New Product Planning Network Group

Digital Innovation (AI) and Advanced Analytics for NPP Professionals

6 Sep 2023

OUTCOMES

2023 NPP Network Schedule of Forums

Bi-monthly event extended to 90 minutes

Feb-28 — Value and Access for NPP Professionals

Apr-12 — Impact of the Inflation Reduction Act on Pipeline Development

Jun-14 — NPP Structures and Models from Emerging Biotech to Large Pharma

Sept - 06 — Digital Innovation (AI) and Advanced Analytics for NPP Professionals

Oct-04 — How to Grow Patients Centricity in Pipeline Decisions?

Dec-08 — Planning Drug-Device Value Creation

Events led by the NPP Network Steering Committee Members

NPP Summit (Fierce Biotech)

NEW PRODUCT PLANNING Summit

We have had several meetings with the conference organizers from Fierce Biotech and believe this will be a good conference for this group to consider attending

When? **October 16 - 17**

Where? **Boston**

Who? All NPP professionals should consider attending

Raffle

We have secured **2 Free Passes** for NPP network members who work in industry (no consultants) to attend this conference. If interested, please email me at michaeljconlon@yahoo.com by EOD tomorrow (9/7)

We have also negotiated a **20% discount** for this group. Please use NPPNETWORK when signing up to get this discount

For more information about the conference: https://www.newproductplanning.com/

Digital Innovation (AI) and Advanced Analytics for NPP Professionals

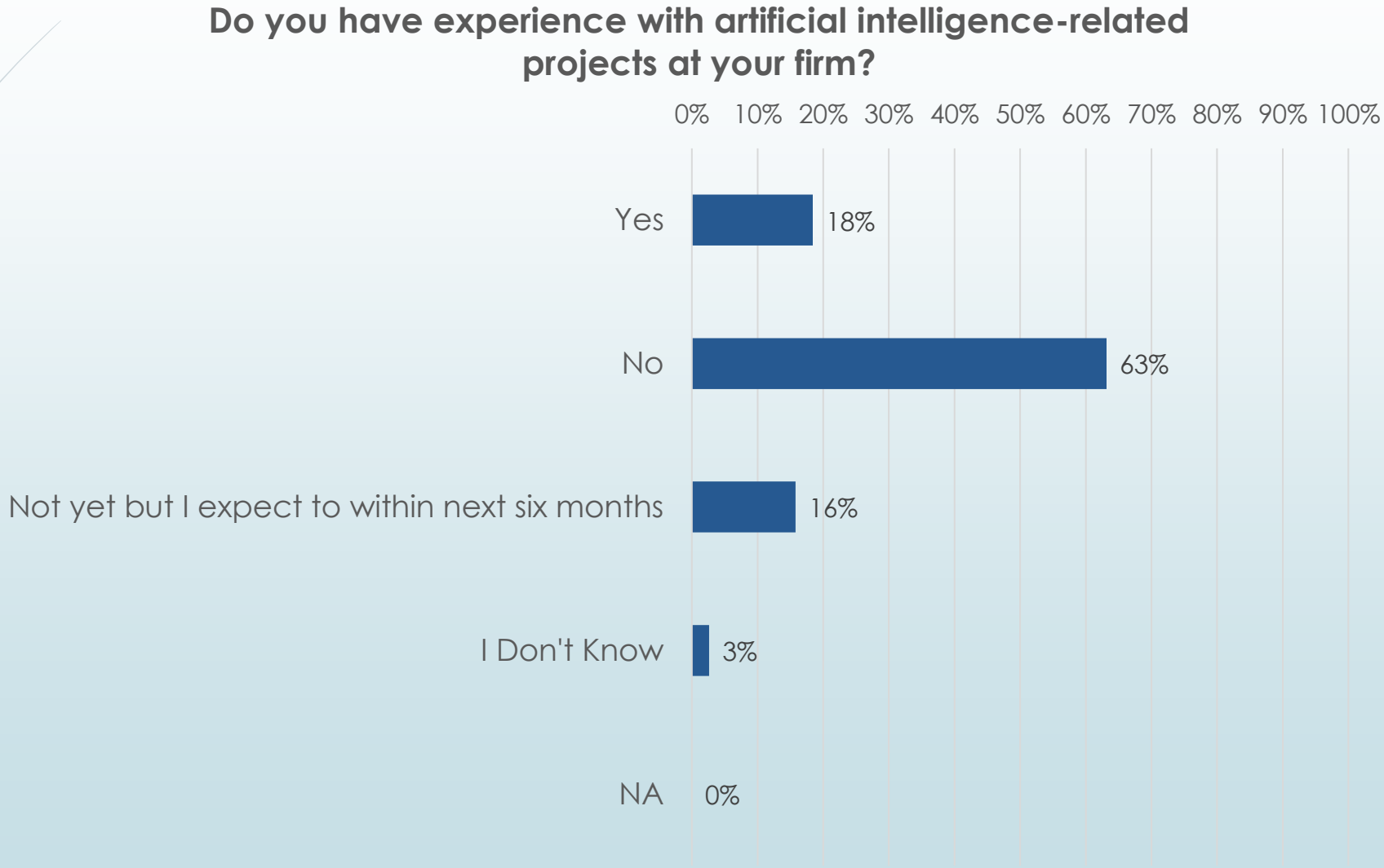
3

Access resources at biopharma-newproductplanning.com

Agenda / Topics

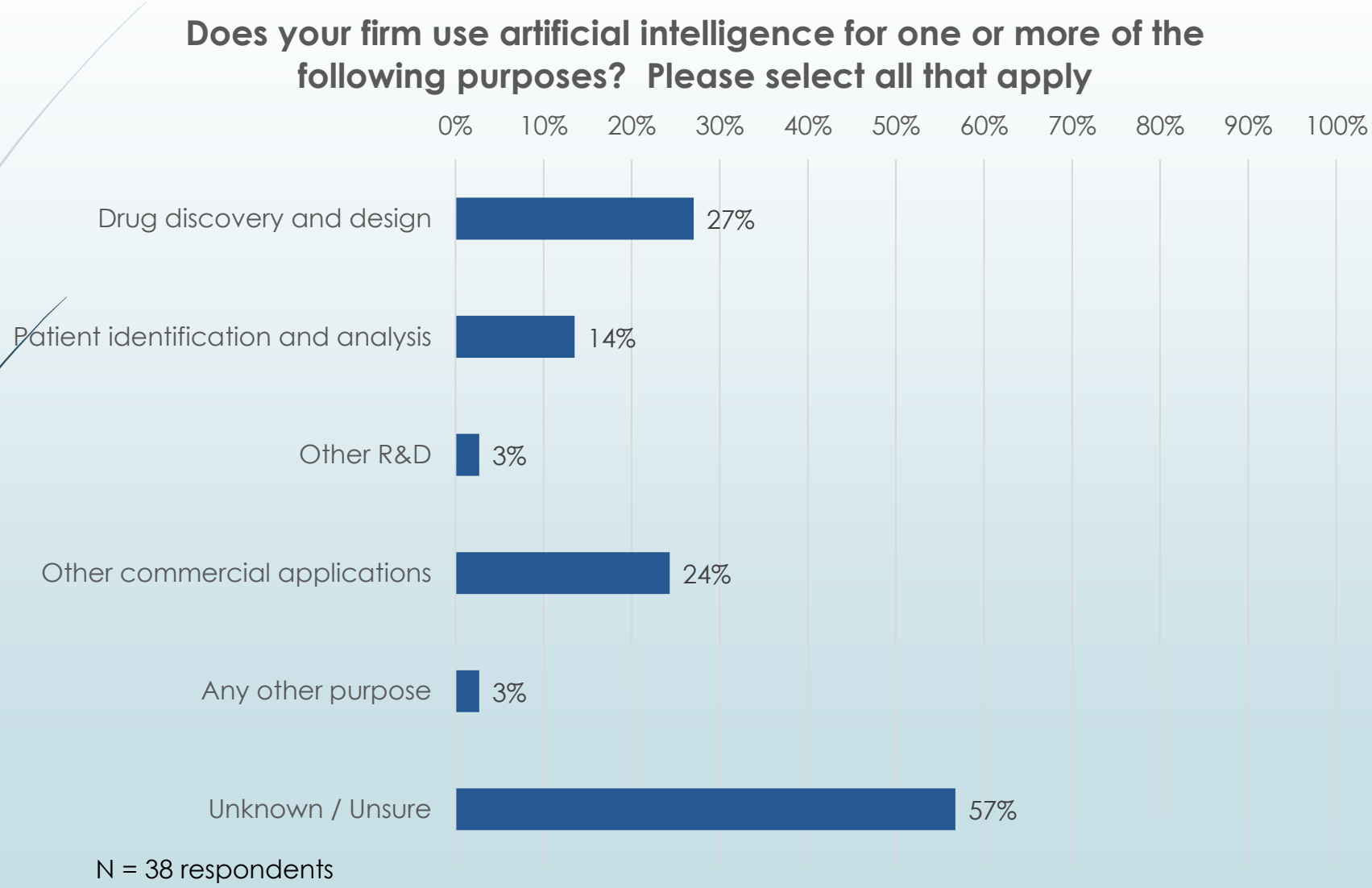
- Use of AI/ML in Drug Discovery
- Implications of AI/ML in Drug Discovery for NPP
- Utility of AI/ML in Commercial Strategy

Pre-Meeting Survey Results



N = 38 respondents

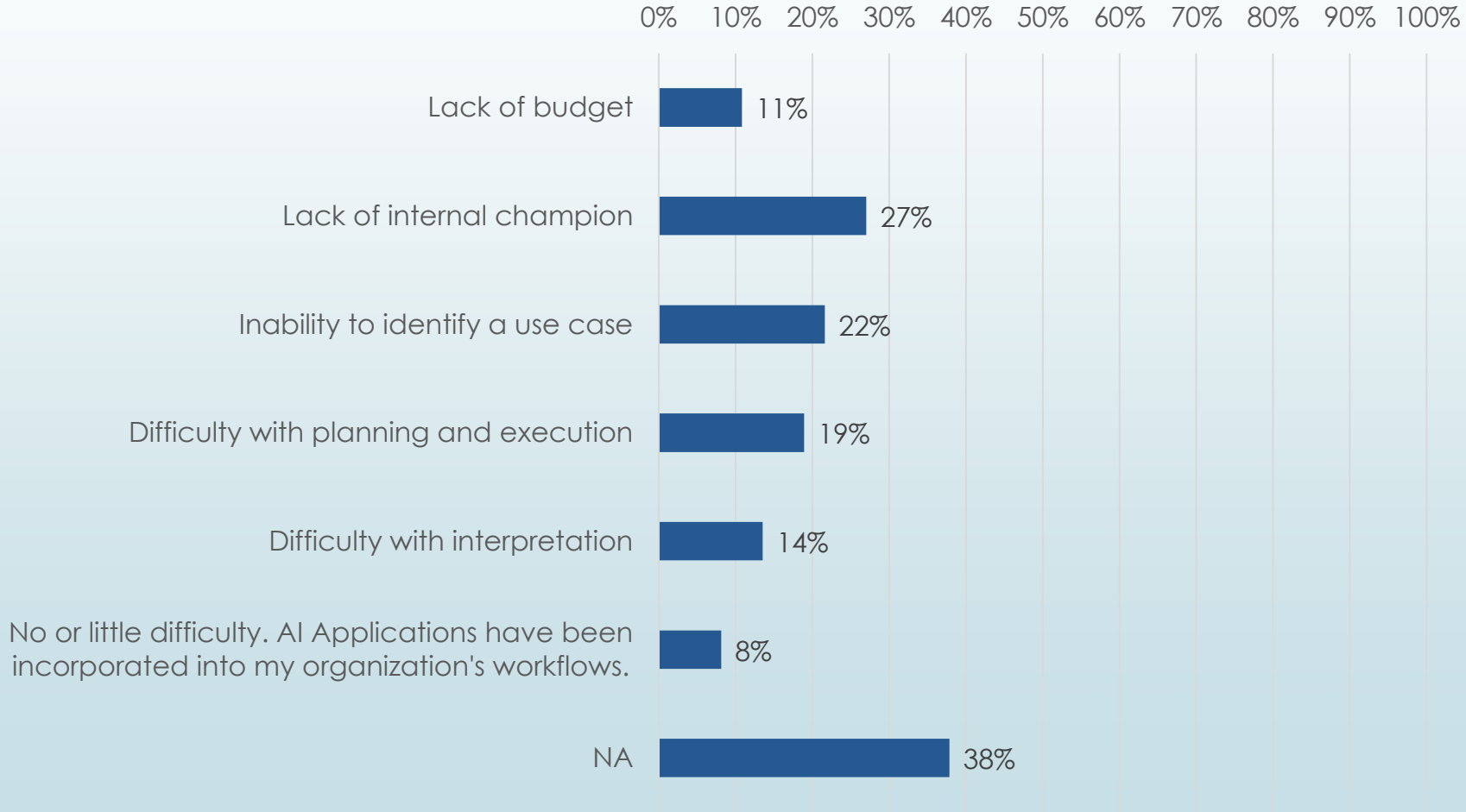
Pre-Meeting Survey Results



N = 38 respondents

Pre-Meeting Survey Results

What have been the biggest challenges with respect to adopting AI practices within your organization? Please select all that apply



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Today's Panel

Jacob Berlin
CEO
Terray Therapeutics

Becca Levin
Director, Corporate Strategy
Eikon Therapeutics

Nitin Choudhary
Commercial Executive.
Experience IMP.ai,
Symphony, Cognizant.

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TERRAY

We're improving human health by transforming the speed, cost and success rate of small molecule drug development using computation integrated with novel data streams at scale.

Founded:
October 2018

Headquarters:
Monrovia, CA

Team:
80 Employees

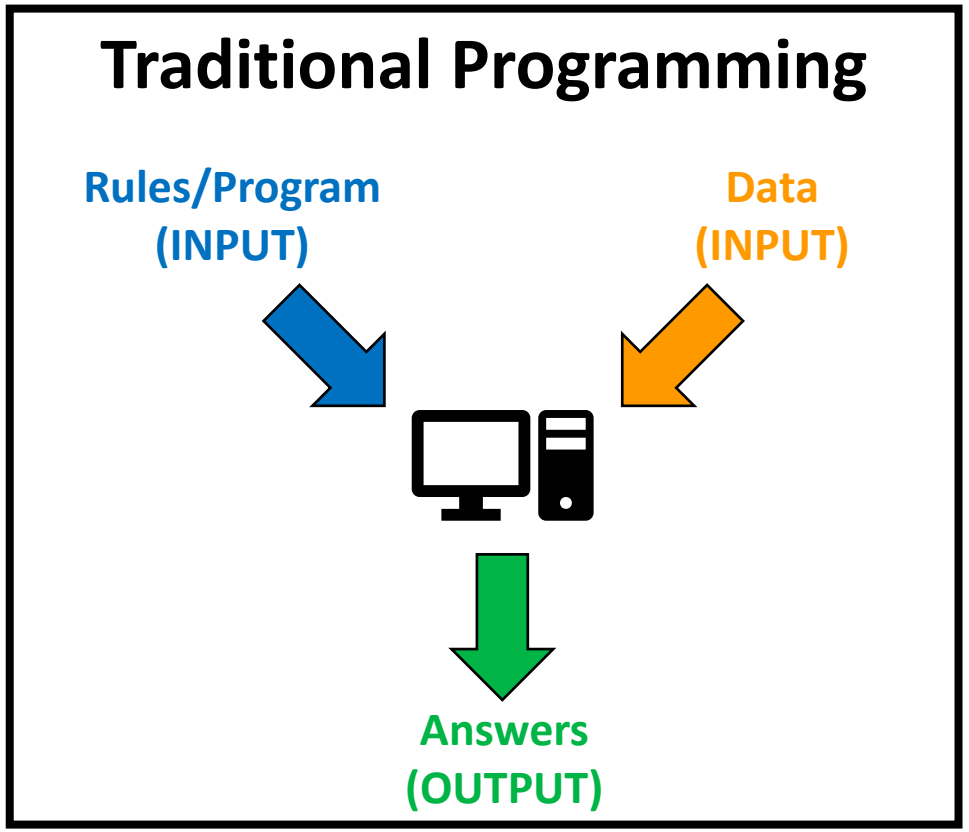
Equity Capital Raised To-Date:
$81.4M

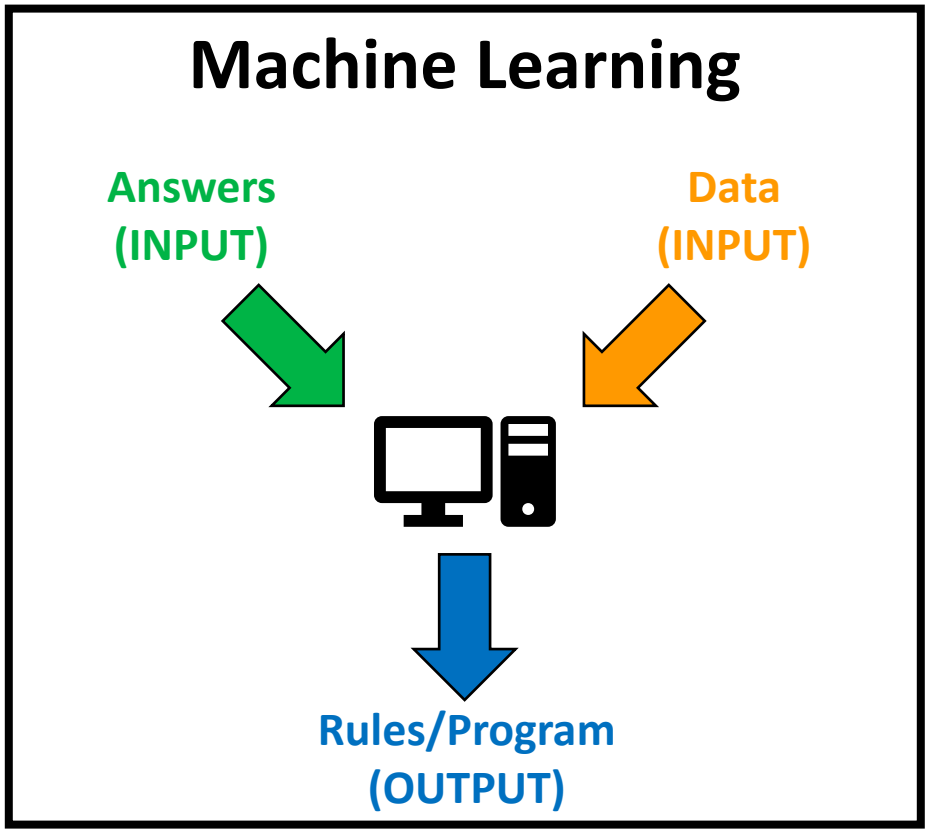
Investors:

MADRONA VENTURE GROUP
2σ
DIGITALIS
GOLDCREST CAPITAL
KdT Ventures
XTX MARKETS
sahsen VENTURES
ALEXANDRIA VENTURE INVESTMENTS

Machine Learning vs. Traditional Programming

"Field of study that gives computers the ability to learn without being explicitly programed." -Arthur Samuel (1959)





Med Chem Example: Traditional Programming

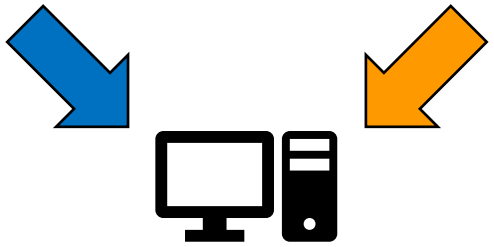
Lipinski's Rule of Five: A rule of thumb to evaluate druglikeness

An orally active drug has no more than one violation of the following criteria:

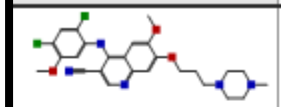
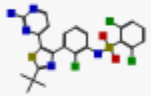
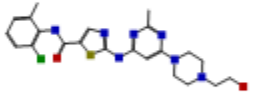
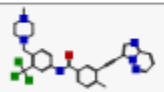
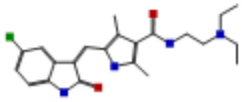
- MW < 500 g/mol
- logP < 5
- HBA < 10
- HBD < 5

Rules

Data



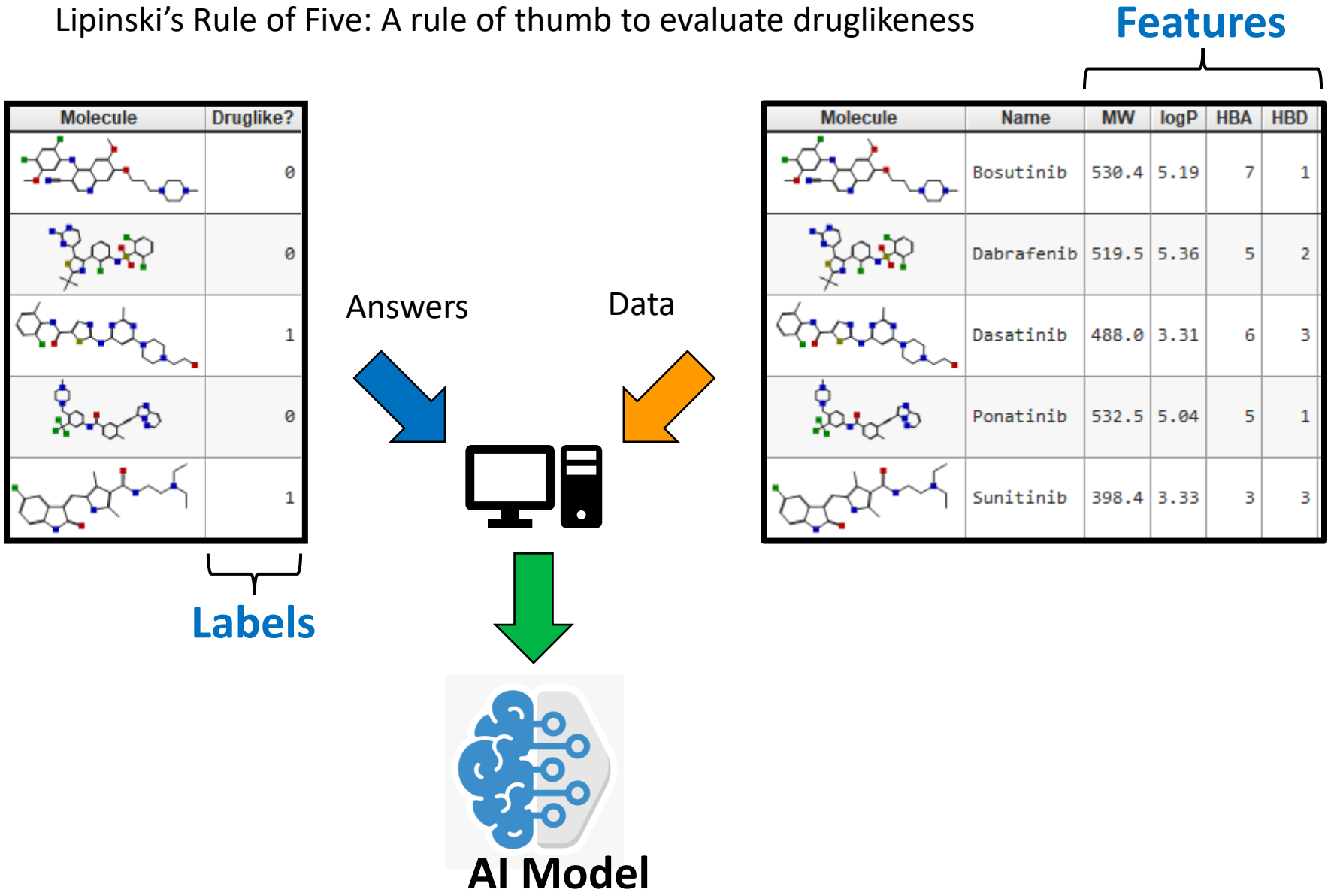
Answers

Molecule	Name	MW	logP	HBA	HBD
	Bosutinib	530.4	5.19	7	1
	Dabrafenib	519.5	5.36	5	2
	Dasatinib	488.0	3.31	6	3
	Ponatinib	532.5	5.04	5	1
	Sunitinib	398.4	3.33	3	3

Name	Druglike?
Bosutinib	0
Dabrafenib	0
Dasatinib	1
Ponatinib	0
Sunitinib	1

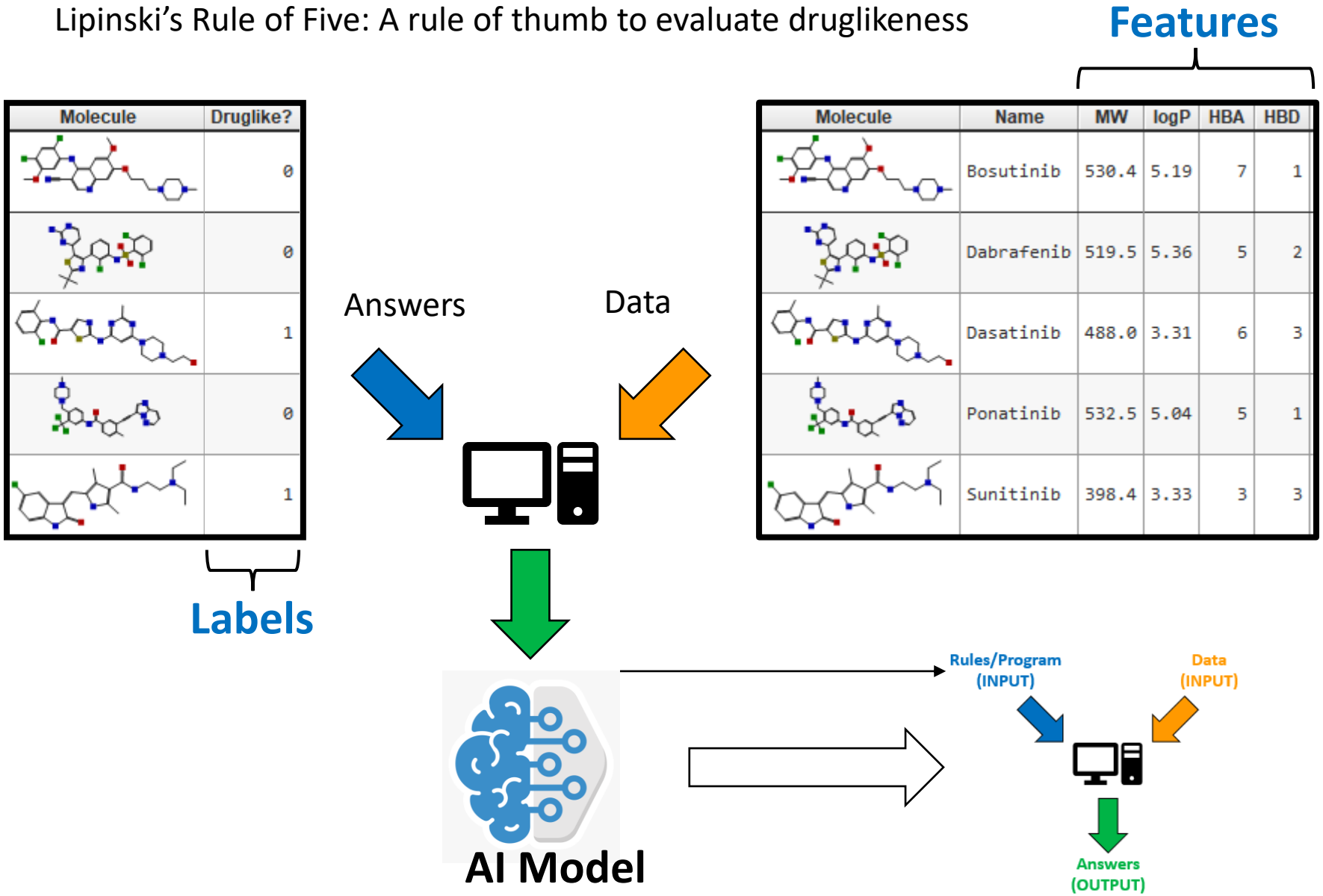
Med Chem Example: Machine Learning (ML)

Lipinski's Rule of Five: A rule of thumb to evaluate druglikeness



Med Chem Example: Machine Learning (ML)

Lipinski's Rule of Five: A rule of thumb to evaluate druglikeness



TERRAY

Computational power and accuracy is at a transformative moment.

avocado armchair_

Text Prompt

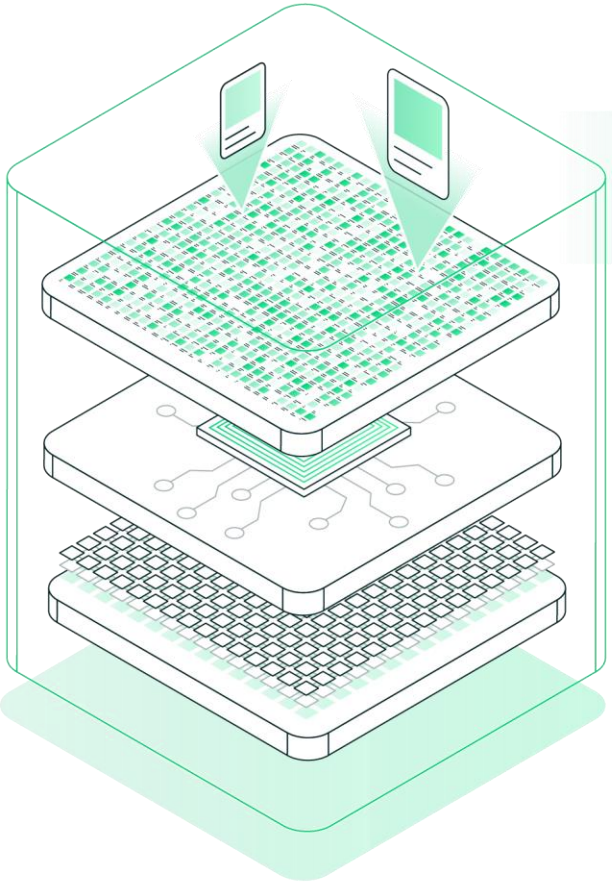
Input

Text-image Pairs

Data at Scale

Compute Power

Storage



Generated Image

Output

DALL•E, Stable Diffusion, Midjourney

AI Text to Image Generators

Precise experimental data at sufficient scale has exponentially increased the biological target opportunity...

MSAWAAASLSRAAARCLLARGPGVRAAPP
RDPRPSHPEPRGCGAAPGRTLHFTAAVPA
GHNKWSKVRHIKGPKDVERSRIFSKLCLNIR
LAVKEGGPNPEHNSNLANILEVCRSKHMP
KSTIETALKMEKSKDTYLLYEGRGPGGSSLLI

Amino Acid Sequences

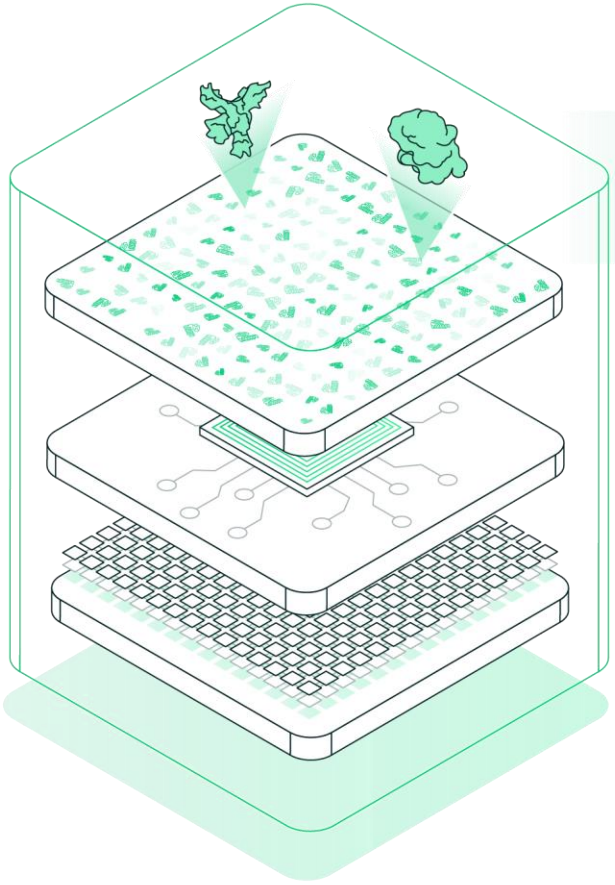
Input

Protein Crystal Structures

Experimental Data at Scale

Compute Power

Storage

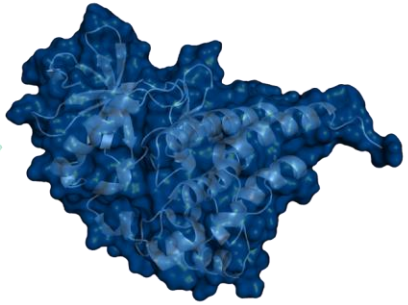


AlphaFold

Protein Structure Prediction

Highly Accurate Protein Structure Predictions

Output



…but the chemistry to solve these biological problems has remained slow and failure prone.

Therapeutic Targets

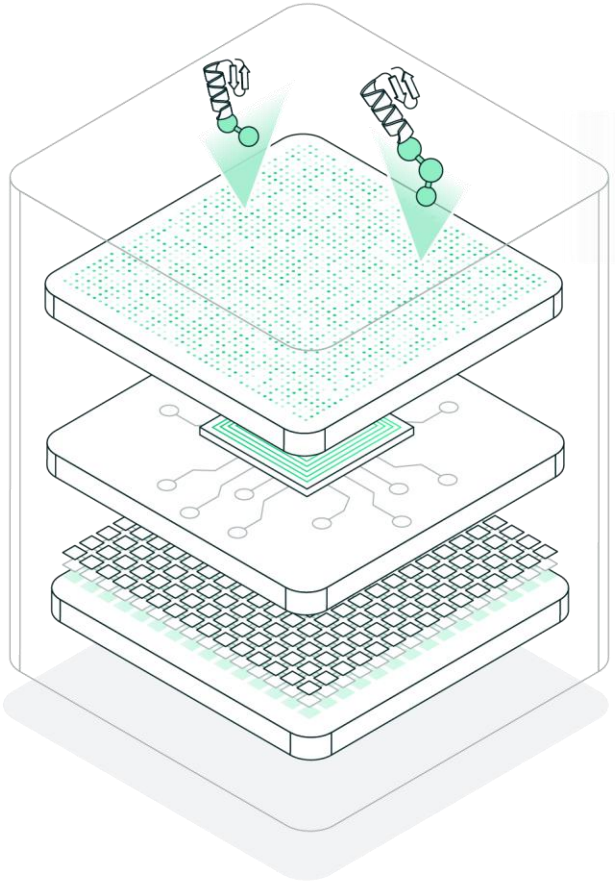
Input

Biochemical Measurements

Experimental Data at Scale

Compute Power

Storage



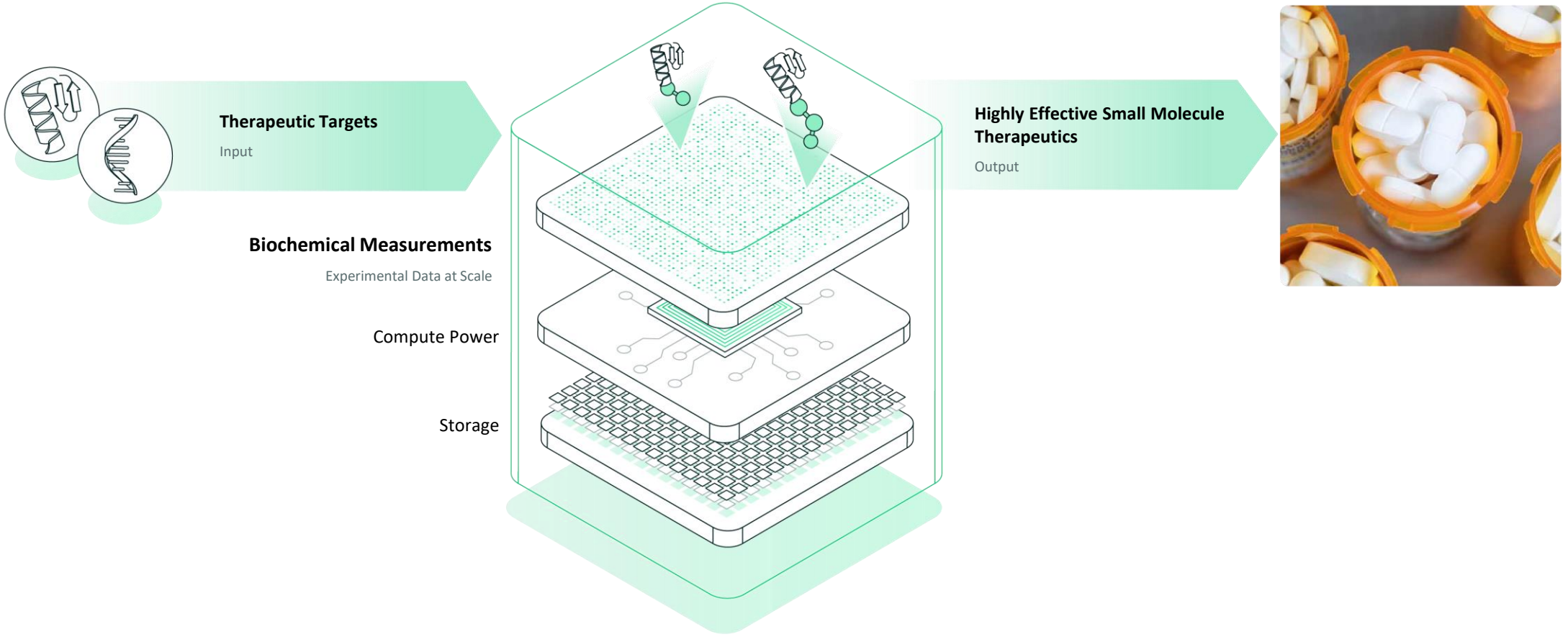
Highly Effective Small Molecule Therapeutics

Output

No Platforms Exist

Novel Small Molecule Therapeutic Discovery

We’re unlocking the power of modern computation in small molecule drug discovery.



tNova: Small Molecule Drug Discovery Platform

TERRAY

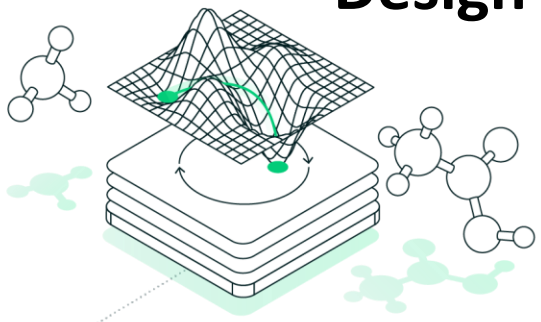
TERRAY

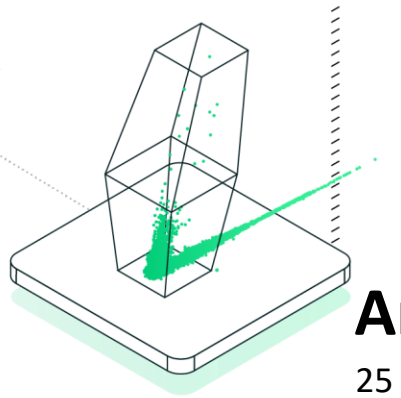
tNova: Small Molecule Drug Discovery Platform

Computation (tCompute)

Design

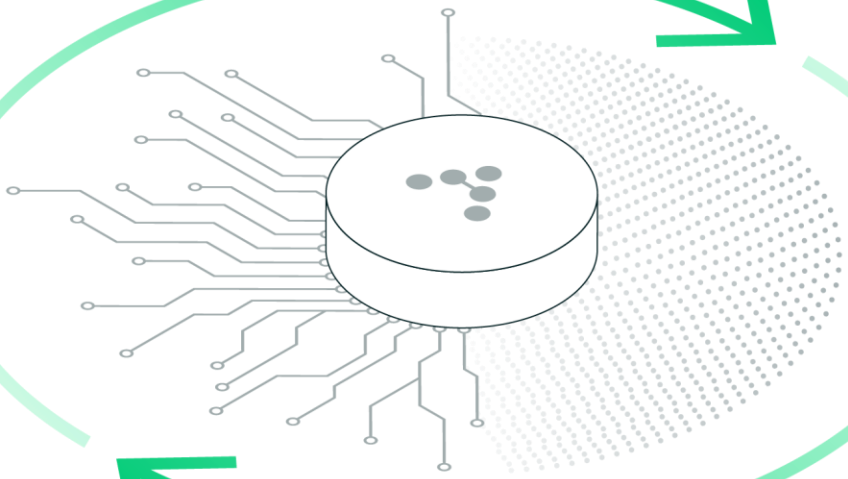
Generative AI leverages a growing database of 50B+ values





Analyze

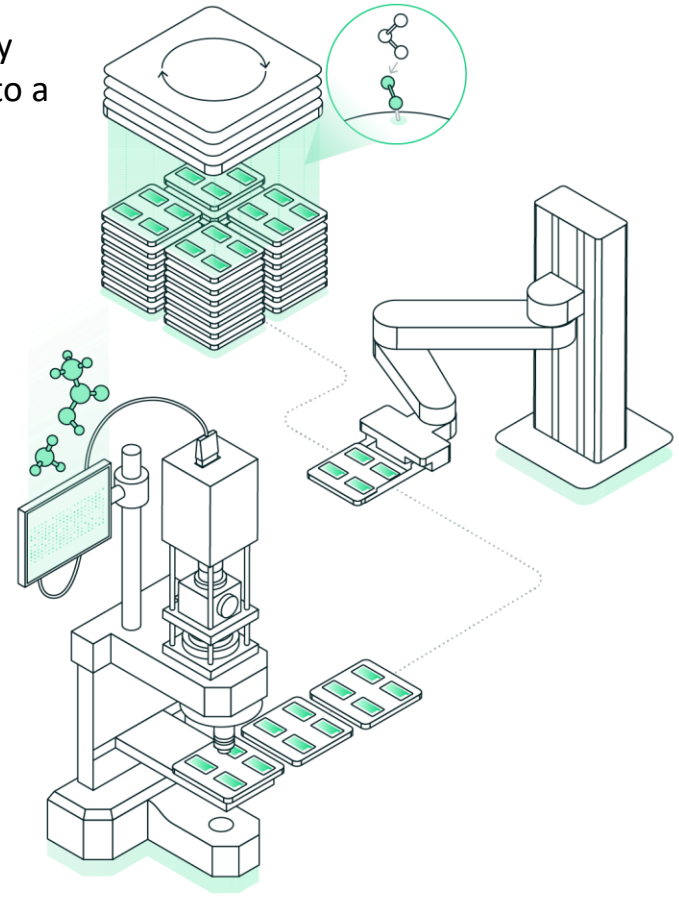
25 TB of image data is converted to binding affinity each day to identify potent and selective molecules



Experimentation (tArray)

Make

Add 4M new library molecules a week to a collection of 60M+

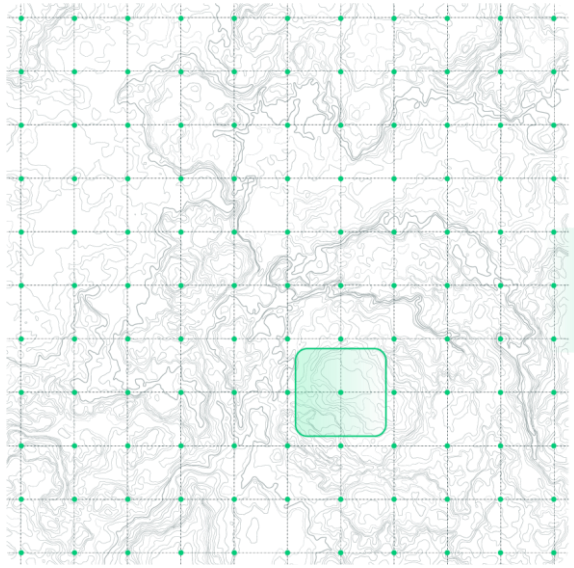


Test

2M molecules against a target in 5 min

How We're Mapping the Molecular World

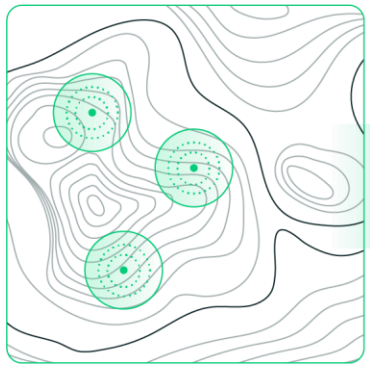
Finding a small molecule drug for a target with tNova is like finding a route to an unknown moutaintop



Grid search of a state

Grid search of a large area to find a region of interest that looks mountainous.

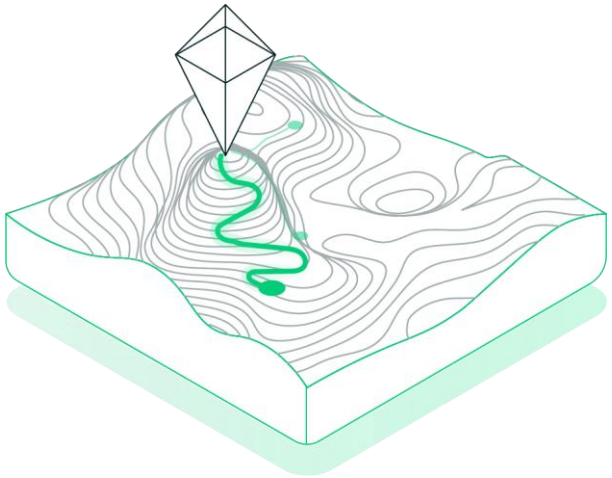
(Diversity Library Screening)



Zoom in, find basecamps

Zoom in on the region of interest to find suitable basecamp locations.

(Focus Libraries)



Uncover the mountain, find the best trail

Use elevation data for a new perspective, revealing the mountain - and the best path to reach the top.

(Generative Design)

Our goal: summiting every peak

With our throughput and scale, we can not only find every mountain – but also the more efficient way to the top.

Our tNova Workflow

Targets of Interest

Diversity Library Screening

First, we measure the interaction of every target with 30M+ unique molecules in our drug-like 2-cycle diversity libraries.

Focused Library (Active Learning)

Then we feed the resulting hit data to ML models to iteratively build and test 2- and 3-cycle focused libraries of 2M+ molecules in just weeks.

Generative Drug Design

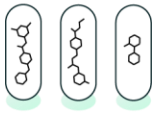
Finally, we use our proprietary ML models to design property-optimized non-combinatorial molecules.

Biological Testing

Biochemical, Cell, ADME, and more.

Many series tested through late preclinical

High Quality Clinical Candidates



FTE synthesis

Scaled-up robotic resynthesis

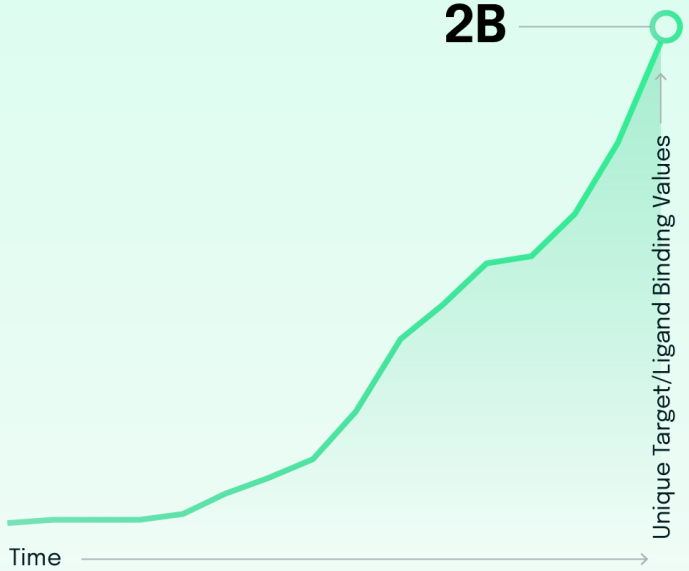
Microscale robotic resynthesis

Hit ID

Hit to Lead / Lead Optimization

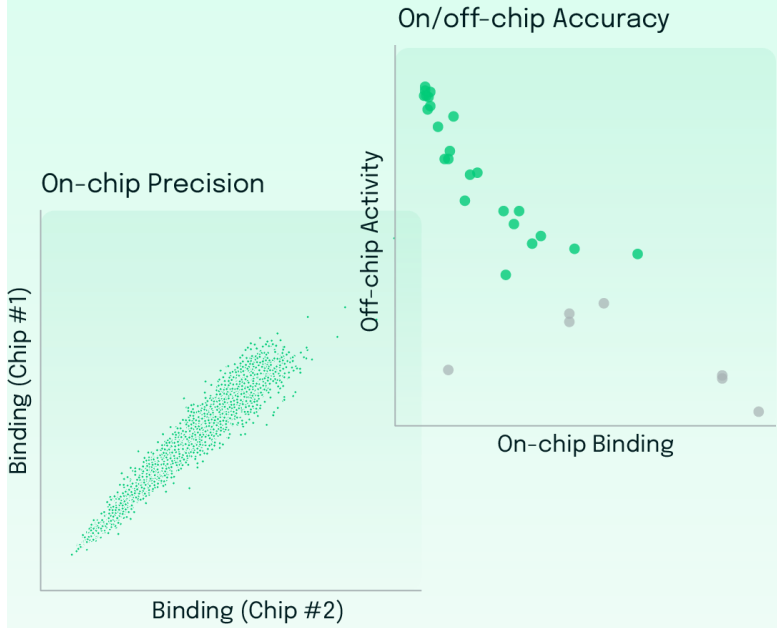
TERRAY

tNova: Small Molecule Drug Discovery Platform



Scale

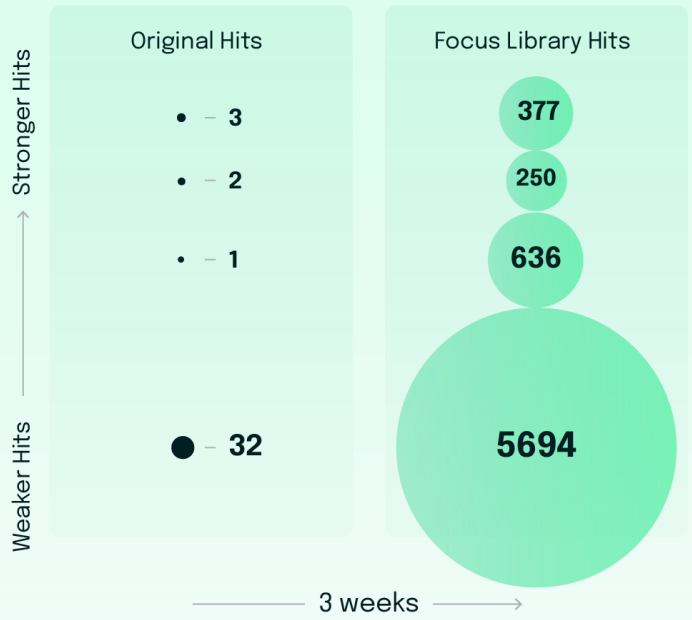
Over 50B individual measurements go into >2B quantitative target-ligand interaction values in our database, enabling us to evaluate selectivity from day 1.



Precision & Accuracy

Each binding value is supported by 20-35 repeat datapoints, resulting in precise measurements that are consistent chip-to-chip, library-to-library, and month-to-month.

These on-chip values accurately correlate with off-chip activity enabling accelerated on-chip optimization.



Iteration

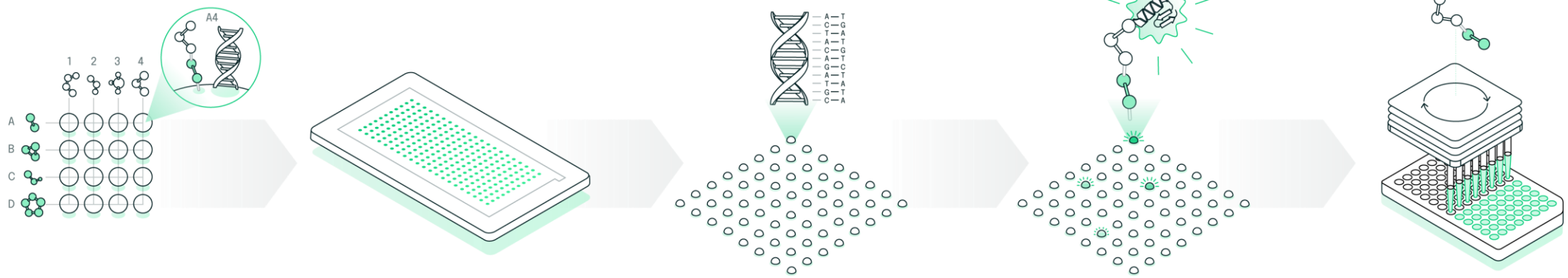
A design-make-test-analyze cycle takes less than 3 weeks per target, enabling an active learning approach that intelligently and smoothly explores chemical spaces millions of

molecules at a time.

tArray: The Foundation of our Experimental Footprint

Enables us to screen hundreds of millions of compounds in minutes and return quantitative data on each compound.

Experimentation (tArray)



Make Nanoparticle Libraries

Combinatorically synthesized molecules and DNA barcodes are attached to nanoparticle beads.

Immobilize Beads on tArray Chip

Beads are randomly placed into 32M wells on a reusable chip the size of a nickel.

Map Position of Beads

DNA barcodes are sequenced to map compound position, then DNA is cleaved off the beads.

Screen Target of Interest

Precise binding affinity is measured based on fluorescence intensity in less than 5 minutes per chip.

Resynthesize and Test

Hits are tested through microscale bead-based resynthesis and high-throughput activity testing.

Computation (tCompute)

Our Workflow

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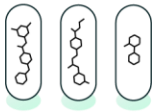


FTE synthesis

Scaled-up robotic resynthesis

Microscale robotic resynthesis

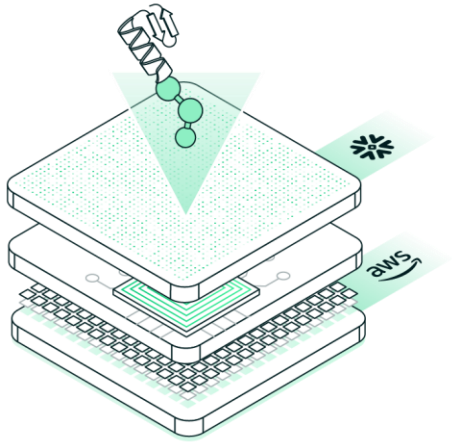
Hit ID

Hit to Lead / Lead Optimization

tCompute: Our Computational Engine

Powered by generative AI and advanced ML models, it enables rapid, iterative design of highly optimized molecules and libraries.

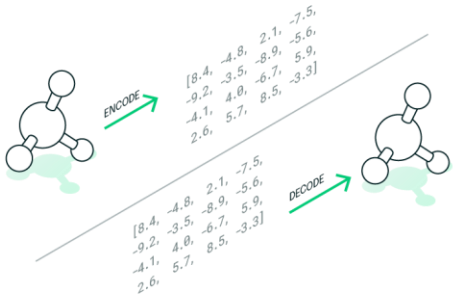
Computation (tCompute)



Molecular data at unprecedented scale

tData

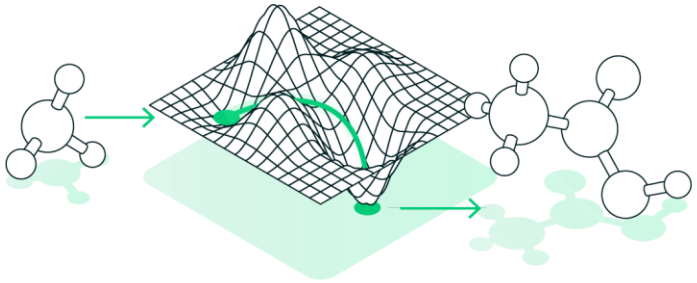
50TB of images a day → cloud processing → billions of actionable target-ligand binding datapoints that can be queried within seconds for understanding SAR, designing molecules and libraries, etc.



Understanding the language of molecules

COATI: **C**ontrastive **O**ptimization for **A**ccelerated **T**herapeutic **I**nference

Multi-modal contrastive pretraining for representing and traversing chemical space (**invertible molecular representation**)



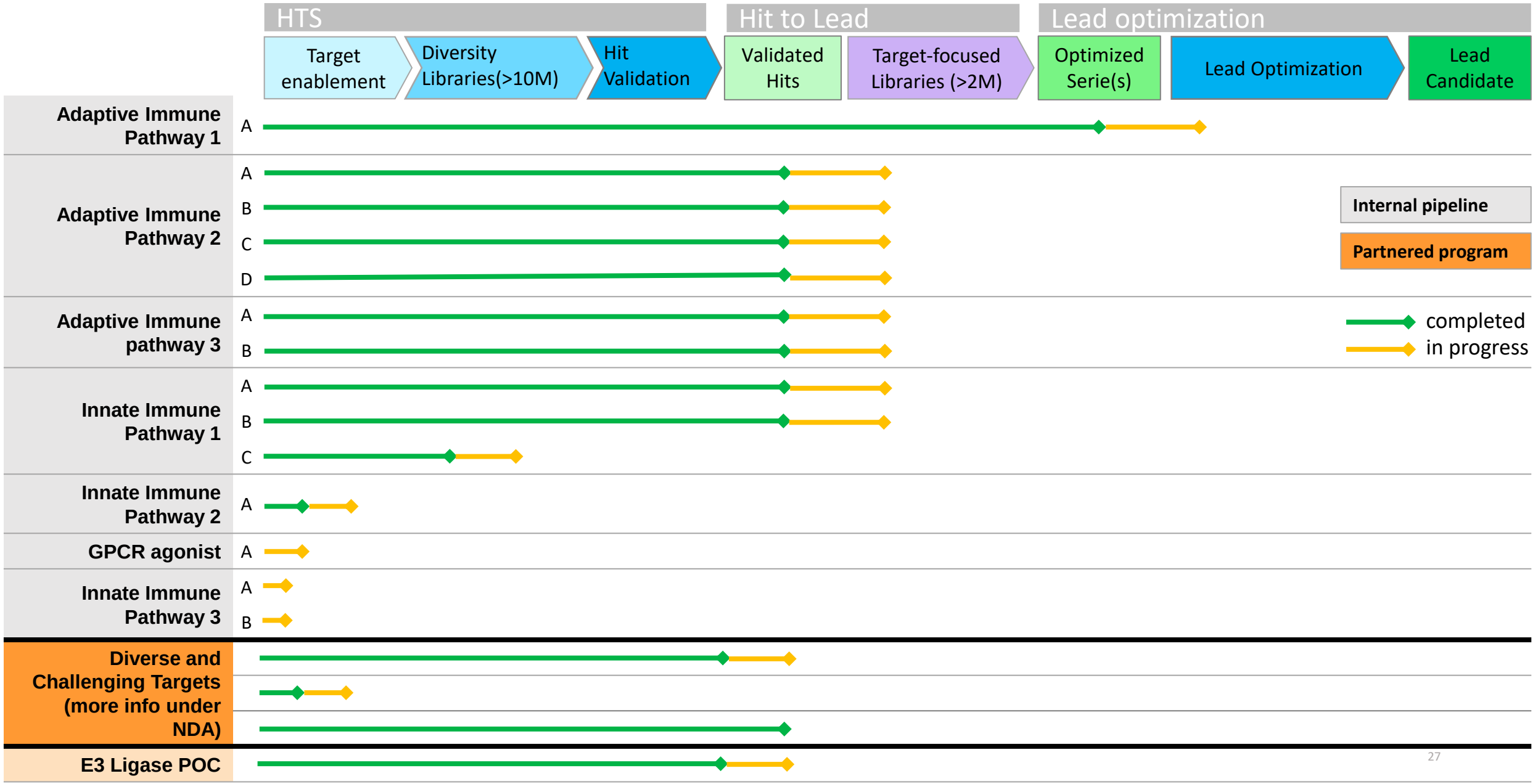
Models for molecular property prediction (affinity, activity, ADME, etc.)

tNet-LB and tNet-SB

Powerful, differentiable ligand-based and structure-based (physics-inspired) **regressors** for predicting molecule properties with **uncertainty quantification**

Experimentation (tArray)

Overview of Terray Pipeline Targets



Where will AI make a difference?

Everywhere there is precise and accurate data at scale that iterates fast enough to test hypotheses and refine models.

Today's Panel

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CEO
Terray Therapeutics

Becca Levin
Director, Corporate Strategy
Eikon Therapeutics

Nitin Choudhary
Commercial Executive.
Experience IMP.ai,
Symphony, Cognizant.

Themes for my discussion today

- Introduce myself & my roles
- Share a bit how AI is used at my current & former co's
- Highlight the impact on those in NPP roles

My background & experience

UCSF
University of California
San Francisco

BCG BOSTON CONSULTING GROUP

"Education"

Recursion

Lead Program & Pipeline Strategy group focused on identifying new targets & advancing through preclinical discovery

Key support for ~$500M IPO in 2021, during heyday of TEDD co's

eikon therapeutics

Focus on corporate planning & strategy including $106M Series C in June

CI support for clinical development team

"Commercial" support for potential Eikon Instruments business

Eikon in summary

World-Class Team	Proprietary Technology	Financially Sound	Growing Pipeline
• Collectively achieved >110 U.S. FDA drug approvals	• Exclusive, Nobel prize-winning microscopy • Unparalleled scale and de-risked	• Top-tier investors • ~$775M raised	• Clinical-stage oncology assets • Near-term catalysts

Superior engineering | High-performance computation | Breakthrough research

= Transformational Medicines

Activity is motion, changes to the system can be read out in protein dynamics and that informs biology

Fast
(e.g. monomers)

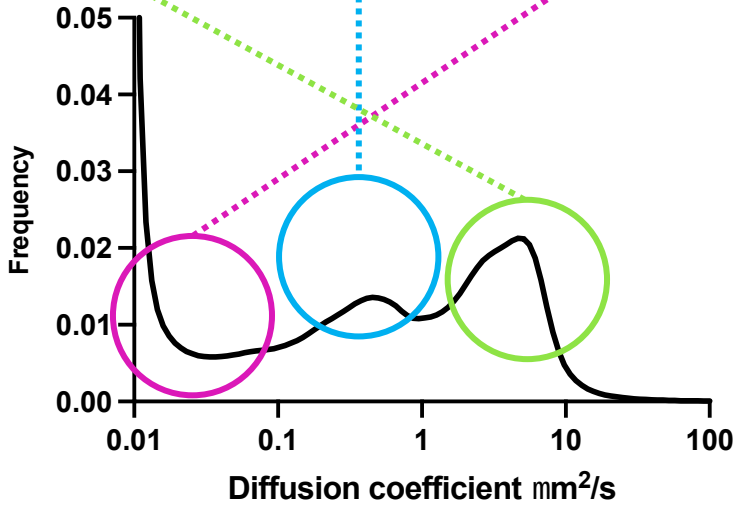
perturbations

Intermediate
(e.g. complexes)

perturbations

Slow
(e.g. bound)

essentially static at the timescale of acquisition



Proteins move to perform their function

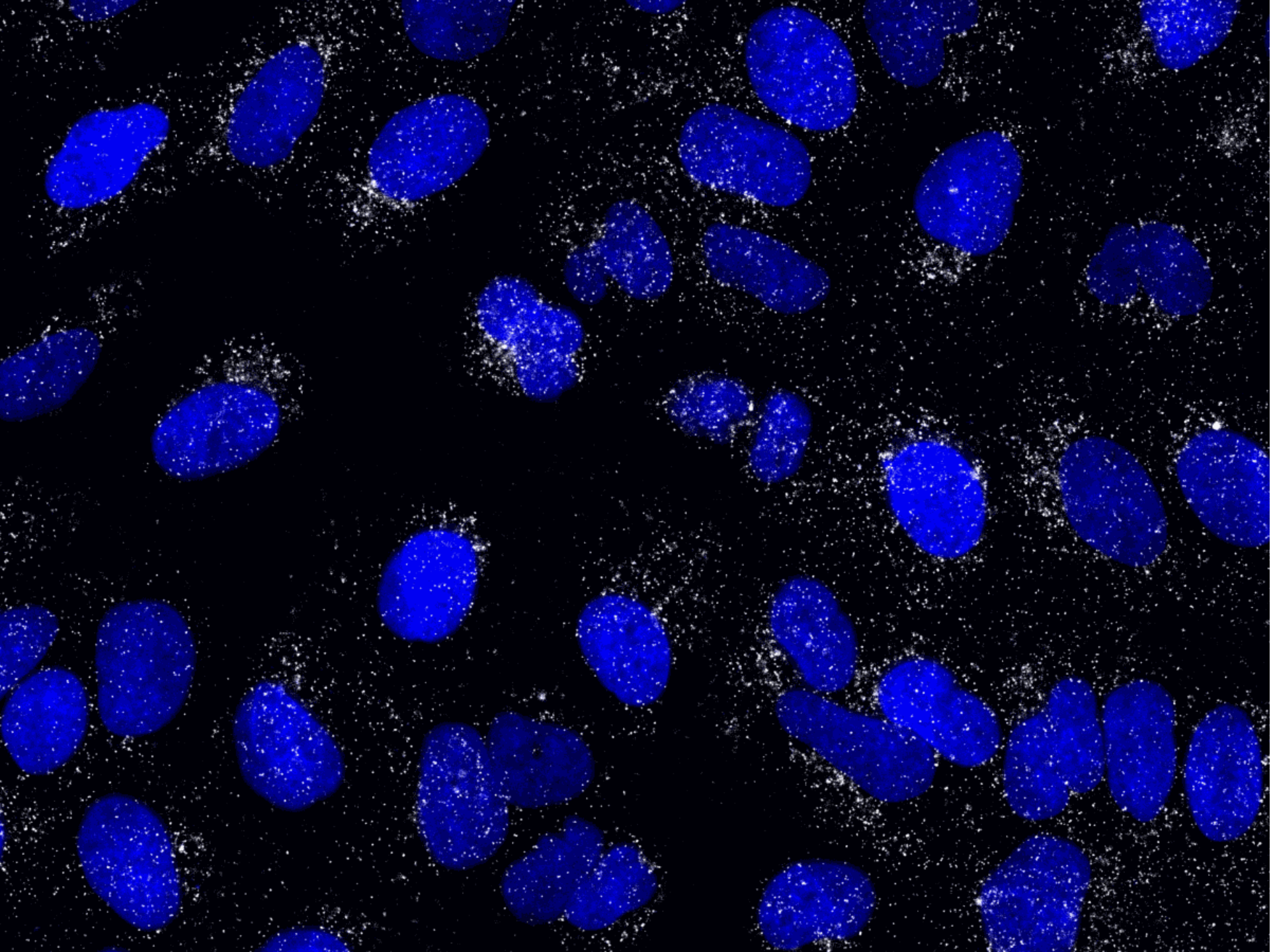
These motions convey information about activity and mechanism

Perturbations

- Chemical
  - Inhibitor
  - Agonist
- Genetic
  - siRNA
  - KO
  - mutant

We can quantify that motion for biological insight…

eikon therapeutics



Proprietary Technology

Studying protein dynamics makes new biology visible

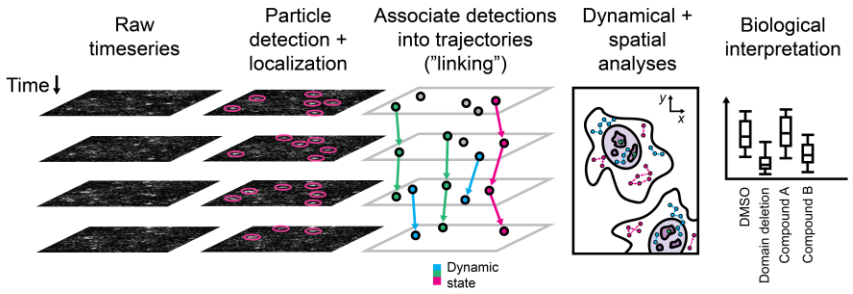
Slow — Fast

Diffusion Coefficient ($\mu m^2/s$)

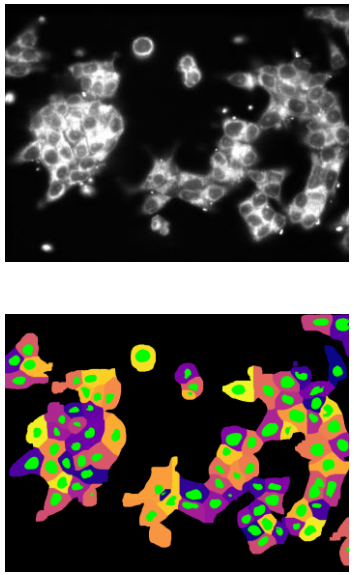
AI/ML are critical to our current SMT analysis pipeline

Quantitate SMT data

Detect, Link, Track Pipeline



Contextualize SMT data

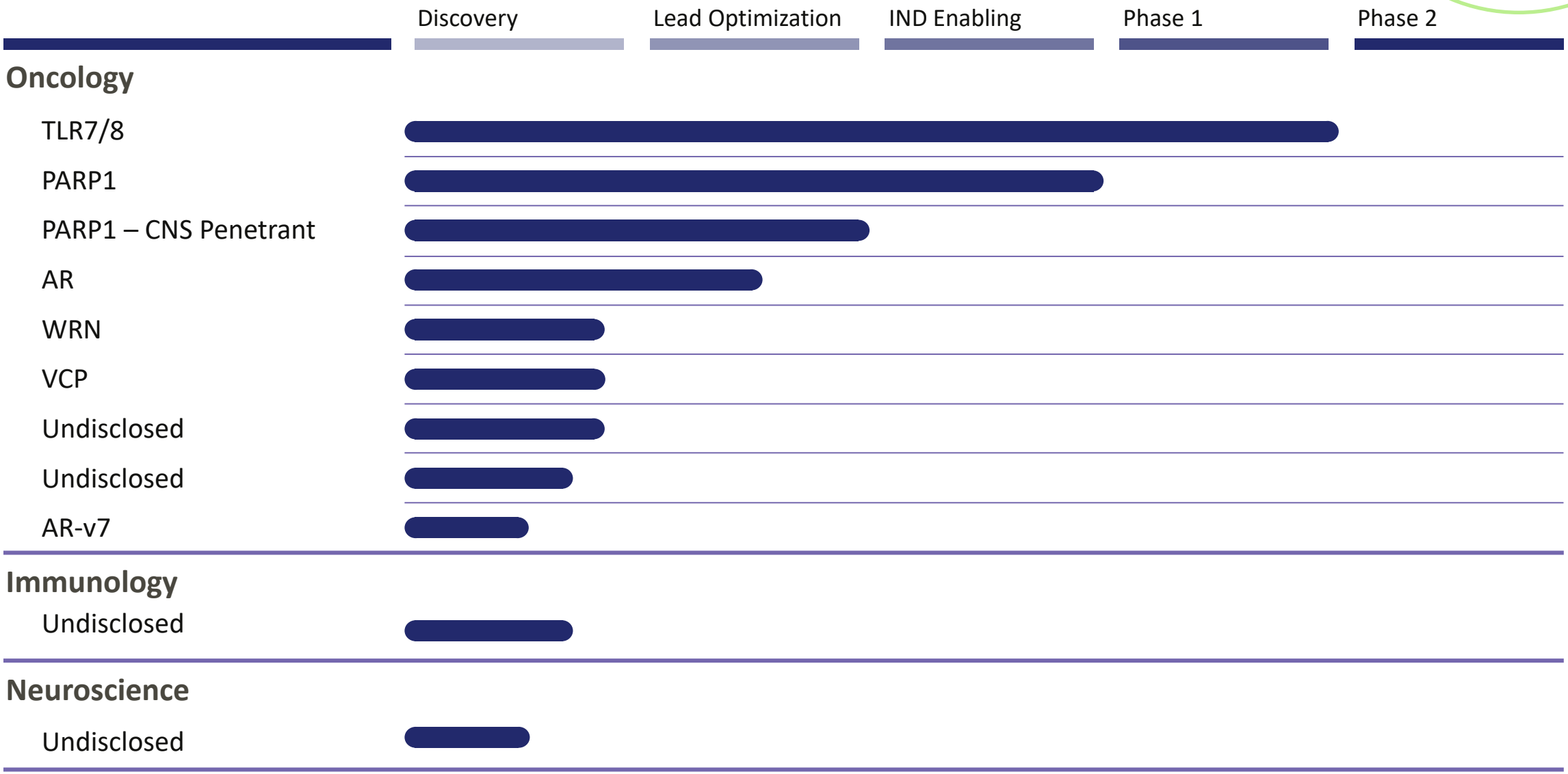


Identify biological activity

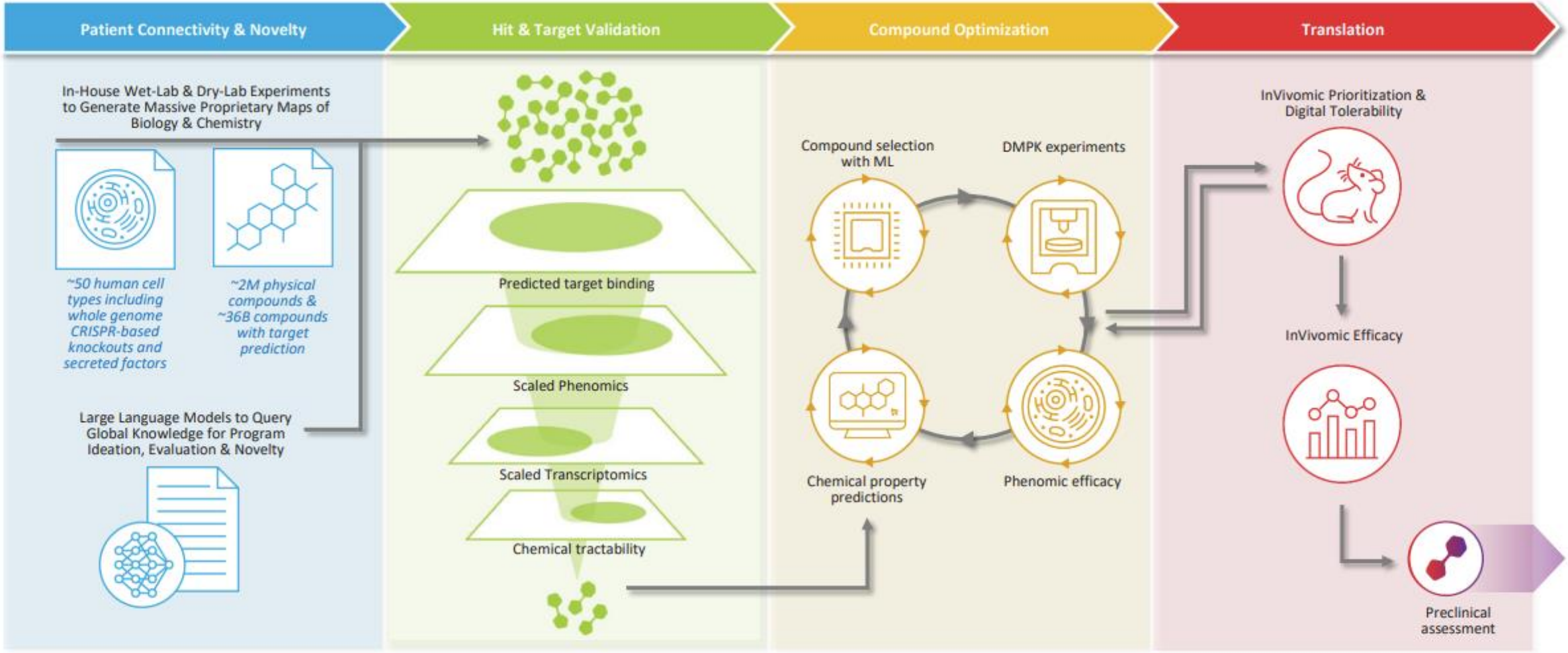
Eikon generates roughly 6PB of data a week that is processed through our AI/ML-enabled data analysis pipeline

Growing pipeline in oncology & beyond

Growing Pipeline



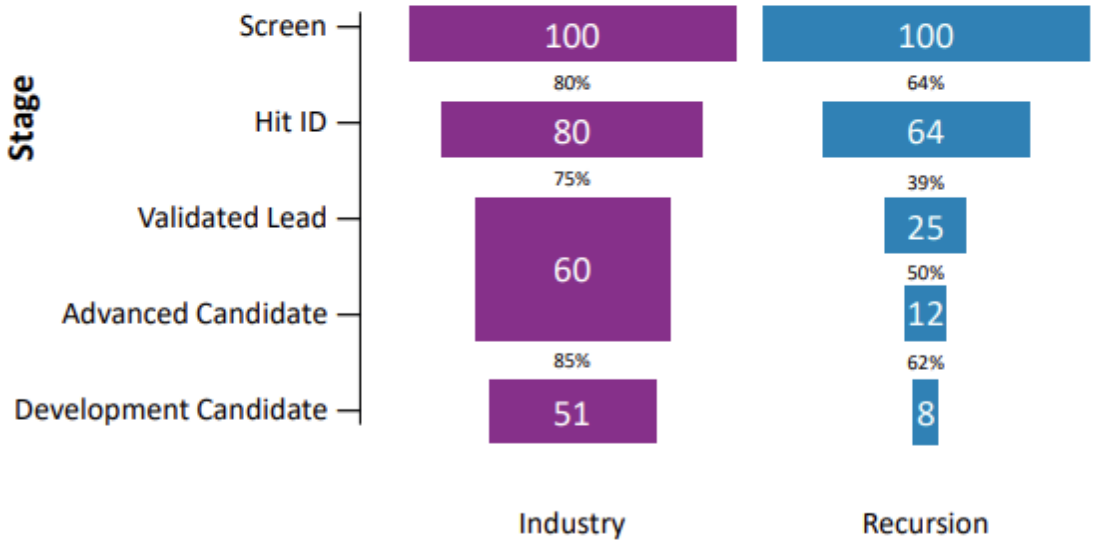
The Recursion OS today: Industrializing drug discovery to transform BioTech into TechBio



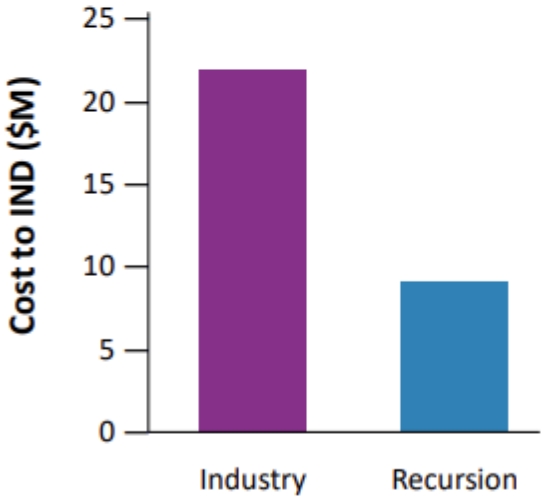
Recursion

Mapping and navigating the complex systems of biology and chemistry has demonstrated leading indicators of efficiency

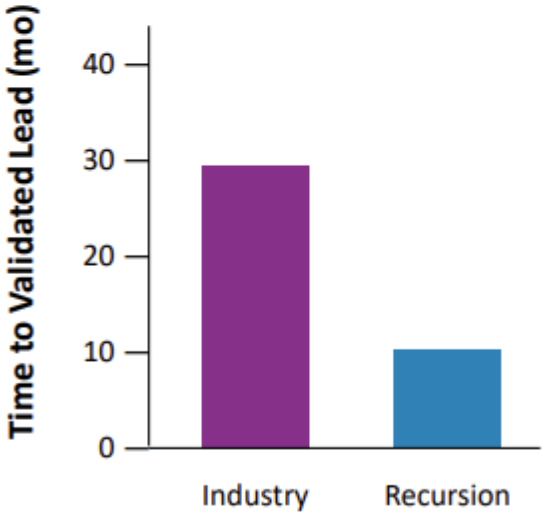
Failing faster and earlier to ›



› spend less ›



› and go faster



Data shown is the average of all our programs since late 2017 through 2022. All industry data adapted from Paul, et al. Nature Reviews Drug Discovery. (2010) 9, 203–214

Our pipeline reflects the scale and breadth of our approach

More than a dozen additional early discovery and research programs in oncology or with our partners

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) Our program has the potential to address several indications in this space. (4) Our program has the potential to address several indications driven by MYC alterations, totaling 54,000 patients in the US and EU5 annually. We have not finalized a target product profile for a specific indication.

Personal perspective: NPP needs to evolve to receive AI insights

AI's impact on drug development ***Resulting impact on NPP***

Increased scale & efficiency

- If you create a truly successful virtuous cycle, you should see a higher volume of programs come through at faster rates. How do you structure your team, time & effort to deliver what is needed, when it is needed?
- Most companies are generating massive quantities of data/relationships/insights – how to quickly triage to find novelty worth pursuing as part of pipeline? Answer: Strong "product" focus

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Novelty – targets, disease relationships

- How do you balance risk if the corporate strategy is focused on novelty & proving platform – how do you balance risk if a pipeline of totally new, unvalidated targets is key to the company's success?
- Epidemiology/market sizing can be tricky if looking at new genetic signatures or other new biomarker driven population
- Need to work across teams – INCLUDING Data science – to truly understand the program and support well

So… am I using AI/ML in NPP today?

Honestly…not yet

- Experimenting with tools like Ferma.ai, ChatGPT, Bard etc but have not been impressed with their functionality for CI work to date
  - Ferma.ai pretty helpful for AACR prep
- Standard databases (Cortellis, Pharmaprojects, Evaluate) are still better curated than the public data ChatGPT has access to
- Would love to see NLP tools layered onto these databases

But, I'm hear to learn!

Today's Panel

Jacob Berlin
CEO
Terray Therapeutics

Becca Levin
Director, Corporate Strategy
Eikon Therapeutics

Nitin Choudhary
Commercial Executive.
Experience IMP.ai,
Symphony, Cognizant.

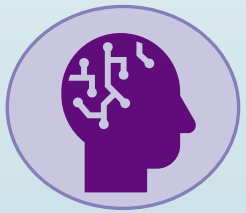
Patient data availability, better integration, and machine learning provides opportunity for efficient decision-making during product launches*

**Applicable to US Market*

Data Democratization

Data integration

Maturity of AI Technology



Focus on specialty markets

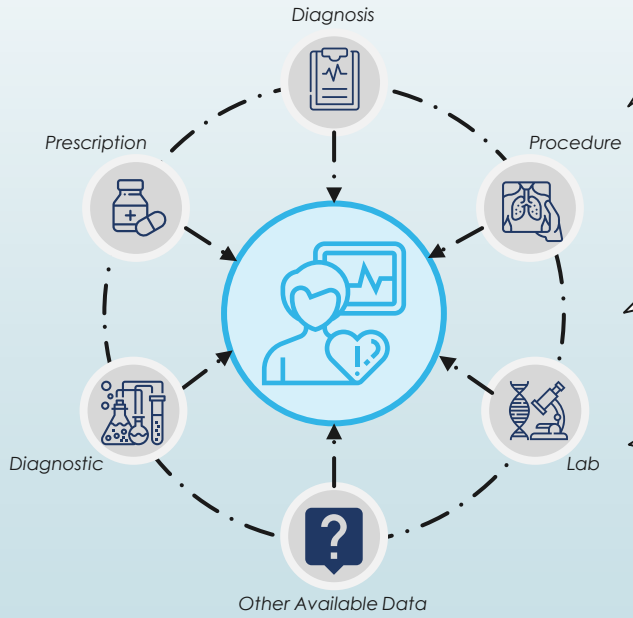
With the patient at the heart of integrated data, a new realm of analytics emerges across the clinical and commercial spectrum

PATIENT FINDING
Which patients are mis-diagnosed and appropriate for therapy?

PATIENT JOURNEY
Can we better understand our patient through longitudinal data?

FORECASTING
Can real-world data refine our baseline forecast or other model inputs?

REFERRAL NETWORK / KOL MAP
What connections exist between prescribers? Who are the most influential HCPs?



HCP TARGETING
How can we identify and prioritize the HCPs & institutions relevant to our brand?

MARKET ASSESSMENT
How large is our addressable market, and who is the competition?

PATIENT / HCP SEGMENTATION
What are the clinical and behavioral profiles of our key customers?

REAL-TIME MARKET ALERTS
How can we notify the field of critical territory activity, as soon as it occurs?

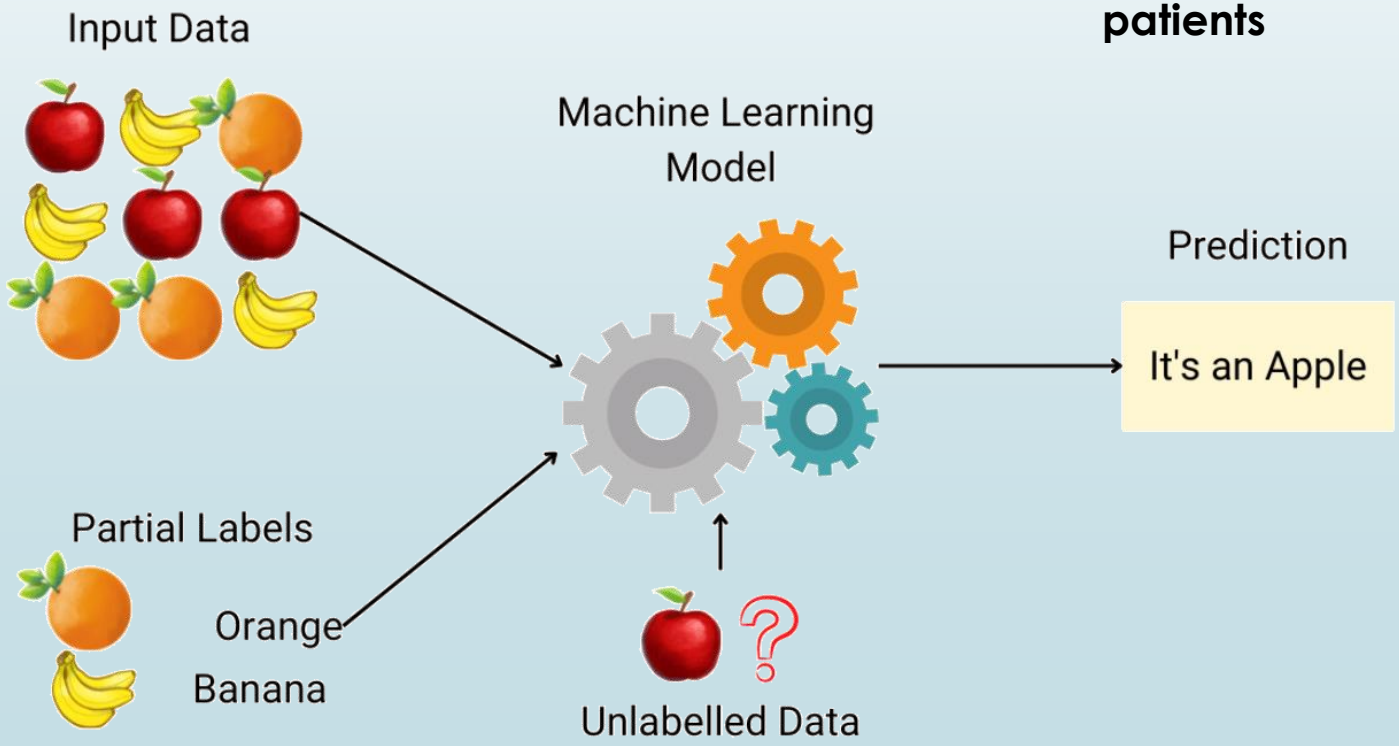
This Analytics can help delivery insights across the product lifecycle

Key Events	Major Activities	Phase I Understand	Phase II Organize	Phase III Deploy	Phase IV Execute
Insight Generation	Market Assessment Patient Journey A&U (Consumer/HCP/ Payor) Segmentation (Patient/HCP) Life Cycle Management	Timing			
Positioning / Branding	Positioning Branding Packaging Development & Refinement				
Communications Development	Message Development & Refinement Creative Development & Refinement Ad Development & Refinement				
Consumer Research	Communications Development Ad & DTC Patient Compliance Program				
Payor / Pricing Research	Market Evolution Pricing Access Strategy Segmentation Messaging				
Competitive Intelligence	Market Evolution Competitive Scenario Planning (War Gamming) Competitive Compound Assessment Competitive Positioning/Communications				
Promotional Response	Channel Strategy and Sales Force Sizing Alignment and people placement IC Design HCP Call Plan				
Launch Tracking	Patient & Physician Triggers Performance Tracking				

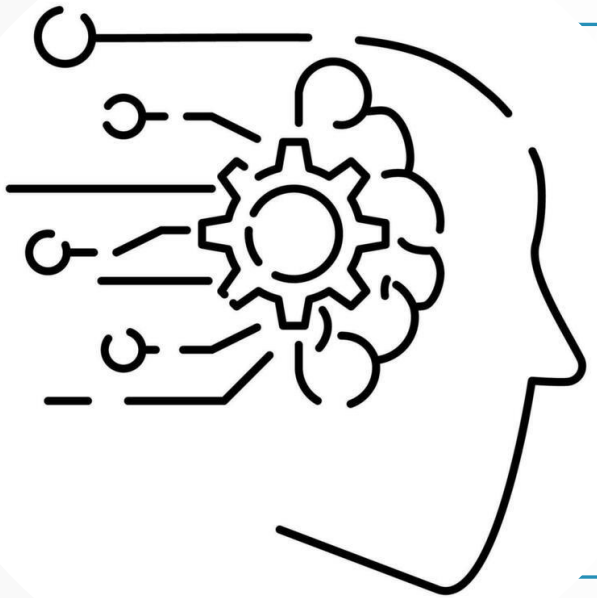
Deep Dive - Patient Finding leveraging Machine Learning

Machine learning predictions are made based on interaction of real-world data: each is a piece of the puzzle

1. **Define and identify positive patients**
2. **Train a machine learning model to find patients who are likely**
3. **Score entire universe of de-identified patient-level data to identify the highest-likely patients**



Learn and deploys AI algorithms to solve various kinds of problems that we encounter



- Undiagnosed / Misdiagnosed Patients
- Patients with Disease progression
- Patients at risk of dropping of therapy

Once the Patient Finding is done, it can inform various key business questions

Payer	Physician	Provider
• Understand the payer associated with patients	• Find the provider/care team that is involved in caring for the patient	• Find the institution/group practice or hospital where the patient is treated

Market Sizing

Stakeholder Segmentation

HCP Targeting

Clear communication, continuous engagement and improvement is essential to success

Robust Planning

Articulate the business objectives, associated messaging and desired outcome behind the analytics undertaking

Expectation setting and Communication

Machine Learning and AI are newer capabilities, and many times the technology don't provide a robust rational for some of the key findings. Hence it requires delicate messaging and expectation setting so as not to overwhelm the stakeholders and at the same time build confidence

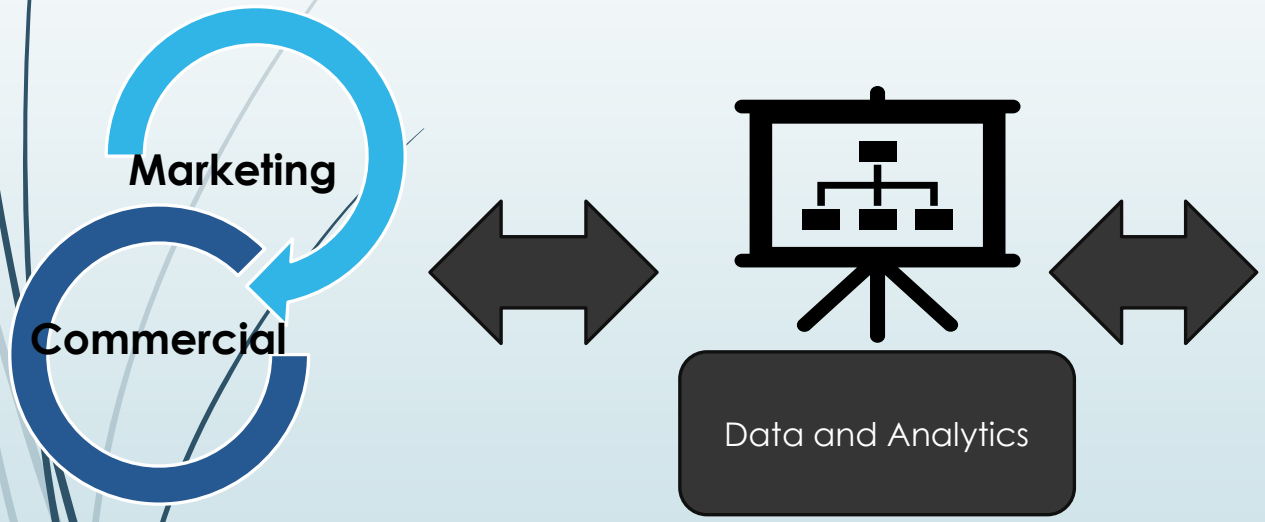
Drive Execution and Gather Feedback

Collect and analyze both short term and long-term feedback

Continuous Improvement and Enhancement

Improve the existing process to ensure optimal results

Many organizations are building the patient analysis as a collaborative initiative



Solution Consultants	Delivery Consultants	Data Analytics	Data Science
Works with Clients to understand, coordinate and explain	Bridge between Data Analytics and Solution team	Data Investigation	Machine Learning and AI experts

What's the opportunity in future

- The integration of healthcare data presents an opportunity for consolidation, despite its current fragmentation.
- By infusing business context into the data, we can unlock valuable insights.
- Addressing the absence of self-service, on-demand analytical tools tailored to specific business requirements can lead to solutions that fulfill crucial operational needs.

Post-Forum Summary Notes

- A big mantra in AI/ML is the "garbage in / garbage out" mentality. If one is building AI tools, regardless of data origin, one needs to have multiple and frequent approaches to validate that one is not spewing out garbage

- Regarding specialized datasets, the field is moving in three ways:
  - ***Size of dataset*** – pick an origin of data type and map the most possible interactions/states in it
  - ***Layers of data*** – you need multiple sources of data (phenomics, proteomics, transcriptomics, etc.) that is all annotated in ways that can "play" with each other (e.g., use same chemical library, use same CRISPR library) to map a set of permutations across all types of data consistently
  - ***New data types*** (e.g., Eikon's Single Molecule Tracking)

Additional Resources

- KPMG recently published white papers on AI applications for the Biopharma industry. They can be accessed via the links below:
  - KPMG AI Trends in Biopharma
  - KPMG AI and Precision Medicine
- Multiple organizations publish white papers and newsletters on artificial intelligence. LinkedIn keyword searches are the best way to identify these resources.