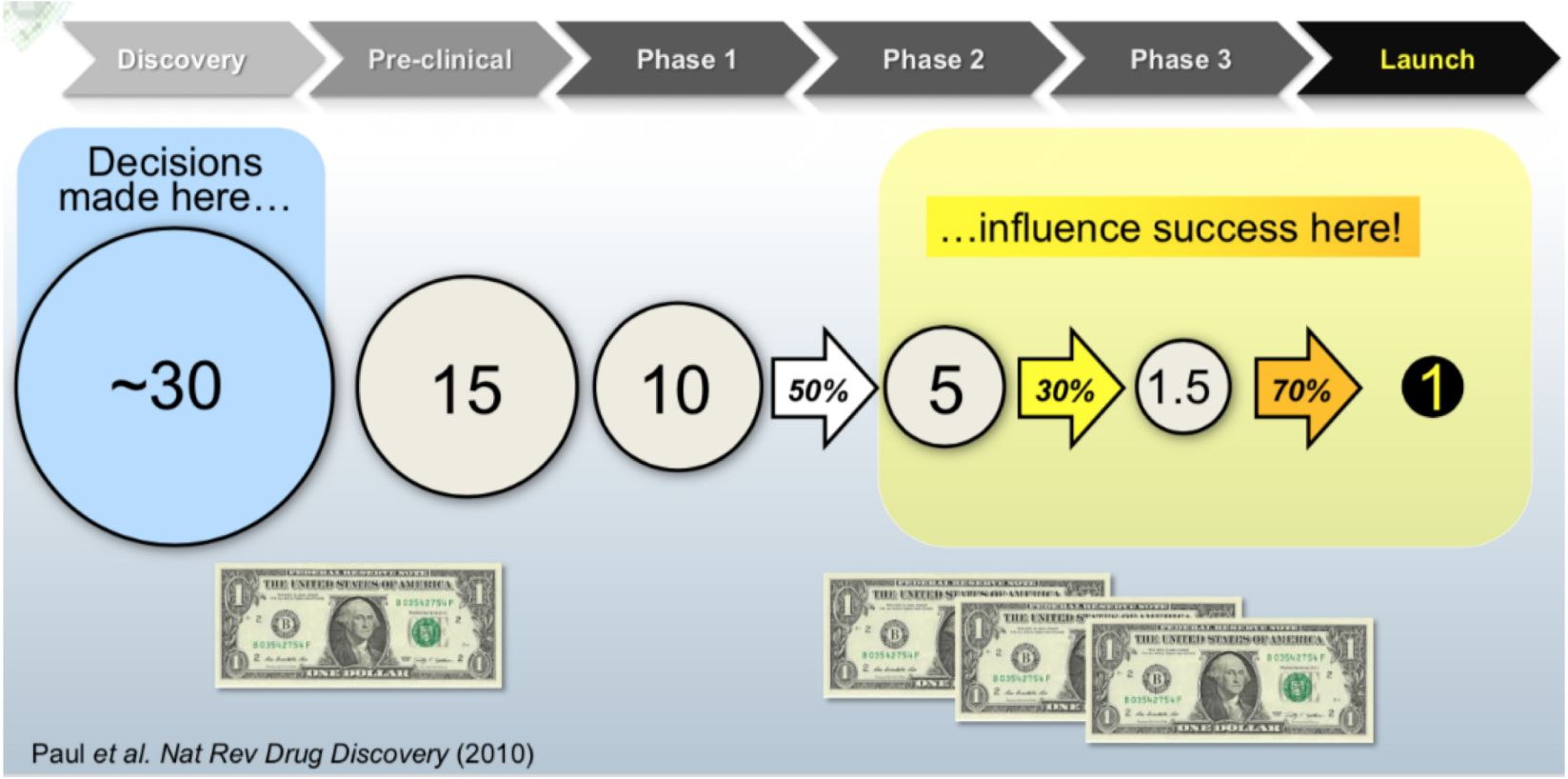
Open Targets: Identifying Drug Targets in a Pre-competitive Framework

Ian Dunham
Director, Open Targets
www.opentargets.org

Open Targets

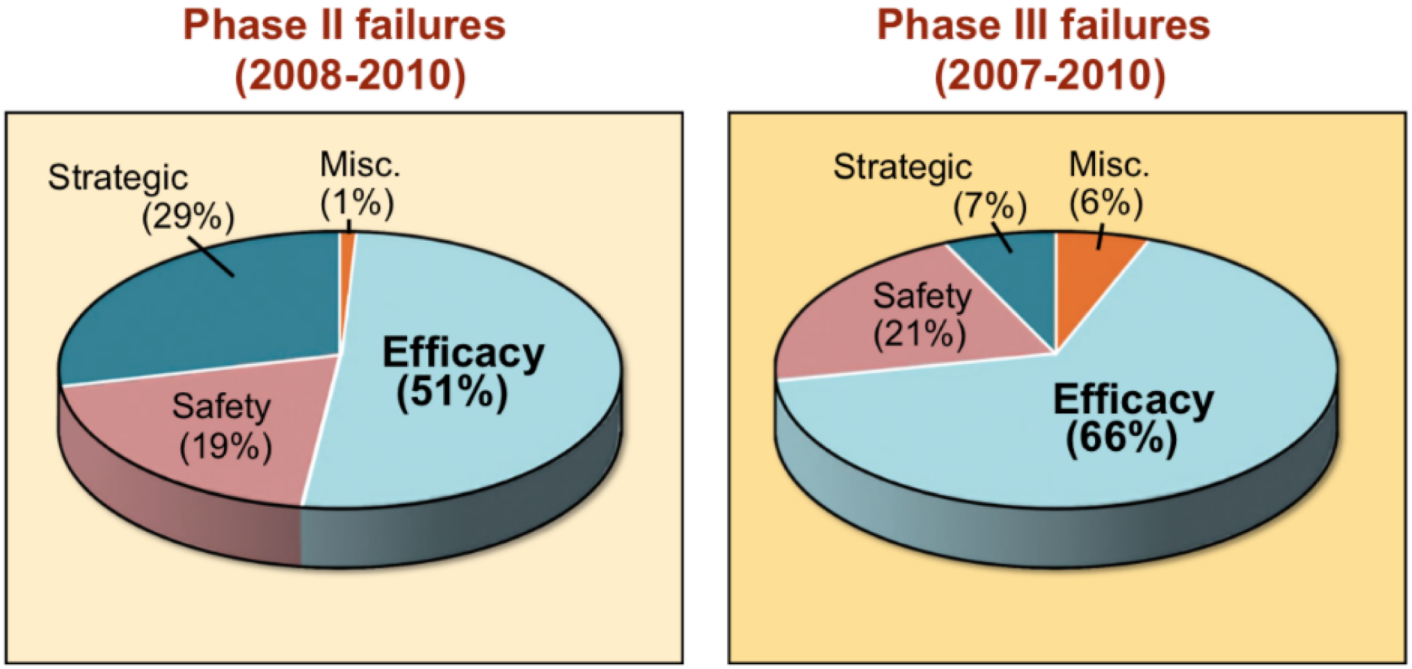
Drug Discovery has High Attrition and Long Lead Times



Credit: Robert Plenge, Celgene

Open Targets

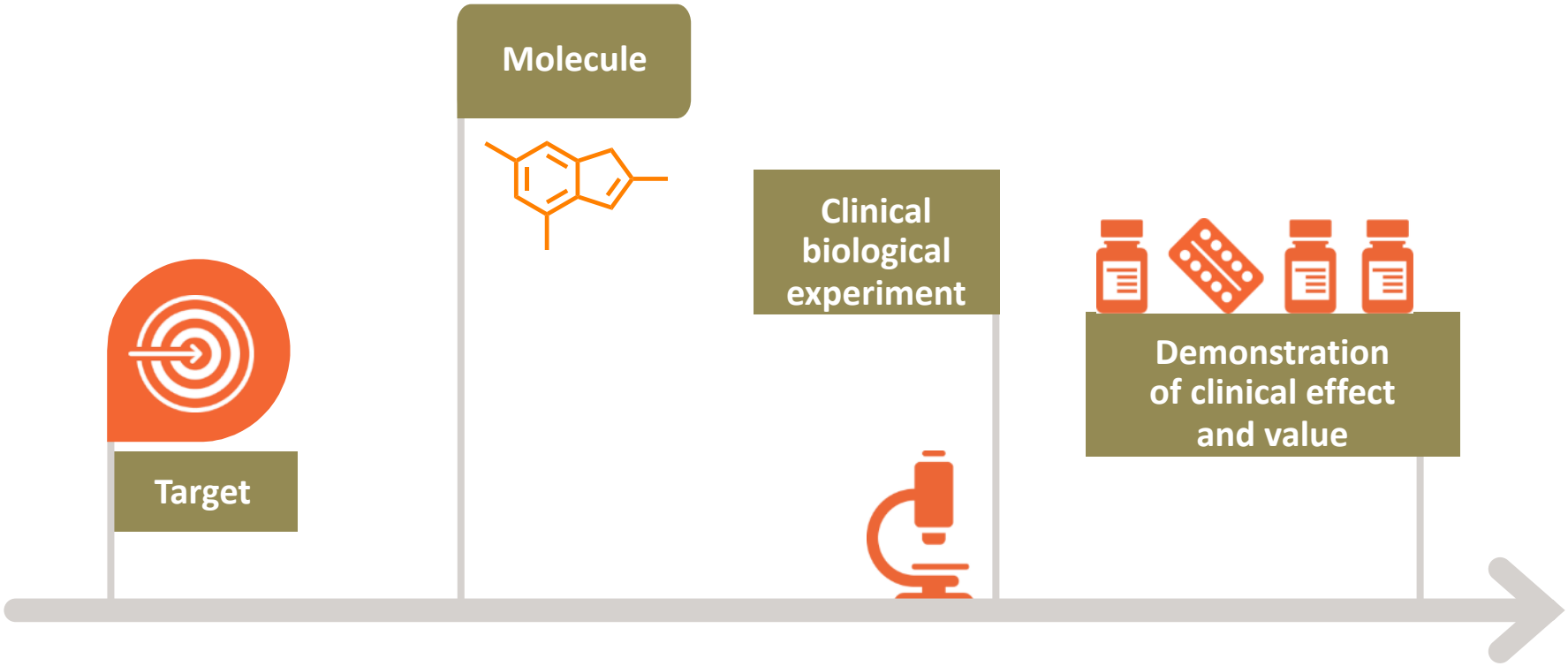
Most Clinical Trial Failures are due to Lack of Efficacy



Arrowsmith *Nature Reviews Drug Discovery* (2011)

Open Targets

Selecting the target is a key decision when making medicines

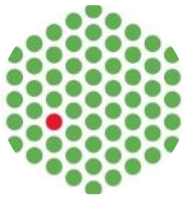


.....and it costs over $1bn and more than a decade to find out if you chose well.

Open Targets

Open Targets

Transforming drug discovery through the systematic identification and prioritisation of targets



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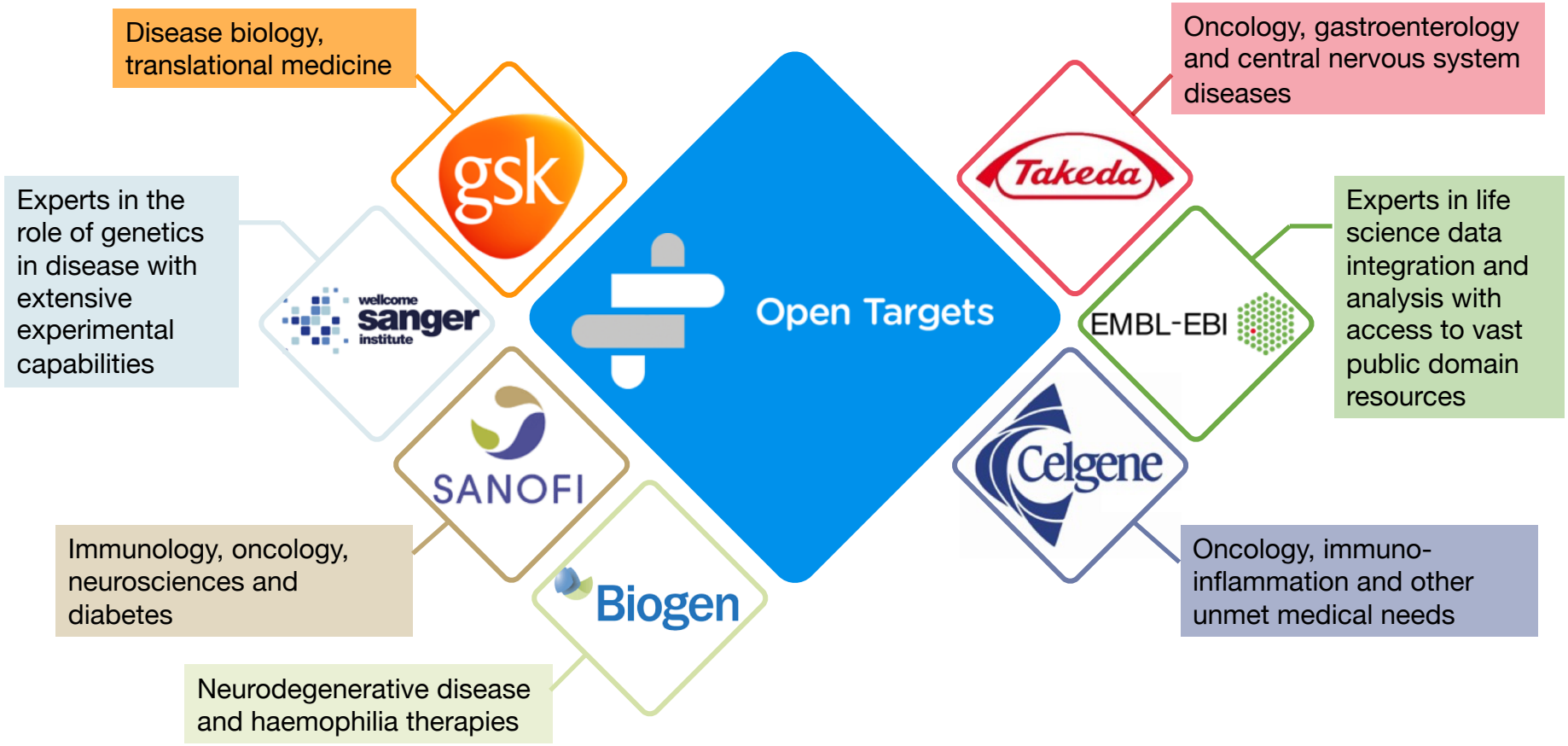
Pioneering Public Private Partnership

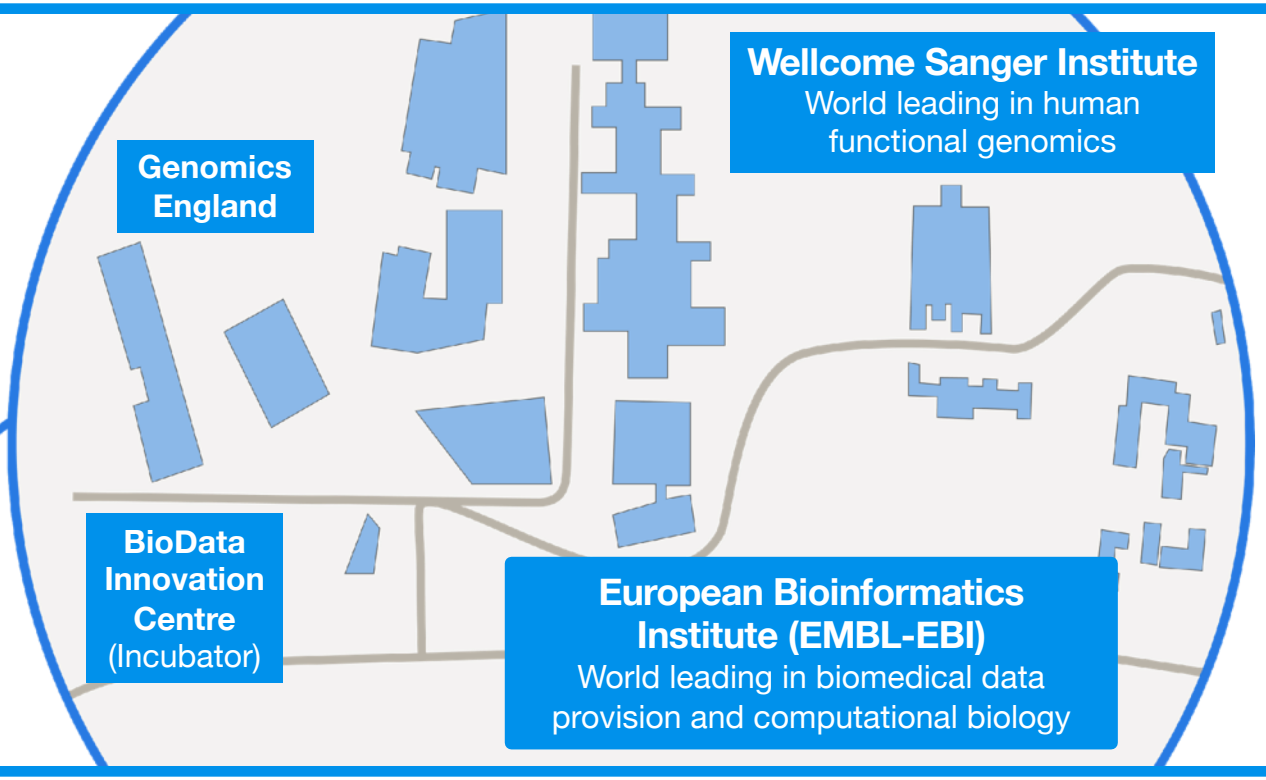


Open Targets

Unique location: Cambridge Cluster & Wellcome Genome Campus, UK

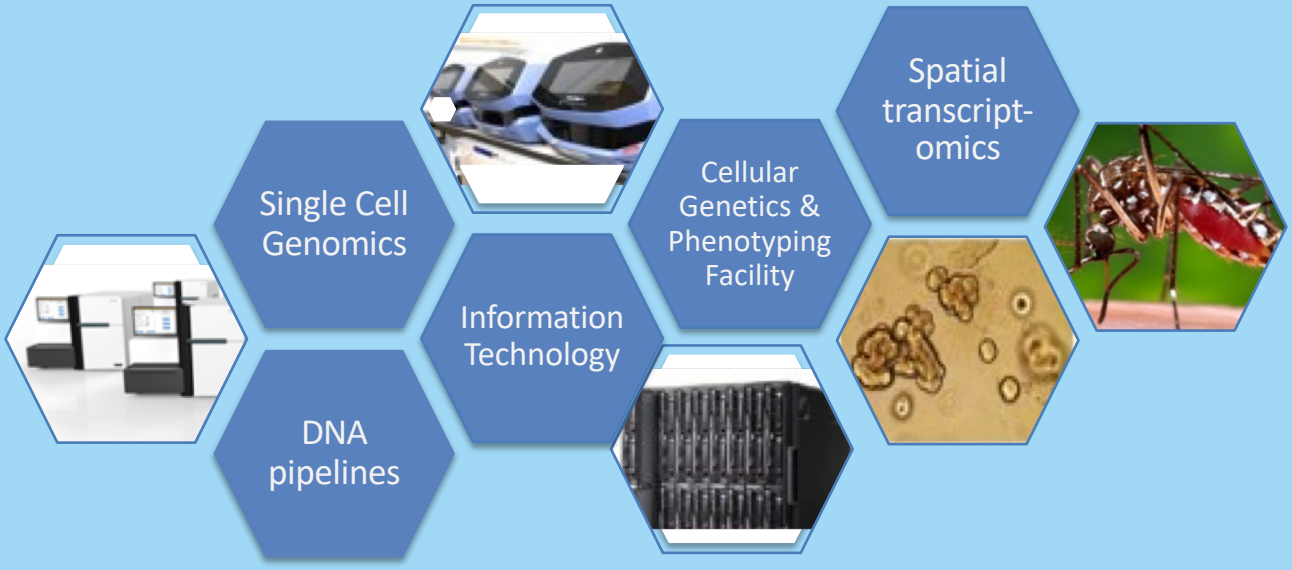
Europe's leading cluster in pharma and biotech

Cambridge, UK



Open Targets

The Wellcome Sanger Institute

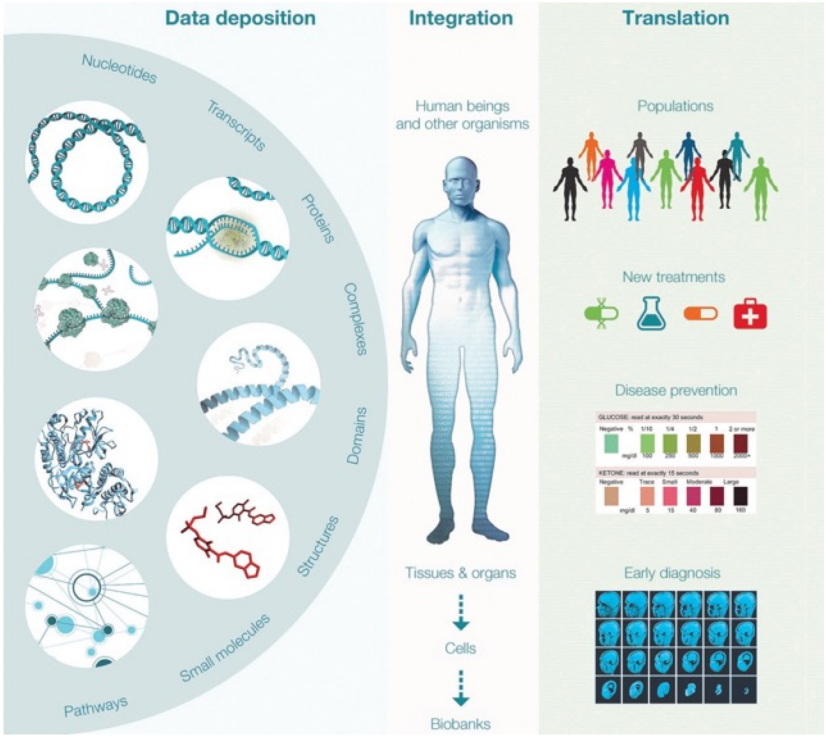


- Human Genetics
- Cancer, Ageing & Somatic Mutation
- Pathogens & Microbes
- Cellular Genetics
- Tree of Life

Open Targets

The European Bioinformatics Institute

EMBL-EBI



Credit: Spencer Phillips, EMBL-EBI

The home for big data in biology

A trusted data provider for the life sciences

Contributes to the advancement of biology through investigator-driven research

Part of the European Molecular Biology Laboratory, an intergovernmental research organisation

International: 650 members of staff from 66 nations

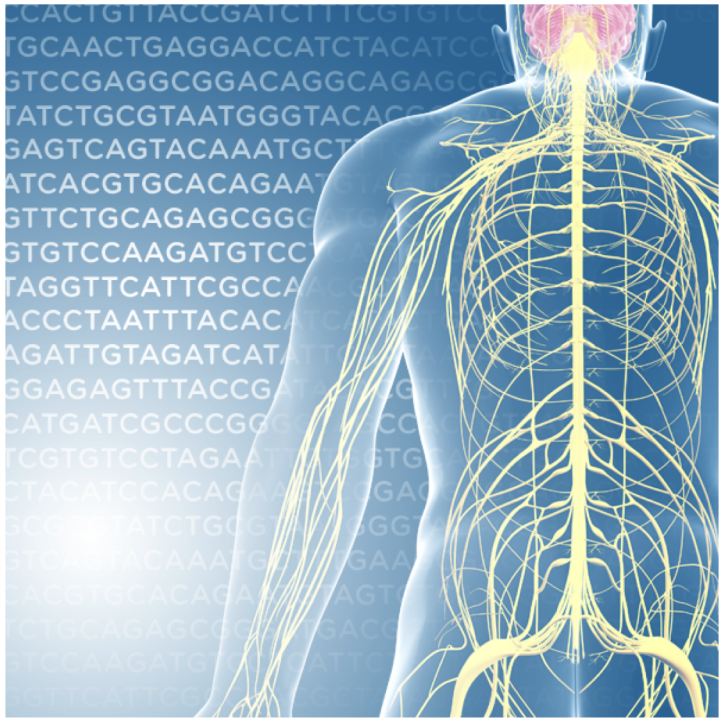
Open Targets

Open Targets Vision and Mission

Improve success rates and be the world-leading centre for human target identification and prioritisation

Identify, pinpoint, understand the processes in the human body that have a demonstrable effect on disease

Combine ground-breaking experimental and computational approaches

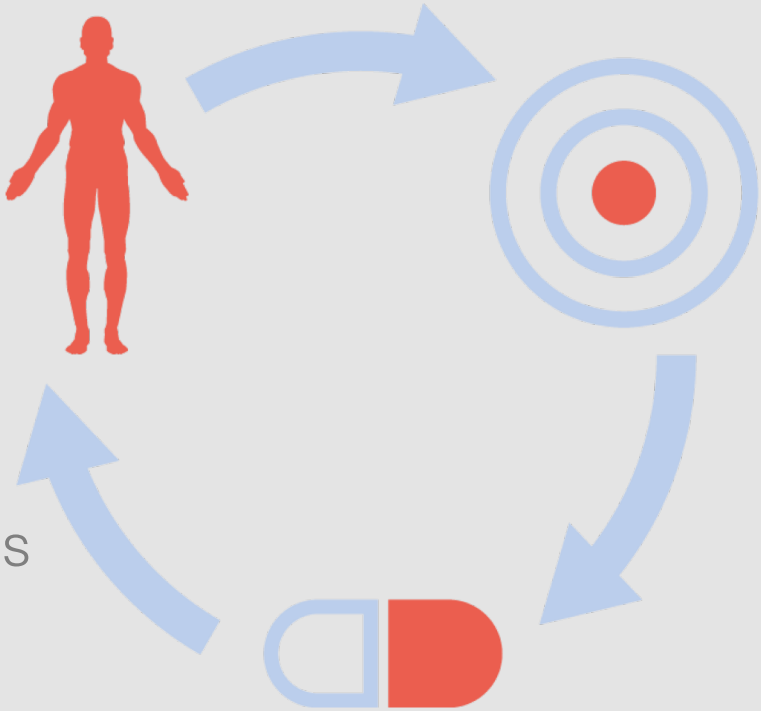


Credit: Spencer Phillips, EMBL-EBI

Open Targets

Open Targets Key Technologies

- WSI cell line collections
- Gene editing (CRISPR)
- iPS cell differentiation and
- phenotyping
- Single cell methods
- Organoid and tissue culture
- Large scale genomics and epigenomics
- Genome wide association studies
- Next-generation sequencing
- Bioinformatics
- High performance computing

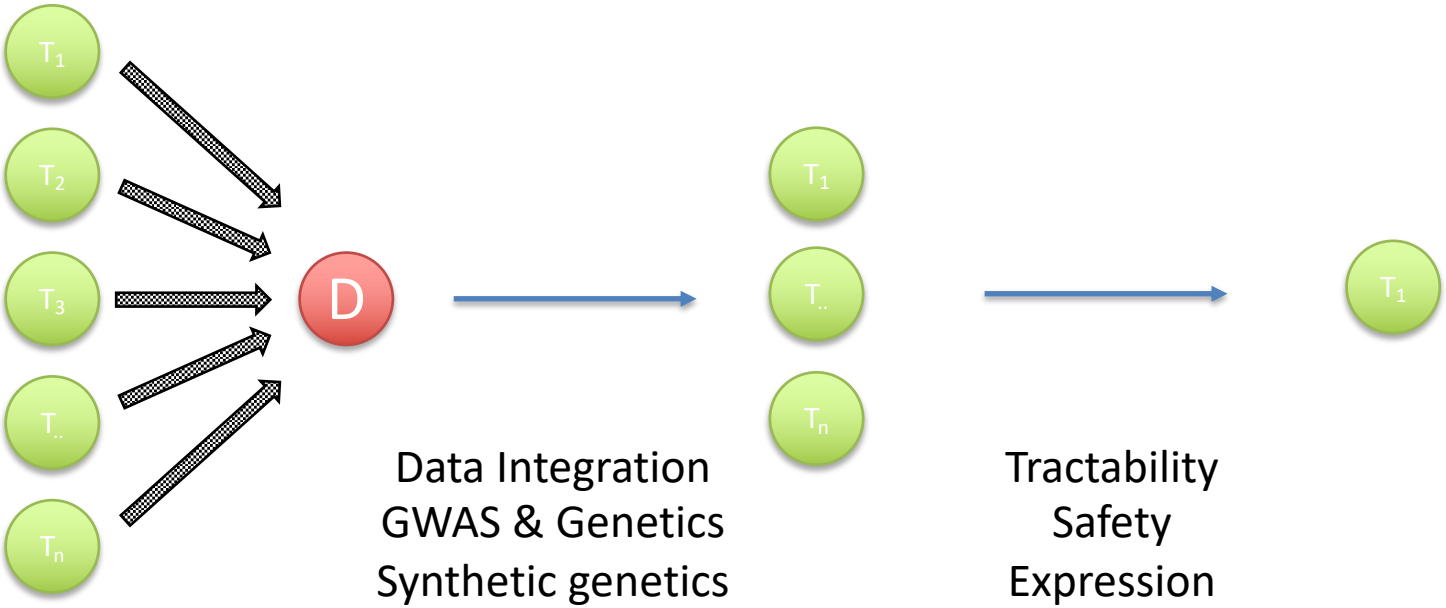


Open Targets

Systematic Identification and Prioritisation

Identification

Prioritisation



Data Integration
GWAS & Genetics
Synthetic genetics

Tractability
Safety
Expression
Biomarkers

Open Targets

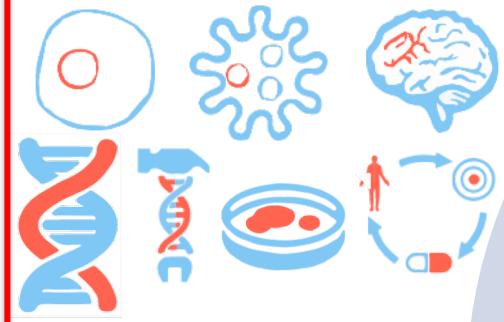
How We Build Projects: Smart Project Sourcing

Collect **Ideas**	Connect **Minds**	Commit **Projects**
Biogen, Celgene, gsk, EMBL, Takeda, SANOFI, wellcome sanger institute		50+
Calls for proposals **Expressions of interest**	**Workshops** **Proposals**	**Review and feedback** **Governance Board Approval**

Open Targets

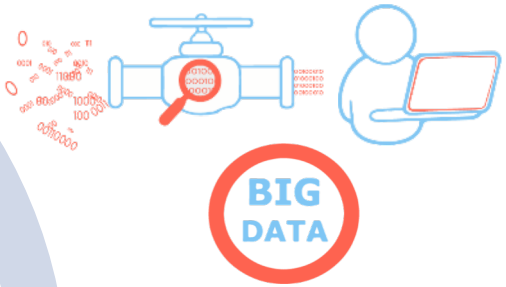
Efficacy Data through Cellular Models

Experimental projects



Public Data

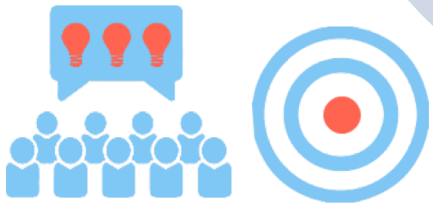
Bioinformatic projects



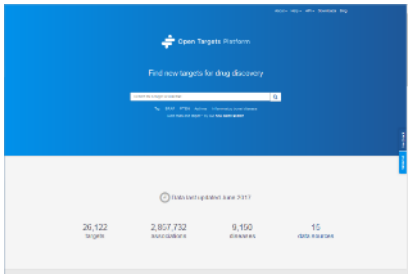
Data Generation

Data Integration

Therapeutic Hypothesis

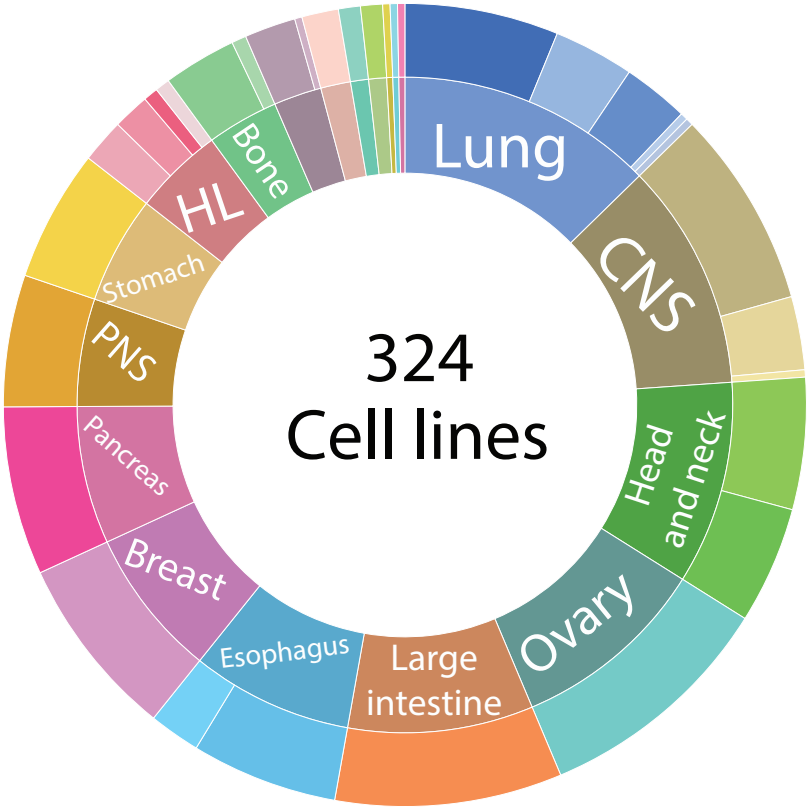


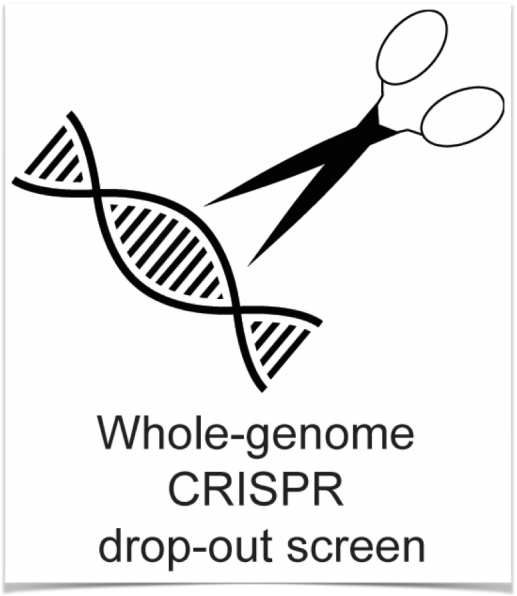
targetvalidation.org



Open Targets

project score

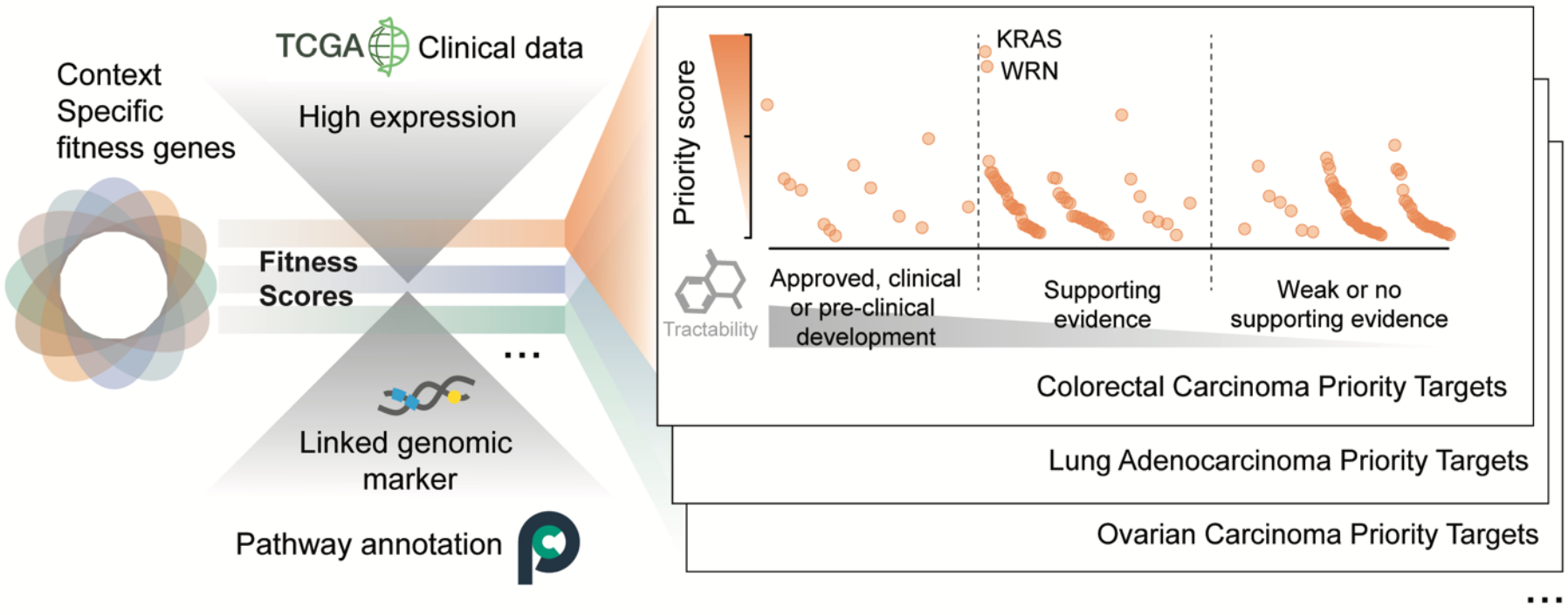




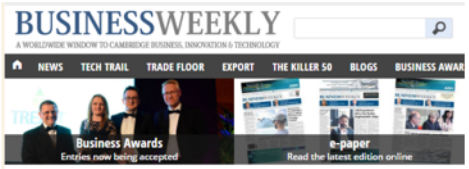
Behan et al *Nature* **568**, 511–516 (2019)

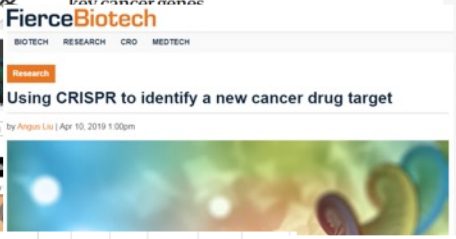
Open Targets

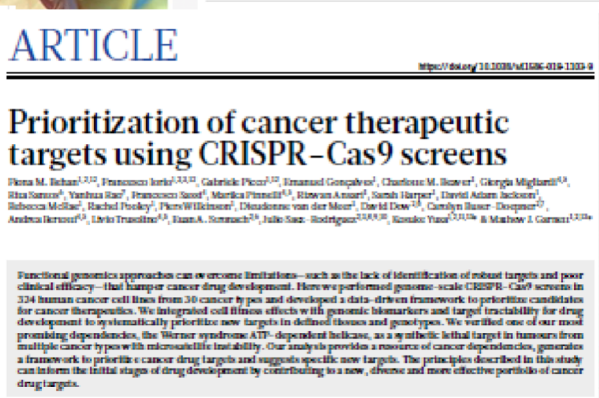
Target Prioritisation & Tractability Assessment

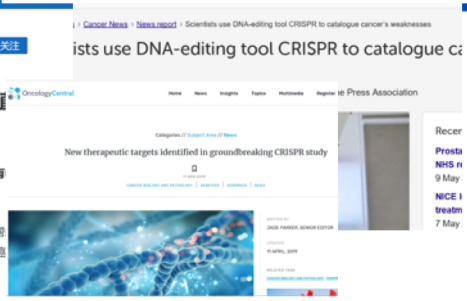


Open Targets

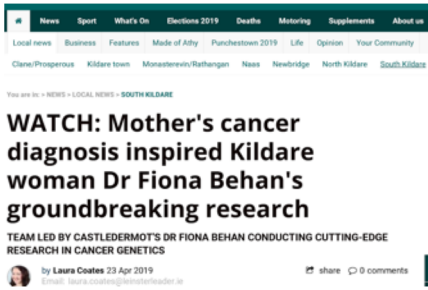








Sanger Institute - Making a difference: Fiona Behan, cancer researcher



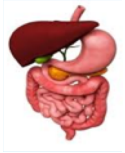
Open Targets

CRISPR Modulation to Identify Targets

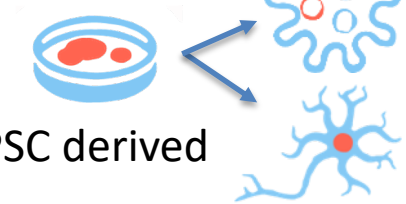
Cancer Cell Line

Immune Cell

Keratinocyte

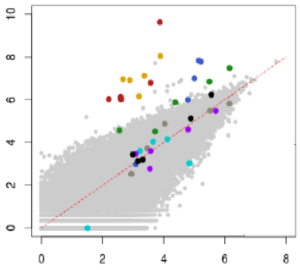


Gut



iPSC derived

Organoid
Organotypic culture
Mixed Culture



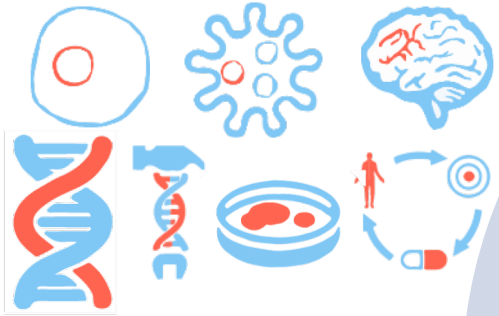
Select on phenotype
- cell death
- fluorescence assay

Target list

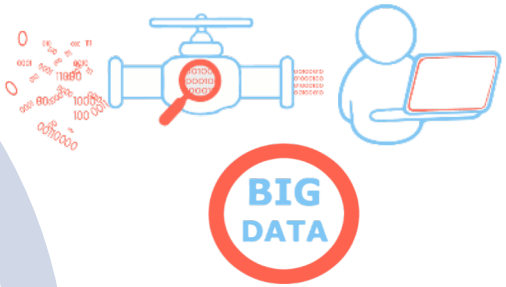
Open Targets

Target Validation Knowledge Cycle

Experimental projects



Bioinformatic projects



Public Data

Data Integration

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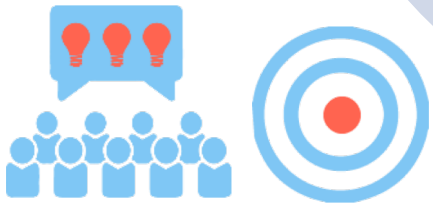
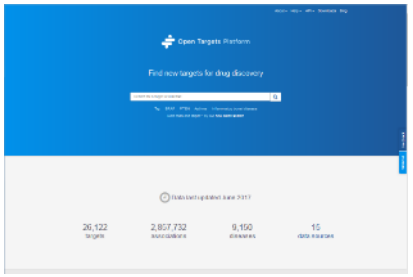


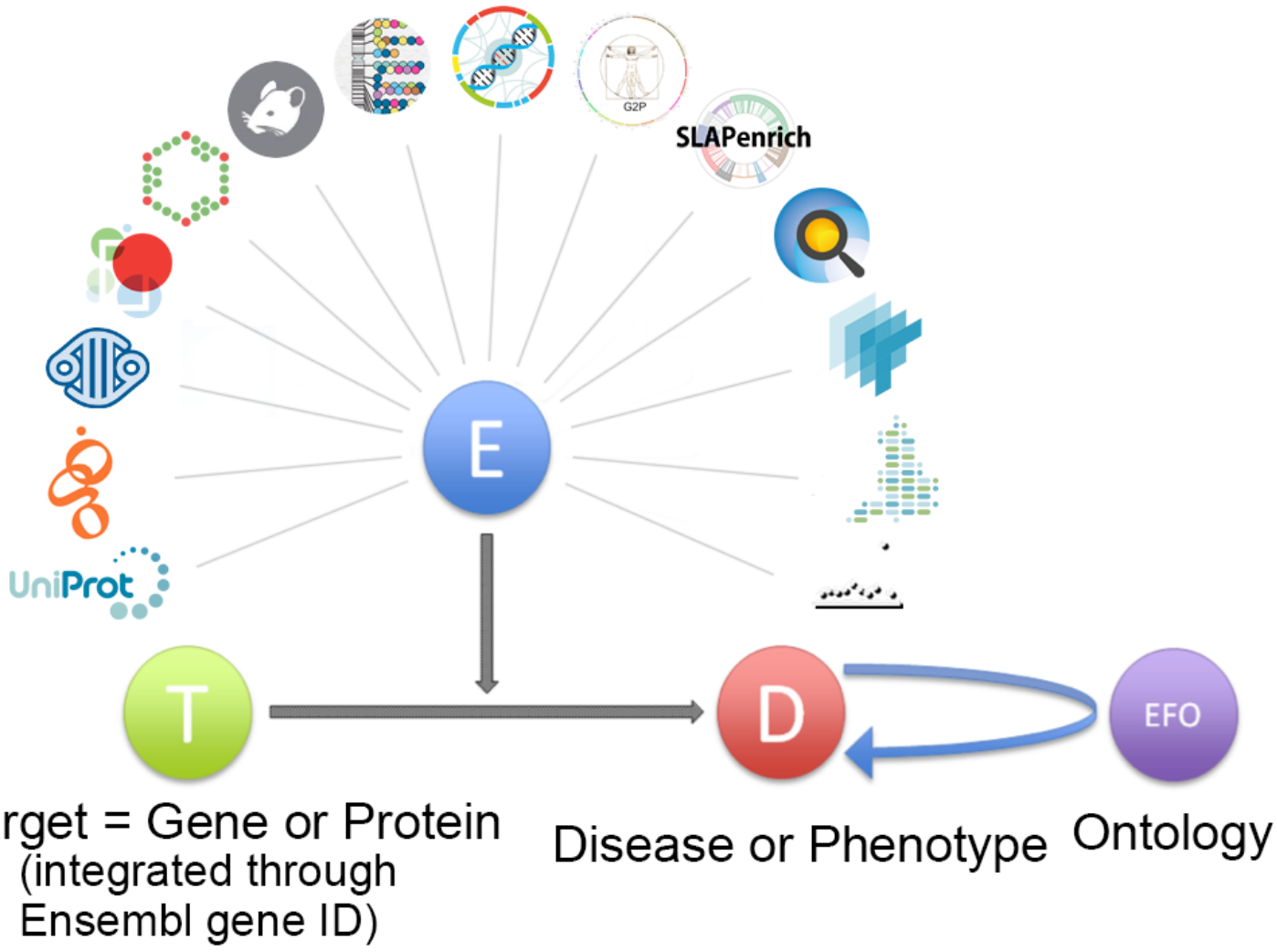
Data Generation

targetvalidation.org



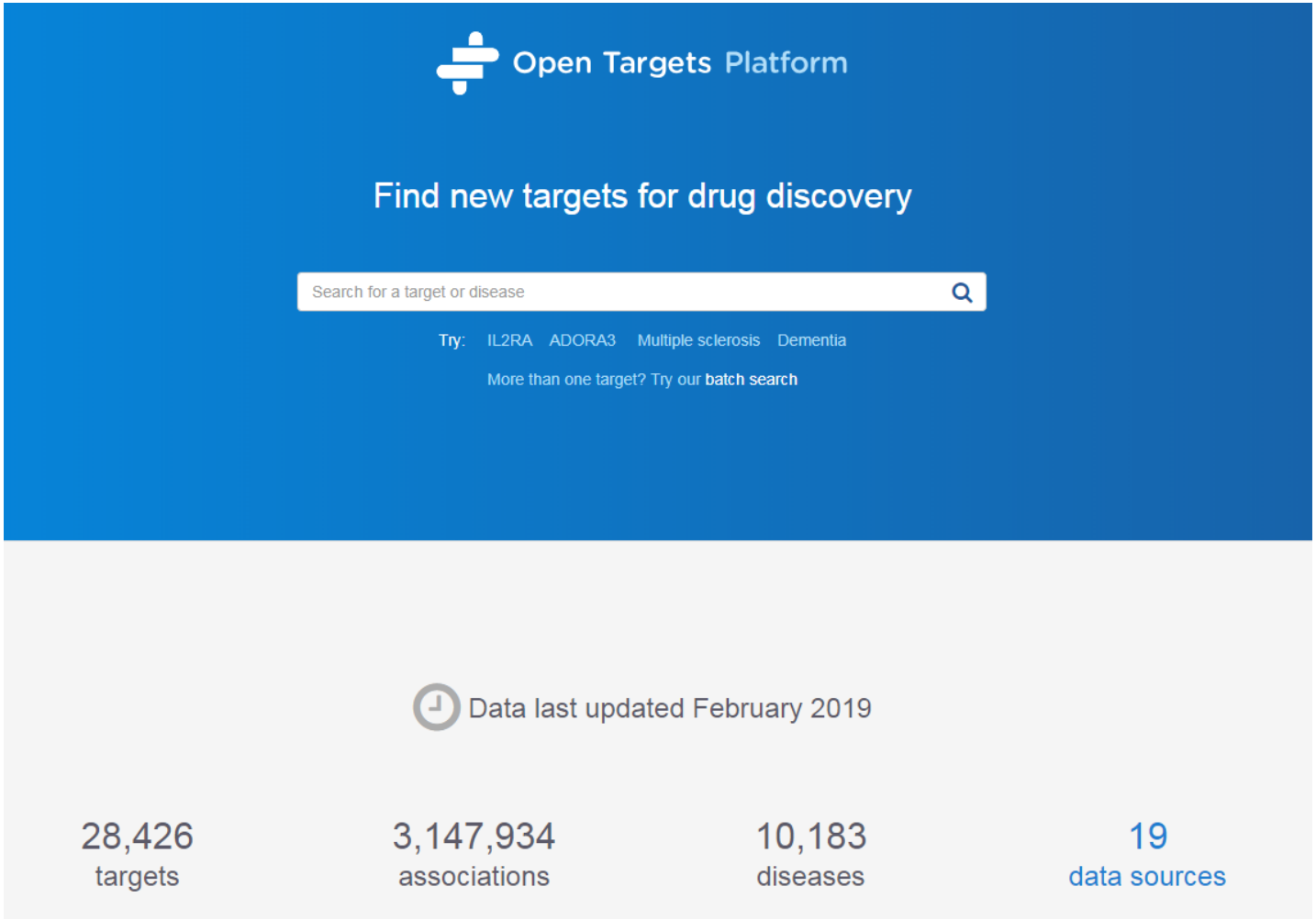
Open Targets

Data Integration for Target ID and Prioritisation



Open Targets

Informatic Products: The Open Targets Platform



targetvalidation.org

Nucleic Acids Research, **2017**, 45, D985-D994
Nucleic Acids Research, **2019**, 47, D1056–D1065

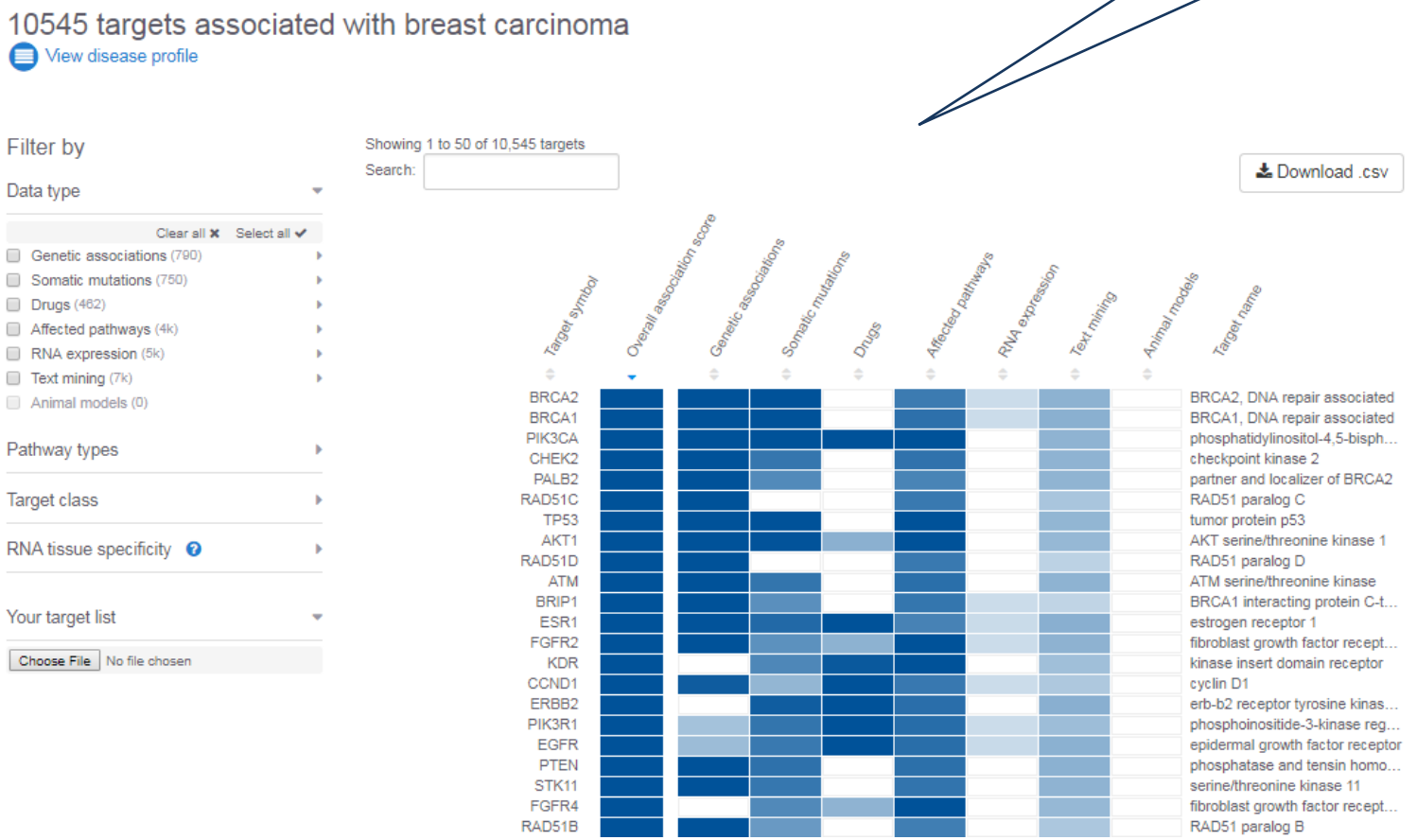
Open Targets

Which targets are associated with breast carcinoma?

Order by evidence type and evidence strength

Filter by evidence type: e.g. 750 targets are supported by somatic mutations

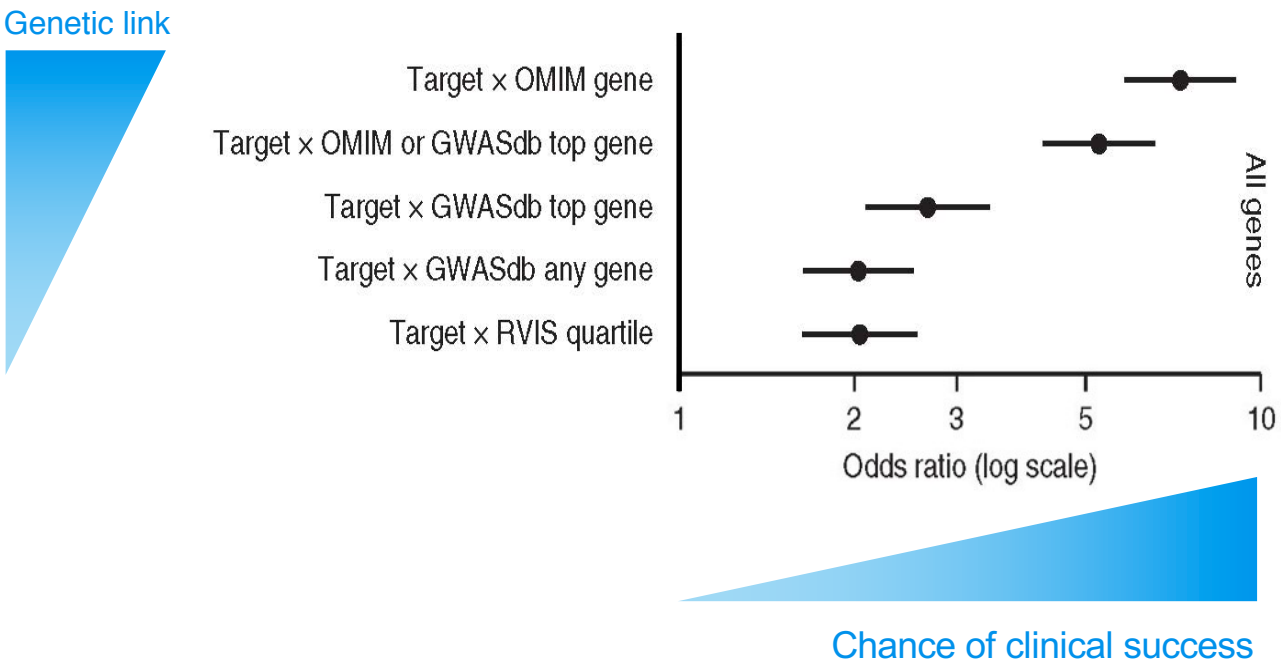
Filter by pathway type and particular pathways



Open Targets

Improved Efficacy through Genetics

Nelson *et al., Nature Genetics, 2013*



Drugs with genetic link between target and disease

Open Targets

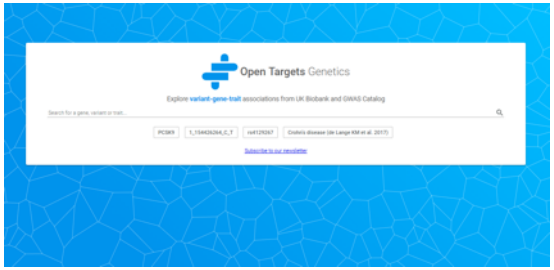
Systematic Identification : Genetics and GWAS

biobank

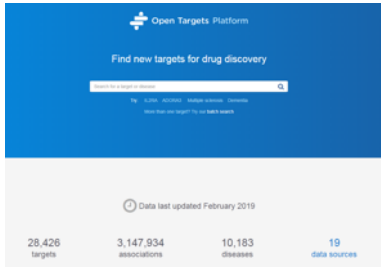
GWAS Catalog
Summary Stats

eQTL Catalogue

Regulation data



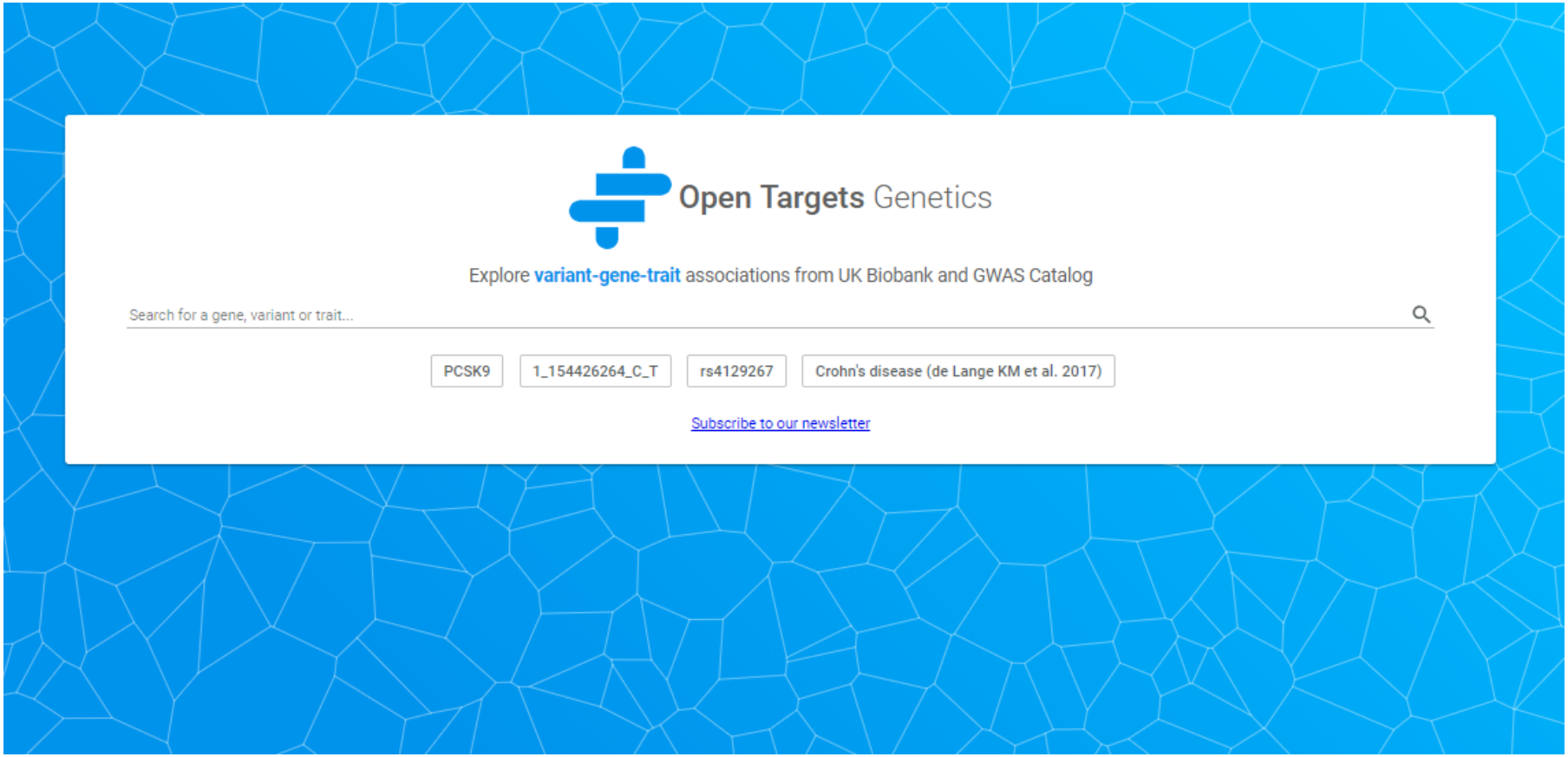
OT Genetics



OT Platform

Open Targets

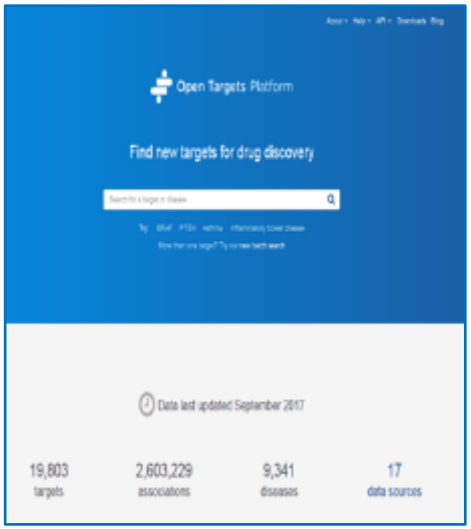
Informatic Products: The Genetics Portal



genetics.opentargets.org

Open Targets

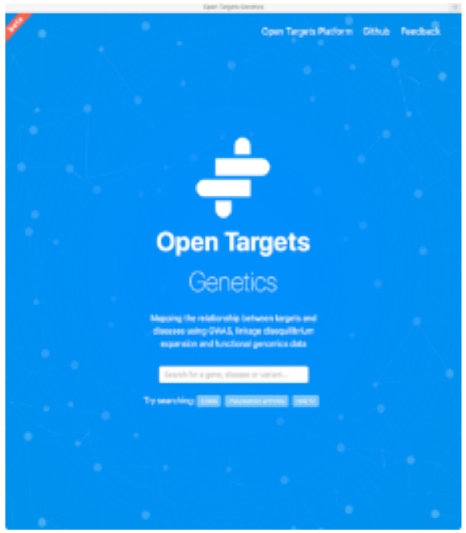
Open Targets Informatics



targetvalidation.org

Aggregate genetics evidence for target

Link out to investigate details of the evidence



genetics.opentargets.org

Detailed investigation of genetics evidence including bespoke tools

https://www.opentargets.org/resources/

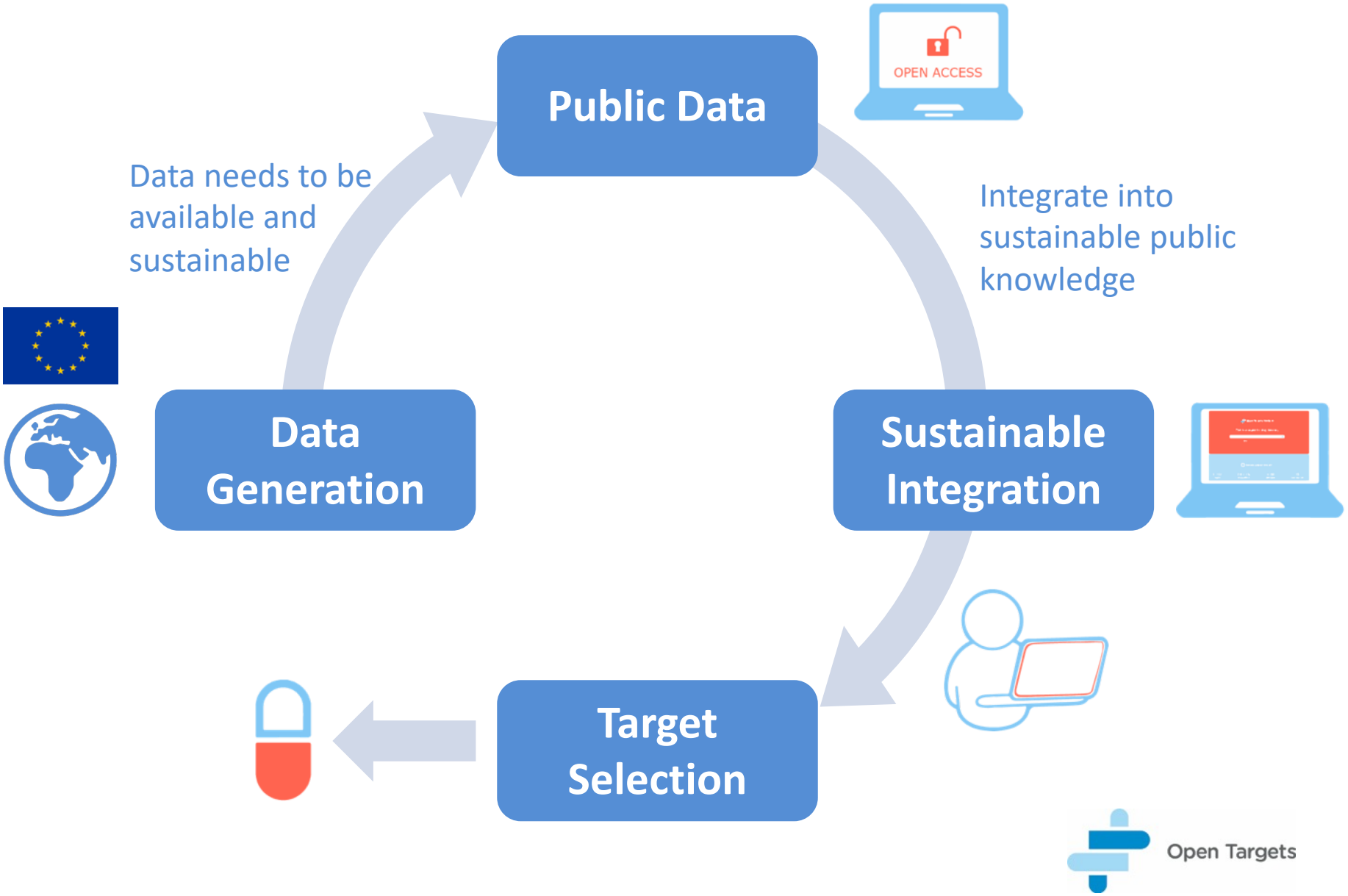
Open Targets

Membership Benefits for Partners

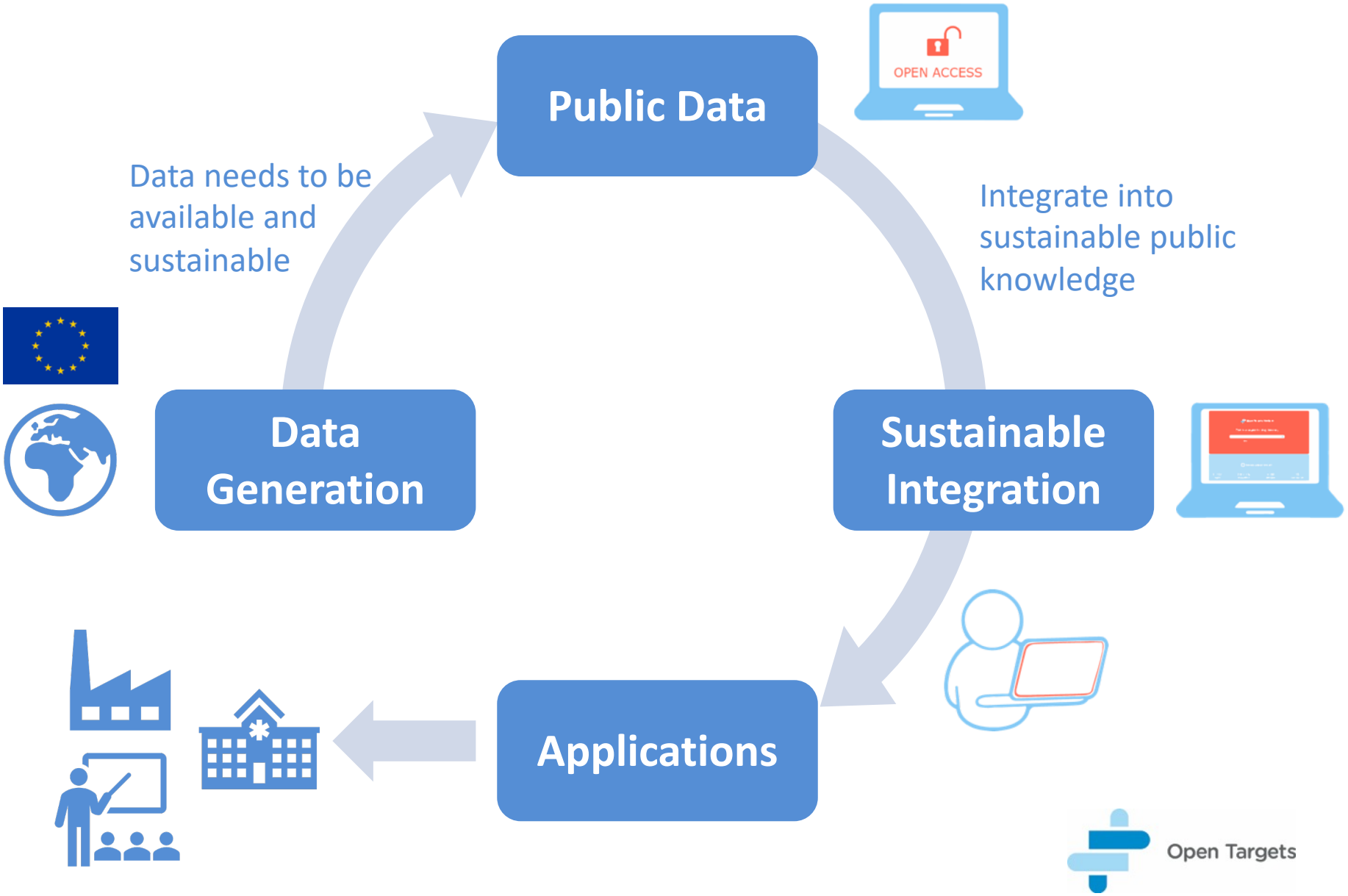
- Direct Open Targets research direction, therapeutic area focus and strategy
- Access to data, methods and technologies to support internal research programmes
- Enhance in-house R&D capability and capacity, de-risk emerging areas
- Work with world-leading teams in genetics, bioinformatics and cell modelling
- Engagement with community transforming therapeutic target selection
- Lean structure, low bureaucratic burden, swift decision-making
- Clear, rapid IP process
- Industry standard project management
- Support for private instance of the bioinformatics platform
- Reputational benefits through partnership and open innovation

Open Targets

Policy Implications – Open Targets



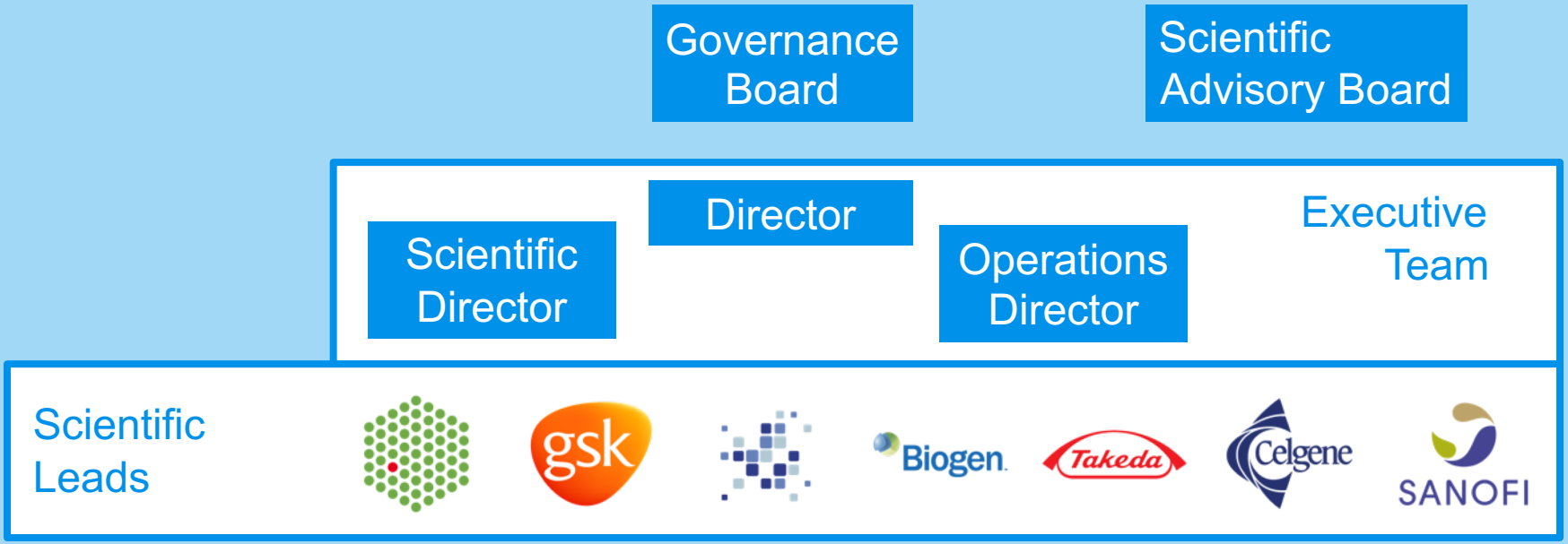
Policy Implications - General



Acknowledgements

Open Targets

Open Targets Governance



Open Targets

Open Targets Governance

Governance Board

Scientific Advisory Board

Scientific Leadership Team

Scientific Director

Director

Operations Director

Executive Team

Scientific Leads

Open Targets

Open Targets Governance

Strategy
Project Approval

Governance Board

Scientific Advisory Board

Scientific Leadership Team

Scientific Director

Director

Operations Director

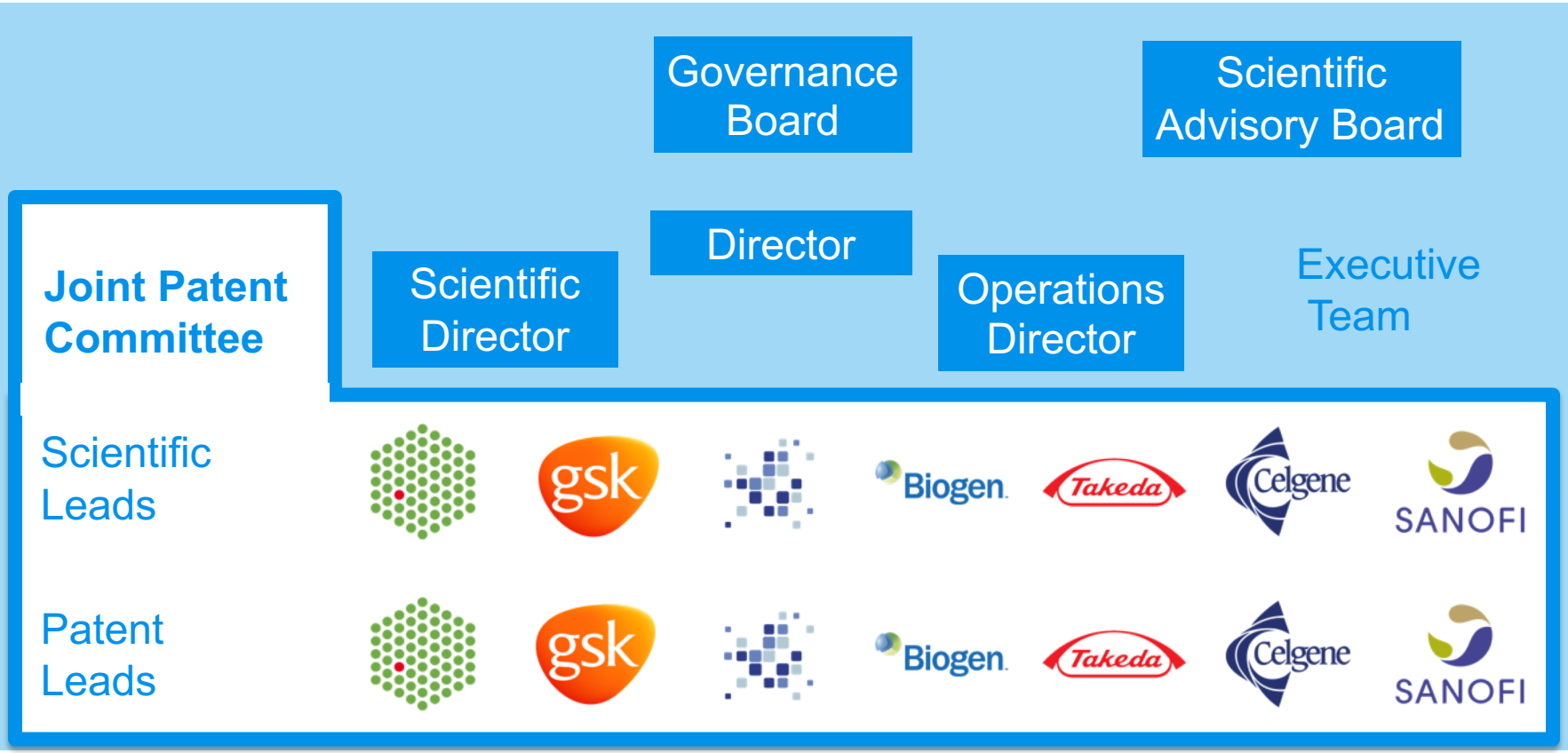
Executive Team

Scientific Leads

Project Review

Open Targets

Open Targets Governance



Open Targets

How can genetics be used to guide therapeutic target identification and Prioritisation?

targetvalidation.org	genetics.opentargets.org
• Rare and complex diseases • Search for **target** or **disease** • Germline and somatic mutations, drugs, pathways, expression, text mining, animal models • Released 2015	• Complex diseases, common genetic variation • Search for **variant**, **target**, or **disease** • Variant-to-gene scoring • Functional genomics, QTLs • Released 2018

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