

absci®

```
from absci import de_novo_model
model = de_novo_model.load_latest()
antigen = model.load_pdb("7olz.pdb",
chain="A")
antibodies = model.predict(antigen, N=300000)
```

```
from absci_library import codon_optimizer
library
= codon_optimizer.reverse_translate(library)
library.to_csv("covid-antibody-designs.csv")
library.to_wet_lab(assay="ACE")
```

```
from absci import lead_opt_model
lead_optimizer = lead_opt_model.load_latest()
library.naturalness =
lead_optimizer.naturalness(library)
lead_optimizer.optimize(library).to_wet_lab(as
say="SPR")
```

DRUG CREATION



CORPORATE PRESENTATION
JULY 2023

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```
from absci import genetic_algorithm; parameters=["maximize|binding_affinity:pH=7.5", "minimize|binding_affinity:pH=6.0",
"maximize|human_naturalness"]; library = genetic_algorithm.multiparametric_optimization(library, parameters, evolutions=100);
library.to_wet_lab(assays=["ACE", "SPR", "Bioassays"])
```

Disclaimers





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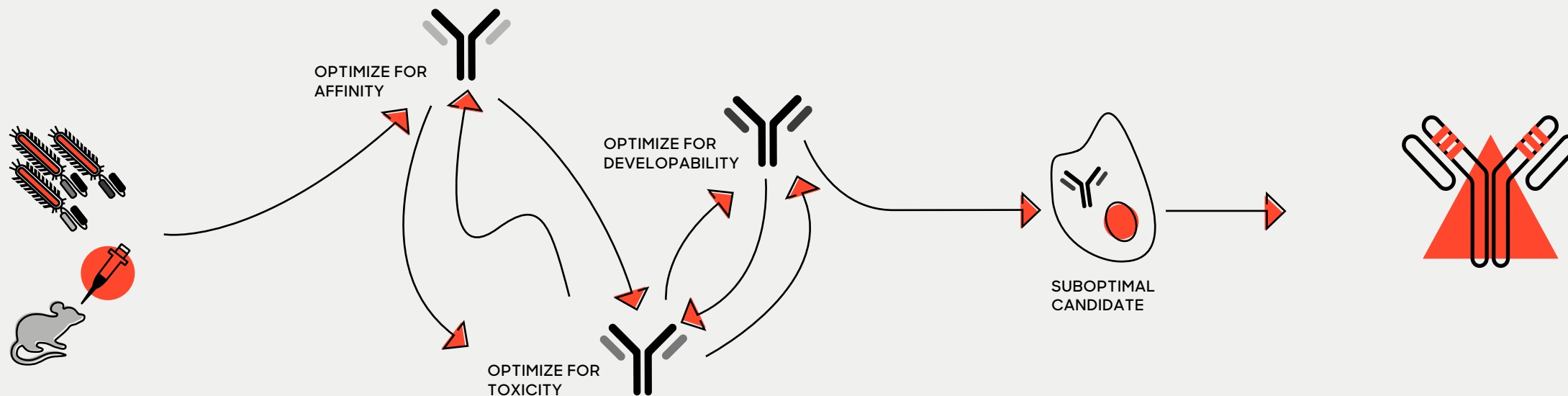
What if the next
transformative drug
was not discovered,
but **created** at a
click of a button?

THE PROBLEM – CURRENT NEED FOR GENERATIVE AI

The drug discovery paradigm is ripe for disruption

5.5 YEARS FROM
DISCOVERY TO IND

<5% SUCCESS RATE FROM
DISCOVERY TO LAUNCH

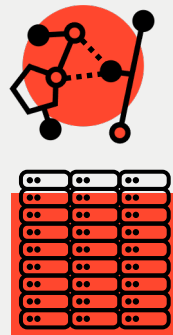


Long iterative process resulting in drug candidates with suboptimal attributes

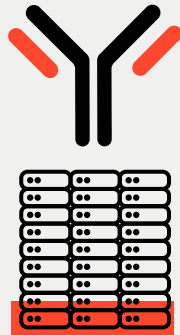
WHY HASN'T GENERATIVE AI TRANSFORMED BIOLOGIC DRUG DISCOVERY?

Unlocking the potential of generative AI in biology requires scalable biological data

Small Molecule v. Biologic

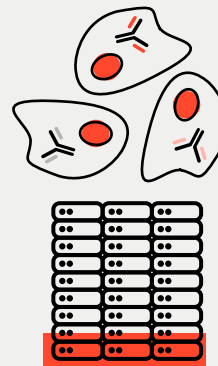


Extensive Libraries



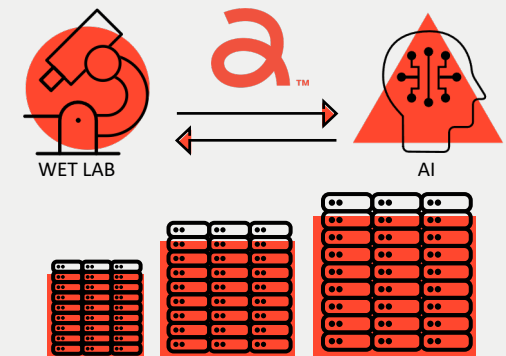
Limited Data

Biologics require living organisms to produce drug variants for testing



Consistency and accurate data is limited

Unlocking the potential of generative AI in biology...



...requires generating scalable biological data

Absci is **solving** the problem of scalable biological data enabling **true generative AI** for biologics drug discovery

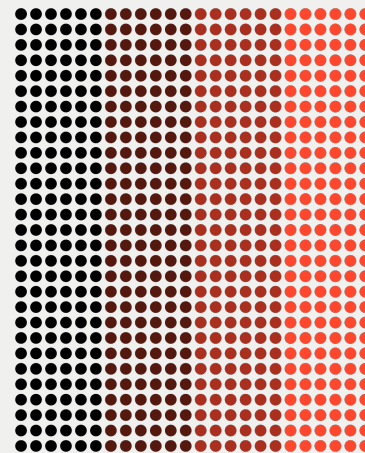
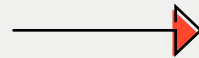
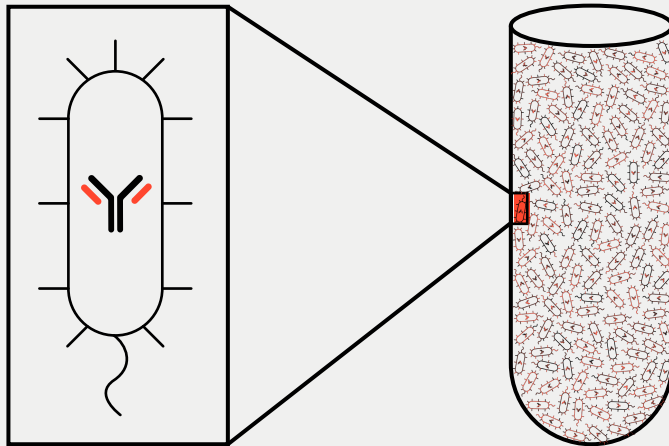


Absci's *E.coli* SoluPro™ cell line

Billions of cells, expressing proteins of interest

Absci's ACE Assay™ screens billions of unique drug variant candidates

High-quality data flows into Absci's generative AI engine



● NON-BINDING
● TIGHT BINDING

ai™

proved, 11.2% of drugs entering clinical trials approved 2006: 22 approved, 11.2% 2007: 18 approved, 10.7% 2008: 24 approved, 6 approved, 7.8% 2010: 21 approved, 6.8% 2011: 35 approved, 6.1% 2012: 39 approved, 5.3% 2013: 27 approved, 5.2% 2014: 41 7% 2015: 45 approved, 13.8%

Instead of finding the needle in the haystack, Absci is creating the needle.

The Solution

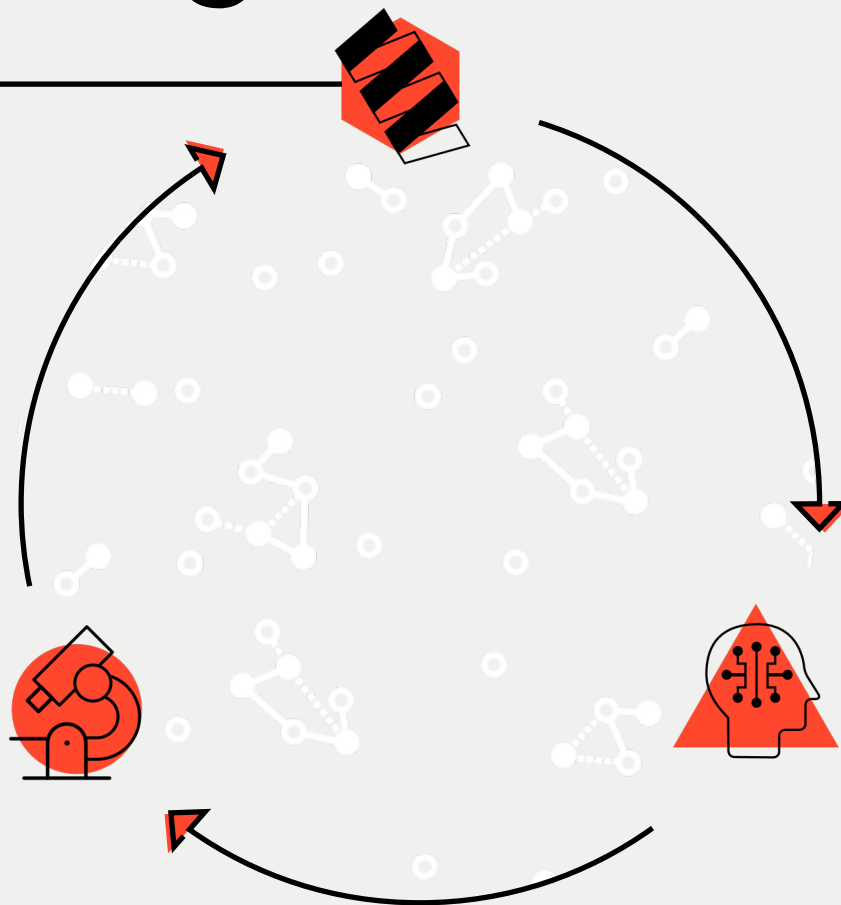
At Absci, the future is **now** with our Integrated Drug Creation™ platform

DATA TO TRAIN

Proprietary wet-lab assays capable of generating **billions** of protein-protein interactions a week for ML training

WET LAB TO VALIDATE

Scalable wet-lab infrastructure capable of validating **2.8 million unique** AI-generated designs a week



AI TO CREATE

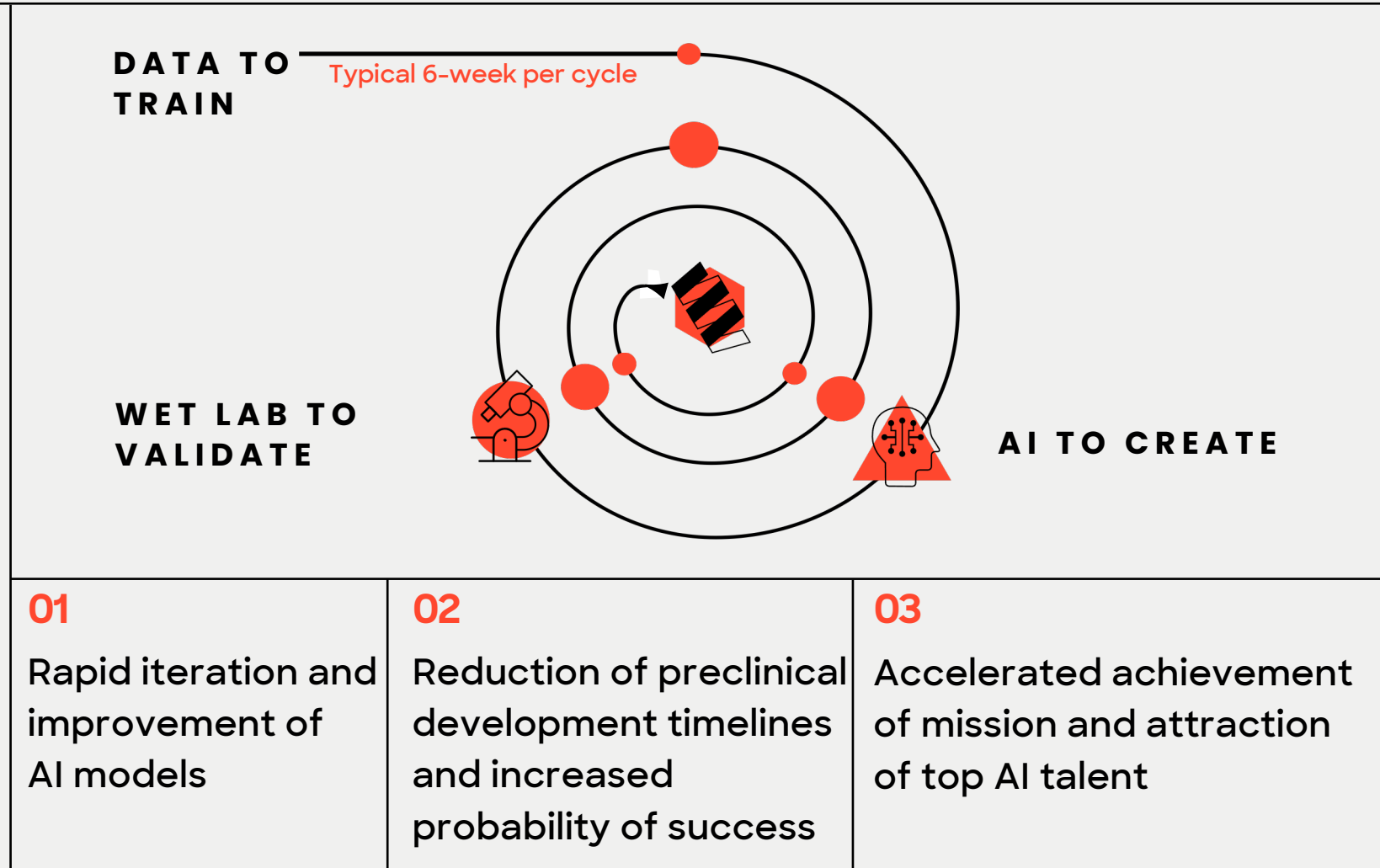
Generative AI engine to create new antibodies and next-gen biologics

ABSCI IS THE LEADER IN GENERATIVE AI DRUG CREATION FOR BIOLOGICS

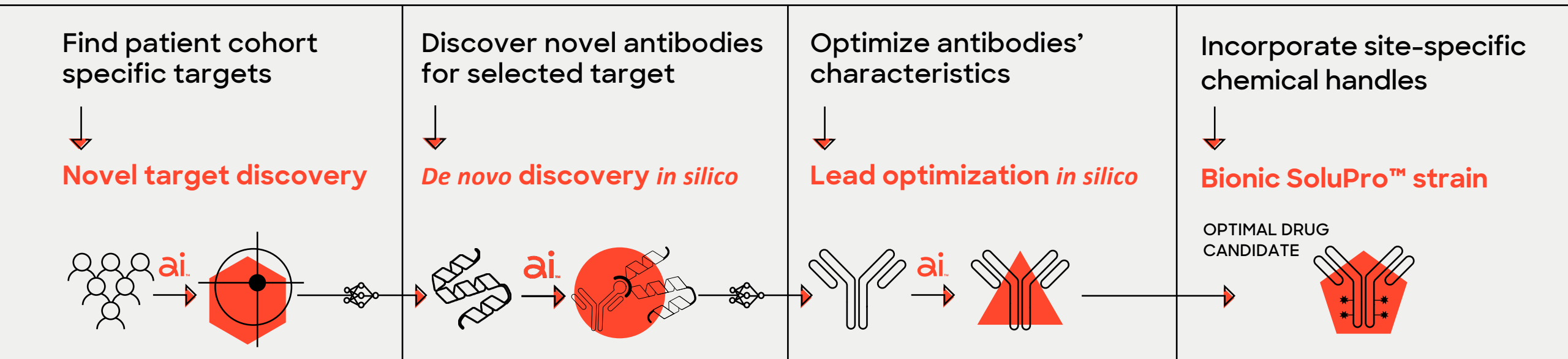
Cycles completed within **weeks**



Absci's rapid cycle times allow for:



The leading full-stack AI platform for **biologics** drug creation





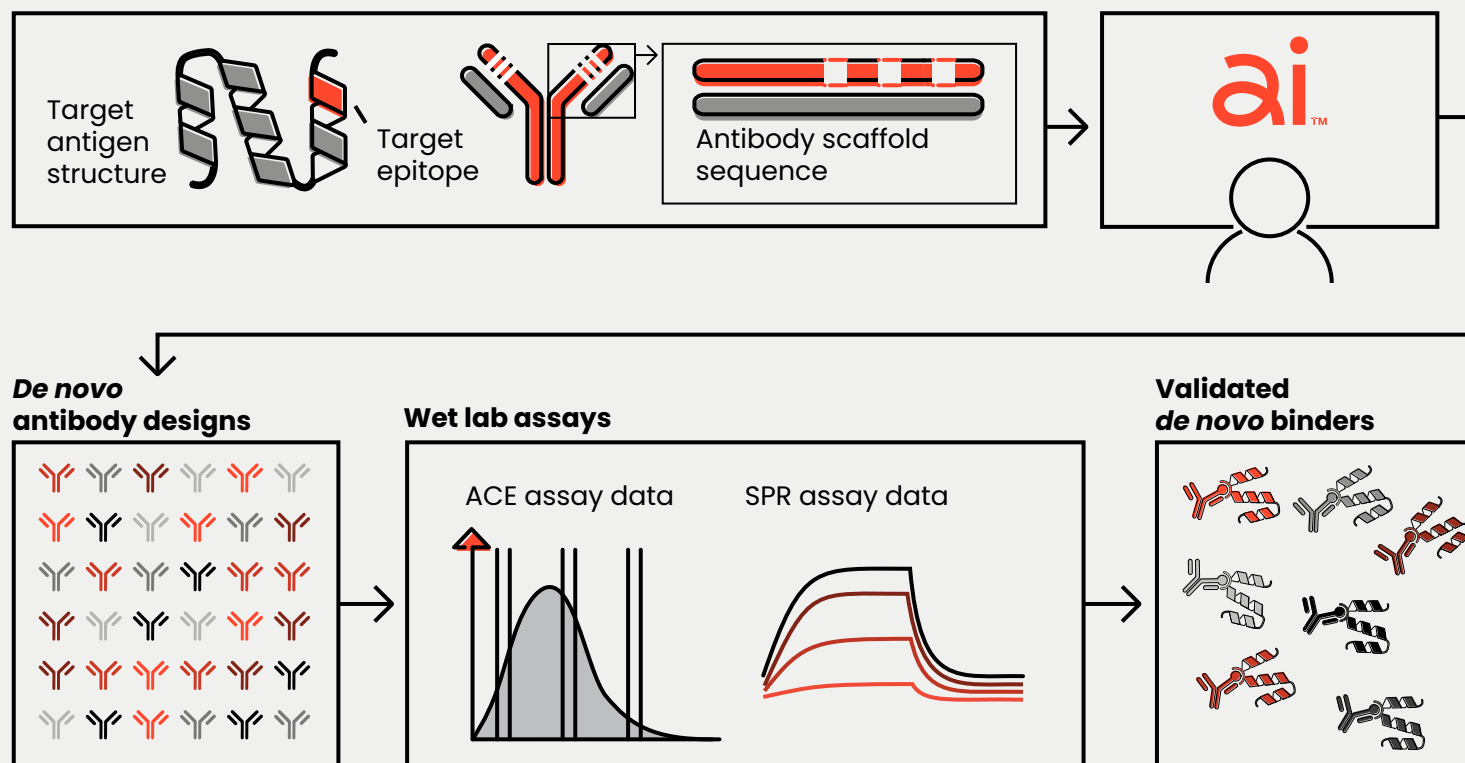
Absci is the **first** to **design and validate** novel antibodies using zero-shot generative AI

Zero-shot: a machine learning technique in which a model is trained to recognize and classify new objects without explicitly being trained on those objects' examples.

For antibodies, this means designing an antibody to bind to an antigen with no previous demonstrations of binders to said antigen.

De novo design in silico

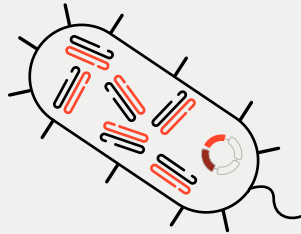
De novo drug creation with 'zero-shot' generative AI



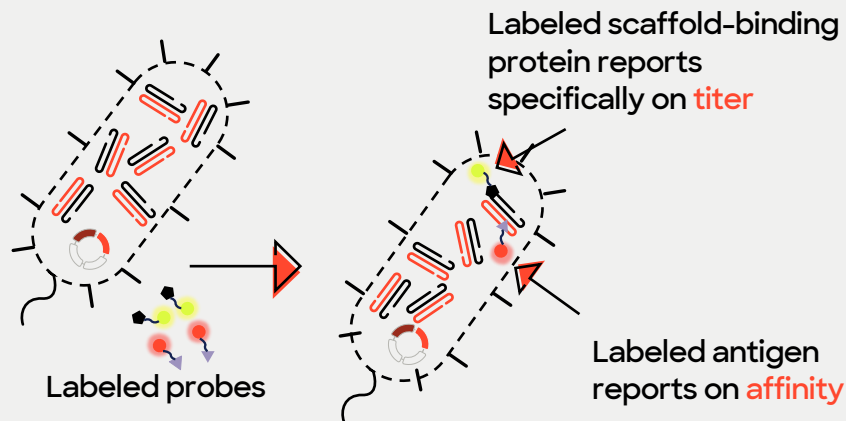
DE NOVO DESIGN IN SILICO REQUIRES LOTS OF HIGH-QUALITY TRAINING DATA

Highly validated ACE Assay generates high-quality and high-throughput data to train deep learning models

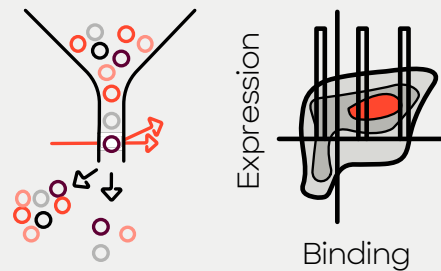
1. Strains expressing unique antibody sequence variants



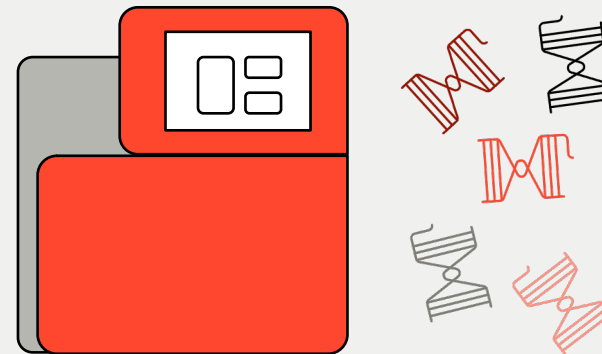
2. Fix and permeabilize cells and add labeled probes



3. Screen and sort by flow cytometry



4. NGS



5. ACE Assay scores (binding classification)

Metric	HCDR3 score	HCDR123 score
Accuracy	95.52%	95.3%
Precision	95.39%	95.65%
Recall	94.83%	92.91%
F1-score	0.9511	0.92426

~5K controls are spiked into libraries of 400k in size:

- ~800 positive controls
- ~1000 negative controls

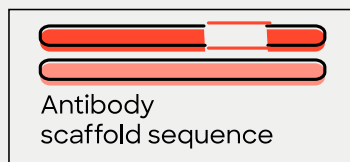
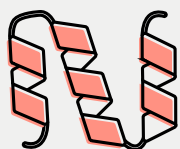
Each included with multiple codon optimized variants

CASE STUDY: DE NOVO DESIGN IN SILICO

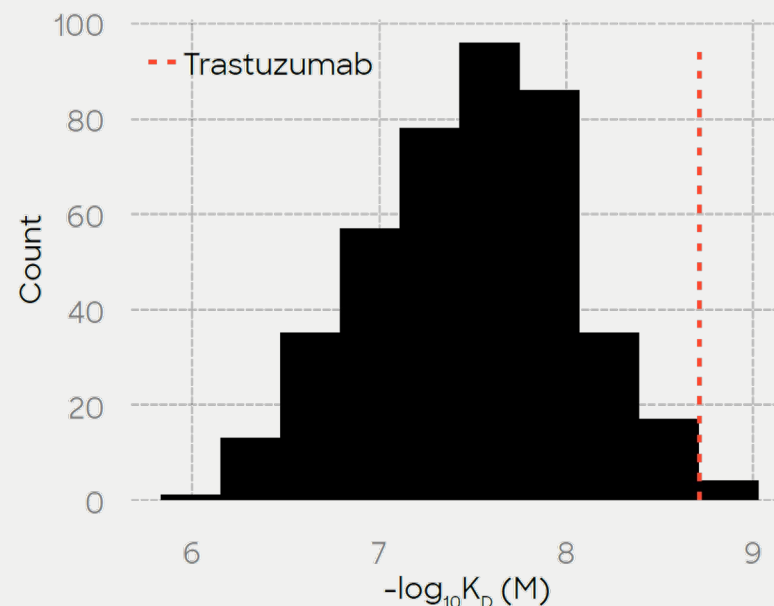
Laboratory validation straight out of the model; 421 designs confirmed by SPR

We selected **trastuzumab**, which binds **HER2**, as a scaffold to test the HCDR3 predictions

The model is conditioned with **HER2 3D structure** and trastuzumab **scaffold excluding HCDR3** designs



Any antibody known to bind to HER2 or any homolog (>40% sequence identity or part of the same homologous superfamily) to HER2 is removed



- 440,354 antibody variants designed
- Approx. 4,000 estimated binders by ACE Assay
- 421 confirmed by SPR
- 71 exhibit <10 nM affinity
- 3 bind tighter than WT trastuzumab

CASE STUDY: DE NOVO DESIGN IN SILICO

AI designs of all HCDRs achieve high binding rates and outperform biological baselines

		HER2 Binding Rate (%) measured via ACE assay	
		HCDR3	HCDR123
Zero-shot de novo generated			
Matched input antigen	Human HER2	10.6	1.8
Mis-matched input antigen	Rat HER2	2.8	0.5
Mis-matched input antigen	HER3	2.9	0.2
Mis-matched input antigen	VEGF	2.5	0.0
Biological baseline			
	OAS	2.68	0.16
	OAS-J	5.25	0.32
	SAbDab	3.16	0.06
Random baseline			
	Permuted sequences	0.33	N/A

AI designs are specific

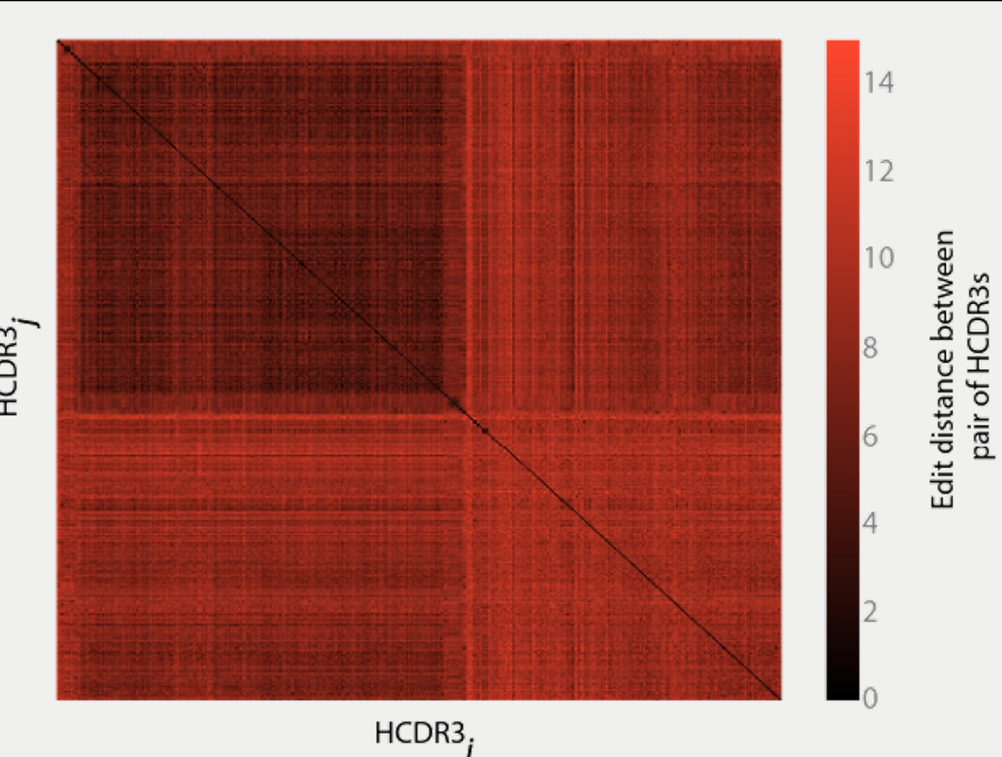
- Inputting a mis-matched undesired antigen (e.g., Rat HER2, HER3, VEGF) into the model results in significant performance decrease towards desired antigen
- Indicates the model's use of antigen information for sequence designs

AI models outperform biological baselines

- De novo designed HCDR3s achieve a **4-fold improvement** over random OAS baseline
- De novo designed HCDR123s achieve an **11-fold improvement** over random OAS baseline

CASE STUDY: DE NOVO DESIGN IN SILICO

High sequence diversity supports patent estate expansion and differentiation



Designs are **sequence diverse** from one another, with a mean edit distance of 7.7 ± 2.1 SD

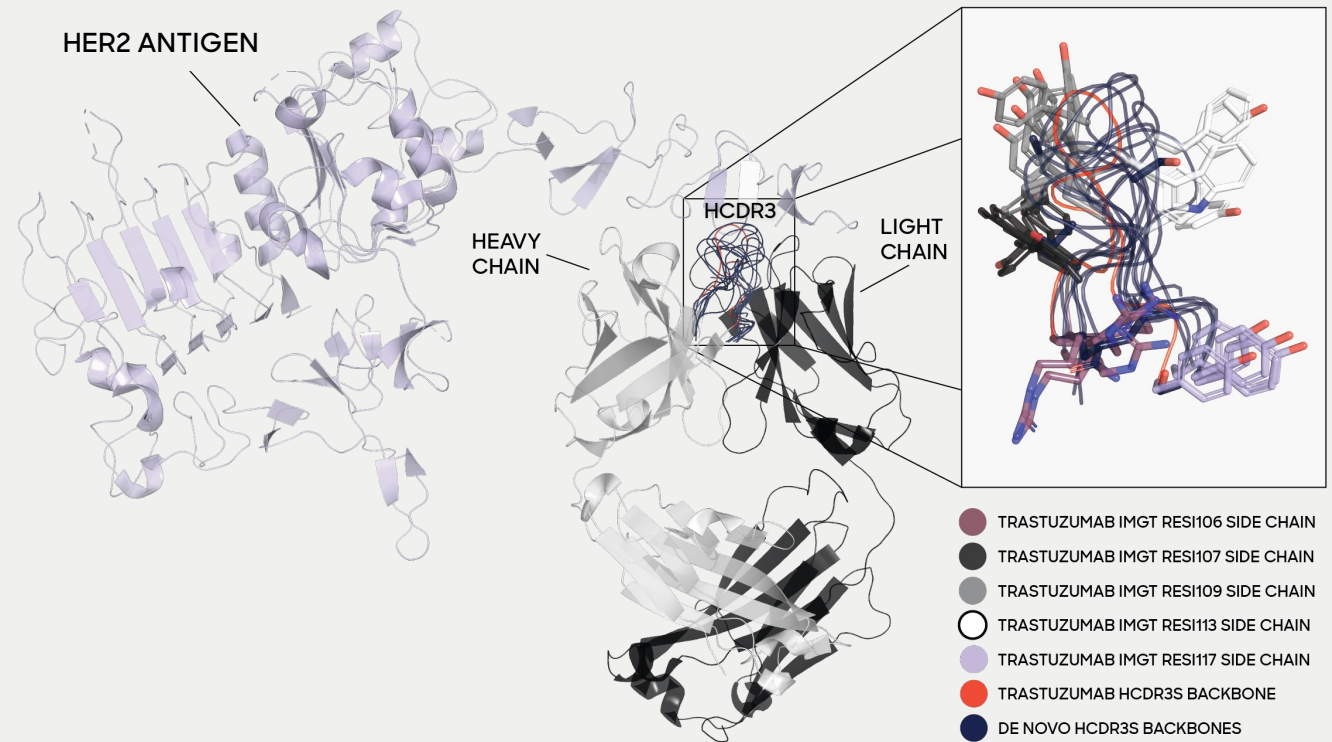
Example HCDR3 designs (edit distance)	$-\text{Log}_{10}(K_D)$
S R W G G D G F Y A M D Y (Wildtype)	8.71
A R W G N Y Y Y M D Y (6)	8.77
A R Y Y Y G F Y Y F D Y (7)	8.92
A R Y A G V E R P G S F A Y (11)	6.24
T R Y F F N G W Y Y F D V (9)	9.03
A F A D S G A Y G I W S F (12)	7.0
A N D I Y I Q G Y D L N R (12)	8.4
A R G Y S G D W P Y E T F Y V (10)	7.01
A R Y D Y G Y Y I Y V S (10)	8.02

Key: Amino acids of the same color belong to the same class

CASE STUDY: DE NOVO DESIGN IN SILICO

‘Zero-shot’ designs of new antibodies from scratch using generative AI

- Zero-Shot: Model has **never seen a binder** to target or homologs
- Binders were identified **straight out of the model** - no lead optimization was performed
- Predicted structures reveal **meaningful biological interactions**
- **Demonstrated across four therapeutic** targets: HER2, VEGF-A, COVID omicron, undisclosed target

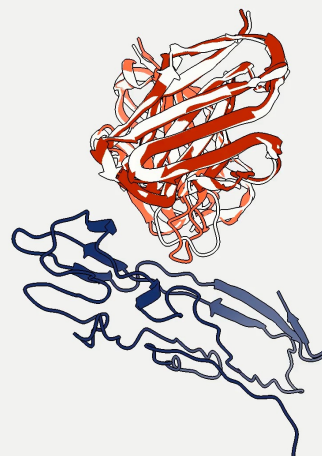


DE NOVO ANTIBODY DESIGN IN SILICO

In silico validation of Zero-shot designs toward diverse targets

- AI-generated Heavy Chain
- AI-generated Light Chain
- Known binder structure¹
- Antigen

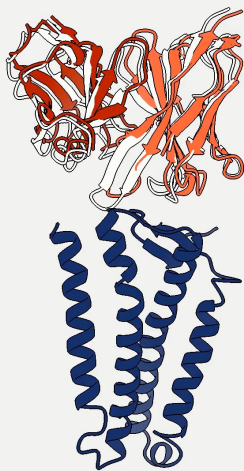
¹Known binder crystal structures are literature sourced



S. aureus α -hemolysin monomer, Fab (4IDJ)



Pekin duck egg lysozyme, Fab (5VJQ)



Prostaglandin E receptor EP4, GPCR, Fab (5YHL)



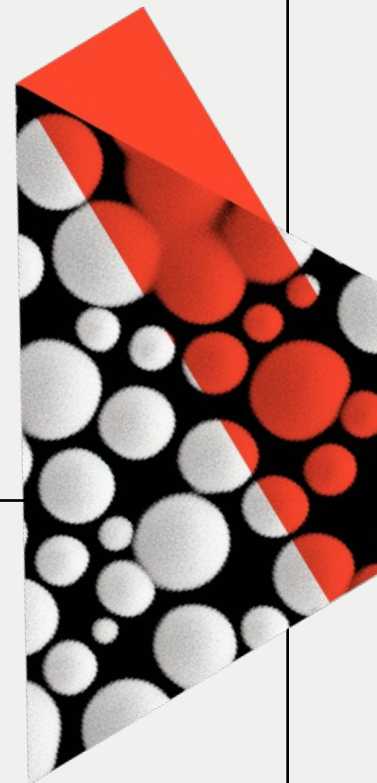
P. vivax RBP2b, monoclonal (6WOZ)



Human urokinase receptor (2FD6)

BREAKTHROUGH IN *DE NOVO* DRUG CREATION

Absci harnesses generative AI to lead a new paradigm of drug creation instead of drug discovery



Unlocking *de novo* antibody design with generative artificial intelligence

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Absci Corporation, New York (NY) and Vancouver (WA), USA

* Equal contribution
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Abstract

Generative artificial intelligence (AI) has the potential to greatly increase the speed, quality and controllability of antibody design. Traditional *de novo* antibody discovery requires time and resource intensive screening of large immune or synthetic libraries. These methods also offer little control over the output sequences, which can result in lead candidates with sub-optimal binding and poor developability attributes. Several groups have introduced models for generative antibody design with promising *in silico* evidence [1–10], however, no such method has demonstrated *de novo* antibody design with experimental validation. Here we use generative deep learning models to *de novo* design antibodies against three distinct targets in a *zero-shot* fashion where all designs are the result of a single round of model generations with no follow-up optimization. In particular, we screen over 400,000 antibody variants designed for binding to human epidermal growth factor receptor 2 (HER2) [11] using our high-throughput wet lab capabilities. From these screens, we further characterize 421 binders biophysically using surface plasmon resonance (SPR), finding three that bind tighter than the therapeutic antibody trastuzumab [12]. The binders are highly diverse and have low sequence identity to known antibodies. Additionally, these binders score highly on our previously introduced *Naturalness* metric [13], indicating that they are likely to possess desirable developability profiles and low immunogenicity. We open source the binders to HER2 and report the measured binding affinities. These results unlock a path to accelerated drug creation for novel therapeutic targets using generative AI combined with high throughput experimentation.

*“...no prior method has demonstrated *de novo* antibody design with experimental validation.”*

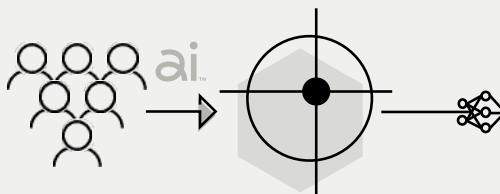


Multiparametric AI lead-optimization can enable **higher potential** therapeutics and **increased PoS**

Find patient cohort specific targets



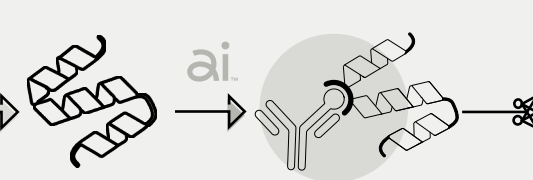
Novel target discovery



Discover novel antibodies for your selected target



De novo discovery *in silico*



Optimize your antibodies' characteristics



Lead optimization *in silico*



Incorporate site-specific chemical handles



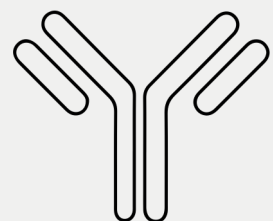
Bionic SoluPro™ strain

OPTIMAL DRUG CANDIDATE



CASE STUDY: AI-DRIVEN LEAD OPTIMIZATION

Multiparametric AI lead-optimization for increased **success rates** & **higher potential** therapeutics

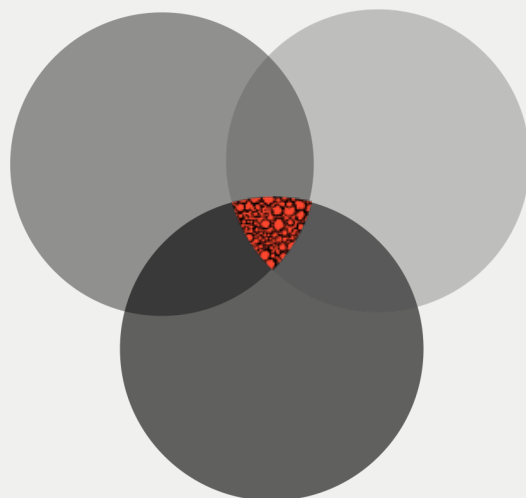


INITIAL LEAD
CANDIDATE



Property 1

Property 2



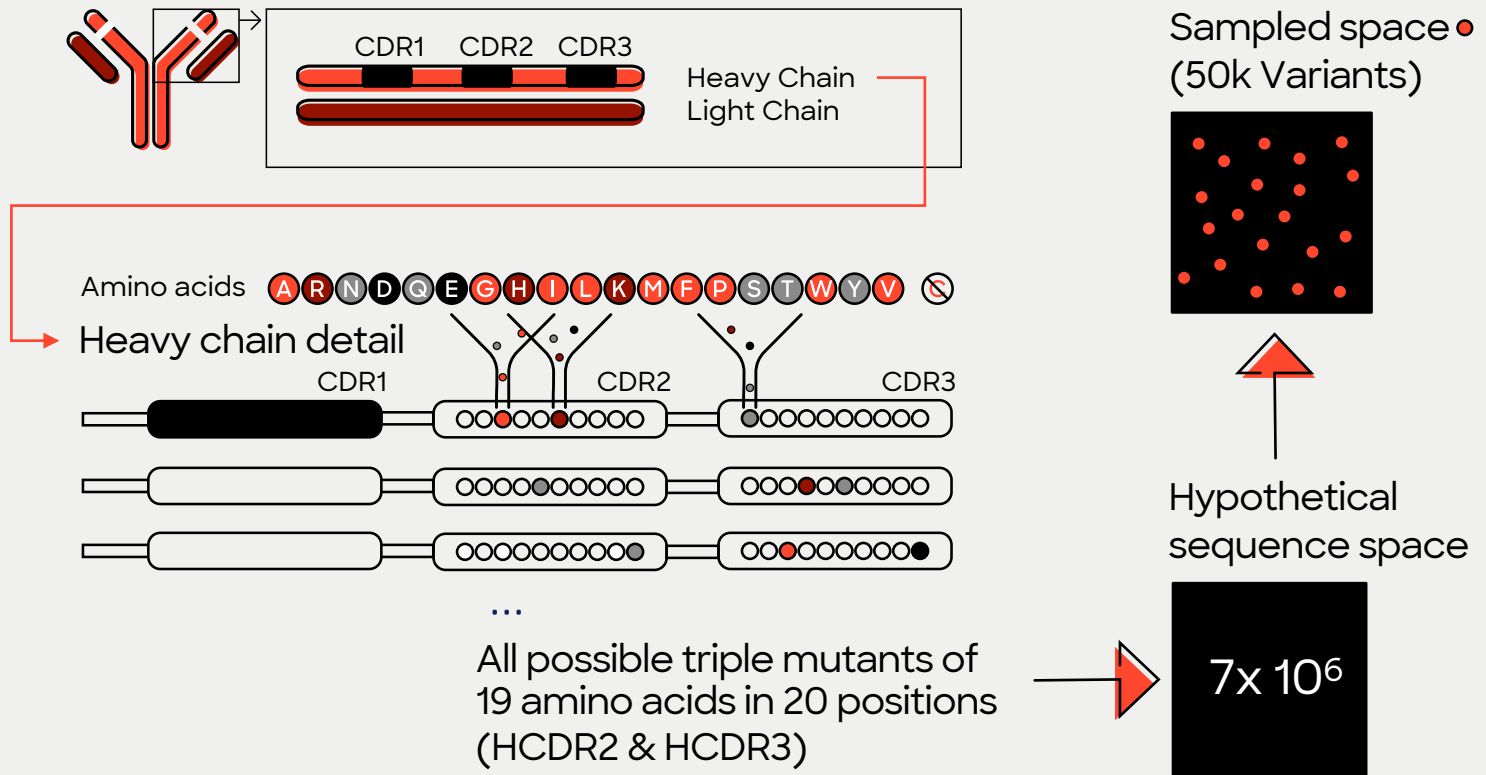
Property 3

Higher potential therapeutics **faster**

- Increased probability of **success**
 - Affinity tailored for desired application
 - Higher Developability
 - Thermostability
 - Self-association
 - Lower immunogenicity
 - S.c. formulation
 - Higher expression levels enabling lower COGS
- Higher **potential** with **novel biology**
 - Dual- or multi-valent binding
 - Conditional biologics

CASE STUDY: DESIGNING BETTER HER2 BINDERS

AI models expanded search space by orders of magnitude

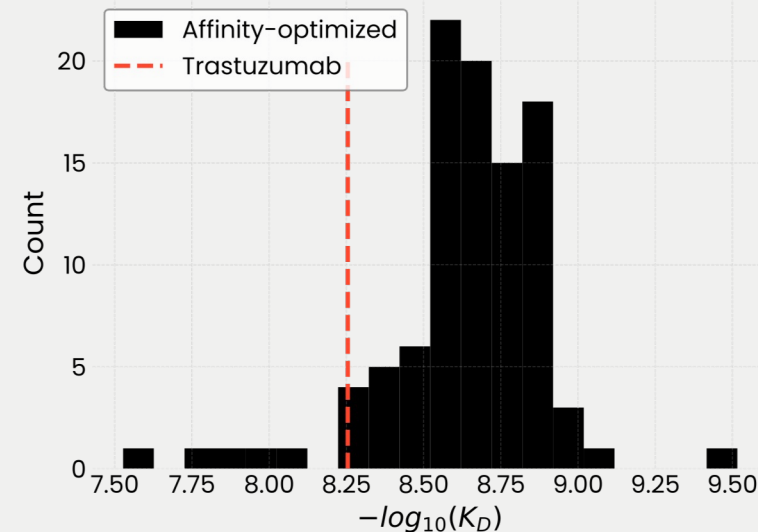
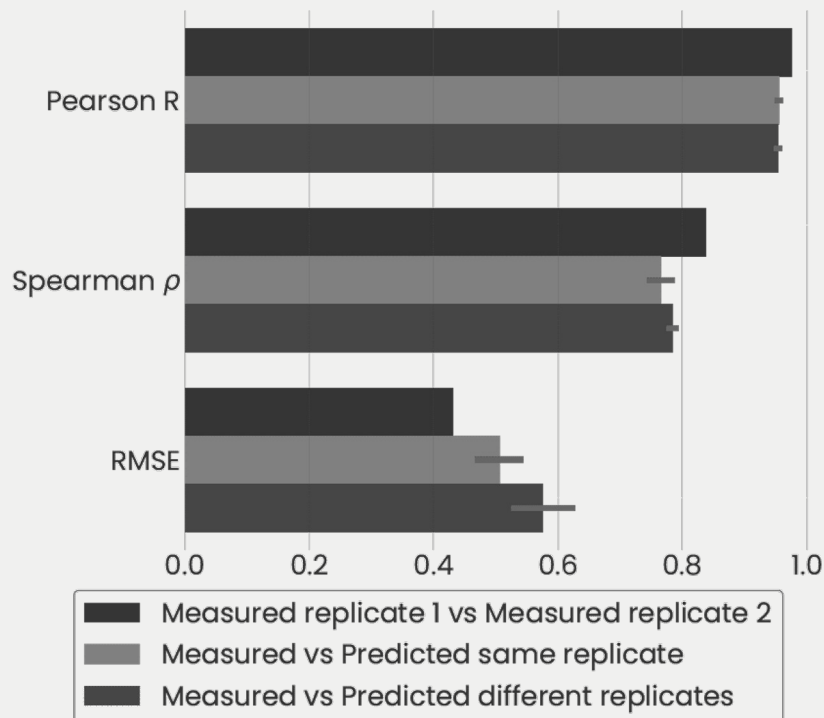
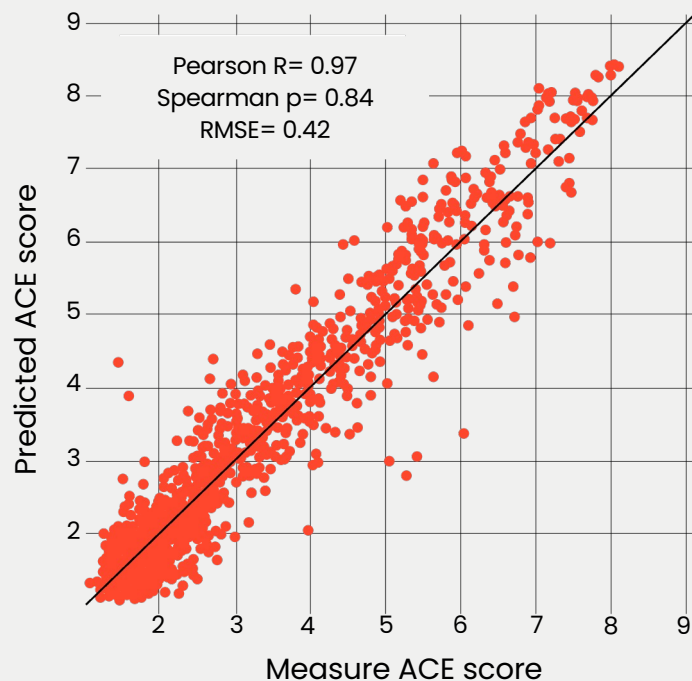


- Combinatorial mutagenesis of up to 3 mutations over ten amino acids each in HCDR2 and HCDR3
- Sampled less than 1% of the sequence space
- Measured binding affinity of nearly 50,000 sequence variants

Bachas, S., Rakocevic, G. et al., "Antibody optimization enabled by artificial intelligence predictions of binding affinity and naturalness," 2022 pre-print in bioRxiv.

CASE STUDY: DESIGNING BETTER HER2 BINDERS

AI quantitatively predicts antibody affinity



HIGH PREDICTIVE PERFORMANCE

Pearson R correlation of 0.93

- Trained on 90% of dataset
- Results shown for 10% of dataset not seen by model

HIGH QUALITY DATA

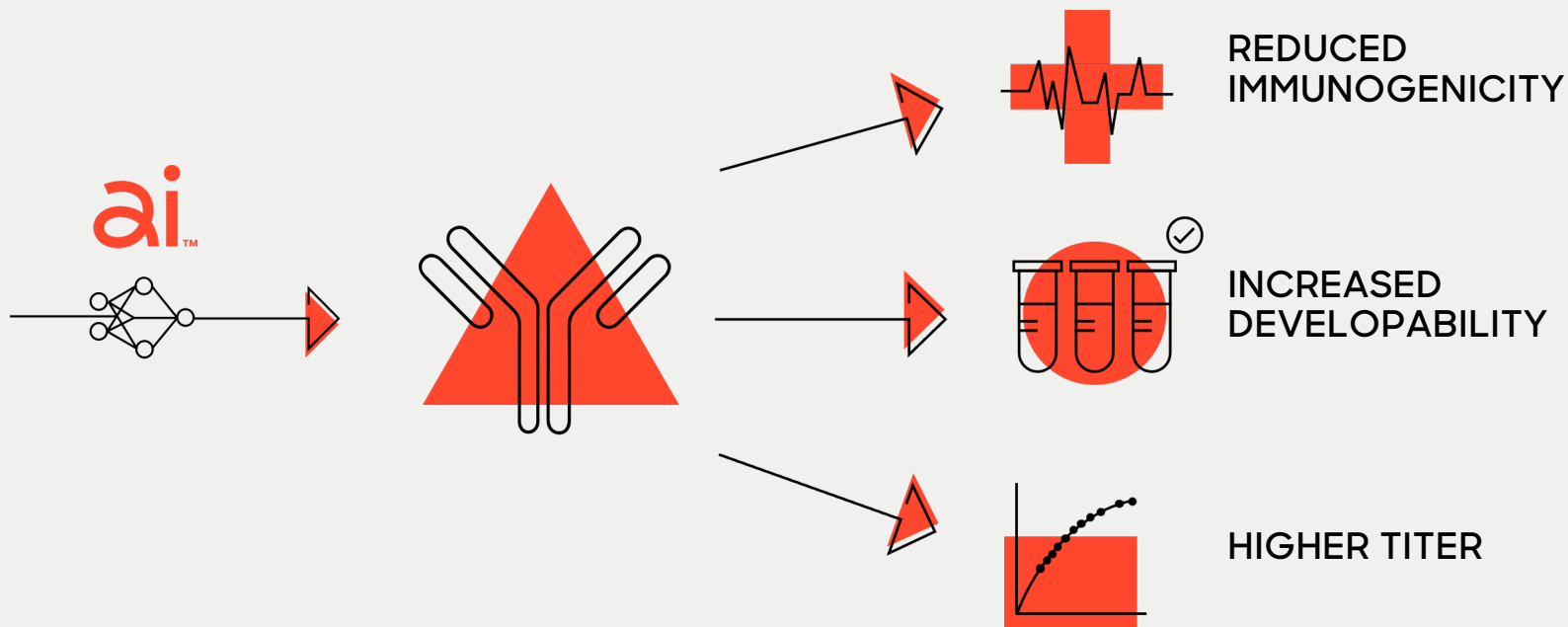
Models trained on one replicate can predict unseen data from a different replicate

HIGH AFFINITY PREDICTIONS

Models can find variants with higher affinity than seen in training data

- 92 of top 100 predicted high-affinity variants bind tighter than trastuzumab

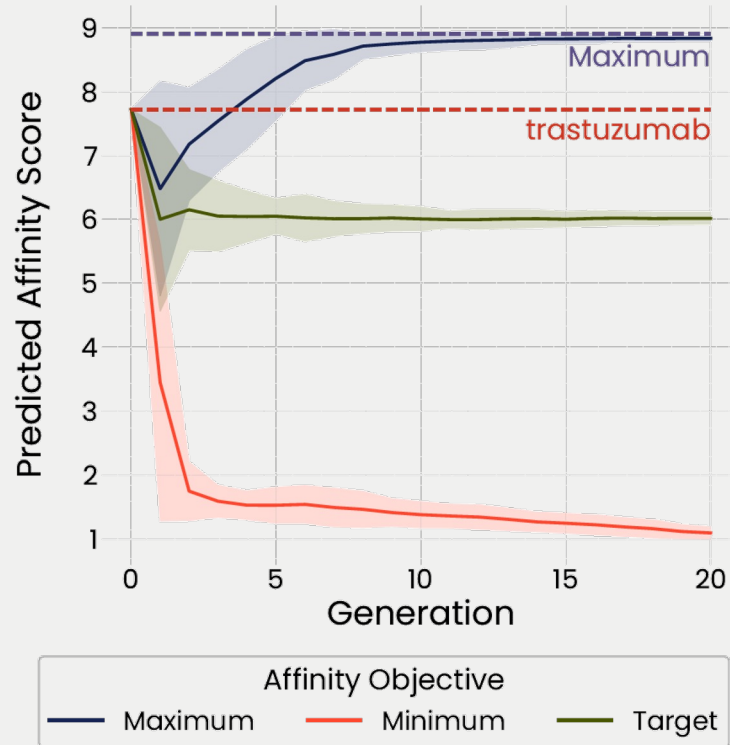
Higher naturalness improves probability of success and expression levels



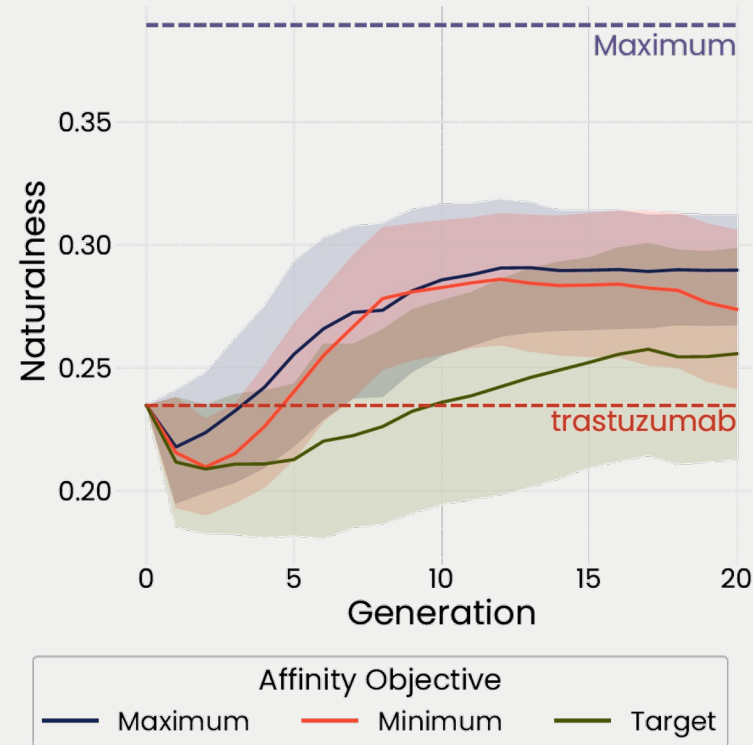
Optimizing for naturalness with Absci's proprietary AI model to overcome major challenges in antibody development

CASE STUDY: OPTIMIZING HER2 BINDERS

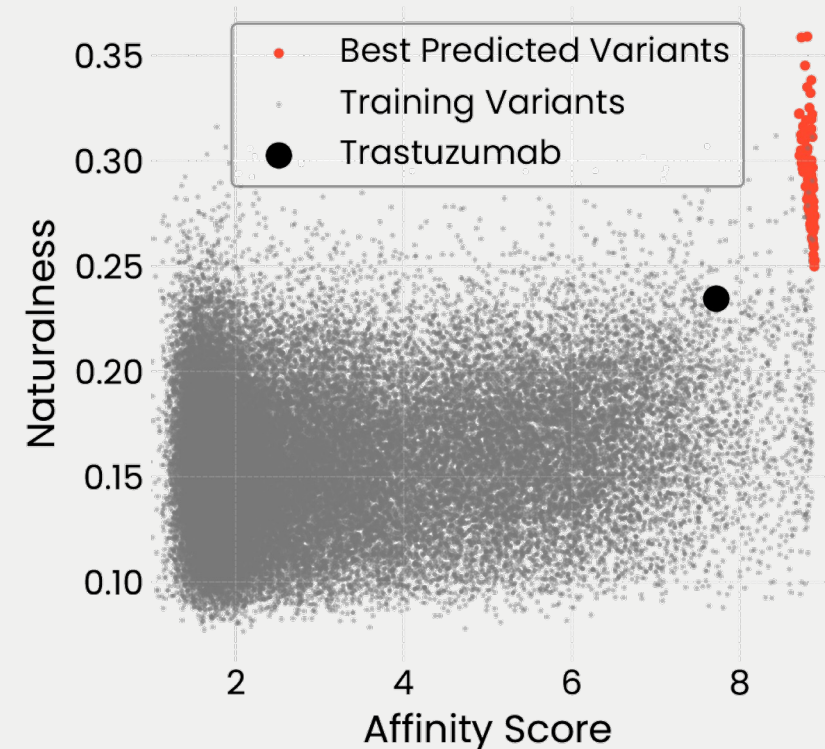
Simultaneous co-optimization of affinity and naturalness



Maximize, minimize, or tailor binding affinity



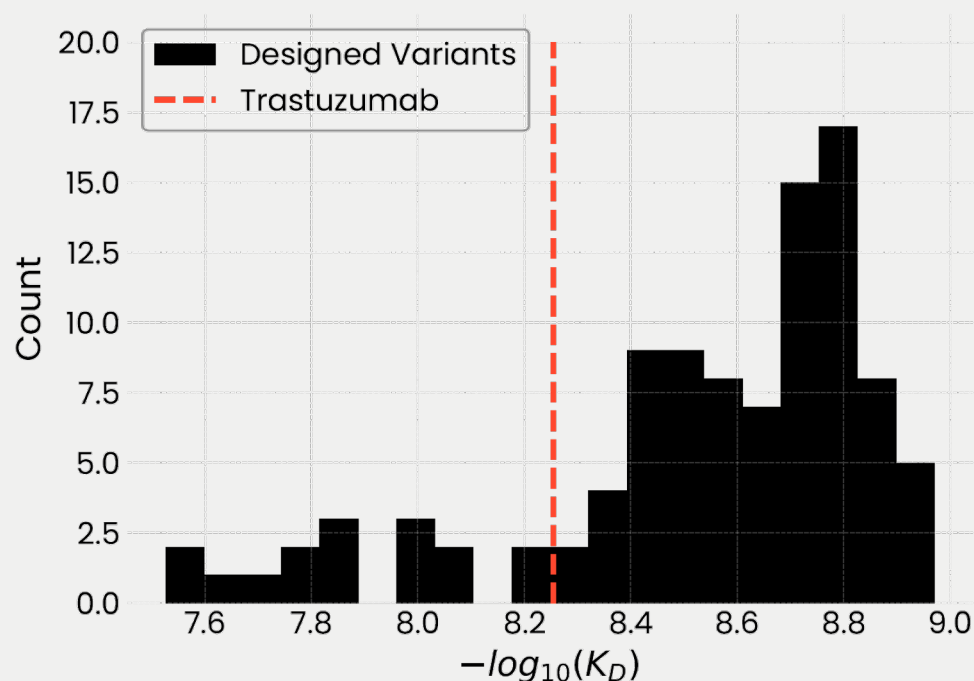
At the same time, ensure sequences appear to come from humans (naturalness)



Models simultaneously tuning for affinity & maximizing naturalness

CASE STUDY: AI-DRIVEN LEAD OPTIMIZATION

85% of Top 100 “**natural**” Trastuzumab variants exhibit higher-affinity than wild-type



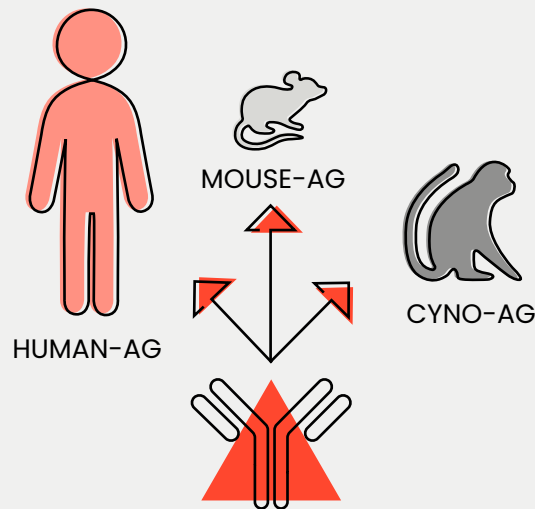
85% of top binders have higher affinity than Trastuzumab

- AI predicts the affinity of **unseen variants** from libraries generated using diverse mutational strategies and combinatorial sequence space
- AI models make predictions with **actionable performance** using <0.1% of the combinatorial sequence space as training set
- Naturalness is associated with **developability** metrics and expression titer
- Enables one-shot multiparametric lead optimization potentially **accelerating time to clinic**

AI-optimization for dual- or multi-valent biologics increases potential

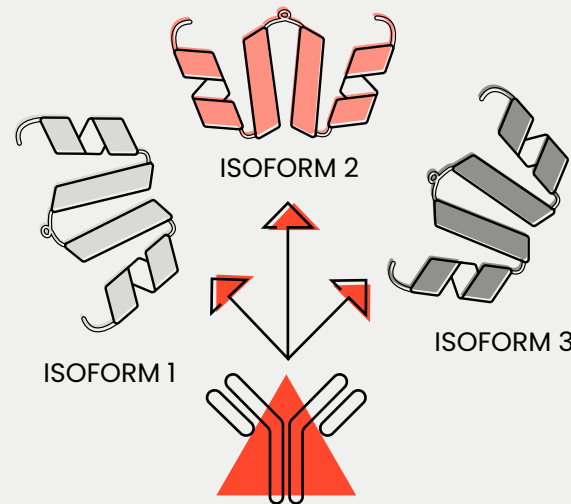
PRECLINICAL DEVELOPMENT

Cross-species binding for improved success rates and speed



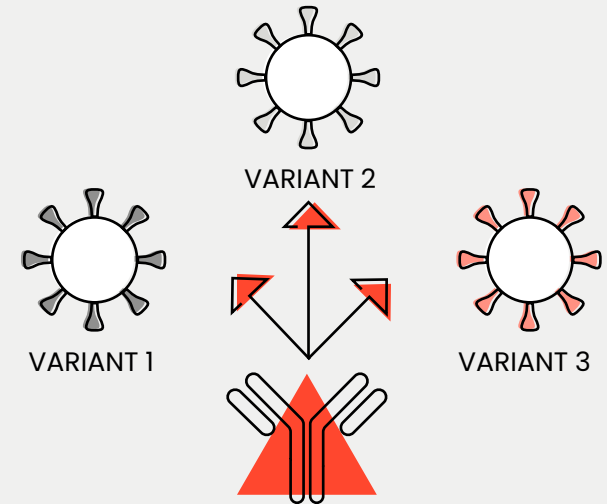
IMMUNOLOGY

Increased efficacy by simultaneous binding to multiple desired **isoforms**



INFECTIOUS DISEASES

Broad spectrum antibodies with simultaneous binding to multiple **viral variants**



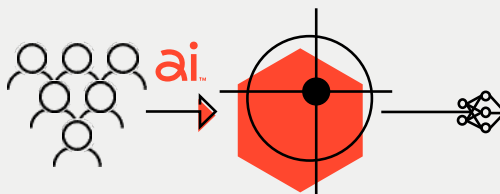
NOVEL TARGET DISCOVERY

The leading AI platform for AI-enabled **biologics** drug creation

Find patient cohort
specific targets



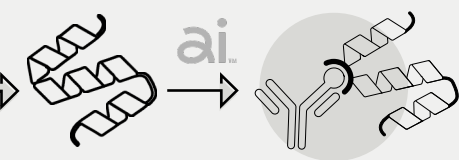
Novel target discovery



Discover novel antibodies
for your selected target



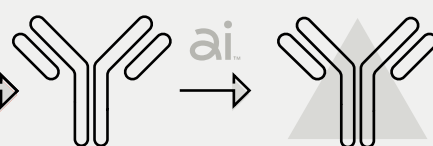
De novo discovery *in silico*



Optimize your
antibodies' characteristics



Lead optimization *in silico*



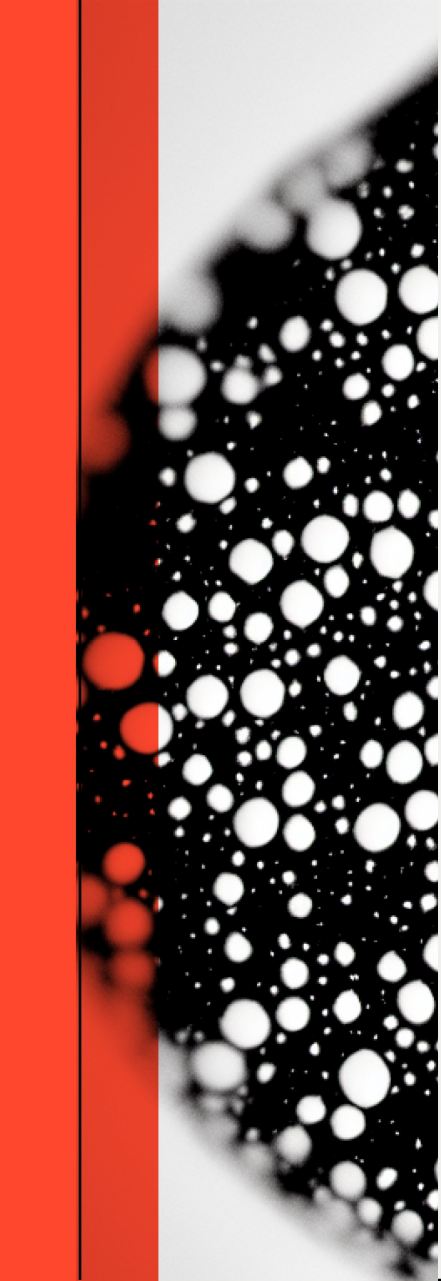
Incorporate site-specific
chemical handles



Bionic SoluPro™ strain

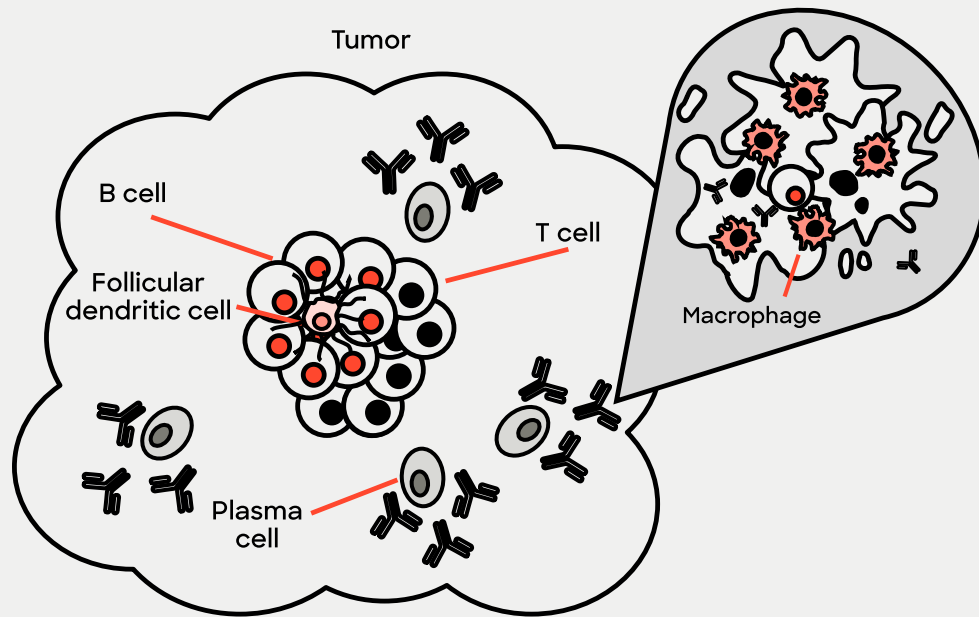
OPTIMAL DRUG
CANDIDATE





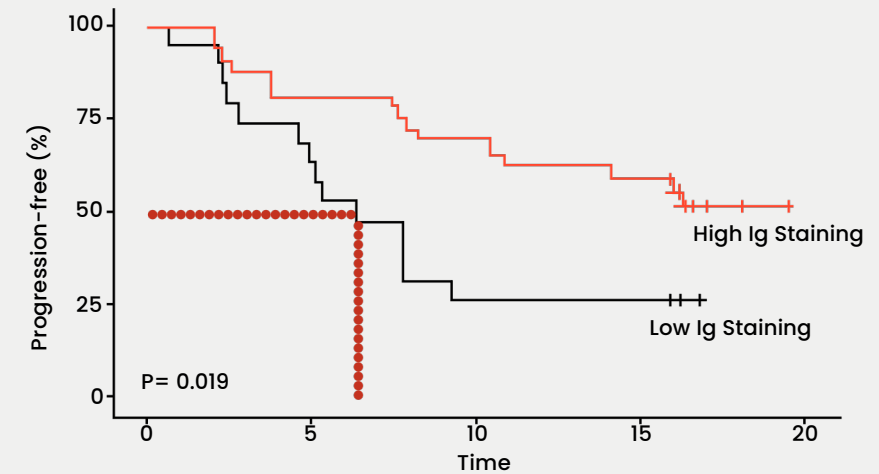
Leveraging
exceptional immune
responses to identify
new potential cancer
specific targets and
therapeutics

Antibodies selected in tertiary lymphoid structures bind to cancer cells and are associated with favorable clinical outcomes



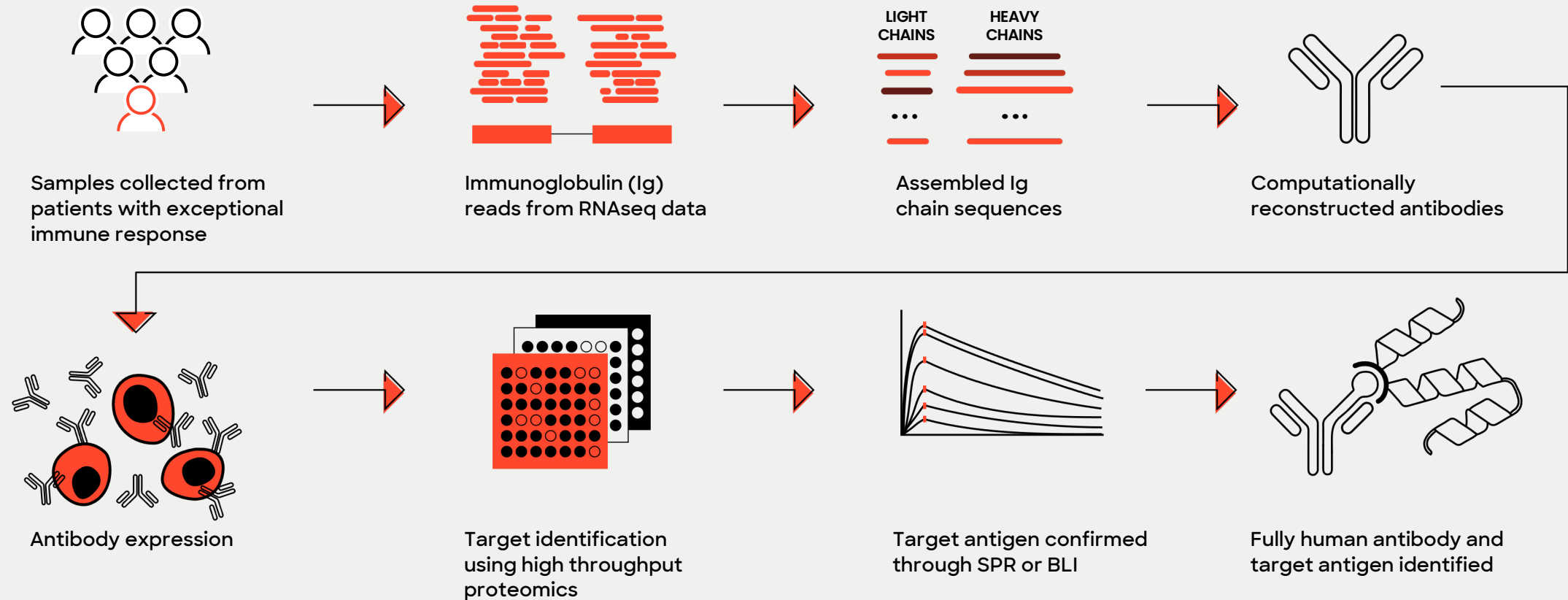
Tertiary Lymphoid Structures (TLS) are centers of immune activity (B-cell proliferation and antibody production) that develop in chronically inflamed tissues such as tumors.

Meylan, Maxime, et al. "Tertiary lymphoid structures generate and propagate anti-tumor antibody-producing plasma cells in renal cell cancer." *Immunity* 55.3 (2022): 527-541.



- The presence of **TLS** is associated with **longer progression-free survival and better response to immune checkpoint inhibitors**.
- Rapidly growing evidence illustrates correlation between **TLS-derived antibodies** in the tumor microenvironment and **positive clinical outcomes**.
- **TLS-derived antibodies** have been shown to be associated with apoptosis of cancer cells in patients.

Our integrated workflow identifies the antigens targeted by exceptional immune responses



Absci's workflow identifies antigens targeted by exceptional immune responses

A Highly Productive Workflow*

>6,600

Reconstructed
antibodies

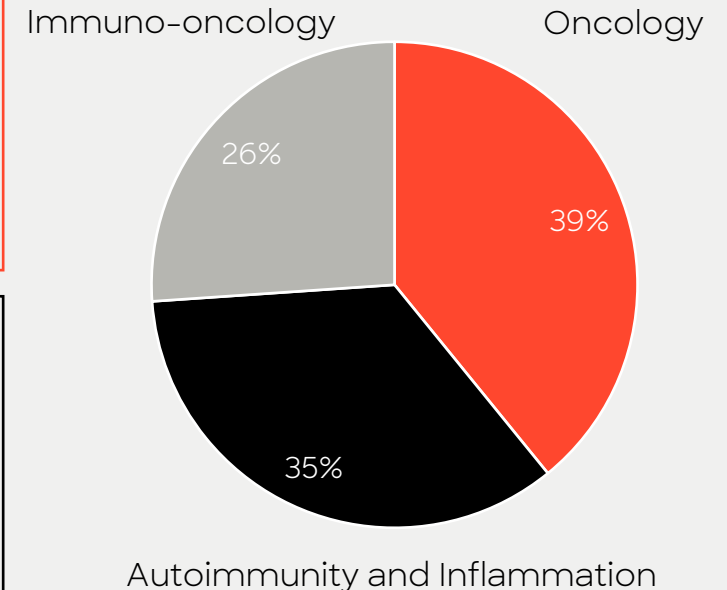
>250

Hits under
evaluation

22

Antibody/Target
pairs

- Expanded network of health care institutions provides continuous access to patient data (melanoma, colorectal cancer, RA, psoriasis, lupus, etc.)
- Validated examples in oncology, immunology and infectious diseases
- Large collection of TLS-derived antibodies targeting **cancer specific antigens, cytokine receptors, checkpoint inhibitors** and other targets



*Information as of 02/09/2023

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NOVEL TARGET DISCOVERY

Absci partners with leading health institutions to drive **novel target discovery**



PARTNERING WITH TOP-CLASS HEALTH INSTITUTES

- Aster Insights
- Avera Health
- Saint John's Cancer
 - Institute Department of Translational Molecular Medicine
- University of Oxford
- Others in progress

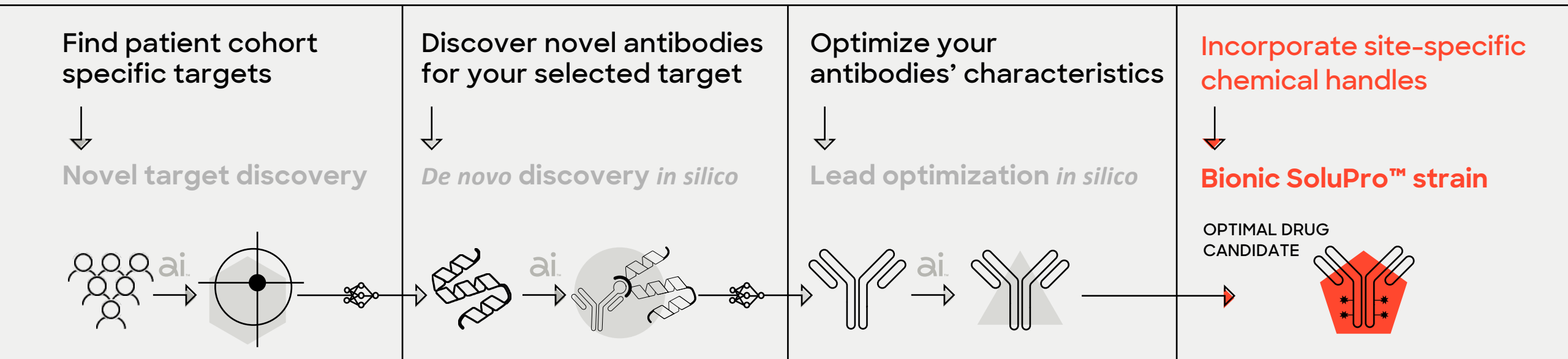


PROVIDES ABSCI WITH

- **access to data from thousands of patients** across relevant oncology and immunology indications
- **continuous funnel of data** for the discovery of **novel** disease-relevant **targets and antibodies**

ABSCI'S END-TO-END PLATFORM SOLUTION

The leading AI platform for AI-enabled **biologics** drug creation



NON-STANDARD AMINO ACID INCORPORATION

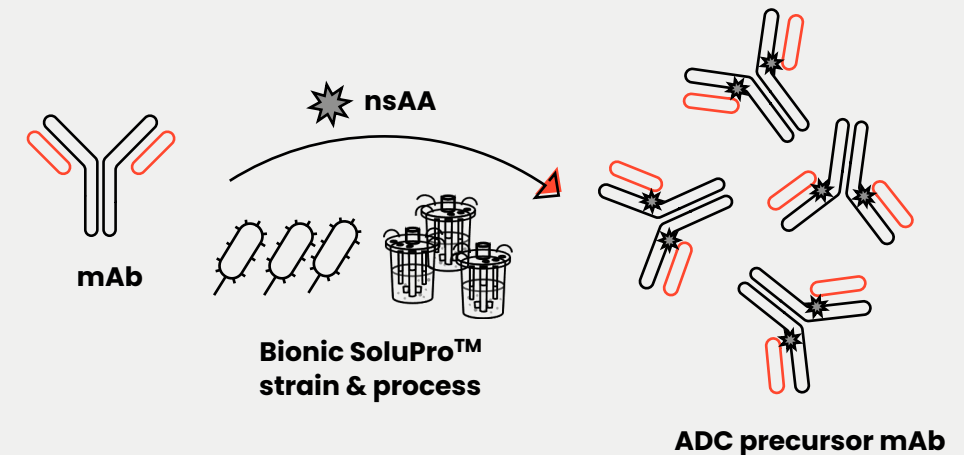
Bionic™ protein technology: non-standard amino acid (nsAA) incorporation

Absci's high-yielding Bionic SoluPro™ strain enables selective site-specific nsAA incorporation into difficult-to-produce biologics (proteins, enzymes, mAbs, fabs, VHHs)

Bionic™ protein technology enables:

- Rapid assessment of payload location
- Precise control over payload location
- **Uniform and homogenous Drug-Antibody-Ratio (DAR) for ADCs**
- Attachment of diverse chemical moieties for novel applications

EXPRESSION OF MAB IN BIONIC SOLUPRO™ CELL LINE (ADC PRECURSOR)



- ★ pAcF - p-acetyl-phenylalanine
- ★ pAzF - p-azido-L-phenylalanine
- ★ oPrY - o-propargyl-L-tyrosine

Unlocking new molecular functionalities and application

Bionic SoluPro™ platform

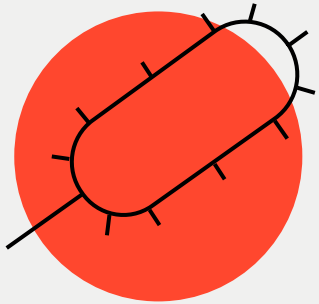
- enables site-specific non-standard amino acid incorporation into difficult-to-produce biologics
- designed for maximum incorporation efficiency
- Unlocks functionalities such as chemical modification, drug conjugation, pegylation, glycosylation

Use in wide range of applications

- development of ADCs with improved therapeutic properties (pharmacokinetic, efficacy, and safety profiles)
- half-life extension
- site-specific, homogeneous, designer glycosylation
- attachment of novel chemical moieties
- enzyme immobilization/modification

NON-STANDARD AMINO ACID INCORPORATION

Bionic SoluPro™ a specialized *E. coli* cell line for non-standard amino acid incorporation

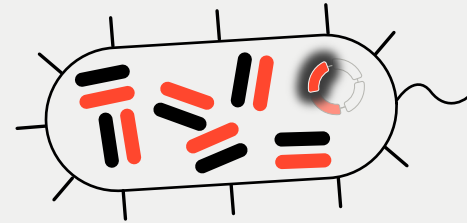
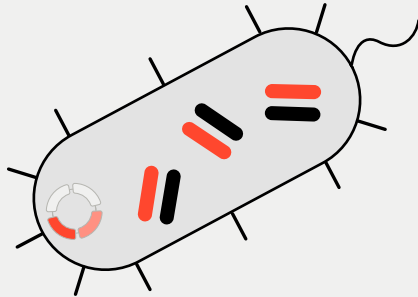


Bionic SoluPro™ cell line

Patented *E. coli* cell line bioengineered for production of mammalian proteins and site-specific incorporation of non-standard amino acids

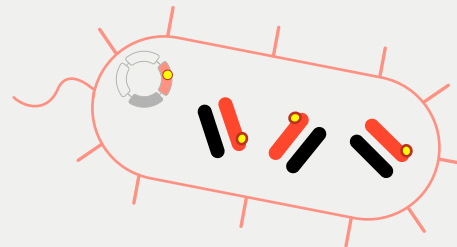
Semi-oxidized cytoplasm

Engineered redox environment to achieve scalable, soluble protein production



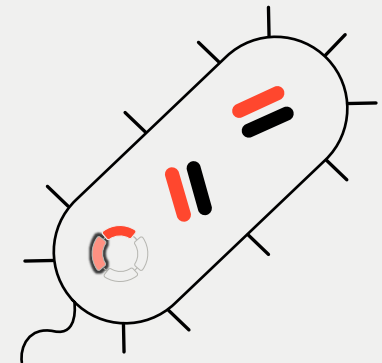
Precise expression control

SoluPro™ cell lines achieve precise control over induction through genetic engineering of metabolic pathways and proprietary plasmid designs



nsAA incorporation

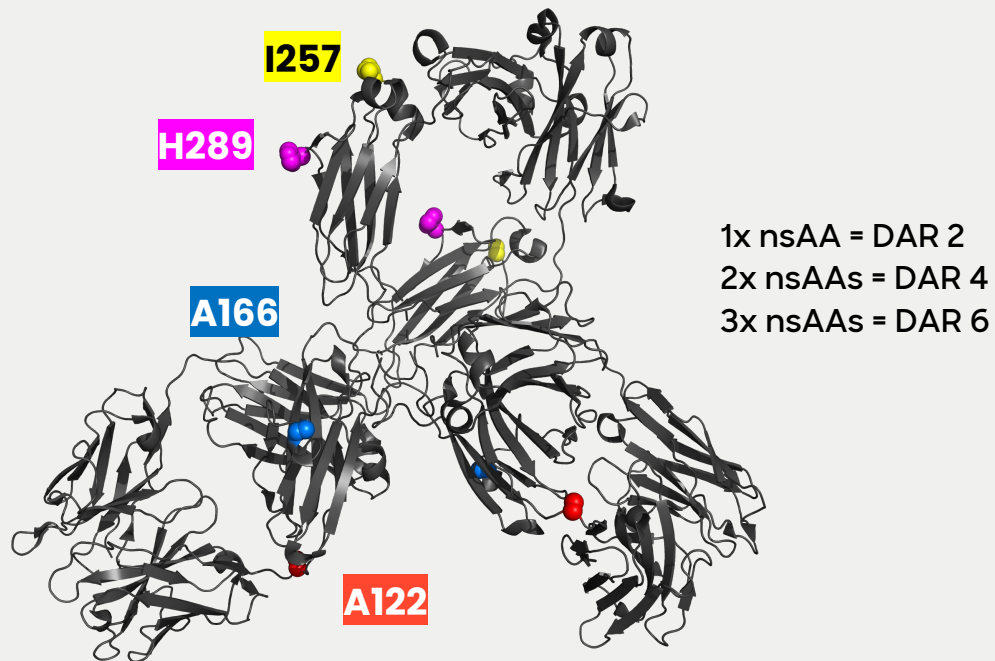
Optimized for high-efficiency incorporation of non-standard amino acids



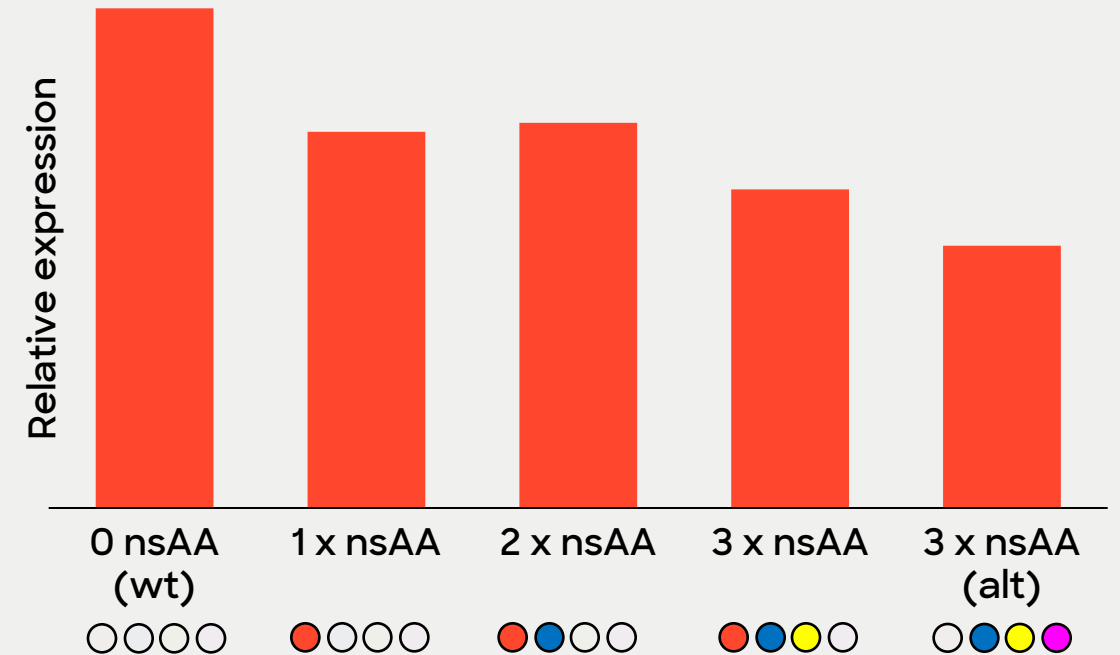
CASE STUDY: MULTIPLE INSERTIONS OF NON-STANDARD AMINO ACIDS

Increased drug to antibody ratio with the incorporation of multiple nsAAs

We investigated our ability to produce bionic Trastuzumab with 1, 2, or 3 nsAA incorporation sites



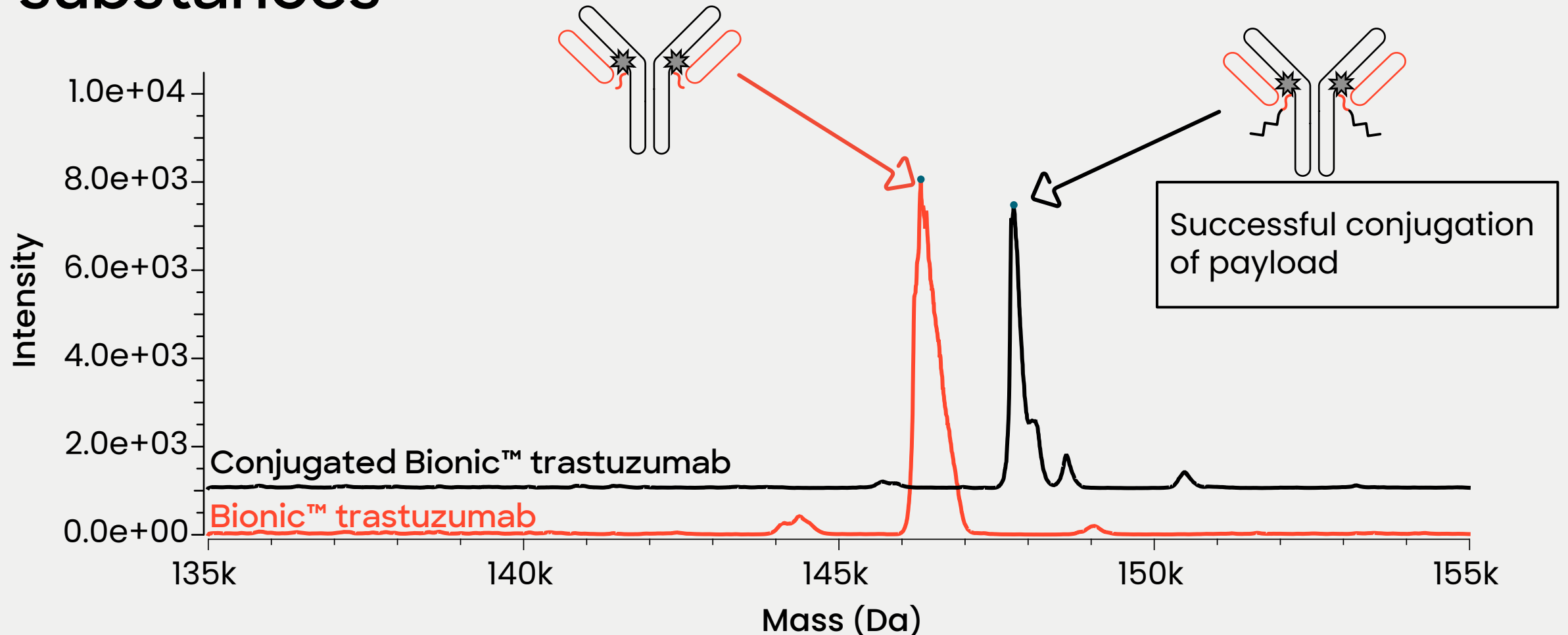
*DAR = Drug-to-Antibody Ratio



Bionic SoluPro™ has been able to incorporate a non-standard amino acid into a total of 3 sites of a heavy chain mAb without major reductions in titer

CASE STUDY: CONJUGATING TO NON-STANDARD AMINO ACIDS

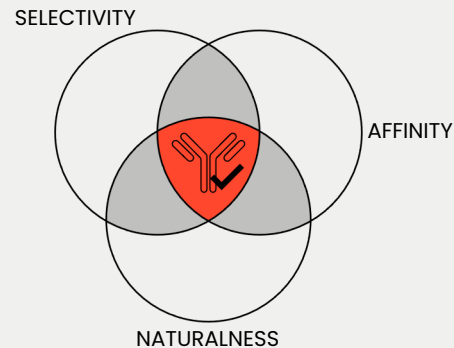
Easy conjugation producing homogenous drug substances



Unlocking new and differentiated value drivers

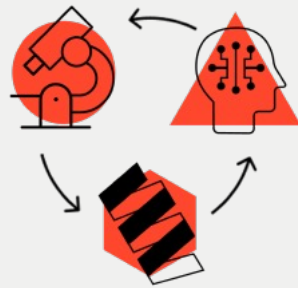
Higher **Potential** Biologics with Increased PoS

Multidimensional optimization in parallel creates **higher quality** biologics with an increased Probability of Success



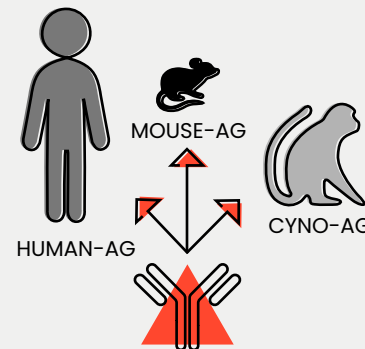
Reducing **Time** & Increasing **Competitiveness**

Drug creation process significantly shortened reducing research costs and **increasing competitiveness**



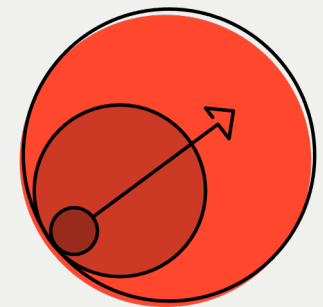
Novel biology: Multi-valent biologics & conditional biologics

Preclinical development: **Cross-species** binding to improve success rates & speed



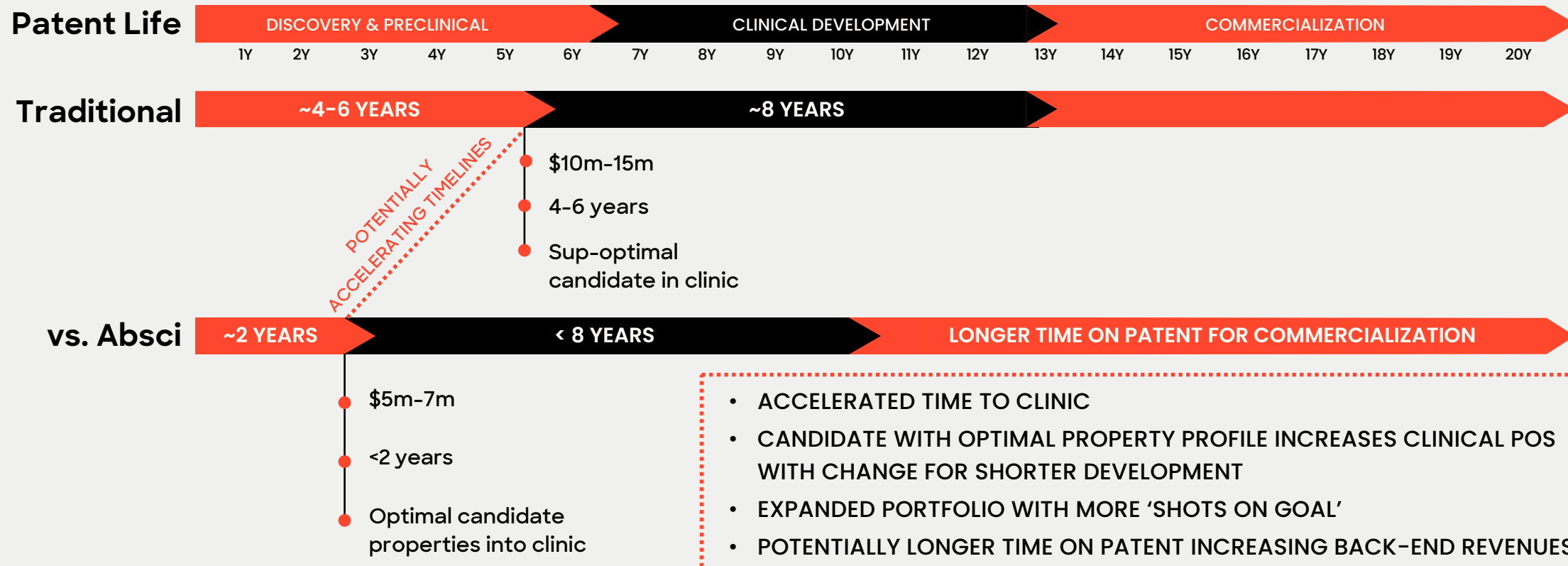
Broadening **Intellectual Property** Space

AI-driven drug creation generates **valuable IP**



BETTER BIOLOGICS FASTER

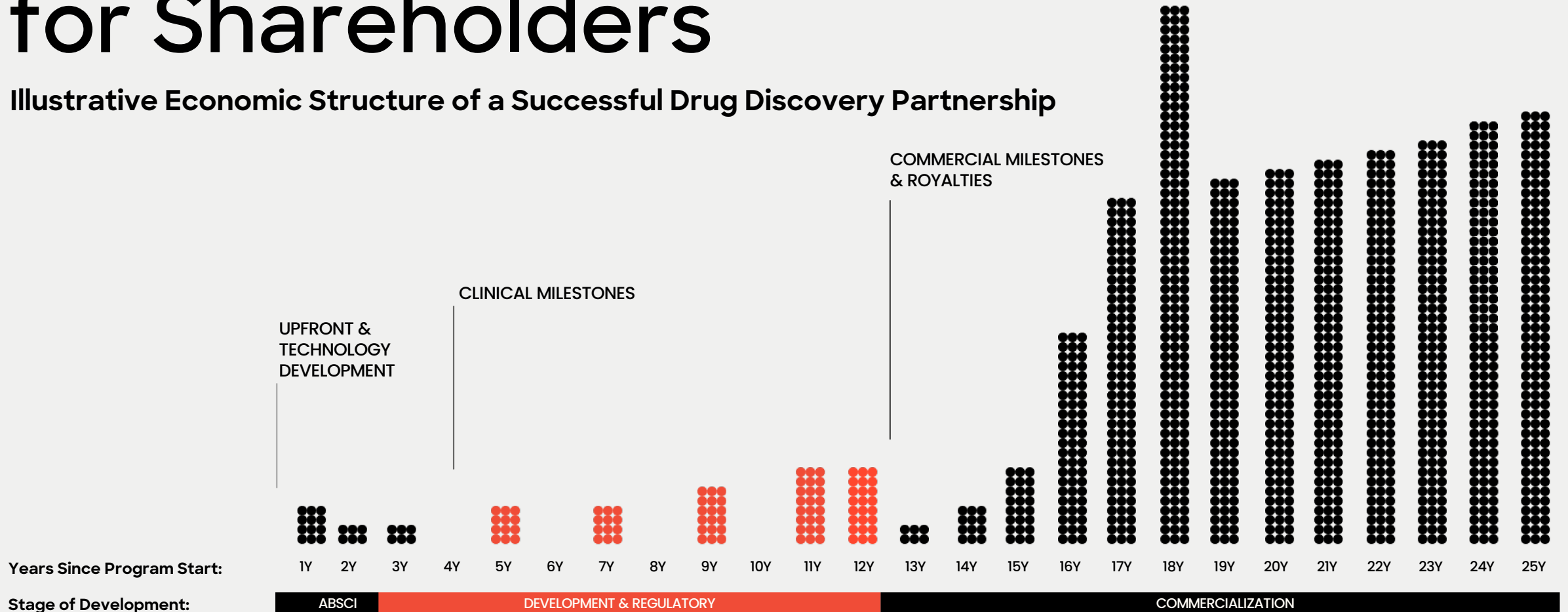
Accelerating time to clinic while increasing PoS



BUSINESS MODEL

Creating Compounding Value for Shareholders

Illustrative Economic Structure of a Successful Drug Discovery Partnership



*Illustrative of Discovery Partnership; assuming successful commercialization. Regulatory milestone captured in clinical development, and single digit royalty rates

Well positioned to revolutionize AI drug creation



>200

Unlimiters with deep experience in AI, immunology, synthetic biology, and protein expression.

Leading AI team with expertise from:



77,000+
Square Feet

State-of-the-art drug creation and wet lab space in Vancouver WA, Absci AI Research (AAIR) lab in NYC, and the Innovation Centre in Zug Switzerland

~\$425M

Capital raised to date

NASDAQ
Listed

\$ABSI IPO July 22, 2021, ten years after founding in a basement lab

PARTNERSHIPS

Technology **validated** through industry-leading collaborations



“Merck leans into AI with \$610M in biobucks for Absci drug discovery pact”

*“At Merck we are continually evaluating new ways to build, expand, and refine our biologics capabilities. Absci’s platform offers a compelling opportunity to design new biologic candidates and explore the expression of complex proteins.”**

Dr. Fiona Marshall

Former SVP, Head of Discovery,
Preclinical and Translational Medicine



“Absci collaborates with NVIDIA, pioneer in AI & compute technology to accelerate vision of creating drugs *in silico*”

“Absci’s powerful data generation and AI protein engineering platform is already helping the drug discovery industry, and NVIDIA is excited to help power and scale Absci’s in silico technologies to achieve the best positive impact.”

Kimberly Powell

Vice President of Healthcare

TRAILBLAZING MANAGEMENT TEAM

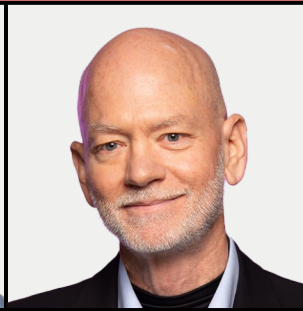
The right leadership team to accomplish the Impossible



SEAN MCCLAIN
Founder & CEO Director



ANDREAS BUSCH, PHD
Chief Innovation Officer



GREG SCHIFFMAN, CPA
Chief Financial Officer



SARAH KORMAN, PHD, JD
Chief Legal Officer



JACK GOLD
Chief Marketing Officer



KARIN WIERINCK
Chief People Officer

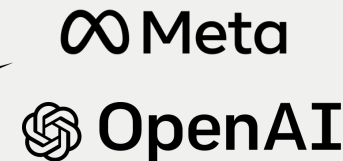


JOSHUA MEIER
SVP, Chief AI Officer



PENELOPE
Chief Morale Officer

Senior leadership bring experience from industry leaders including:



Backed by a Board of industry, platform, and scientific **innovators**

Board of Directors



SEAN MCCLAIN
Founder & CEO Director,
Absci



KAREN MCGINNIS, CPA
Former CAO,
Illumina



ZACH JONASSON, PHD
Managing Partner,
PVP



AMRIT NAGPAL
Managing Director,
Redmile Group



JOSEPH SIROSH, PHD
Vice President,
Alexa Shopping, Amazon



DAN RABINOVITSJ
VP Connectivity,
Meta



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Head of Development, CMO,
AiCuris

Redmile Group

Meta

amazon

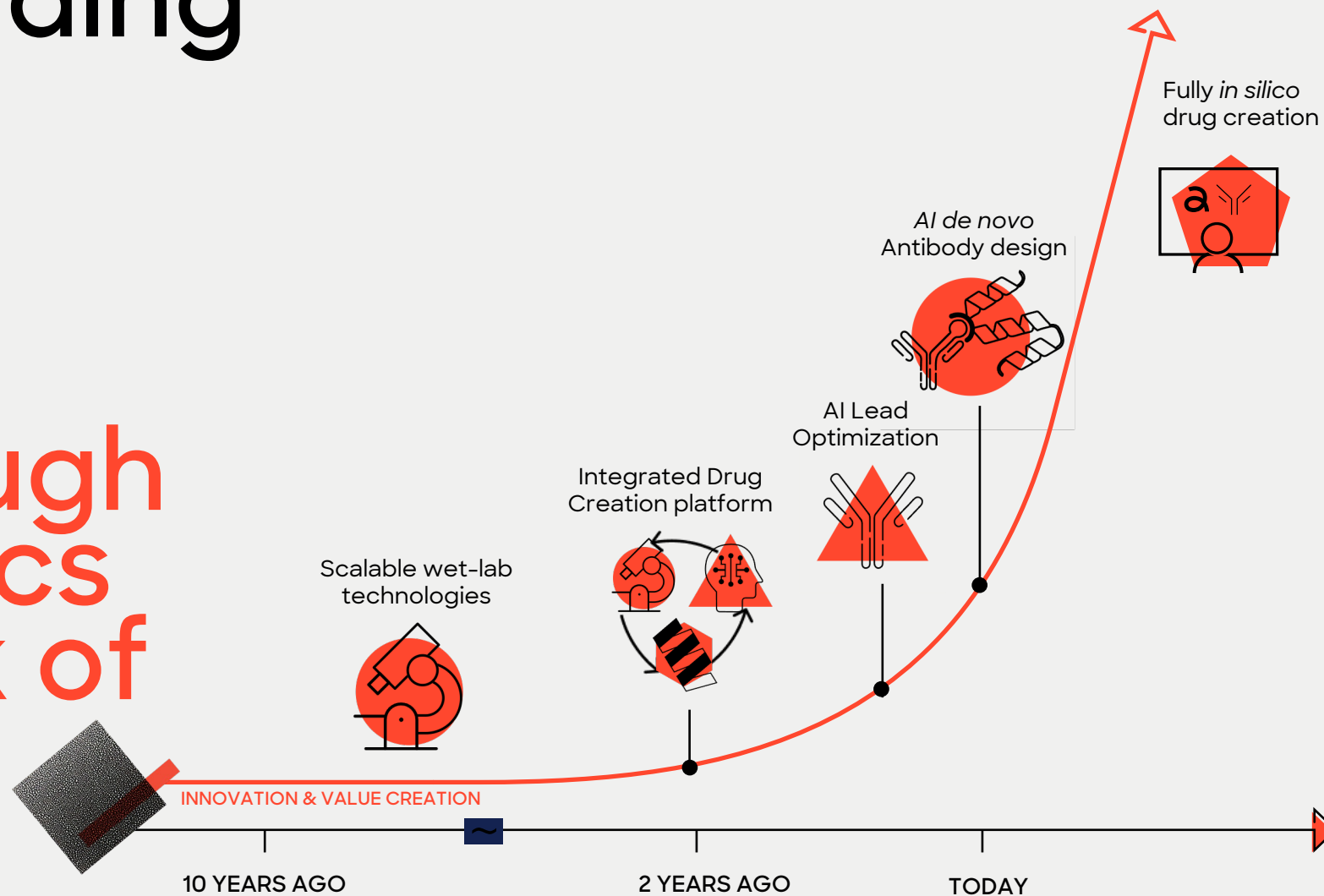
illumina



HARVARD
UNIVERSITY



Absci is leading the way in AI drug creation towards breakthrough therapeutics at the click of a button



absci®



This **revolution** is
only just beginning.