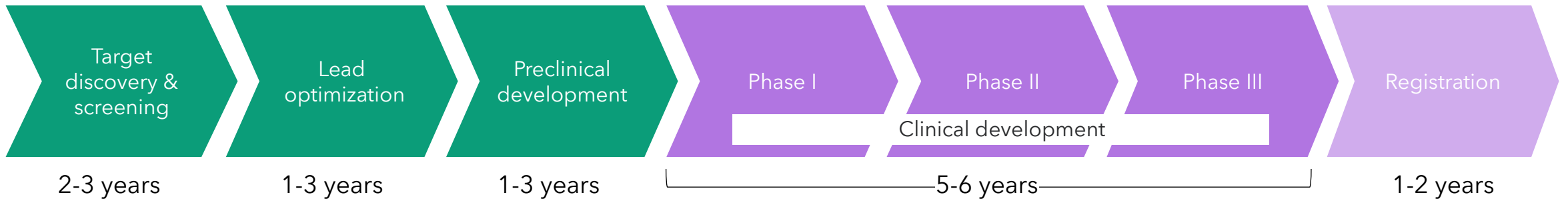
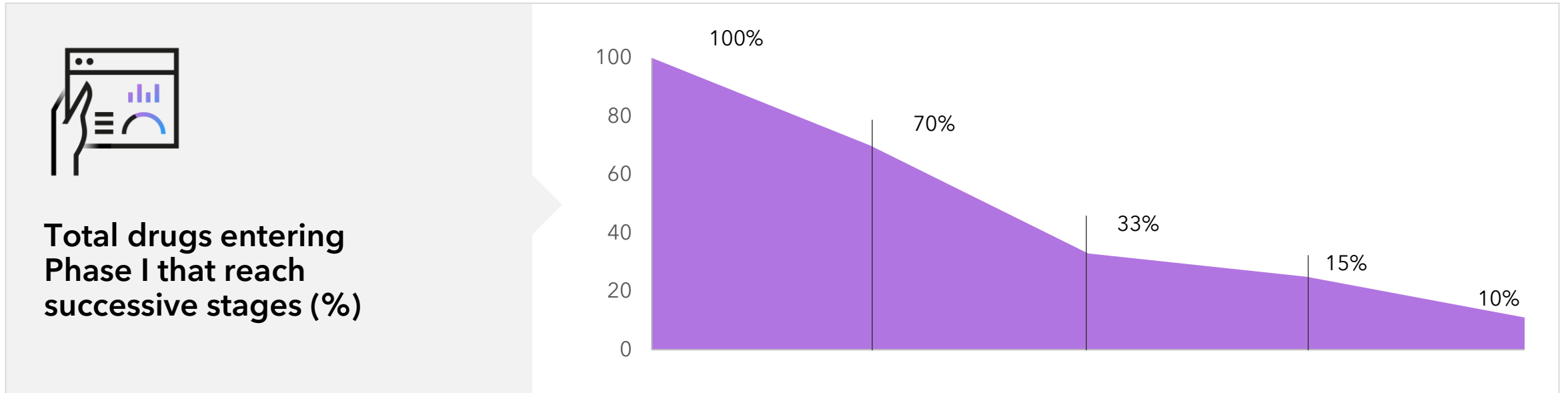


Drug Target Prediction and Repositioning using Machine Learning Integration of Network-based, Pathway Enrichment- based and Disease Enrichment-based Analyses

Traditional de novo drug development pipeline



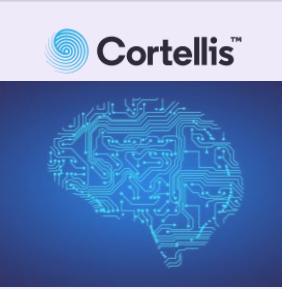
Target ID overview

Indication of interest

Biomarkers


Disease targets

Gene expression signatures



Cortellis™

Integration through machine learning



Expert analysis:
Top target recommendation

Universe of protein targets

Prioritized targets for indication of interest

Assessment:

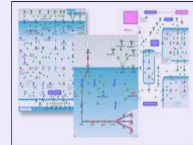
- Novelty
- Tissues
- Druggability

Top selected targets

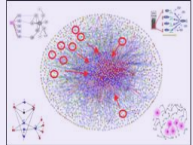
Mechanisms for top targets

Identify drugs



Pathways



Network algorithms




Disease similarity

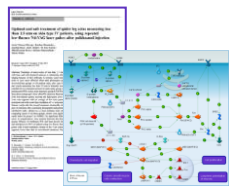


560K+ Drugs and biologics

6.7K+ Targets



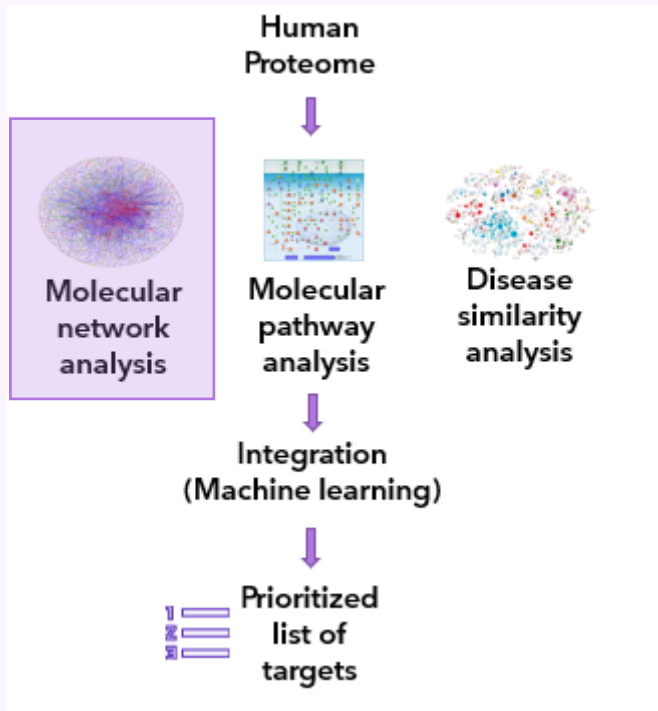
GTExPortal **RCSB PDB** PROTEIN DATA BANK



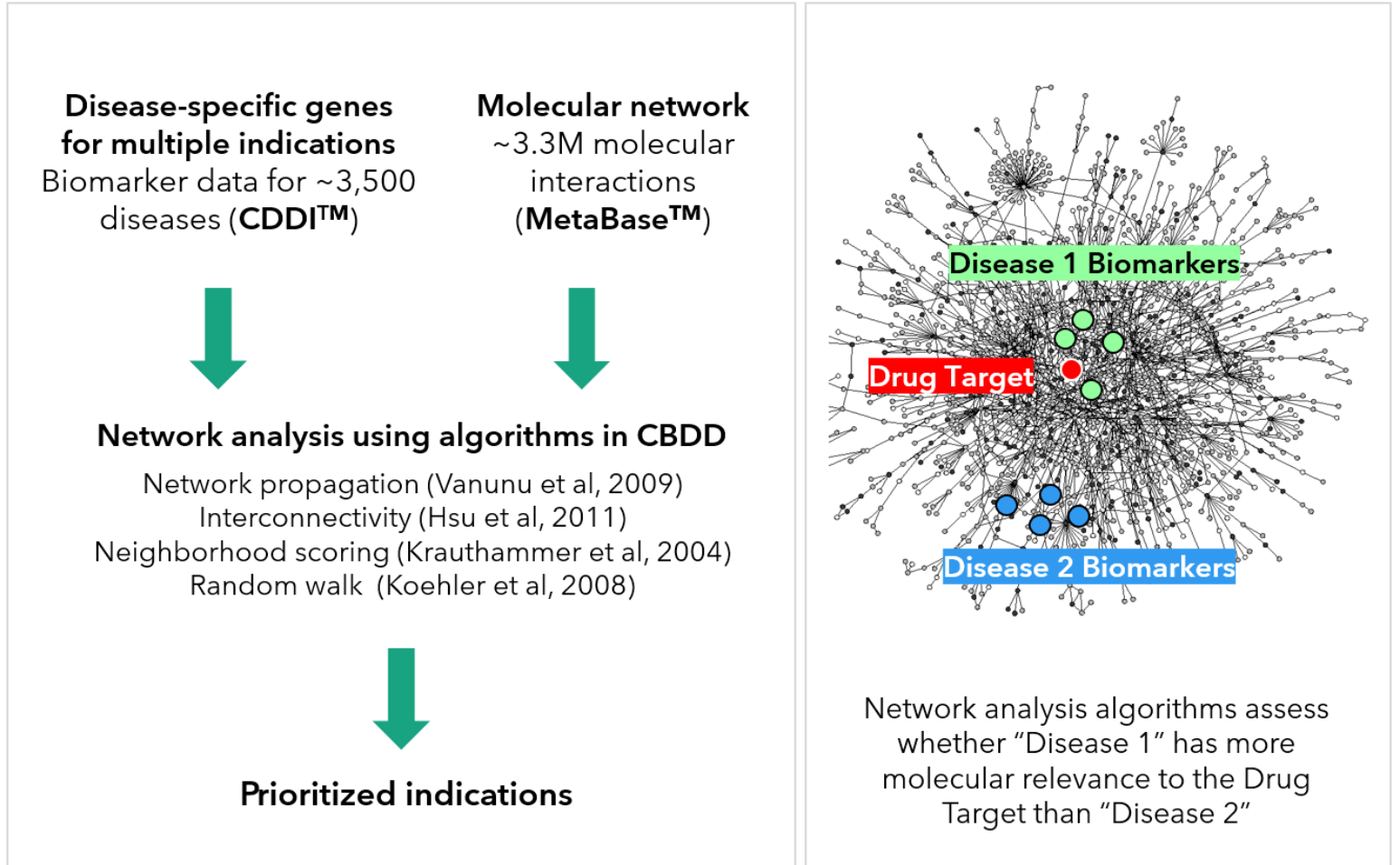
Expert analysis:
Manual mechanism reconstruction



Approaches for Target ID and Prioritization

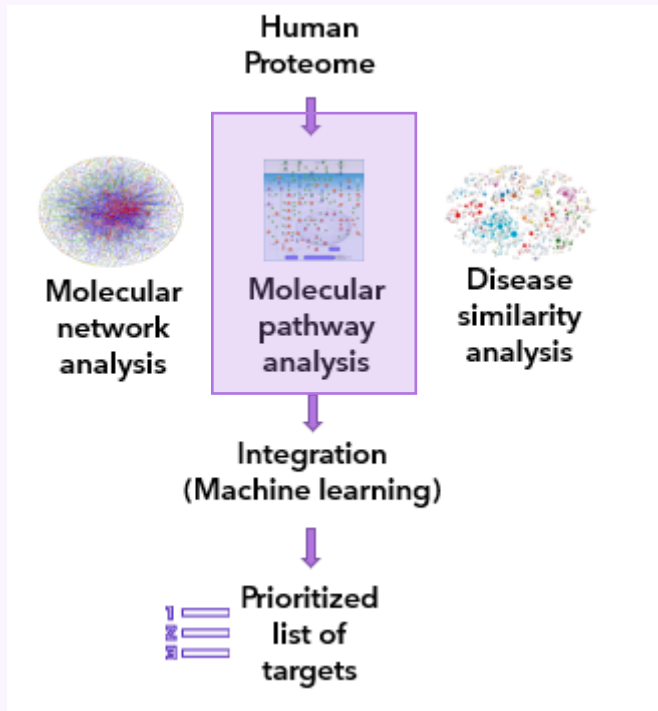


Molecular network analysis



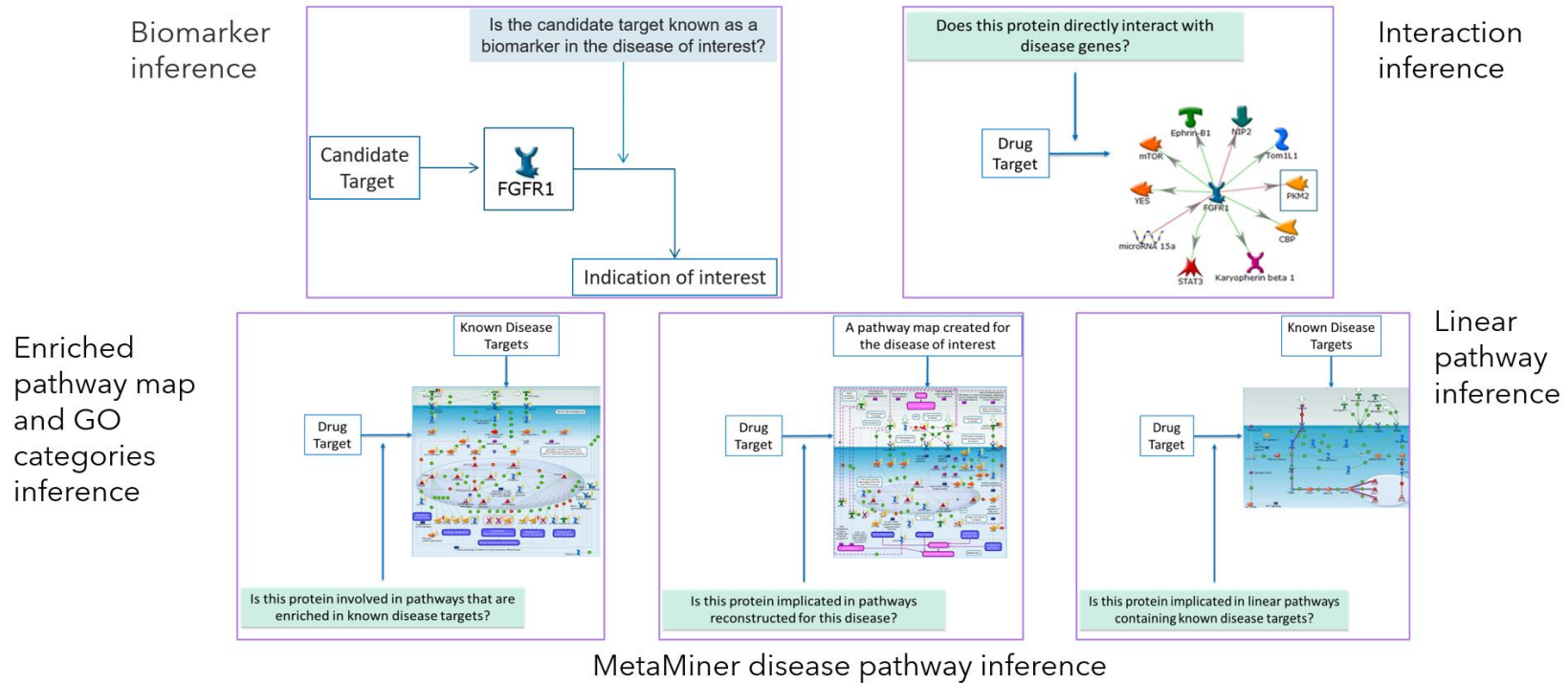
For further details see Emig et al, PLOS ONE 2013

Approaches for Target ID and Prioritization

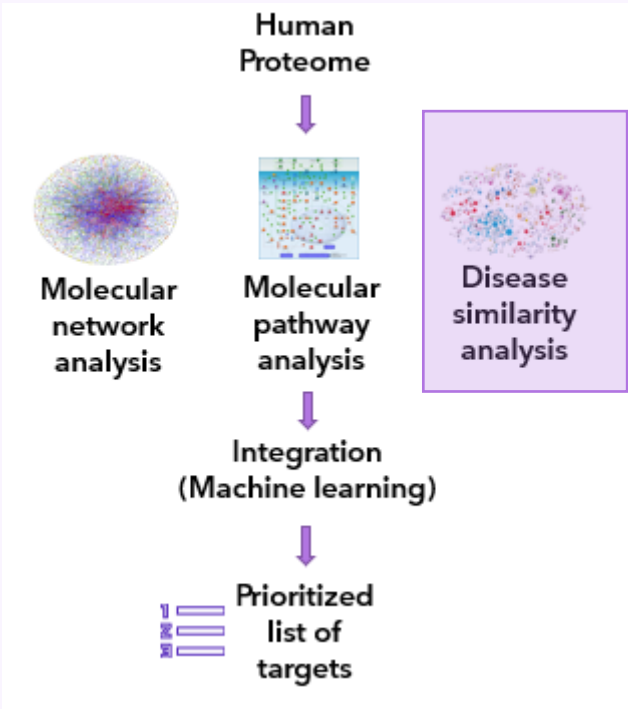


Molecular pathway analysis

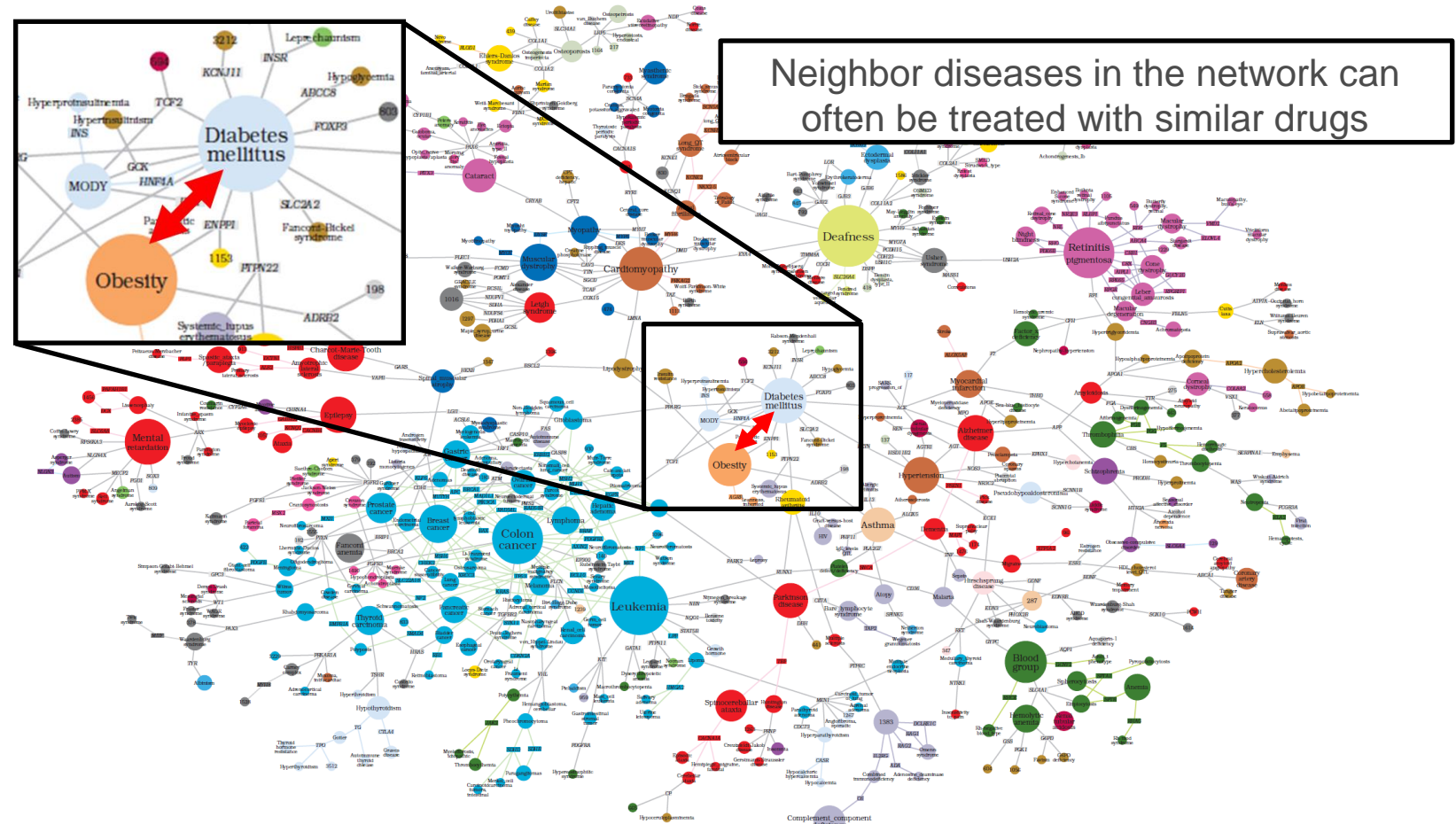
Pathways and biomarkers-based approach



Approaches for Target ID and Prioritization



Target repositioning between similar diseases

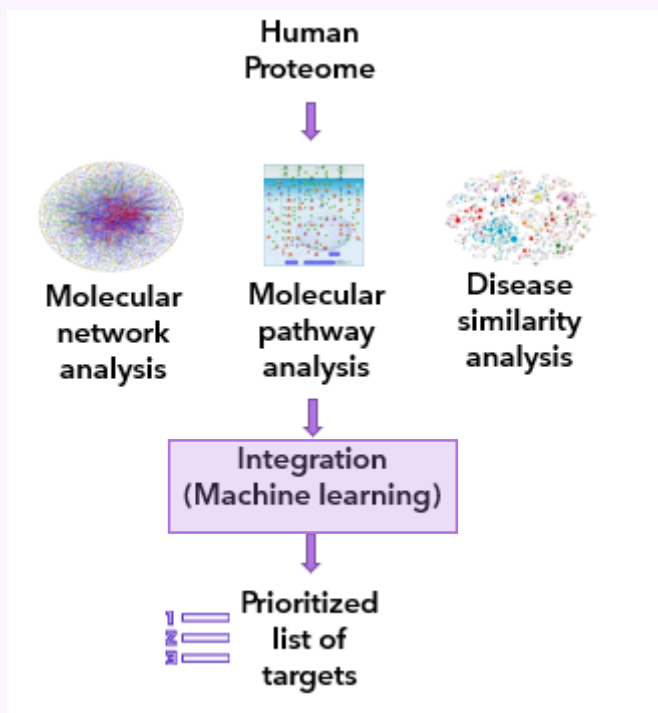


The human disease network

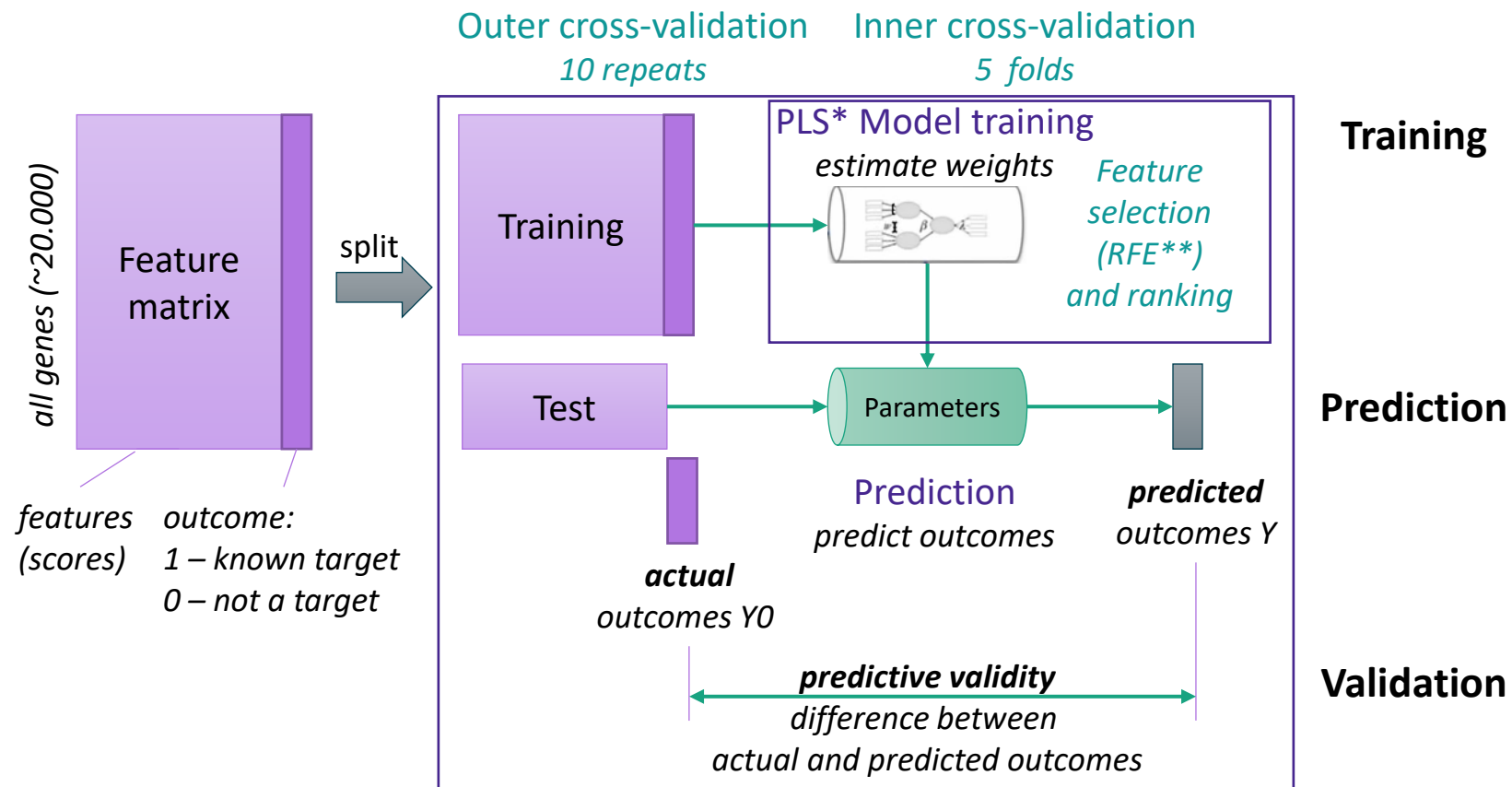
Goh K-I, Cusick ME, Valle D, Childs B, Vidal M, Barabási A-L (2007) *Proc Natl Acad Sci USA* 104:8685-8690



Approaches for Target ID and Prioritization



Machine Learning Model for target prioritization



Machine learning techniques:

* Partial Least Squares

** Recursive Feature Elimination (RFE)

Target ID overview

Indication of interest

Biomarkers

Disease targets

Gene expression signatures

Cortellis™
Integration through machine learning

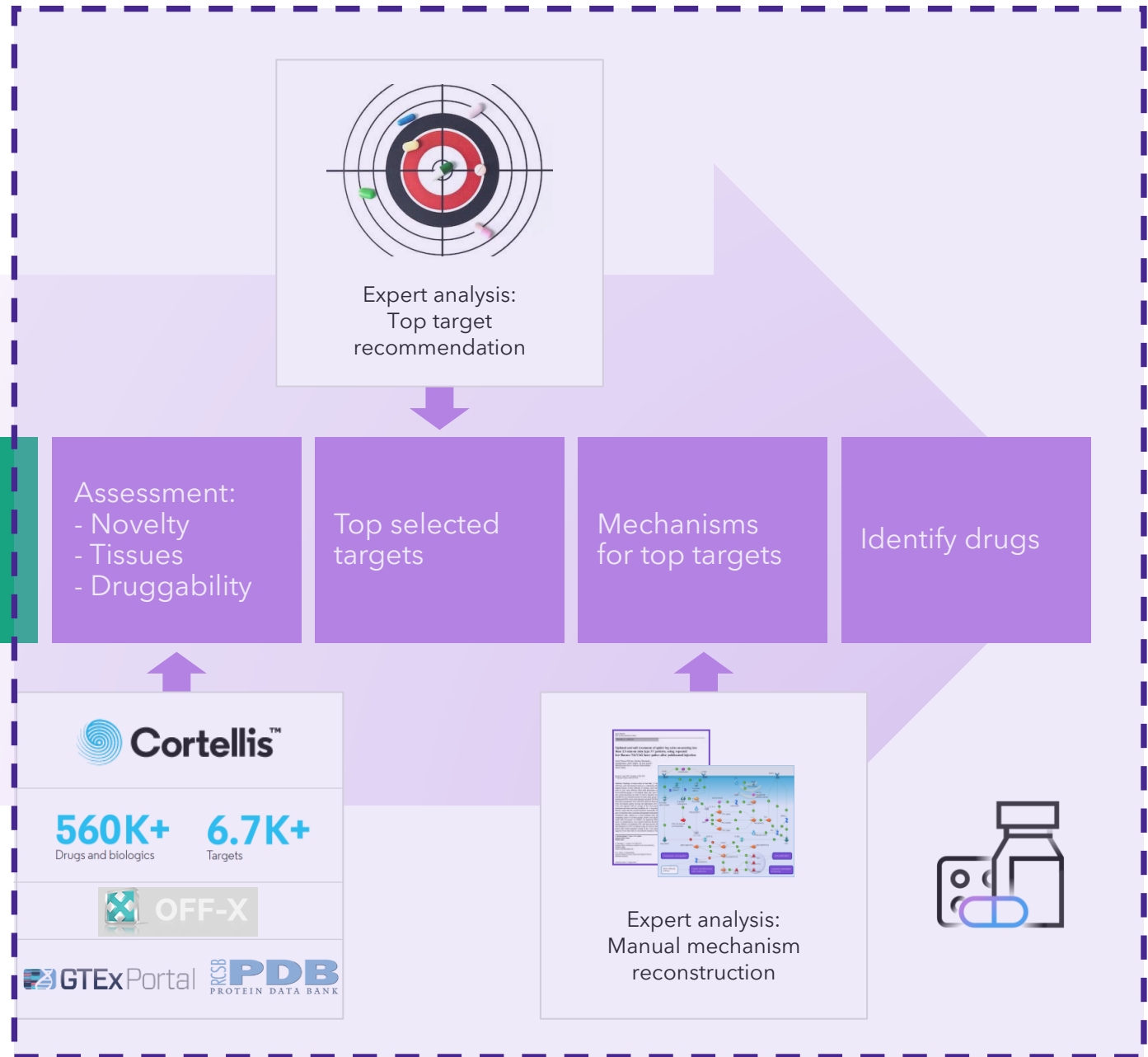
Universe of protein targets

Prioritized targets for indication of interest

Pathways

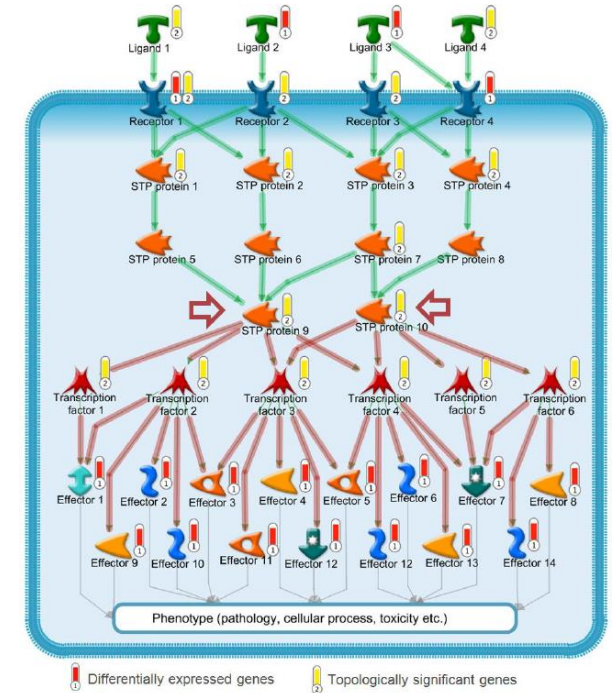
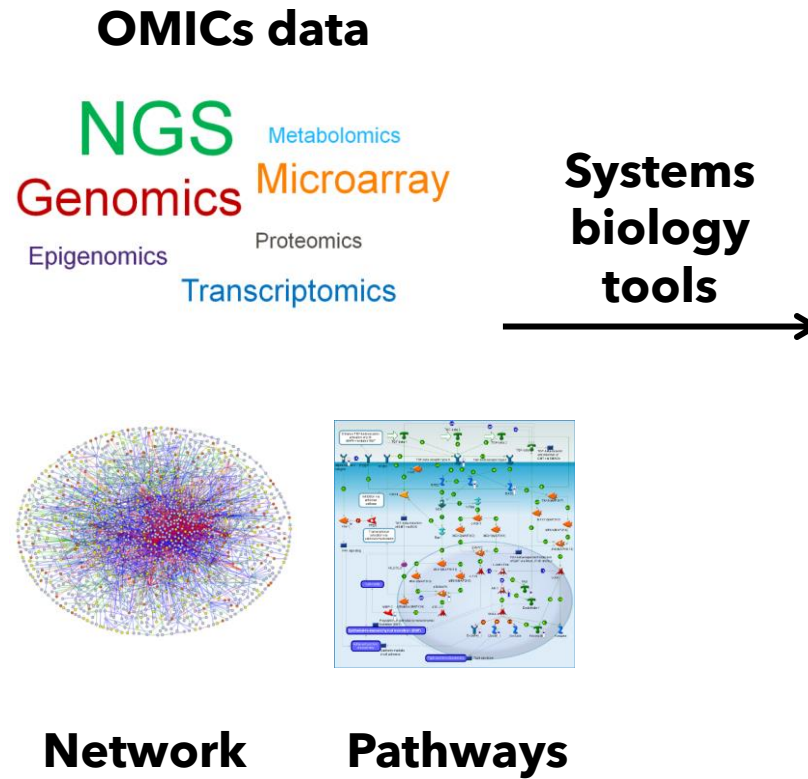
Network algorithms

Disease similarity



Biological mechanism reconstruction

- Why was this target predicted?
- How is the target related to the disease mechanism?
- What is the strength of evidence linking the target to the disease mechanism?

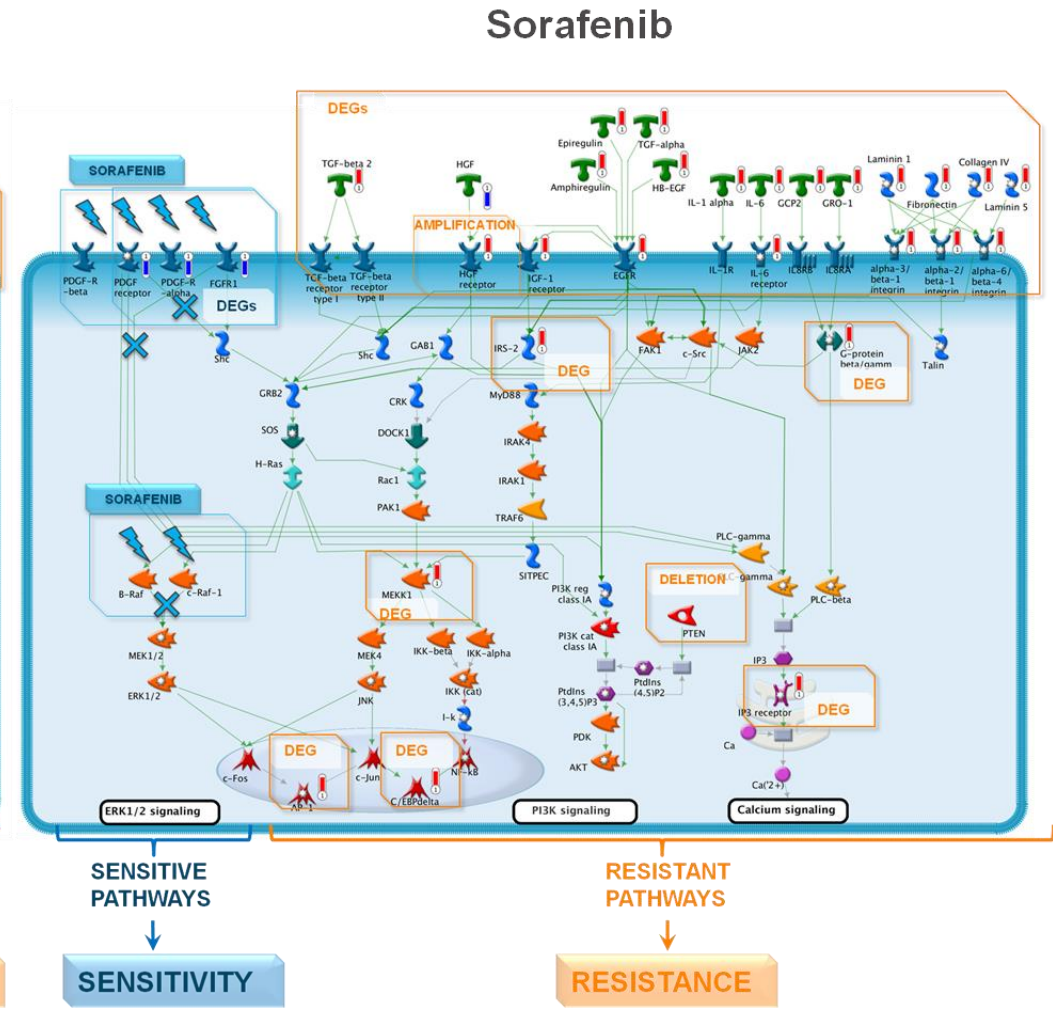
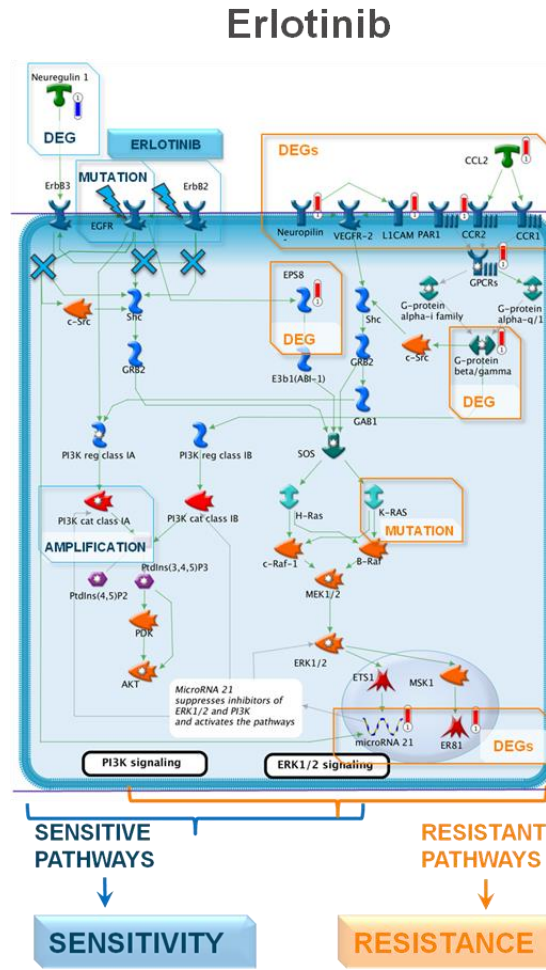


- ✓ Disease biology
- ✓ Drug action
- ✓ Drug resistance
- ✓ Drug toxic effects




Reconstruction of drug sensitivity and resistance mechanisms

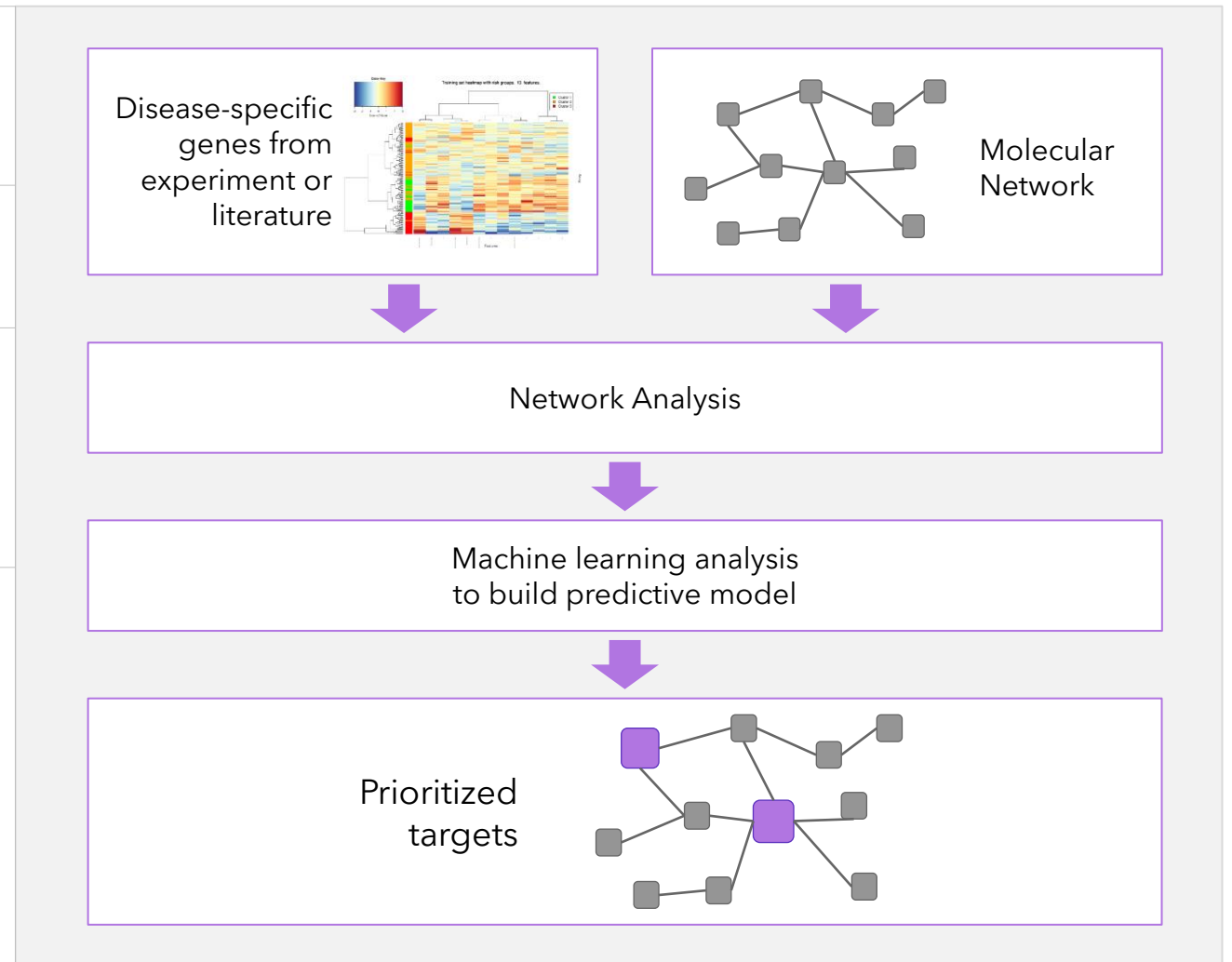
Case study for the patient stratification and biomarker discovery services



Target identification and repositioning for Parkinson's disease (PD)

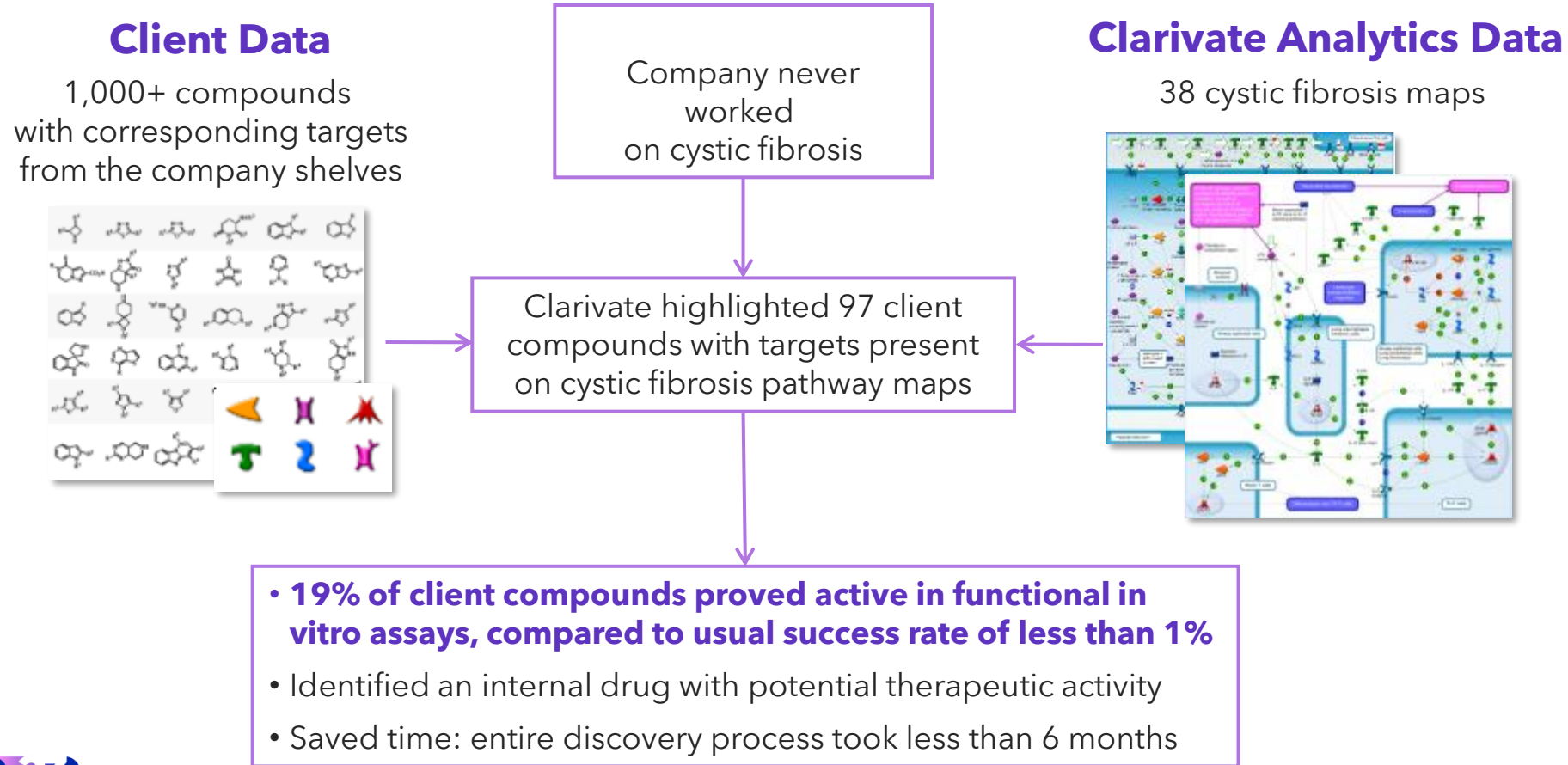
Case study for the target identification and drug prioritization services

Client	
Aim	Identify candidate targets for repositioning in PD
Solution	<ul style="list-style-type: none">Used as input gene expression data from multiple brain regions of PD patientsApplied proprietary network analysis workflow for repositioning
Results	<ul style="list-style-type: none">23 candidate targets for repositioning undergoing clinical development with no existing consideration for PD2 out of these 23 targets were tested and validated in animal models by UCB PharmaResults presented in the Benelux Bioinformatics Conference



Pathway approaches to target identification and drug prioritization

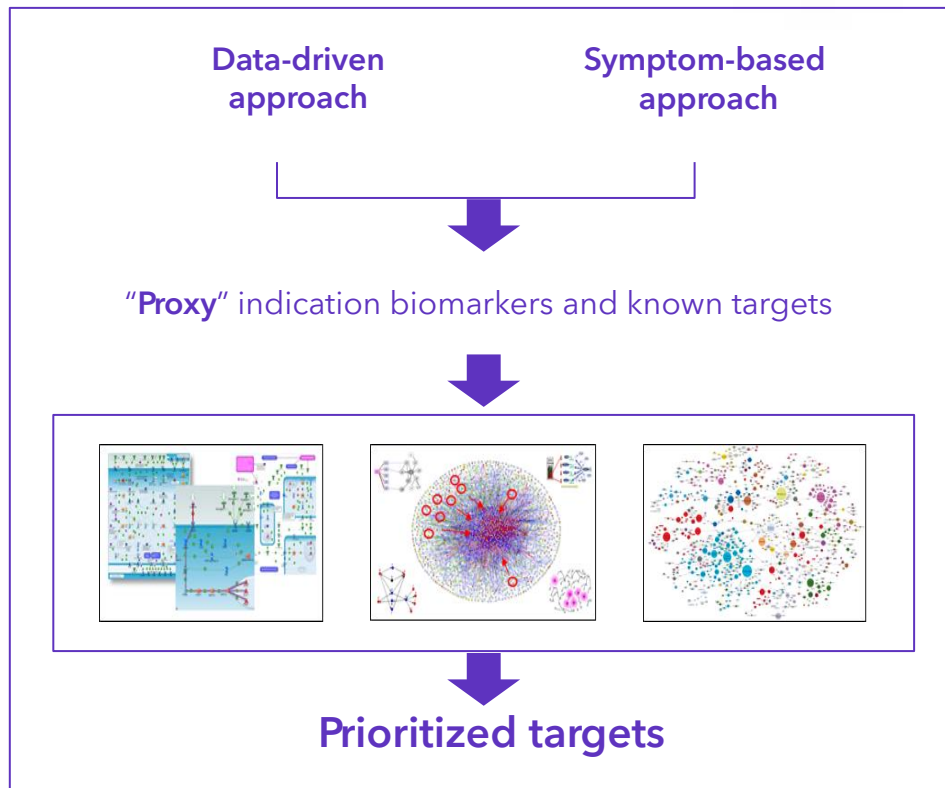
Case study for the target identification and drug prioritization services



Tailored analysis: Drug repurposing for chemical agent exposure

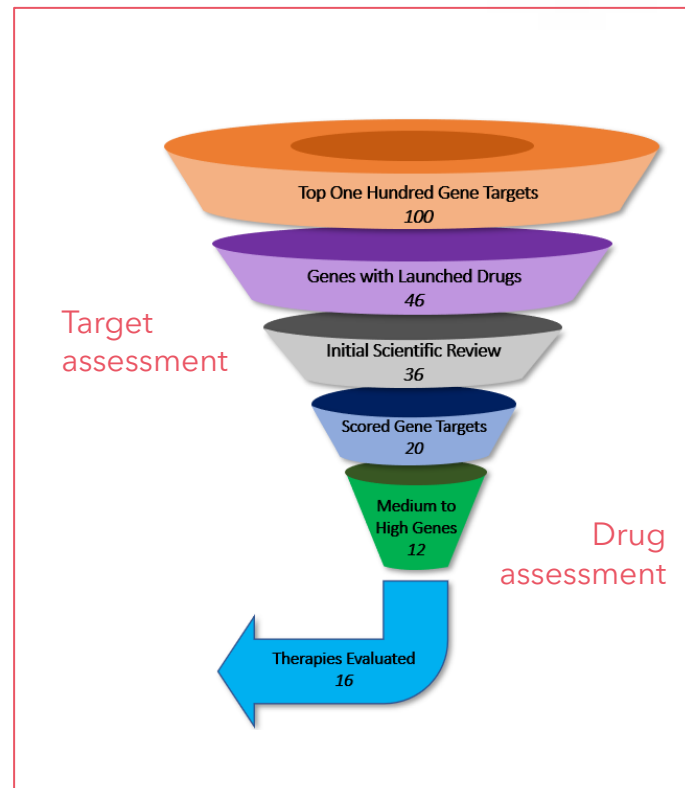
Target identification and prioritization

01



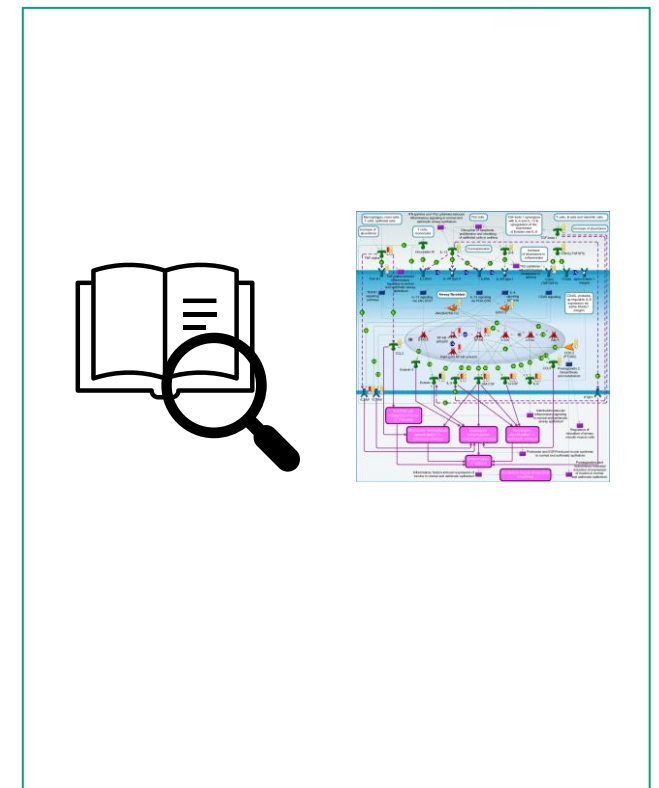
Drug factor analysis

02



Pathway reconstruction

03



The value of the data powering the pipelines

Accelerate preclinical development

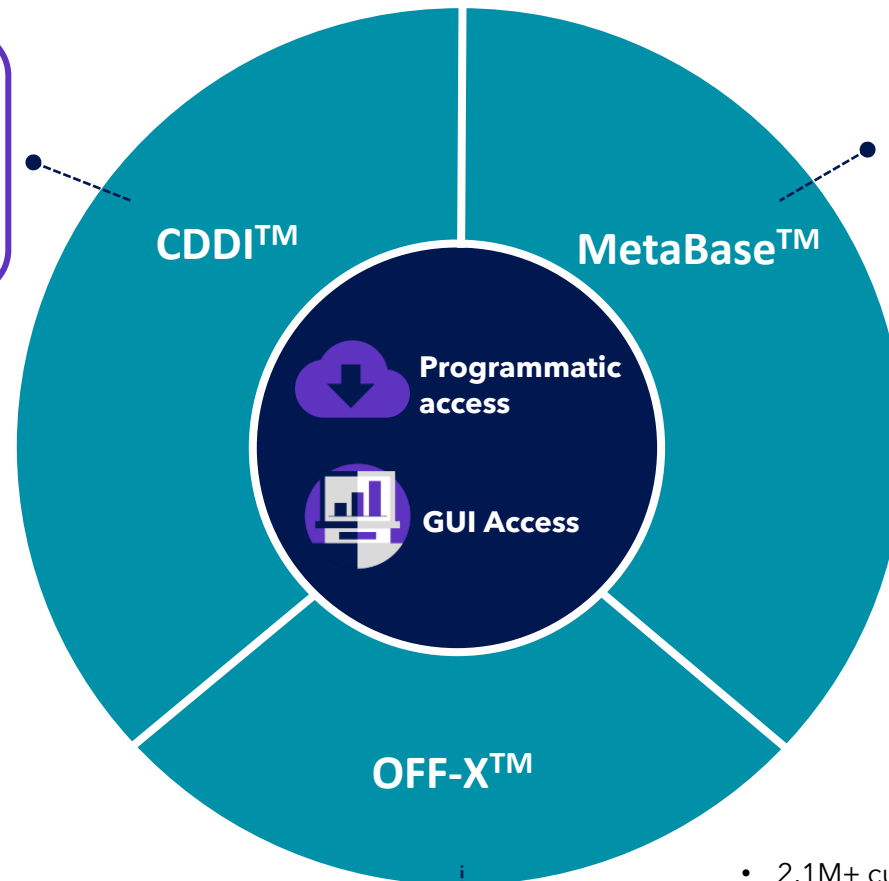
Avoid late-stage failures with drug intelligence that integrates biological, chemical and pharmacological data into one platform.

- 49K+ genes and targets
- 270K+ genetic variants
- 709K+ drugs and biologics
- 47K+ biomarkers
- 169K experimental models
- 2.6M+ preclinical and clinical uses
- 3.4M+ pharmacological studies
- 2.9M+ publication references

Accelerate drug discovery research

Understand the molecular basis of disease and generate hypotheses for biomarkers, targets and mechanisms of action.

- 3.5M+ molecular interactions
- Disease associations covering 3600+ therapeutic indications
- 1500+ molecular pathways
- 1100+ molecular networks
- 2.9M+ publication references



Preclinical and Clinical Safety Intelligence

Translational tool providing drug and class safety intelligence to anticipate risks and drive new competitive value

- 2.1M+ curated safety and toxicity alerts
- 15K+ targets and genes
- 32K+ drugs and biologics
- 12K+ adverse events and toxicity endpoints
- From peer-reviewed journals, congresses, clinical trial registries, company and regulatory agency communications around the world, and FDA, EMA, and PDMA approval packages



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Thank you

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