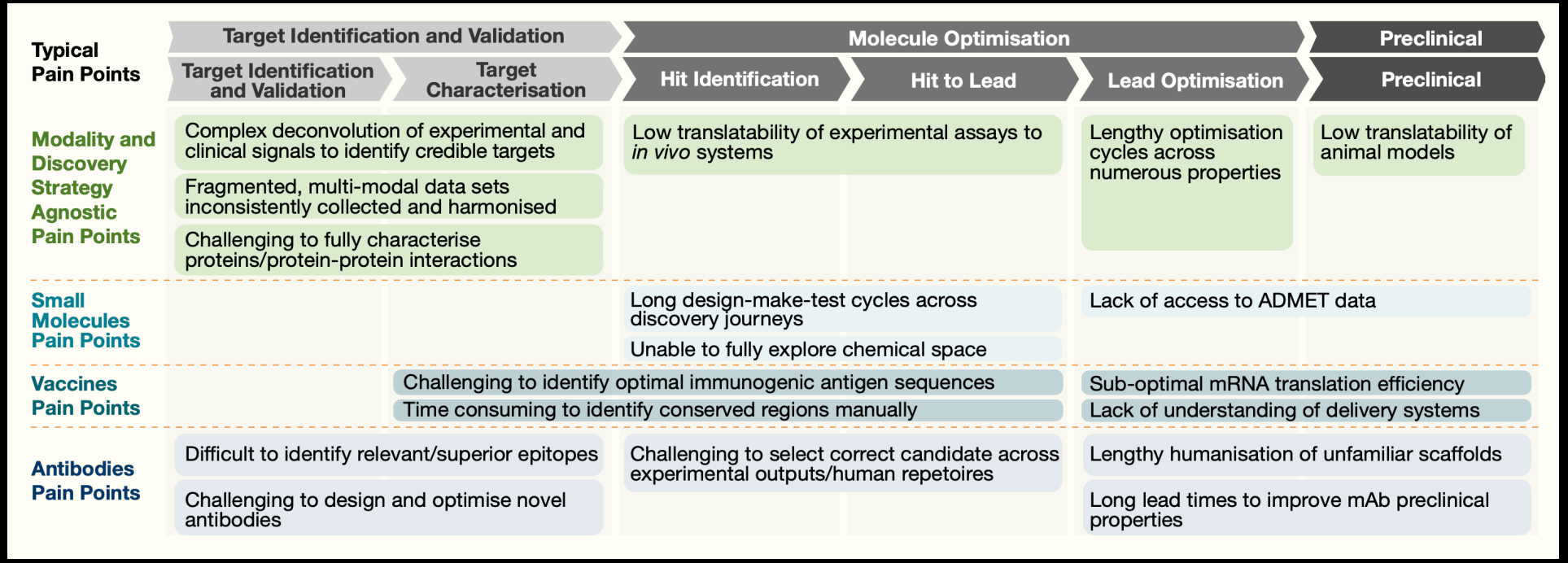
Unlocking the potential of AI in Drug Discovery

Current status, barriers and future opportunities

Key Pain Points



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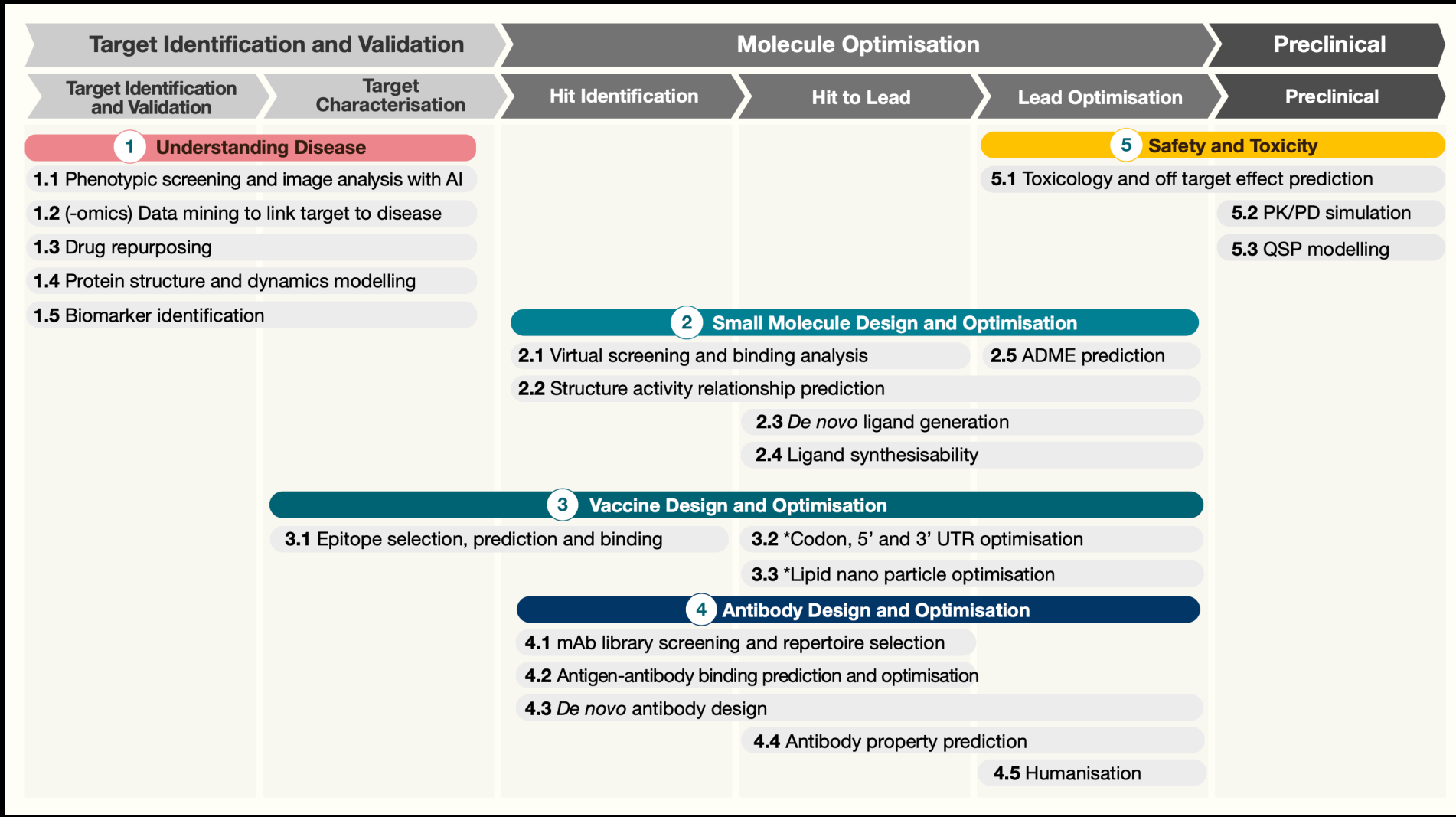
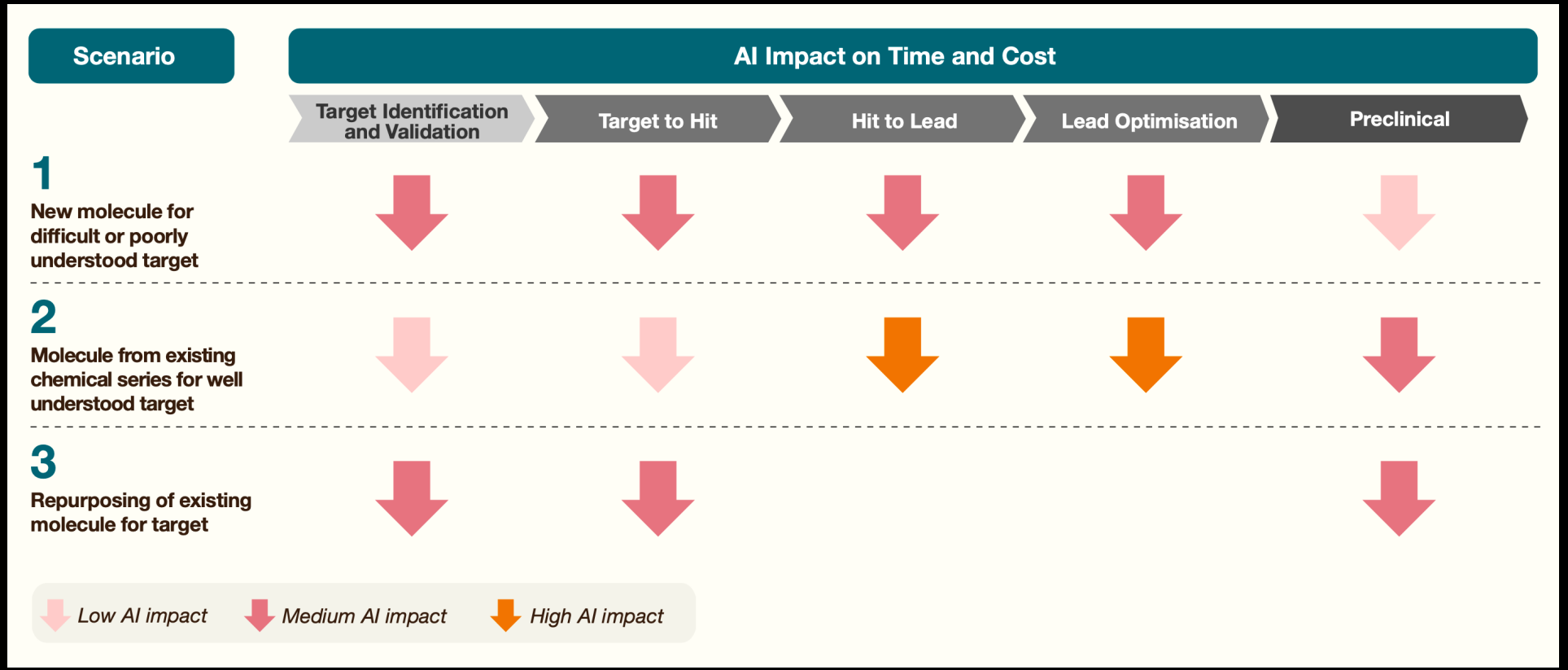

Target Identification and Validation
Molecule Optimisation
Preclinical
Target Identification and Validation
Target Characterisation
Hit Identification
Hit to Lead
Lead Optimisation
Preclinical
1 Understanding Disease
1.1 Phenotypic screening and image analysis with AI
1.2 (-omics) Data mining to link target to disease
1.3 Drug repurposing
1.4 Protein structure and dynamics modelling
1.5 Biomarker identification
5 Safety and Toxicity
5.1 Toxicology and off target effect prediction
5.2 PK/PD simulation
5.3 QSP modelling
2 Small Molecule Design and Optimisation
2.1 Virtual screening and binding analysis
2.5 ADME prediction
2.2 Structure activity relationship prediction
2.3 De novo ligand generation
2.4 Ligand synthesisability
3 Vaccine Design and Optimisation
3.1 Epitope selection, prediction and binding
3.2 *Codon, 5' and 3' UTR optimisation
3.3 *Lipid nano particle optimisation
4 Antibody Design and Optimisation
4.1 mAb library screening and repertoire selection
4.2 Antigen-antibody binding prediction and optimisation
4.3 De novo antibody design
4.4 Antibody property prediction
4.5 Humanisation

AI Impact on Time & Cost



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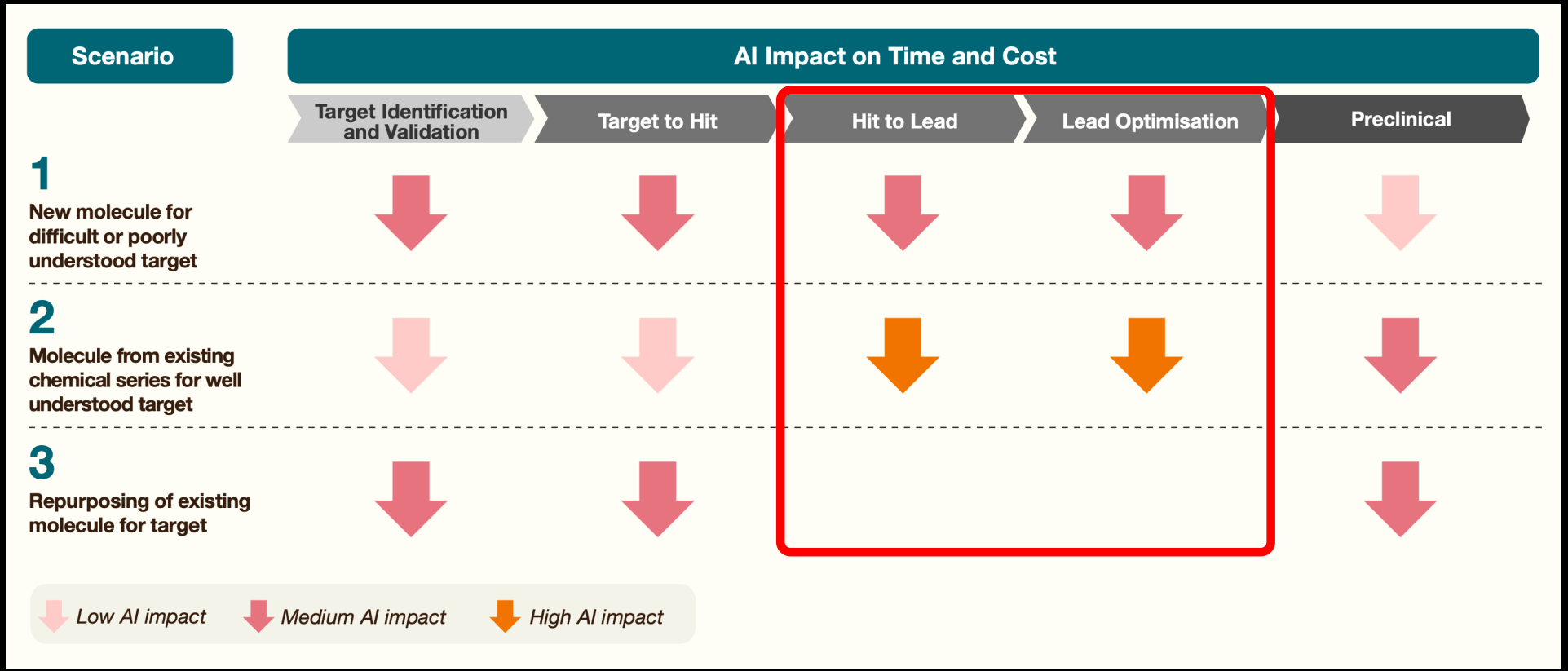

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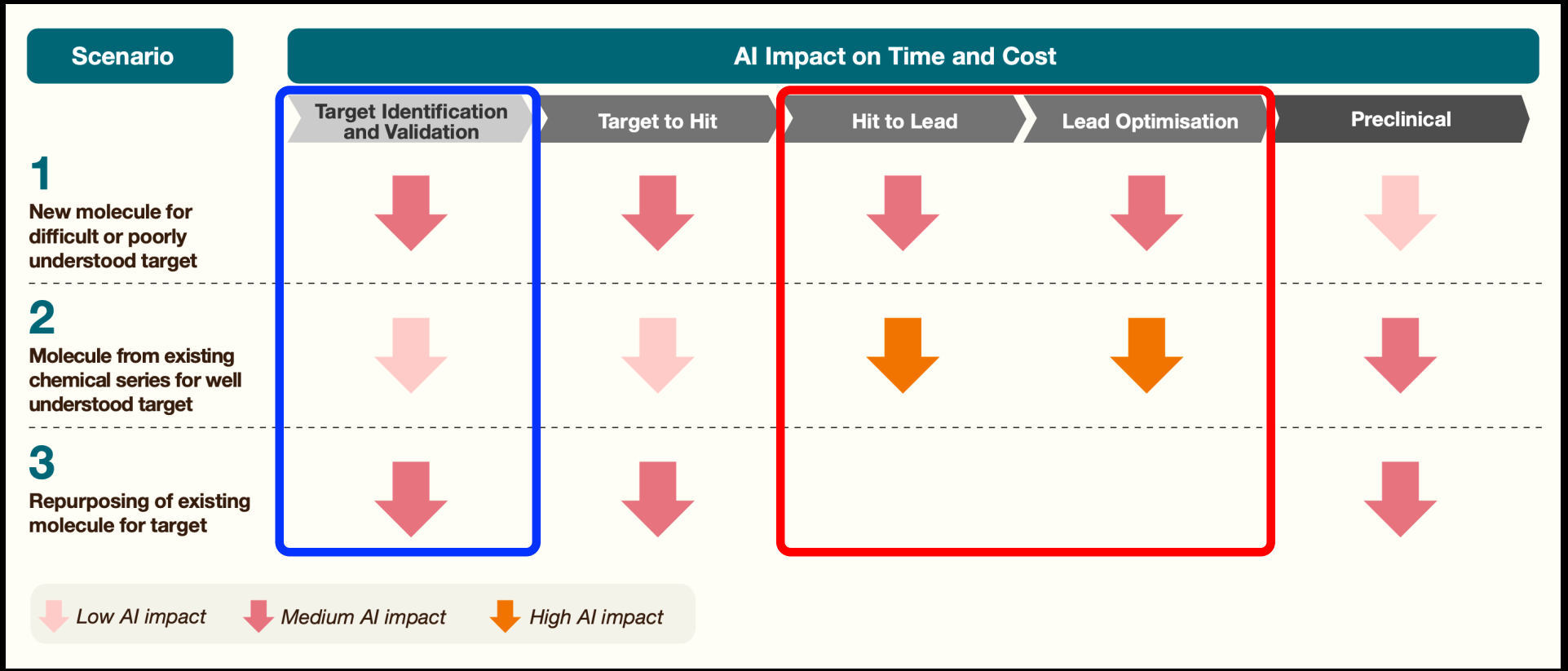

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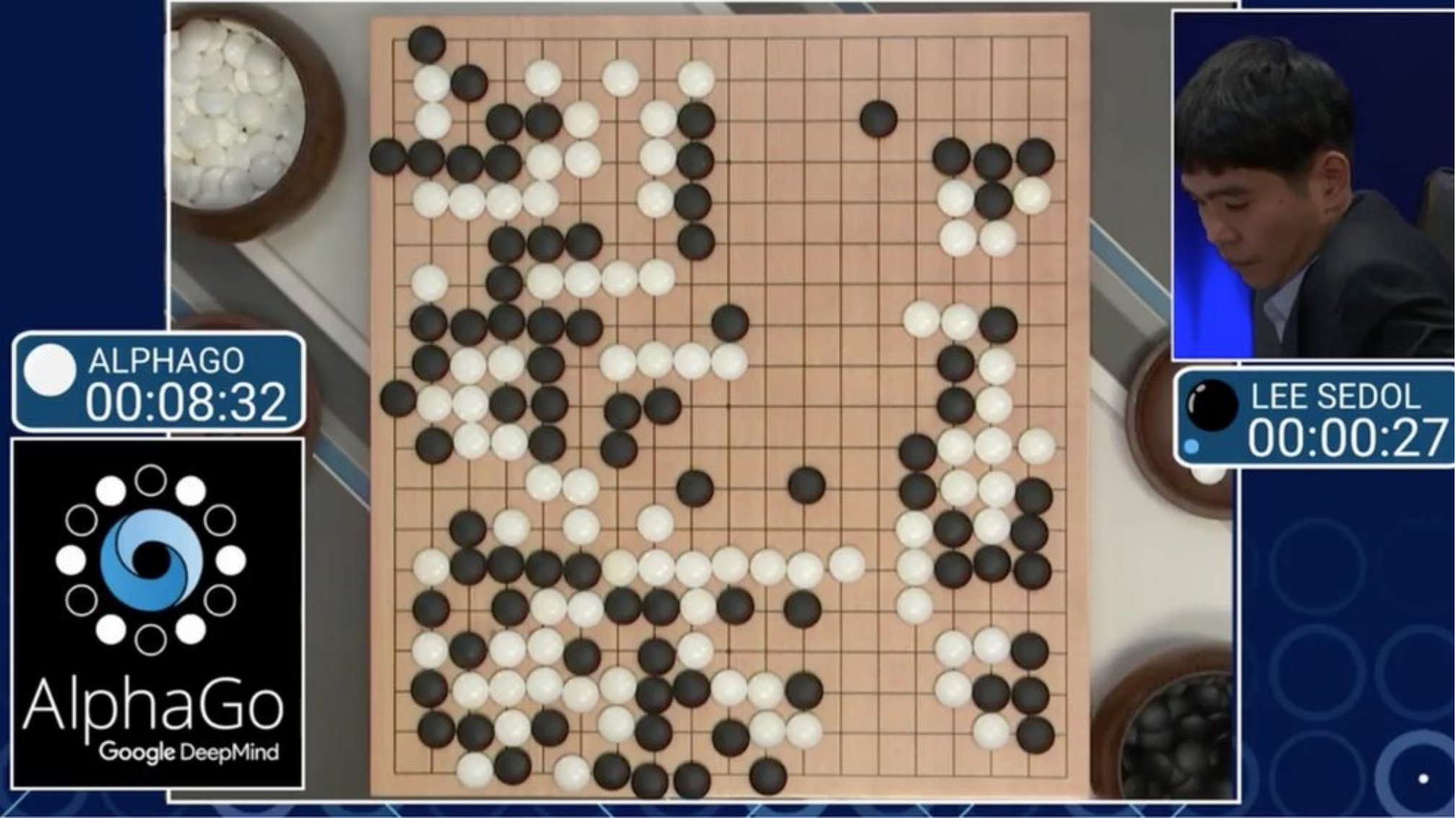
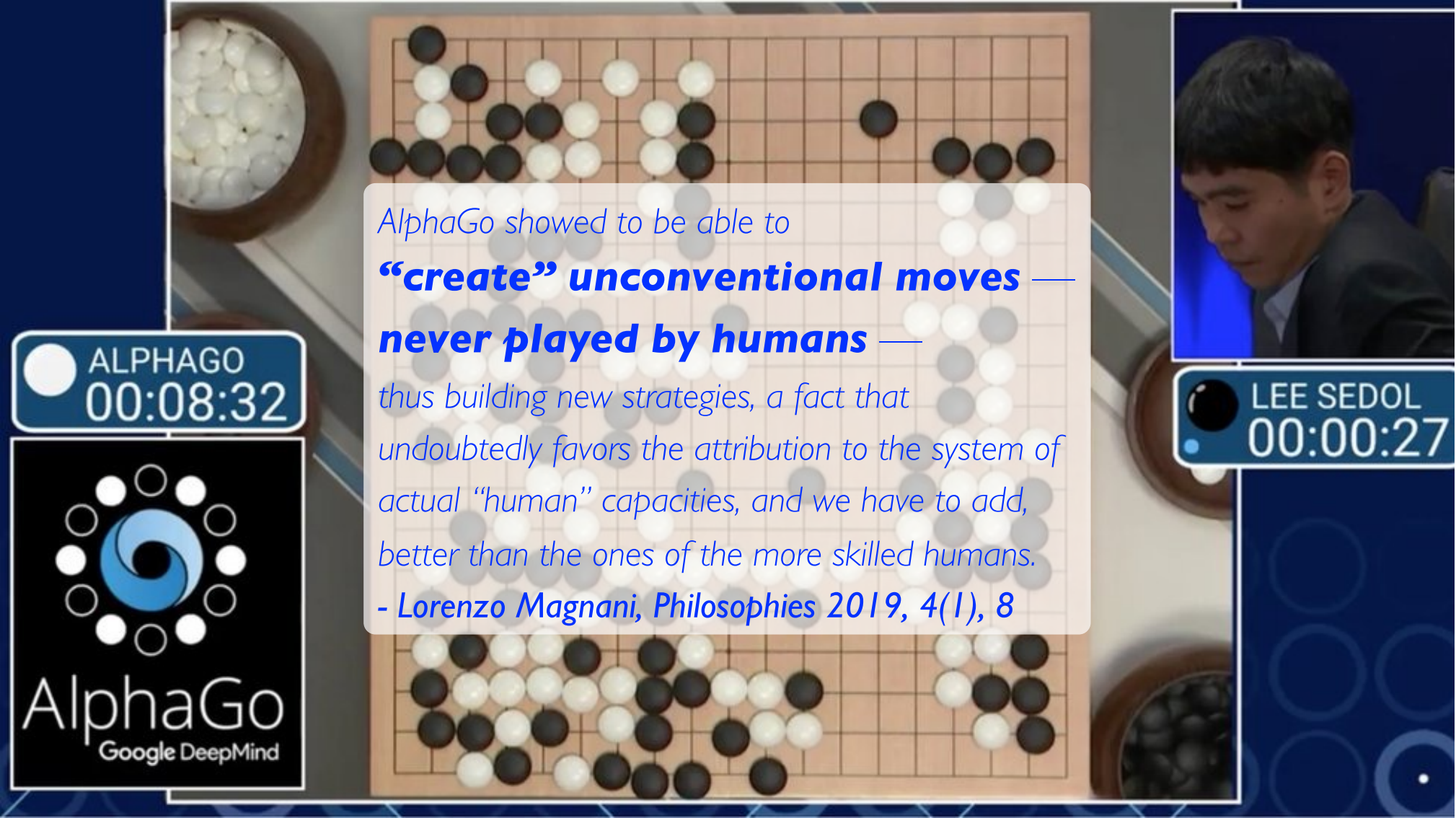
AI Impact on Unmet Medical Needs


ALPHAGO
00:08:32
AlphaGo
Google DeepMind
LEE SEDOL
00:00:27



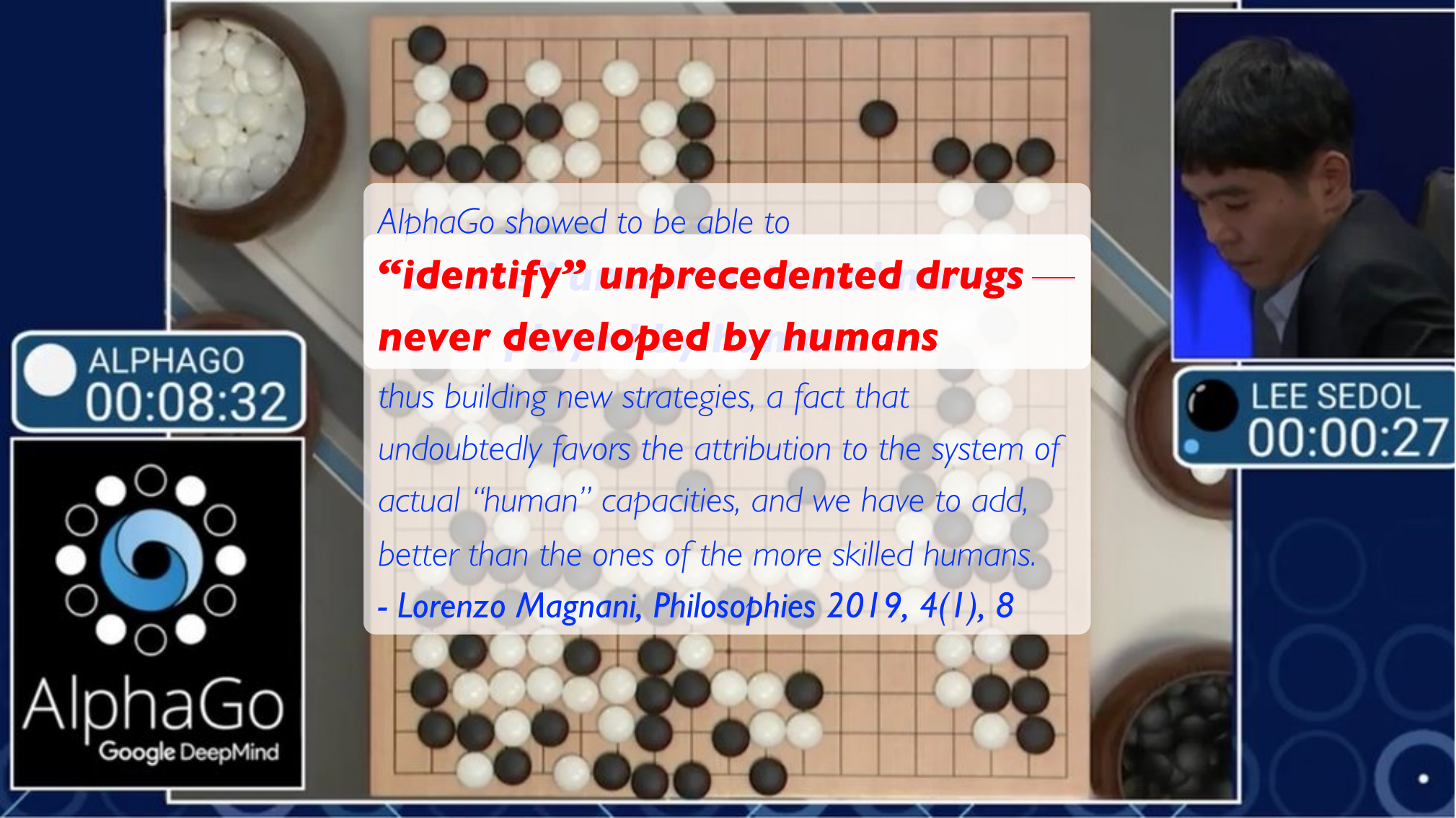
AlphaGo showed to be able to

"create" unconventional moves —

never played by humans —

thus building new strategies, a fact that undoubtedly favors the attribution to the system of actual "human" capacities, and we have to add, better than the ones of the more skilled humans.

- Lorenzo Magnani, Philosophies 2019, 4(1), 8



AlphaGo showed to be able to

"identify" unprecedented drugs — never developed by humans

thus building new strategies, a fact that undoubtedly favors the attribution to the system of actual "human" capacities, and we have to add, better than the ones of the more skilled humans.

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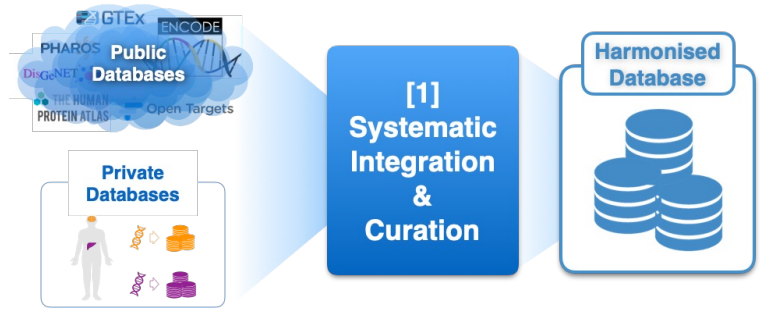
in silico Drug Discovery Pipeline



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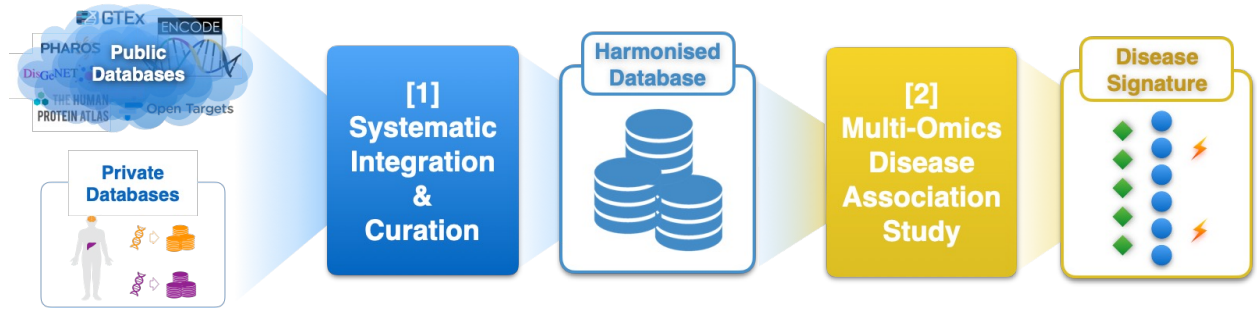

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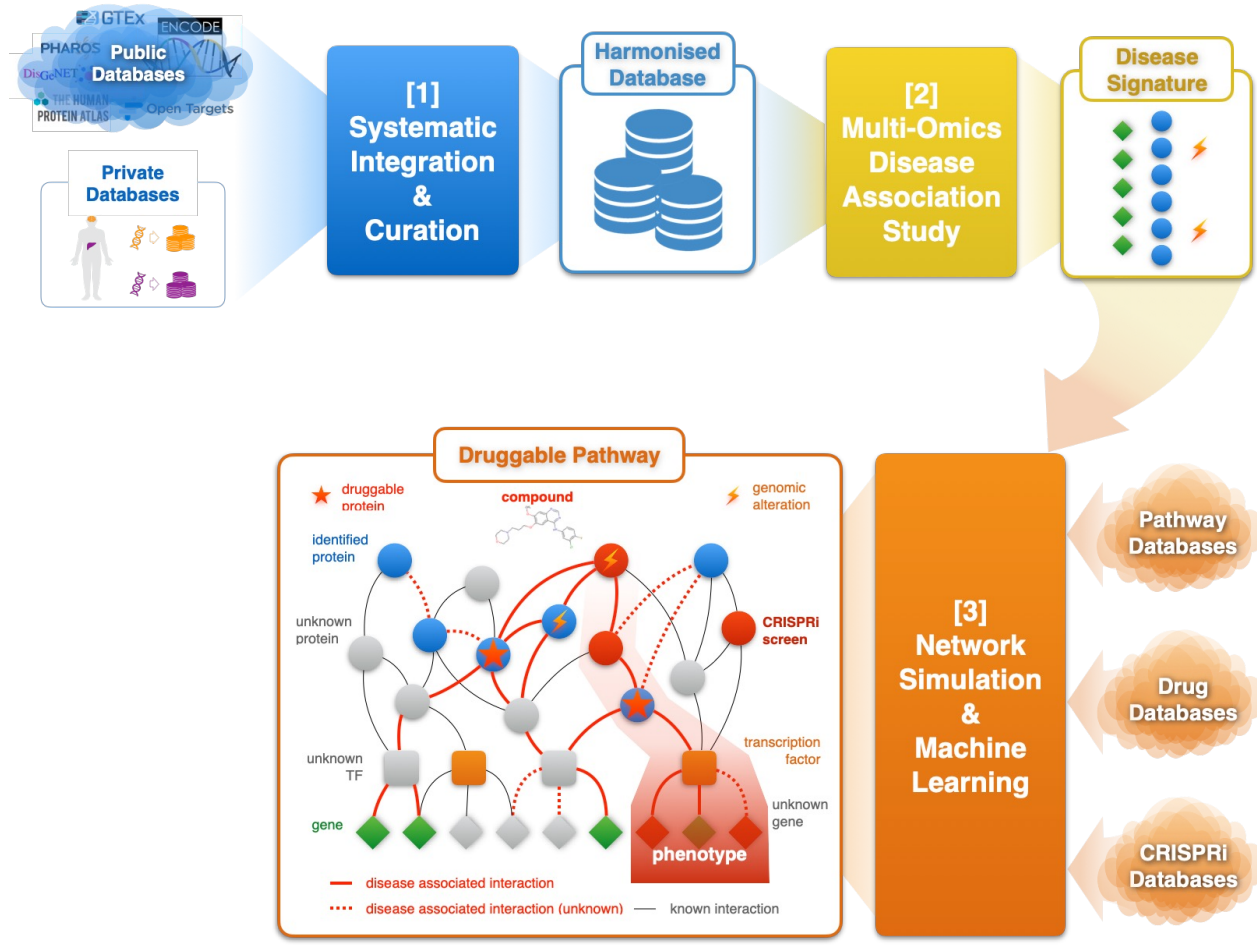
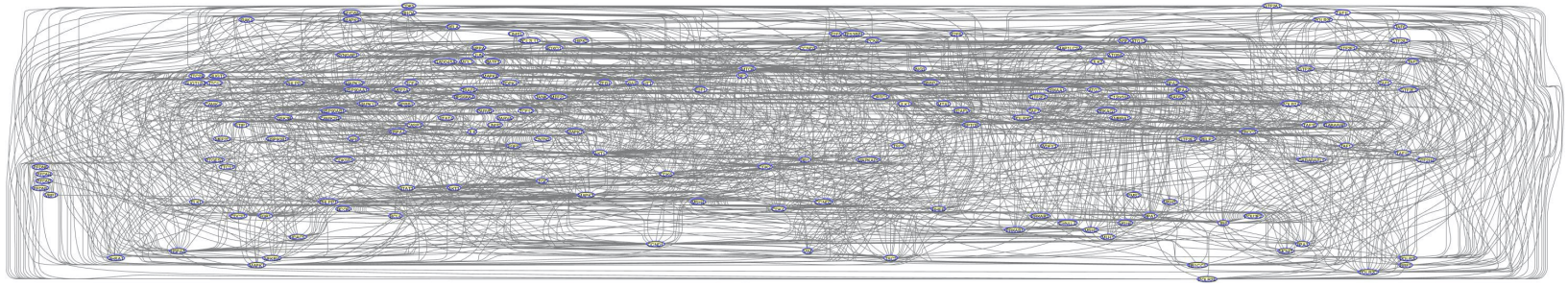


Network Analysis



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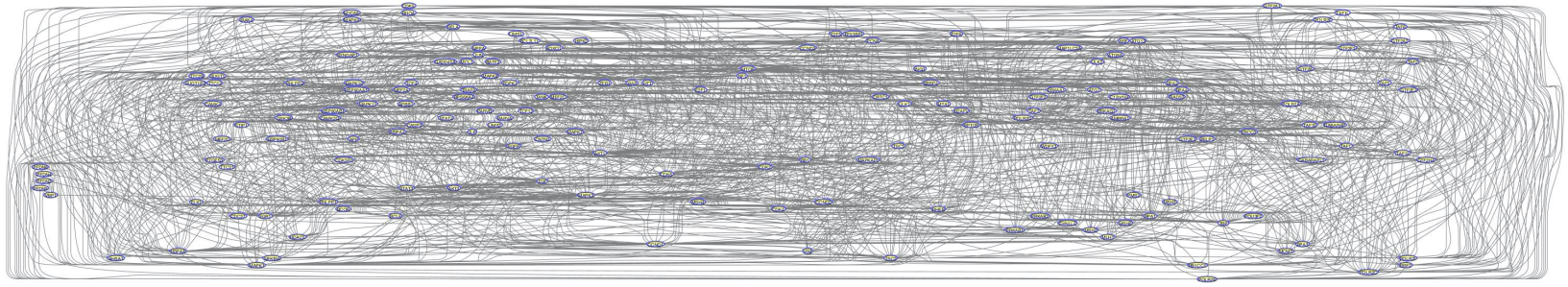

$$\vec{r}_i = c\tilde{W}\vec{r}_i + (1-c)\vec{e}_i$$

Ranking vector — Adjacent matrix — starting vector

$$\begin{pmatrix}0.13\\0.10\\0.13\\0.22\\0.13\\0.05\\0.05\\0.08\\0.04\\0.03\\0.04\\0.02\end{pmatrix} = 0.9\times \begin{pmatrix}0 & 1/3 & 1/3 & 1/3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\ 1/3 & 0 & 1/3 & 0 & 0 & 0 & 0 & 1/4 & 0 & 0 & 0 & 0\\ 1/3 & 1/3 & 0 & 1/3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\ 1/3 & 0 & 1/3 & 0 & 1/4 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 1/3 & 0 & 1/2 & 1/2 & 1/4 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 1/4 & 0 & 1/2 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 1/4 & 1/2 & 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 1/3 & 0 & 0 & 1/4 & 0 & 0 & 0 & 1/2 & 0 & 1/3 & 0\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1/4 & 0 & 1/3 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1/2 & 0 & 1/3 & 1/2\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1/4 & 0 & 1/3 & 0 & 1/2\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1/3 & 1/3 & 0\end{pmatrix} \begin{pmatrix}0.13\\0.10\\0.13\\0.22\\0.13\\0.05\\0.05\\0.08\\0.04\\0.03\\0.04\\0.02\end{pmatrix} + 0.1\times \begin{pmatrix}0\\0\\0\\1\\0\\0\\0\\0\\0\\0\\0\\0\end{pmatrix}$$

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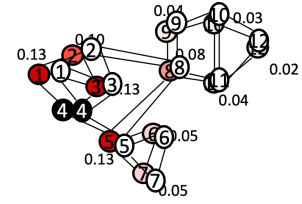

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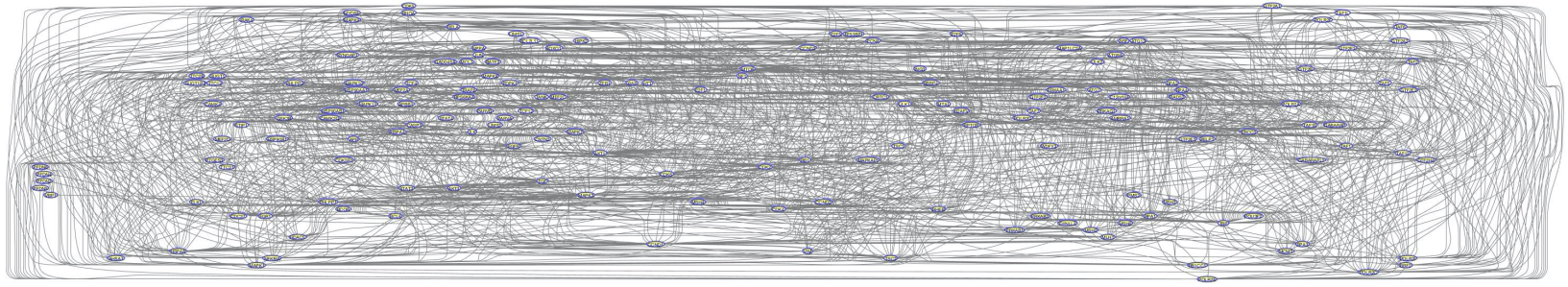

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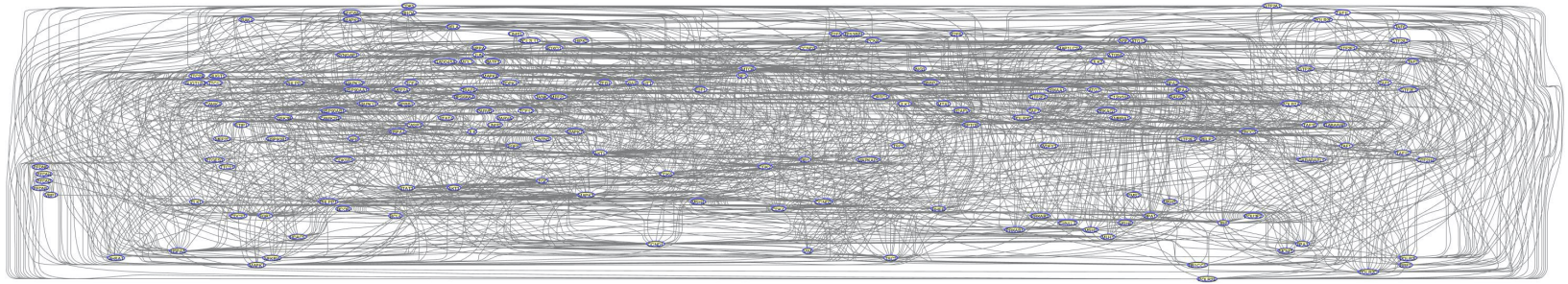
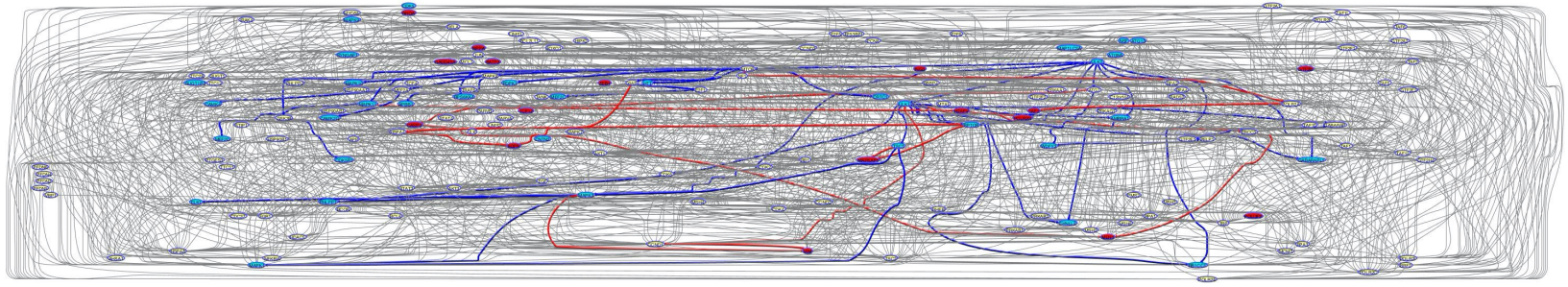
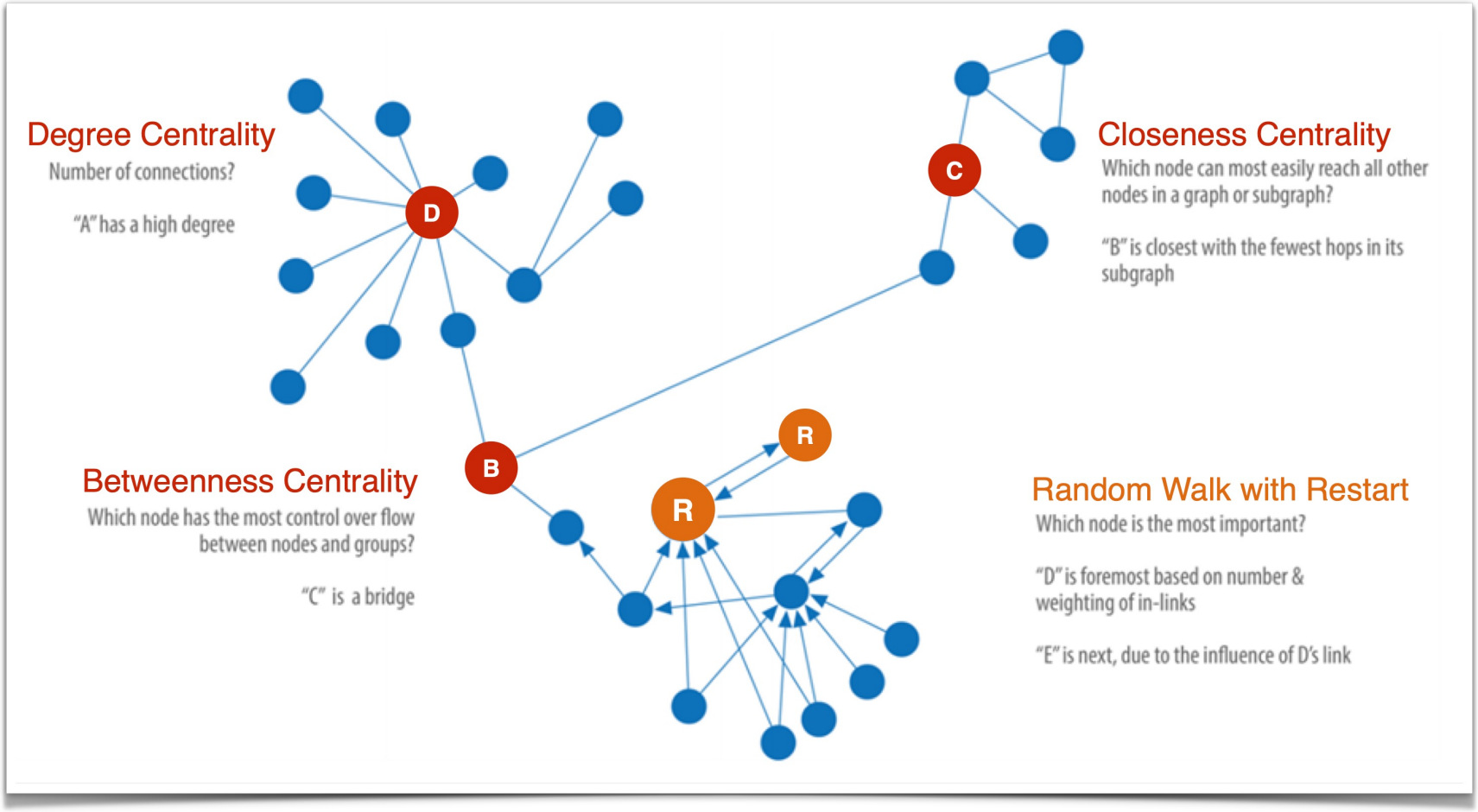




Network Algorithms



Mark Needham & Amy Hodler (2019)

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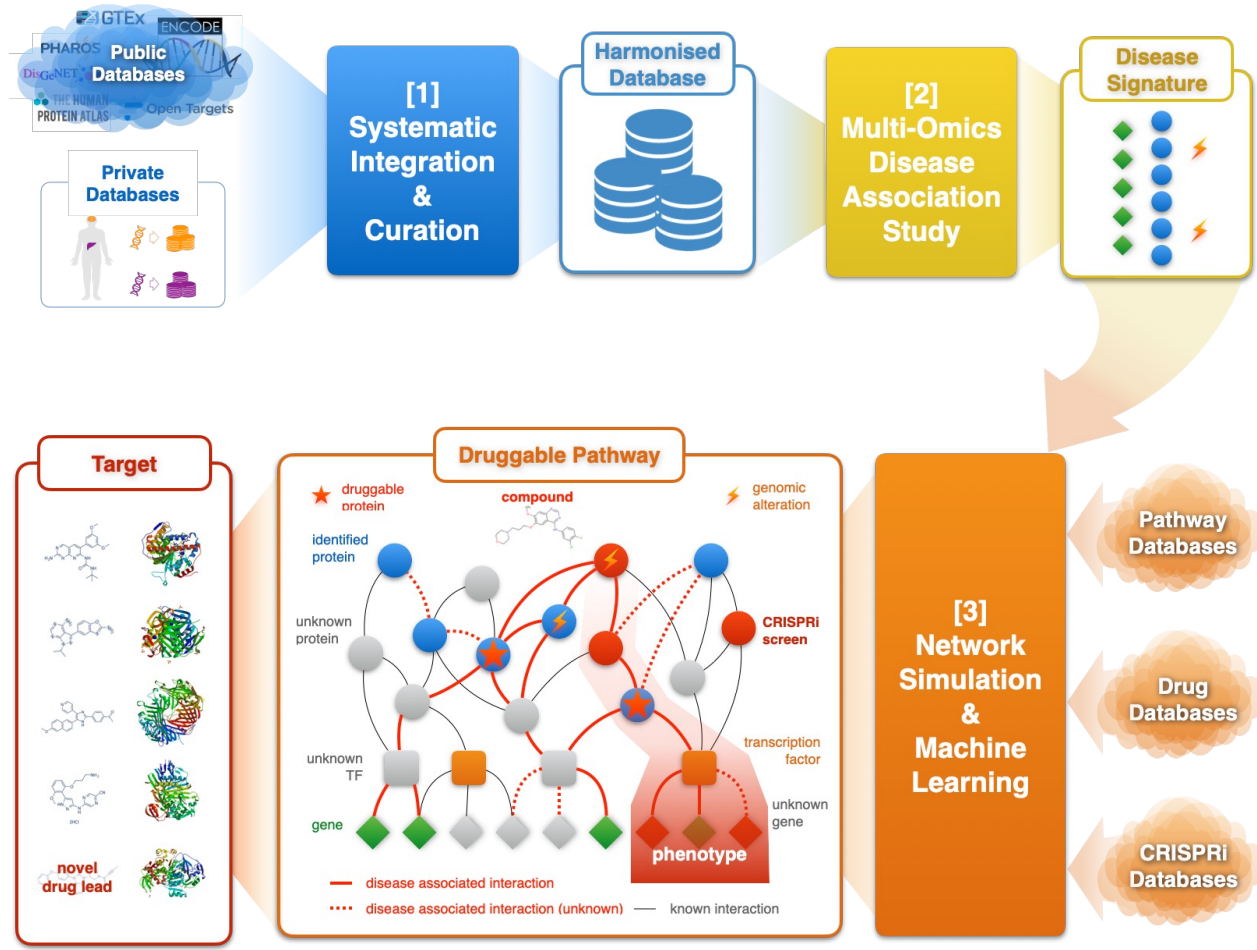

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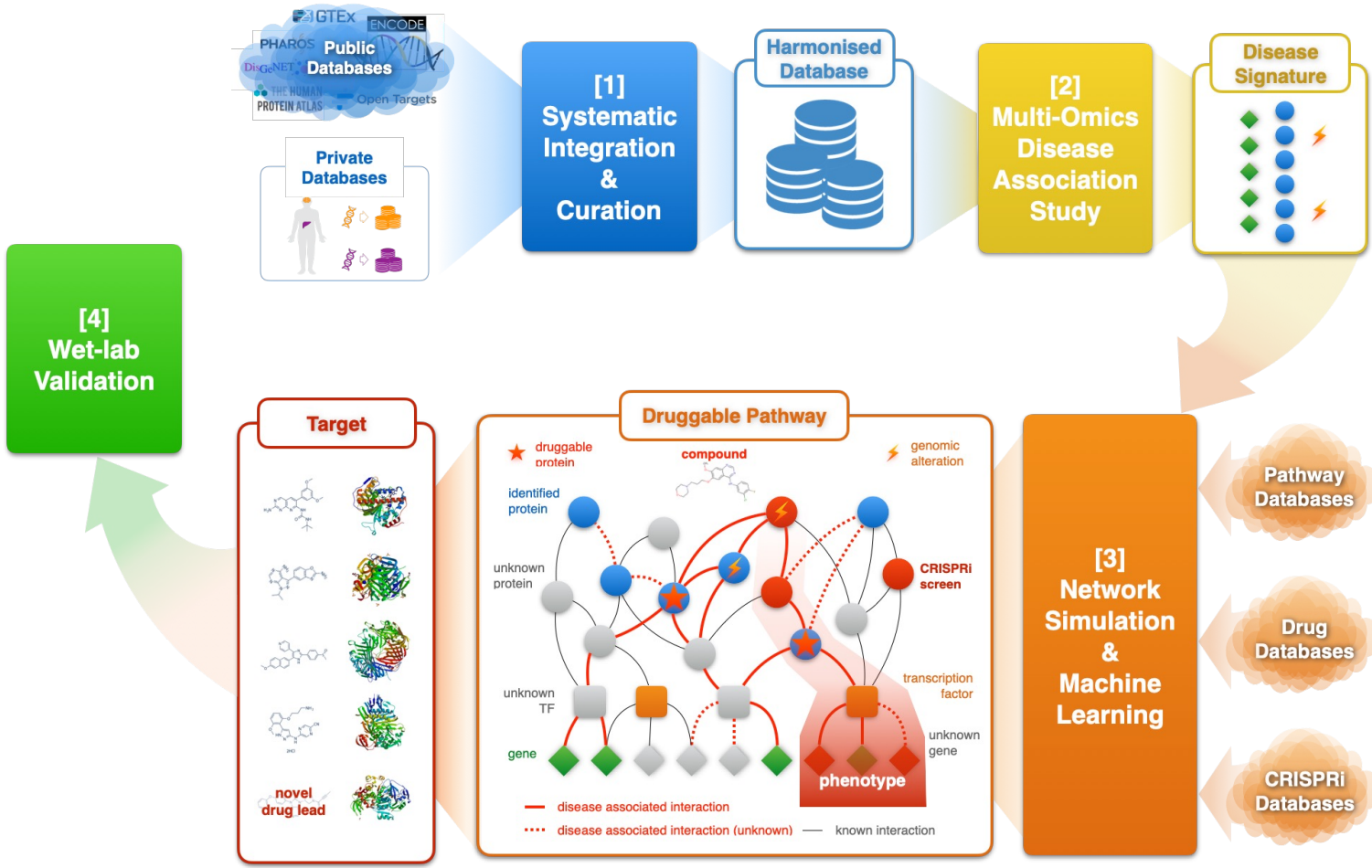

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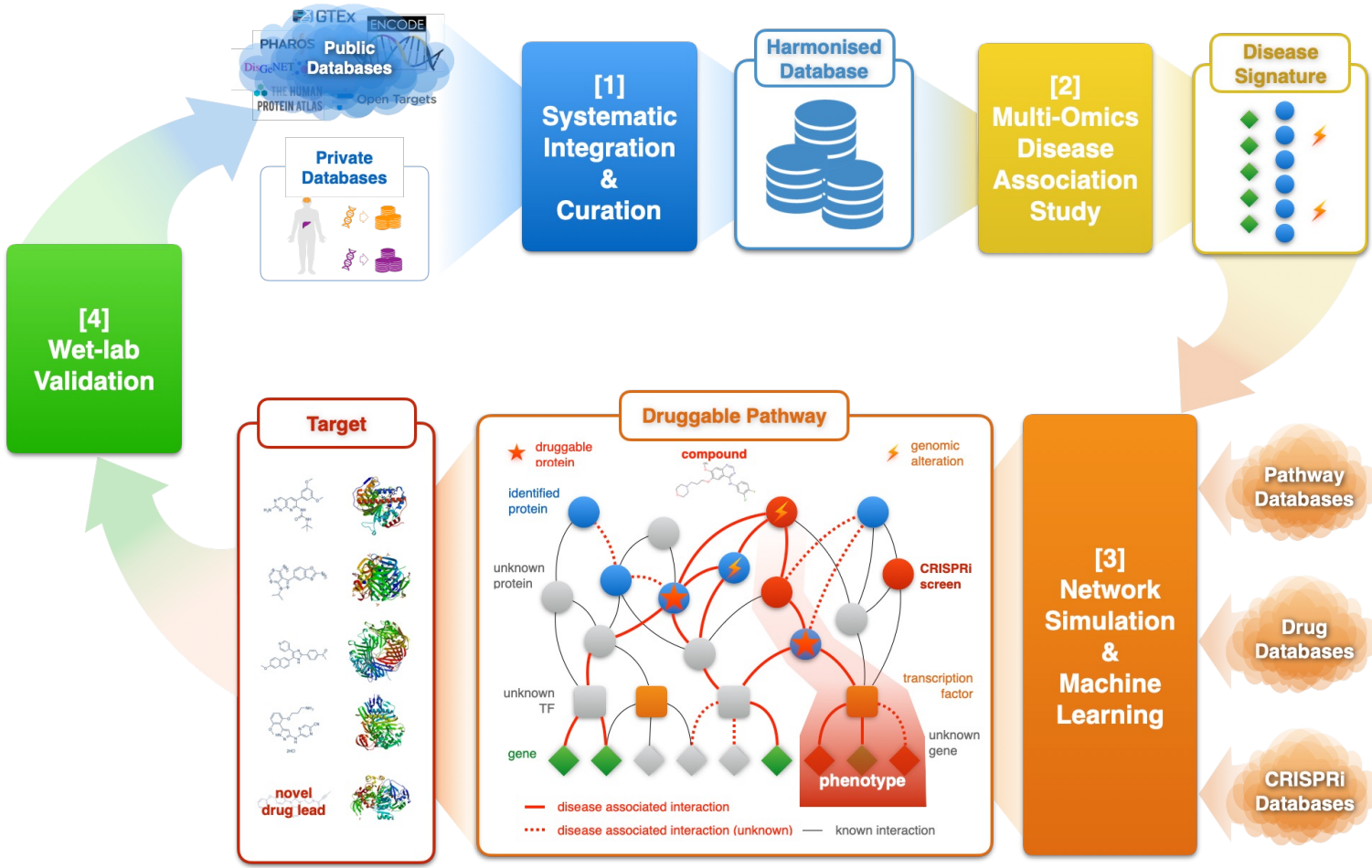

Lab Members, Collaborators & Funders

University of Cambridge School of Clinical Medicine
NHS Cambridge University Hospitals
Frank McCaughan & Nick Morrell
Kourosh Saeb-Parsv
Sarah Welsh & Grant Stewart
Nazima Pathan

Alzheimer's Research UK – The Power to Defeat Dementia
University of Cambridge
DRUG DISCOVERY INSTITUTE
John Skidmore & William Kuan

University of Cambridge Chemical Engineering and Biotechnology
David Fairen-Jimenez

IMS Institute of Metabolic Science Metabolic Research Laboratories
Toni Vidal-Puig

wellcome-MRC cambridge stem cell institute
Bertie Göttgens
Dan Hodson
Matthias Zilbauer

Early Cancer Institute
Harveer Dev

University of Cambridge Department of Engineering
Yan Yan Shery Huang

Open Targets
Ellen McDonagh
David Ochoa

wellcome sanger institute
Tom Mitchell

University of Portsmouth
Dariusz Gorecki, Murphy Wan

University of Bath
Milner Centre for Evolution
Laurence Hurst

University of Exeter
Soojin Ryu

CHARITÉ
Milad Rezvani

KAIST
Doheon Lee

Yonsei University College of Medicine
Jaeho Cheong

UCI University of California, Irvine
Young Jik Kwon

Mayo Clinic
Tae Hyun Hwang

Cleveland Clinic
David Wold

Memorial Sloan Kettering Cancer Center
Ioo-Hveon Lee

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David Powell & Andrew Leach

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Oliver Rausch & Hendrik Weisser

gsk GlaxoSmithKline
Valeriu Damian

Cancer Research UK
AstraZeneca
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Julie Little & Maria Groves

Standigm
Sojung Yun

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Thank you

Namshik Han

nh417@cam.ac.uk

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ai@cam