
Recursion
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Day 2024

Recursion

# Download Day 2024

# Agenda

**Breakfast & Arrival at Recursion** (Upper Level) — 8:30 am – 9:30 am

## Morning Session — 9:30 am – 12:30 pm

### Welcome

### State of Recursion
Chris Gibson PhD – Co-Founder & CEO

### Recursion OS
Lina Nilsson PhD – Senior VP of Inception Labs

### Preclinical
Laura Schaevitz PhD – Senior VP and Head of Research

### Fireside Chat with Deepak Nijhawan, MD, PhD
David Mauro MD PhD – Chief Medical Officer
Deepak Nijhawan MD PhD – UT Southwestern, Distinguished Chair in Biomedical Science

### Tours & Demos
Senior Management

**Lunch & Break** (Upper Level, High Throughput Feeding) — 12:30 – 1:30 pm

## Afternoon Session — 1:30 pm – 4:30 pm

### Afternoon Convocation
Najat Khan PhD – Chief R&D Officer & Chief Commercial Officer

### Partnerships
Matt Kinn – Senior VP of Business Development & Corporate Initiatives
John Marioni PhD – Genentech, Senior VP and Head of Computational Sciences

### Clinical Programs
David Mauro MD PhD – Chief Medical Officer

### Company & Milestones
Michael Secora PhD – Chief Financial Officer

### Break

### Fireside Chat with Jensen Huang
Chris Gibson PhD – Co-Founder & CEO
Jensen Huang – NVIDIA, Founder & CEO

### Closing Remarks
Chris Gibson PhD – Co-Founder & CEO

**Dinner — Mar Muntanya** (Hyatt Regency) — 5:00 – 7:00 pm

Recursion

# Welcome

State of the Company

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# Disclaimers

This presentation and any accompanying discussion and documents contain information that includes or is based upon "forward-looking statements" within the meaning of the Securities Litigation Reform Act of 1995. These forward-looking statements are based on our current expectations, estimates and projections about our industry and our company, management's beliefs and certain assumptions we have made. The words “plan,” “anticipate,” “believe,” “continue,” “estimate,” “expect,” “intend,” “may,” “will” and similar expressions are intended to identify forward-looking statements. Forward-looking statements made in this presentation include outcomes and benefits expected from the Tempus partnership, including our ability to leverage the datasets acquired through the license agreement into increased machine learning capabilities and accelerate clinical trial enrollment; outcomes and benefits expected from the Enamine partnership, including the generating and co-branding of new chemical libraries; outcomes and expected benefits from the Helix partnership, including the development of causal AI models and biomarker and patient stratification strategies; expected BioHive supercomputer capabilities; outcomes and benefits from licenses, partnerships and collaborations, including option exercises by partners, additional partnerships, and the ability to house tools on the BioNeMo Marketplace; the potential for additional partnerships and making data and tools available to third parties; advancements of our Recursion OS, including augmentation of our dataset; outcomes and benefits expected from the Large Language Model-Orchestrated Workflow Engine (LOWE); the occurrence or realization of any near- or medium-term potential milestones; the initiation, timing, progress, results, and cost of our research and development programs and our current and future preclinical and clinical studies, including timelines for enrollment in studies, data readouts, and progression toward IND-enabling studies; the potential size of the market opportunity for our drug candidates; our ability to identify viable new drug candidates for clinical development and the accelerating rate at which we expect to identify such candidates; our expectation that the assets that will drive the most value for us are those that we will identify in the future using our datasets and tools, and many others. Forward-looking statements made in this presentation are neither historical facts nor assurances of future performance, are subject to significant risks and uncertainties, and may not occur as actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. For a discussion of factors that could affect our business, please refer to the "Risk Factors" sections in our filings with the U.S. Securities and Exchange Commission, including our Annual Report for the Fiscal Year ended December 31, 2023, on Form 10-K and our most recent Quarterly Report on Form 10-Q. This presentation does not purport to contain all the information that may be required to make a full analysis of the subject matter. We undertake no obligation to correct or update any forward-looking statements, whether as a result of new information, future events or otherwise.

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Cross-trial or cross-candidate comparisons against other clinical trials and other drug candidates are not based on head-to-head studies and are presented for informational purposes; comparisons are based on publicly available information for other clinical trials and other drug candidates.

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# Our Hopes for Today

Share details and updates on our:

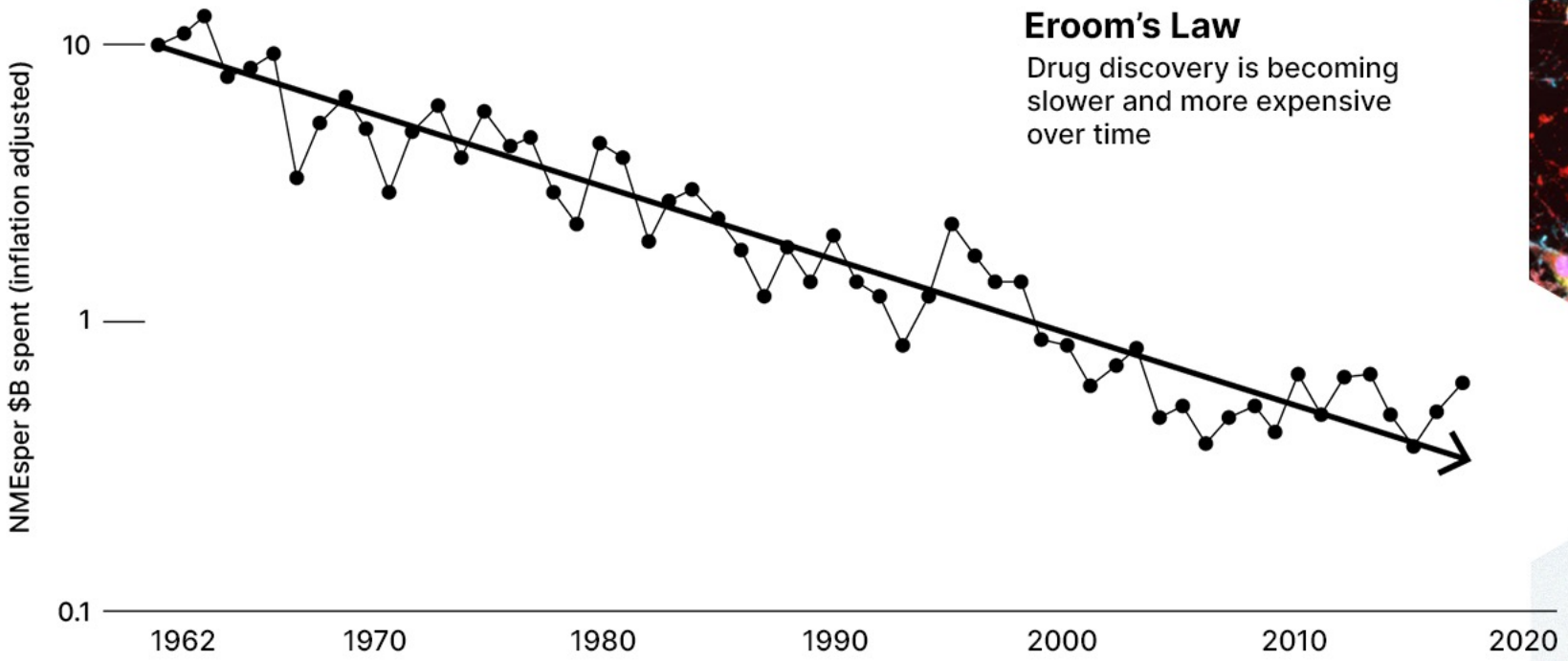
- Pipeline – with 7 clinical trial readouts expected in the next ~18 months
- Partnerships - with potential near term options on both maps and programs
- Platform - with industry-leading data generation and compute

Help define what we view as a tipping point moment as BioTech transitions to TechBio and understand why Recursion is uniquely positioned to take advantage of this

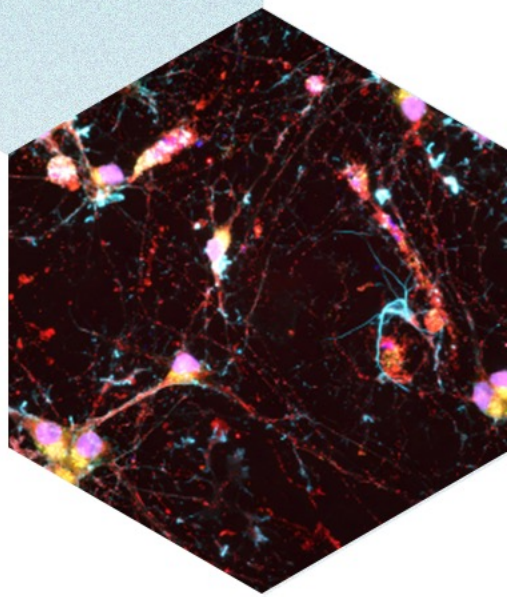
Let you get a feel for Recursion and hear from expert partners from outside Recursion about the current and potential future impact of our work

# The Moment: A Tale of Two Cities

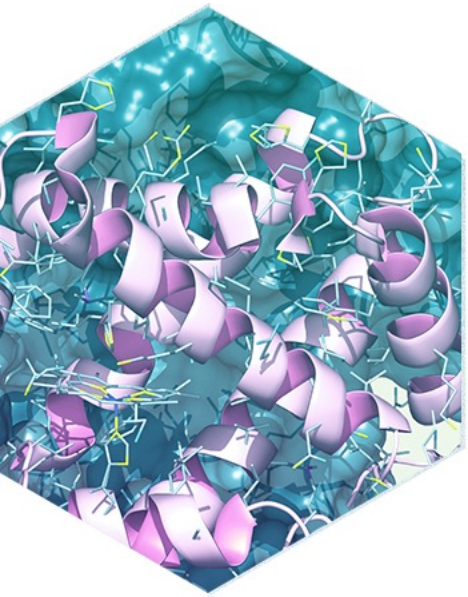

# A Tale of Two Cities: BioPharma




Scannell et al., *Nature Reviews Drug Discovery* 11:191, 2012



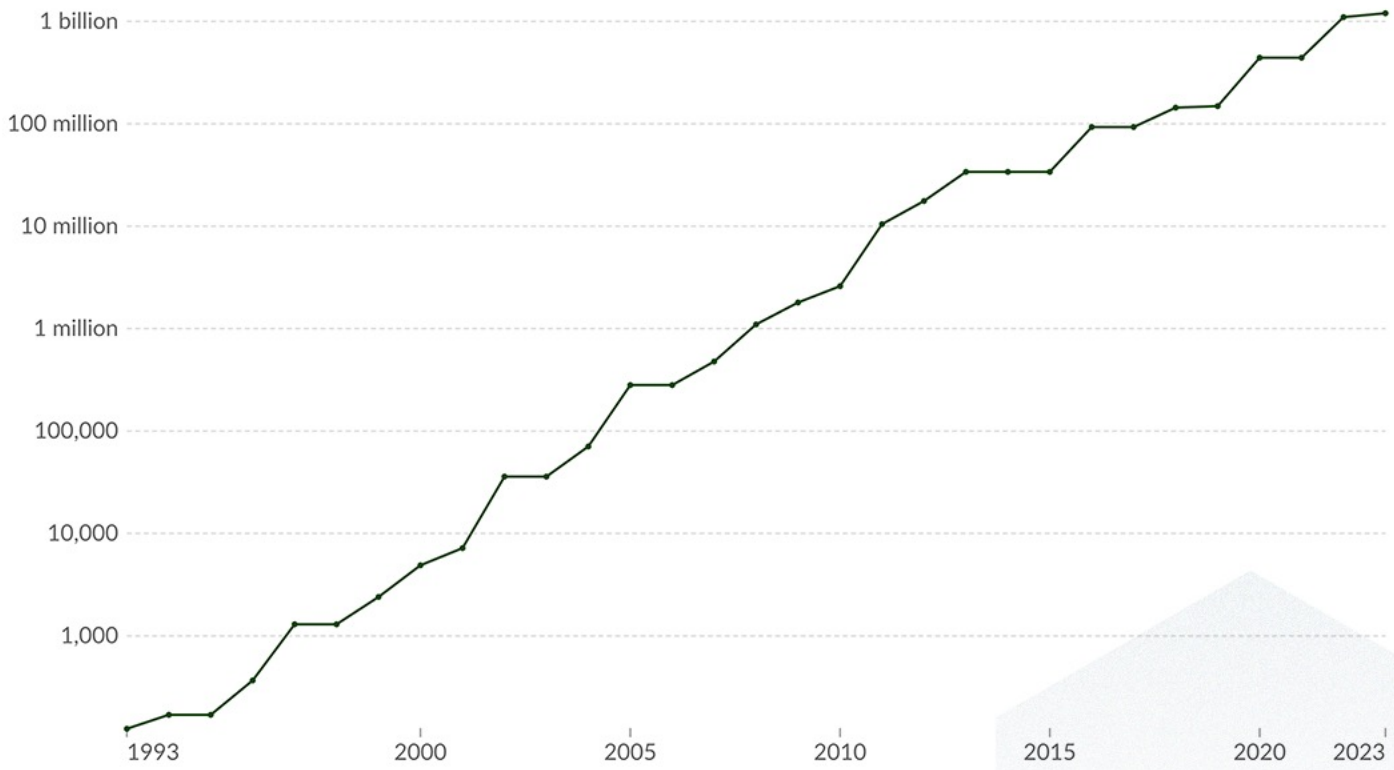
# A Tale of Two Cities: Tech



## Computational capacity of the fastest supercomputers

Our World in Data

The number of floating-point operations[1] carried out per second by the fastest supercomputer in any given year.
This is expressed in gigaFLOPS, equivalent to $10^9$ floating-point operations per second.




**Data source:** Dongarra et al. (2023)

OurWorldInData.org/technological-change | CC BY

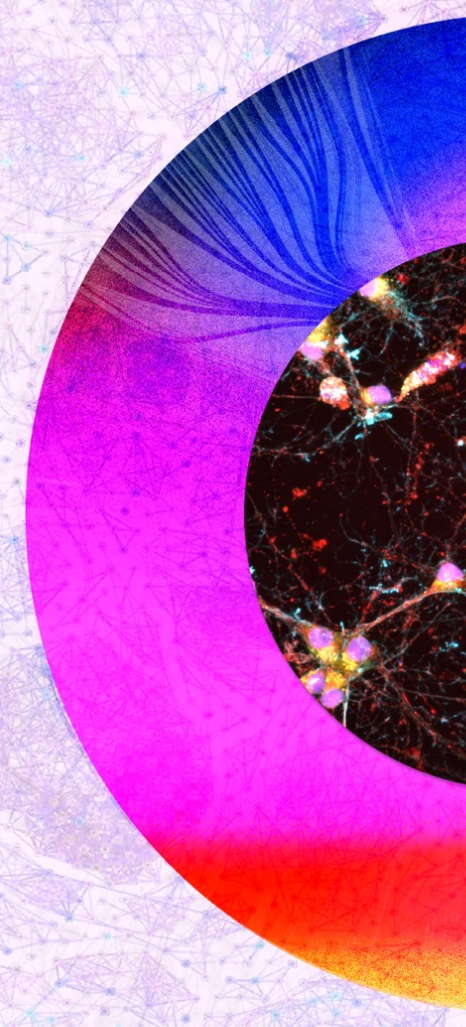
**1. Floating-point operation**: A floating-point operation (FLOP) is a type of computer operation. One FLOP represents a single arithmetic operation involving floating-point numbers, such as addition, subtraction, multiplication, or division.

# The Evolution of BioTech into TechBio

We believe the transformation of BioPharma through AI is inevitable, just as we are seeing in so many industries — we believe it is a matter of who, how and when

New types of companies have emerged that are truly “bilingual” in tech and science

Data, compute, and automation are shifting the speed, cost, and quality of novel insights today, and we are nearing the stage where we can harvest the earliest of this jump forward

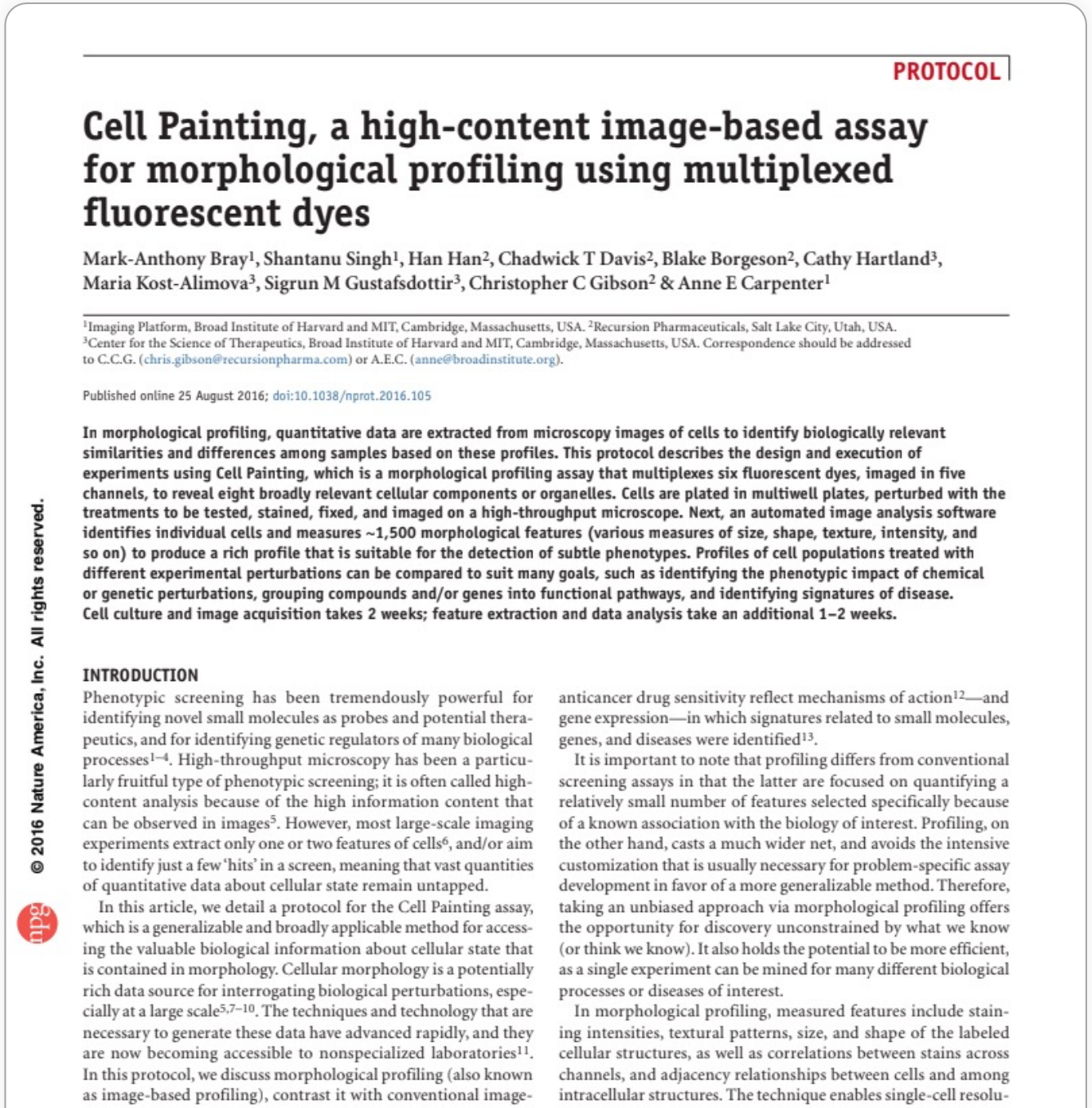


# TechBio Origins: Point Solutions

Most BioTech companies have built a point solution - they've developed a tool, process, model or analysis to accomplish an important step in drug discovery.

**This is how we started too.**

But discovering and developing medicines requires hundreds of steps…



PROTOCOL

## Cell Painting, a high-content image-based assay for morphological profiling using multiplexed fluorescent dyes

Mark-Anthony Bray[1], Shantanu Singh[1], Han Han[2], Chadwick T Davis[2], Blake Borgeson[2], Cathy Hartland[3], Maria Kost-Alimova[3], Sigrun M Gustafsdottir[3], Christopher C Gibson[2] & Anne E Carpenter[1]

[1]Imaging Platform, Broad Institute of Harvard and MIT, Cambridge, Massachusetts, USA. [2]Recursion Pharmaceuticals, Salt Lake City, Utah, USA. [3]Center for the Science of Therapeutics, Broad Institute of Harvard and MIT, Cambridge, Massachusetts, USA. Correspondence should be addressed to C.C.G. (chris.gibson@recursionpharma.com) or A.E.C. (anne@broadinstitute.org).

Published online 25 August 2016; doi:10.1038/nprot.2016.105

**In morphological profiling, quantitative data are extracted from microscopy images of cells to identify biologically relevant similarities and differences among samples based on these profiles. This protocol describes the design and execution of experiments using Cell Painting, which is a morphological profiling assay that multiplexes six fluorescent dyes, imaged in five channels, to reveal eight broadly relevant cellular components or organelles. Cells are plated in multiwell plates, perturbed with the treatments to be tested, stained, fixed, and imaged on a high-throughput microscope. Next, an automated image analysis software identifies individual cells and measures ~1,500 morphological features (various measures of size, shape, texture, intensity, and so on) to produce a rich profile that is suitable for the detection of subtle phenotypes. Profiles of cell populations treated with different experimental perturbations can be compared to suit many goals, such as identifying the phenotypic impact of chemical or genetic perturbations, grouping compounds and/or genes into functional pathways, and identifying signatures of disease. Cell culture and image acquisition takes 2 weeks; feature extraction and data analysis take an additional 1–2 weeks.**



### INTRODUCTION

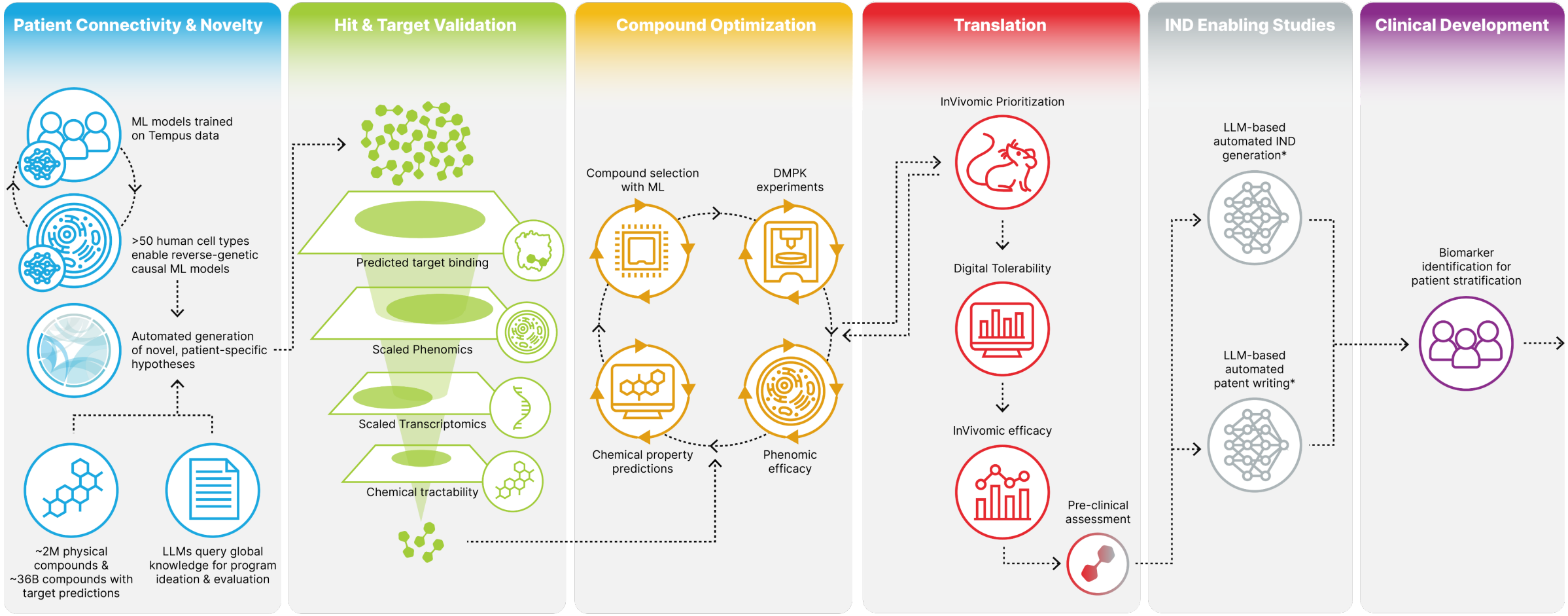
Phenotypic screening has been tremendously powerful for identifying novel small molecules as probes and potential therapeutics, and for identifying genetic regulators of many biological processes[1–4]. High-throughput microscopy has been a particularly fruitful type of phenotypic screening; it is often called high-content analysis because of the high information content that can be observed in images[5]. However, most large-scale imaging experiments extract only one or two features of cells[6], and/or aim to identify just a few 'hits' in a screen, meaning that vast quantities of quantitative data about cellular state remain untapped.

In this article, we detail a protocol for the Cell Painting assay, which is a generalizable and broadly applicable method for accessing the valuable biological information about cellular state that is contained in morphology. Cellular morphology is a potentially rich data source for interrogating biological perturbations, especially at a large scale[5,7–10]. The techniques and technology that are necessary to generate these data have advanced rapidly, and they are now becoming accessible to nonspecialized laboratories[11]. In this protocol, we discuss morphological profiling (also known as image-based profiling), contrast it with conventional image-anticancer drug sensitivity reflect mechanisms of action[12]—and gene expression—in which signatures related to small molecules, genes, and diseases were identified[13].

It is important to note that profiling differs from conventional screening assays in that the latter are focused on quantifying a relatively small number of features selected specifically because of a known association with the biology of interest. Profiling, on the other hand, casts a much wider net, and avoids the intensive customization that is usually necessary for problem-specific assay development in favor of a more generalizable method. Therefore, taking an unbiased approach via morphological profiling offers the opportunity for discovery unconstrained by what we know (or think we know). It also holds the potential to be more efficient, as a single experiment can be mined for many different biological processes or diseases of interest.

In morphological profiling, measured features include staining intensities, textural patterns, size, and shape of the labeled cellular structures, as well as correlations between stains across channels, and adjacency relationships between cells and among intracellular structures. The technique enables single-cell resolu-

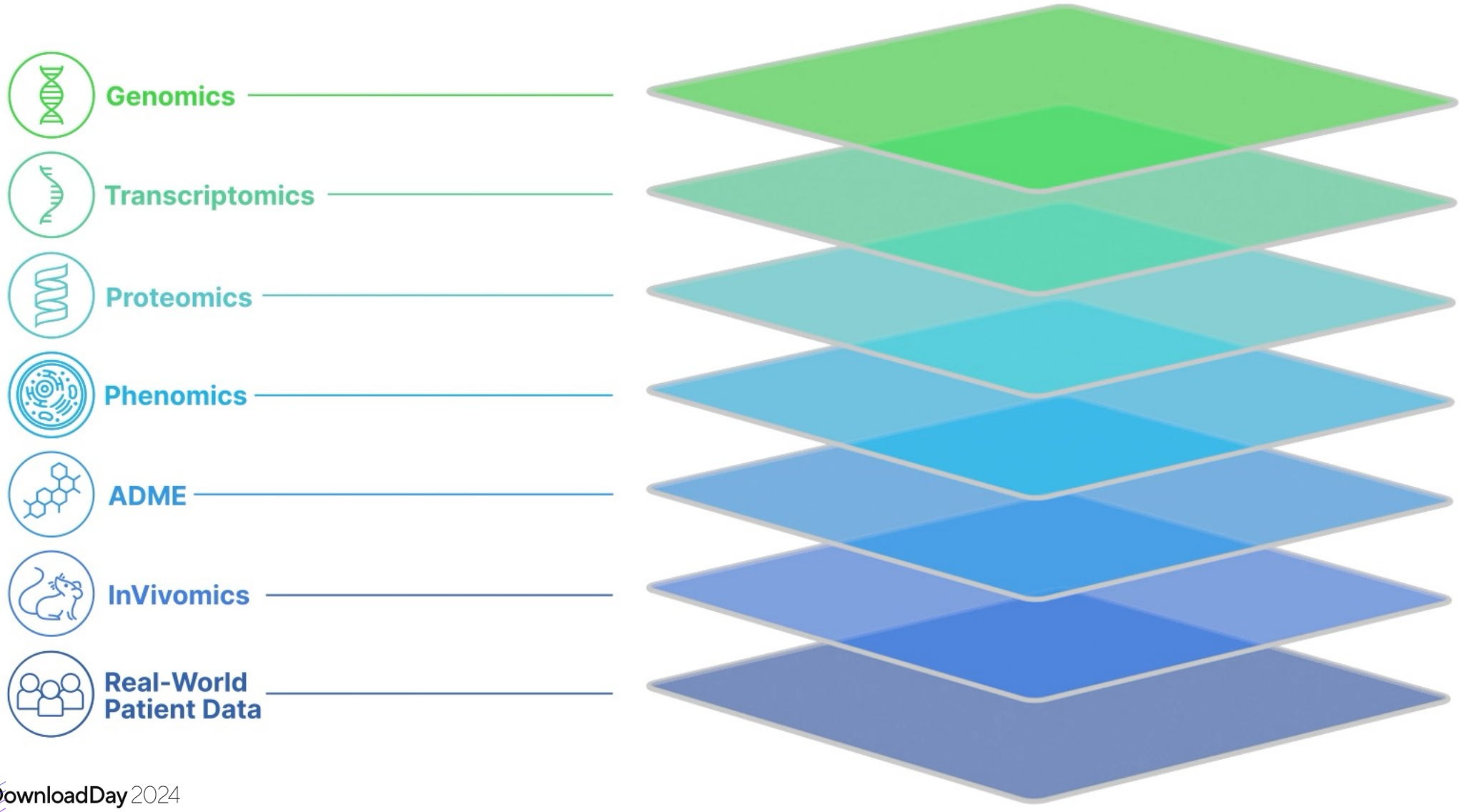
# To truly industrialize drug discovery, point solutions must be integrated as modules across many diverse steps



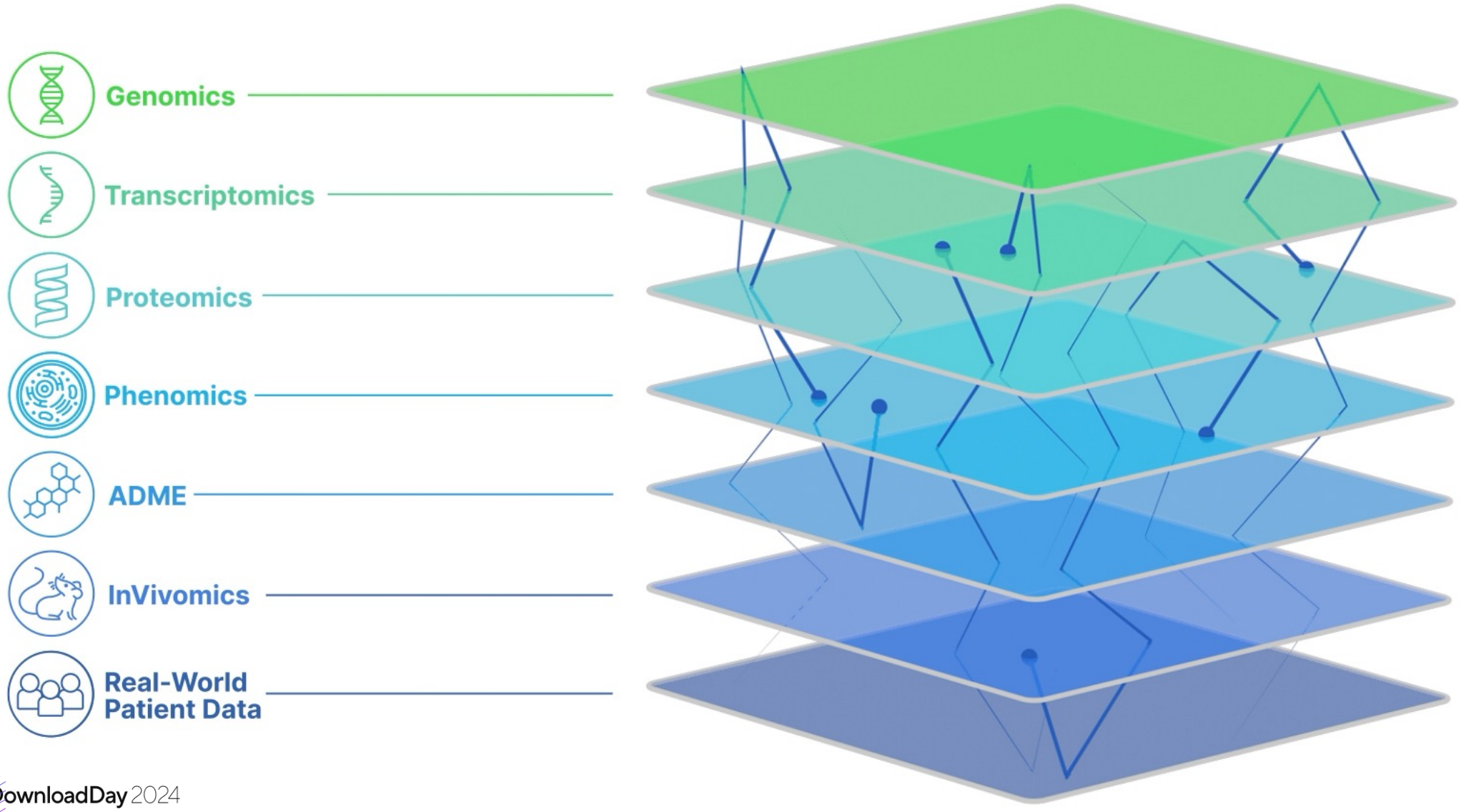

*Currently being explored


LOWE

# Connecting data layers to build digital maps of biology

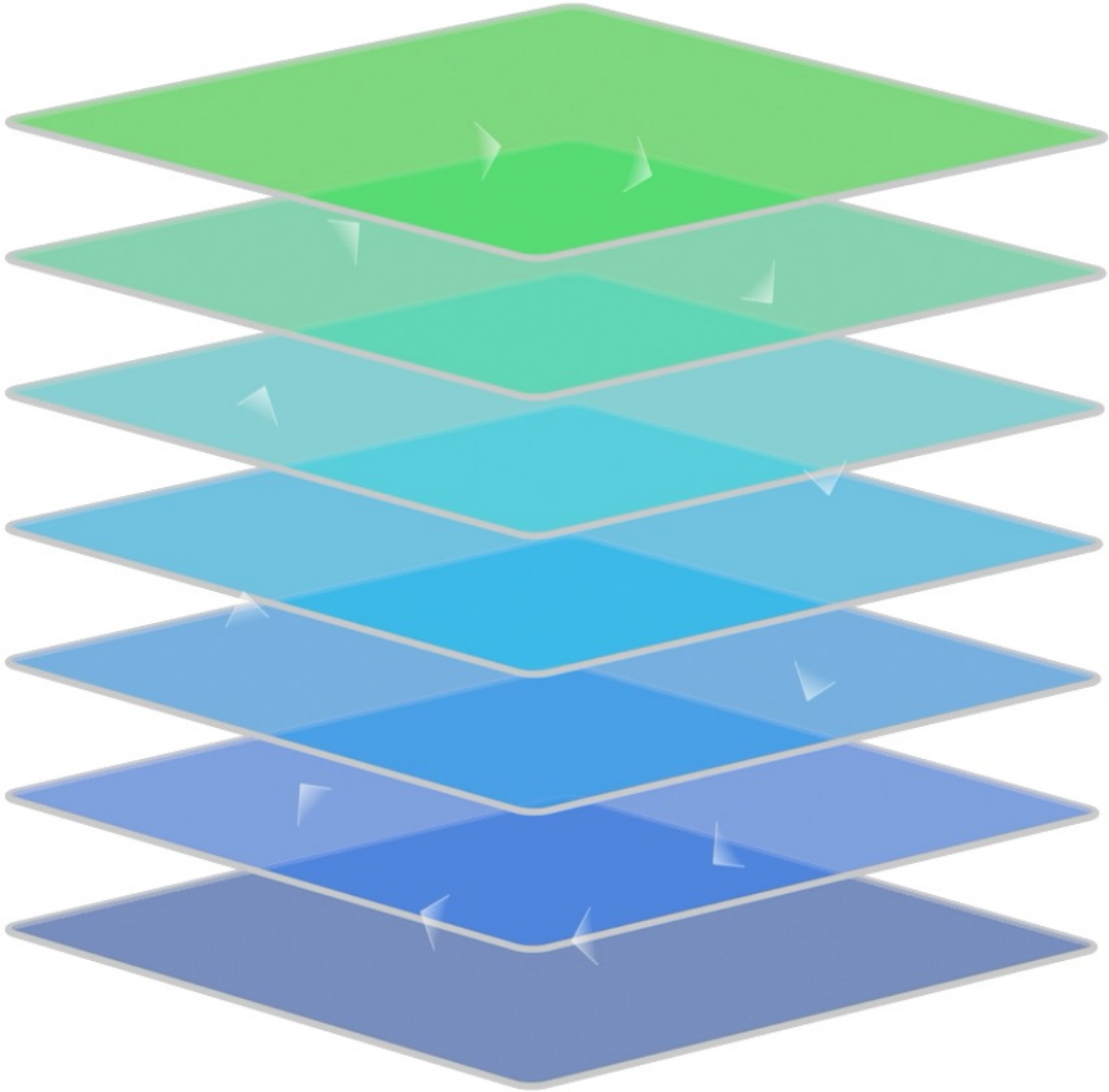


# Connecting data layers to build digital maps of biology



# Connecting data layers to build digital maps of biology

- Genomics
- Transcriptomics
- Proteomics
- Phenomics
- ADME
- InVivomics
- Real-World Patient Data



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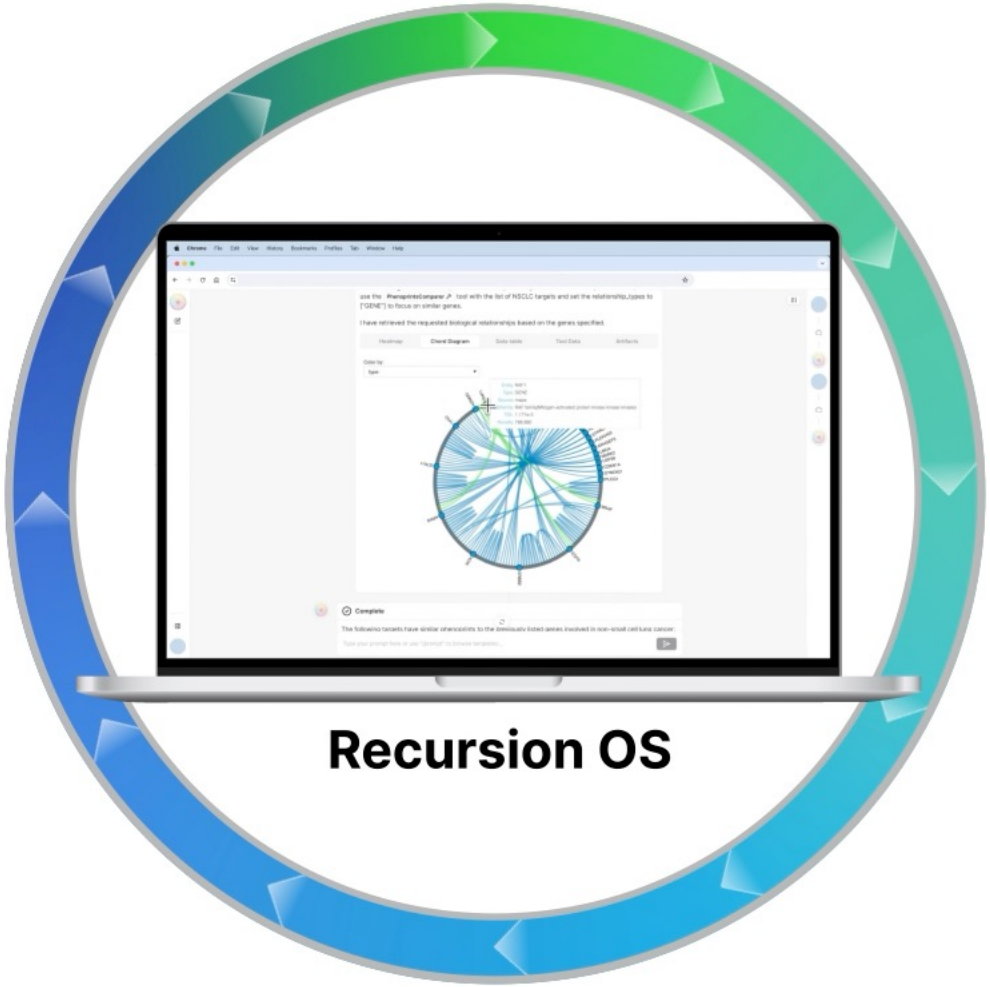
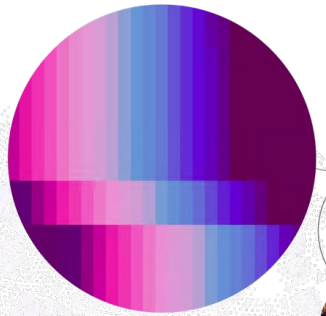
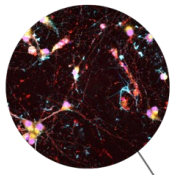


# Where are we right now?

# What have we learned?





Fit for Purpose Data is Critical and the primary bottleneck

More Compute is needed and few are investing at our scale

More data and compute enables more generalizable Models

# Industrializing stages of our drug discovery efforts leads to massive efficiency improvements

**2022**
Pre-Industrialization

**2023**
Post-Industrialization

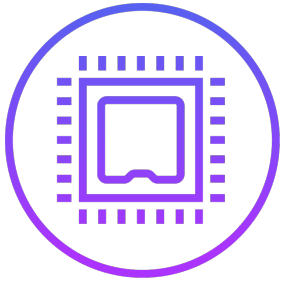
**Half of 2024**
Continued Improvement

| | | |
|---|---|---|
| Team of **40** people → | Team of **7** people → | **~1** FTE equivalent |
| **30** program hypotheses explored → | **115** program hypotheses explored → | **201** program hypotheses *initiated* |

# Four ingredients needed to continue leading TechBio at the tipping point

People

Data



Compute

Capital

# Four ingredients needed to continue leading TechBio in an industry at the tipping point


People

# Four ingredients needed to continue leading TechBio in an industry at the tipping point

Data

# Four ingredients needed to continue leading TechBio in an industry at the tipping point

Compute

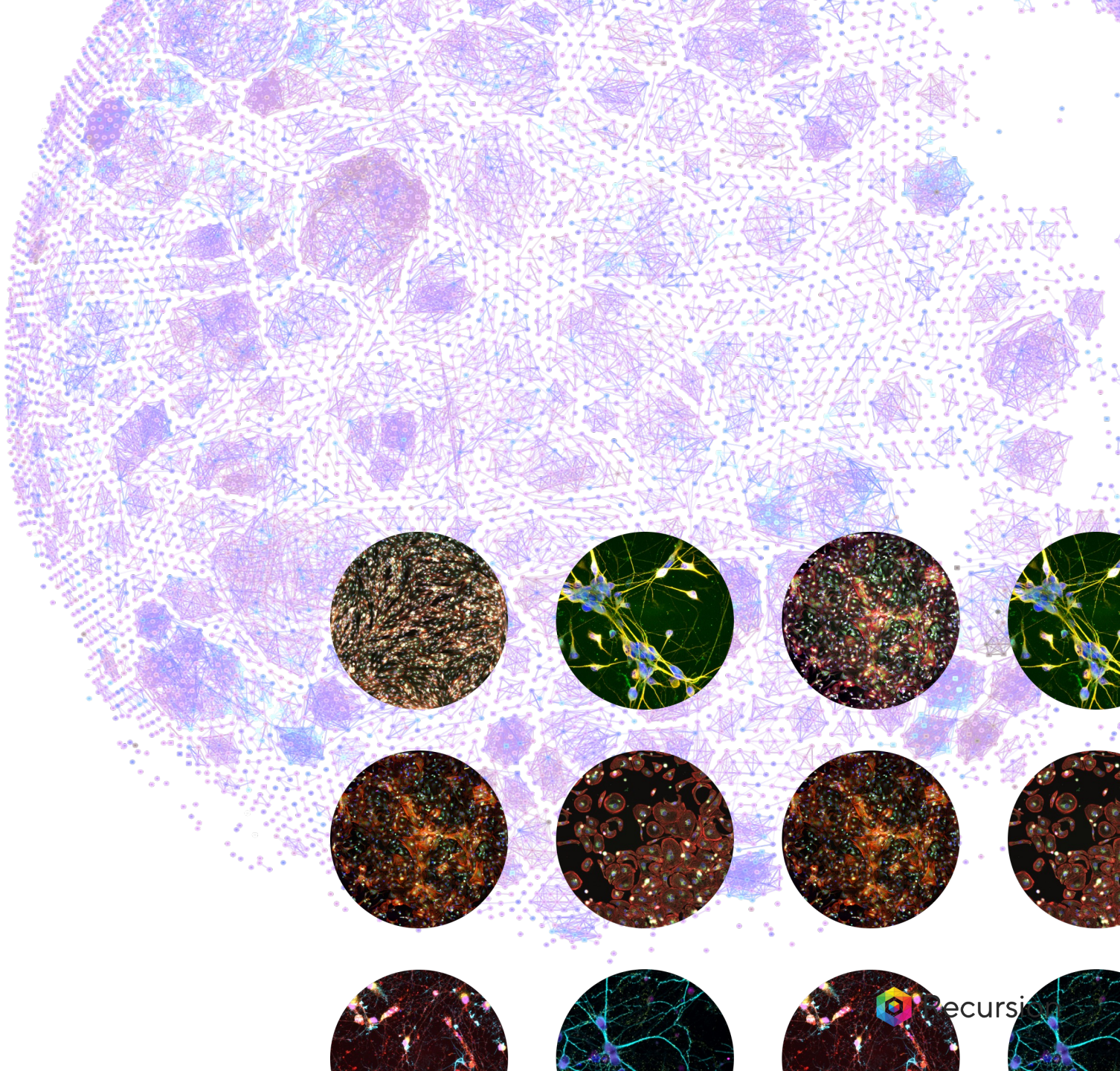
# Four ingredients needed to continue leading TechBio in an industry at the tipping point

# Our Purpose

We exist to run an experiment...

….An experiment to determine if there might be a better way to discover and develop drugs...

...We need this sort of ambition in BioTech if we hope to have a chance of transforming our ability to impact patients and drive down the cost of medicines.



# What to Expect from Recursion in the Near Term

**Pipeline**

- 7 clinical trial readouts expect over the next ~18 months with new programs embracing our tools to drive novel chemistry against novel targets advancing quickly

**Partnership**

- Roche & Genentech: program optioned in oncology continues to progress with potential additional near-term program & very near-term map options
- Bayer: On track to complete 25 unique multi-modal data packages in Q3 2024 with first joint Project now advancing rapidly towards Lead Series nomination

**Platform**

- Internal programs now initiated by LLM with multiple hit nominations for LLM-generated programs with more on the way
- Moving towards large-scale multi-omics and generalizable foundation models with first genome-scale transcriptomics map and patient data
- Data and tools available to biopharma and commercial users: Bayer will be 1st beta-user of LOWE for drug discovery and development

Recursion

# The Recursion Operating System

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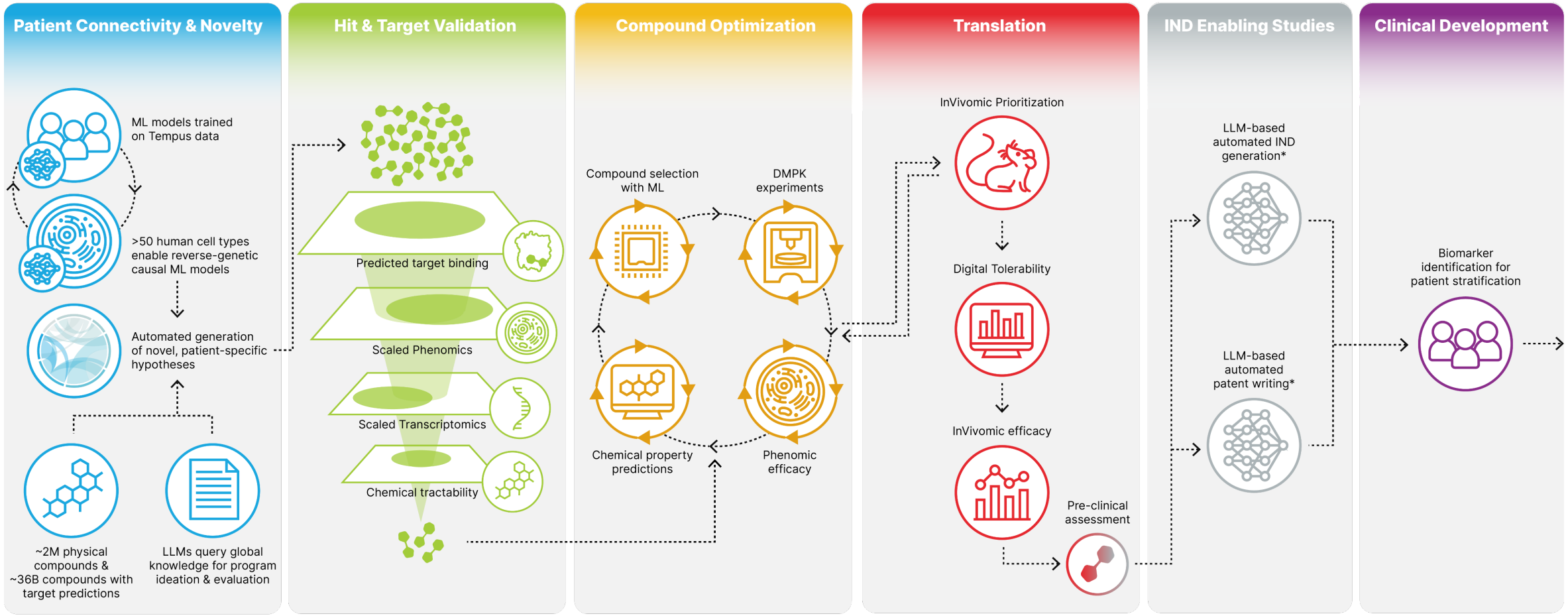
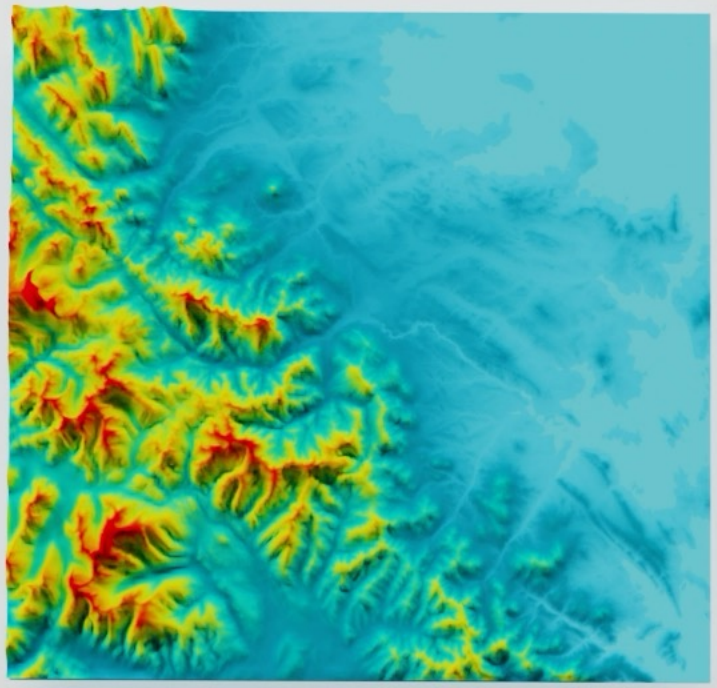
Wet Lab
Dry Lab

# Virtuous Cycles Connect Systems for Efficient End-to-End Drug Discovery




*Currently being explored

# Virtuous Cycles Enable Efficient Exploration of Biological Variability



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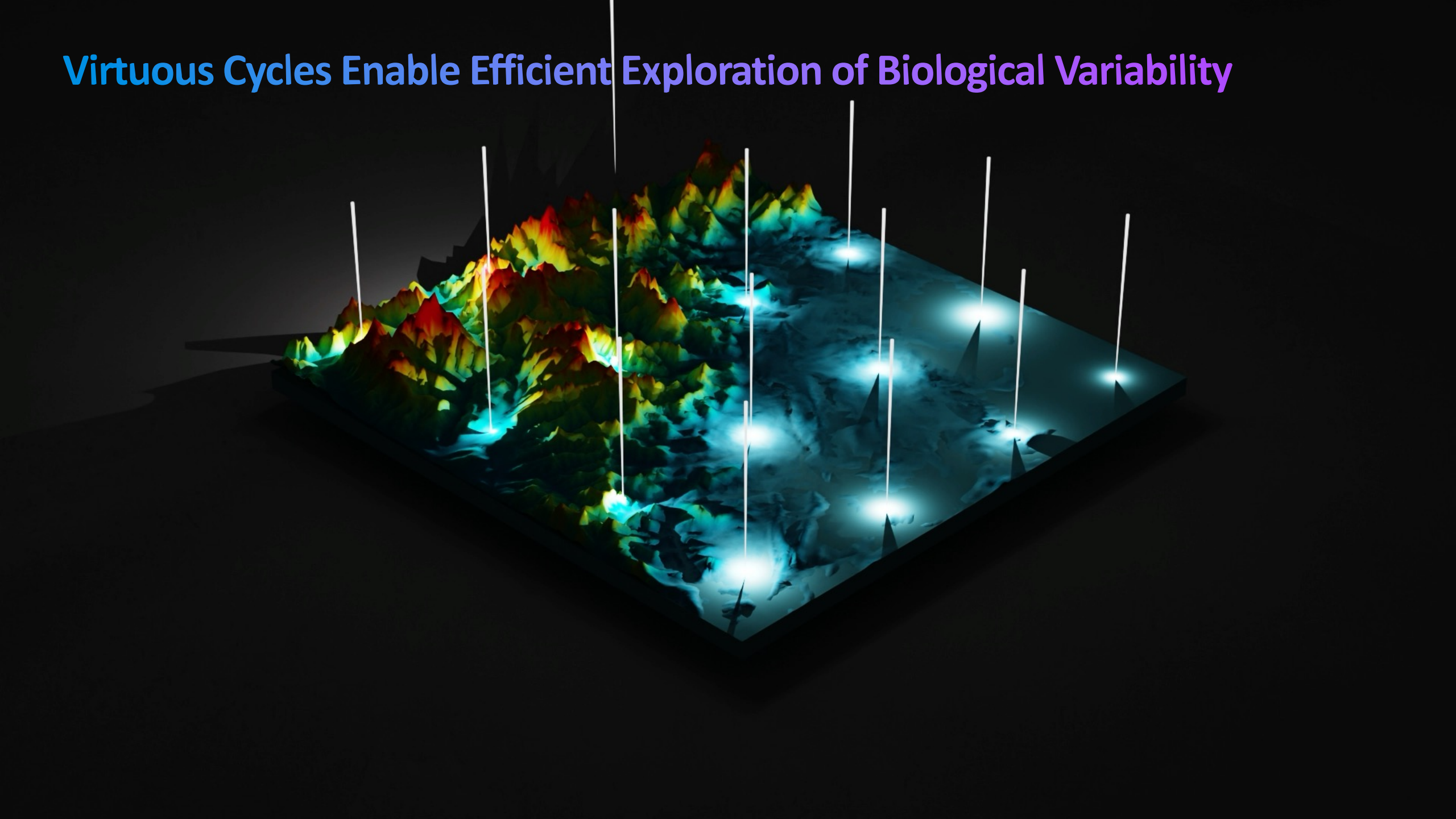

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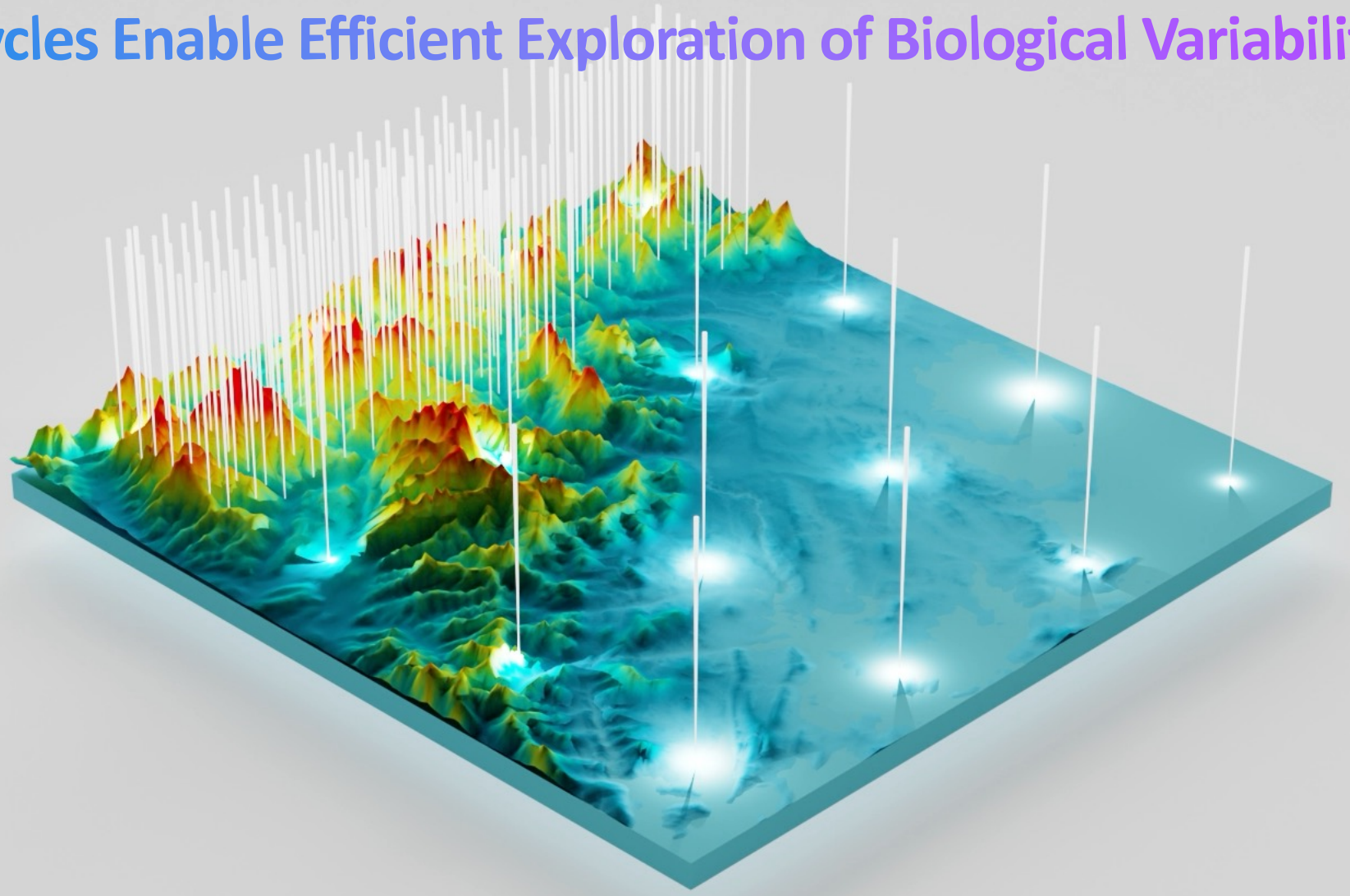
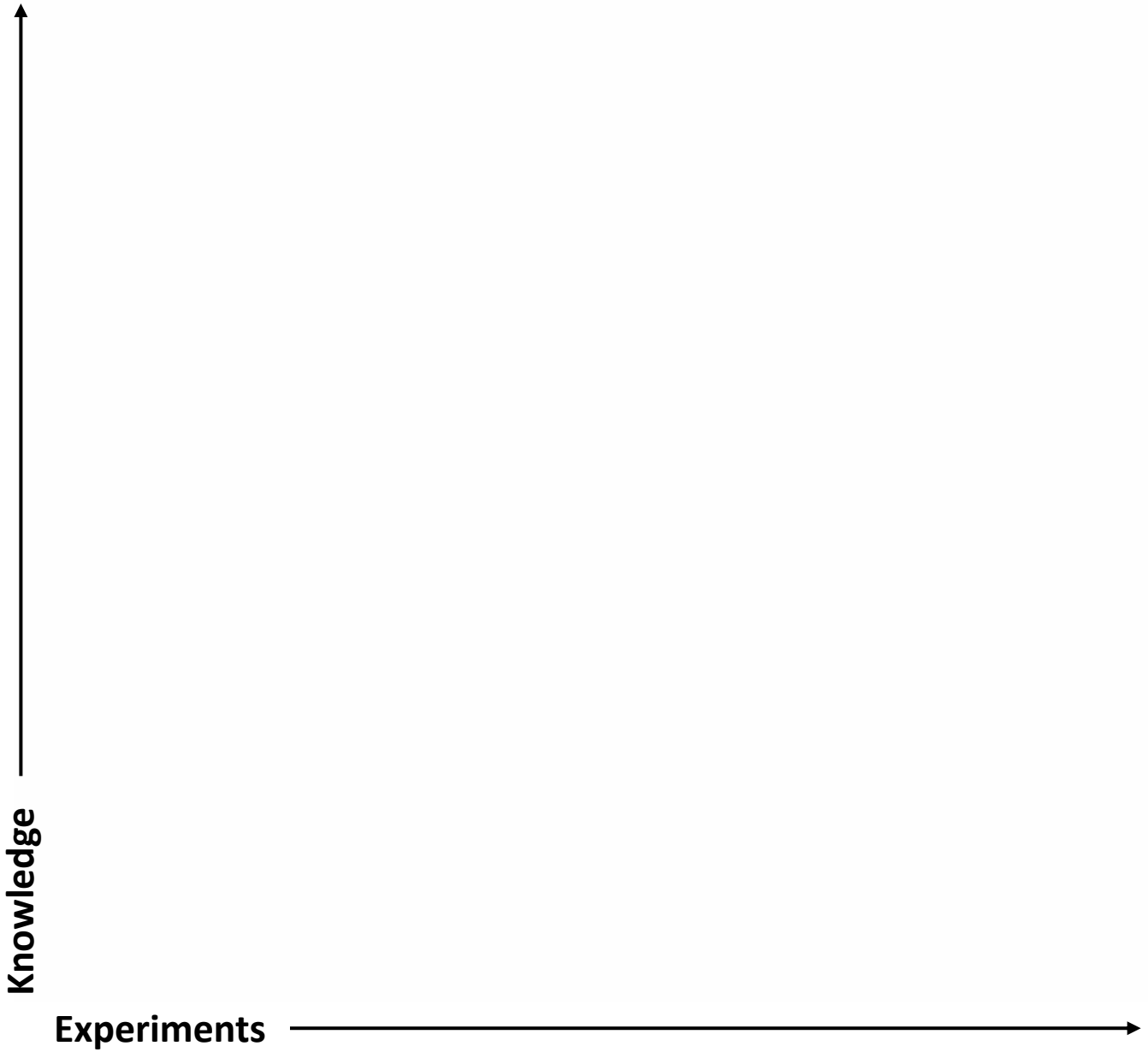
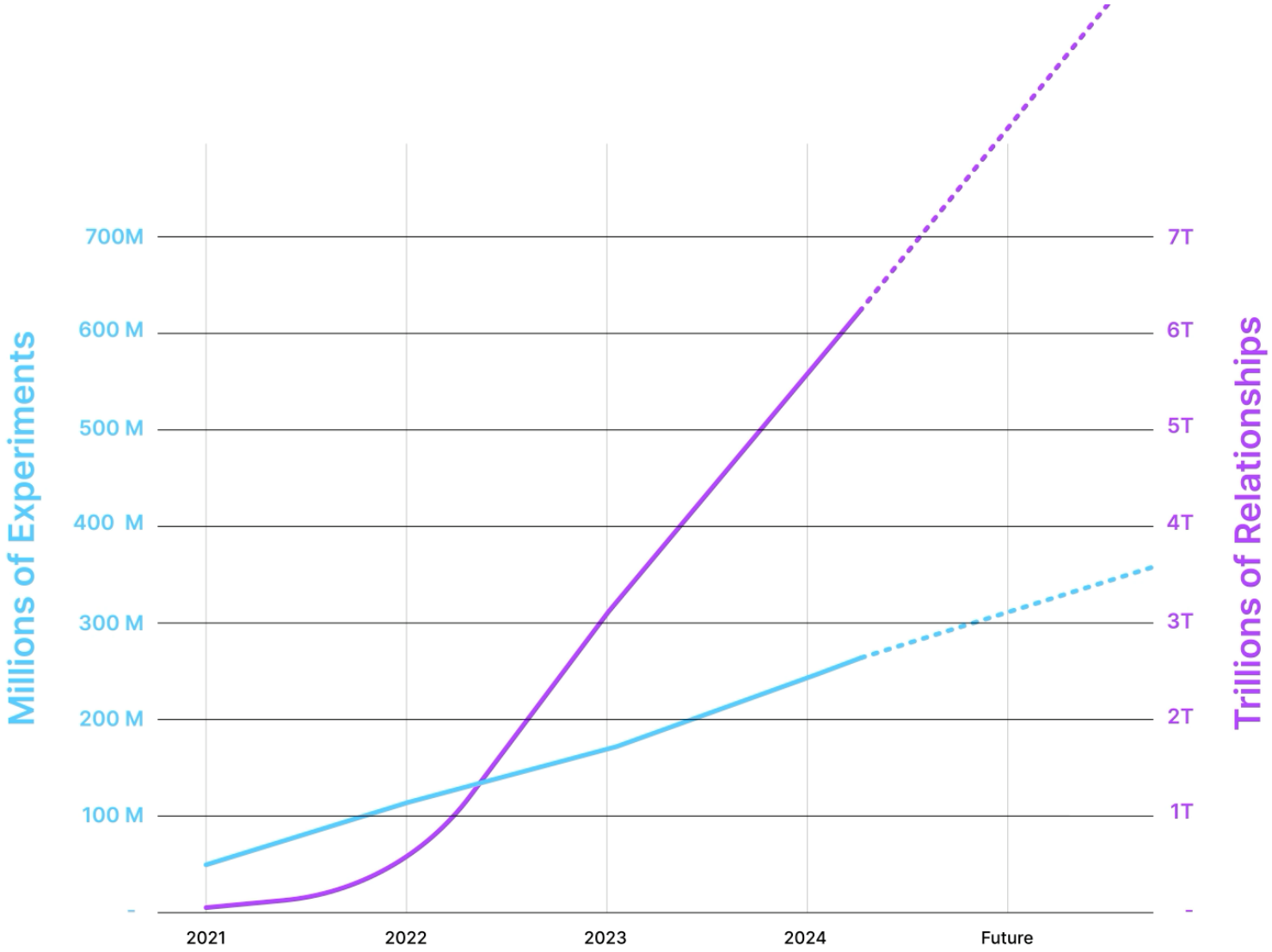


AI Strategy Experiments

Randomized Experiments



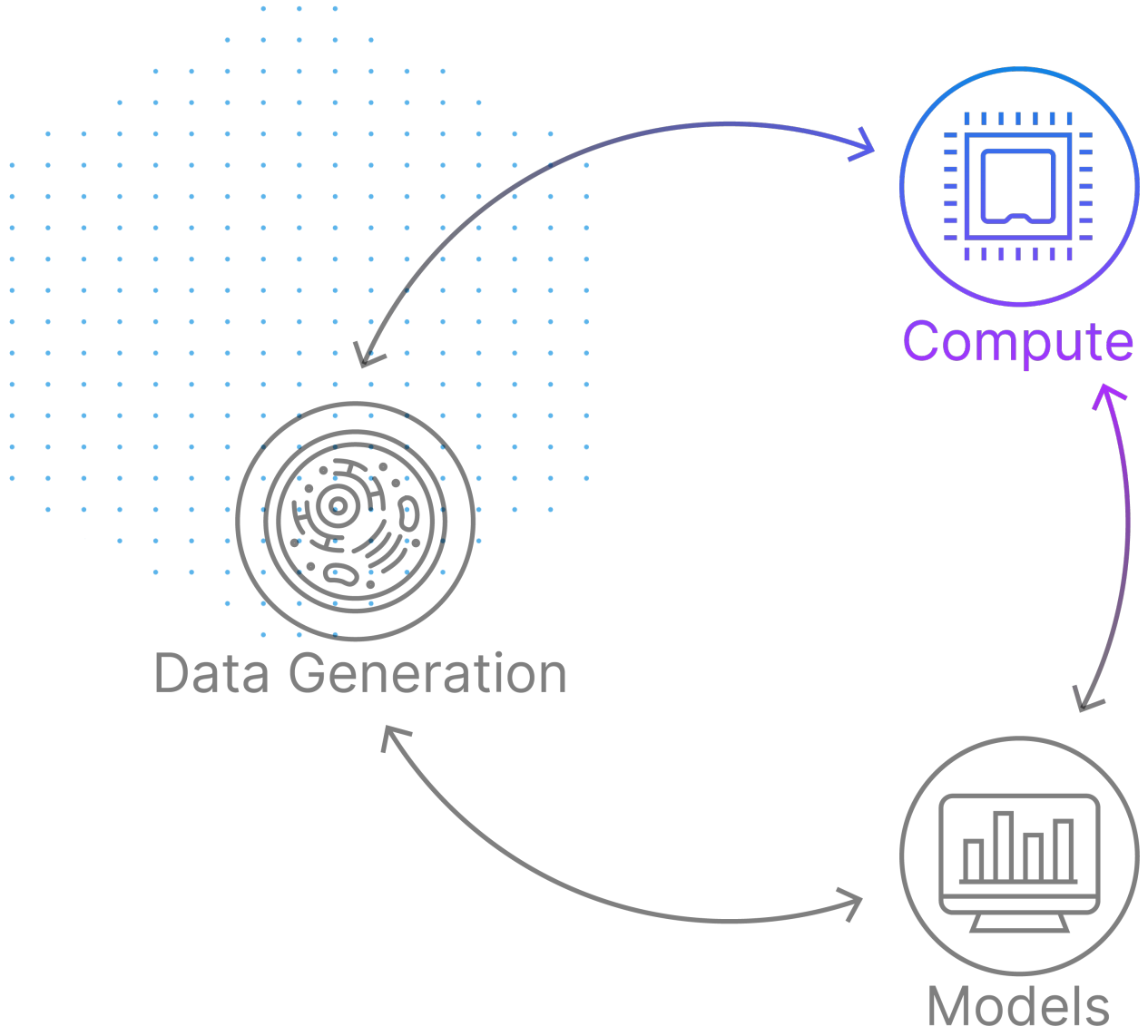
# Virtuous Cycles Drive Superlinear Knowledge Creation




Compute
Data generation
Models

Recursion

# Compute



# Ahead of the curve: our supercomputer journey

**BioHive-1:**
- 320 NVIDIA A100's
- #84 on TOP500 list when built

**BioHive-2**:
- 504 NVIDIA H100's, 4X BioHive-1
- Top ranked supercomputer in pharma
- #35 on TOP500 list

2020
Initial discussions began

2021

2023

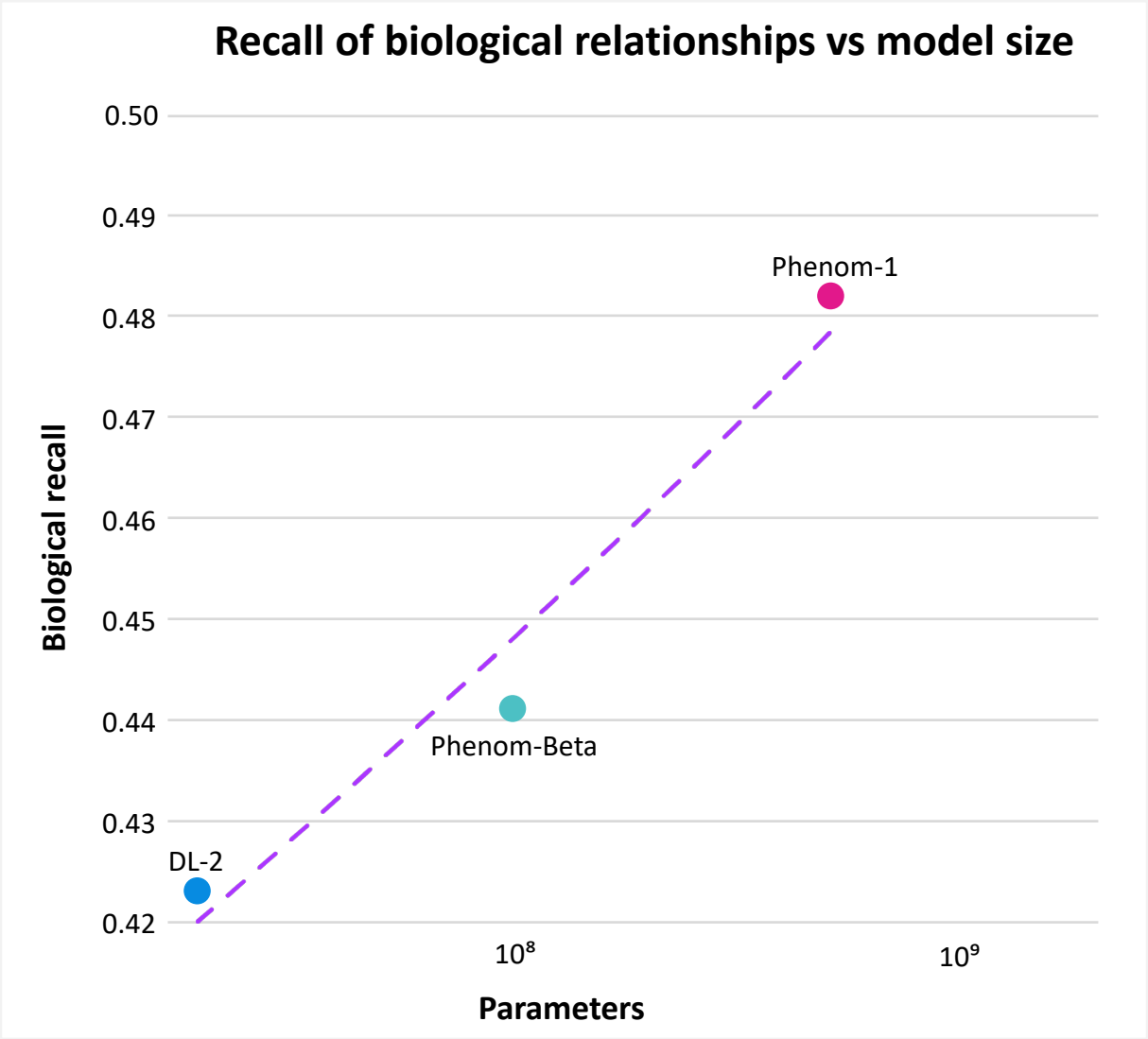
2024

NVIDIA

CNBC

**Nvidia invests $50 million in biotech company Recursion for A.I. drug discovery**

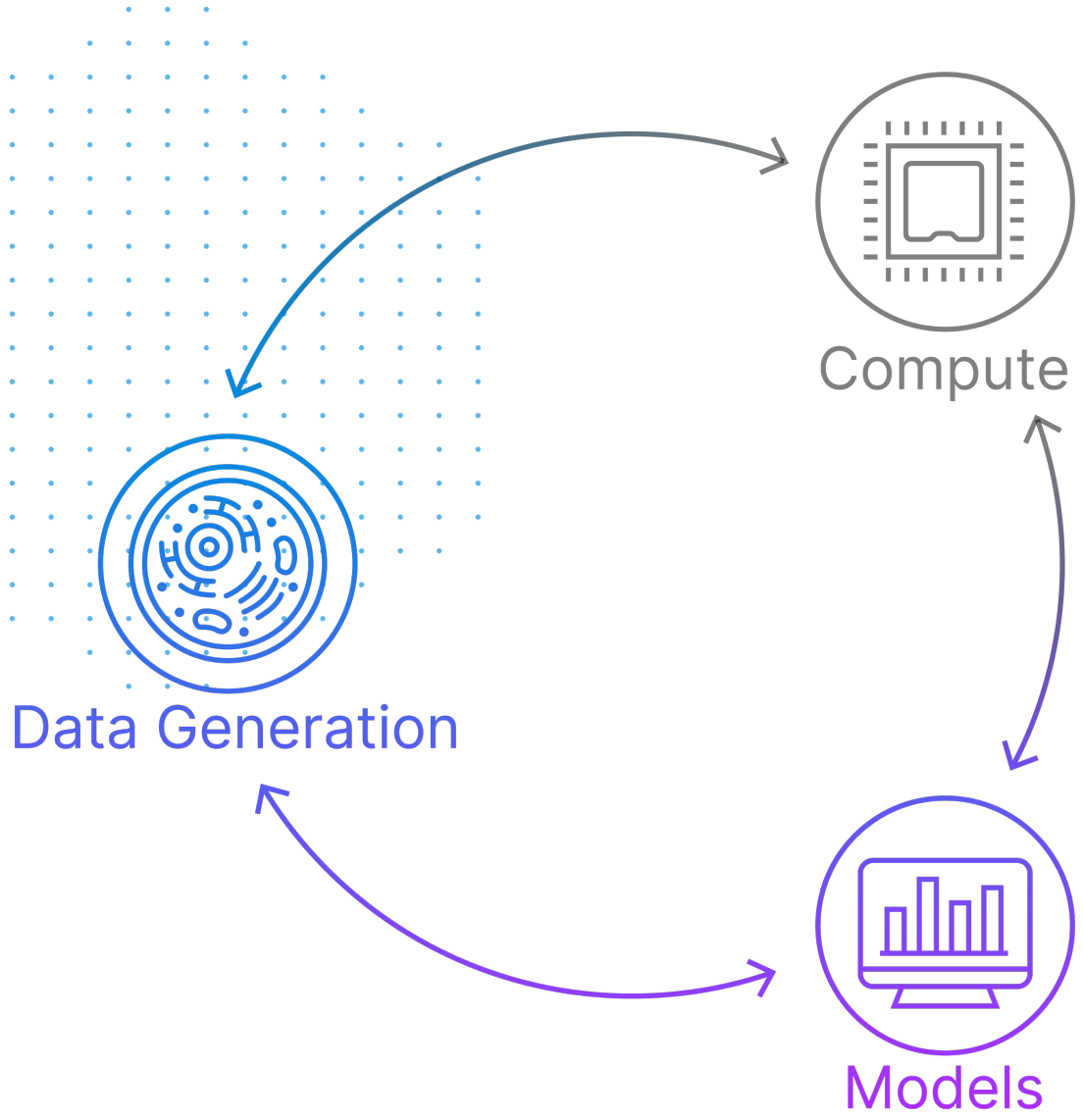
# Larger datasets and Increased Computation Yield Superior Models



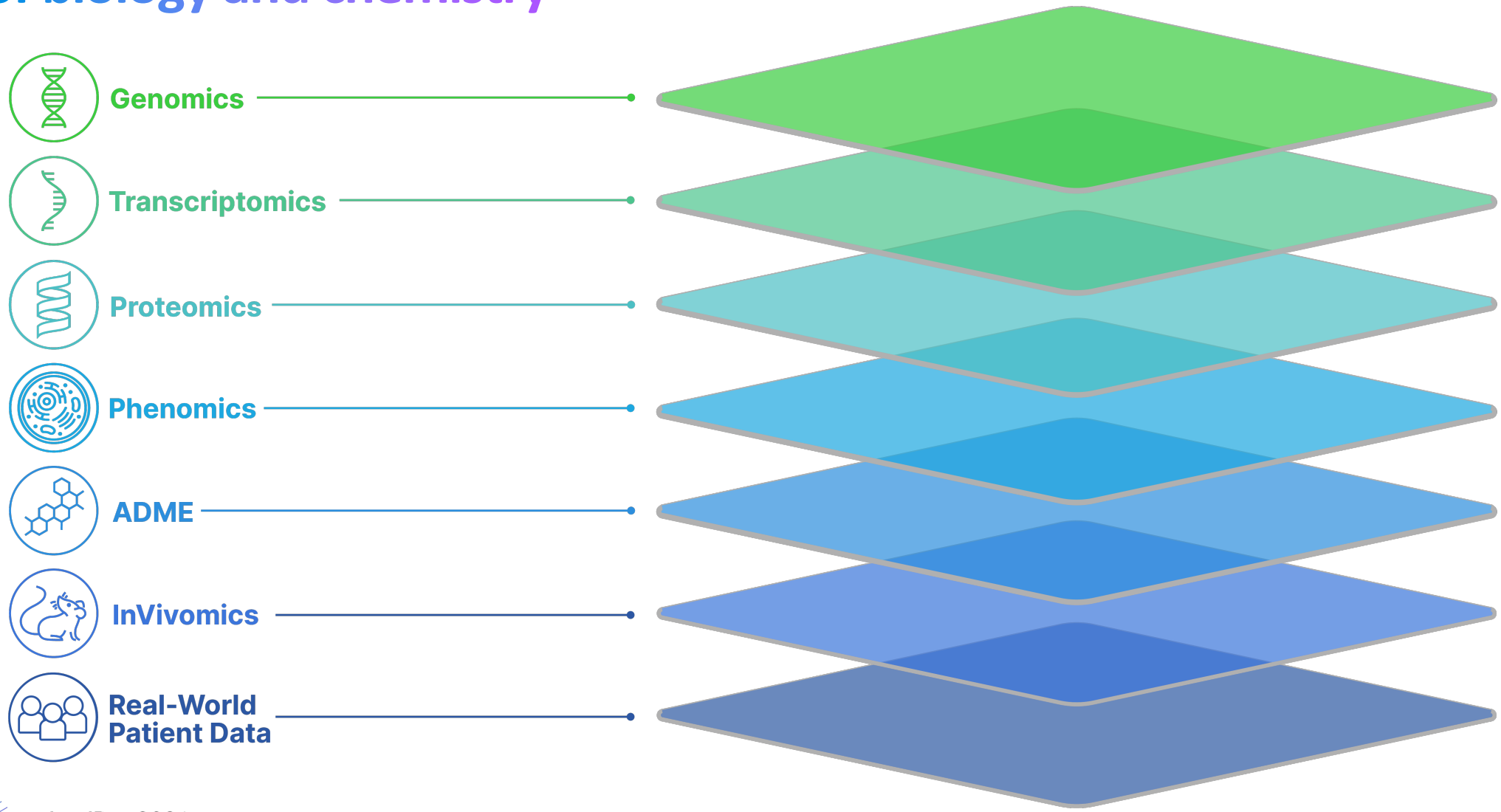
# 35th fastest supercomputer in the world!

Recursion

# Data Generation and Models



# Standardizing and automating experiments to capture multiple layers of biology and chemistry



# Phenomics: Foundation models improve at detecting biology

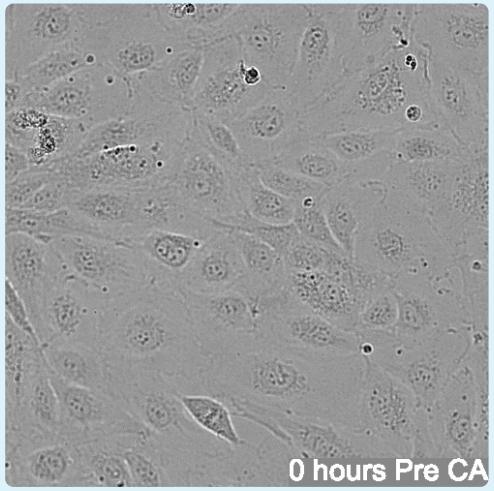
## DATA GENERATION

**>250 million** experiments

**>50** human cell types

**>1 trillion** neurons generated

Brightfield to capture dynamics

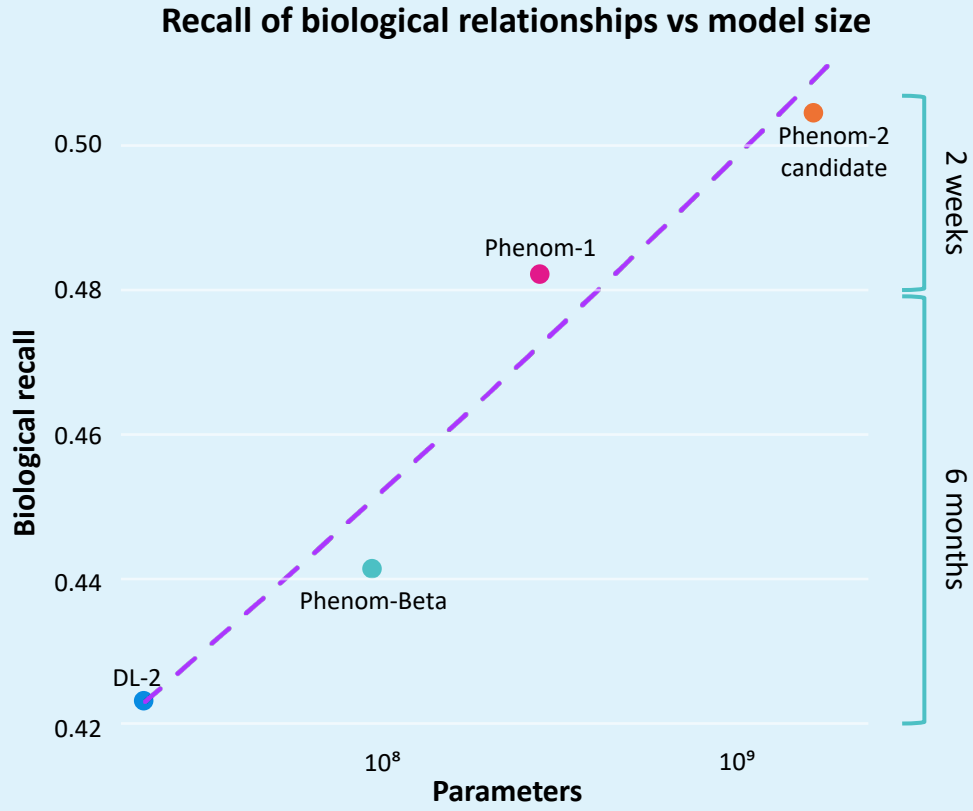



## MODELS

2 weeks of rapid iteration on Biohive-2 enabled

**25.7%**

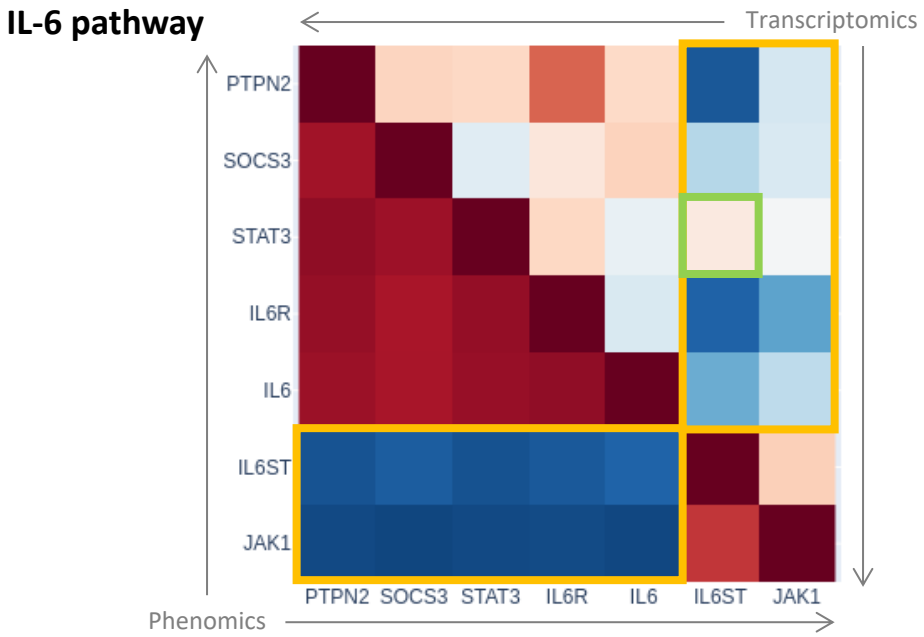
increase in expressed gene knock-outs detected



# Transcriptomics: Multimodal data scales validation and mapping

## DATA GENERATION

**>1M** samples sequenced
**First** genome-scale transcriptomic map




## MODELS

Replaced time-consuming, disease-specific validation assays with portfolio-wide **multimodal model** workflow

**90%**

Ability to predict compounds that *failed* later disease-relevant assays in internal tests

**60%**

Ability to predict compounds that *passed* later disease-relevant assays in internal tests

# ADME: Data and scale lead to State of the Art models

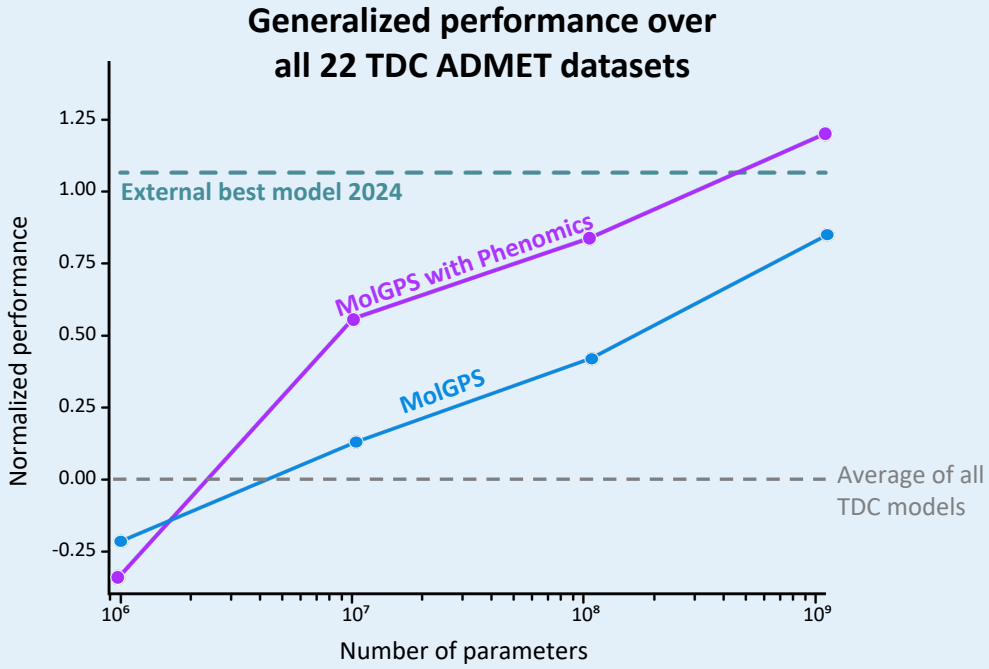
## DATA GENERATION

Estimated **90x** throughput over manual approach

**>750** compounds per week

## MODELS

**Our single generalizable model** improves with multimodal data and model size



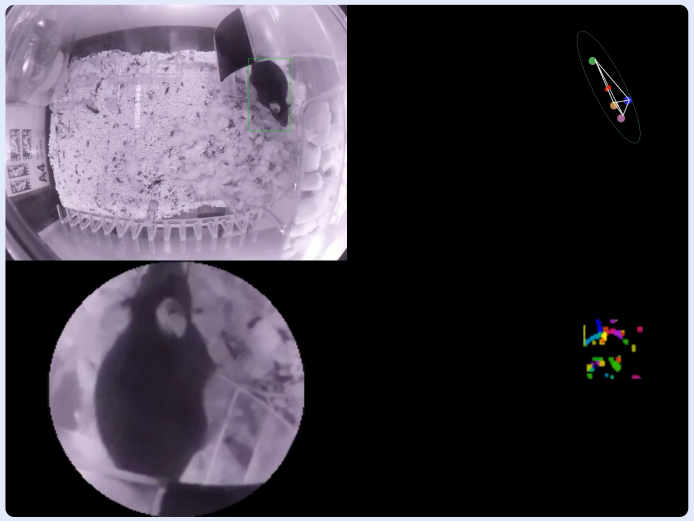
# InVivomics accelerates decision-making in late discovery

## DATA GENERATION

**>1,000** digital mouse cages

150 digital **rat cages** in 2024

**Social housing** increases relevance



## MODELS

- Machine learning enables scale by extracting signals from video and temperature sensors
- Applied across breadth of Recursion portfolio
- Designed to select the right molecule at the right dose before entering studies

# Patient Data: Path to uncover novel disease drivers with Maps

## DATA GENERATION

TEMPUS

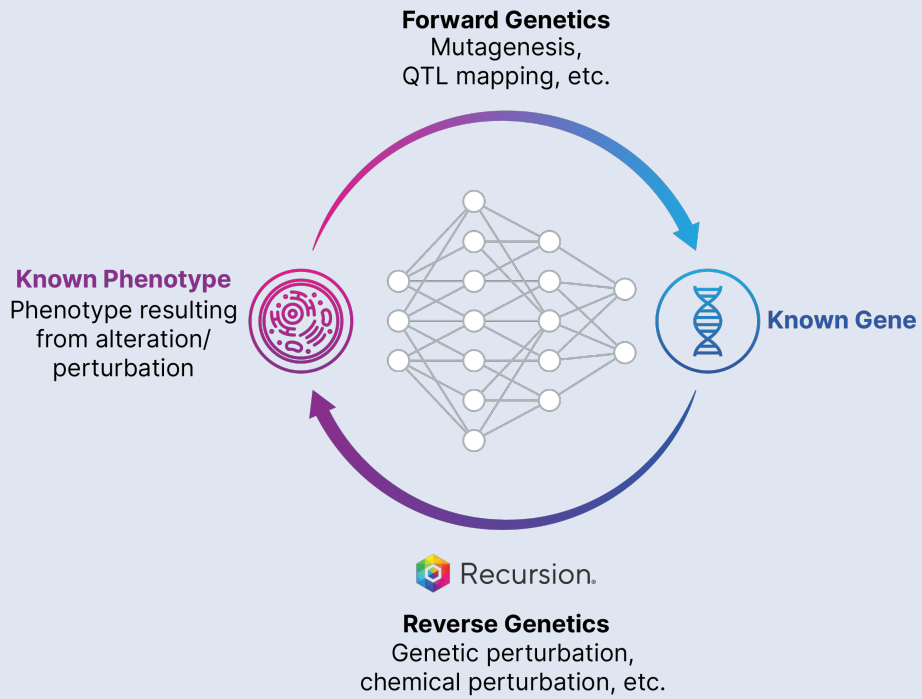
**>20 PB** of real-world multi-modal oncology data

Helix

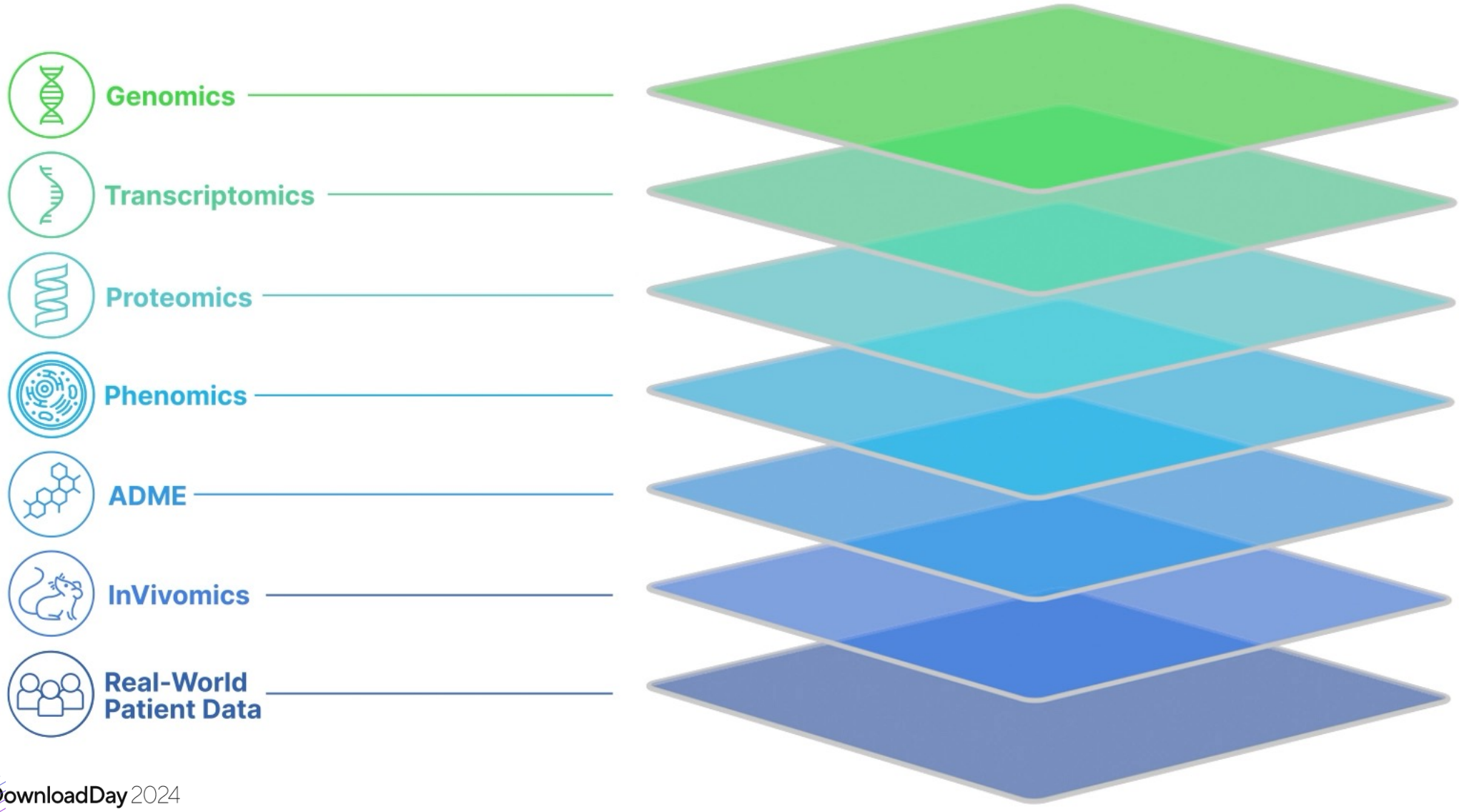
**Hundreds of thousands** of unique de-identified patient records across diverse therapeutic areas

## MODELS

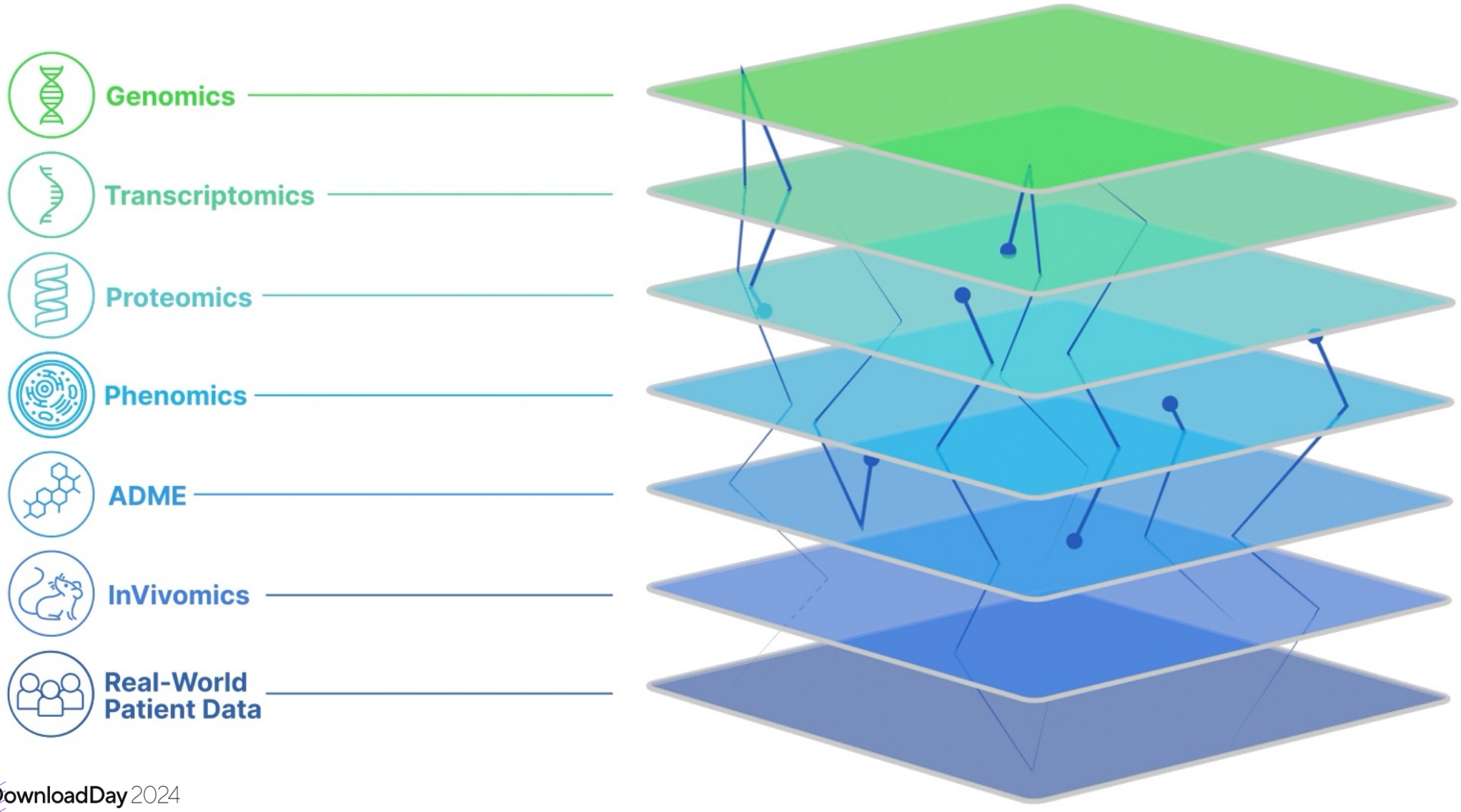
Combining Recursion maps of biology with patient clinical data unlocks causal modeling to find novel targets



# Connecting data layers to build digital maps of biology

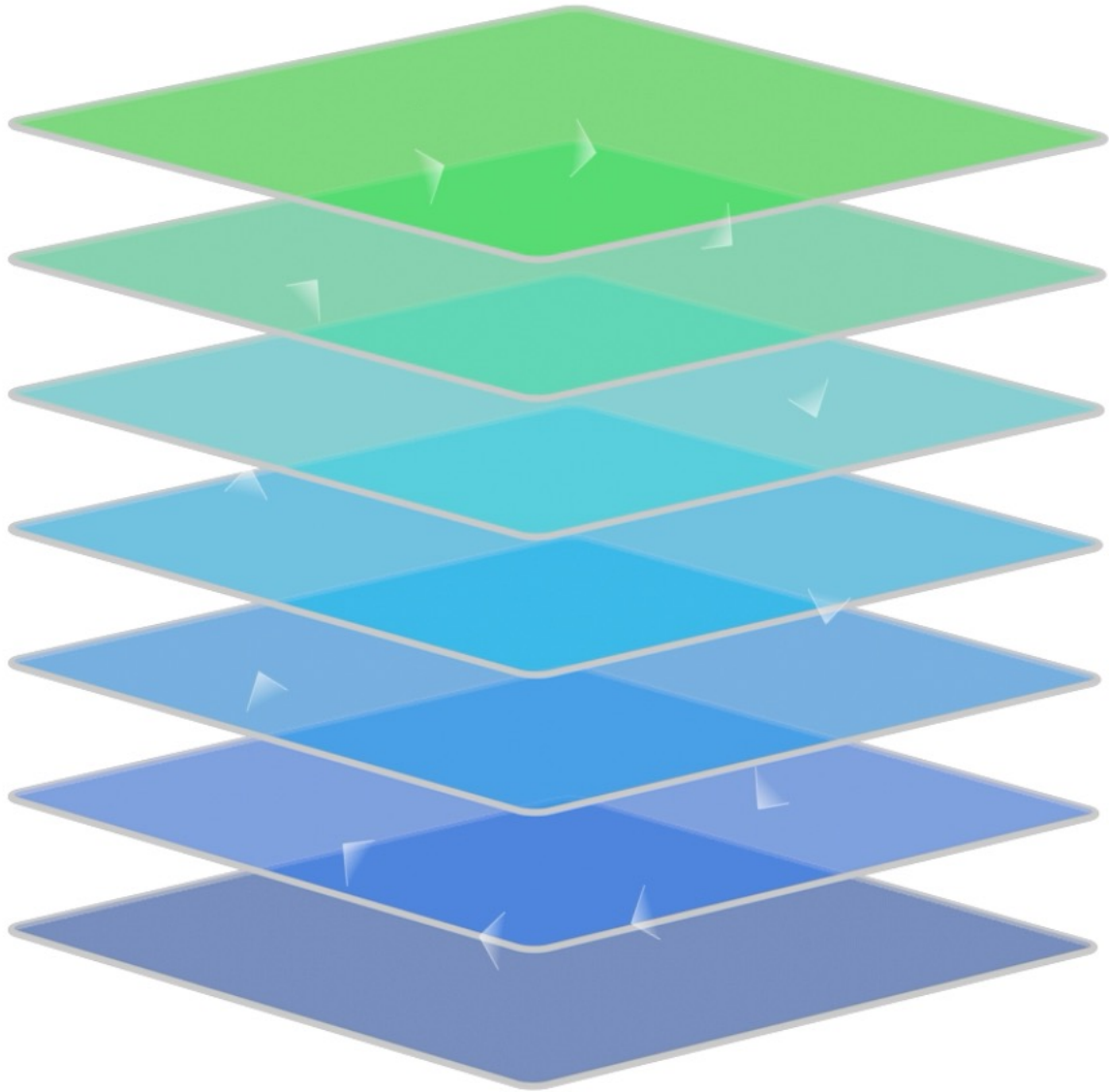


# Connecting data layers to build digital maps of biology



# Connecting data layers to build digital maps of biology

- Genomics
- Transcriptomics
- Proteomics
- Phenomics
- ADME
- InVivomics
- Real-World Patient Data



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- Genomics
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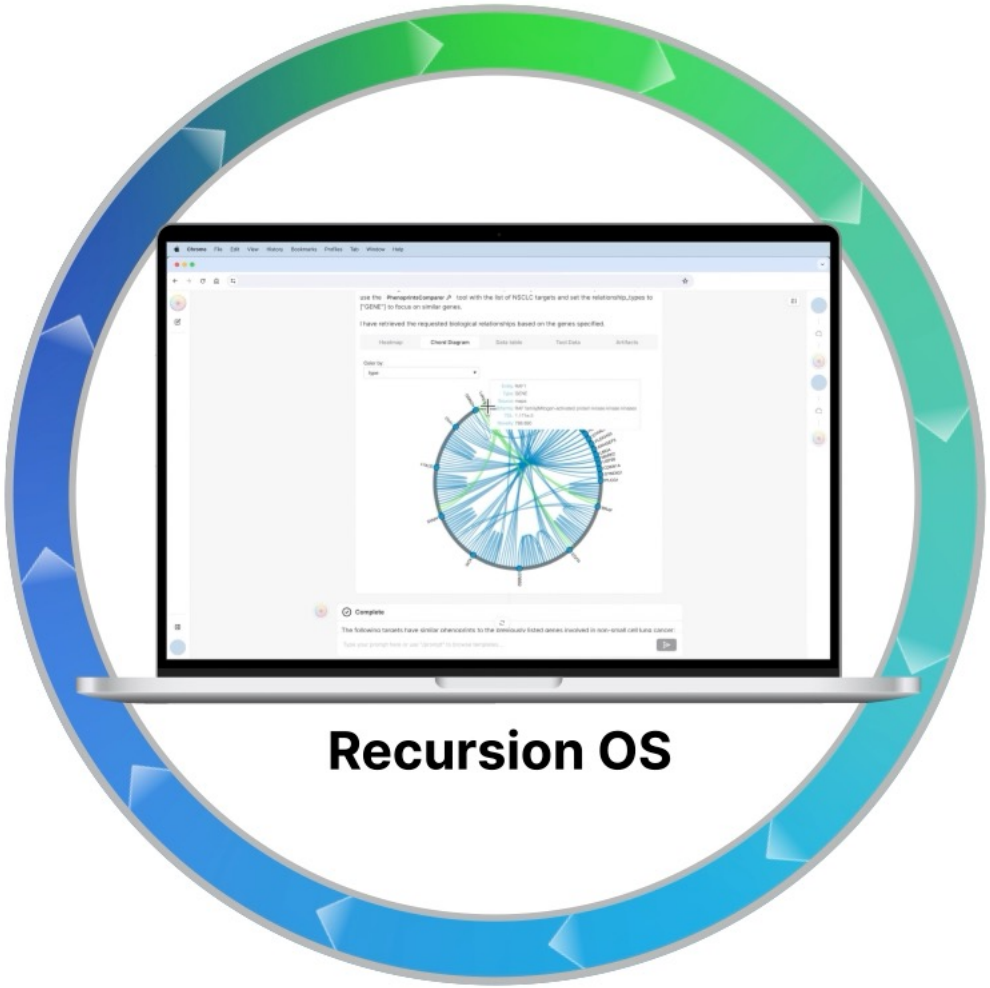
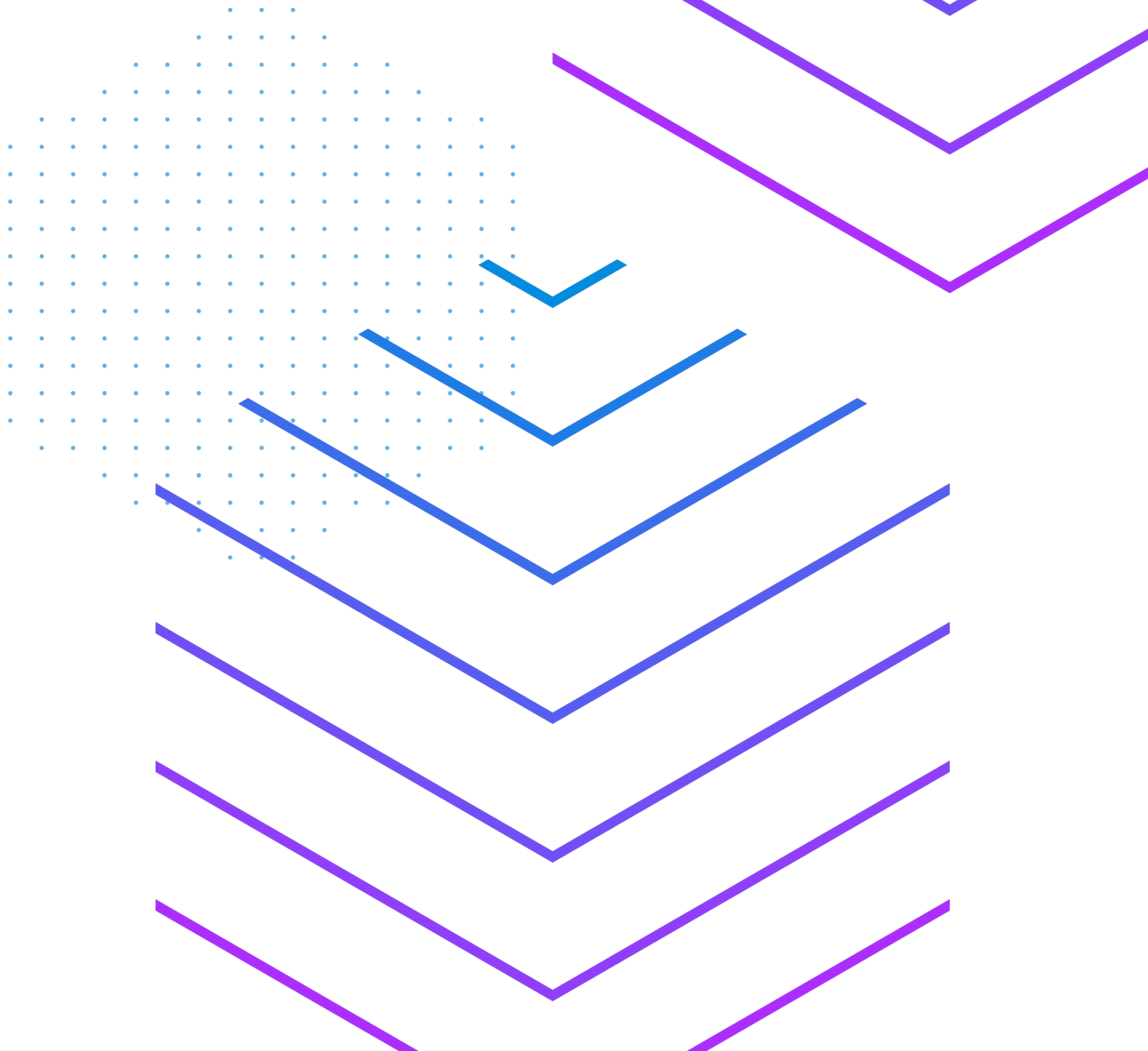


Recursion

# Utility of the OS



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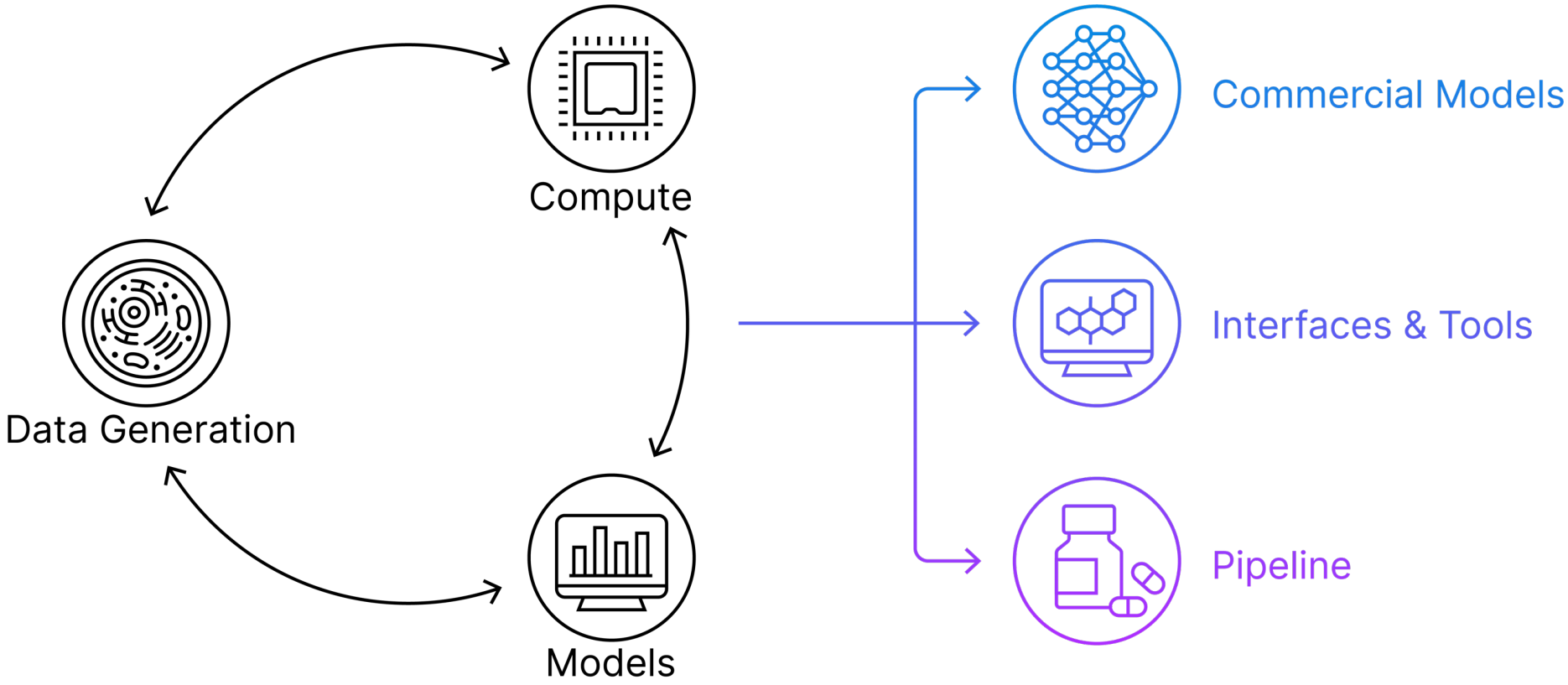
# The Recursion OS: Utility across multiple potential product verticals



# Commercial Models: Capitalizing on our data and foundation models

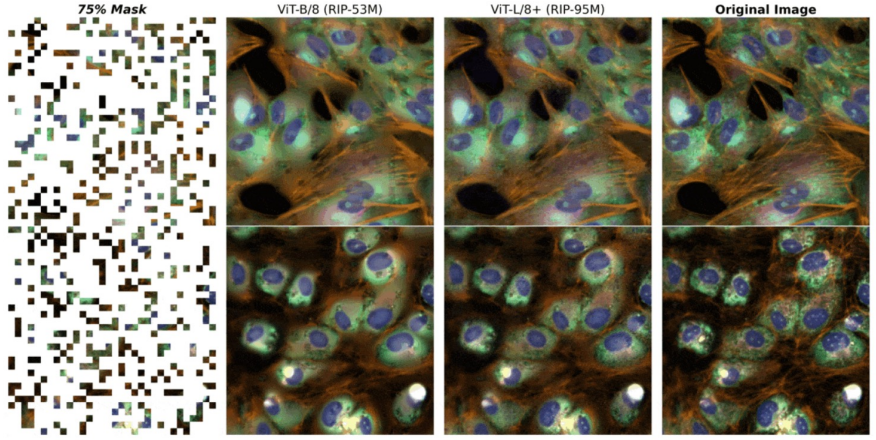
NVIDIA

Home AI Data Center Driving Gaming Pro Graphics Rc

## Phenomenal AI for Pharma: Recursion Brings Phenom-Beta Model to BioNeMo

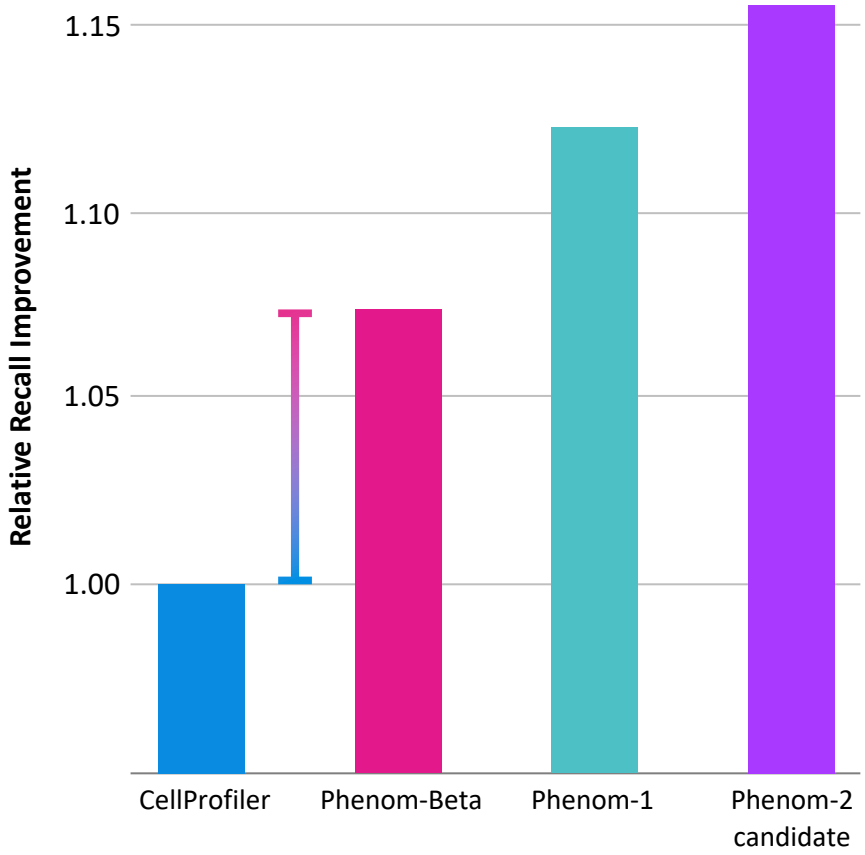
Recursion is the first hosting partner offering an AI model through BioNeMo cloud APIs: Phenom-Beta, a vision transformer model that extracts biologically meaningful features from cellular microscopy images.

This capability can provide researchers with insights about cell function and help them learn how cells respond to drug candidates or genetic engineering.




Phenom-Beta performed well on image reconstruction tasks, a training metric to evaluate model performance. Read the NeurIPS workshop paper to learn more.

**Phenom-Beta, available on NVIDIA BioNeMo, outperforms open-source "gold standard" CellProfiler**



# Interfaces and Tools: bringing together modules spanning the drug discovery process

Phenomics

Compound selection with ML

Patient-specific hypotheses

Phenom-1

Chemical tractability

InVivomic prioritization

LLMs & literature search

InVivomic efficacy

Chemical property predictions

Predicted target binding

Tempus data ML models

Phenomic efficacy

Patient stratification

Transcriptomics

MatchMaker

Digital tolerability

DMPK

Compound ordering

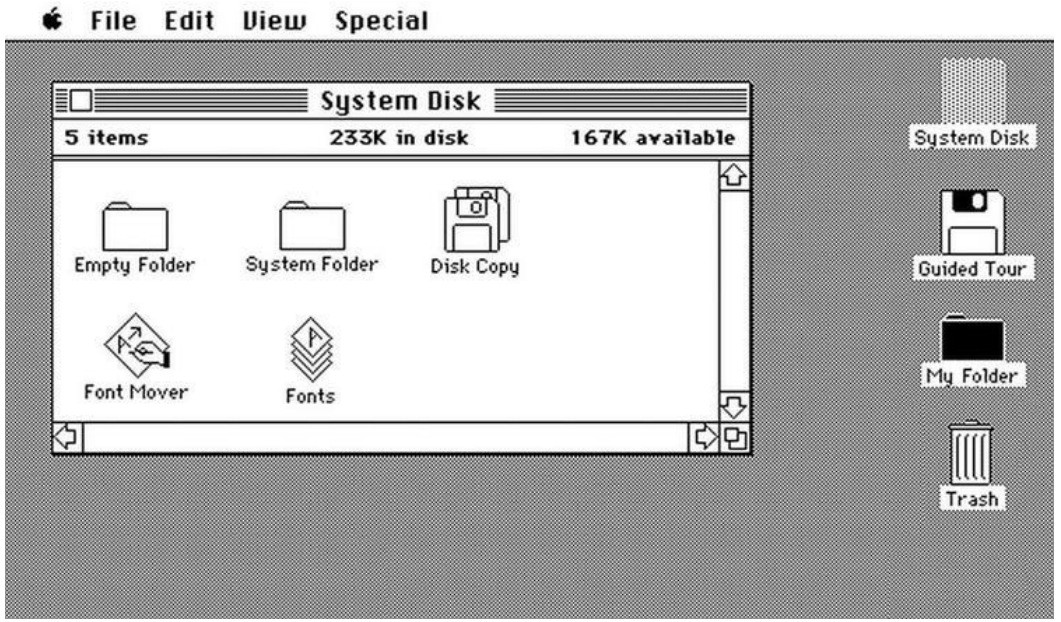

LOWE

# The Future of TechBio

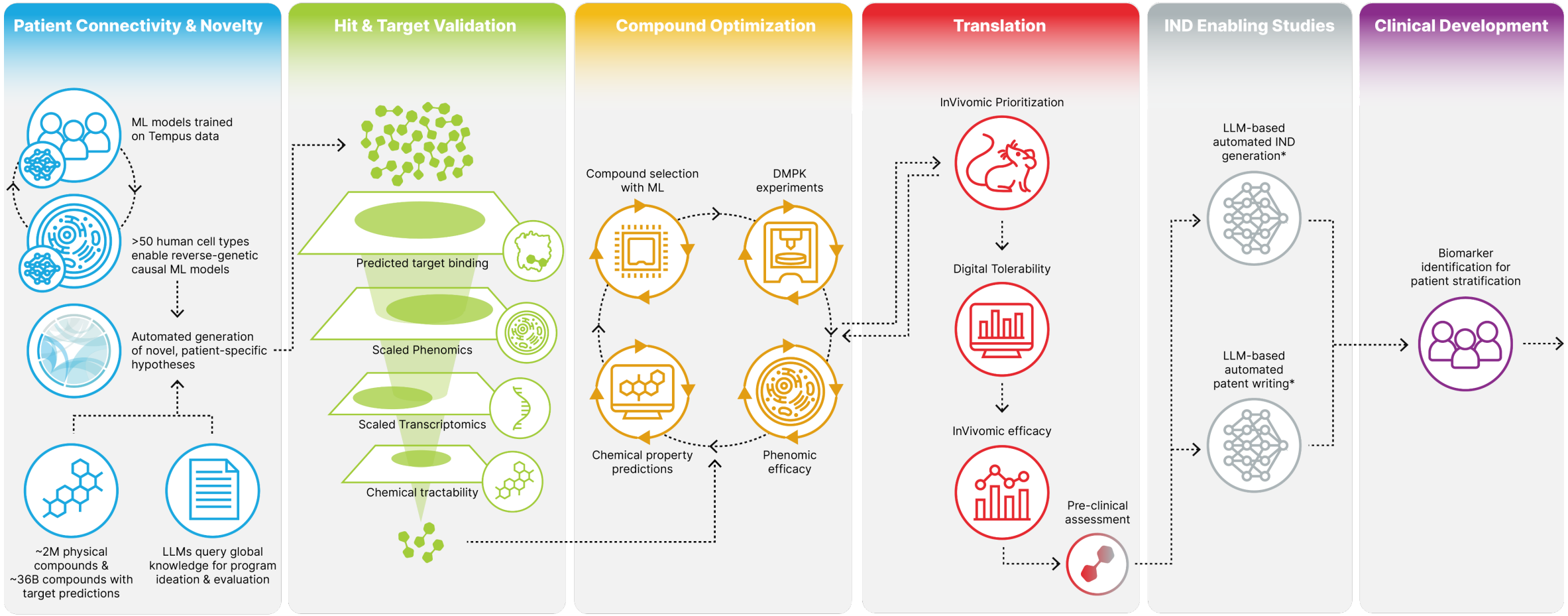
Turning drug discovery into a search problem

# The Future of TechBio

Turning drug discovery into a search problem



# Pipeline: connecting systems into Industrialized Workflows




*Currently being explored

Recursion

# Preclinical: The Power of Prediction

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# Traditional approach to initiating a new drug discovery program


Novel opportunity

↓

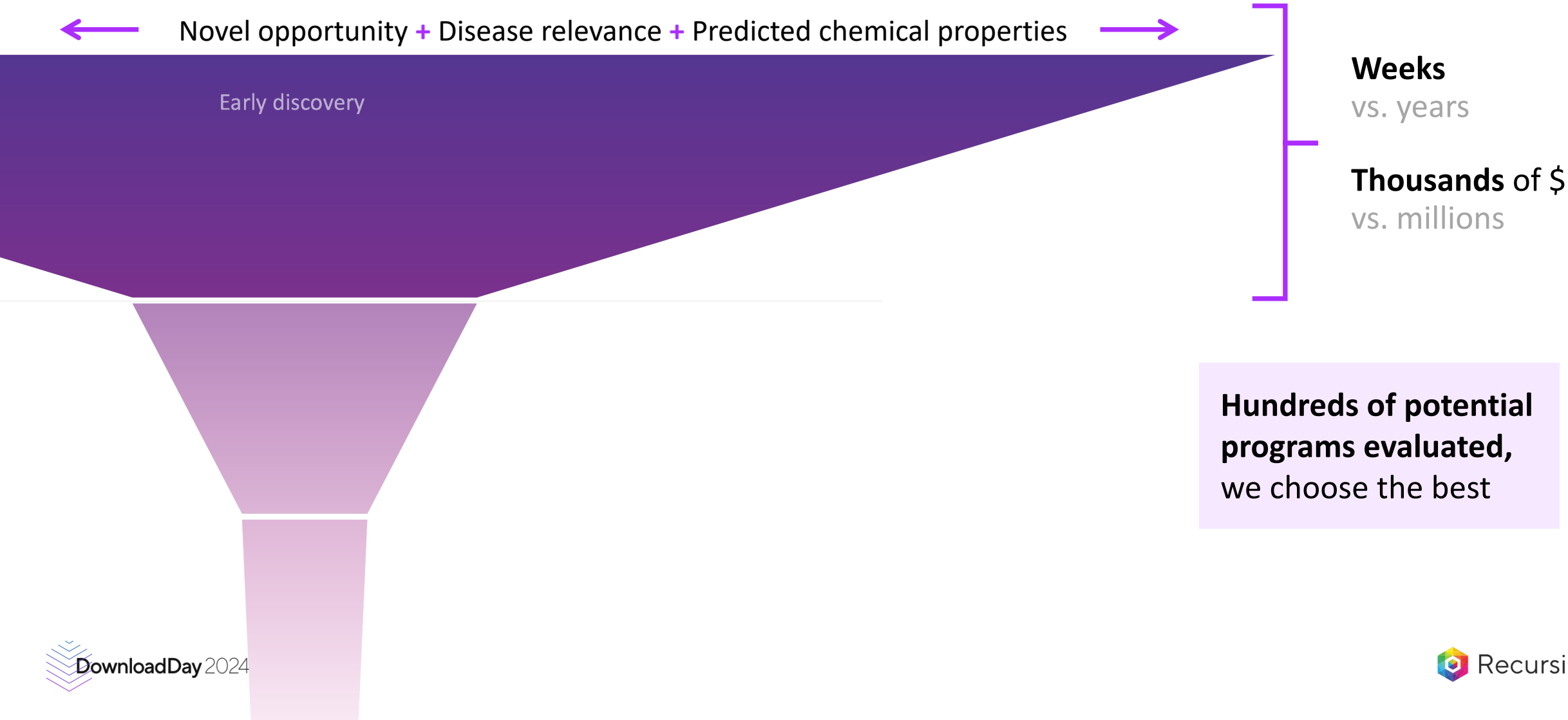
Disease relevance

1-2 **years**

**Millions** of $

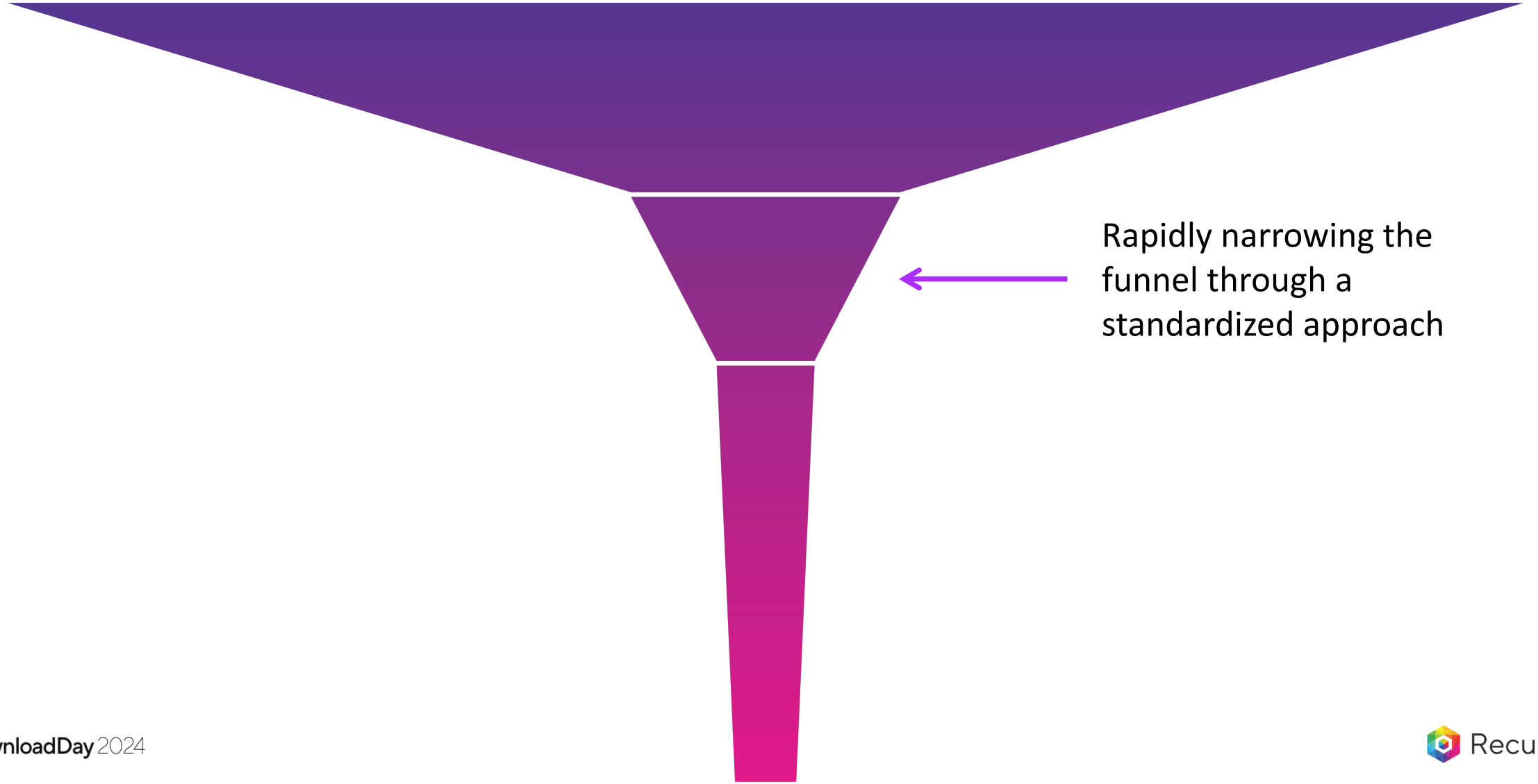
~One potential program

# We are turning this into a search problem, evaluating new programs in bulk

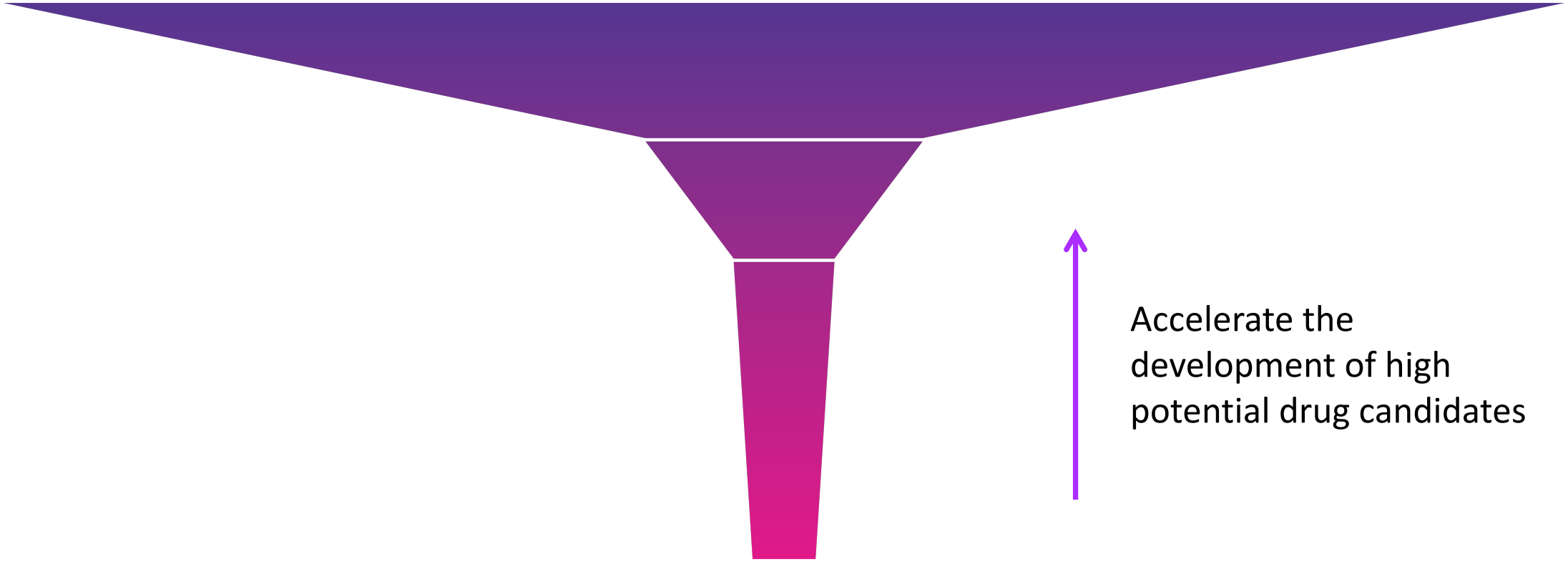



**Hundreds of potential programs evaluated,** we choose the best

# Recursion is designed to impact drug discovery productivity…

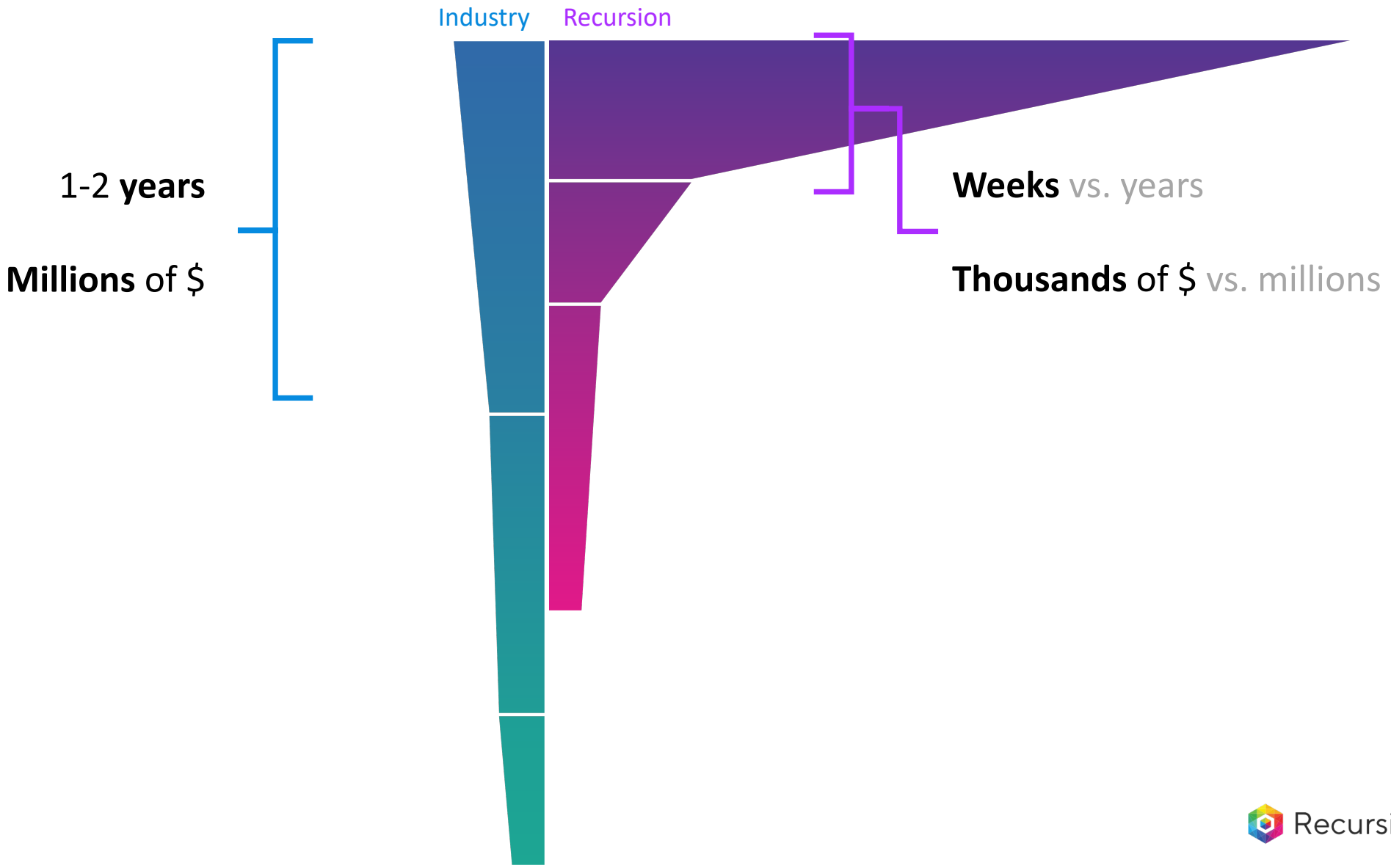


# Recursion is designed to impact drug discovery productivity…



Accelerate the development of high potential drug candidates

# Reshaping the timelines and shape of drug discovery research



Recursion

# Case Study: Target Epsilon

Identifying novel targets and optimizing novel chemistry

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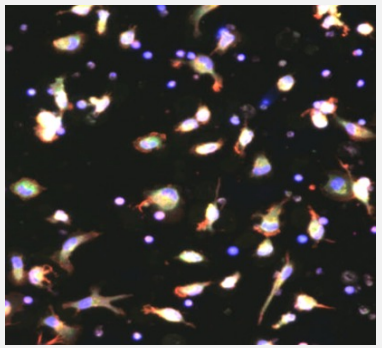
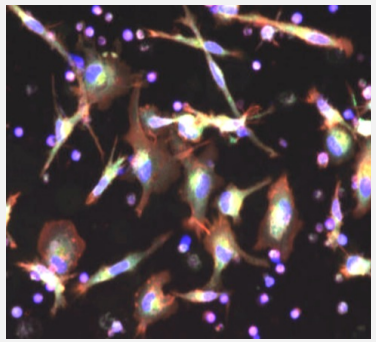
# Power of Phenomics: Identify complex phenotypic rescue at scale

## *PBMC-derived fibrocyte assay*



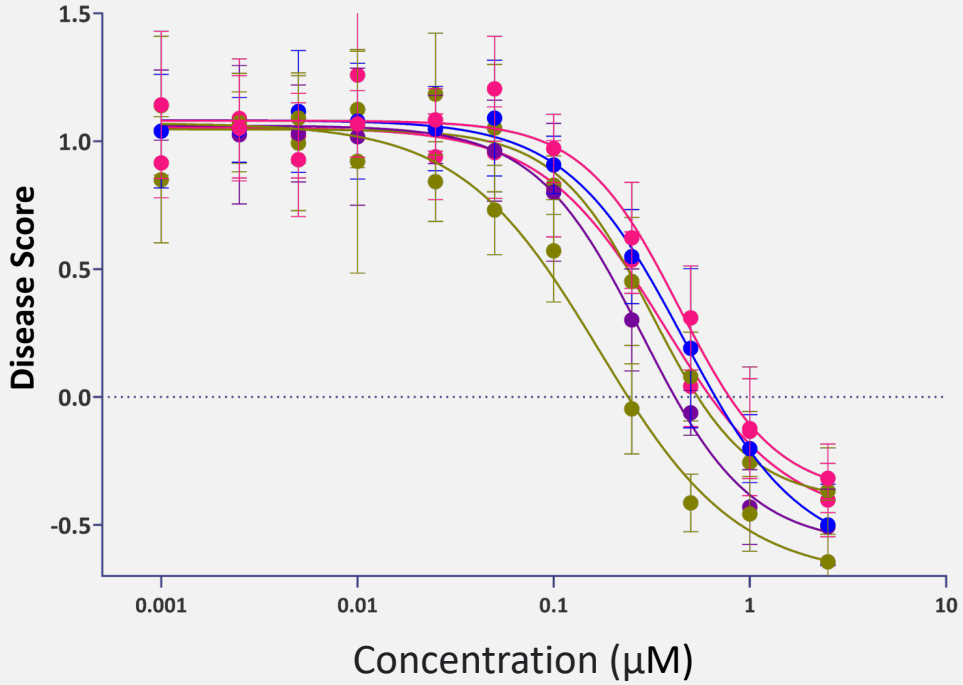
**Control State:**
10 µg/mL control peptide



**Disease State:**
Undisclosed treatment

- Human-PBMCs are differentiated to fibrocytes
- Treatment with a control peptide gives desired impact on fibrocytes (**control state)**

## *Promising hits from phenotypic screen*

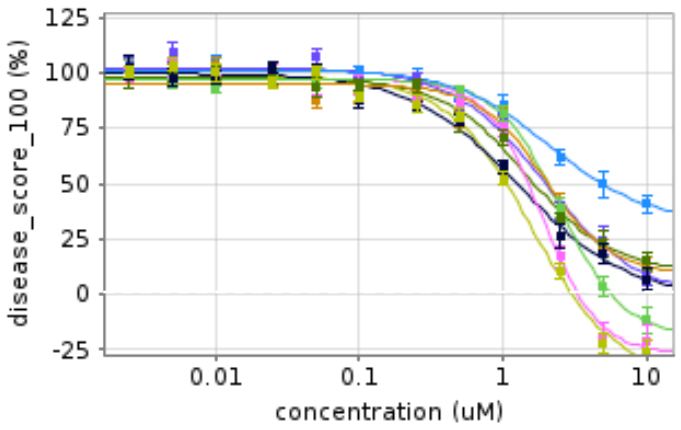


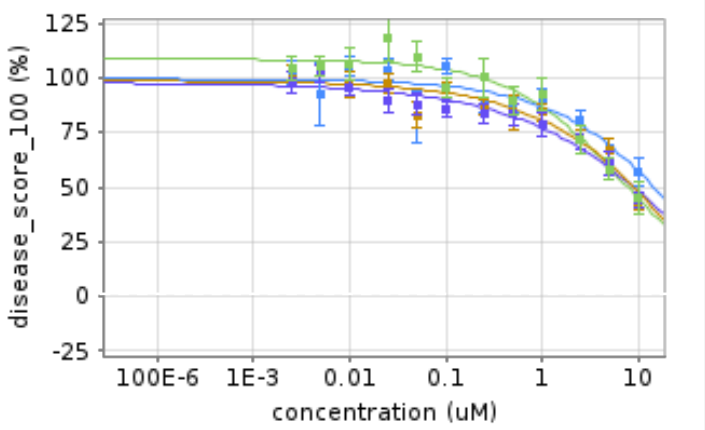
# ~100x potency gains driven entirely on phenomics assay

**Representative concentration response curves (CRC) from the phenotypic assay**

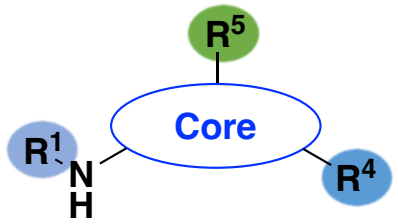
Disease State

Healthy Control State



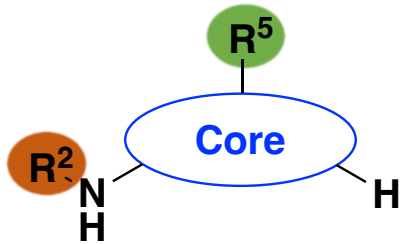




Significant reduction of disease modifying activity




**REC-A**

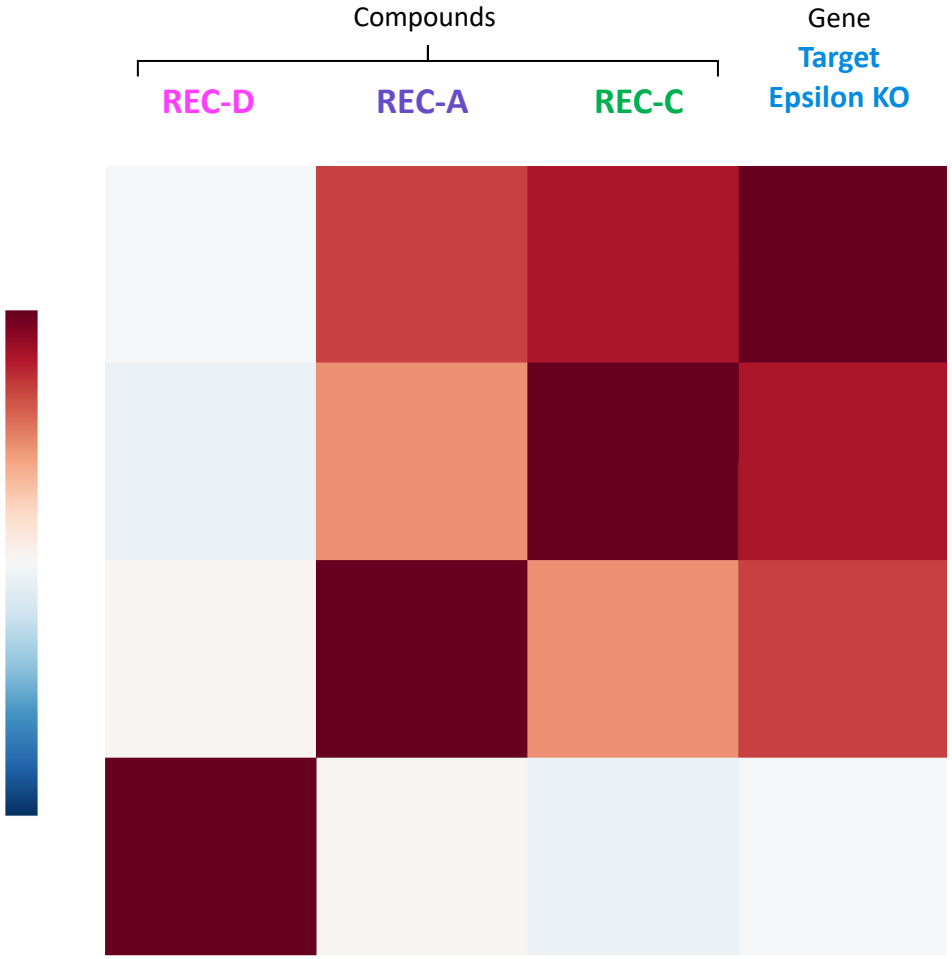
50% Rescue 1.5 µM

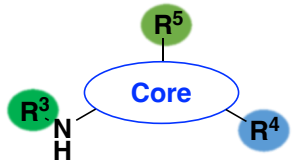
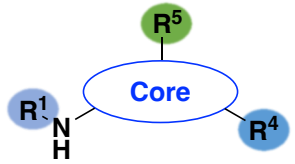
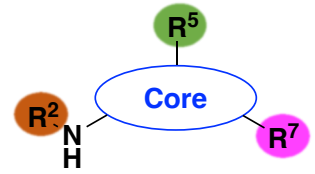



**REC-B**

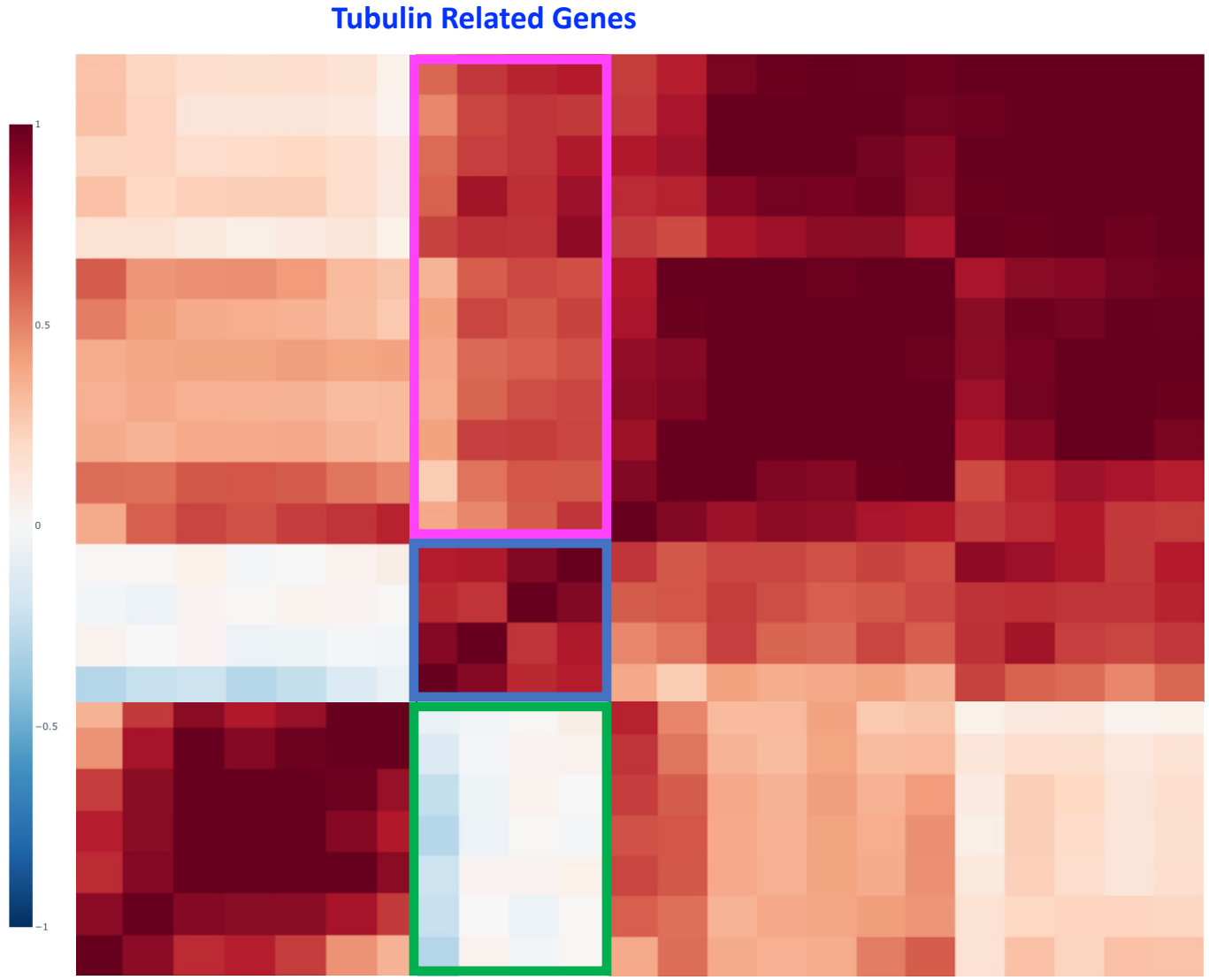
50% Rescue ~10 µM

# Phenomics identified mechanism of action as a novel approach for treating fibrosis

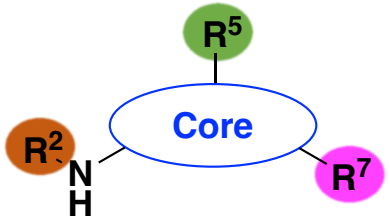



| | | ***Epsilon*** **biochemical confirmation** |
|---|---|---|
| **Target Epsilon KO** | | **n/a** |
| **REC-C** **2.5 µM** |  | Target Epsilon $IC_{50}$ **= 31.5 nM** |
| **REC-A** **2.5 µM** |  | Target Epsilon $IC_{50}$ **= 106 nM** |
| **REC-D** **2.5 µM** |  | Target Epsilon $IC_{50}$ **= 3600 nM** |

# Power of Phenomics: Track and minimize off-target liabilities




Compounds with
**<10 µM tubulin $IC_{50}$**

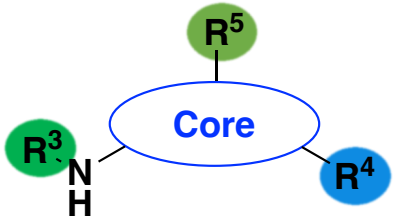



REC-D

Phenomap correlates with tubulin polymerization inhibition assay

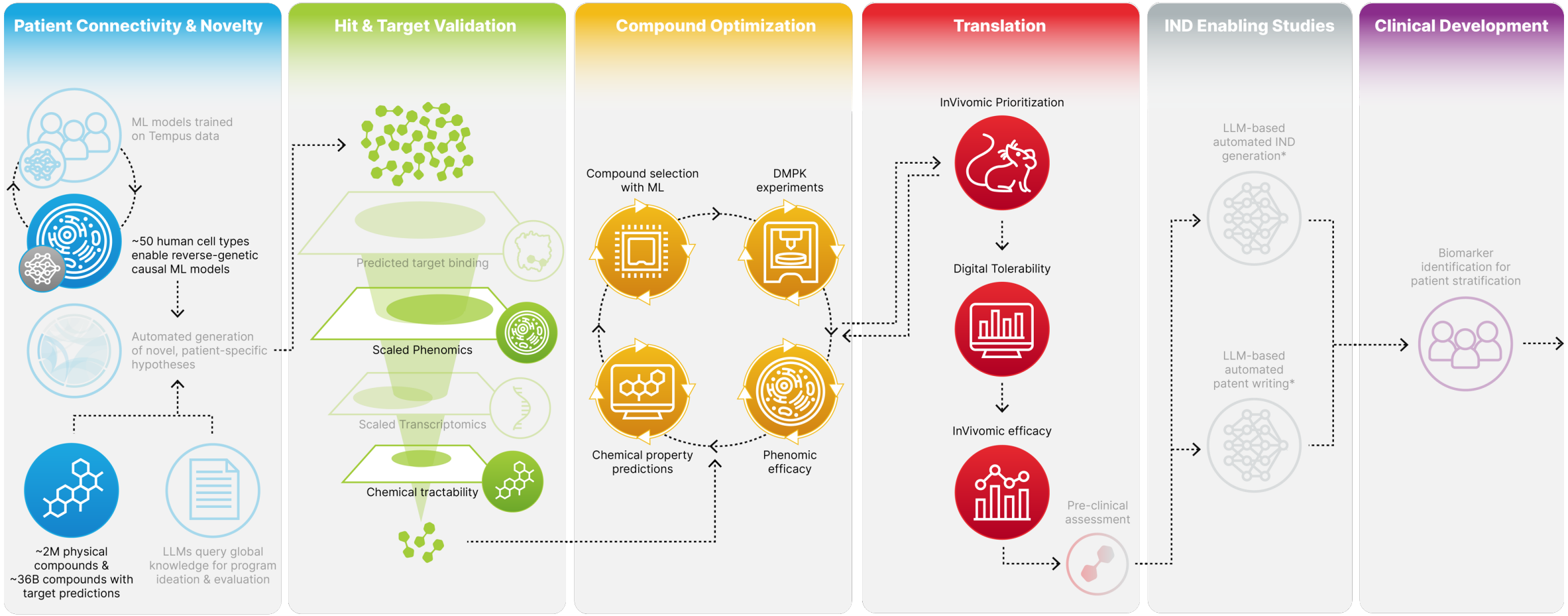
**Tubulin Related Genes**

Compounds with
**>30 µM tubulin $IC_{50}$**




REC-C

# Industrialized Drug Discovery: Optimizing novel chemical matter

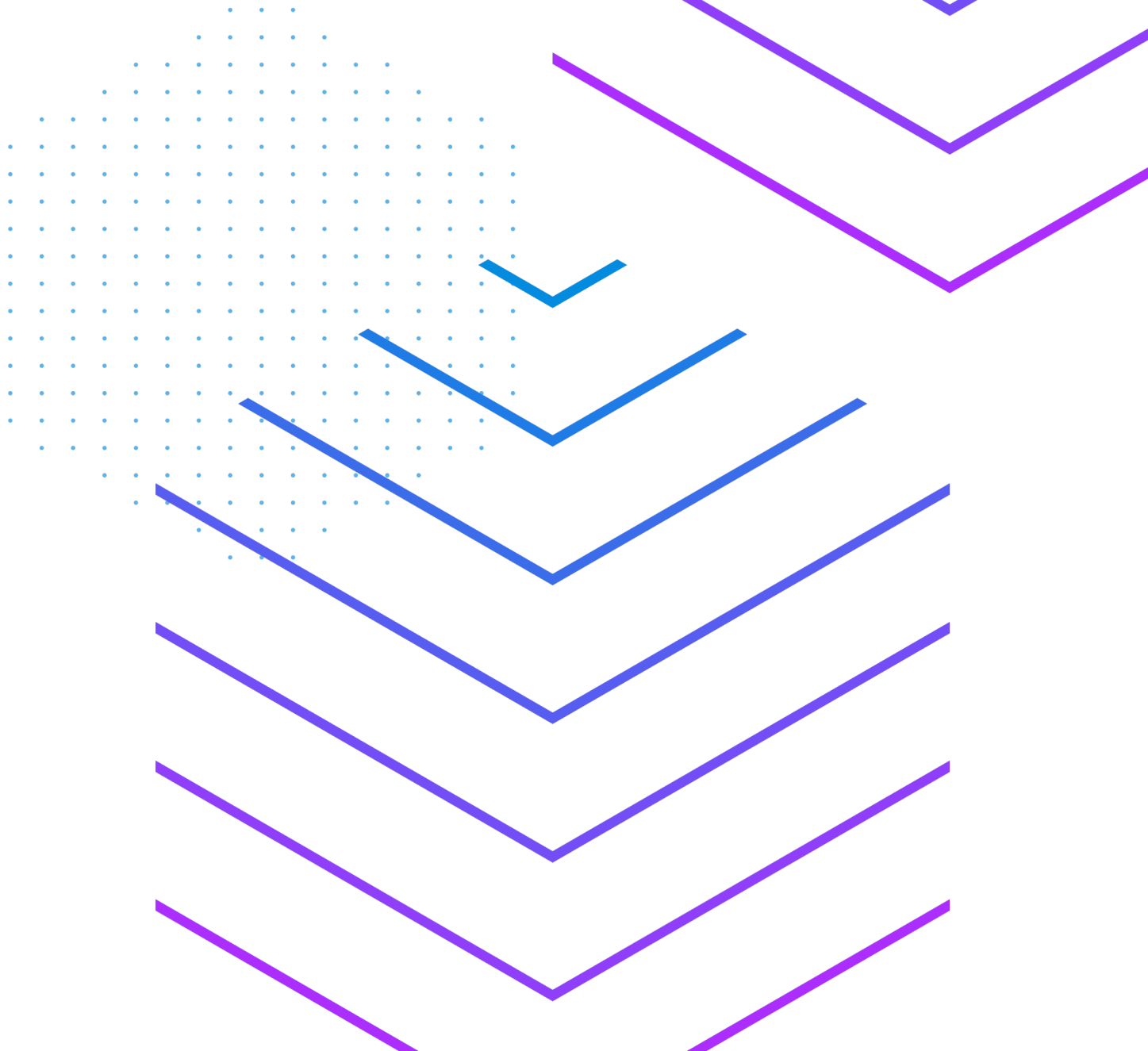



*Currently being explored

Recursion

# Case Study: RBM39

Accelerating to IND enabling studies through in silico novel target prediction



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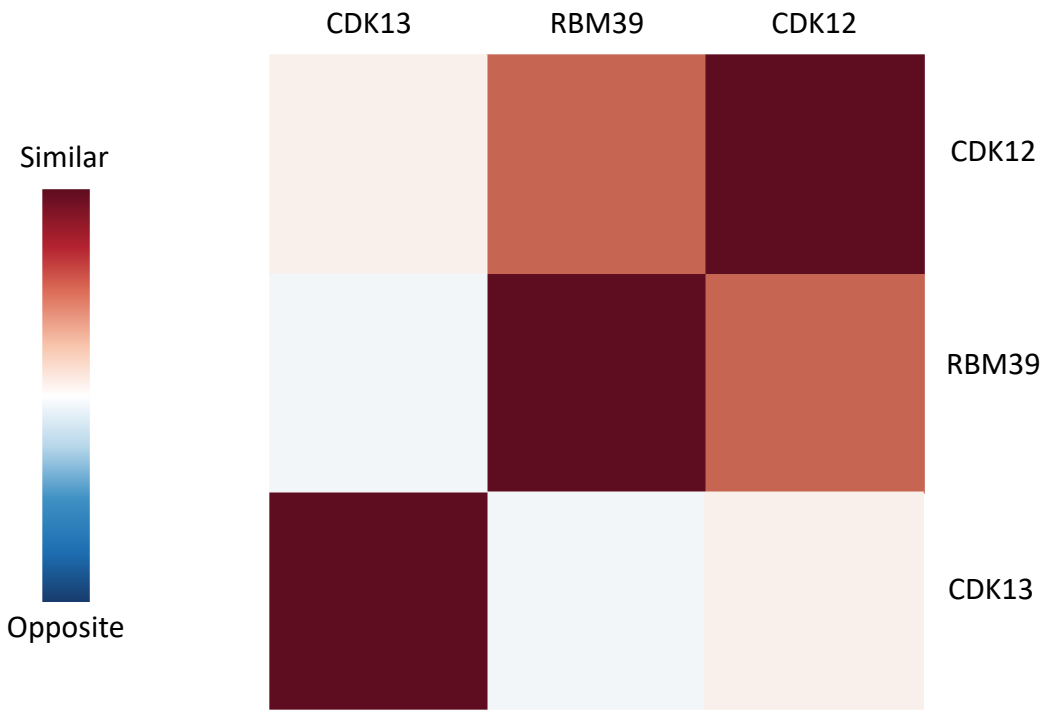
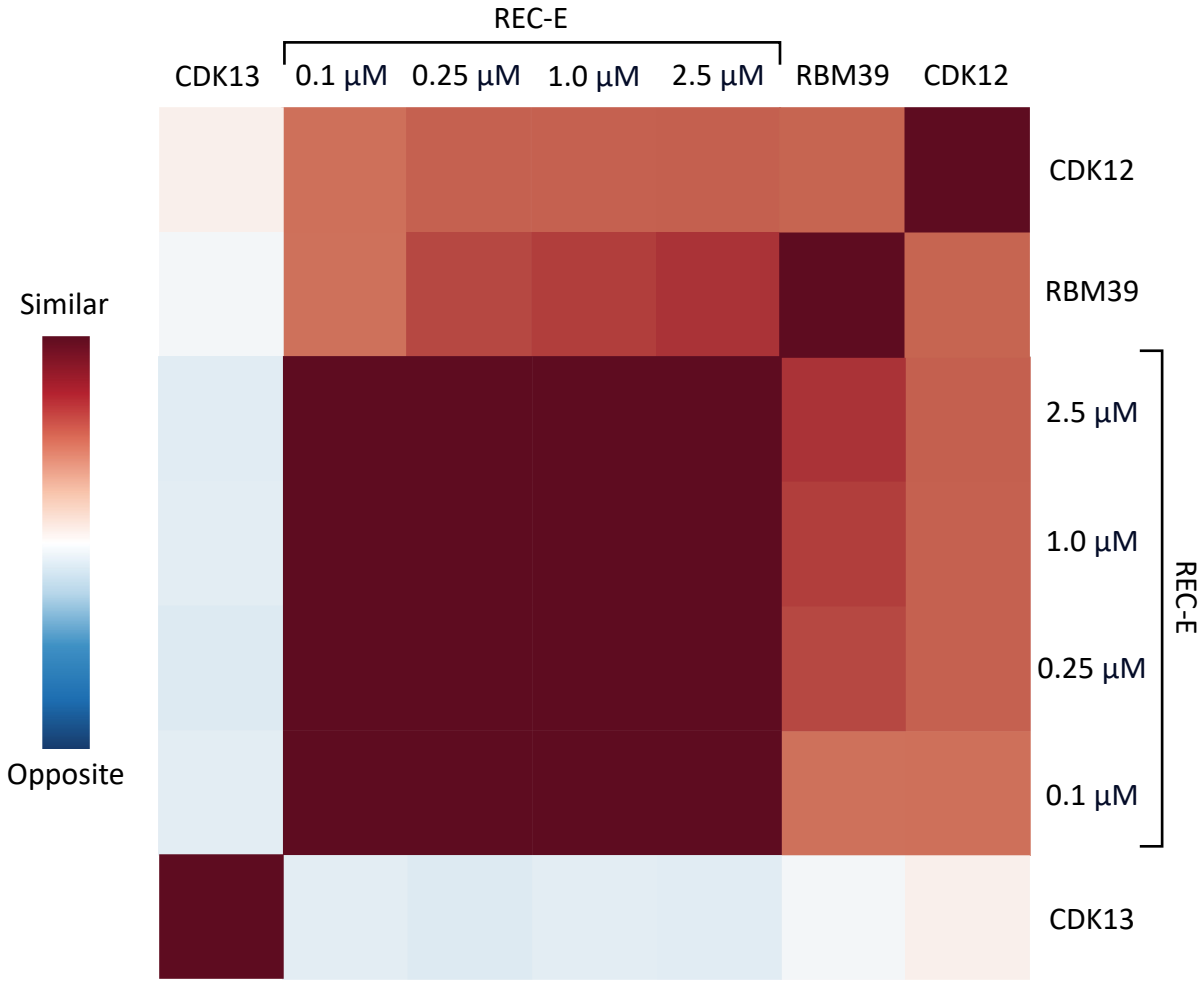
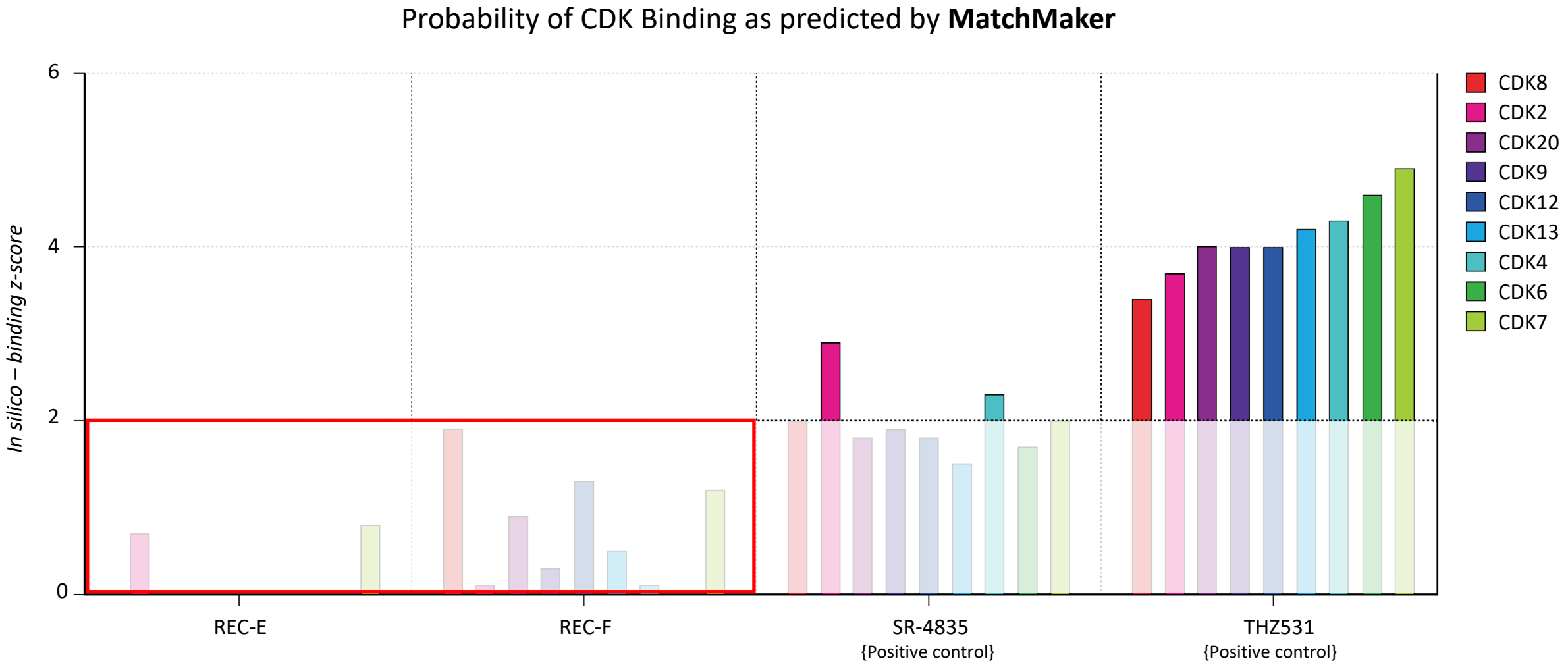
# Inference search reveals novel CDK12 adjacent target RBM39 and selective small molecule hits



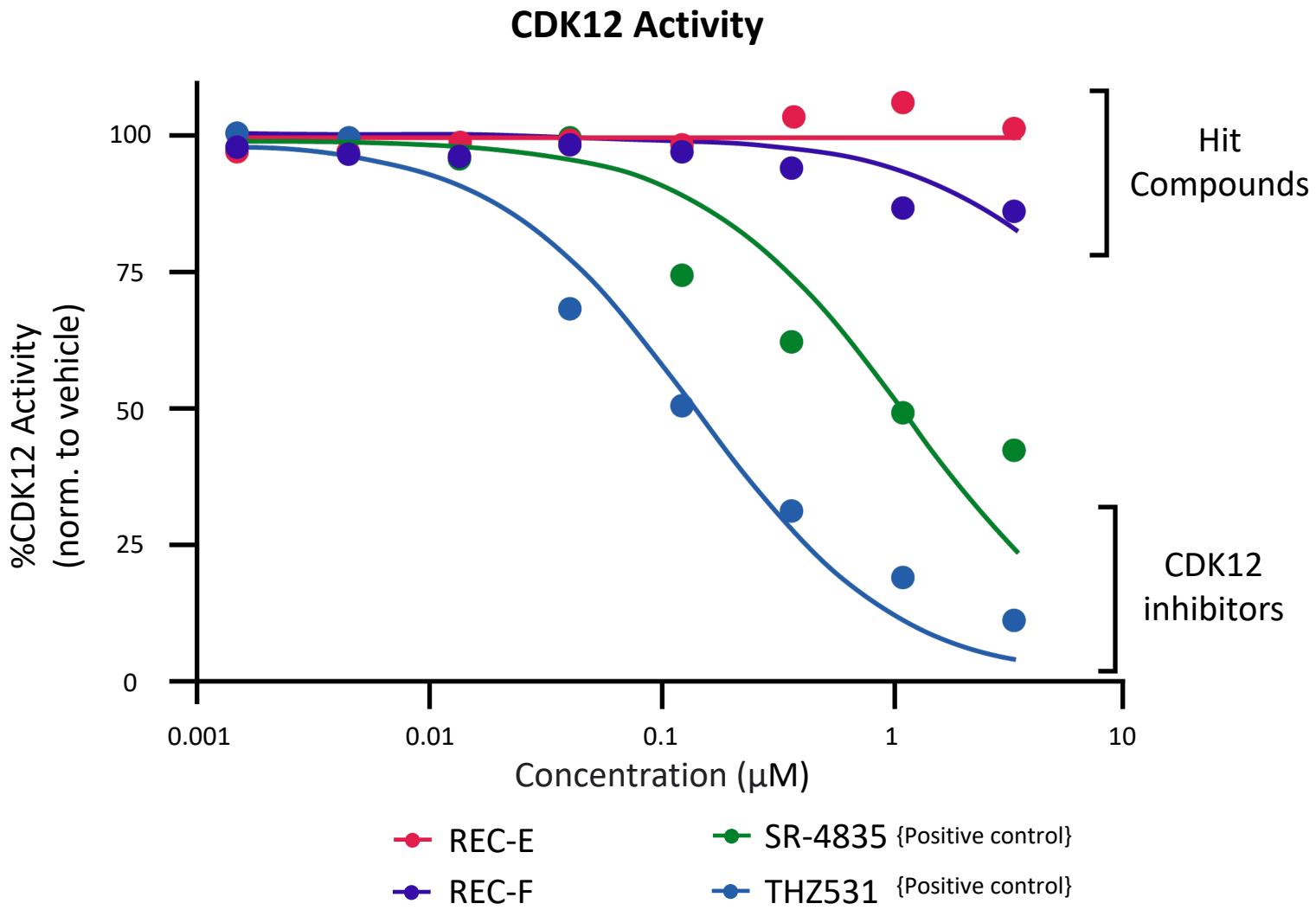
# Inference search reveals novel CDK12 adjacent target RBM39 and selective small molecule hits



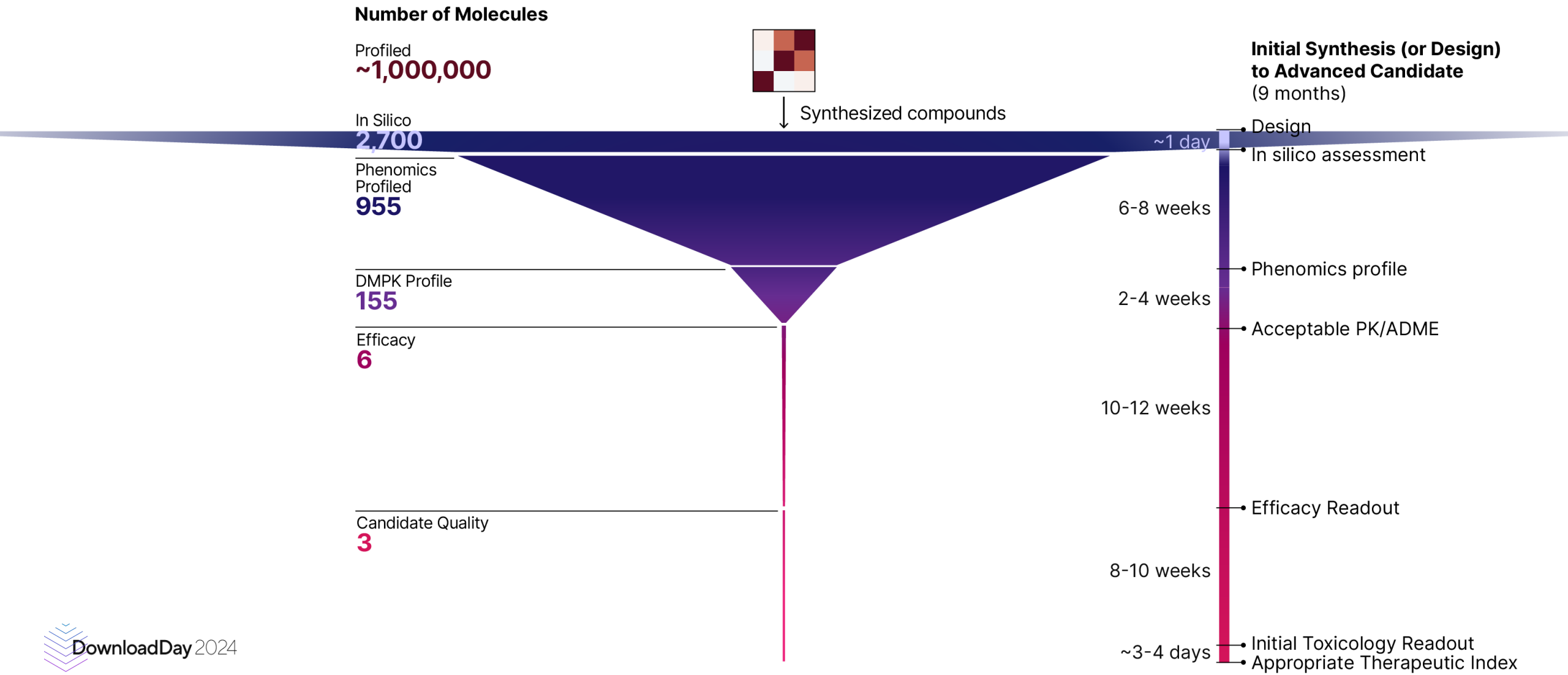
# In silico MatchMaker predicts hit compounds are NOT CDK inhibitors



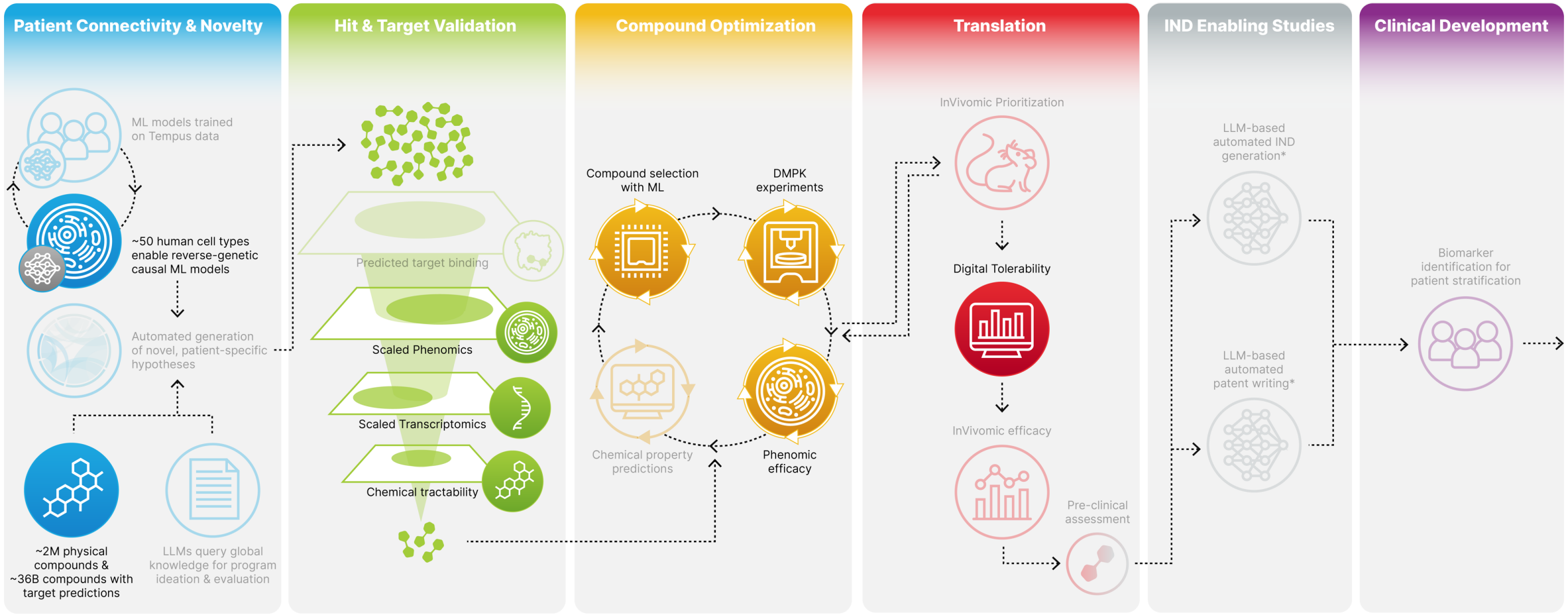
# Physical data confirms digital hypothesis



# Predictions and minimal standard experiments enabled rapid and efficient identification of development candidate



# Rapid in silico novel target identification



# Time from target ID to IND enabling study

Recursion


Industry

Recursion

# Case Study: Undisclosed Oncology Target 1

Connecting data layers end-to-end improves quality and speed of insights

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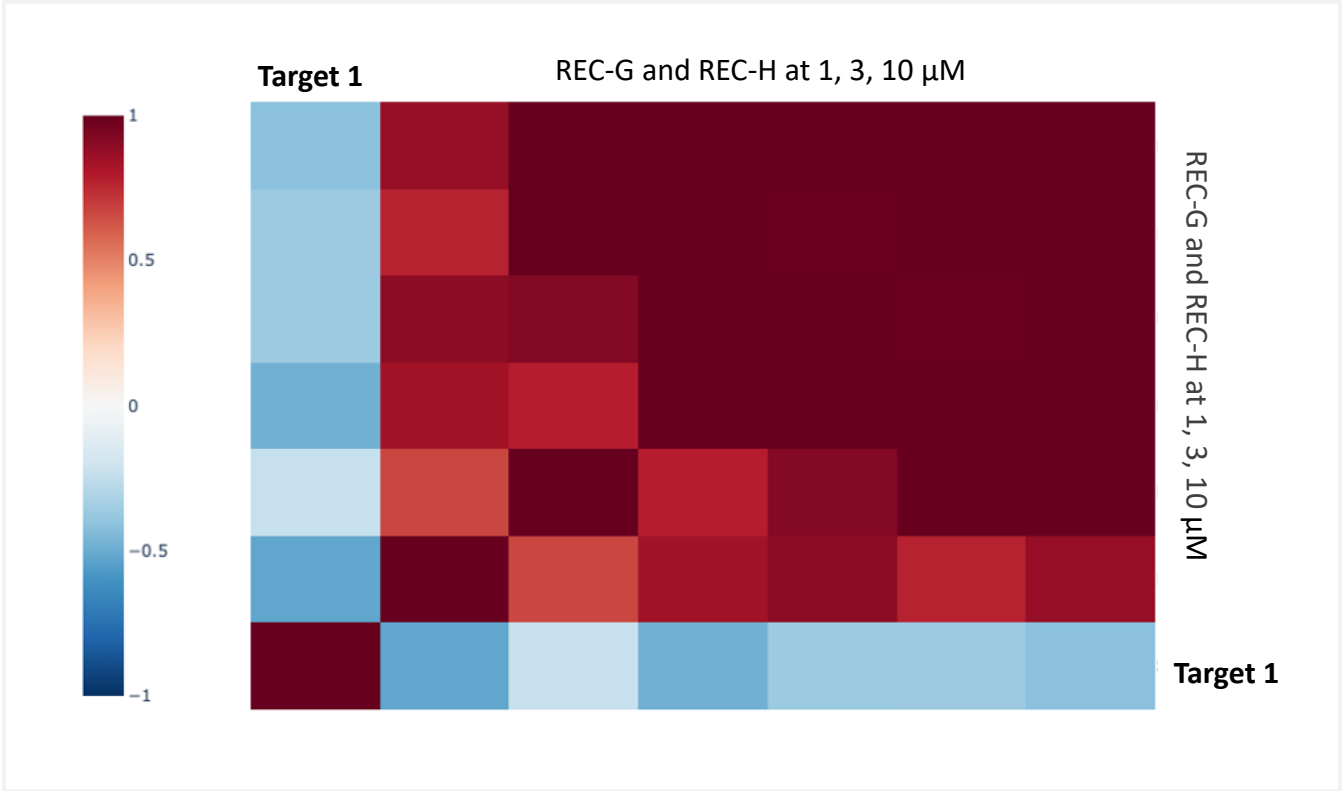
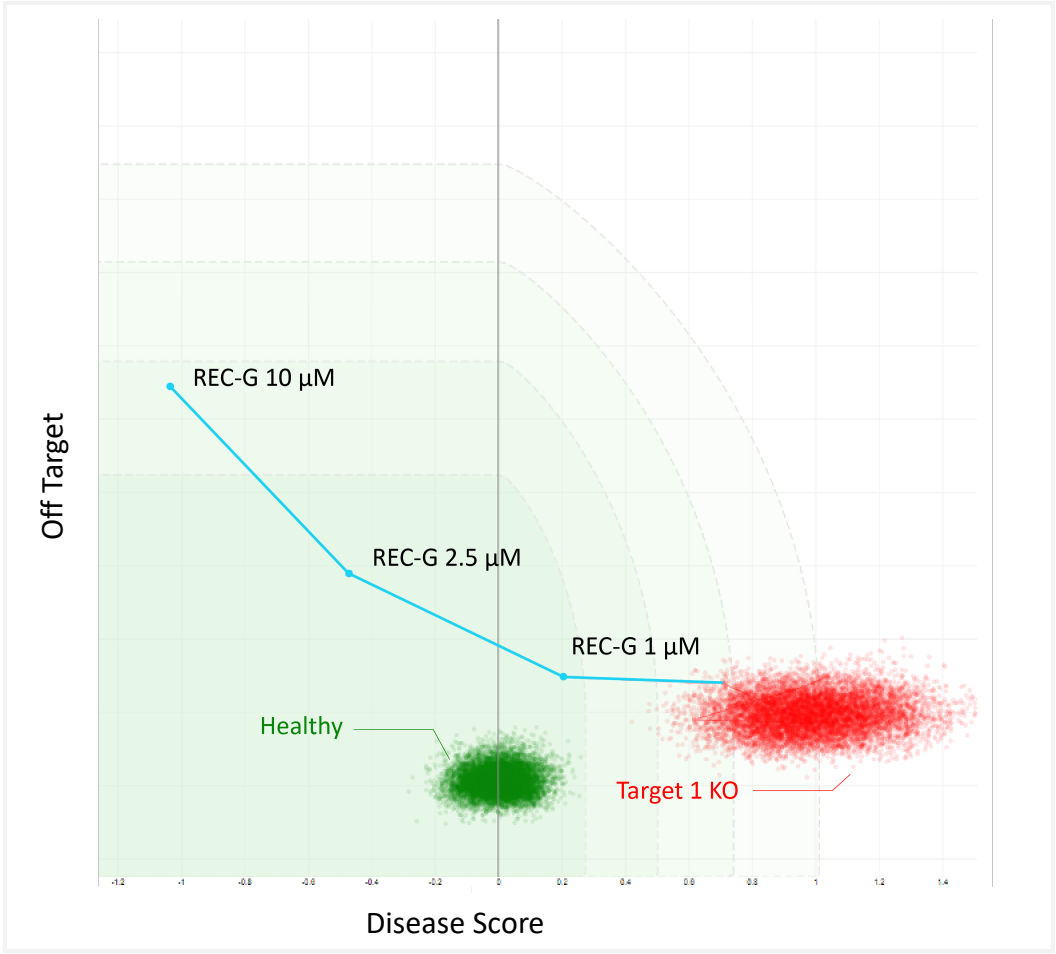
# Identifying novel Target 1 and opposing molecules through automated, in silico analysis

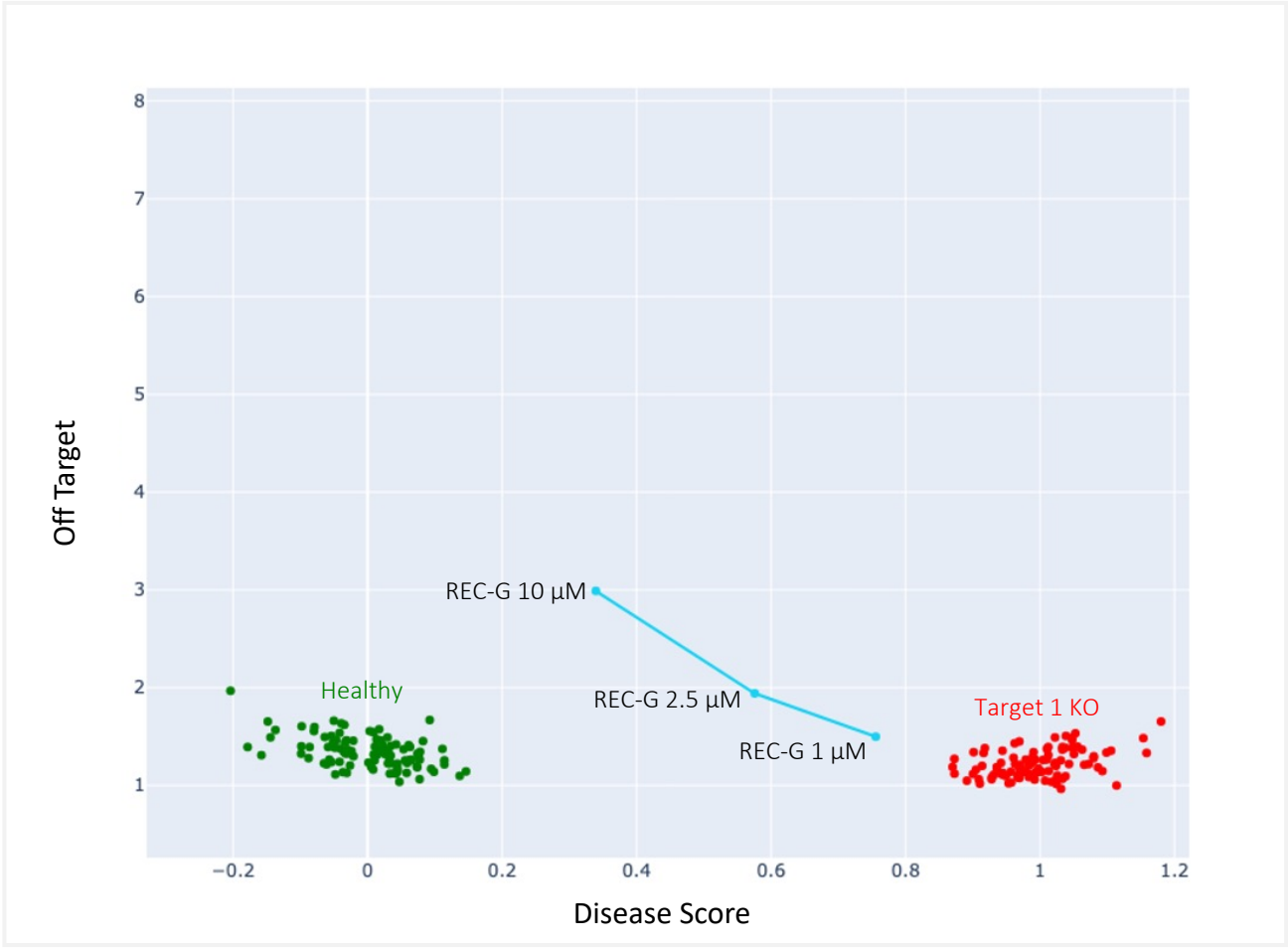


# Physical data confirms digital hypothesis

## Phenomics Confirmation Screen

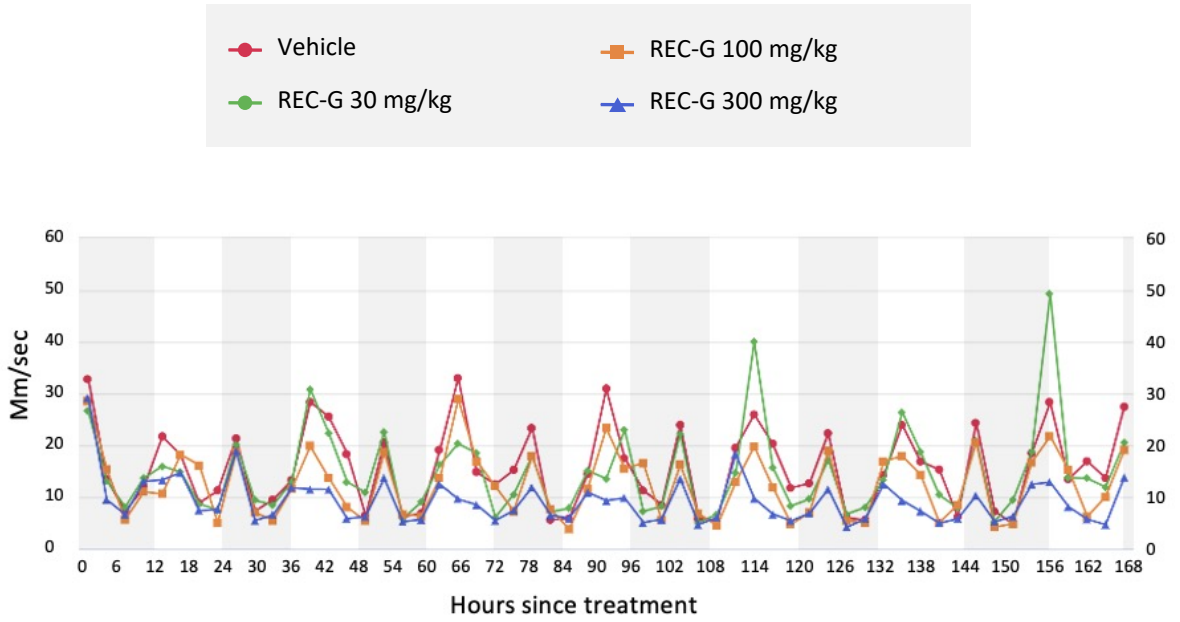



## Transcriptomics Confirmation Screen

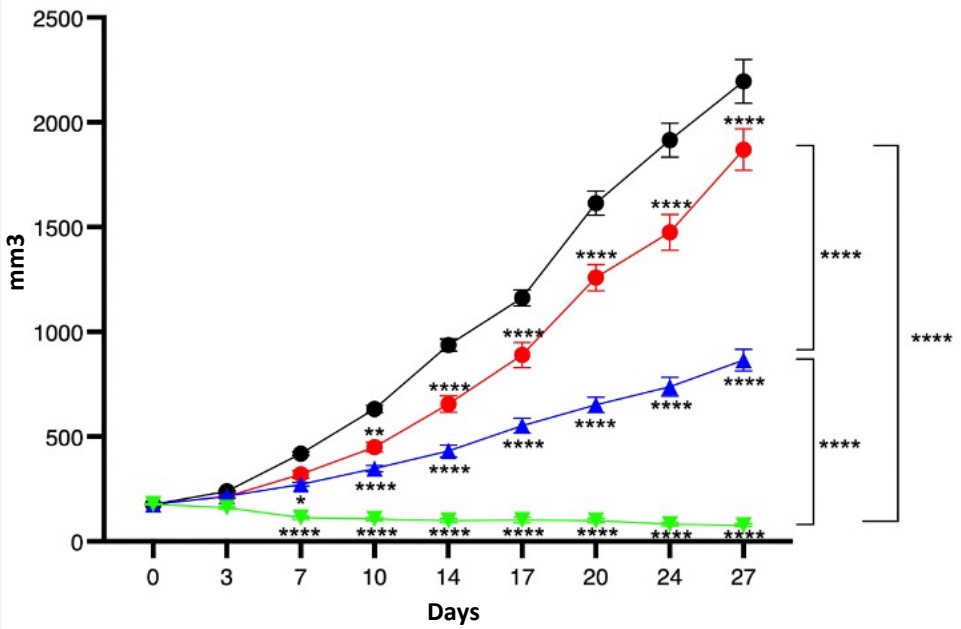


# InVivomics enables identification of tolerable dose for rapid positive proof of concept readouts for unoptimized molecules

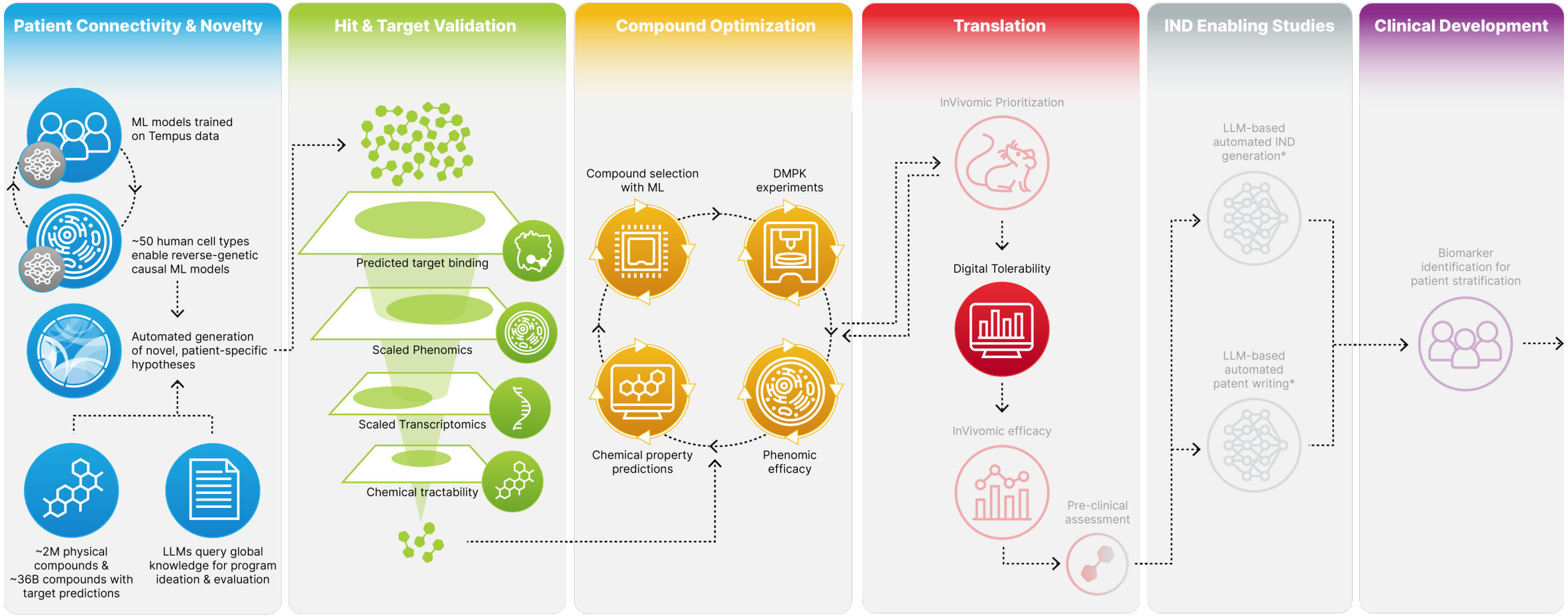
## Daily Motion




## Tumor Volume



# End-to-end automation drives significant efficiency gains to deliver lead in 10 months




*Currently being explored

Recursion

# Case Study: Undisclosed Oncology Target 2

Identifying novel molecules for a previously undruggable target

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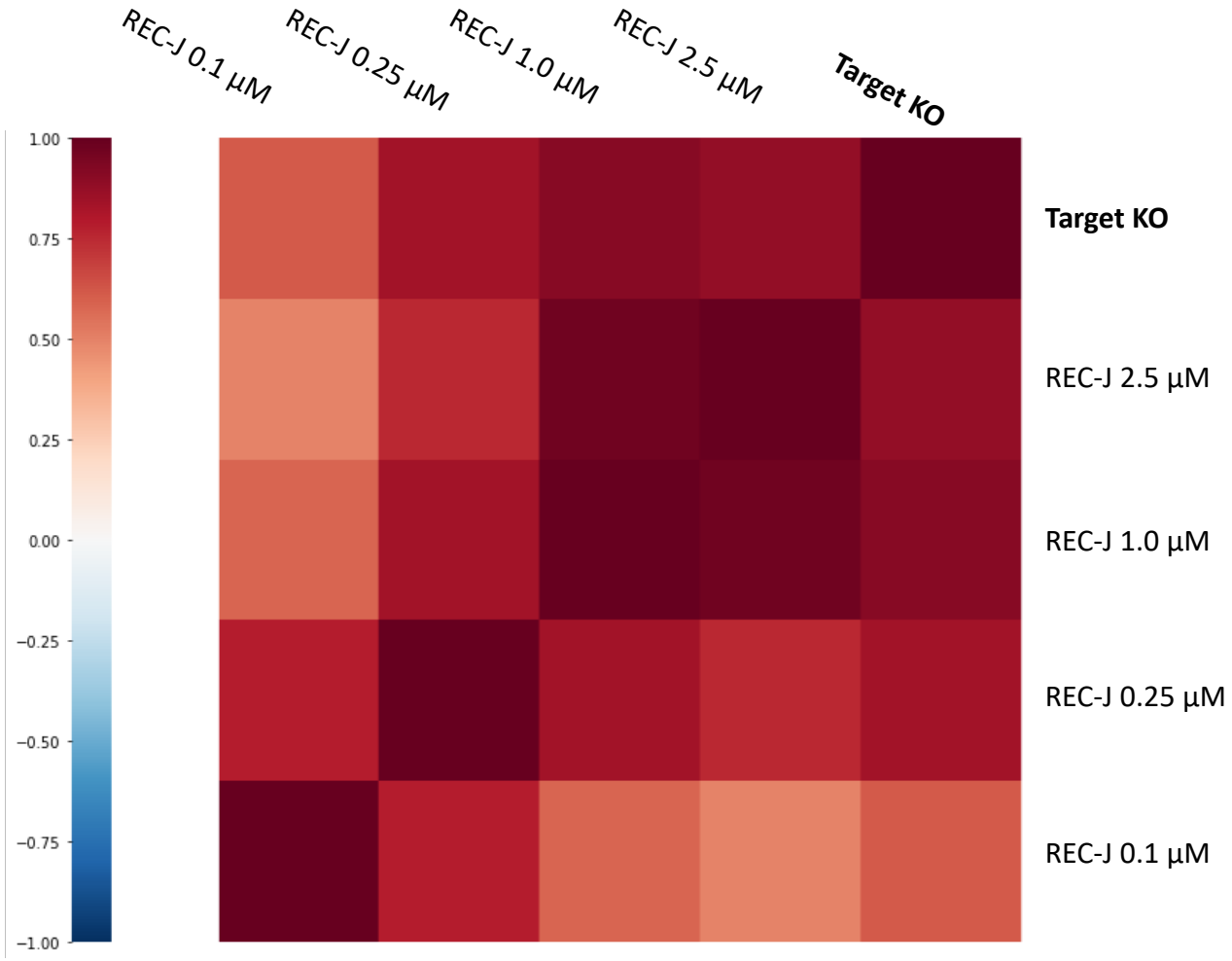
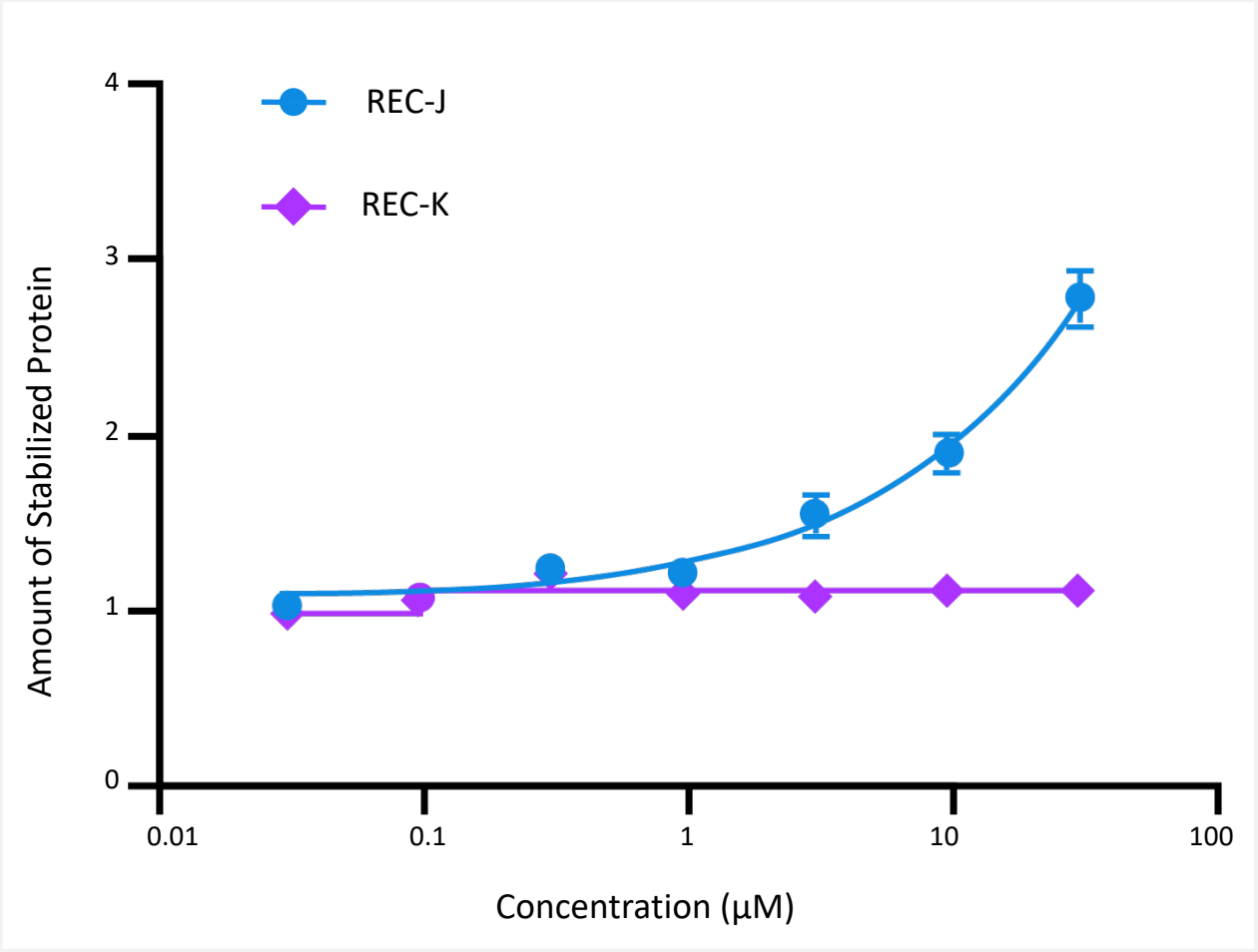
# In silico analysis reveals compound highly phenosimilar to Target KO



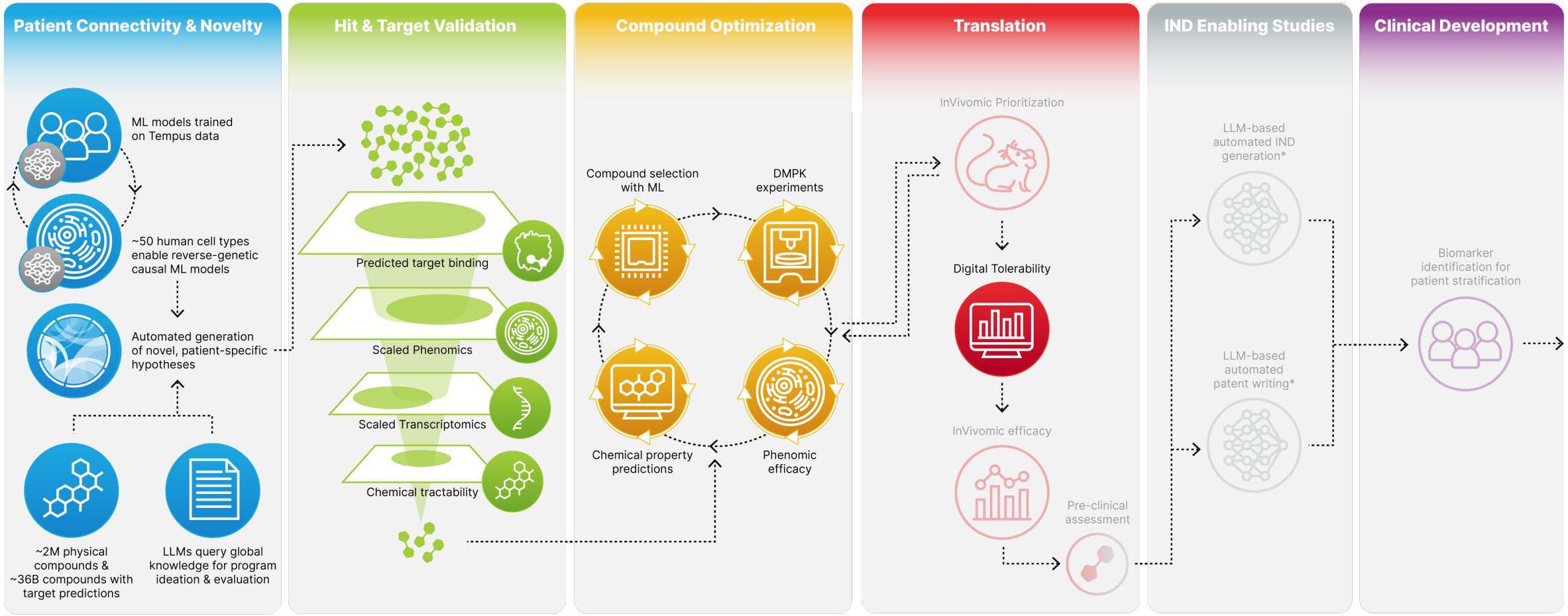
# Compound with high predicted phenosimilarity bind to Target 2




REC-J
$EC_{50}$ = 100 µM

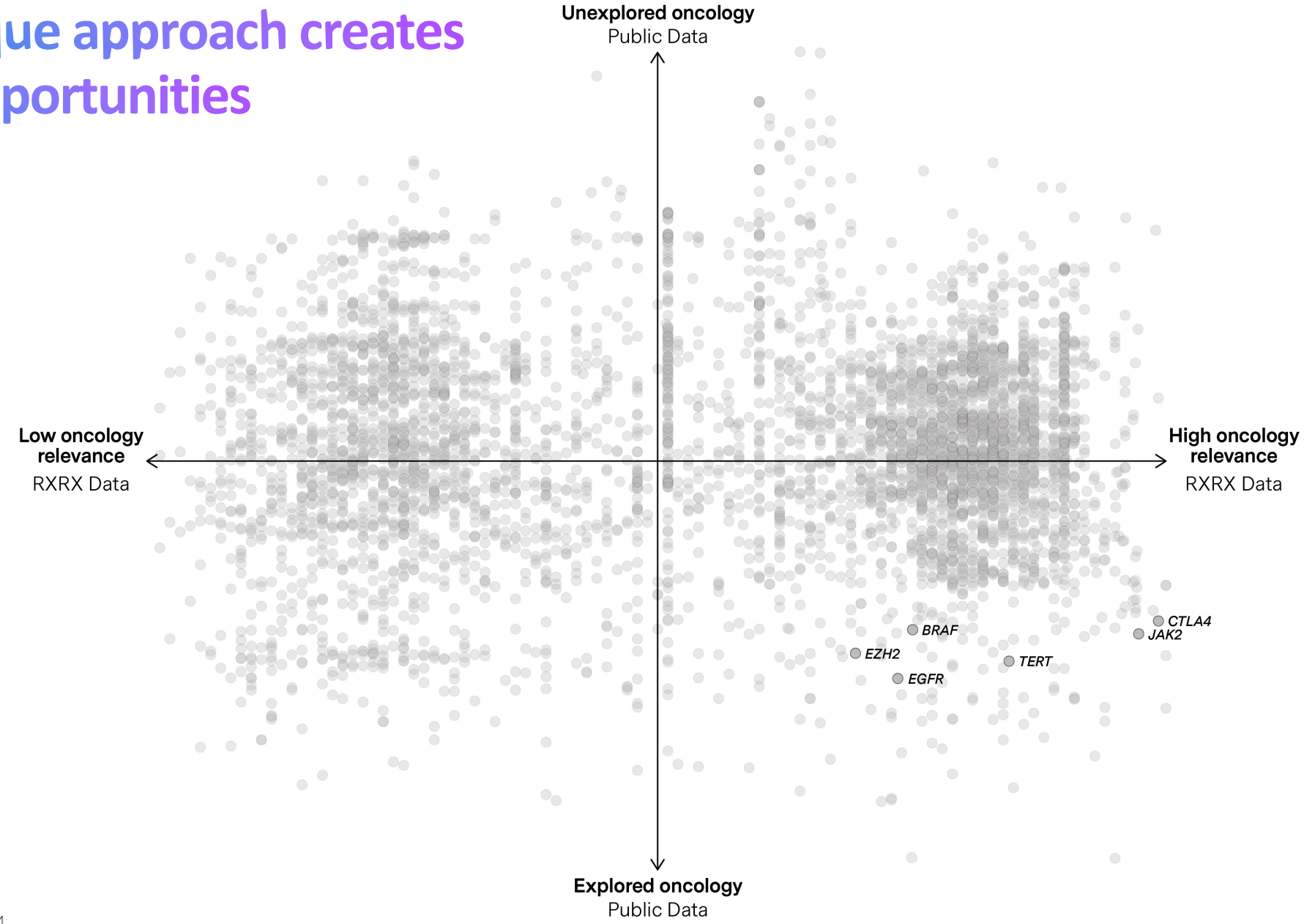
REC-K
$EC_{50}$ = >10 µM

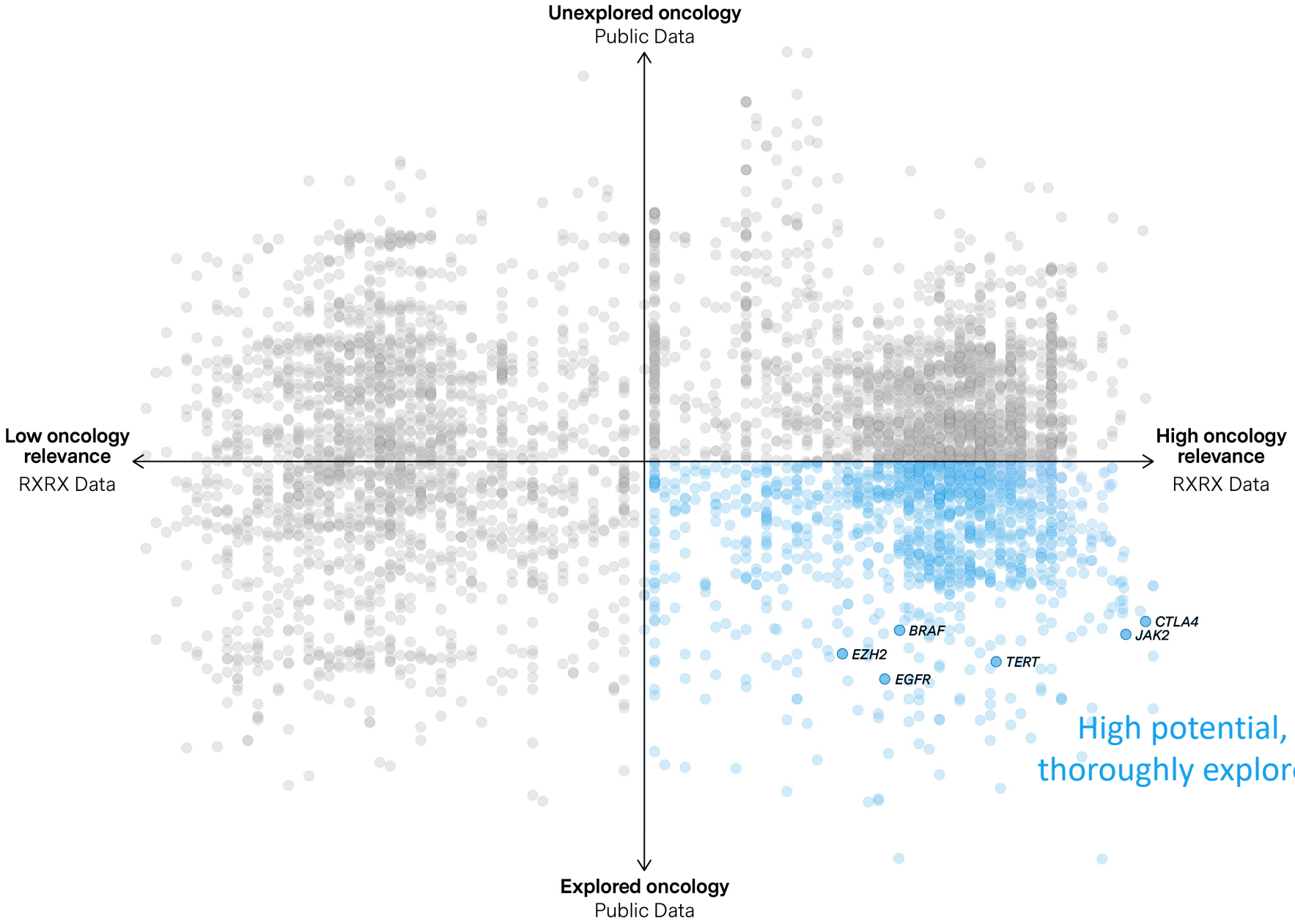
# Overcoming the hurdles of drug discovery: undruggable targets

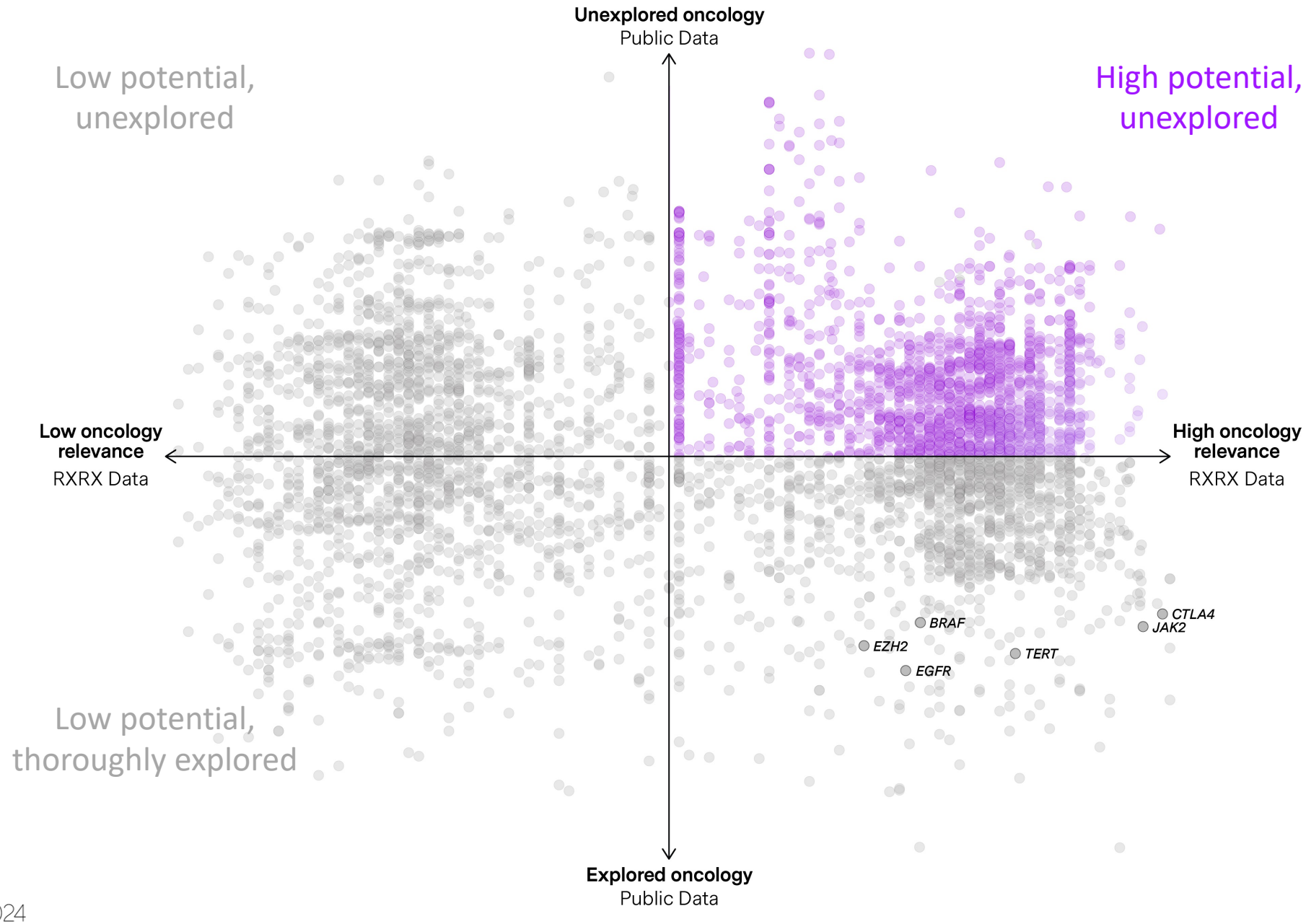


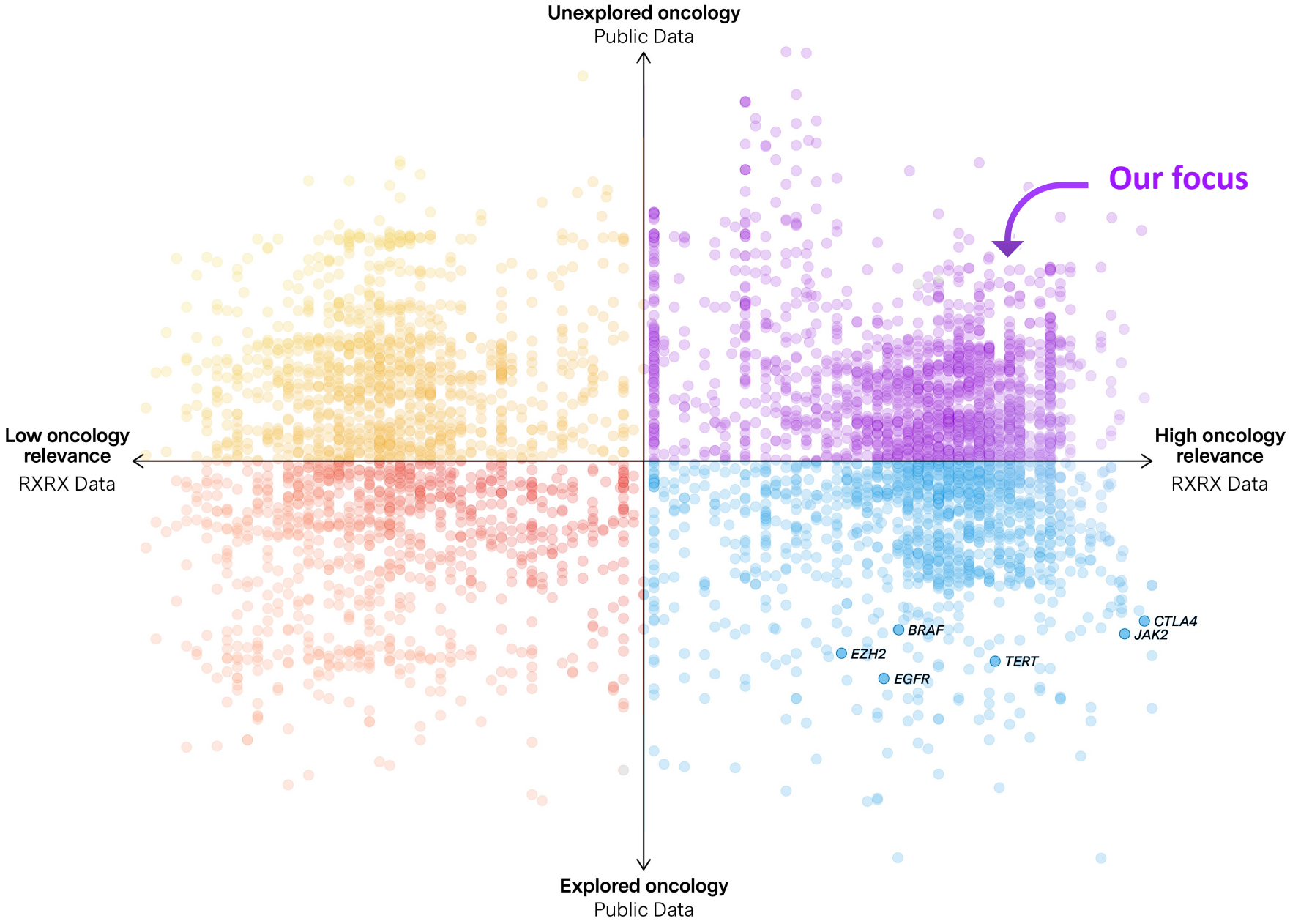

*Currently being explored

# Our unique approach creates novel opportunities



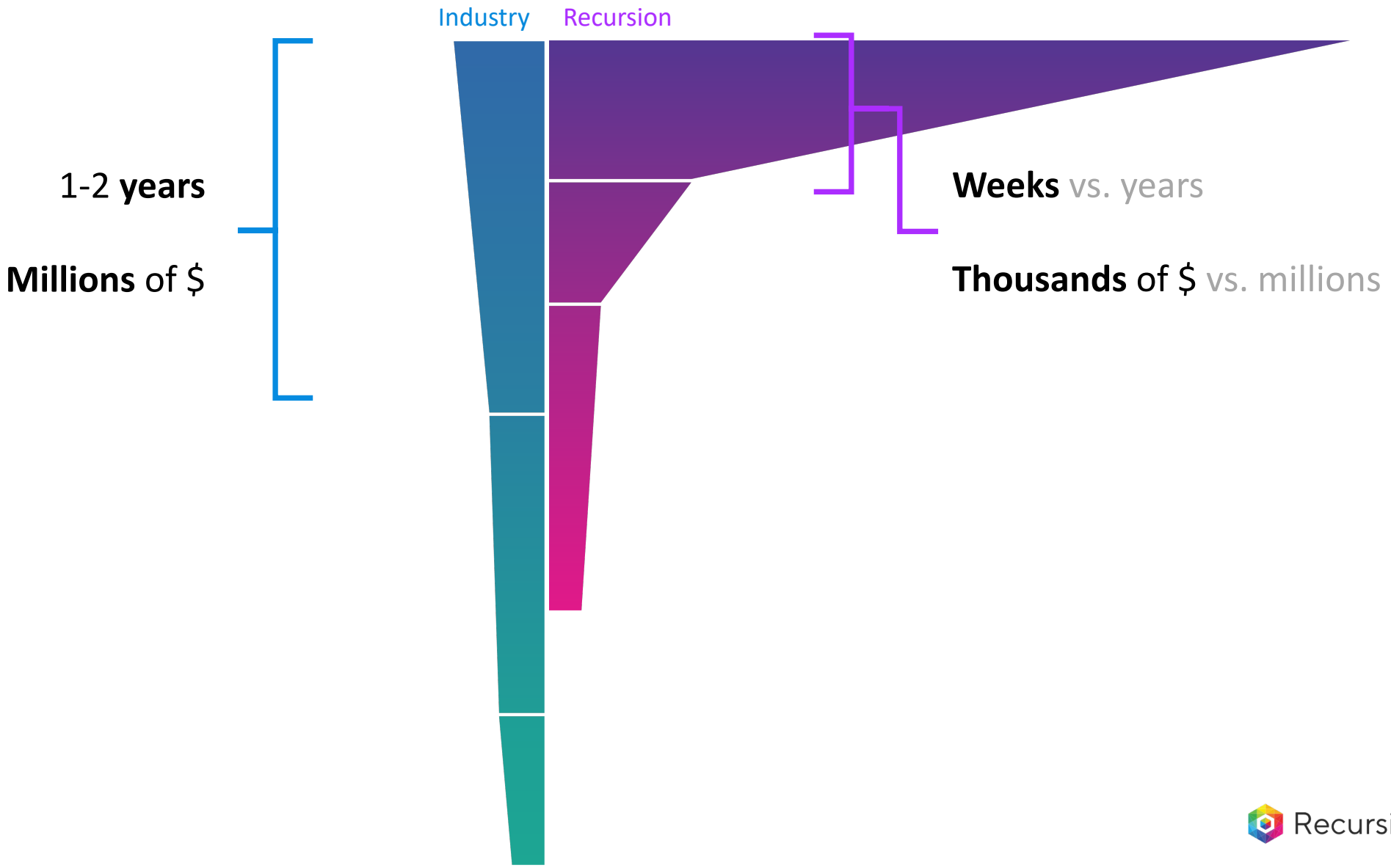

Unexplored oncology
Public Data
Low oncology relevance
RXRX Data
High oncology relevance
RXRX Data
Explored oncology
Public Data
CTLA4
JAK2
BRAF
EZH2
TERT
EGFR
High potential, thoroughly explored


Unexplored oncology
Public Data
Low potential,
unexplored
High potential,
unexplored
Low oncology
relevance
RXRX Data
High oncology
relevance
RXRX Data
BRAF
CTLA4
JAK2
EZH2
TERT
EGFR
Low potential,
thoroughly explored
Explored oncology
Public Data


Unexplored oncology
Public Data
Our focus
Low oncology relevance
RXRX Data
High oncology relevance
RXRX Data
CTLA4
JAK2
BRAF
EZH2
TERT
EGFR
Explored oncology
Public Data

# We are turning this into a search problem, evaluating new programs in bulk

# Reshaping the timelines and shape of drug discovery research



Recursion

# Fireside Chat:
# Dr Deepak Nijhawan

Associate Professor in the Departments of Internal Medicine and Biochemistry at UT Southwestern Medical Center

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Recursion

# Afternoon Convocation

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AI impact in healthcare

# Patients are waiting

# Why: Impact of AI & healthcare for patients

**Predict risk factors** and holistic understanding **disease causality** using **multiomics** and **clinical insights**

Prediction

Diagnosis

**Achieve earlier diagnosis** through **AI-enabled diagnostic methods, biomarkers**, clinical decision support and more

**Boost productivity** through **automated operations** and **elevate** the **quality of care** with virtual assistants

Organizational Productivity

Therapeutic Generation

**Generate and optimize new molecules**, biologics, cell therapies, etc. leveraging **generative AI**

**Achieve precision medicine** by ensuring **access and adoption**, delivering ***the right treatment*** *to the* ***right patient*** *at the* ***right time***

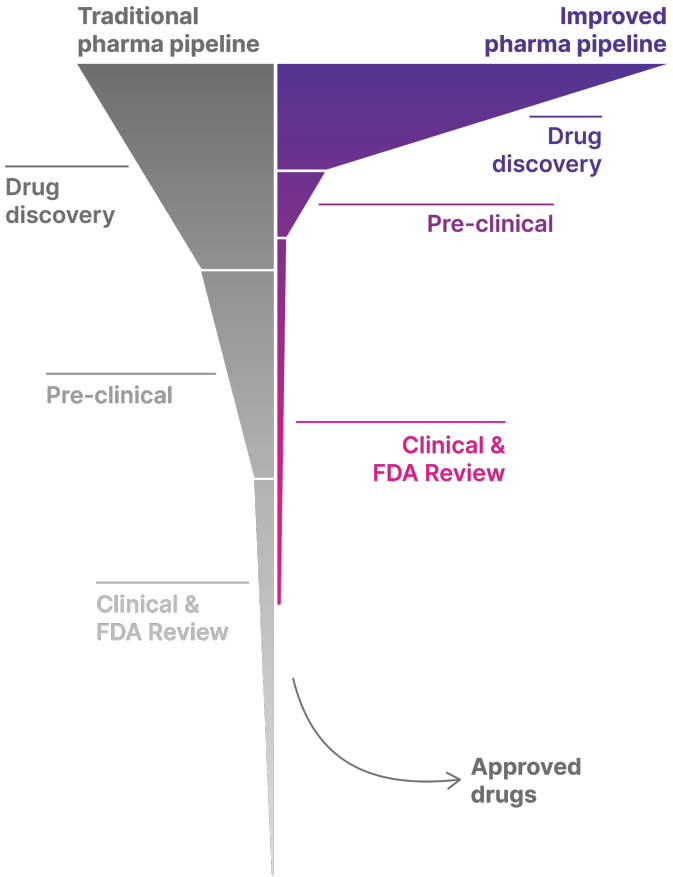
Personalization & Access

Therapeutic Development

**Optimize clinical development** with **precision medicine, digital endpoints, real-world evidence**, and AI-driven execution of clinical trials.

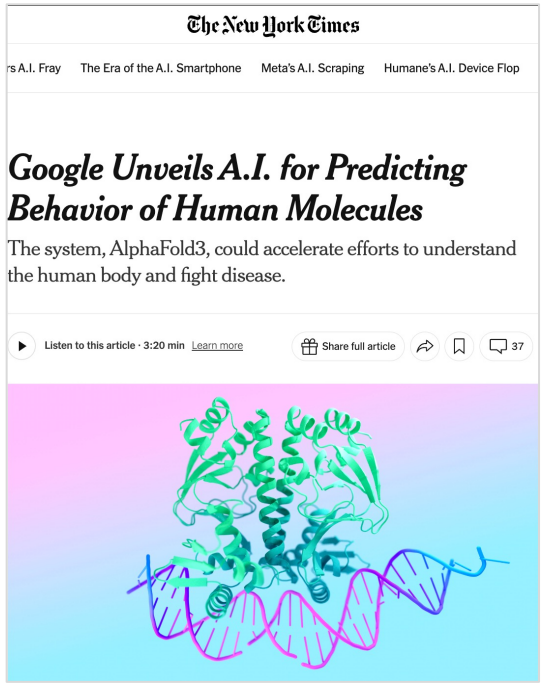
# Why: Current state and the opportunity ahead

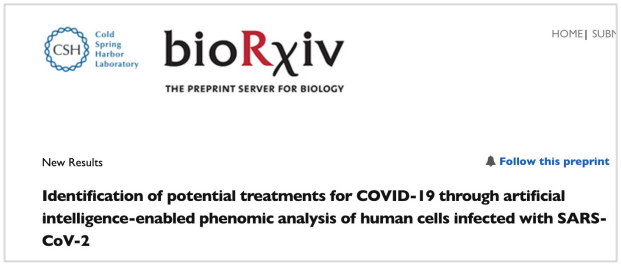
| | Therapeutic hypothesis | Molecular invention | Precision development | Digital commercialization |
|---|---|---|---|---|
| From | Pathway-specific research, genomics | Heuristics-based design, molecular modeling, immunization | Lengthy, linear clinical processes, imprecise disease definition, high failure rates | Broad, one-size-fits-all marketing |
| To | **Industrialized, AI-powered** discovery<br><br>**Multiomics**-based, image-based, **holistic** | **ML, generative AI and physics-based design**, optimization, predictive models | **Precision medicine,** adaptive trial design<br><br>**RWE and ML-driven enrollment,** improved likelihood of success, and faster | **Personalized medicine,** AI-enabled patient and provider engagement |

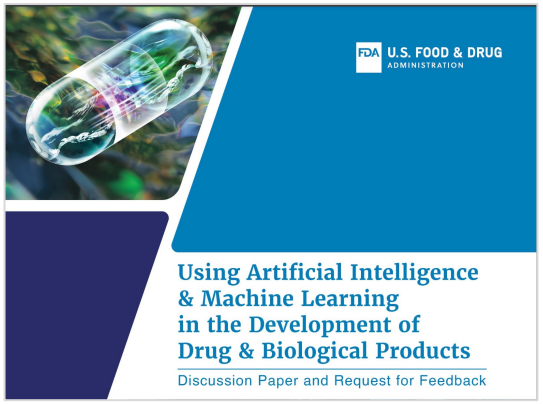



## Improve success rates, faster execution

# What: Industry's current state








Relentlessly **outcomes focused** vs. *point solutions*

**Investing to innovate** *where it matters the most*

**Agility to adopt** new waves of tech + bio innovation

**Bilingual** talent and culture (science + AI)

# What: The pharma of tomorrow

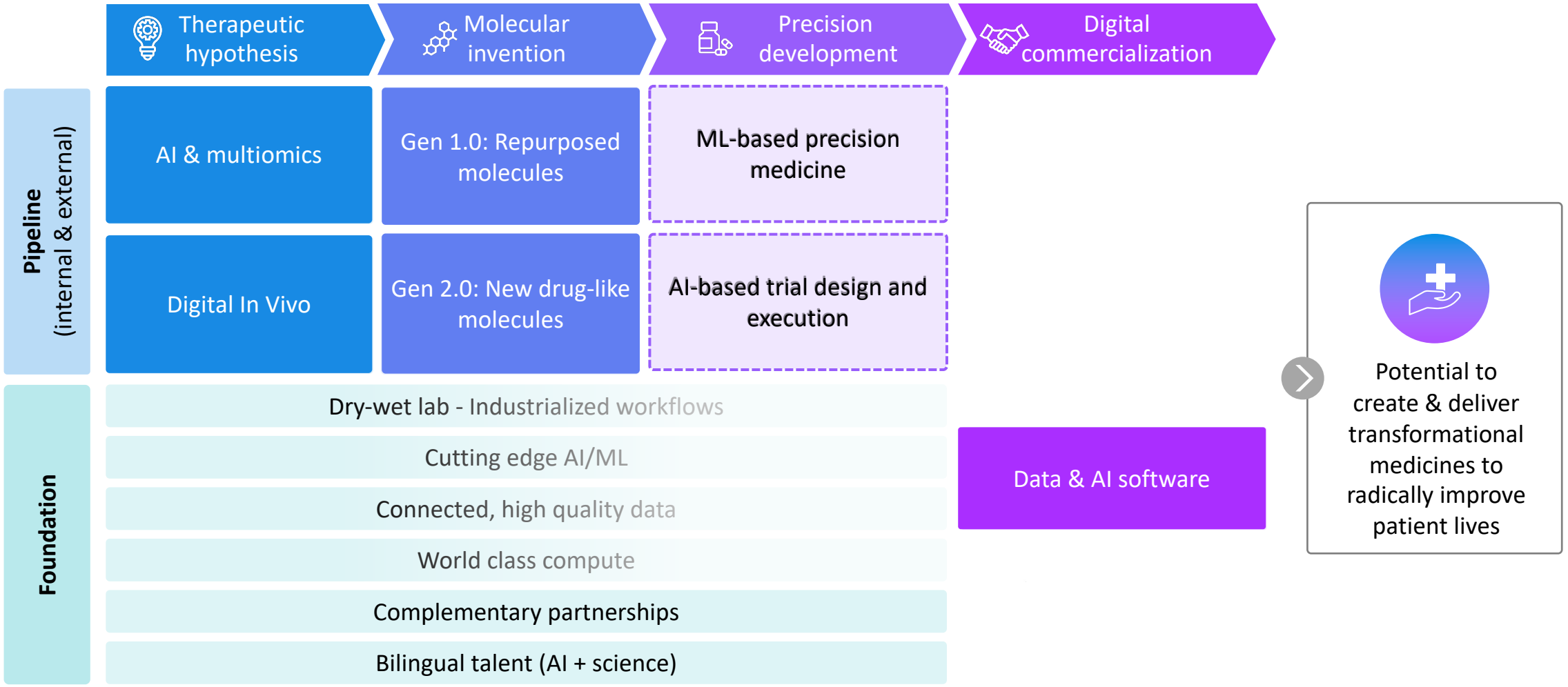
## Breadth and depth in AI and pharma excellence

| | Therapeutic hypothesis | Molecular invention | Precision development | Digital commercialization |
|---|---|---|---|---|
| **Pipeline** (internal & external) | AI and multiomics to identify novel targets and comprehensive biological pathways | Gen AI-driven novel drug-like molecular entities[1] | ML-based precision medicine<br>AI-based trial design and execution | AI-based personalized sales, marketing<br>AI/RWE based DTC, market access, and adoption |
| **Foundation** | Dry-wet lab combo - Industrialized workflows | | | |
| | Cutting edge AI/Machine Learning | | | |
| | Connected, high quality data at scale (proprietary + public) | | | |
| | World class compute | | | |
| | Complementary partnerships | | | |
| | Bilingual talent (AI + science) | | | |

Potential to create & deliver transformational medicines to radically improve patient lives

1. with optimized PK/PD profiles

# RXRX Gen 1.0: The Rise of a TechBio



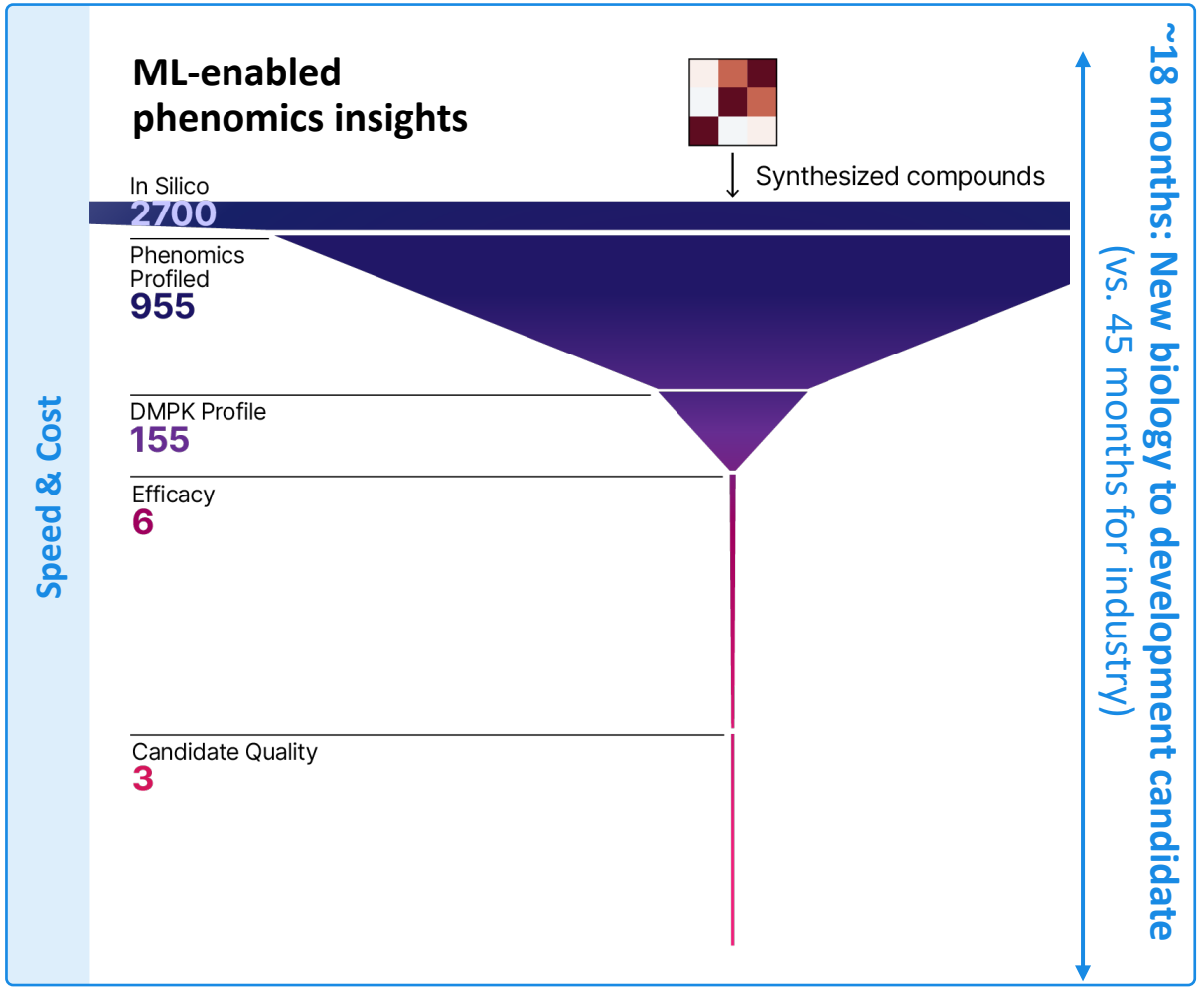
# RXRX Gen 1.0: Emerging proof points

| | Therapeutic hypothesis | Molecular invention | Precision development | Digital commercialization |
|---|---|---|---|---|
| **Pipeline** (internal & external) | **Novel biology:**<br>✓ **RBM39, 12+** in early and late discovery<br>• **Roche – GI Onc, Neuroscience**<br>✓ **Bayer – Oncology** | **Repurposed molecules to novel molecules:**<br>✓ **RBM39, Epsilon, 12+** in early and late discovery, **60%** using Gen AI<br>✓ **Roche – RG1**<br>✓ **2.5x lower** cost to IND<br>✓ **3x faster** time to lead | **Pipeline: 7 programs**<br>• 5 in clinical stage<br><br>**AI-based trial execution**<br>• **AXIN1/APC** Ph 2 | |
| **Foundation** | **Phenom-1** | **MatchMaker** (Hit ID)<br>**MolE** (ADME)<br>**GFlowNets** (Lead Op) | **Causal AI** | **Phenom-Beta** |
| | **LOWE** (LLM to orchestrated workflows) | | | |
| | **50 PB+** high quality data (biological, chemical, clinical) | | | |
| | **BioHive-2** | | | |
| | **Roche/Genentech, Bayer, Nvidia, Enamine, Tempus, Helix, and more** | | | |

Potential to create & deliver transformational medicines to radically improve patient lives

# Use case 1: RBM39 – new biology and chemistry

| | Therapeutic hypothesis | Molecular invention | Precision dev. | Commercial-ization |
|---|---|---|---|---|
| **Pipeline** (internal & external) | • Novel biology: **RBM39** | Gen 2.0 NCE: • **RBM39** | Pipeline: & programs • 5 in clinical stage | |
| | | • **~2.5x lower cost to IND** • **~3x faster time to lead** | Just-in-time recruitment: • AXN1/APC | |
| **Foundation** | **Phenom-1** | **MatchMaker MolE GFlowNets** | Precision medicine – Causal AI | Phenom-Beta |
| | **LOWE** | | | |
| | **50 PB+** | | | |
| | **BioHive-2** | | | |
| | **Cross-industry partnerships – Enamine, Tempus** | | | |



# Use case 2: Faster execution, lower cost for preclinical programs

| | Therapeutic hypothesis | Molecular invention | Precision dev. | Commercial-ization |
|---|---|---|---|---|
| **Pipeline** (internal & external) | • Novel biology: **RBM39** | Gen 2.0 NCE: • **RBM39** | Pipeline: & programs • 5 in clinical stage | |
| | | • **~2.5x lower cost to IND** • **~3x faster time to lead** | Just-in-time recruitment: • AXN1/APC | |
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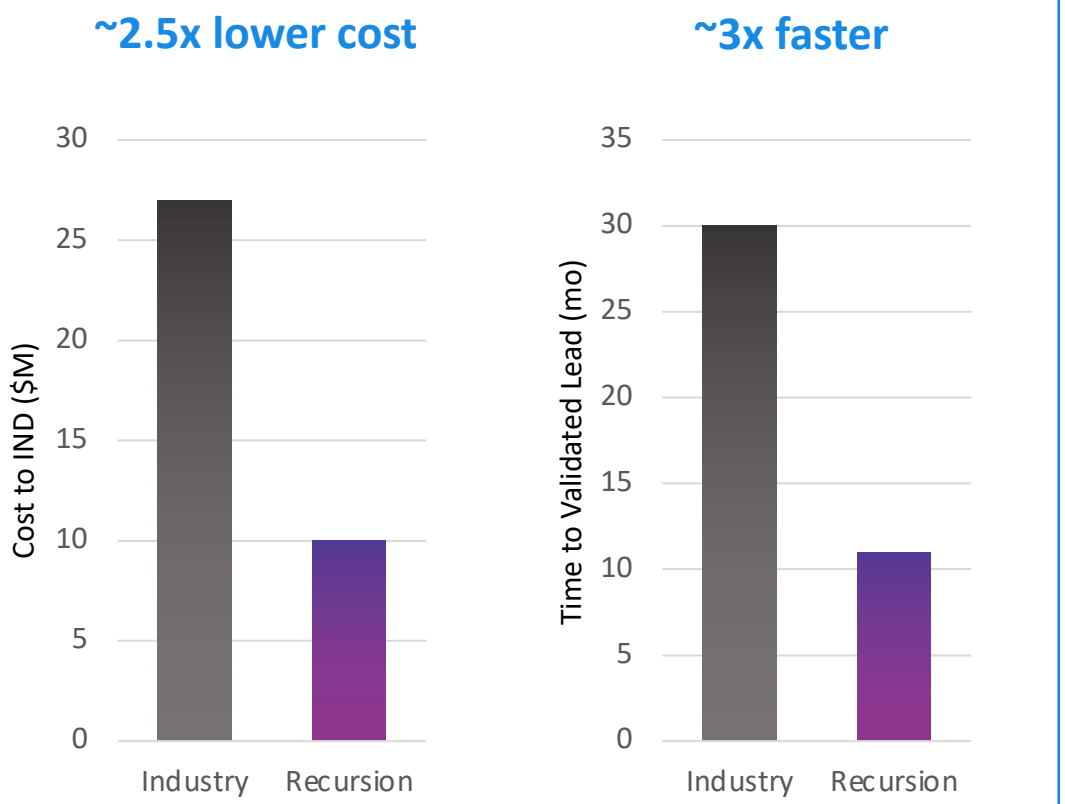
| | **LOWE** | | | |
| | **50 PB+** | | | |
| | **BioHive-2** | | | |
| | **Cross-industry partnerships – Enamine, Tempus** | | | |

**Speed & Cost**

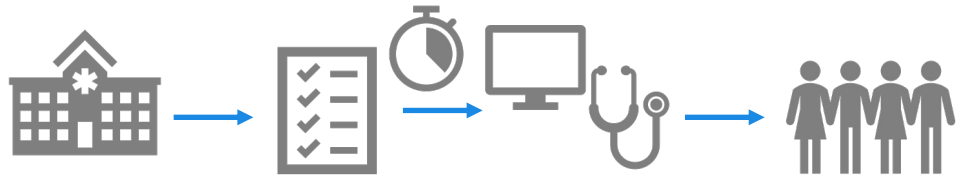


# Use case 3: Advancing clinical execution using AI

| | Therapeutic hypothesis | Molecular invention | Precision dev. | Commercial-ization |
|---|---|---|---|---|
| **Pipeline** (internal & external) | • Novel biology: RBM39 | Gen 2.0 NCE: • RBM39 | Pipeline: & programs • 5 in clinical stage | |
| | | • ~2.5x lower cost to IND • ~3x faster time to lead | **Just-in-time recruitment: • AXN1/APC** | |
| **Foundation** | Phenom-1 | MatchMaker MolE GFlowNets | Precision medicine – Causal AI | Phenom-Beta |
| | **LOWE** | | | |
| | **50 PB+** | | | |
| | BioHive-2 | | | |
| | **Cross-industry partnerships – Enamine, Tempus** | | | |

**Faster recruitment**

## AXIN1/APC Ph2 enrollment



**Traditional → 4-6 months**

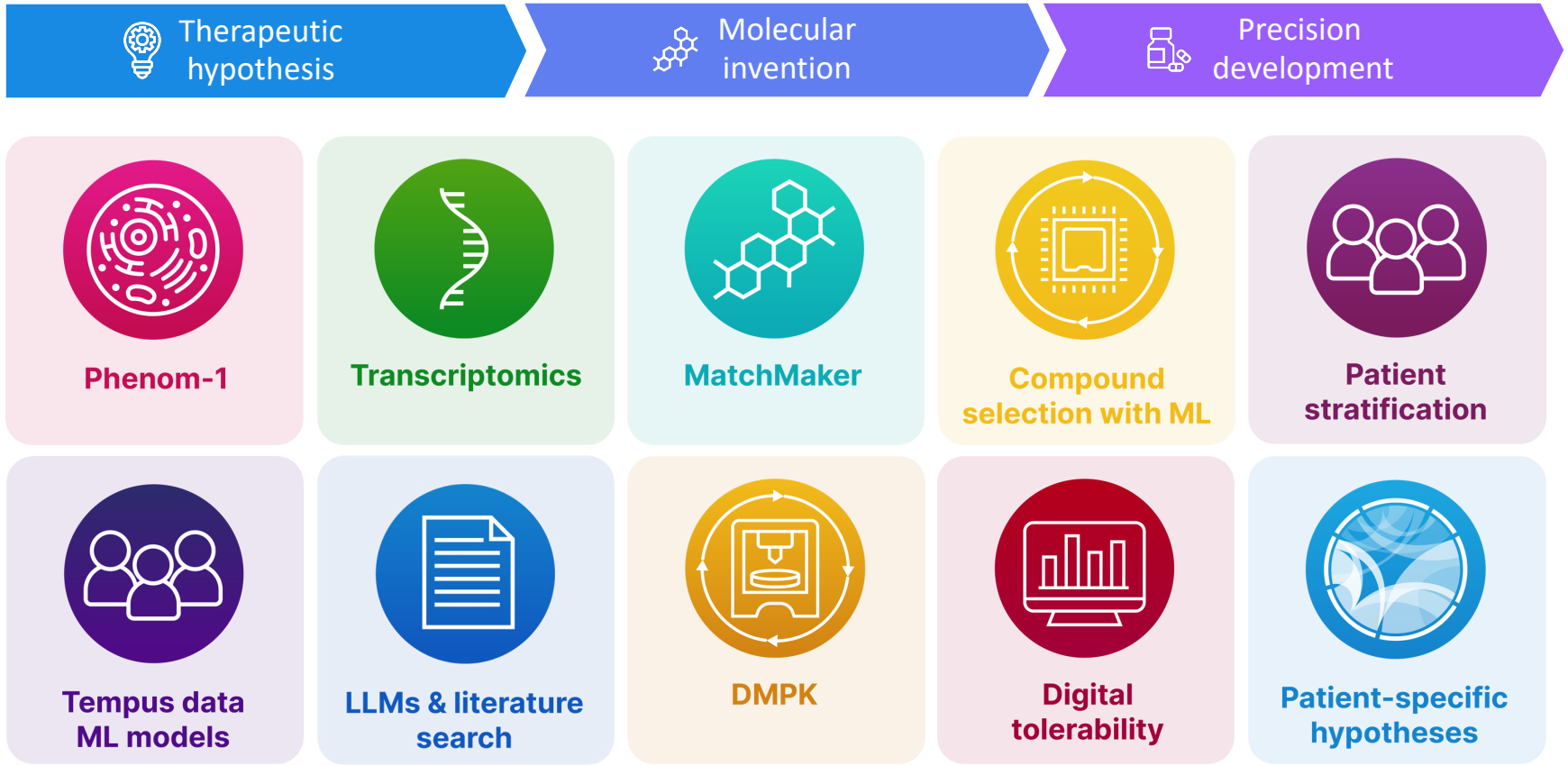
**Data-driven, just-in-time → 4-6 weeks**

**Genomics & RWD + AI** ✓

**Site Partnerships + Master Agreements + Central IRBs** ✓

**Sites/participants engaged in real time at point of care** ✓

# Use case 4: Suite of AI-first models



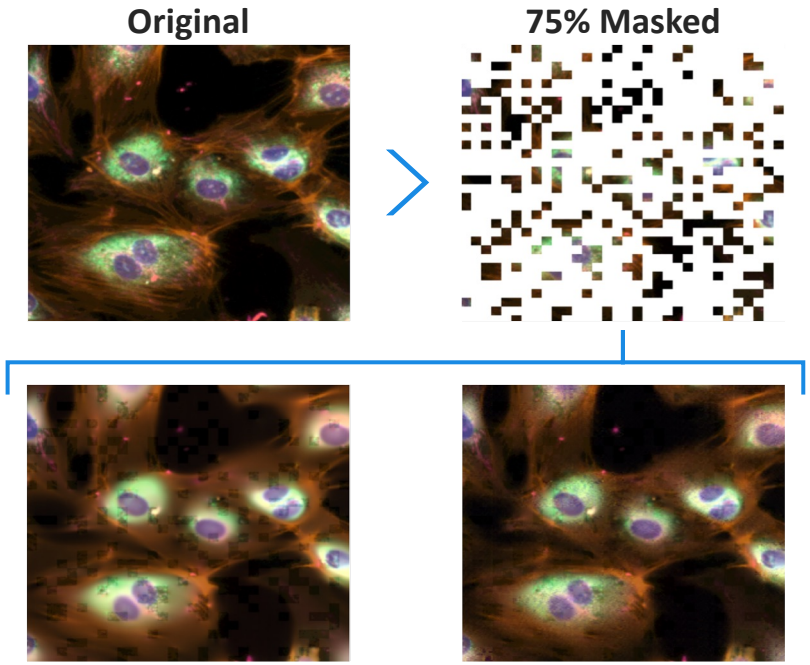
# Use case 5: Foundational models for external use

| | Therapeutic hypothesis | Molecular invention | Precision dev. | Commercial-ization |
|---|---|---|---|---|
| **Pipeline** (internal & external) | • Novel biology: RBM39 | Gen 2.0 NCE: • RBM39 | Pipeline: & programs • 5 in clinical stage | |
| | | • ~2.5x lower cost to IND • ~3x faster time to lead | Just-in-time recruitment: • AXN1/APC | |
| **Foundation** | Phenom-1 | MatchMaker MolE GFlowNets | Precision medicine – Causal AI | **Phenom-Beta** |
| | **LOWE** | | | |
| | **50 PB+** | | | |
| | BioHive-2 | | | |
| | Cross-industry partnerships – Enamine, Tempus | | | |

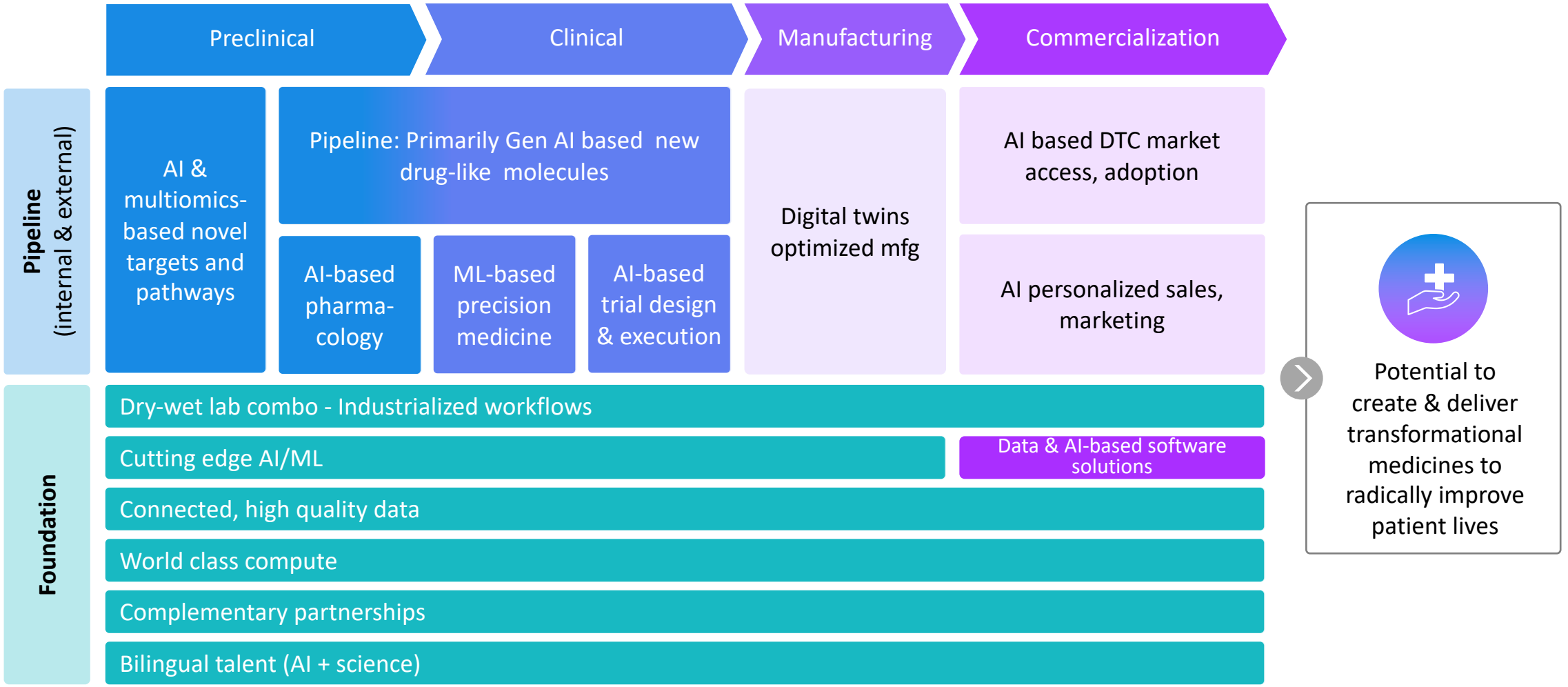
**Foundational models for external use**

## Phenom-Beta

*Hosted on Nvidia BioNeMo platform*



# What's next?


Preclinical
Clinical
Manufacturing
Commercialization
Pipeline (internal & external)
AI & multiomics-based novel targets and pathways
Pipeline: Primarily Gen AI based new drug-like molecules
AI-based pharma-cology
ML-based precision medicine
AI-based trial design & execution
Digital twins optimized mfg
AI based DTC market access, adoption
AI personalized sales, marketing
Foundation
Dry-wet lab combo - Industrialized workflows
Cutting edge AI/ML
Data & AI-based software solutions
Connected, high quality data
World class compute
Complementary partnerships
Bilingual talent (AI + science)
Potential to create & deliver transformational medicines to radically improve patient lives

# Path forward objectives – next 12 months

Advance Preclinical and Clinical Stage Programs

Enhance AI-Driven Chemistry

Innovate with AI across Clinical Development

Continue Investment in Scalable Infrastructure – wet and dry lab

Deliver on Strategic Partnerships

Create additional SaaS opportunities to advance the creation of medicines

Recursion

# Partnerships

# We harness value from the Recursion OS with a multi-pronged capital-efficient business strategy


**Pipeline**

## Pipeline Strategy

Build internal pipeline in indications with potential for **accelerated path** to approval

- **Precision Oncology**
- **Rare Disease**

**Partnerships**

## Partnership Strategy

Partner in **complex therapeutic areas** requiring large financial commitment or competitive arbitrage

**Leverage partner knowledge** and clinical development capabilities

- **Neuroscience***
- **Undruggable Oncology**
- **Other large, intractable areas of biology (e.g., CV/Met)**

**Data**

## Data Strategy

**License** subsets of data and key tools

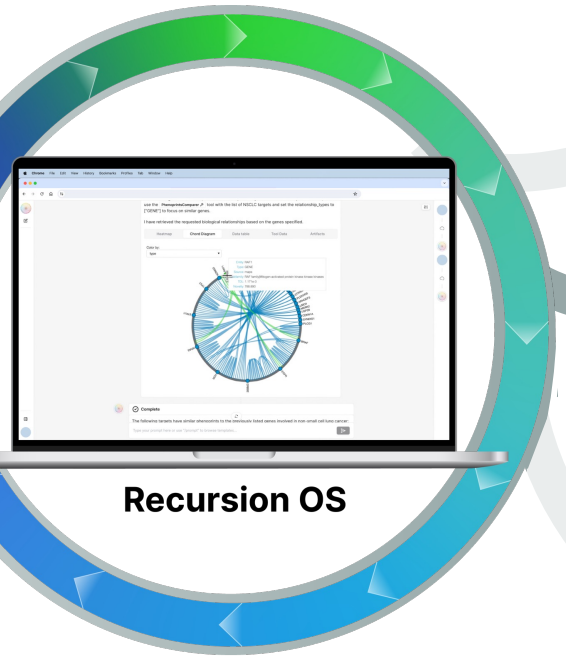
Direct generation of new data internally **to maximize pipeline and partnership value-drivers**

- **Licensing**
- **Augment Recursion OS**



**Includes a single oncology indication from our Roche and Genentech collaboration.*

# We harness value from the Recursion OS with a multi-pronged capital-efficient business strategy




Pipeline

## Pipeline Strategy

Build internal pipeline in indications with potential for **accelerated path** to approval

- Precision Oncology
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Data

## Data Strategy

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- Licensing
- Augment Recursion OS



*Includes a single oncology indication from our Roche and Genentech collaboration.

# Roche Genentech Partnership

**Neuroscience**
(and single oncology indication)
Announced Dec 2021



**Undruggable oncology targets**

Announced Sept 2020
Amended Nov 2023

# Computational Sciences in Drug Development

John Marioni, PhD FMedSci

Senior Vice President & Head of Computational Sciences, gRED

Genentech

Schema XI

Fig: 1.

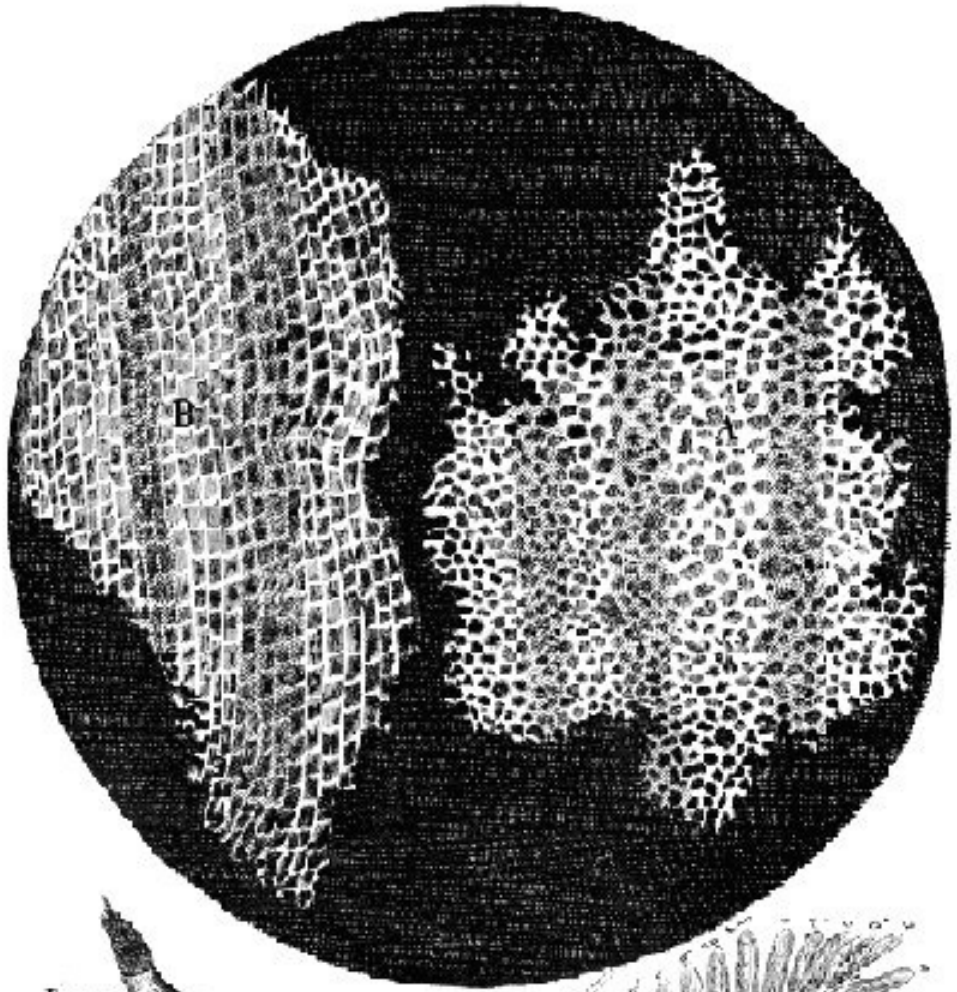



Fig: 2.

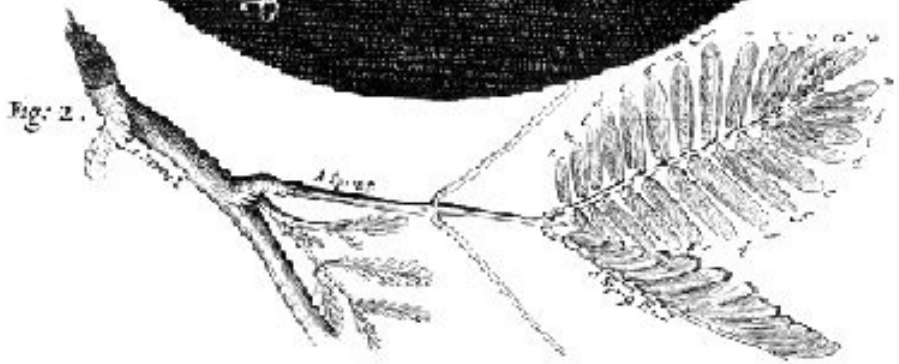


Fig: 5.

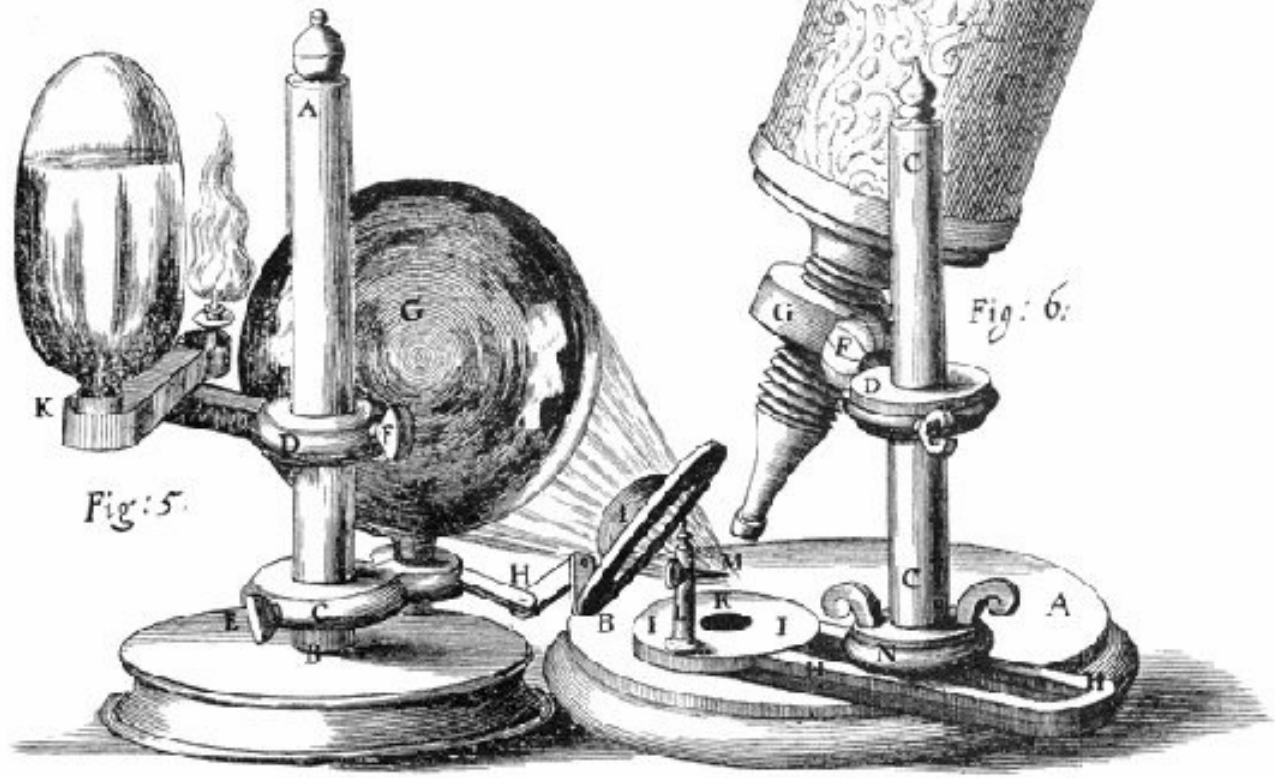
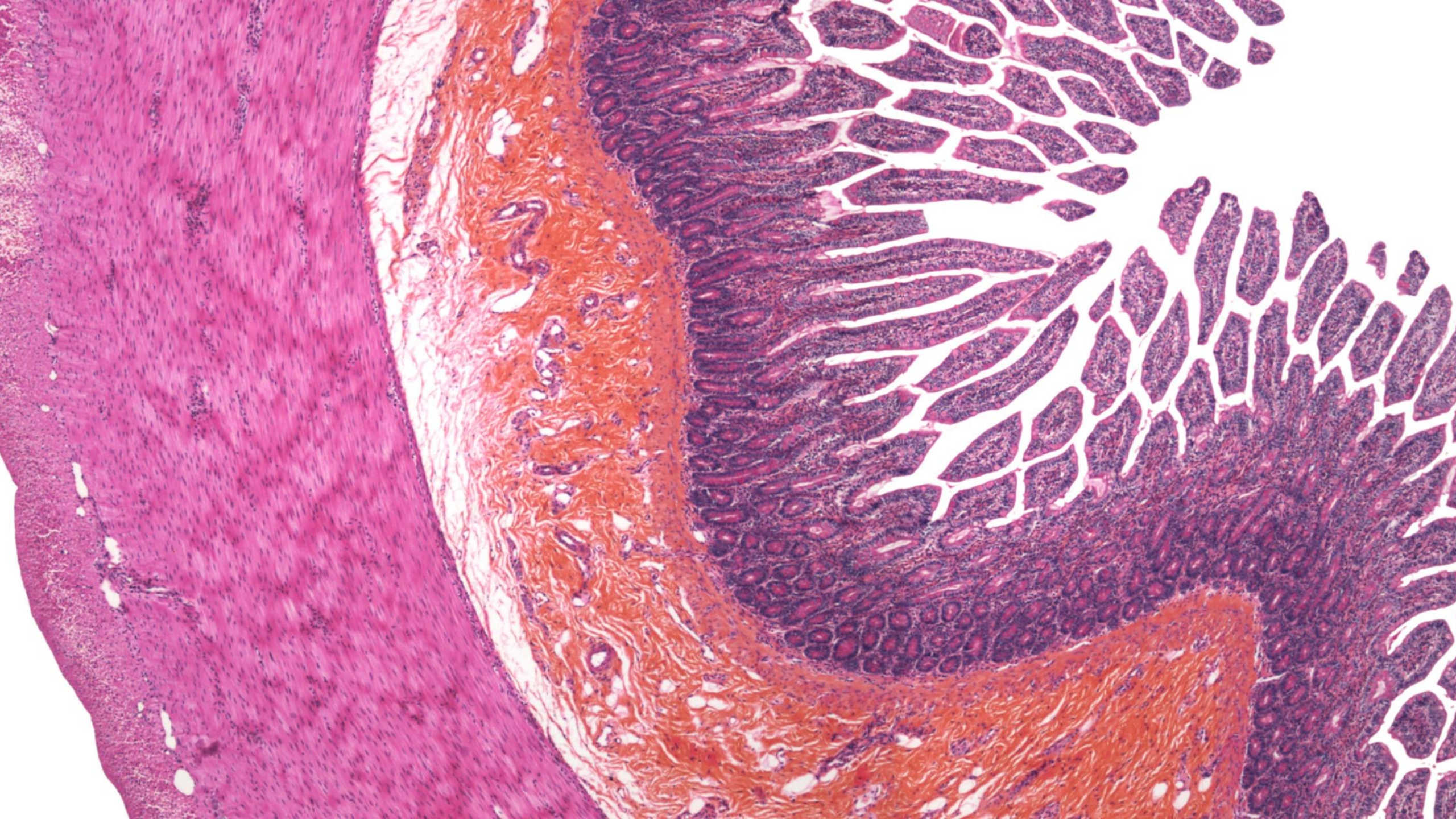
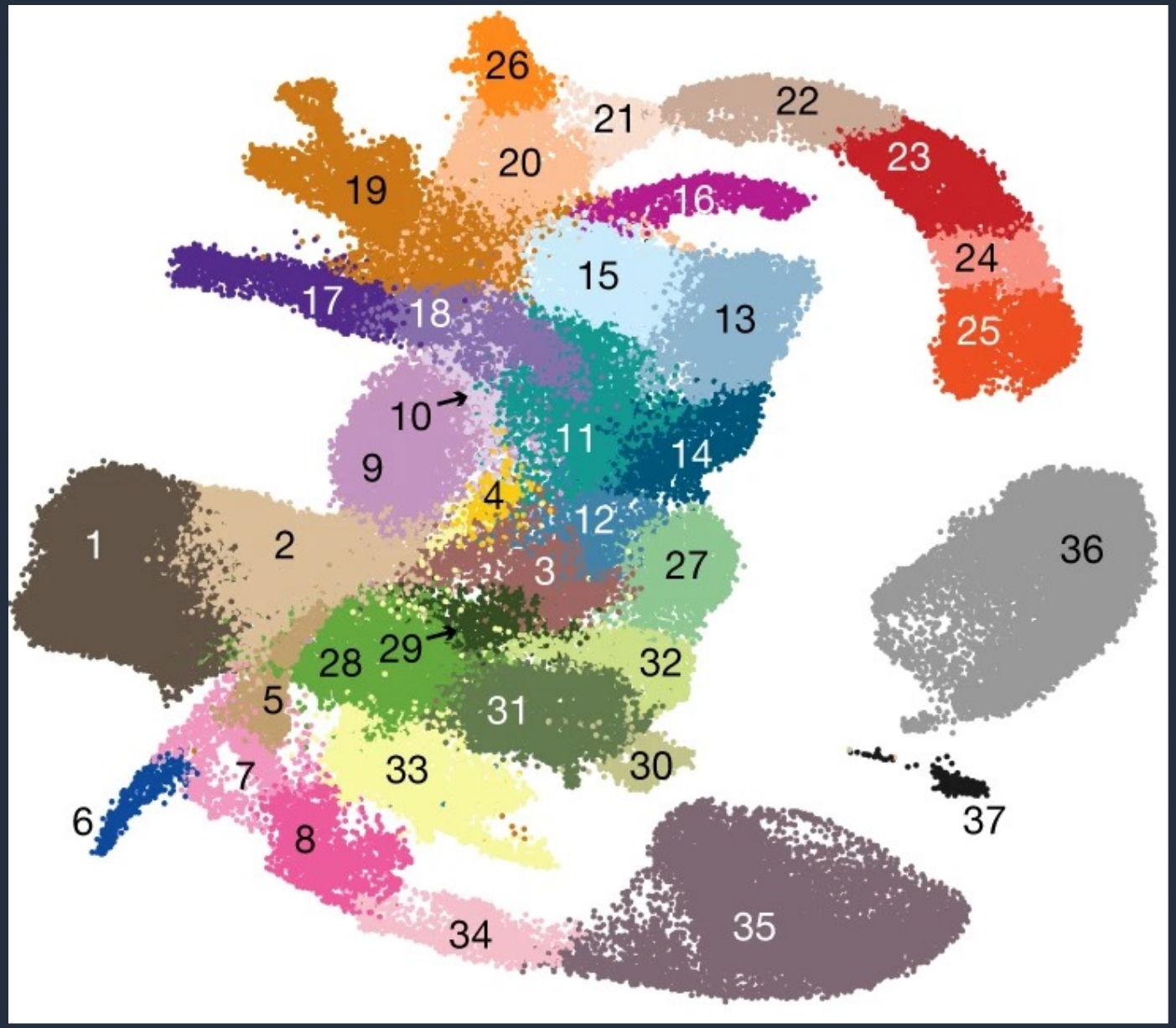



Fig: 6.






Pijuan-Sala, Griffiths, Guibentif, et al., Nature, 2019

We can generate **huge amounts of data**—from both **healthy** and **perturbed** conditions… but how will we make sense of these data and make predictions about perturbations we have not seen?

$10^4$

CELL TYPES AND STATES

$2x10^4$

GENES

$4^{2.4x10^8}$

VARIANT COMBINATIONS

$10^{13}$

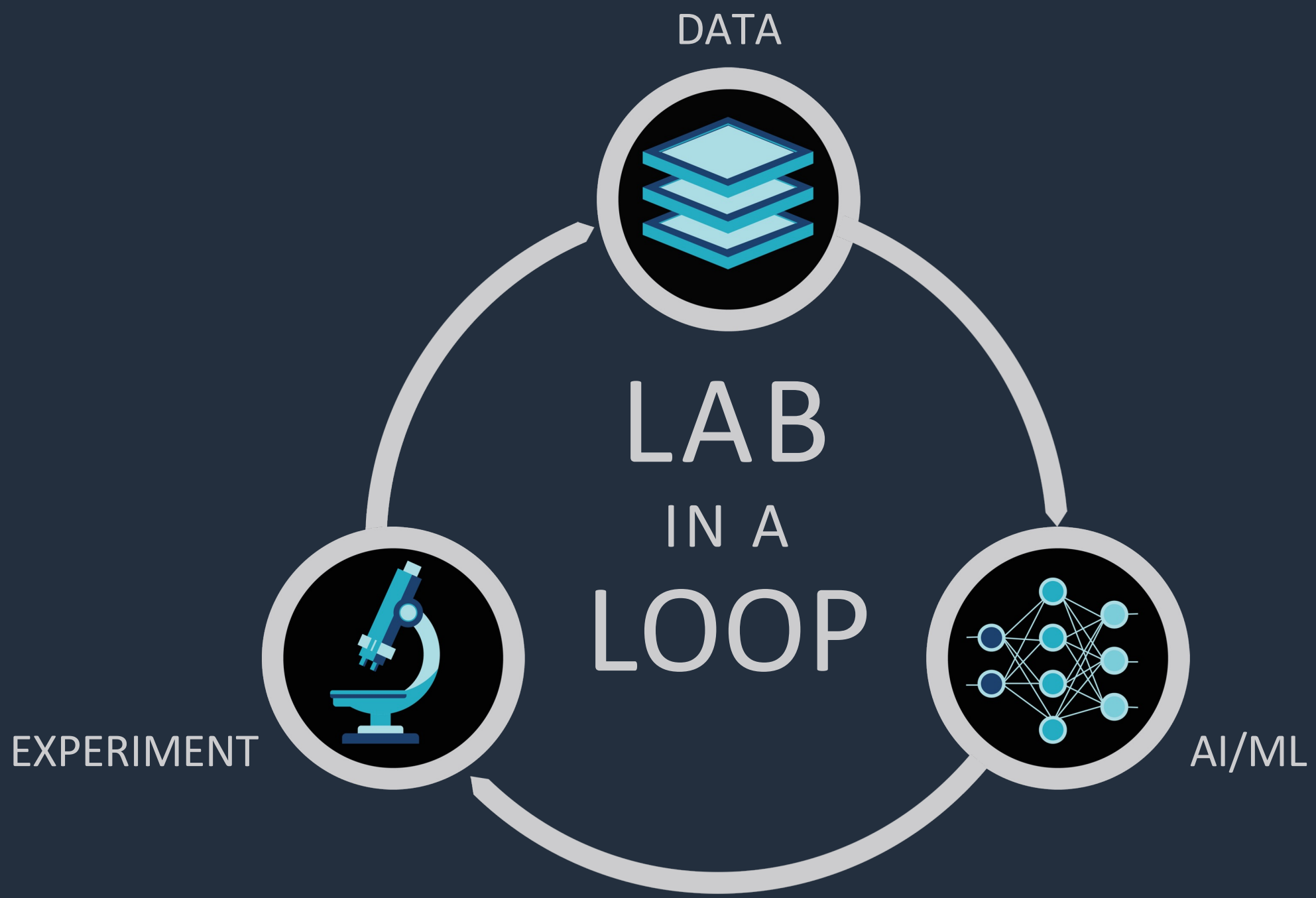
GENE COMBINATIONS

This is one example where computational models, especially **foundation models** and **generative AI** can **transform** how we discover and develop **medicines**

This is one example where computational models, especially **foundation models** and **generative AI** can **transform** how we discover and develop **medicines**

gRED Computational Sciences (gCS) seeks to make this vision a reality

# HOW?


DATA
LAB
IN A
LOOP
EXPERIMENT
AI/ML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GGGATCCTCATCAAGCGACGGCAGCAGAAGATCCGGAAGTACACGATGCGGAGACTGCTGCAGGAAACGGAGCTGGT
GACACCTAGCGGAGCGATGCCCAACCAGGCGCAGATGCGGATCCTGAAAGAGACGGAGCTGAGGAAGGTGAAGGTGC
CGCTTTTGGCACAGTCTACAAGGGCATCTGGATCCCTGATGGGGAGAATGTGAAAATTCCAGTGGCCATCAAAGTGTT
CATCCCCCAAAGCCAACAAAGAAATCTTAGACGAAACGATCTCAAACTTATTCTCAAACTTCGCCCCGAGAGGGCCCT
CCGACCTGCTGGTGCCACTCTGGAAAGGGCCAAGACTCTCTCCCCAGGGAAGAATGGGGTCGTCAAAGACGTTTTTG

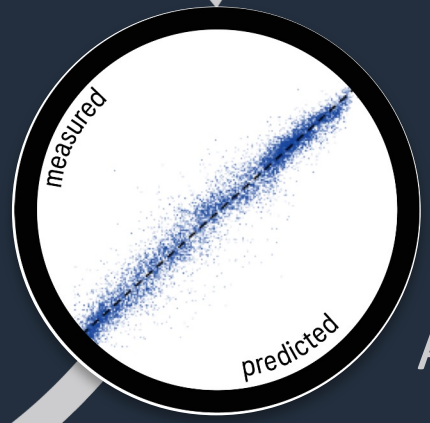
DATA

TRANSFORMER

BASED ORACLE

EXPERIMENT

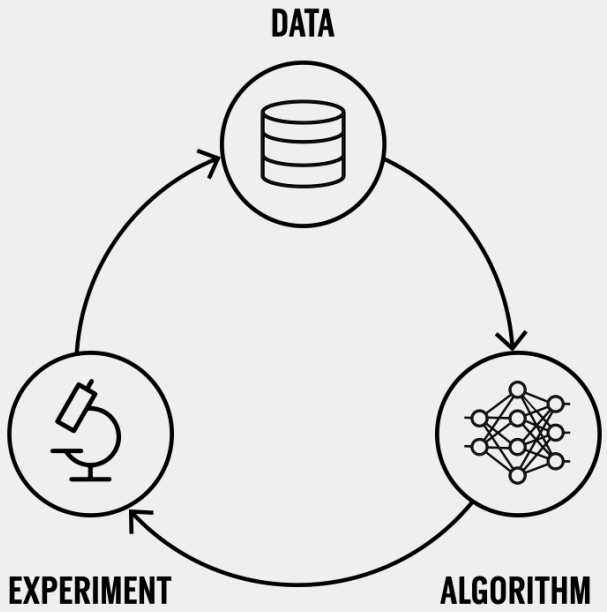
$4^{80}$ possibilities




AI/ML

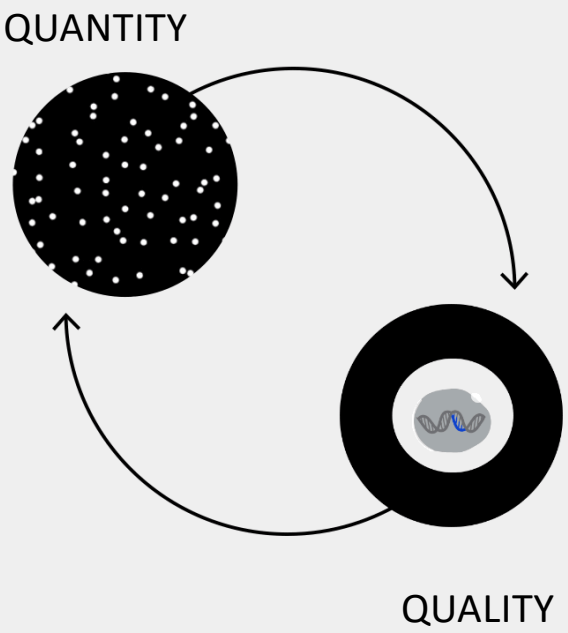
# Our AI strategy for R&D

## Lab in a Loop, integrated




Full stack, across all aspects of R&D; up to “self drive”

## Scale & resolution




Maximize benefit of large size: proprietary legacy data and data generation capacity

## Strategic partnerships

Key partnerships:

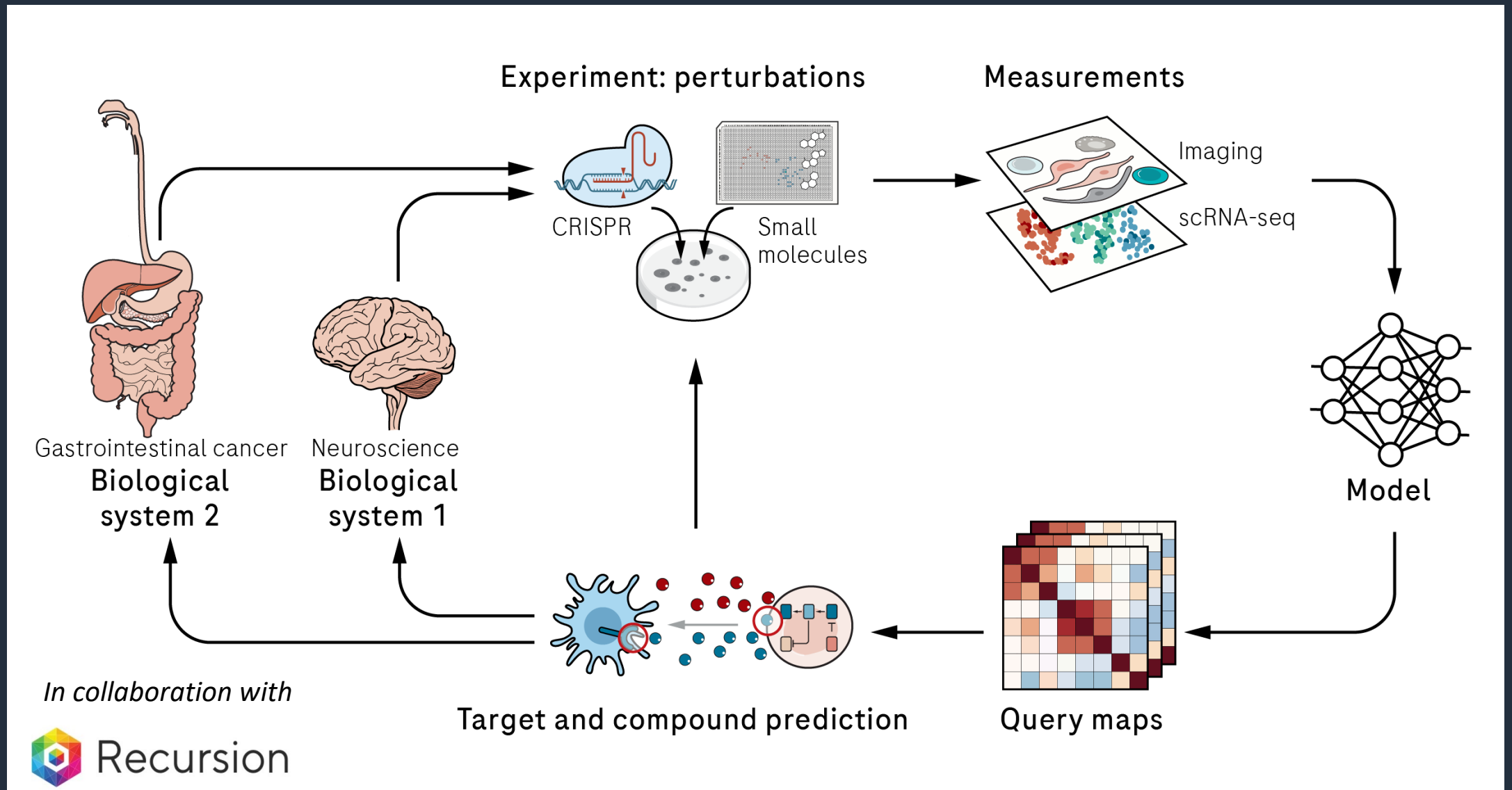
NVIDIA

Recursion

aws

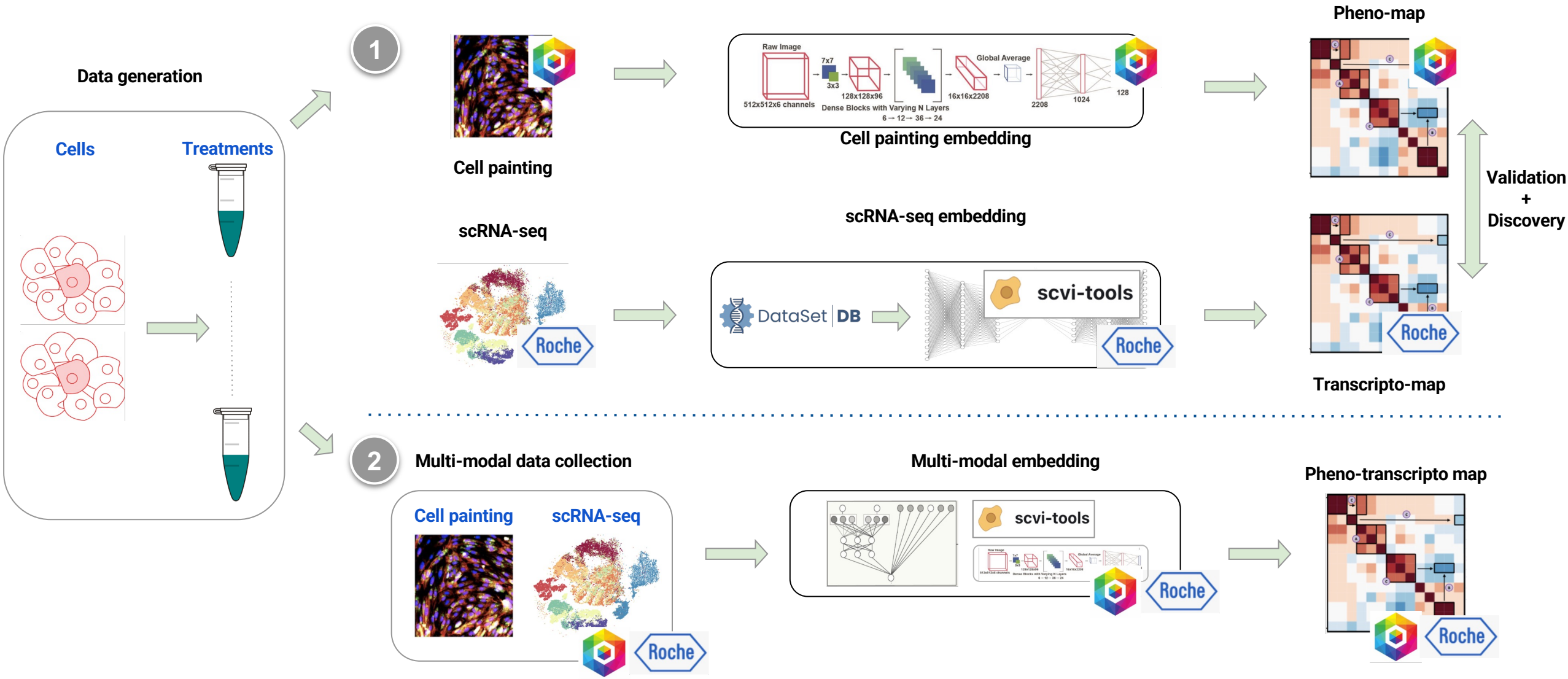
Partnership around unique data generation, AI/ML model development and hardware

# RIGHT TARGET OR CHEMICAL MATTER FOR THE DISEASE


Experiment: perturbations
Measurements
CRISPR
Small molecules
Imaging
scRNA-seq
Gastrointestinal cancer
Biological system 2
Neuroscience
Biological system 1
Model
Target and compound prediction
Query maps
In collaboration with
Recursion

# RIGHT MOLECULE

# Multi-Modal Model Development



# MODELS ARE ONLY AS GOOD AS THE DATA

## Challenges

Data management, metadata and access

Integrating expertise from multiple disciplines

Access to scalable scientific computing for fitting/fine-tuning models

Democratizing access and ensuring use of data and models

## Challenges... But already driving to solutions

Data management, metadata and access: modernizing our data stack and exploiting the cloud and associated tools

Integrating expertise from multiple disciplines: internal organizational structure and external partners

Access to scalable scientific computing for fitting/fine-tuning models: partnering with outstanding companies in the industry

Democratizing access and ensuring use of data and models: Autonomous agents as the next-generation scientific assistant

# THANK YOU!

# Bayer Partnership

**Neuroscience**
(and single oncology indication)
Announced Dec 2021

**Undruggable oncology targets**

Collaboration announced Sept 2020
Amended Nov 2023

# Scientific Collaborations: Undruggable Oncology Targets

Nov 2023
pivot to Oncology

Q1

Work initiated

Q2

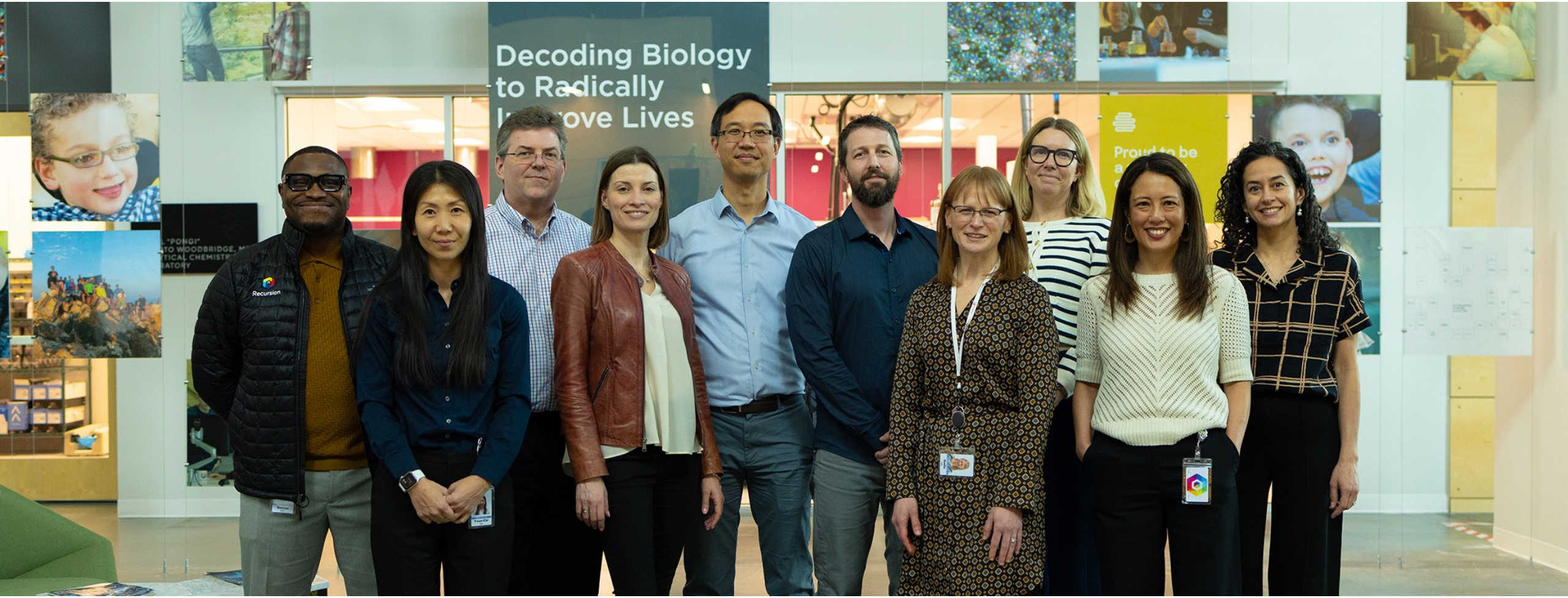
Initiated 1st joint Project which will now be advancing rapidly towards Lead Series nomination

Q3

On track to complete 25 unique multi-modal data packages in Q3

**Bayer expected to be the first beta-user of our LOWE LLM-orchestrated workflow software**

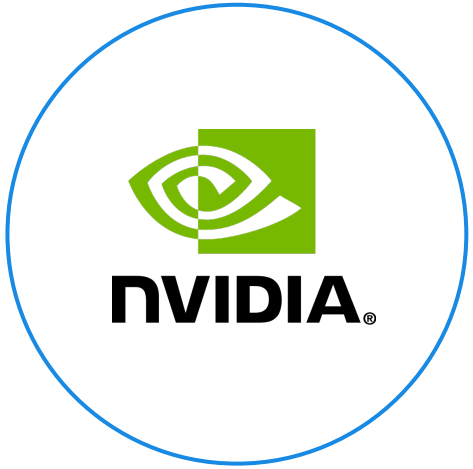
# Scientific Collaborations: Undruggable Oncology Targets



# Scientific Collaborations: Platform, Tech, and Data

Computation and ML/AI

Announced July 2023



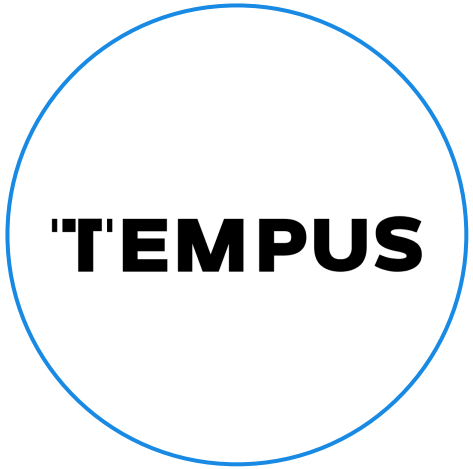


Cheminformatics and chemical synthesis

Announced Dec 2023

Real-world data access (oncology)

Announced Nov 2023





Real-world data access (non-oncology)

Announced May 2024

# Scientific Collaborations: Real world (de-identified) data


- Multi-site network protocol continuously aggregating in **various therapeutic areas**
- **Geographically** and **demographically diverse** population consented for re-contact
- **Whole exome sequencing** paired with rich, **longitudinal clinical data** for all consenting patients
- Access to **hundreds of thousands of unique records** each year

# We harness value from the Recursion OS with a multi-pronged capital-efficient business strategy



Recursion

# Clinical

DownloadDay 2024

# Our pipeline reflects the scale and breadth of our approach

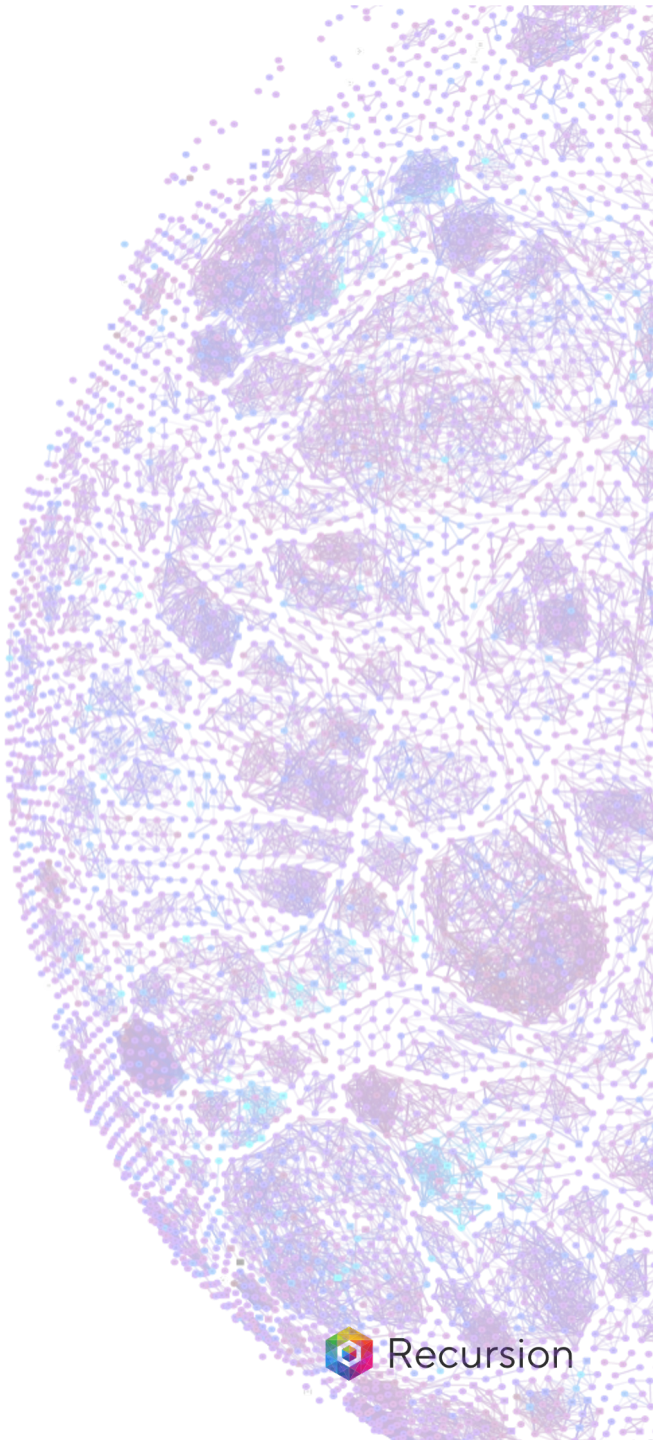
| | Program | Indication | Target | Patient Population | Preclinical | Phase 1 | Phase 2 | Phase 3 | Anticipated Near-Term Milestones |
|---|---|---|---|---|---|---|---|---|---|
| Rare & Other | **REC-994** | Cerebral Cavernous Malformation | Superoxide | ~ 360K[1] | *SYCAMORE* | | | | Topline readout in September 2024 |
| | **REC-2282** | Neurofibromatosis Type 2 | HDAC | ~ 33K[2] | *POPLAR* | | | | Preliminary data readout in Q4 2024 |
| | **REC-4881** | Familial Adenomatous Polyposis | MEK | ~ 50K[3] | *TUPELO* | | | | Preliminary data readout in H1 2025 |
| | **REC-3964** | *Clostridioides difficile* Infection | TcdB | ~730K | *ALDER* | | | | Ph2 initiation in Q4 2024 |
| | **Epsilon** | Fibrotic Diseases | Undisclosed | ~ 50K[4,5,6] | | | | | IND submission in early 2025 |
| Oncology | **REC-4881** | Advanced AXIN1/APC-mutant Cancers | MEK | ~ 104K[7] | *LILAC* | | | | Preliminary data readout in H1 2025 |
| | **RBM39** | Advanced HR-Proficient Cancers | RBM39 | ~ 220K[8] | | | | | IND submission in Q3 2024, Ph 1/2 initiation in Q4 2024 |

**More than a dozen discovery and research programs in oncology or with our partners – first program optioned by Roche-Genentech in GI-oncology**

All populations defined above are US and EU5 incidence unless otherwise noted. EU5 is defined as France, Germany, Italy, Spain, and UK. (1) Prevalence for hereditary and sporadic symptomatic population. (2) Annual US and EU5 incidence for all *NF2*-driven meningiomas. (3) Prevalence for adult and pediatric population. (4) Our program has the potential to address several indications. (5) We have not finalized a target product profile for a specific indication. (6) Incidence for US only. (7) 2L+ drug-treatable population. (8) 2L+ drug-treatable population comprising ovarian, prostate, breast, and pancreatic cancers.

# **REC-994** for the Treatment of Symptomatic Cerebral Cavernous Malformations (CCM)

| | |
|---|---|
| **Target / MOA** | Superoxide Scavenger |
| **Molecule Type** | Small Molecule |
| **Lead Indication(s)** | Cerebral Cavernous Malformations |
| **Status** | Phase 2 |
| **Designation(s)** | US & EU Orphan Drug |
| **Source of Insight** | Recursion OS |



Clinical: CCM

# SYCAMORE Clinical Trial: REC-994 for CCM Phase 2 Fully Enrolled

## PREVALENCE & STANDARD OF CARE

~360,000

**Symptomatic US + EU5,** >1 million patients worldwide live with these lesions today

**>5x larger** US patient population than other rare diseases like Cystic Fibrosis (>31k patients)

**No approved therapy**

- Most patients receive no treatment or only symptomatic therapy
- Surgical resection or stereotactic radiosurgery not always feasible because of location and is not curative

## CAUSE

**LOF mutations in genes *CCM1*, *CCM2* & *CCM3***, key for maintaining the structural integrity of the vasculature due to unknown mechanisms

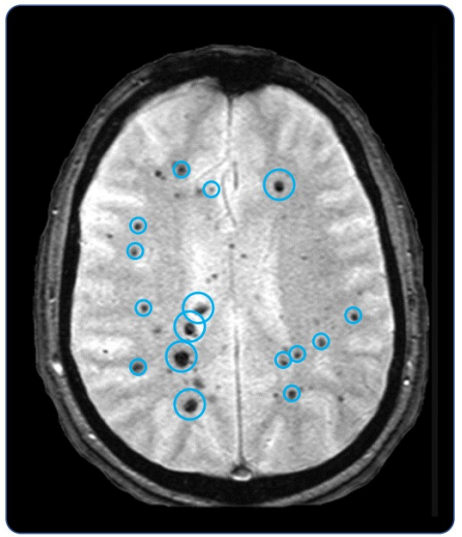
## PATHOPHYSIOLOGY & REASON TO BELIEVE

**Vascular malformations of the CNS** leading to focal neurological deficits, hemorrhage and other symptoms

Efficacy signal in Recursion OS as well as functional validation via scavenging of massive superoxide accumulation in cellular models; reduction in lesion number with chronic administration in mice

## KEY ELEMENTS

- Targeting **sporadic and familial symptomatic CCM** patients with *CCM1*, *CCM2*, and *CCM3* mutations
- Superoxide scavenger, small molecule
- Phase 2 readout **expected September 2024**
- US & EU **Orphan Drug Designation**



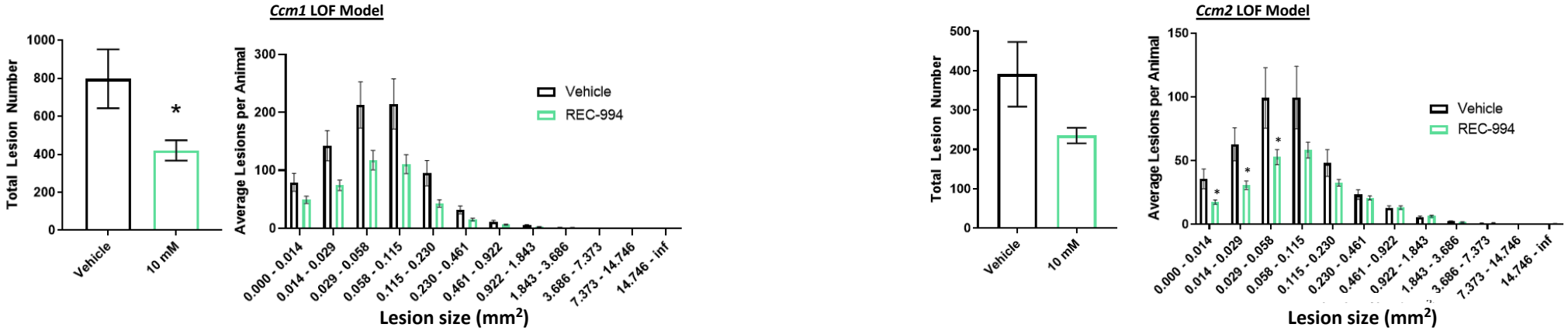
Vascular malformations (cavernomas)

Julia – living with CCM

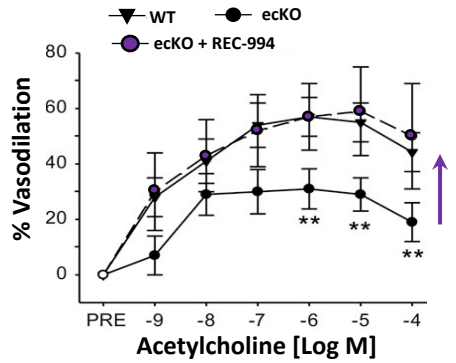
# Preclinical Studies Confirm Insight

**Preclinical Studies: REC-994 reduces lesion burden and ameliorates vascular defects in genetic mouse models of CCM**

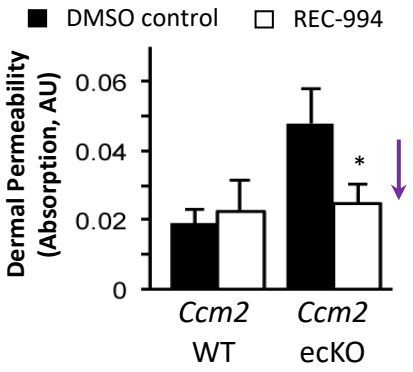
## 1 Reduces lesion number & size in *Ccm1* and *Ccm2* LOF mouse models




## 2 Rescues acetylcholine-induced vasodilation defect




## 3 Rescues dermal permeability defect in CCM2 mice




- **REC-994 stabilizes the integrity of vasculature against challenges to permeability**
- **Altered vascular permeability is a clinically relevant feature of CCM lesions**



*Source: Data above from Gibson, et al. Strategy for identifying repurposed drugs for the treatment of cerebral cavernous malformation. Circulation, 2015 or Recursion internal data (Ccm1 mouse model)*

# SYCAMORE Clinical Trial : REC-994 for CCM Phase 2 Fully Enrolled

**Topline Data Expected September 2024**

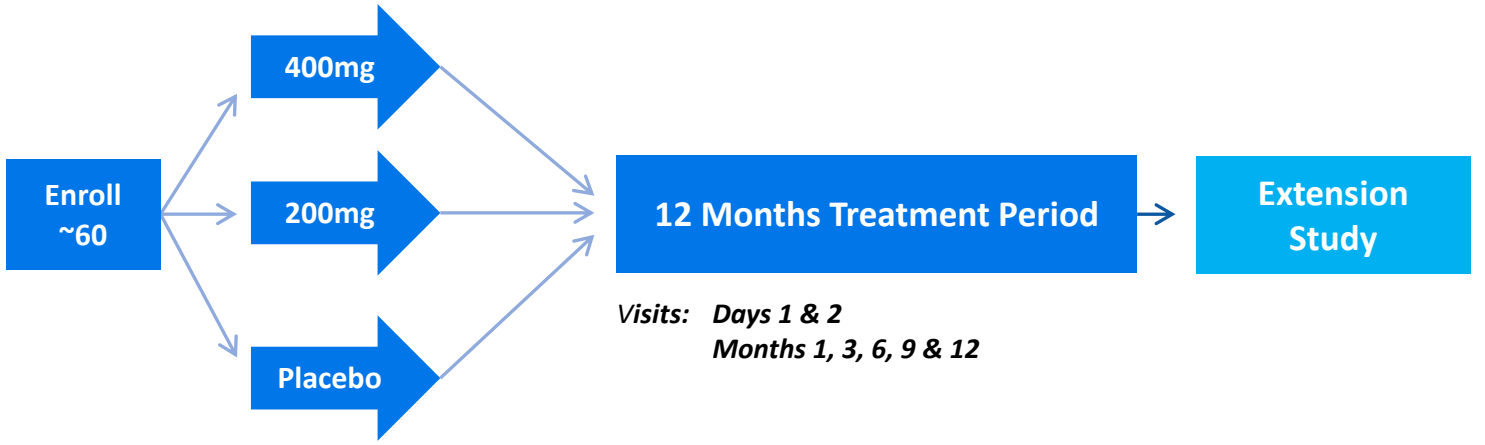
## Enrollment Criteria

- MRI-confirmed CCM lesion(s)
- Familial or sporadic
- Symptoms directly related to CCM

## Outcome Measures

- Primary: Safety and tolerability
- Secondary: Efficacy
- Exploratory: Biomarkers

| Screening & Randomization 1:1:1 | Treatment | Follow-up |
|---|---|---|




*Source : The Symptomatic Cerebral Cavernous Malformation Trial of REC-994 (SYCAMORE)*

# REC-994 for CCM: Expectations

## Outcome Measures

- **Primary: Safety and Tolerability**
  - **Adverse events & symptoms**
- **Secondary & Exploratory:**
  - **Efficacy**
    - **Clinician-measured outcomes** (CGI, PGI)
    - **MRI Imaging**
    - **Impact of acute stroke** (mRS, NIHSS)
    - **Patient and Investigator reported outcomes** (SMSS, PROMIS-29, CCM-HI, symptom questionnaires)

## Trial Update

- **Enrollment is complete**
- **Vast majority of participants** who completed 12 months of treatment continue to enter **long-term extension**
- **Analysis**
  - Identification of **trends across multiple endpoints**
  - **Changes in vascular permeability**
    - E.g., hemosiderin deposition
  - **Change in lesion burden**
  - **Subgroup**



Source: https://clinicaltrials.gov/study/NCT05085561

# **REC-2282** for the Treatment of Progressive Neurofibromatosis Type 2 (NF2) Mutated Meningiomas

| | |
|---|---|
| **Target / MOA** | HDAC Inhibitor |
| **Molecule Type** | Small Molecule |
| **Lead Indication(s)** | NF2 Mutated Meningiomas |
| **Status** | Phase 2/3 |
| **Designation(s)** | Fast Track; US and EU Orphan Drug |
| **Source of Insight** | Recursion OS |

Clinical: NF2

# POPLAR Clinical Trial: REC-2282 for NF2 Part A Underway

## PREVALENCE & STANDARD OF CARE

~33,000 **Treatable US + EU**

**No approved therapy**

- Surgery/RT is standard of care (when feasible)
- Location may make complete resection untenable, leading to hearing loss, facial paralysis, poor balance and visual difficulty
- **Stasis or shrinkage of tumor could improve prognosis**

## CAUSE

**LOF mutations in *NF2* tumor suppressor gene**, leading to deficiencies in the tumor suppressor protein merlin

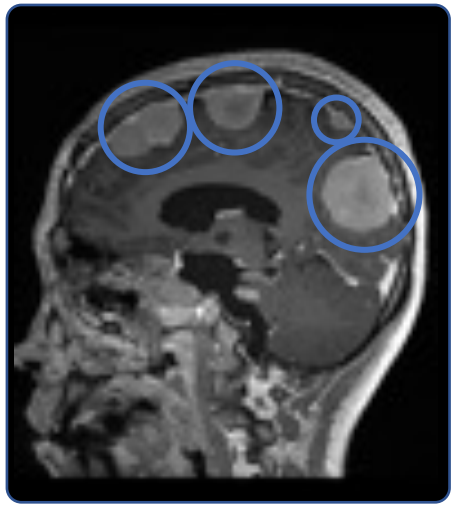
## PATHOPHYSIOLOGY & REASON TO BELIEVE

Inherited rare **CNS tumor syndrome** leading to loss of hearing and mobility, other focal neurologic deficits

Efficacy signal in Recursion OS, cellular, and animal models; suppression of aberrant ERK, AKT, and S6 pathway activation in a Phase 1 PD Study in NF2 patient tumors

## KEY ELEMENTS

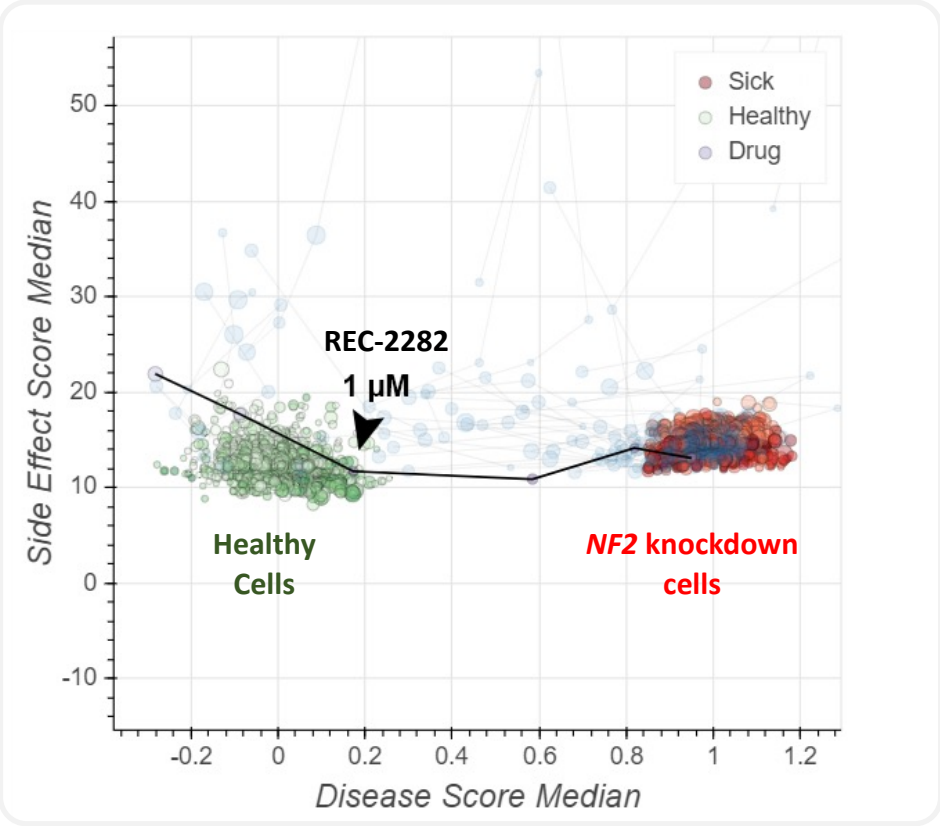
- Targeting **familial & sporadic NF2 meningioma** patients
- HDAC inhibitor, small molecule
- Oral dosing
- Preliminary readout **expected Q4 2024**
- **Fast-Track** and US & EU **Orphan Drug Designation**



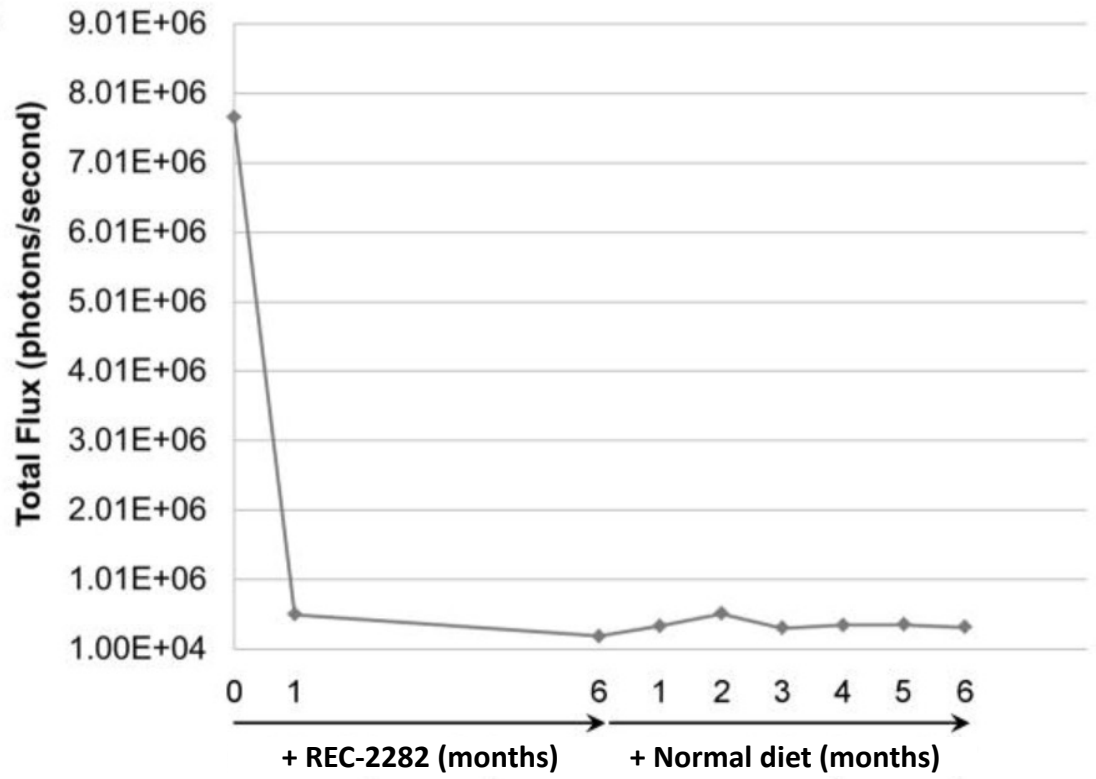
Intracranial meningiomas

Ricki – living with NF2

# Insight from OS : REC-2282 Rescued Loss of NF2




**Prevents growth & regrowth of NF2-deficient meningioma model in mice**






*HUVEC, human umbilical vein endothelial cells; NF2, neurofibromatosis type 2; siRNA, small interfering RNA.*

# POPLAR Trial: REC-2282 for NF2 Part A Underway

## Key Enrollment Criteria

- MRI-confirmed progressive meningioma
- Sporadic meningioma with confirmed NF2 mutation
- Familial NF2 meningioma
- Have documented progression with past 24 months

## Outcome Measures

- Primary: PFS6 defined as proportion of patients who are alive or progression free after
- Secondary: ORR, Safety, PK/PD

**Phase 2/3 trial initiated in Q2 2022**

*Phase 2 portion*

40 mg TIW
~6 Sporadic
~6 Familial

60 mg TIW
~6 Sporadic
~6 Familial

→ **6-month PFS (Futility Analysis)** →

FDA Mtg

- ***Go/No-go to Ph3***
- ***Safety/Tolerability***
- ***PK***
- ***PFS***

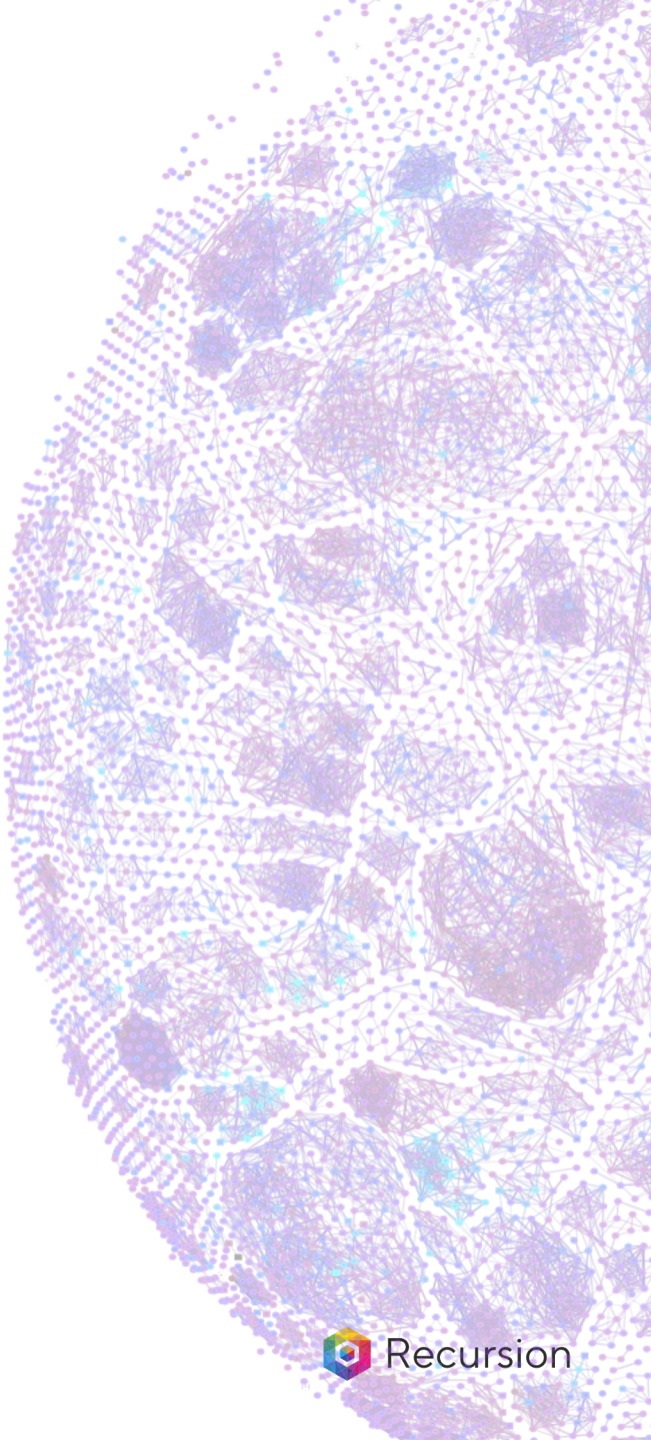
**Preliminary Phase 2 readout** (safety & preliminary efficacy) expected in **Q4 2024**



*Source : Efficacy and Safety of REC-2282 in Patients With Progressive Neurofibromatosis Type 2 (NF2) Mutated Meningiomas (POPLAR-NF2)*

# **REC-4881** for the Treatment of Familial Adenomatous Polyposis (FAP)

| | |
|---|---|
| **Target / MOA** | MEK Inhibitor |
| **Molecule Type** | Small Molecule |
| **Lead Indication(s)** | Familial Adenomatous Polyposis |
| **Status** | Phase 2 |
| **Designation(s)** | Fast Track; US and EU Orphan Drug |
| **Source of Insight** | Recursion OS |



Clinical: FAP

# TUPELO Clinical Trial : REC-4881 for FAP Phase 2 Underway

## PREVALENCE & STANDARD OF CARE

**~50,000** **Diagnosed US + EU**

**No approved therapy**

- Colectomy during adolescence (with or without removal of rectum) is standard of care
- Post-colectomy, patients still at significant risk of polyps progressing to GI cancer
- Significant decrease in quality-of-life post-colectomy (continued endoscopies, surgical intervention)

## CAUSE

**Inactivating mutations in the tumor suppressor gene *APC***

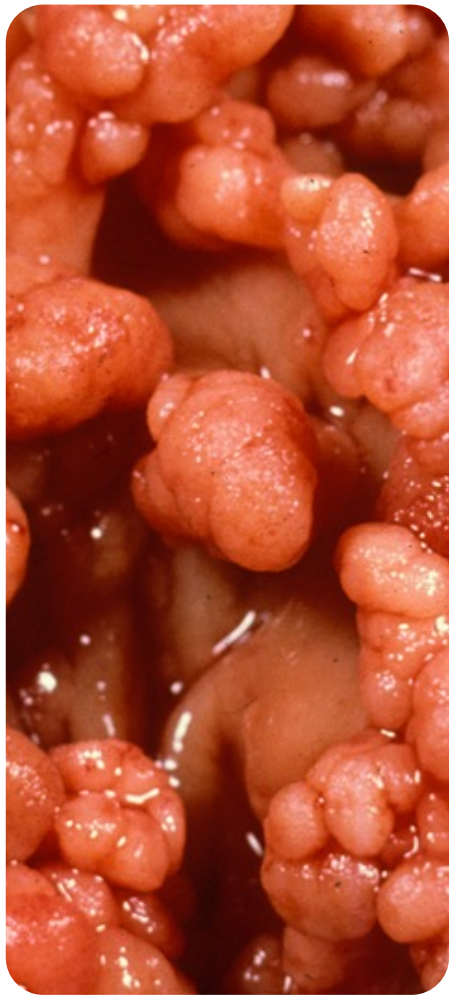
## PATHOPHYSIOLOGY & REASON TO BELIEVE

**Polyps throughout the GI tract** with extremely high risk of malignant transformation

Efficacy signal in the Recursion OS showed specific MEK 1/2 inhibitors had an effect in context of *APC* LOF. Subsequent $APC^{min}$ mouse model showed potent reduction in polyps and dysplastic adenomas

## KEY ELEMENTS

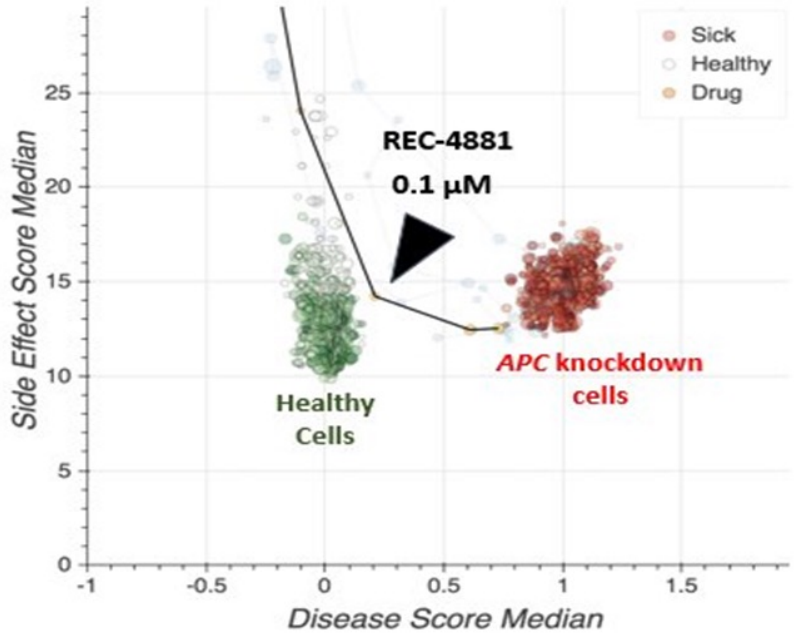
- Targeting **classical FAP patients (with *APC* mutation)**
- MEK inhibitor, small molecule
- Oral dosing
- Preliminary readout **expected H1 2025**
- **Fast-Track** and US & EU **Orphan Drug Designation**



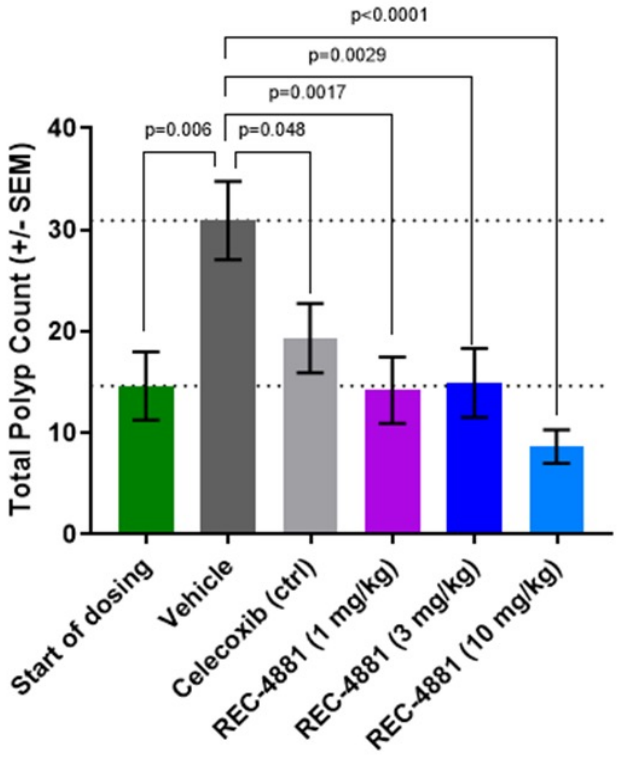
Polyps Found in Colon and Upper GI Tract

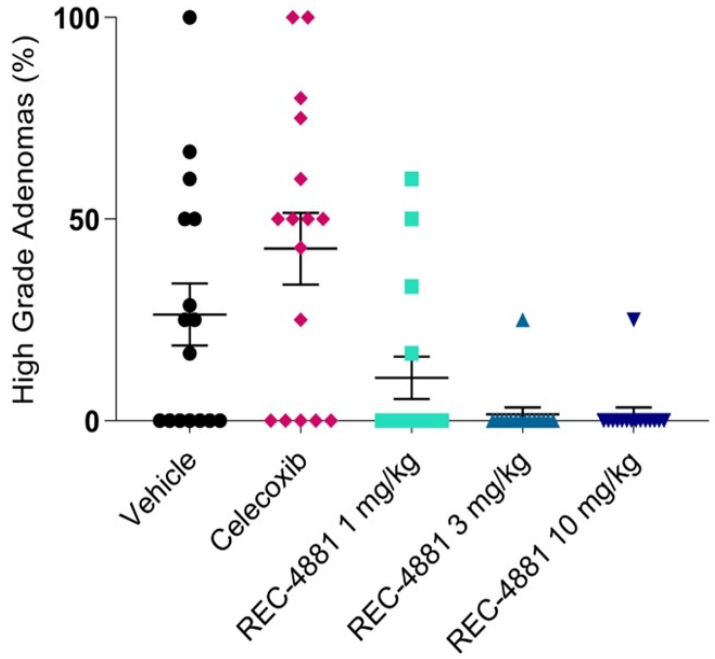
# Preclinical Validation of Novel OS Insight in Relevant FAP Models

## REC-4881 rescued phenotypic defects of cells with APC knockdown




## ↓ polyp count



# TUPELO Clinical Trial : REC-4881 for FAP Phase 2 Underway

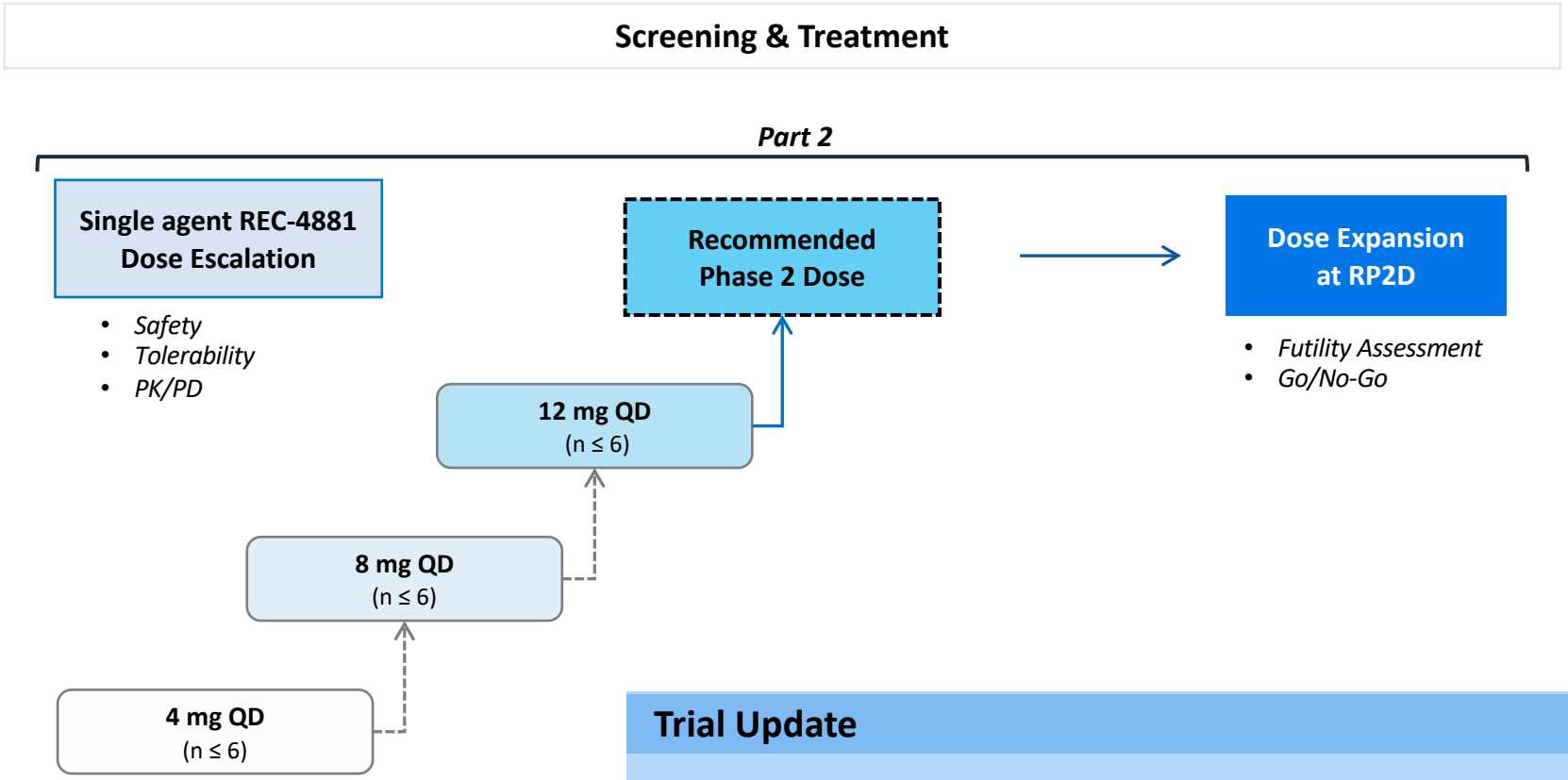
## Part 2 Enrollment Commenced

### Key Enrollment Criteria

- Confirmed *APC* mutation
- ≥ 55 years old
- Post-colectomy/proctocolectomy
- No cancer present
- Polyps in either duodenum (including ampulla of vater) or rectum/pouch

### Outcome Measures

- Primary:
  - Safety & Tolerability
  - Change from baseline in polyp burden at 12 weeks
  - RP2D
- Secondary:
  - PK/PD




### Trial Update

**Phase 2 initiated** preliminary **readout** expected by H1 **2025**



*Source : Evaluate REC-4881 in Patients With FAP (TUPELO)*

# **REC-4881** for the Treatment of Solid Tumors with AXIN1 or APC Mutations

| | |
|---|---|
| **Target / MOA** | MEK Inhibitor |
| **Molecule Type** | Small Molecule |
| **Lead Indication(s)** | Solid Tumors with AXIN1 or APC Mutations |
| **Status** | Phase 2 |
| **Source of Insight** | Recursion OS |

# LILAC Clinical Trial: REC-4881 for AXIN1 or APC mutant cancers

**~104,000** **Treatable US + EU5**

**Substantial need** for developing therapeutics for patients harboring mutations in *AXIN1* or *APC*, as these **mutations are considered undruggable**

To our knowledge, REC-4881 is the **only industry sponsored small molecule therapeutic** designed to enroll solid tumor patients harboring mutations in *AXIN1* or *APC*

## CAUSE

**LOF mutations in *AXIN1* or *APC* tumor suppressor genes**

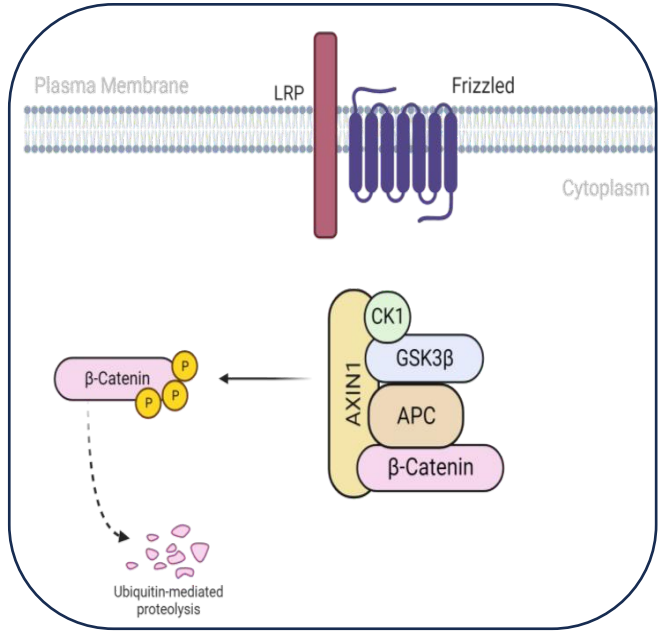
## PATHOPHYSIOLOGY & REASON TO BELIEVE

**Alterations in the WNT pathway** are found in a **wide variety of tumors** and confer poor prognosis and resistance to standard of care

Efficacy signal in the Recursion OS and favorable results in PDX models harboring *AXIN1* or *APC* mutations vs wild-type leading to a significant PFS benefit only in mutant models

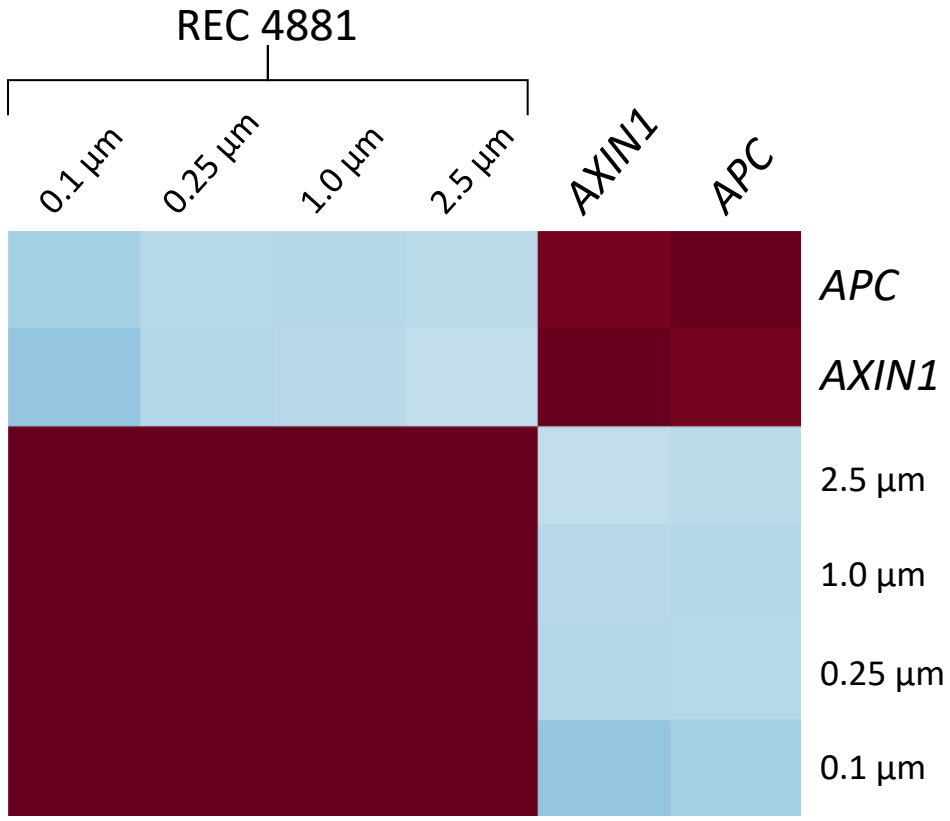
## KEY ELEMENTS

- Targeting ***AXIN1* or *APC* mutant cancers**
- MEK inhibitor, small molecule
- Oral dosing
- **Enrollment ongoing**
- Phase 2 initial readout **expected H1 2025**




AXIN1/APC regulate WNT pathway

# Recursion OS Identified Novel Insight of AXIN1 & APC biology



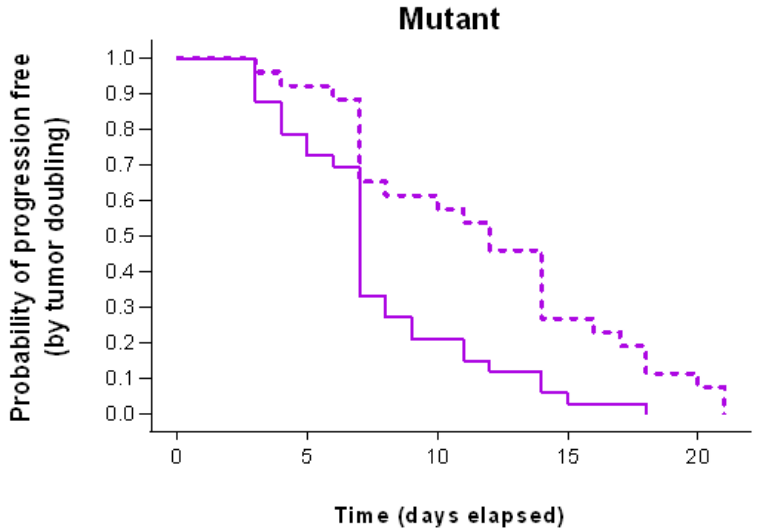

**REC-4881 is phenotypically opposite to the genetic KO of *APC* and *AXIN1* providing a novel mechanism that may restore the disease state modeled by the loss of these genes**

**Significantly greater antitumor activity in mutant models led to significant PFS benefit**

| | Median PFS (days) | 95% CI |
|---|---|---|
| REC-4881 (n = 33) | 12.0 | (7.18 - 20.01) |
| Vehicle (n = 33) | 7.0 | (4.19 - 11.70) |

**Log-rank p value < 0.001**

HR = 0.49 (95% CI 0.29 - 0.83)



# LILAC Clinical Trial: REC-4881 for AXIN1 or APC mutant cancers

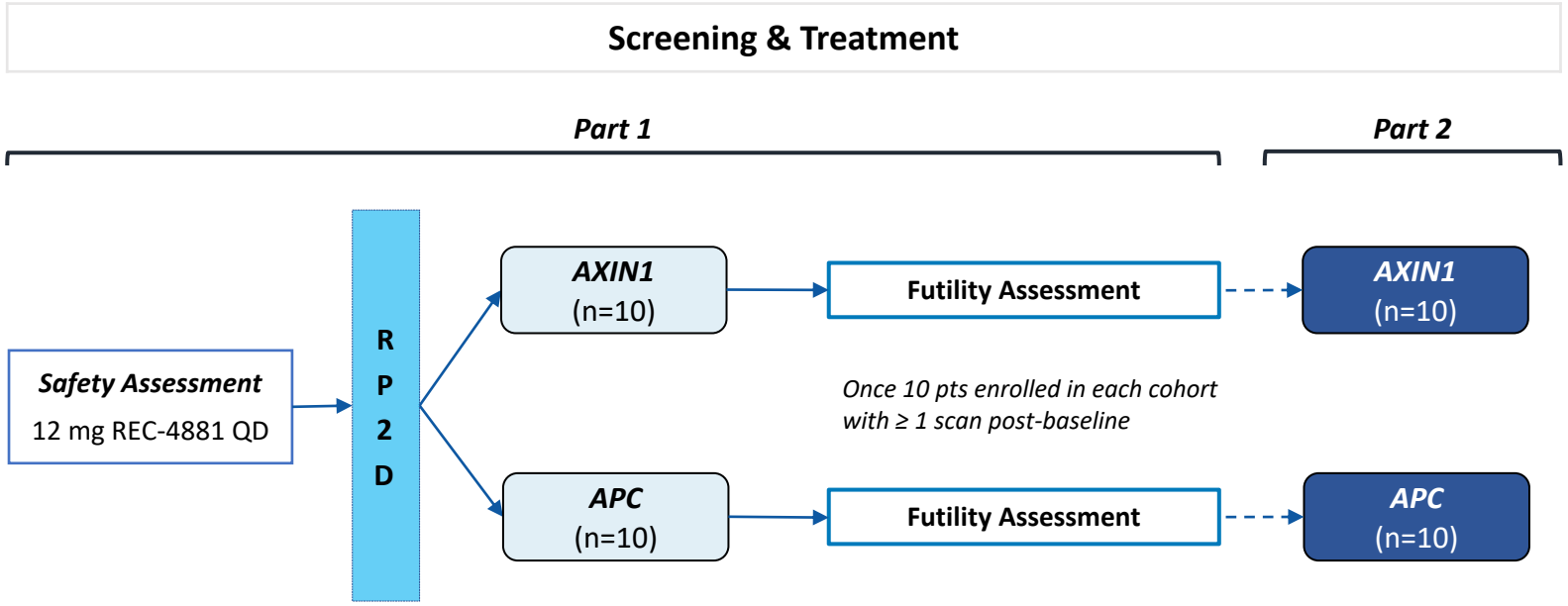
**FPI achieved Q1 2024**

## Enrollment Criteria

- Unresectable, locally advanced, or metastatic cancers
- ≥ 55 years old
- *AXIN1* or *APC* mutation confirmed by NGS (tissue or blood)
- CRC patients must be *RAS / RAF* wildtype
- No MEK inhibitor treatment within 2 months of initial dose
- ≥ 1 prior line of therapy
- ECOG PS 0-1

## Outcome Measures

- Primary
  - Safety/tolerability
  - ORR (RECIST 1.1)
- Secondary
  - PK
  - Additional efficacy parameters




## Trial Update

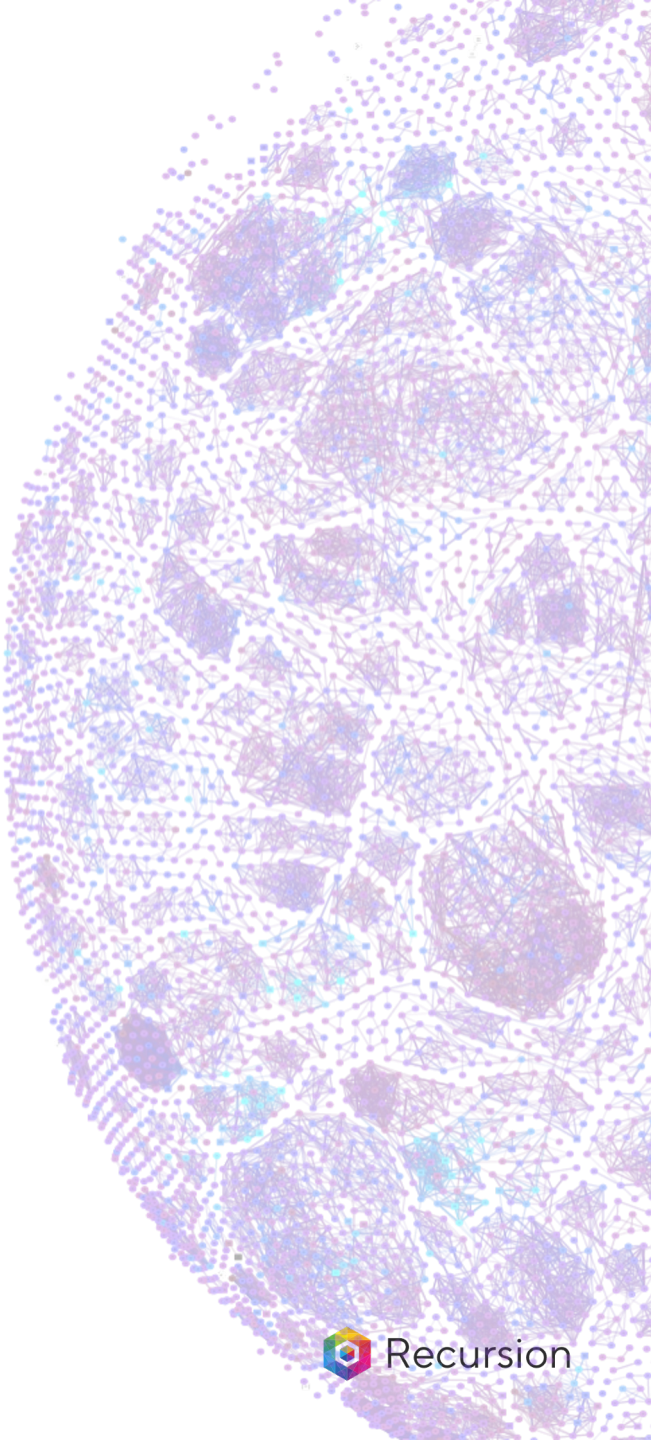
- Utilizing genomics & RWD data for patient/site matching
- **Phase 2** initial **readout** expected **H1 2025**



Source : A Study of REC-4881 in Participants With Cancers Which Have an AXIN1 or APC Mutation

# **REC-3964** for the Prevention of *C. difficile* Infection (CDI)

| | |
|---|---|
| **Target / MOA** | Selective *C. difficile* Toxin Inhibitor |
| **Molecule Type** | Small Molecule |
| **Lead Indication(s)** | Prevention of CDI |
| **Status** | Phase 2 |
| **Source of Insight** | Recursion OS |



Clinical: C. difficile

# ALDER Clinical Trial: REC-3964 for *C. Difficile*

## PREVALENCE & STANDARD OF CARE

~730,000 Diagnosed US + EU5 patients

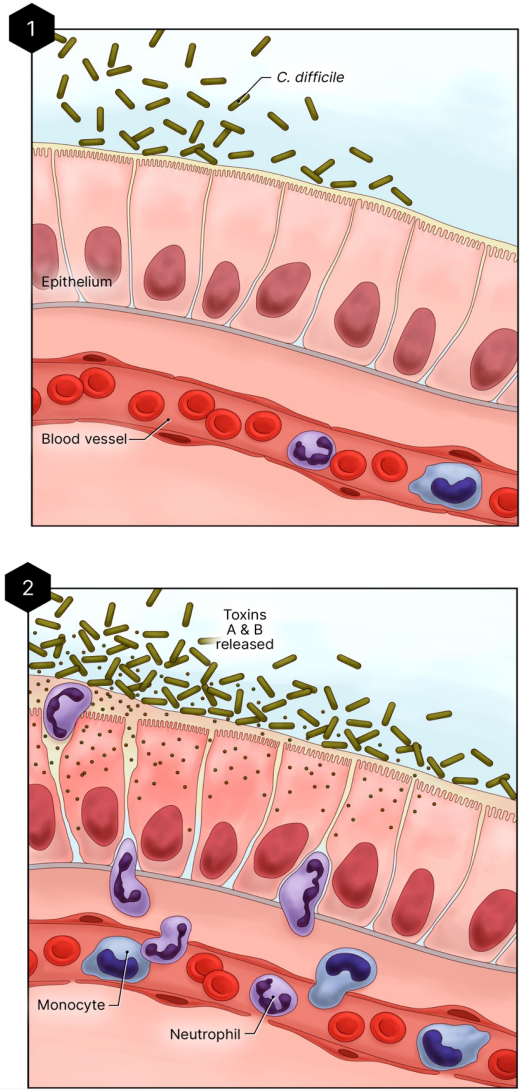
- **Severity of infection varies and can range from mild to severe, requiring colectomy**
  - **>29,000 patients** die in the US each year from CDI
- **Cost burden of up to $4.8bn annually**

## TREATMENT PARADIGM

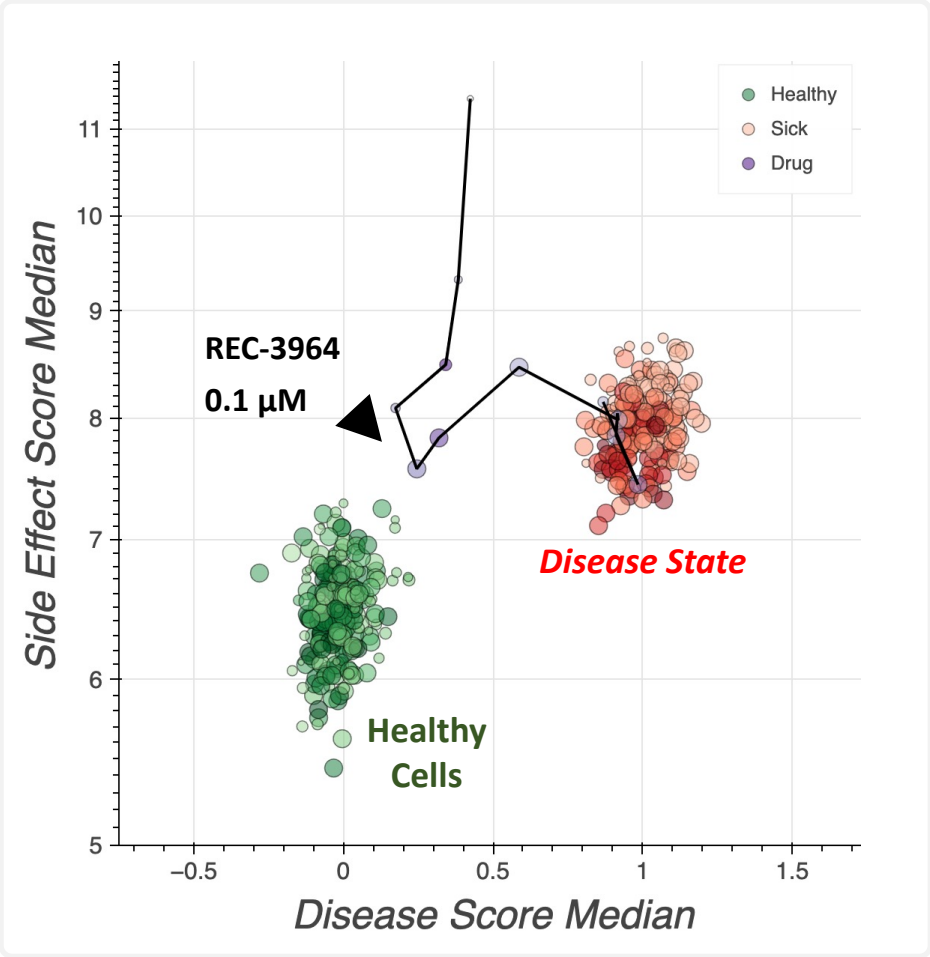
- Standard of care for 1st occurrence: Antibiotics alone
- Recurrence (20-30% of patients) treated with antibiotics ± adjunct therapy (bezlotoxumab IV or fecal transplant)
- REC3964 inhibits the C. difficile toxins and is a non-antibiotic therapy

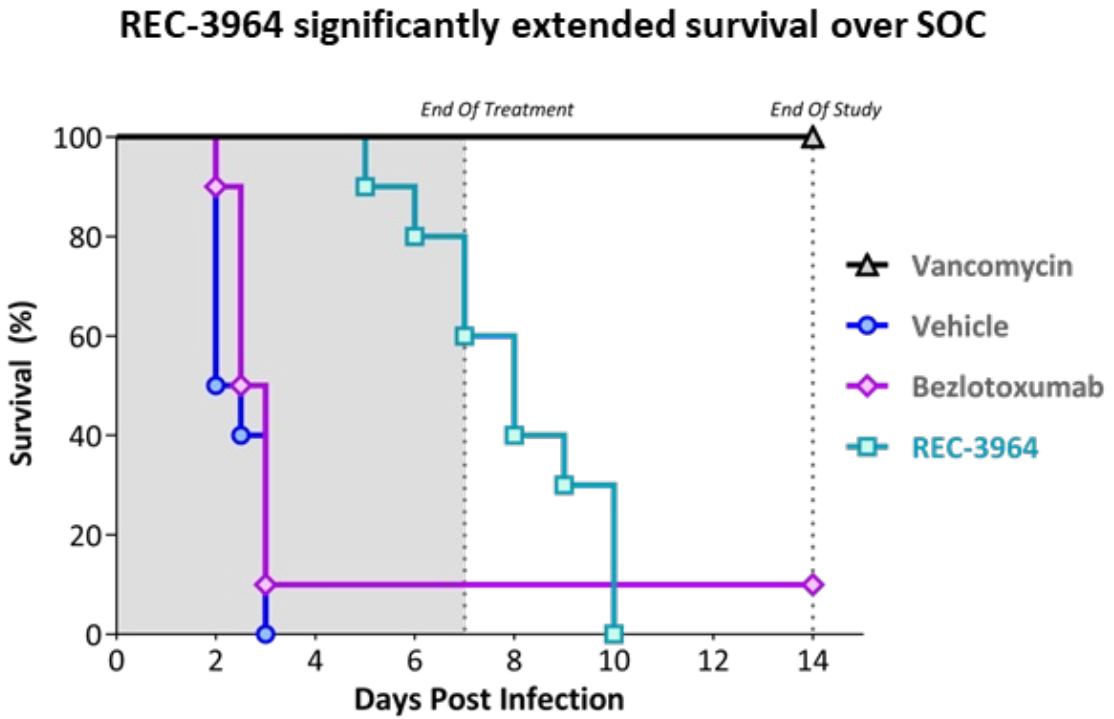
## PATHOPHYSIOLOGY & REASON TO BELIEVE

- Selective Inhibitor of C. difficile Toxins
- Recursion's 1st Small Molecule NCE to Reach the Clinic
- Binds and blocks catalytic activity of the toxin's innate glucosyltransferase, but not the host's



# Insight from OS: REC-3964 Rescued Cells Treated with *C. diff* Toxins




- REC-3964 potently inhibits toxin B with residual activity against toxin A, while bezlotoxumab is specific to toxin B.
- Significant difference in probability of survival vs bezlotoxumab alone at the end of treatment (**p<0.001**, log-rank test)

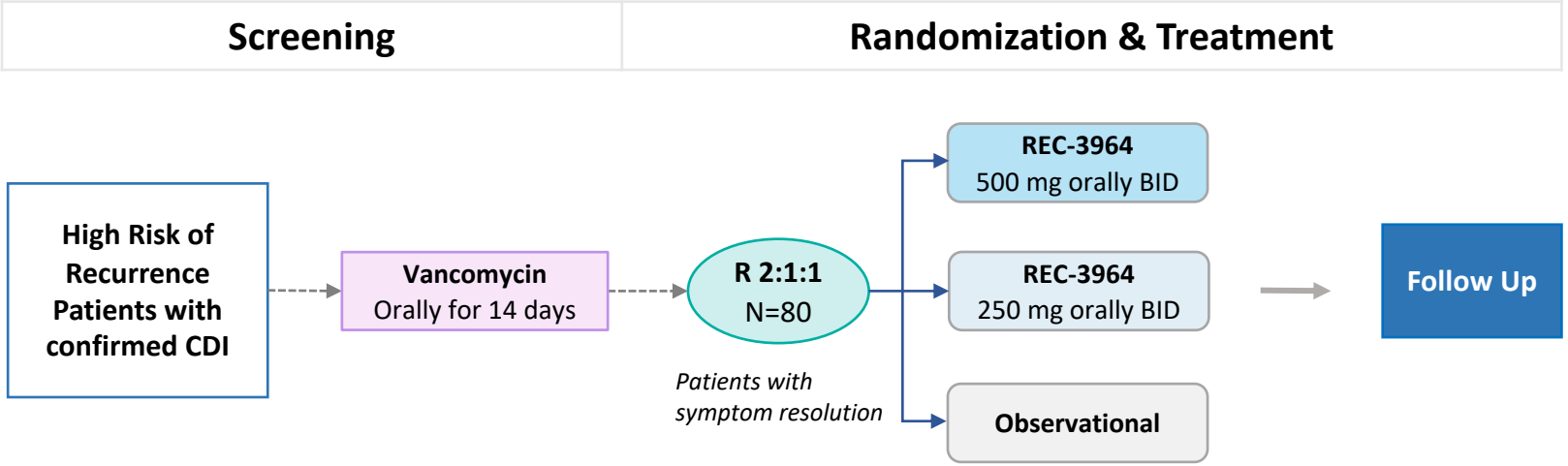
# ALDER Clinical Trial: POC Phase 2 REC-3964 in Patients at High Risk of *C. Diff* Recurrence

## Enrollment Criteria

- Patients at high risk of recurrence
- ≥3 bowel movements in 24 hours
- Confirm CDI using EIA (toxin)
- No fulminant CDI
- No history of chronic diarrheal illness due to other causes

## Outcome Measures

- Primary
  - Rate of recurrence
- Secondary
  - Additional efficacy measures
  - Safety / tolerability
  - PK




## Trial Updates

- Phase 1 and DDI studies **completed**
- **Phase 2 initiation** expected in **Q4 2024,** preliminary **readout** expected by end of **2025**

# Novel Insights into **RBM39** Degradation for the Treatment of Select HR-Proficient Solid Tumors

| | |
|---|---|
| **Target / MOA** | RBM39 Molecular Glue Degrader |
| **Molecule Type** | Small Molecule |
| **Lead Indication(s)** | TBD |
| **Status** | IND submission in Q3 2024,<br>Phase 1/2 initiation in Q4 2024 |
| **Source of Insight** | Recursion OS |

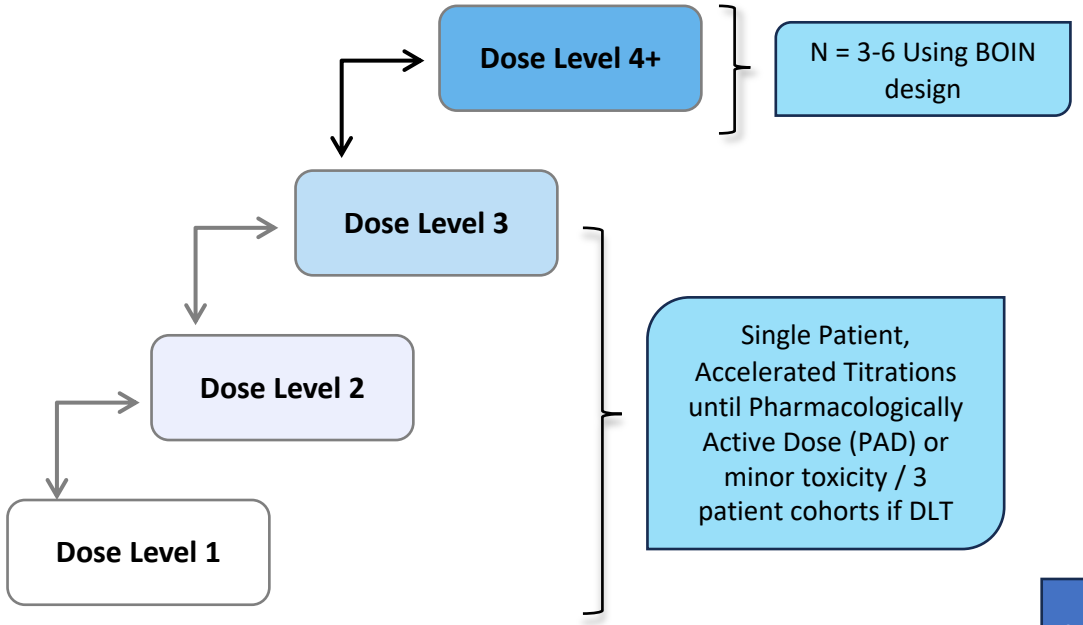
# Anticipated RBM39 Trial Design

## Planned Phase 1/2 study of RBM39 degrader in Biomarker Selected Relapsed Refractory HR-Proficient Solid Tumors

**Phase 1A**
Dose Finding
(Accelerated Titration BOIN)
N=30

**Phase 1B**
Dose Confirmation
N=20

**Phase 2**
N=10-30




**Dose #1**
N=10

***Indication #1***

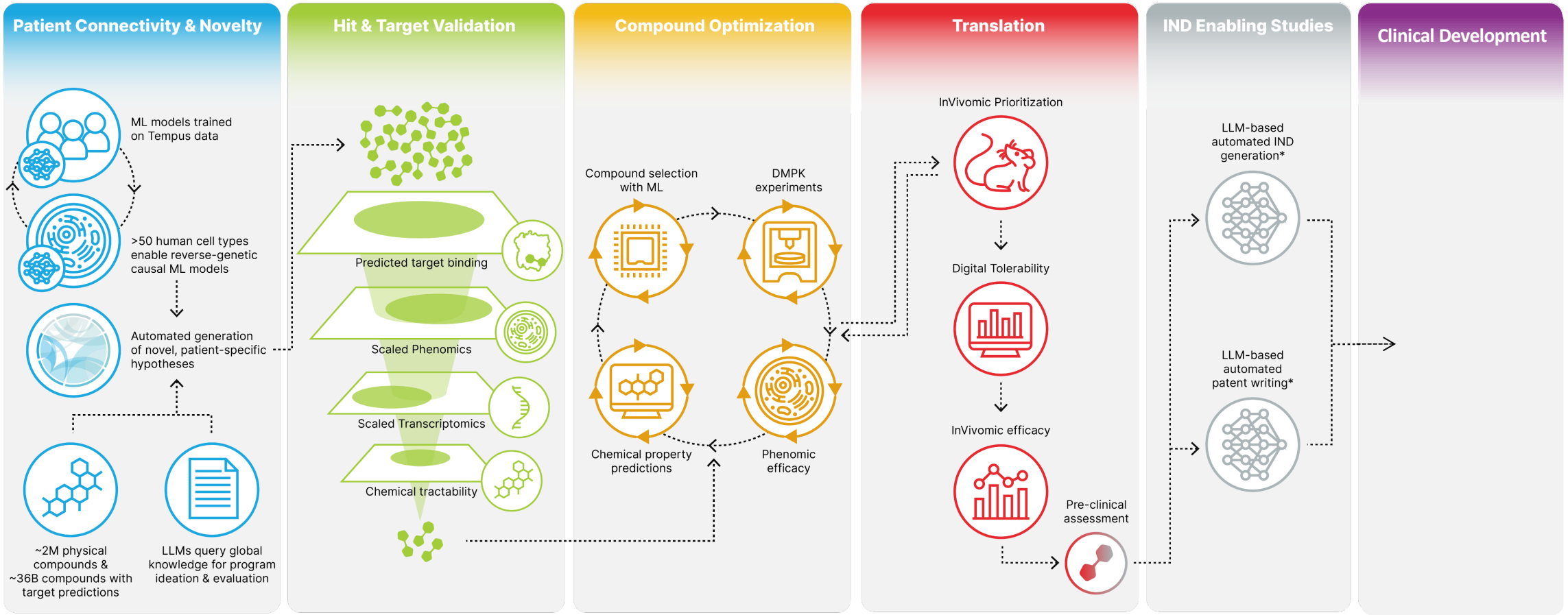
**Dose #2**
N=10

***Indication #1***

- **IND** submission expected in **Q3 2024**
- **Phase 1/2 initiation** expected in **Q4 2024**
- **Phase 1** dose-escalation **readout** by end of **2025**

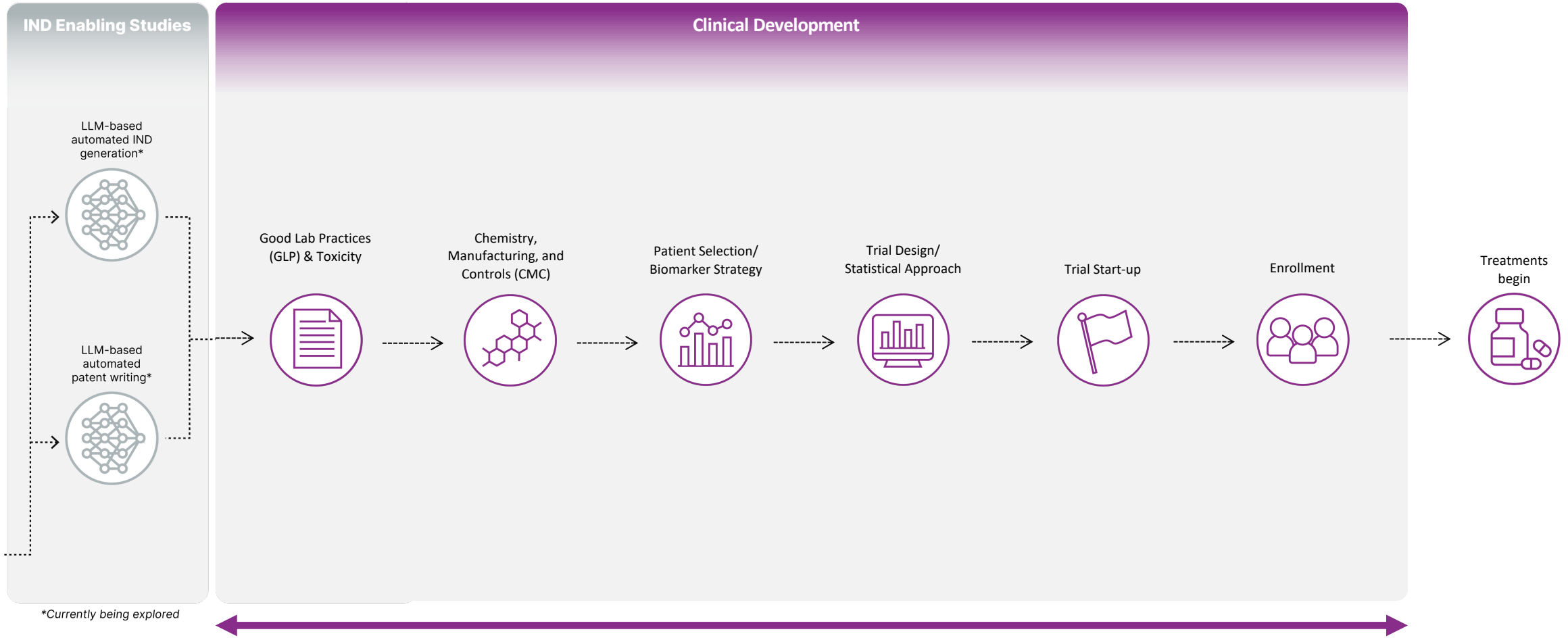
# Machine Learning:

to truly industrialize drug discovery, data and AI solutions must be integrated as modules across many steps
Exciting scientific collaborations span biopharma, tech & data

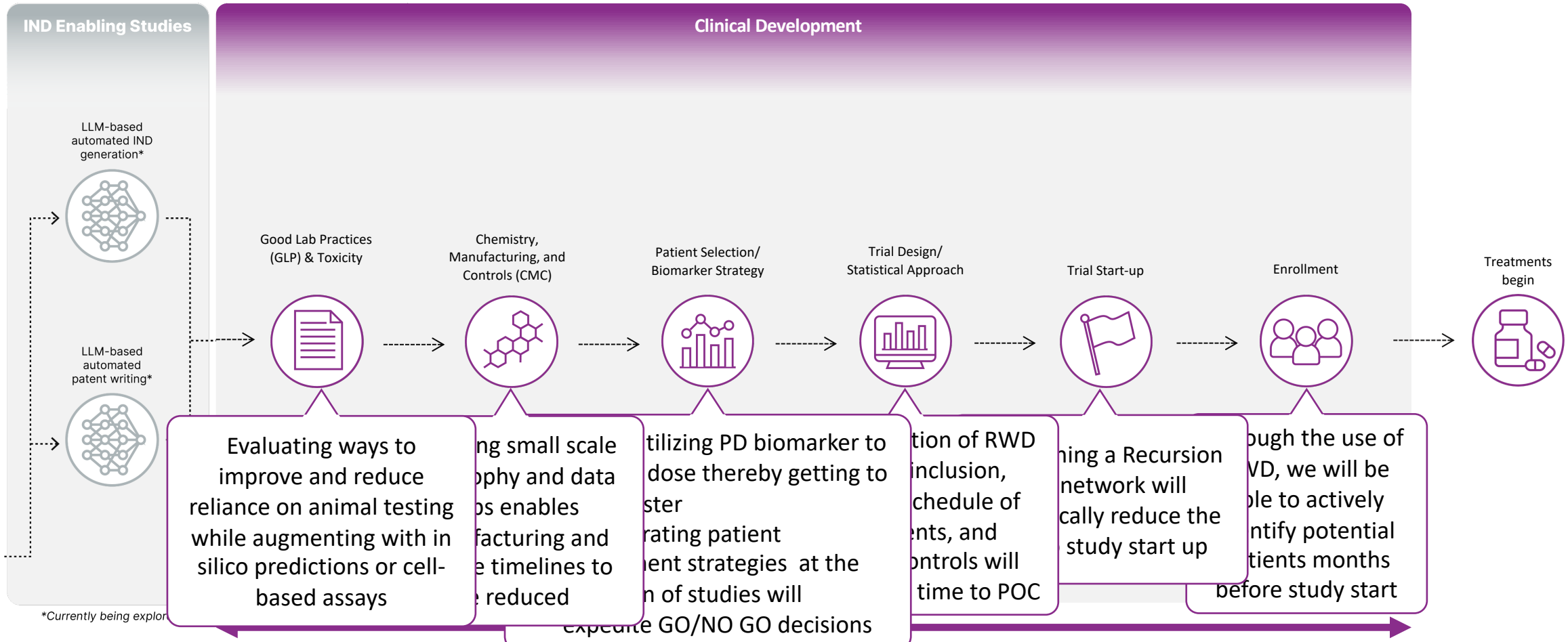



*Currently being explored

# Industrializing the clinical process, through data and operational efficiency



# Industrializing the clinical process, through data and operational efficiency




Collectively we believe these processes could significantly reduce time from IND enabling studies to 1st patient dosed

Recursion

# Company & Milestones

# Our Culture and People are Key to Driving Value

MISSION

## Decoding Biology to Radically Improve Lives

PRINCIPLES

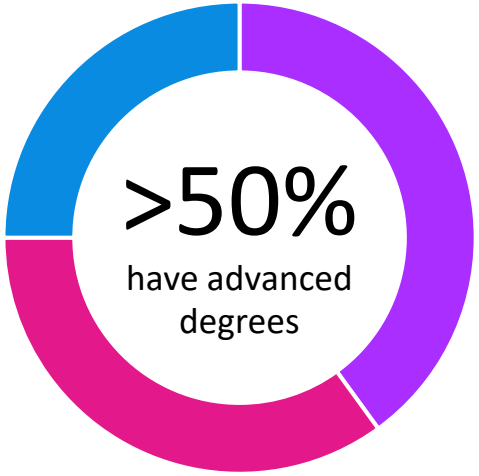
Explore the Uncharted
Create Virtuous Cycles
Build Connected Data
Industrialize to Scale
Optimize for the Portfolio
Challenge Assumptions

VALUES

We Care
We Deliver
We Learn
Act Boldly with Integrity
We are One Recursion

# Our People

## Functional Breakdown




### >500 employees

- Technology – data science, software engineering, automation, etc.
- Life Sciences – biology, chemistry, development, etc.
- Strategic Operations

~43% Female

~55% Male

~1% Non-Binary

*Data shown reflective of Q1 2024, gender statistics include participating individuals*

***Parity Pledge Signer***
gender parity and people of color parity

## Locations


Headquarters in **Salt Lake City, Utah** with additional locations in:

- San Francisco, California
- Toronto, Ontario
- Montréal, Québec
- London, England

# Our Operating Model – Organizing Ourselves in line with Our Drug Discovery Process

**Inception / Valence**

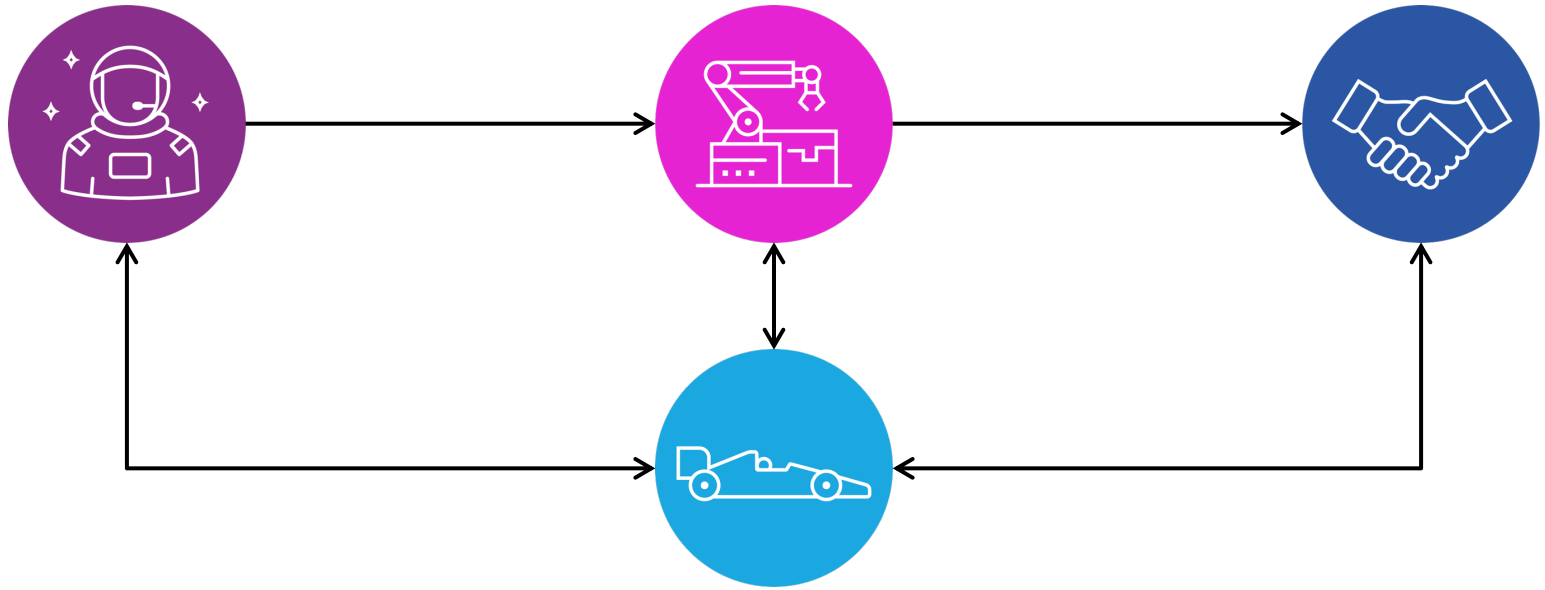
De-risks novel capabilities to expand the Recursion OS to the point of minimum viable product

**OS**

Develops, deploys, and improves the platform and workflows that make up the Recursion OS

**Value**

Translates data and insights into value for our patients, partners, investors, and others



**Accelerator**

Drives company-wide efficiencies and paves the way for achieving the Recursion mission

# Milestones: Pipeline – 7 Clinical Trial Readouts Expected in ~18 Months

**Pipeline**

- **CCM: Ph2** readout expected in **September 2024**
- **NF2: Ph2** safety & preliminary efficacy expected in **Q4 2024**
- **FAP: Ph2** safety & preliminary efficacy expected in **H1 2025**
- **AXIN1 or APC Mutant Cancers: Ph2 FPI** achieved in **Q1 2024** with safety & preliminary efficacy expected in **H1 2025**
- ***C. difficile* Infection: Ph2 initiation** expected in **Q4 2024** with preliminary **readout** expected by end of **2025**

- **Target RBM39 / HR-Proficient Cancers: IND** submission expected in **Q3 2024** and **Ph1/2 initiation** expected in **Q4 2024** with **Ph1 dose-escalation readout** by end of **2025**
- **Target Epsilon** (novel target in fibrotic diseases): **IND** submission expected in **early 2025** with **Ph1 healthy volunteer readout** by end of **2025**

- **Dozens of internal & partner programs** in early stages with first **LLM & causal model driven programs entering pipeline**

SYCAMORE

POPLAR

TUPELO

LILAC

ALDER

# Milestones: Partnerships & Platform

## Partnerships

- **Roche & Genentech:** validation **program option exercised** for 1st validated hit series in oncology, potential **program & map options** on the near or very near-term
- **Bayer:** delivered **multiple oncology data packages,** on track to complete **25 unique data packages** in **Q3 2024**, initiated and advancing **1st joint project** towards lead series nomination, potential near-term **program options**, agreed to be **1st beta-user of LOWE** for drug discovery and development
- **Tempus & Helix:** building large-scale **causal AI models** to generate **target hypotheses** across cancer and other disease areas, exploring **novel NSCLC targets**
- Potential for **additional partnership(s)** in large, intractable areas of biology

## Platform

- Built our 1st genome-scale **transcriptomics KO map**, moving towards **multiomics foundation models**
- **Active learning** and exploration of **proteomics, organoids, spheroids, & automated synthesis**
- Potential to **make some data and tools available** to biopharma and commercial users
- OS moving towards **autonomous discovery**

### Strong Financial Position

**~$296M in cash Q1 2024**

*Cash refers to cash and cash equivalents at the end of Q1 2024*

Recursion

# Fireside Chat with Jensen Huang

DownloadDay 2024

Recursion

Recursion

# Closing Remarks

# Our Hopes for Today

Let you get a feel for Recursion and hear from expert partners from outside Recursion about the current and potential future impact of our work

Help define what we view as a tipping point moment as BioTech transitions to TechBio and understand why Recursion is uniquely positioned to take advantage of this

Share details and updates on our:

- Pipeline – with 7 clinical trial readouts expected in the next ~18 months
- Partnerships - with potential near term options on both maps and programs
- Platform - with industry-leading data generation and compute