

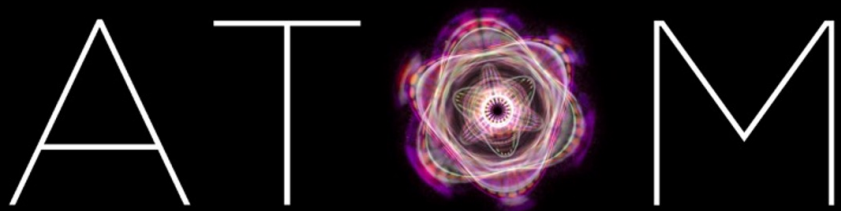
Partnerships to Accelerate AI Health Research

**GUIRR: Enhancing U.S. Science and Innovation with
Novel Cross-Sector Partnerships**

June 29, 2022

Washington, DC

John Baldoni

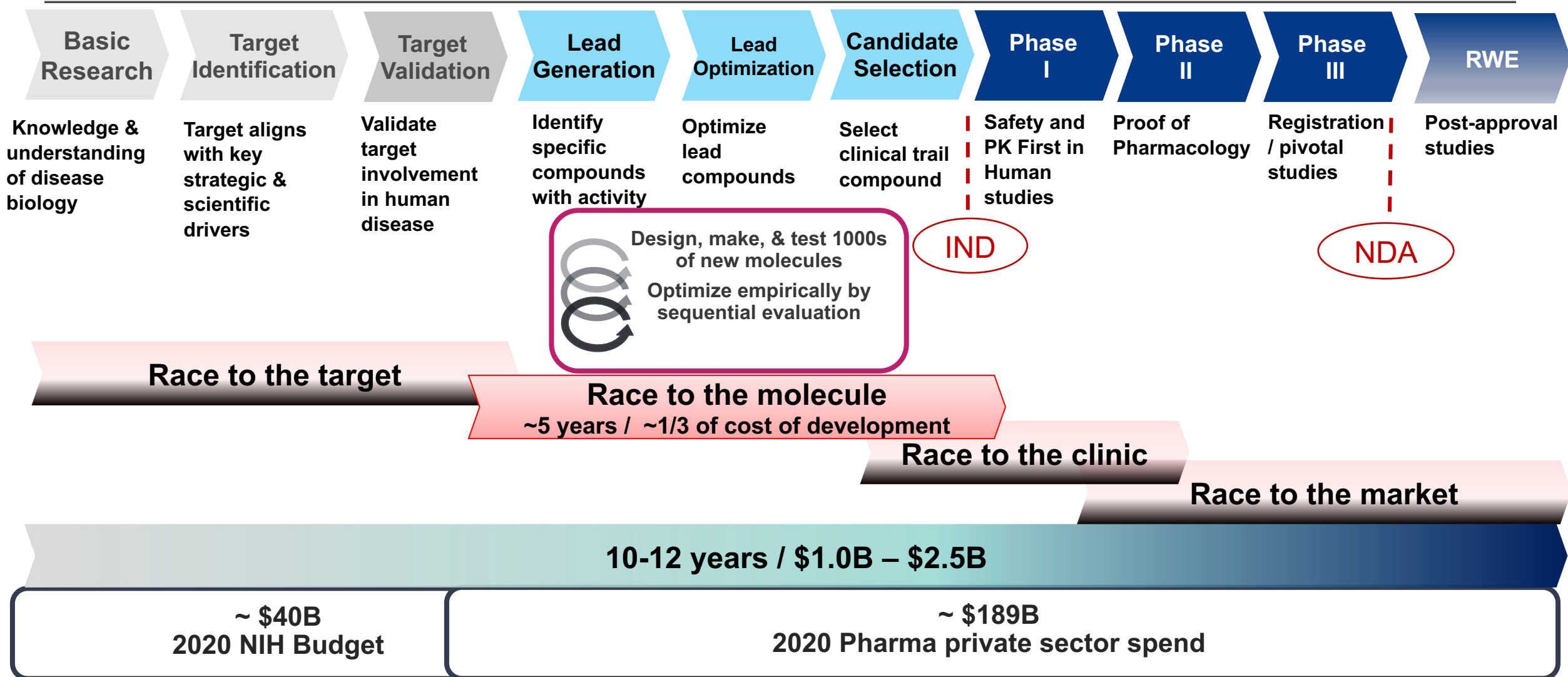


A Public – Private Partnership to accelerate discovery & development of more effective therapies for patients

Topics to be covered

- **The drug discovery challenge and opportunity**
- **The business experiment we chose to conduct**
- **Operational successes**
- **Things we could have done better**
- **ATOM's evolution**
- **AI in healthcare: opportunity, ecosystem and impact**
- **For what it's worth, what I recommend**

The Linearity of Drug Discovery and Development



ATOM's Formation

Founding Member Recognized the Need to Integrate SMEs and Technologies

Support from the highest levels of each organization

4-Way CRADA – two different government agencies, a university and a UK-based private pharma



High performance
computing and
data science



Drug discovery
biology, chemistry,
and data sciences



Cancer center,
biology, and
experimental
facilities

Frederick National Laboratory
for Cancer Research

sponsored by the National Cancer Institute

Experimental
biology and data
analytics

ATOM

Computationally driven drug discovery workflows

Timeline...

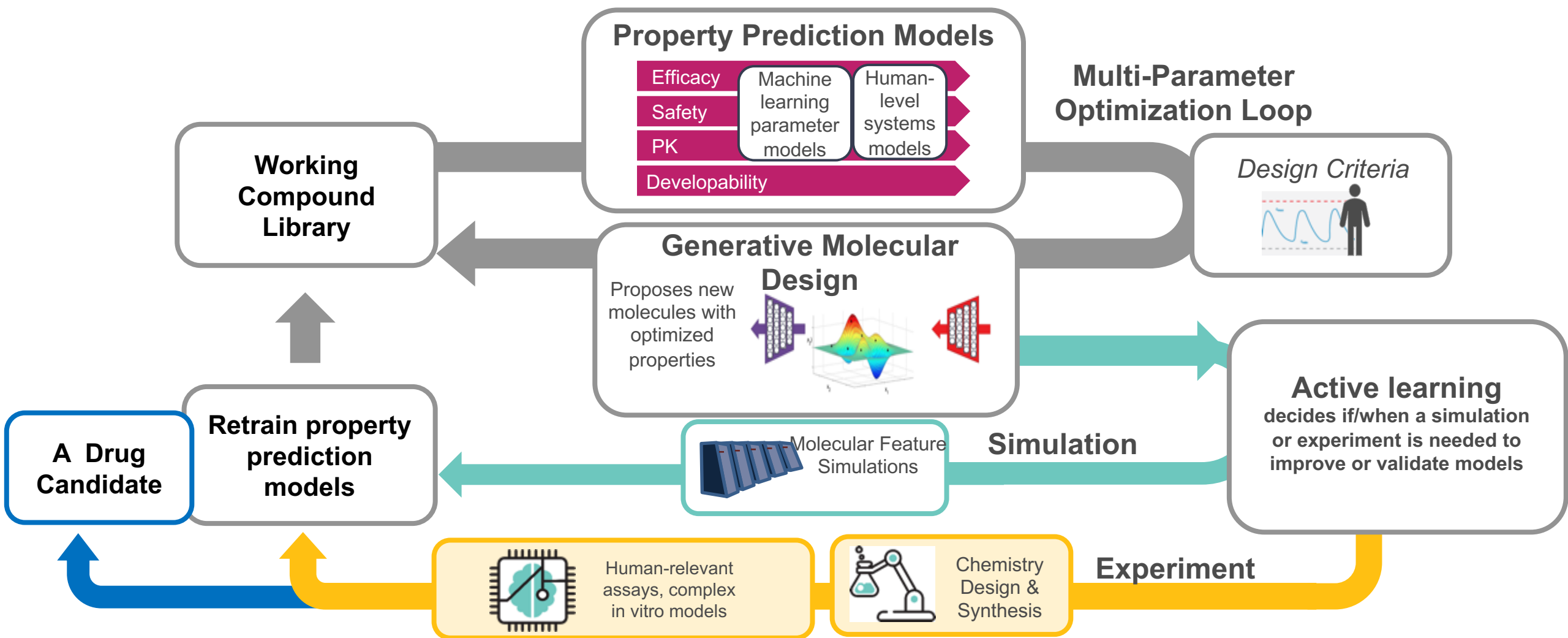
- Early 2016: DOE / NCI discussions with Pharma
- June 2016: Three-way letter of intent to form ATOM, a public-private partnership
- Early 2017: UCSF indicates its interest to participate
- October 2017: Four-way CRADA signed, ATOM launch
- November 2017: Ingestion of ~3M GSK “dead” compounds
- February 2018: R&D work started in ATOM

What we talked about as we put it together...

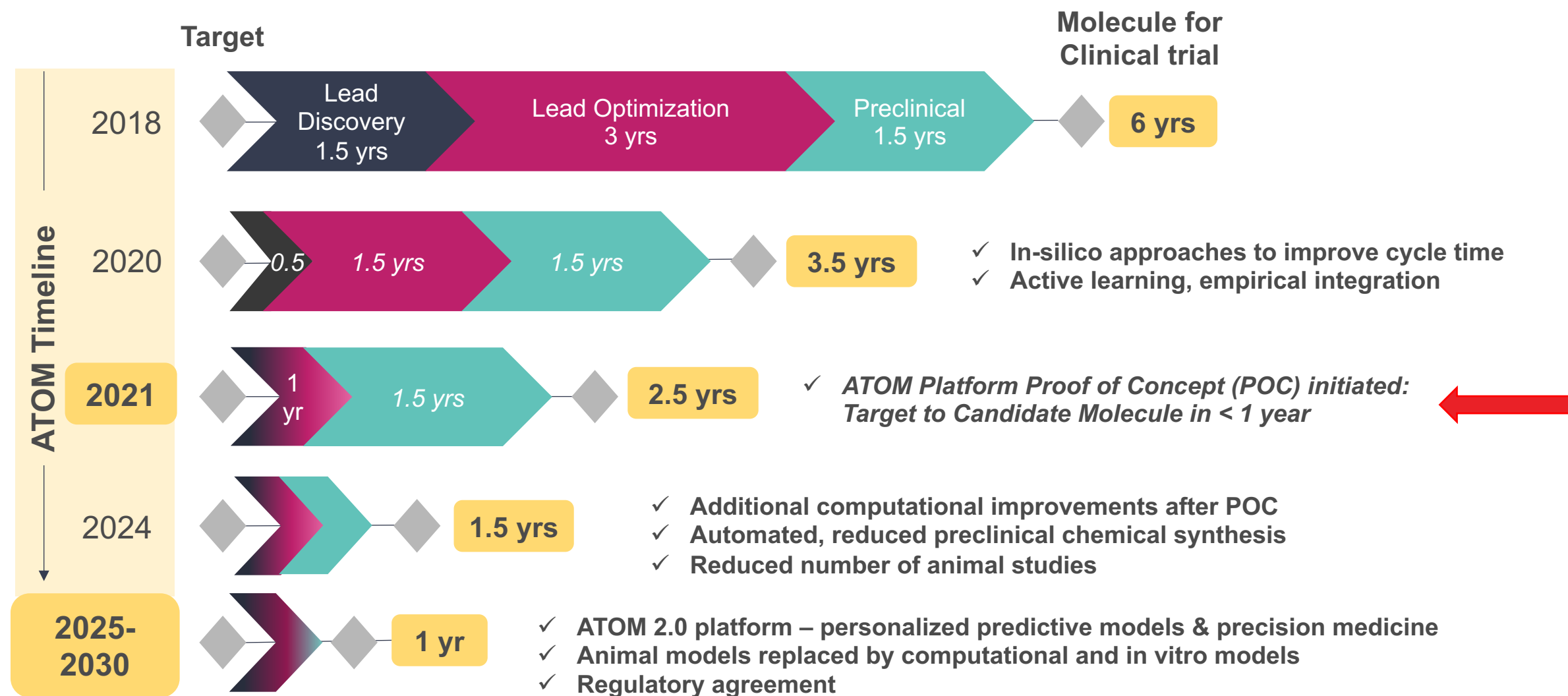
- Democratizing drug discovery,
- Open sourcing tools and capabilities,
- A place for disciplines to merge,
- Training next generation of drug discovery scientists and engineers,
- Create a drug molecule in less than 1 year vs. the industry standard of 5 years,
- Identify gaps so new tools could be invented in drug discovery.

The Foundational ATOM Molecular Design Workflow

Generative Molecular Design



“2017” ATOM target-to-clinical trial roadmap

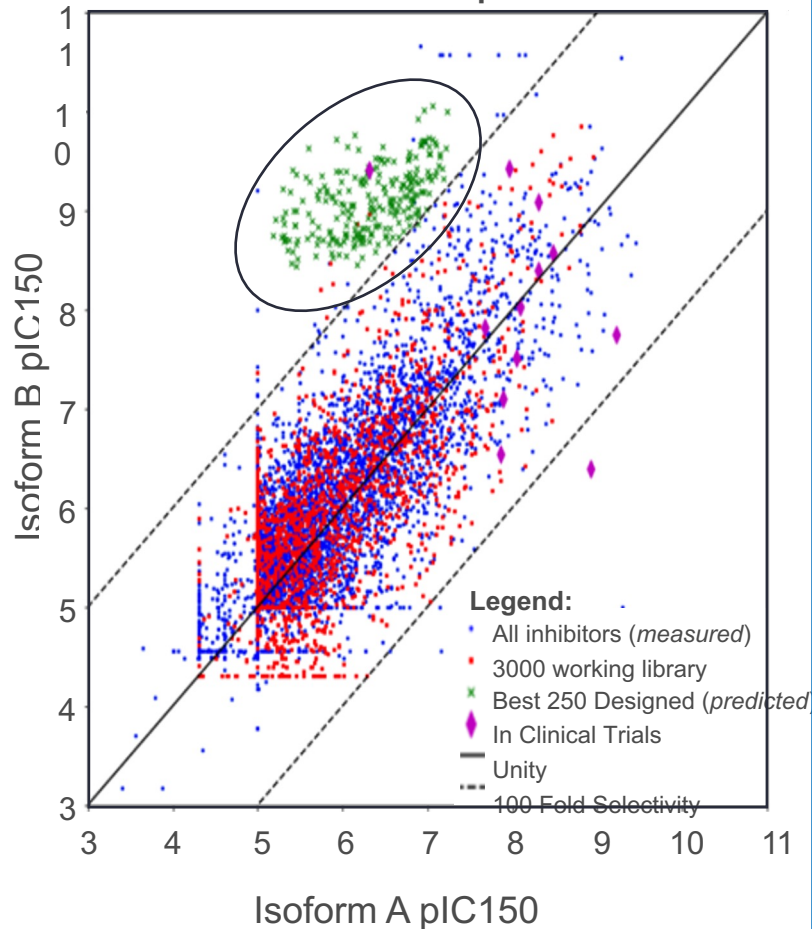


Molecule Design Projects (plus, Covid protease inhibitor and SARS-CoV2 mAb design)

1: Kinase inhibitor

8 parameters co-optimized

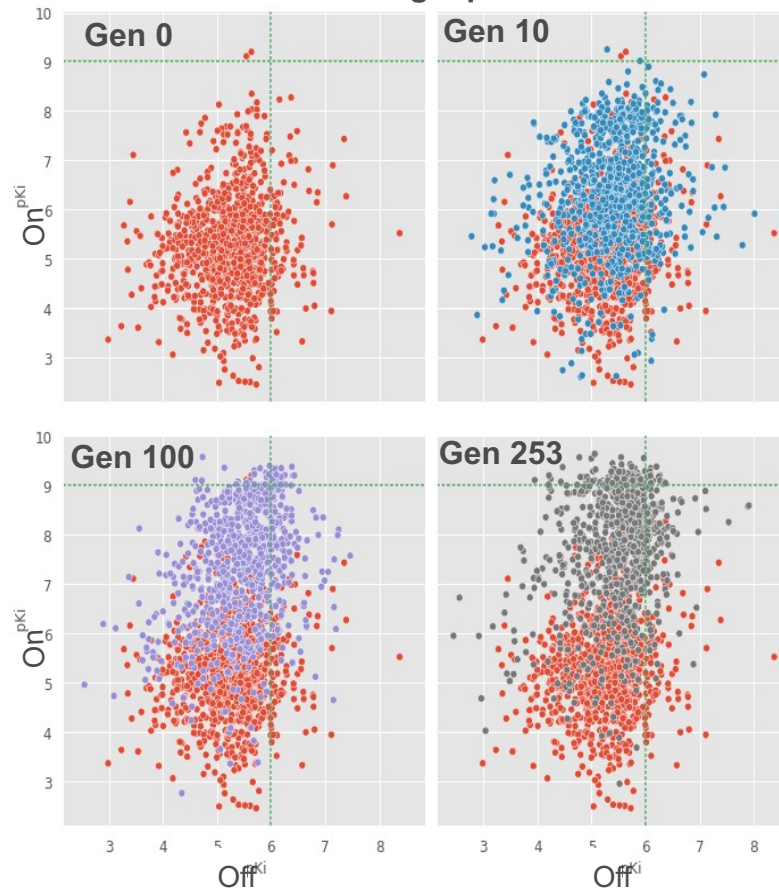
Isoform B vs. Isoform A pIC50



2: Receptor antagonist

10 parameters co-optimized

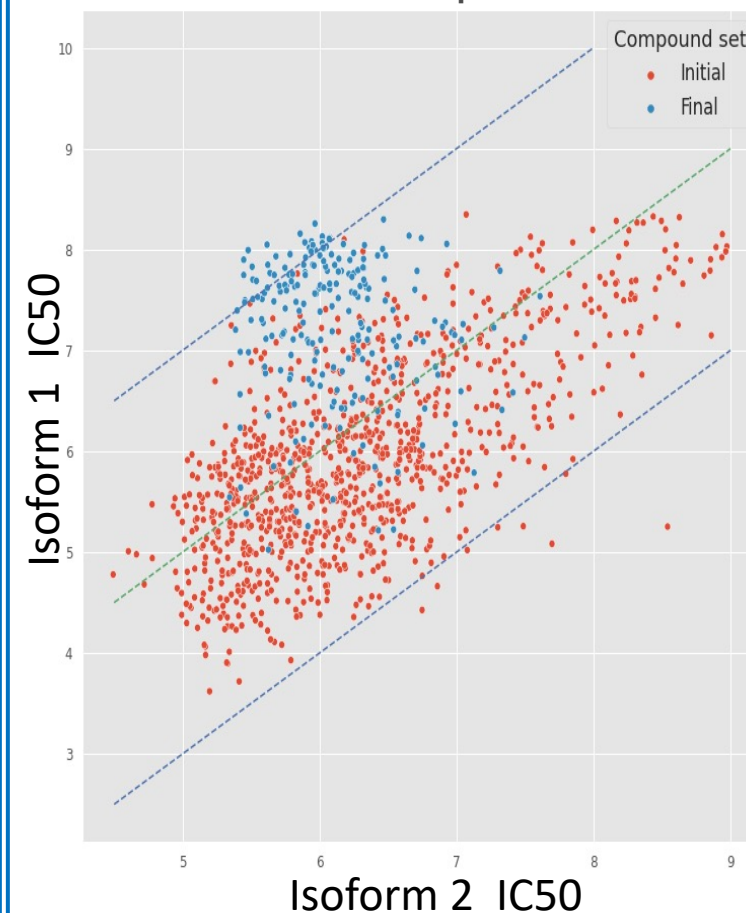
Predicted off- vs on-target pKi values



3: Enzyme inhibitor--PoC

12 parameters co-optimized

Isoform 1 vs. Isoform 2 pIC50



Sampling of work placed the public domain

Machine Learning Models to Predict Inhibition of the Bile Salt Export Pump

<https://dx.doi.org/10.1021/acs.jcim.0c00950>

Artificial Intelligence and Pharmacometrics: Time to Embrace, Capitalize, and Advance?

<https://pubmed.ncbi.nlm.nih.gov/31006175/>

Accelerating Therapeutics for Opportunities in Medicine: A Paradigm Shift in Drug Discovery

<https://www.frontiersin.org/articles/10.3389/fphar.2020.00770/full>

Improved Protein–Ligand Binding Affinity Prediction with Structure-Based Deep Fusion Inference

<https://pubs.acs.org/doi/10.1021/acs.jcim.0c01306>

High-Throughput Virtual Screening of Small Molecule Inhibitors for SARS-CoV-2 Protein Targets with Deep Fusion Models

<https://doi.org/10.1145/3458817.3476193>

Enabling rapid COVID-19 small molecule drug design through scalable deep learning of generative models

<https://doi.org/10.1177/10943420211010930>

Predicting Volume of Distribution in Humans: Performance of in silico Methods for A Large Set of Structurally Diverse Clinical Compounds

<https://dmd.aspetjournals.org/content/early/2020/11/25/dmd.120.000202>

Artificial Intelligence and Pharmacometrics: Time to Embrace, Capitalize, and Advance?

<https://doi.org/10.1002/psp4.12418>

Rethinking drug design in the artificial intelligence era

<https://www.nature.com/articles/s41573-019-0050-3>

AMPL: A Data-Driven Modeling Pipeline for Drug Discovery

<https://pubs.acs.org/doi/10.1021/acs.jcim.9b01053>

<https://github.com/ATOMScience-org/AMPL>

Solving Hard Problems with AI: Dramatically Accelerating Drug Discovery Through A Unique Public-Private Partnership

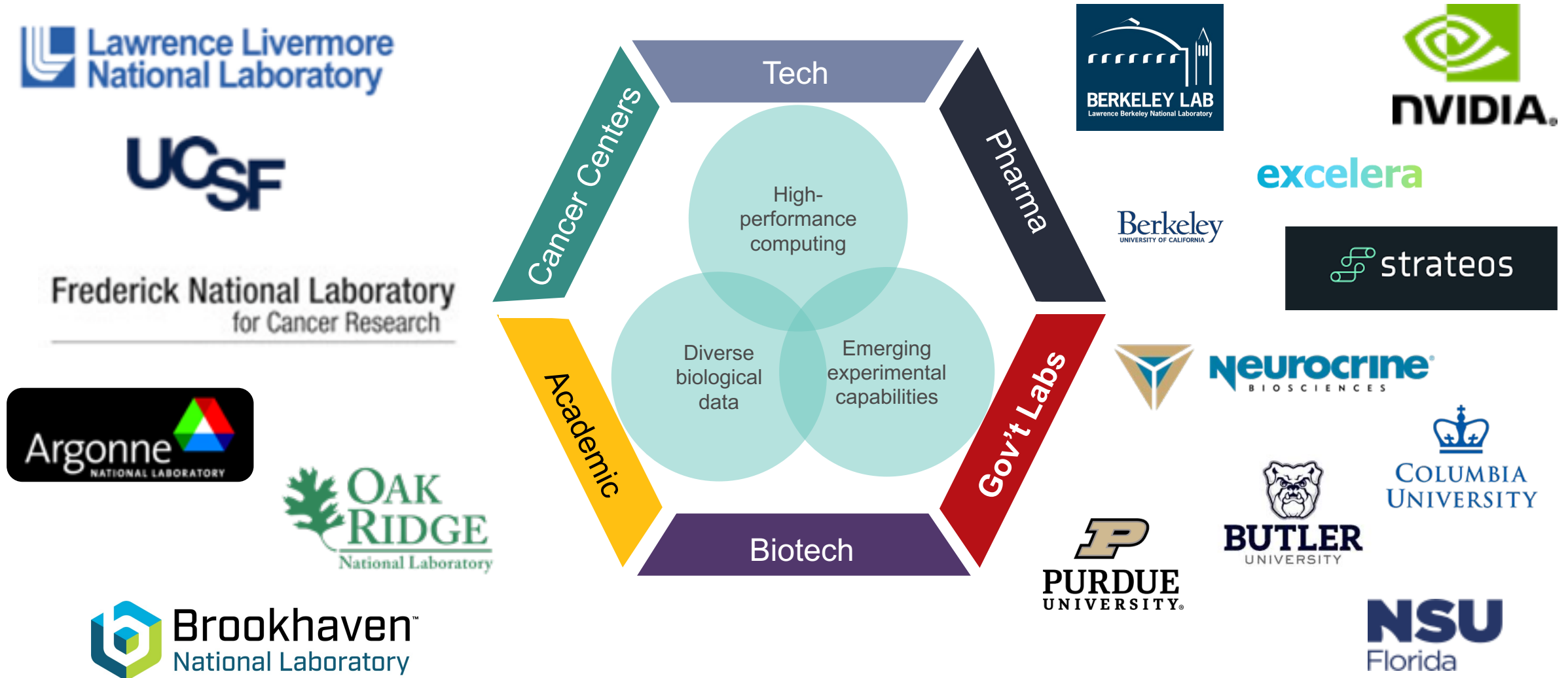
<https://www.commercialbiotechnology.com/index.php/jcb/article/view/954>

Integrating Experiments and Machine Learning Models: Examples from the ATOM Consortium

[https://docs.google.com/file/d/1-](https://docs.google.com/file/d/1-WeORfWy6DpU0KceBAFC9IGz0tyDy3ag/edit?filetype=mspresentation)

[WeORfWy6DpU0KceBAFC9IGz0tyDy3ag/edit?filetype=mspresentation](https://docs.google.com/file/d/1-WeORfWy6DpU0KceBAFC9IGz0tyDy3ag/edit?filetype=mspresentation)

ATOM Network Today



Accelerating Therapeutics for Opportunities in Medicine



ATOM Research Alliance

ATOM

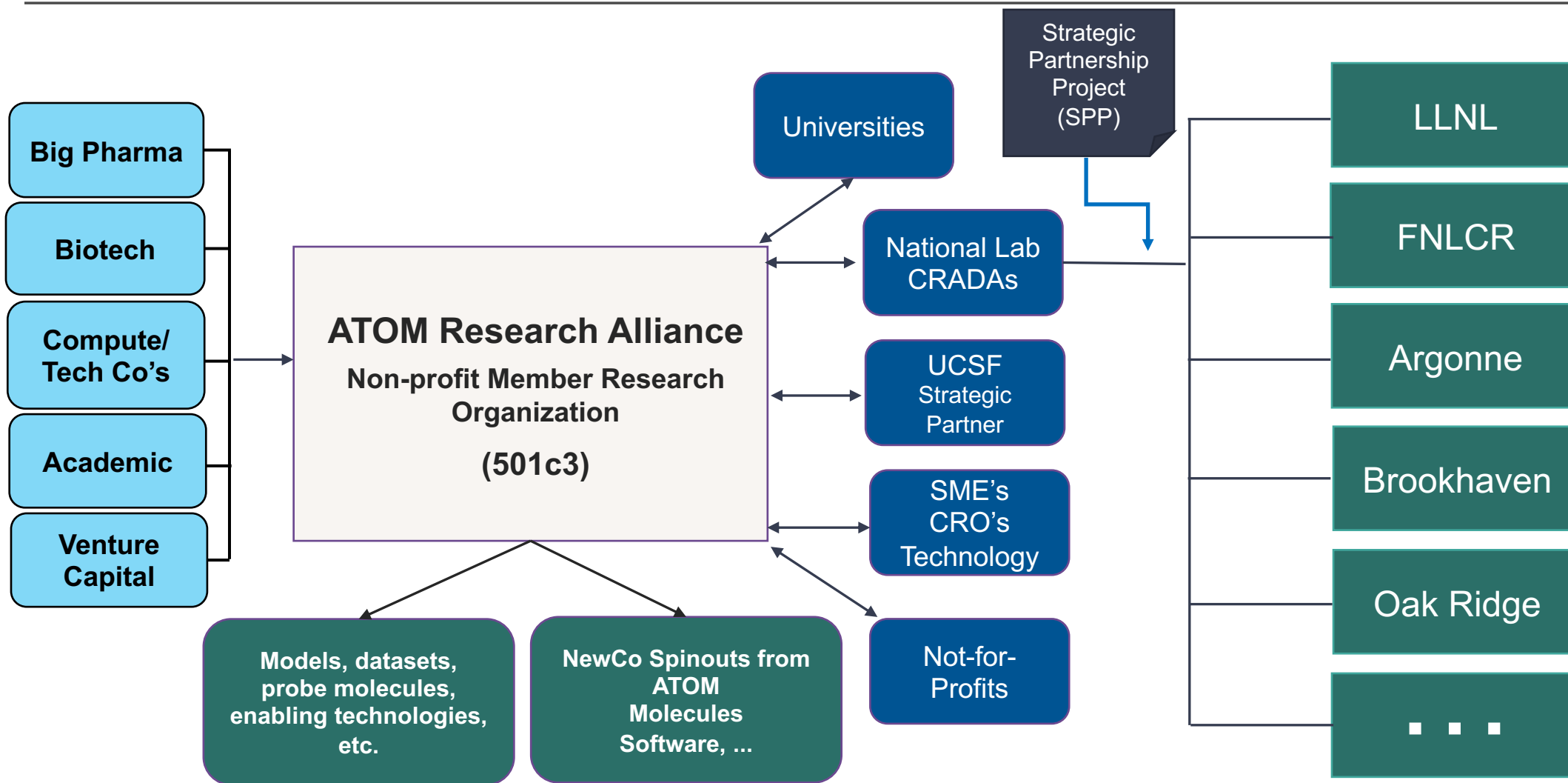
A Public – Private Partnership to accelerate discovery & development of more effective therapies for patients

ATOM

R e s e a r c h A l l i a n c e

A 501(c)(3) corporation established to accelerate discovery & development of more effective therapies for patients

ATOM Research Alliance Ecosystem



Membership

Strategic Members

- (i) an academic institution, pharmaceutical or biotechnology company, philanthropic organization, national laboratory, or other organization that actively promotes ATOM's primary purposes; and
- (ii) contribute substantial financial resources or in-kind support to ATOM

Associate Members

- an organization that recognizes mutual benefit from actively working with ATOM
- ARA sees these as core to its mission to the public good

Membership dues are based on a financial sliding scale

AI in Drug Discovery



AI in Healthcare -- High impact areas

Real world consequences

Outcomes

Biomarker shift

Comparison to other patients

Computationally derived digital biomarkers

Longitudinal surveillance.

Progression potential

Diagnose

Clinical chemistry

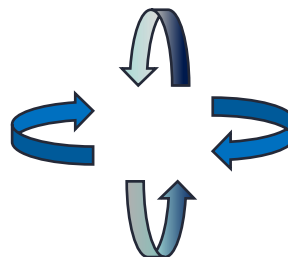
Image analysis

Patient history

Genetics

Known biomarkers

Computationally derived digital biomarkers



Understand Clinical Potential

Patient stratification

Individualized therapy

Efficacy

Emergent adverse event signals

Drug/drug interactions

Derived digital biomarkers

Biochemical biomarkers

Modulate Biology

Molecular design

Molecular features

Molecule attribute predictors

On-/off-target effects-- ADME/Tox

MOA, efficacy and pathway impact

Human-relevant assays

Human-relevant simulations

Understand Biology

Genetics, genomics, 'omics

Gene editing

Target/pathway understanding

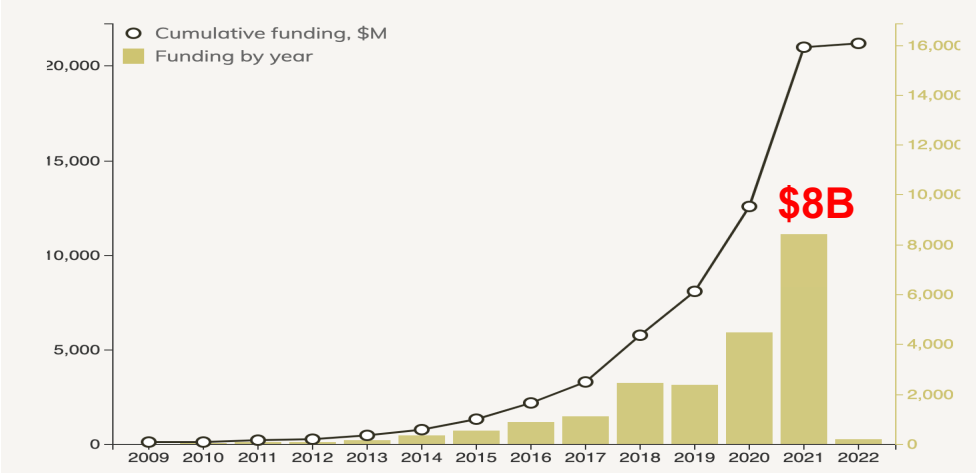
Patient-relevant in vitro systems

In vitro biochemical biomarkers

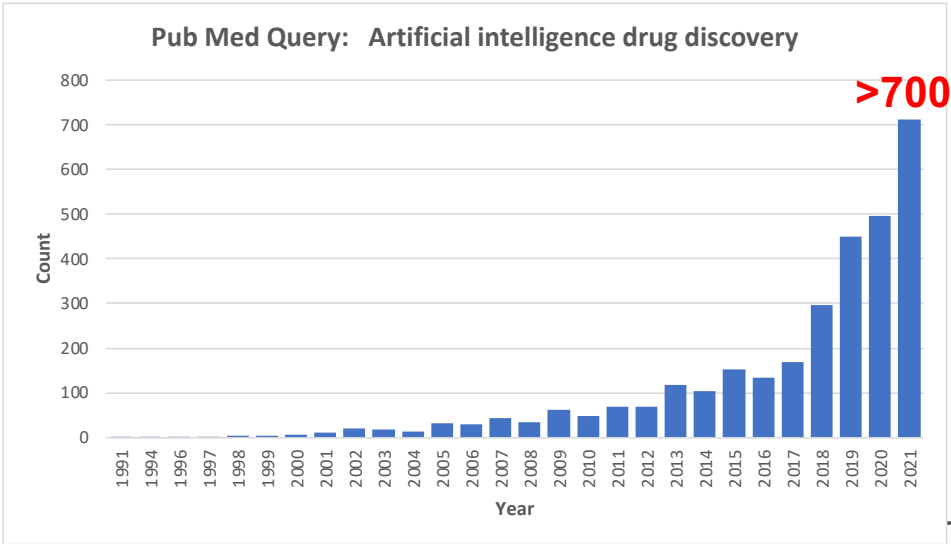
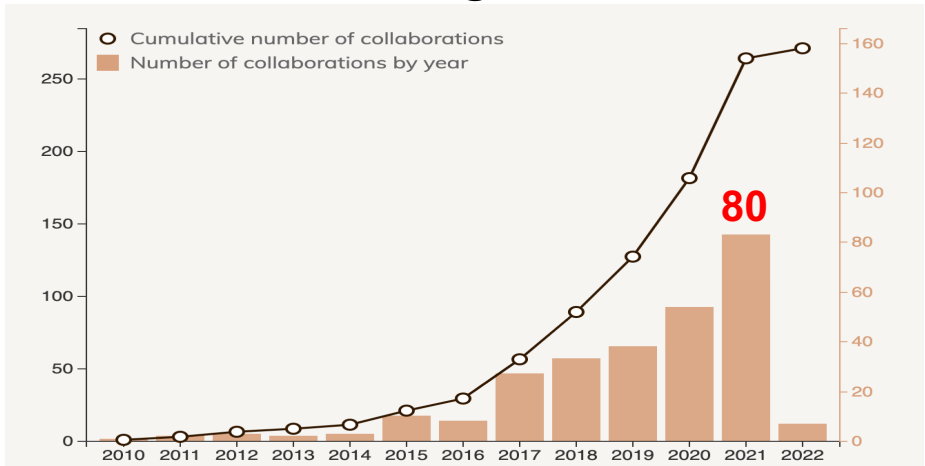
Responder identification

Investment in AI-assisted Drug Discovery

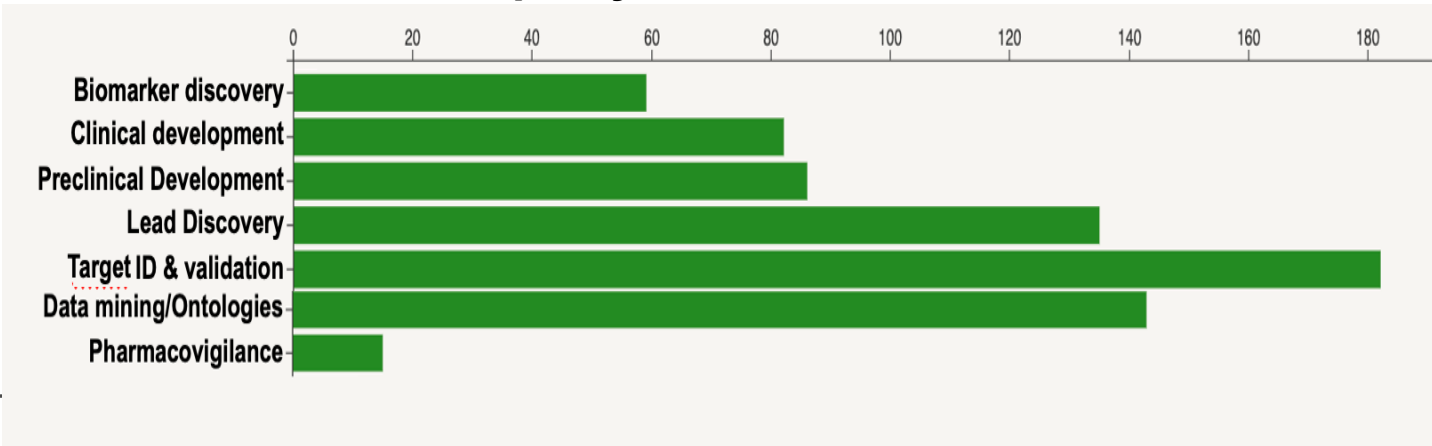
Venture Funding In AI Healthcare Companies



Number of Deals--Big Pharma and AI Startups



AI startups by Pharma Research Use Case



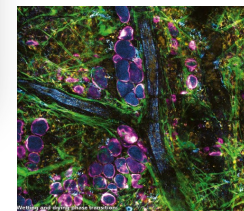
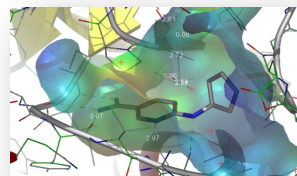
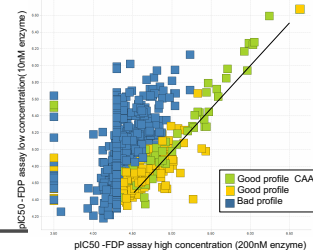
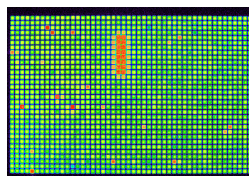
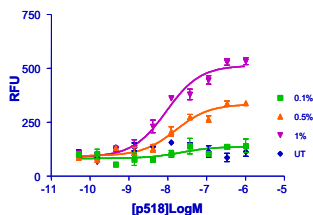
2010-2019 NIH Contribution to Drug Discovery and Development

356 drug approvals / 219 biological targets			NIH Funding
All publications relating to drug discovery and development	Publications	2M	
	Publications referencing NIH funding	424k	\$195B
Publications relating to 356 approved drugs	Publications associated with approved drugs	244k (12%)	
	Publications referencing eventually approved drugs and NIH funding	39k (9.2%)	\$36B (18.5%)
<p>NIH funding is associated with every approved drug</p> <p>Total NIH funding for all 356 approved drugs = \$230B</p> <p>Drugs represent 10% of US healthcare costs: ~\$476.2B in 2018</p>			

The currency of AI-enabled drug discovery is data

Are these data strategic to the U.S?”


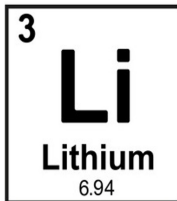
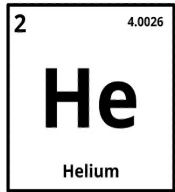
- Who paid for it and who owns it?
- How is access granted?
- It is very different than clinical data
 - No personal identifiable information
 - No patient consent required—in vitro and animal work
 - It is predominantly structured numeric datasets
- So, it should be readily available, but it's not.
- Is such data a strategic asset for the U.S. to be deployed to solve hard problems in healthcare?
- Where are the data associated with molecule discovery and characterization?



Merriam-Webster

Strategic: Of great importance within an integrated whole or to a planned effect

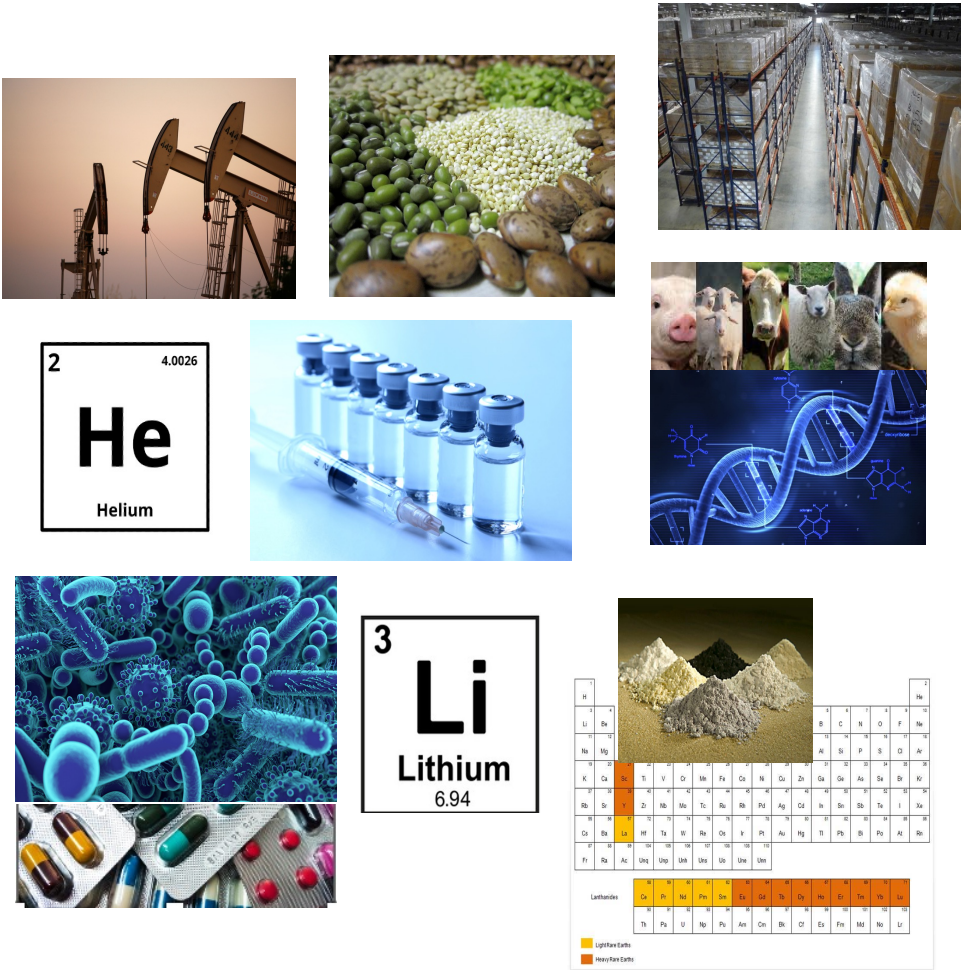
U.S. Strategic Stockpiles



H	He																	Li					
1	2																	3					
U	Pu																	B	C	N	O	F	Ne
92	94																	5	6	7	8	9	10
Na	Mg																	Al	Si	P	S	Cl	Ar
11	12																	13	14	15	16	17	18
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Cu	Ni	Cd	Zn	Ga	Ge	As	Se	Br	Kr						
19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36						
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe						
37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54						
Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn						
55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72						
Fr	Ra	Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr							
		Lanthanides																					
		La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu							
		57	58	59	60	61	62	63	64	65	66	67	68	69	70	71							
		Actinides																					
		Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr								
		88	89	90	91	92	93	94	95	96	97	98	99	100	101	102							
		Lighter Elements																					
		Heavier Elements																					

Strategic: Of great importance within an integrated whole or to a planned effect

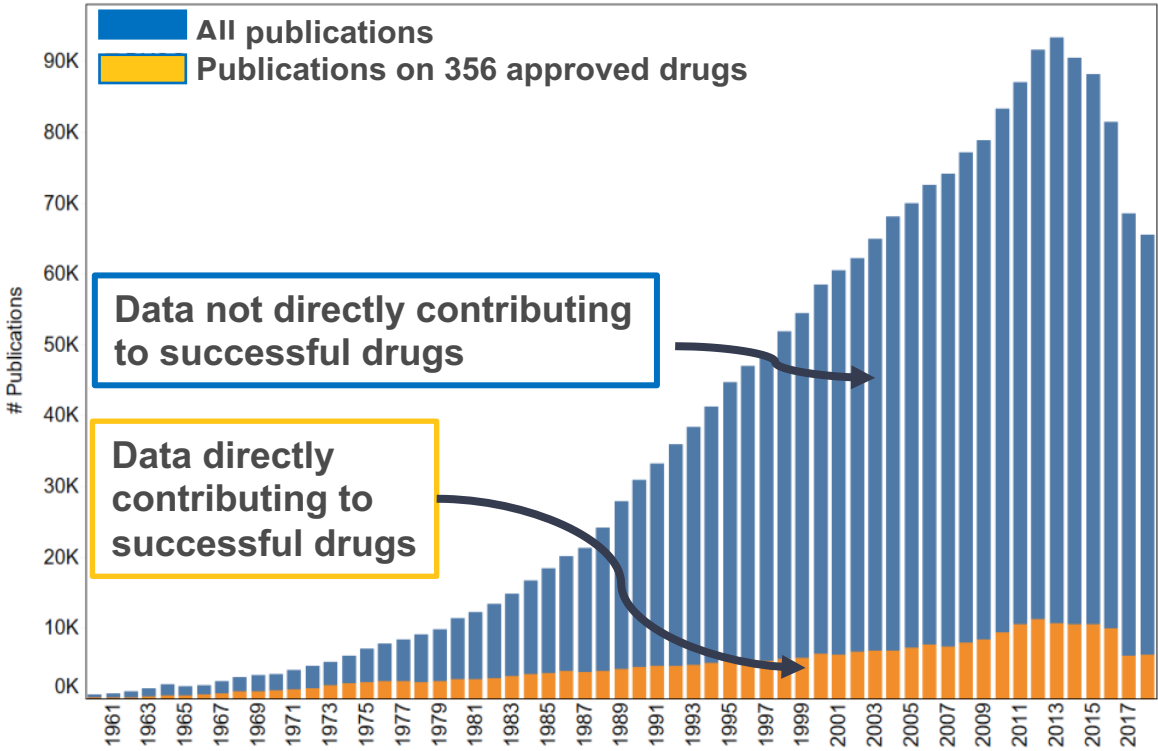
US Strategic Stockpiles



US “Strategic Drug Discovery Data Stockpile”

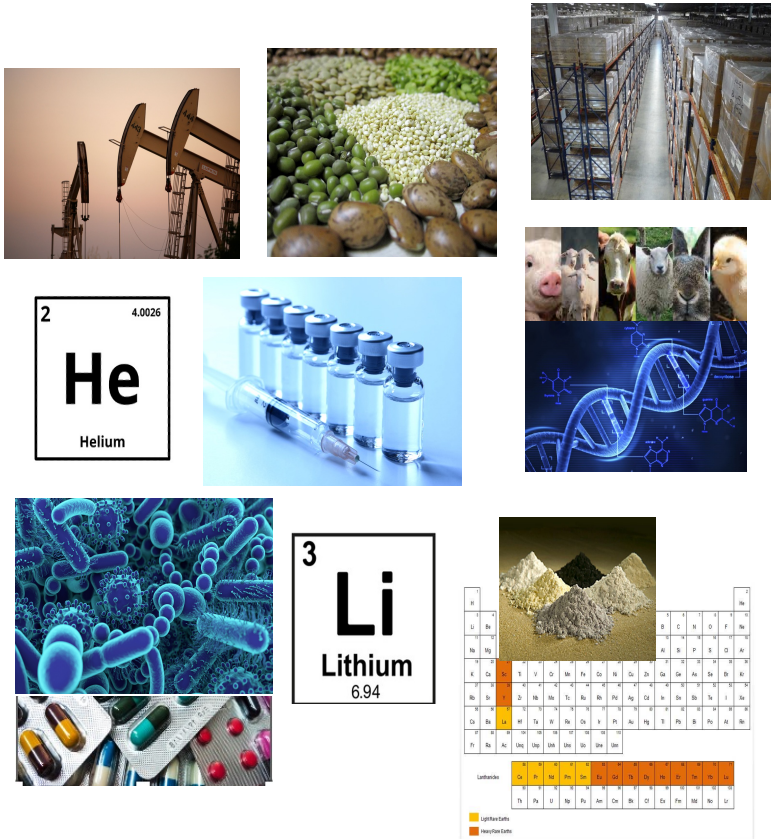
Publications ref. NIH funding	424k	\$195B
Publications ref. app. drugs & NIH funding	39k (9.2%)	\$36B (18.5%)

Publications associated with ALL Searches and DRUG Searches



Dark data of drug development

US Strategic Stockpiles



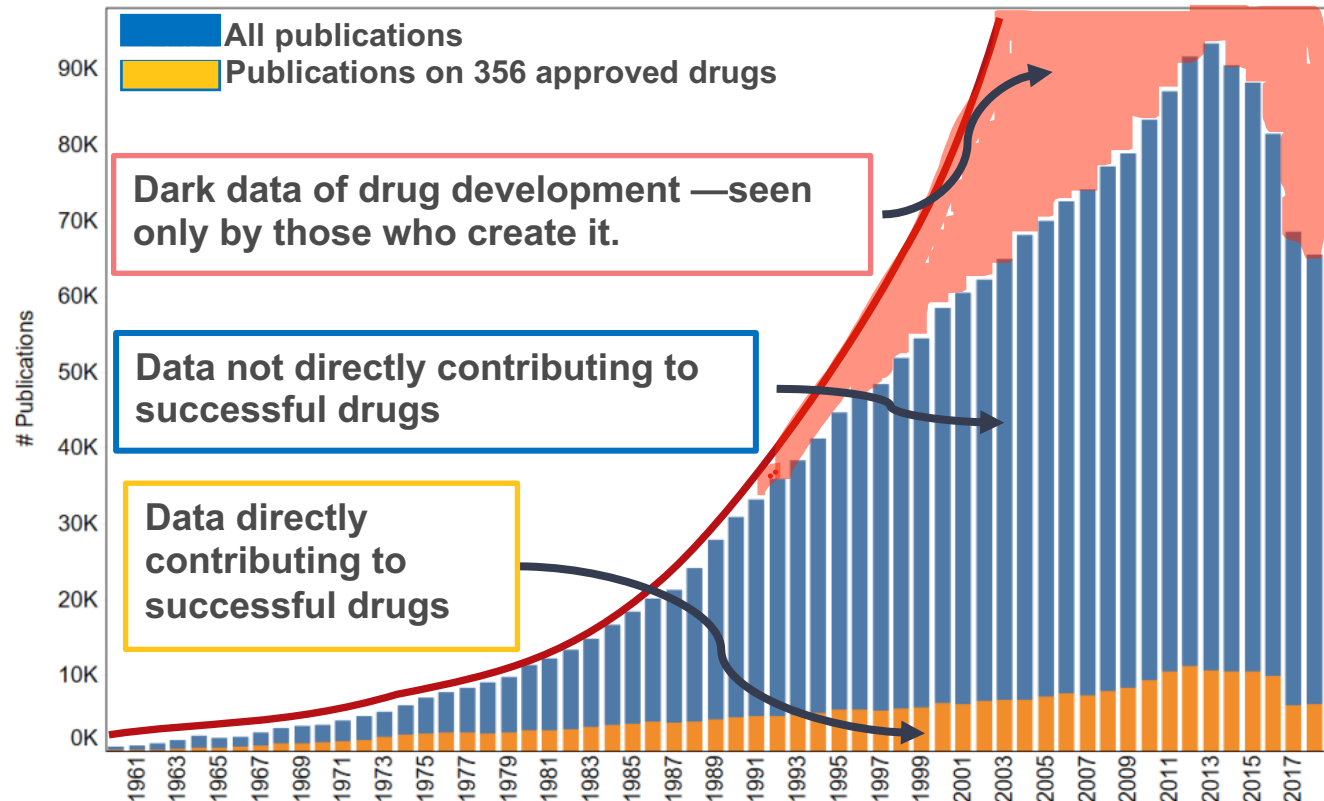
US “Strategic Drug Discovery Data Stockpile”

Race to the target

Race to the molecule

~5 years / ~1/3 of cost of development

Publications associated with ALL Searches and DRUG Searches



Recommendations to enable rapid drug discovery

- **Government**

- Create a Drug Discovery Data Strategic Reserve (3DSR)
- Legislation to incentivize data-generators to fill it—carrot or stick approach
- Tools and capability to use it
- Keep the Labs focus in “molecular recognition”

- **Universities**

- Create collaboration networks at the “big problem” level—the STEM equivalent of the NCAA
- Teach biology as a mathematics and physics discipline
- Encourage curious and imaginative business development offices

- **Industry**

- Pharma—release your failed compound dark data
- Tech—listen to the users on what is needed and build it. It isn’t as hard as it is being made out to be



Thank you and Questions

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