

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  
SUMMER 2024

```
from absci import genetic_algorithm; parameters=["maximizebinding_affinity:pH=7.5", "minimizebinding_affinity:pH=6.0",
"maximizehuman_naturalness"]; library = genetic_algorithm.multiparametric_optimization(library, parameters, evolutions=100);
library.to_wet_lab(assays=["ACE", "SPR", "Bioassays"])
```

# Disclaimers

## Forward-Looking Statements

Certain statements in this presentation that are not historical facts are considered forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995, Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements containing the words “will,” “may,” “anticipates,” “plans,” “believes,” “forecast,” “estimates,” “expects,” “predicts,” “advancing,” “aim,” “potential,” and “intends,” or similar expressions. We intend these forward-looking statements, including statements regarding our strategy, estimated speed, cost advantages, improved success rates, and expanded intellectual property opportunities from developing therapeutics leveraging our AI drug creation platform, potential milestone and royalty payments due under our collaboration agreements, projected costs, prospects, plans and objectives of management, our technology development efforts and the application of those efforts, including for generalizing our platform, accelerating drug discovery and development timelines, increasing probability of successful drug development and developing better product candidates, our drug discovery and development activities related to drug creation partnerships and our internal therapeutic asset programs, the progress, milestones and success of our internal asset programs, including ABS-101, including our clinical development strategy, the progress and timing for various stages of development including candidate selection, IND enabling studies, initiating clinical trials and the generation and disclosure of data related to these programs, the translation of preclinical results and data into product candidates, and the significance of preclinical results, including in comparison to competitor molecules for ABS-101 and in leading to differentiated clinical efficacy or product profiles, to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Securities Exchange Act, and we make this statement for purposes of complying with those safe harbor provisions. These forward-looking statements reflect our current views about our plans, intentions, expectations, strategies, and prospects, which are based on the information currently available to us and on assumptions we have made. We can give no assurance that the plans, intentions, expectations, or strategies will be attained or achieved, and, furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a variety of risks and factors that are beyond our control, including, without limitation, risks and uncertainties relating to our ability to secure milestone payments and royalties, obtaining and maintaining necessary approvals from the FDA and other regulatory authorities, replicating in clinical trials positive results observed in preclinical studies, our dependence on third parties to support our internal asset programs, including for the manufacture and supply of preclinical and clinical supplies of our product candidates or components thereof, our ability to effectively collaborate on research, drug discovery and development activities with our partners or potential partners, our existing and potential partners’ ability and willingness to pursue the development and commercialization of programs or product candidates under the terms of our partnership agreements, and overall market conditions and regulatory developments that may affect our and our partners’ activities under these agreements; along with those risks set forth in our most recent periodic report filed with the U.S. Securities and Exchange Commission, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the U.S. Securities and Exchange Commission. Except as required by law, we assume no obligation to update publicly any forward-looking statements, whether as a result of new information, future events, or otherwise.

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# Absci is a Data-First Generative AI Drug Creation Company

Our Integrated AI & Wet Lab  
Platform Aims to Engineer  
**Better Biologics Faster**

- Ultra-Efficient Discovery
- Best-in-Class Properties
- Access Difficult Targets
- Unlock Novel Biology

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DIFFERENTIATED LAB-IN-A-LOOP:  
'DATA TO TRAIN',  
'AI TO CREATE', &  
'WET LAB TO VALIDATE' IN RAPID  
**6-WEEK CYCLES**

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PLATFORM VALIDATED THROUGH  
**INDUSTRY-LEADING PARTNERSHIPS**  
INCLUDING WITH ASTRAZENECA, MERCK  
AND NVIDIA

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INTERNAL PIPELINE OF POTENTIALLY  
'**BEST-IN-CLASS**' & '**FIRST-IN-CLASS**'  
ASSET PROGRAMS FOCUSED ON  
CYTOKINE BIOLOGY

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LEAD ASSET ABS-101, A DIFFERENTIATED  
TL1A ANTIBODY DESIGNED USING  
**ABSCI'S DE NOVO AI** ADVANCING  
TOWARDS CLINIC IN **EARLY 2025**

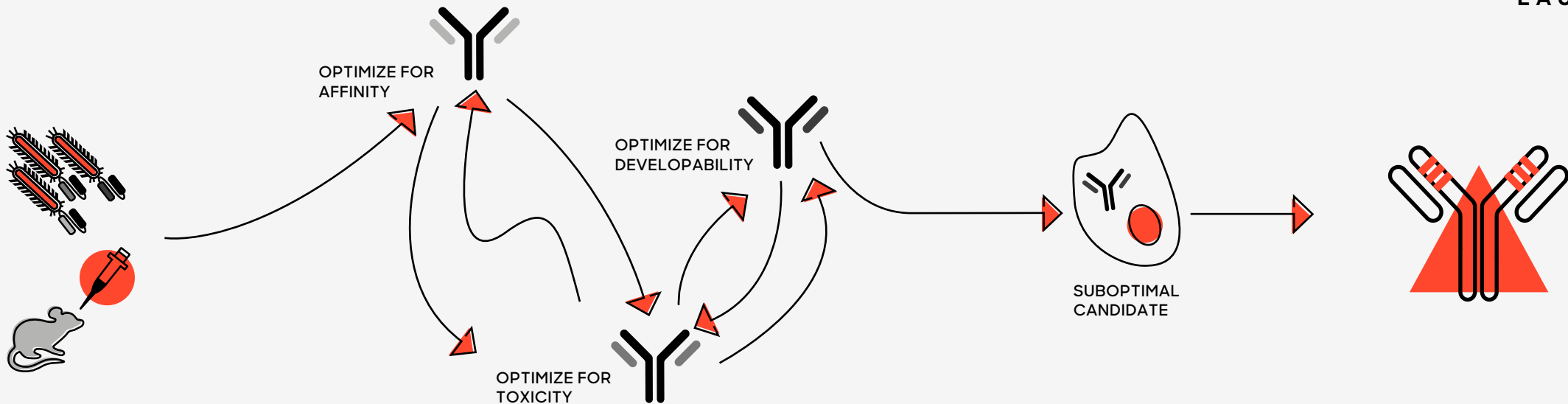
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# THE PROBLEM – CURRENT NEED FOR GENERATIVE AI

## The Drug Discovery Paradigm is Ripe for **Disruption**

5.5 YEARS FROM  
DISCOVERY TO IND

<5% SUCCESS RATE  
FROM DISCOVERY TO  
LAUNCH



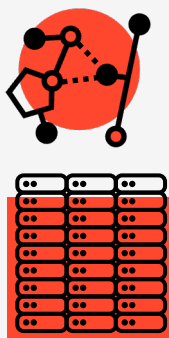
LONG ITERATIVE PROCESS RESULTING IN DRUG CANDIDATES WITH SUBOPTIMAL ATTRIBUTES  
LIMITED CONTROL OF ATTRIBUTES OF THERAPEUTICS  
NO ABILITY TO SELECT EPITOPE

# WHY HASN'T GENERATIVE AI TRANSFORMED BIOLOGIC DRUG DISCOVERY?

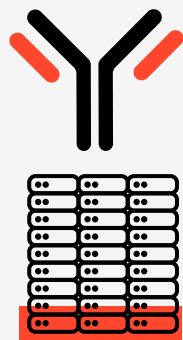
## Unlocking the Potential of Generative AI in Biology Requires Scalable Biological Data

SMALL MOLECULE

v. BIOLOGIC

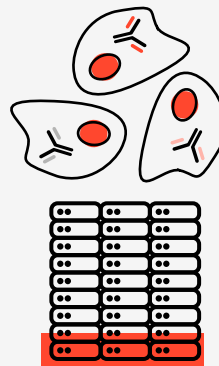


Extensive Libraries



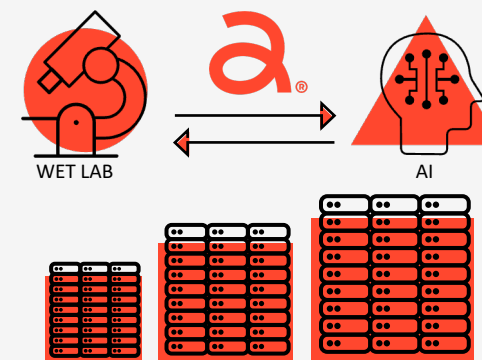
Limited Public Data and technologies to scale data

BIOLOGICS REQUIRE LIVING ORGANISMS TO PRODUCE DRUG VARIANTS FOR TESTING



Consistent and accurate data is limited

UNLOCKING THE POTENTIAL OF GENERATIVE AI IN BIOLOGY...



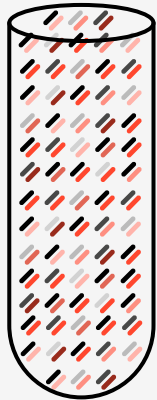
...requires generating scalable biological data

## THE SOLUTION

# Absci is Solving the Problem of Scalable Biological Data to Enable True Generative AI for Biology

Absci's *E. coli* SoluPro cell line generates billions of cells, expressing proteins of interest

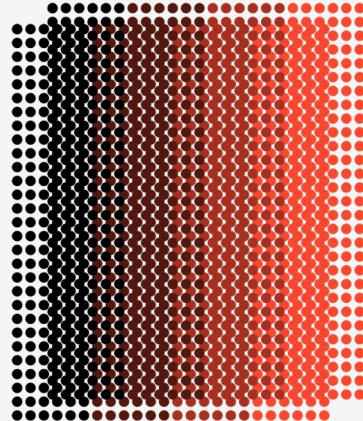
### SOLUPRO™ CELL LINE



Billions of cells, expressing proteins of interest

Absci's ACE Assay™ technology generates data at >4,000x the throughput of traditional HT assays

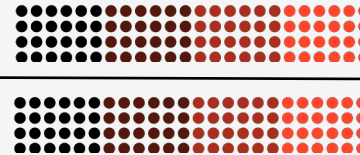
### ACE ASSAY™



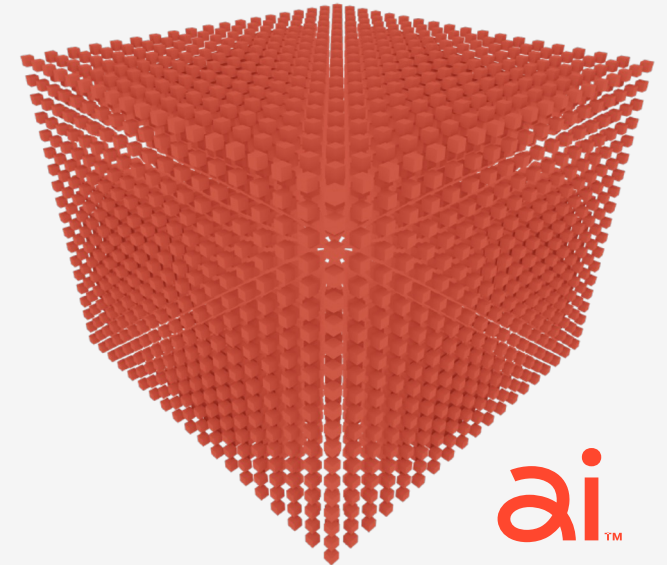
Millions of antibody sequence variants + billions of parameters in weeks

Massive and Growing Training Data Sets

### PUBLIC DATA SETS



### PROPRIETARY ASSAYS



# Integrated Drug Creation™ Platform: Lab-in-a-Loop + Proprietary Data + Advanced Generative AI Models

## DATA TO TRAIN

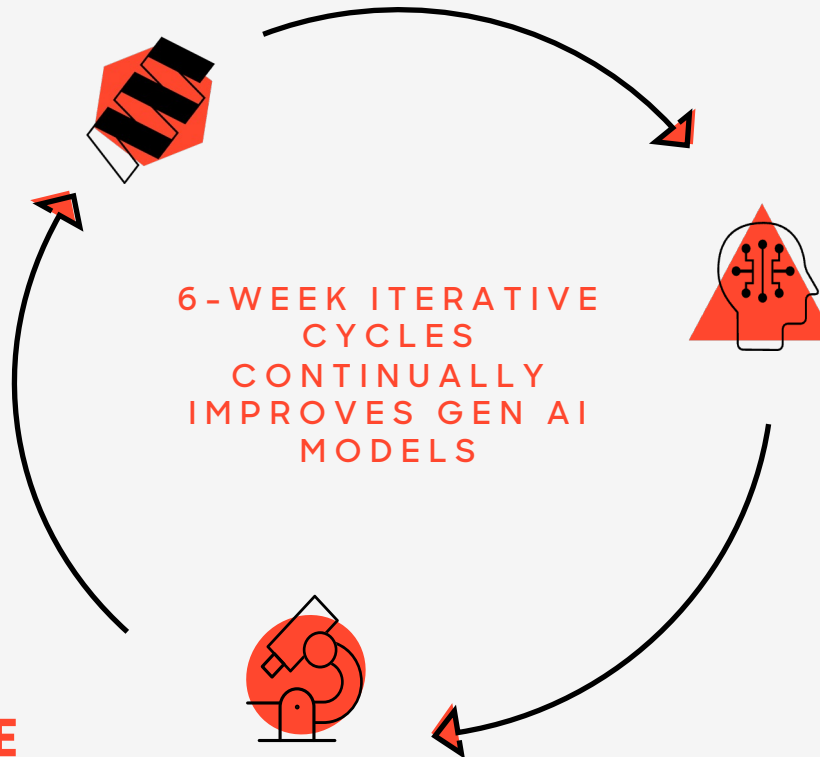
Wet lab assays generate massive quantities of high-quality data for generative AI model training

- ACE Assay™ measures binding affinity and target specificity of millions of antibody sequences in a single week.
- ACE Assay™ data is combined with additional proprietary generated data and public data sets.

## WET LAB TO VALIDATE

77,000 sq ft+ lab to validate AI-generated designs

- Assess binding affinity and target specificity for up to 3 million of ranked antibody sequences from billions of AI-designed antibodies.
- Lower throughput assays confirm other predicted properties for lead designs:
  - Potency
  - Self-association
  - Polyreactivity
  - FcRn recycling
  - Hydrophobicity
  - Solubility
  - Thermostability
  - Resistance to stress

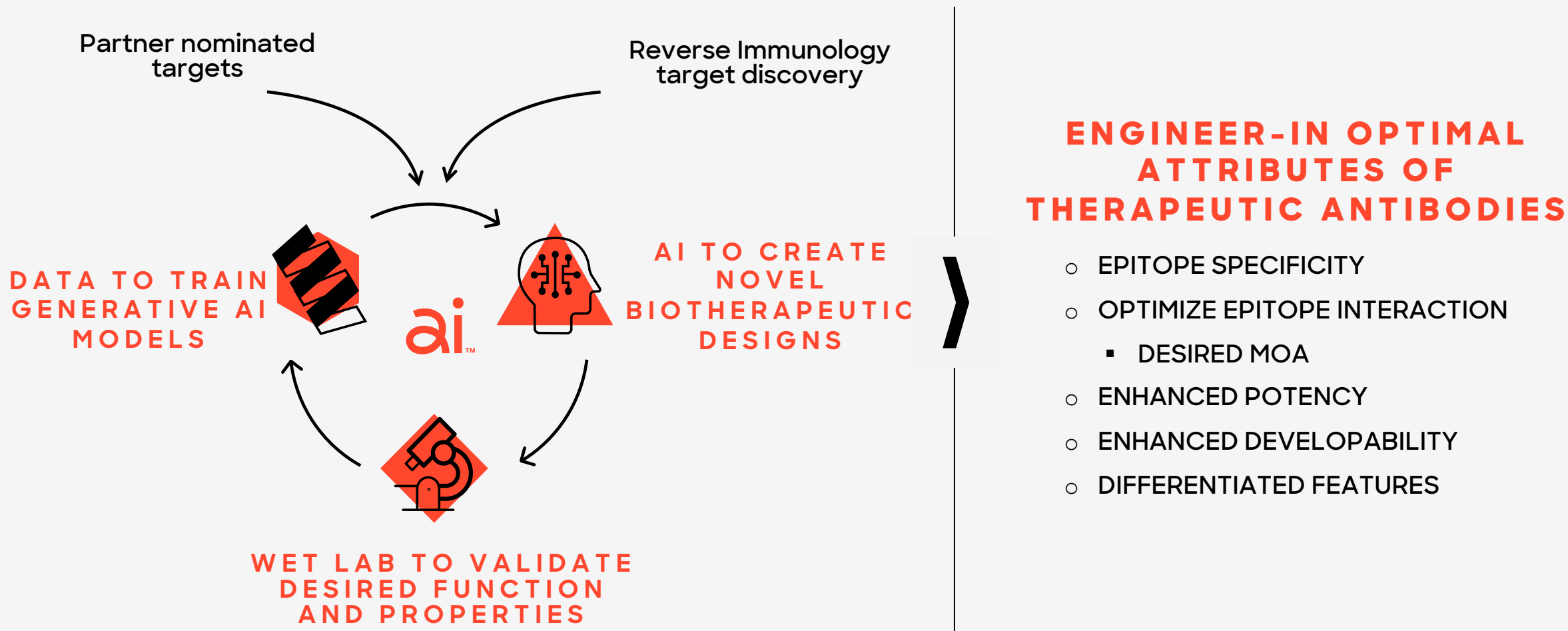


## AI TO CREATE

Advanced generative AI models used to create antibodies and next-gen biologics through *de novo* design and optimization

- *De novo* antibody creation is prompted with antigen structure, epitope location, and framework sequences and returns designed CDRs
- Proprietary generative AI models use architectural innovations to access a massive sequence search space, up to  $\sim 20^{55}$ , to design antibody-antigen complex structures and sequences *in silico*

# Absci's Integrated Drug Creation™ Platform to Engineer Optimal Drug Attributes





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



**\* MAR 2023 - UPDATED JAN 2024**  
Functional **wet-lab validation** of novel antibodies designed using **zero-shot** generative AI - demonstrating the potential to go from target to therapeutic antibody at a click of a button  
(Shanehsazzadeh et al. 2024)



**DEC 2023**  
*in vitro* validated antibody design against **multiple therapeutic antigens** using generative inverse folding model  
(Shanehsazzadeh et al. 2023)



**AUG 2022**  
Used artificial intelligence to **simultaneously optimize** multiple parameters important to drug discovery and development  
(Bachas et al. 2022)



# Leveraging Generative AI Capabilities to Access Novel Biology and Rapidly Design Therapeutics with Best-in-Class Properties

## Design of therapeutic antibodies to novel and challenging targets

- Novel targets including GPCRs and ion channels

## Rapid design of fast follower therapeutic antibodies to validated targets

- 12-14 months to Drug Candidate
- Best-in-class Potential

DE NOVO AI  
FOUNDATION  
MODEL

- ✓ Epitope specificity
- ✓ Global epitope landscaping to identify epitopes with desired MoA
- ✓ Local epitope landscaping to identify desired epitope interactions for potentially improved potency and MoA

AI LEAD  
OPTIMIZATION  
MODEL

- ✓ Local epitope interface evolution to improve desired epitope interactions for potentially improved potency and desired MoA
- ✓ Multi-parametric developability optimization

AI DESIGNED  
FEATURES

Novel Features:

- ✓ pH depending binding
- ✓ Half-life extension
- ✓ Multi-valency / multiple targets

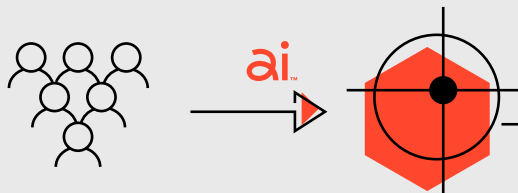
# Integrated Drug Creation™ Platform

Leveraging AI Throughout the **End-to-End** Drug Discovery Process

## TARGET DISCOVERY WITH NOVEL APPROACHES



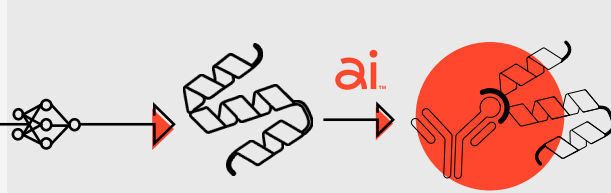
*Reverse Immunology for target discovery*



## AI-GUIDED ANTIBODY DRUG CREATION



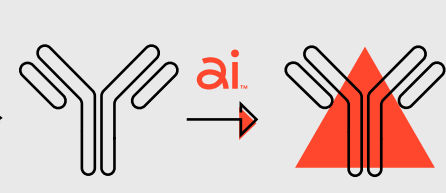
*De novo antibodies designed by AI*



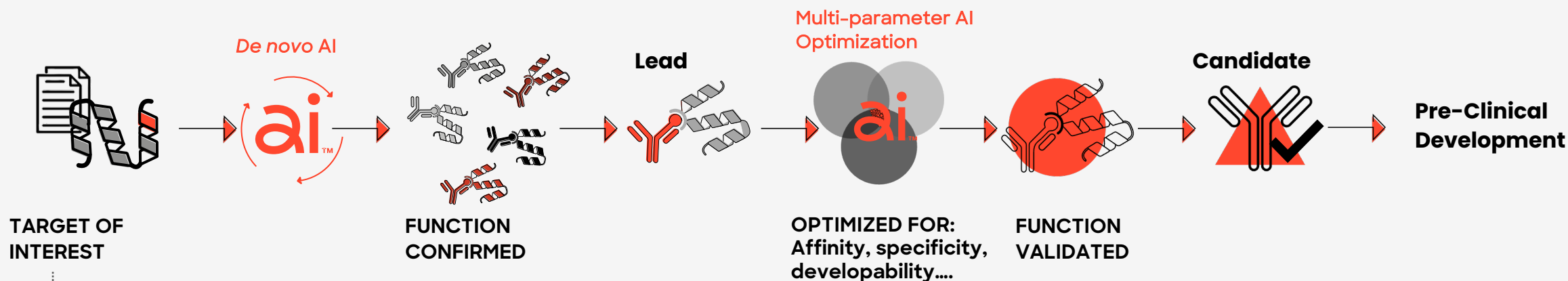
## AI-GUIDED LEAD OPTIMIZATION



*Multi-parameteric optimized antibodies*



# Generative AI Drug Creation™ workflow



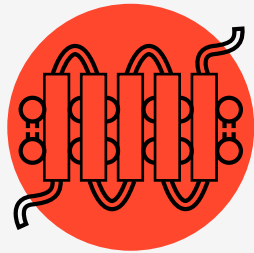
Absci works with its partners to set the goals of partnership programs:

- (1) Target antigen
- (2) Target antigen epitope(s) if known OR global epitope landscaping to identify optimal epitope / MOA
- (3) Drug modality, e.g. mAb, bi-specific, fusion protein
- (4) Target TPP parameters

## VALUE DRIVERS

# Platform Enables the Potential to Deliver Differentiated Biologics, Faster at Lower Cost

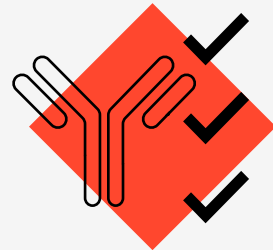
### ACCESS NOVEL DISEASE BIOLOGY



Ability to address elusive drug targets, e.g. GPCRs, Ion Channels

ENABLING FIRST-IN-CLASS

### INCREASED PROBABILITY OF SUCCESS



Superior Drug Attributes and Multidimensional optimization creates higher quality biologics

ENABLING BEST IN CLASS & HIGHER PROGRAM NPVS

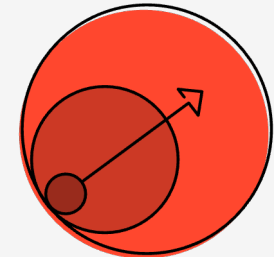
### REDUCED TIME & COST TO CLINIC



2 years and \$14-16M from Target to IND; significant reduction compared to industry estimates

FASTER TIME TO IND

### EXPANDED INTELLECTUAL PROPERTY SPACE



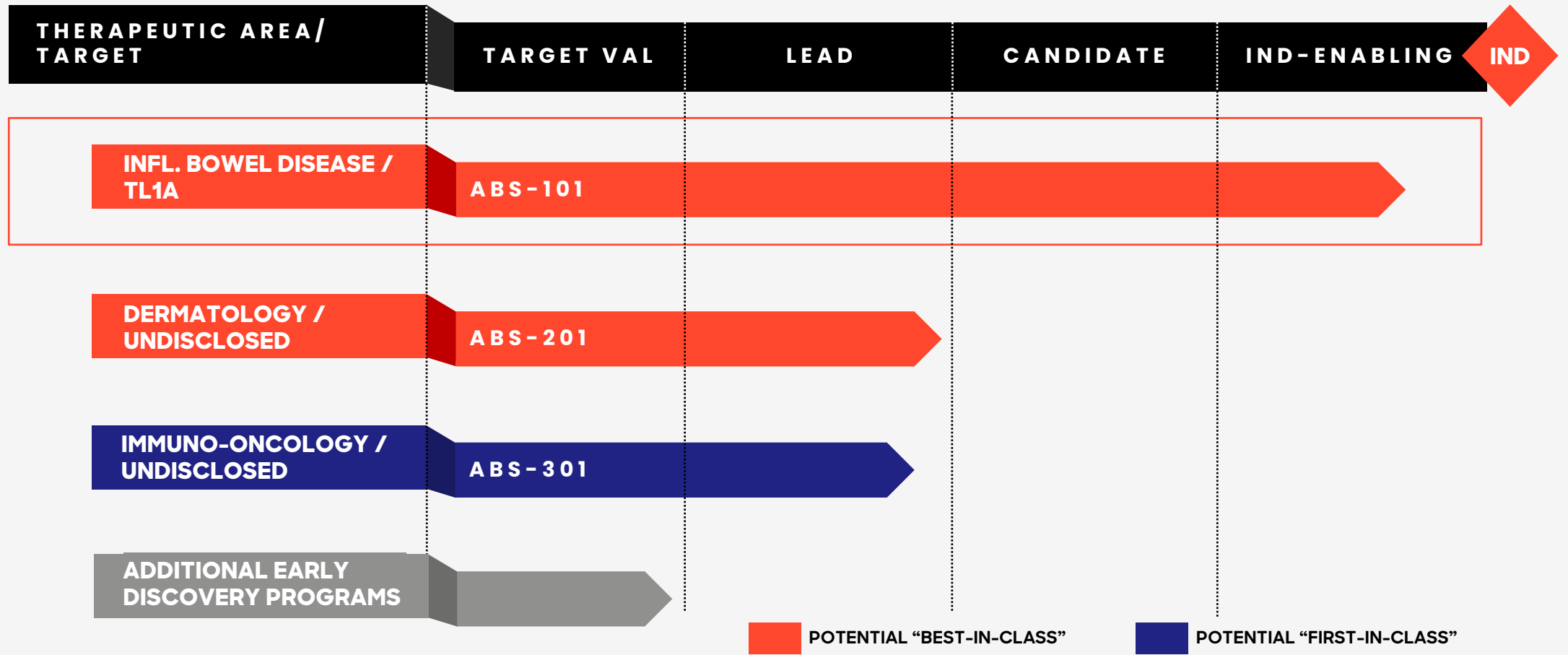
Generates broader IP for First-in-Class therapies and finds new IP for Best-in-Class therapies

ENHANCED IP PROTECTION

# PIPELINE HIGHLIGHTS

## Internal Pipeline of Potential First-in-Class and Best-in-Class Assets

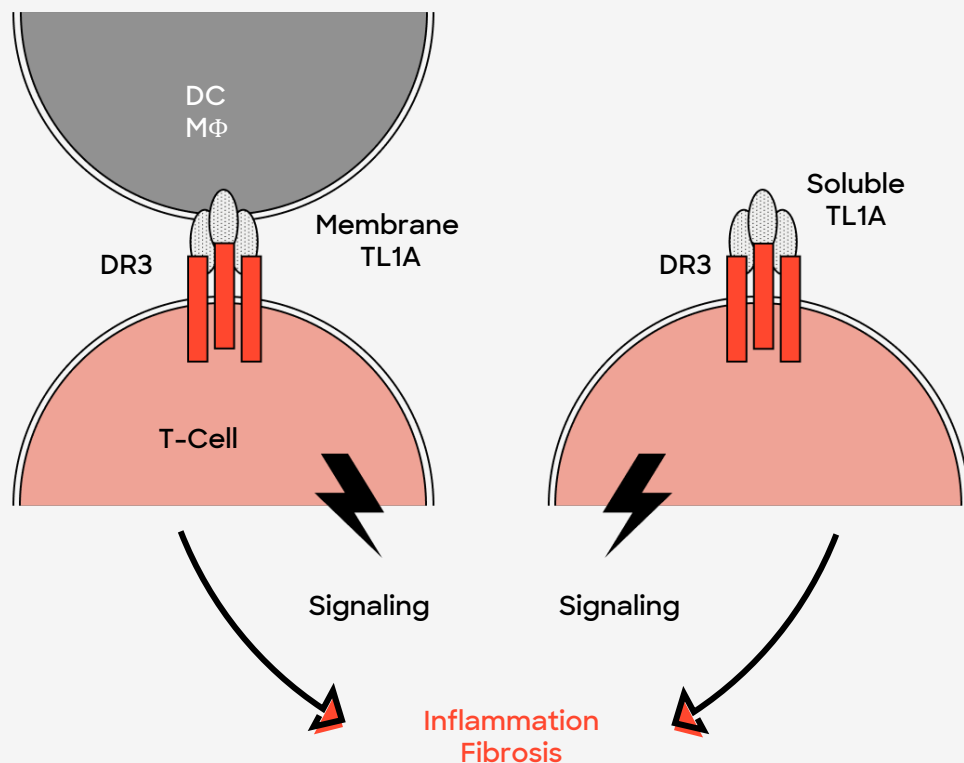
*Focus on cytokine biology - first frontier of AI-driven disruption*



# ABS-101 TL1A DATA HIGHLIGHTS

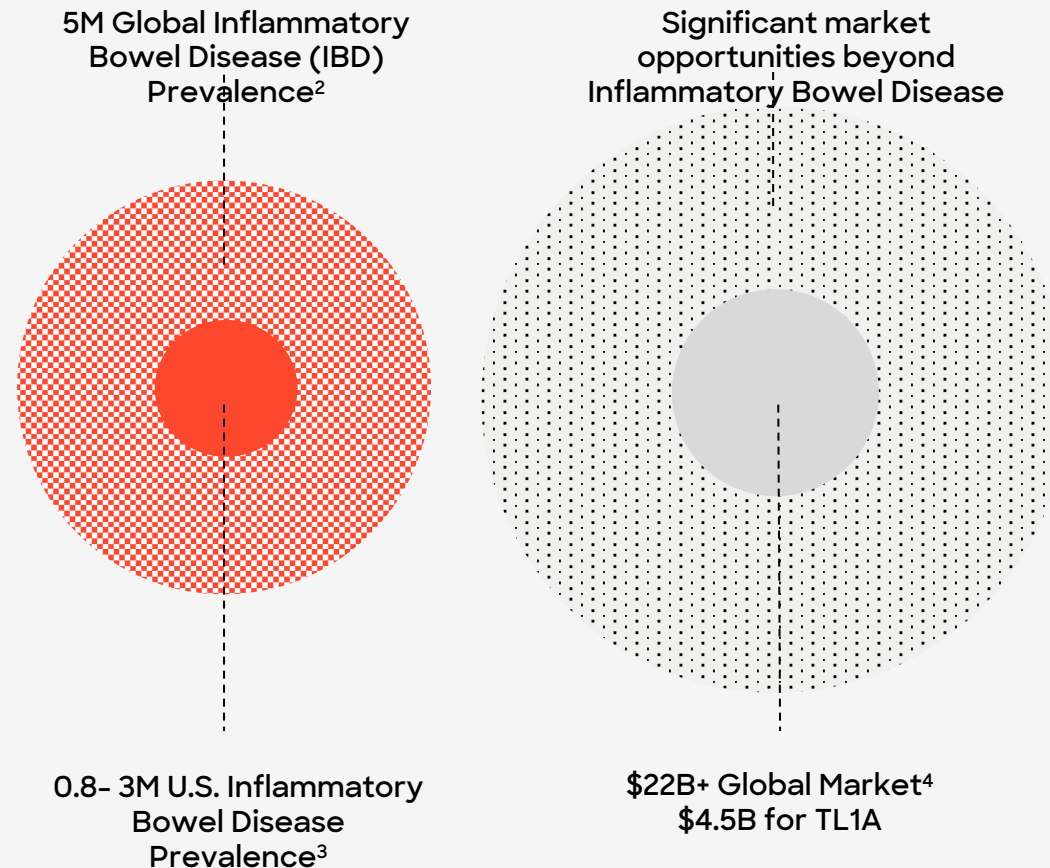
## Clinically Validated Mechanism of Action in Large Underserved Market

**TL1A: DR3 SIGNALING CLINICALLY SHOWN TO INDUCE PRO-INFLAMMATORY RESPONSES<sup>1</sup>**



<sup>1</sup> Adapted from Takedatsu 2008 doi: [10.1053/j.gastro.2008.04.037](https://doi.org/10.1053/j.gastro.2008.04.037)

**POTENTIAL RELEVANCE IN WIDE RANGE OF AUTOIMMUNE INDICATIONS**



<sup>2</sup> Wang 2023 <http://dx.doi.org/10.1136/bmjopen-2022-065186>

<sup>3</sup> Dahlhamer, James M., et al. "Prevalence of inflammatory bowel disease among adults aged ≥ 18 years—United States, 2015." *Morbidity and mortality weekly report* 65.42 (2016): 1166-1169.

<sup>4</sup> Evaluate Pharma Oct 2023.

## Potential Best-in-Class TL1A mAb Designed using Generative AI



### **DE NOVO AI-DESIGNED AND AI-OPTIMIZED**

- Target to promising candidates in just over 1 year

### **SUPERIOR PRE-CLINICAL PROFILE AND POTENTIAL FOR SUPERIOR CLINICAL PROFILE**

- High Affinity & Potency
  - High affinity to both the TL1A trimer and monomers
- Extended Half-life & Longer Dosing Intervals
  - Q8W to once quarterly
- Low immunogenicity
- Sub-Q Dosing
  - High bioavailability
- Favorable Developability

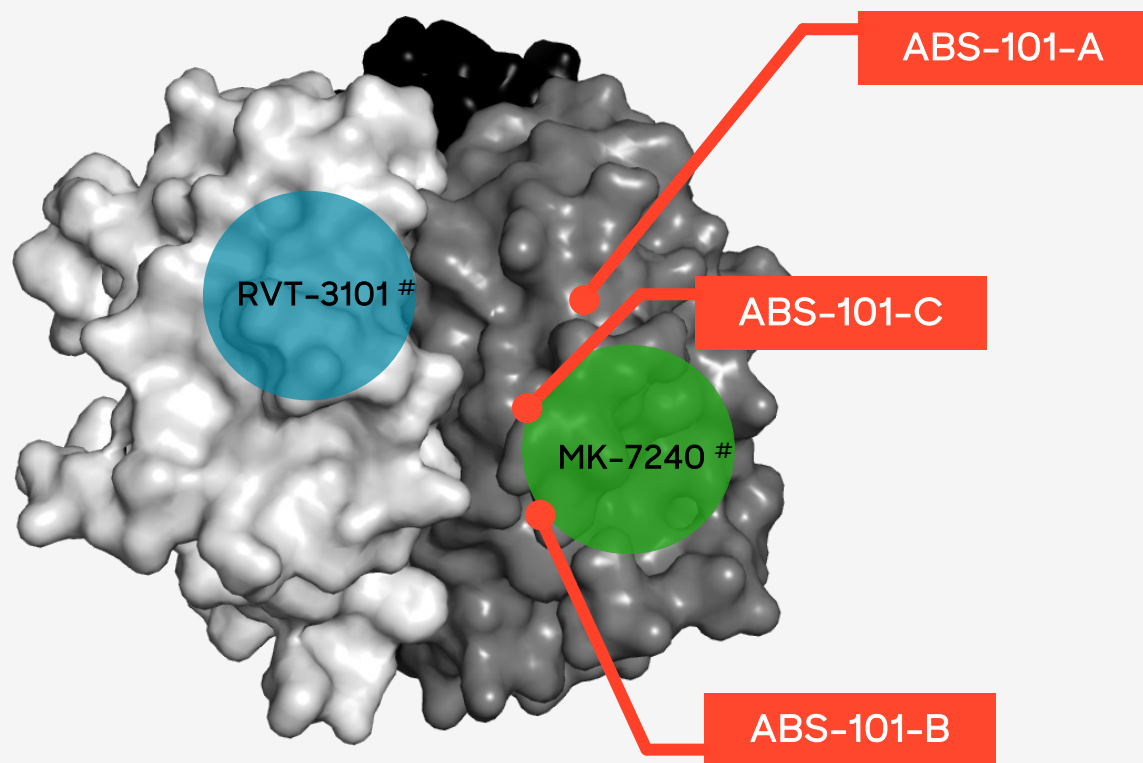
### **DIFFERENTIATED INTELLECTUAL PROPERTY**



## ABS-101 TL1A DATA HIGHLIGHTS

# AI Platform Designed Leads Span Diverse Set of Epitopes Leading to IP Differentiation and Superior Preclinical Profile

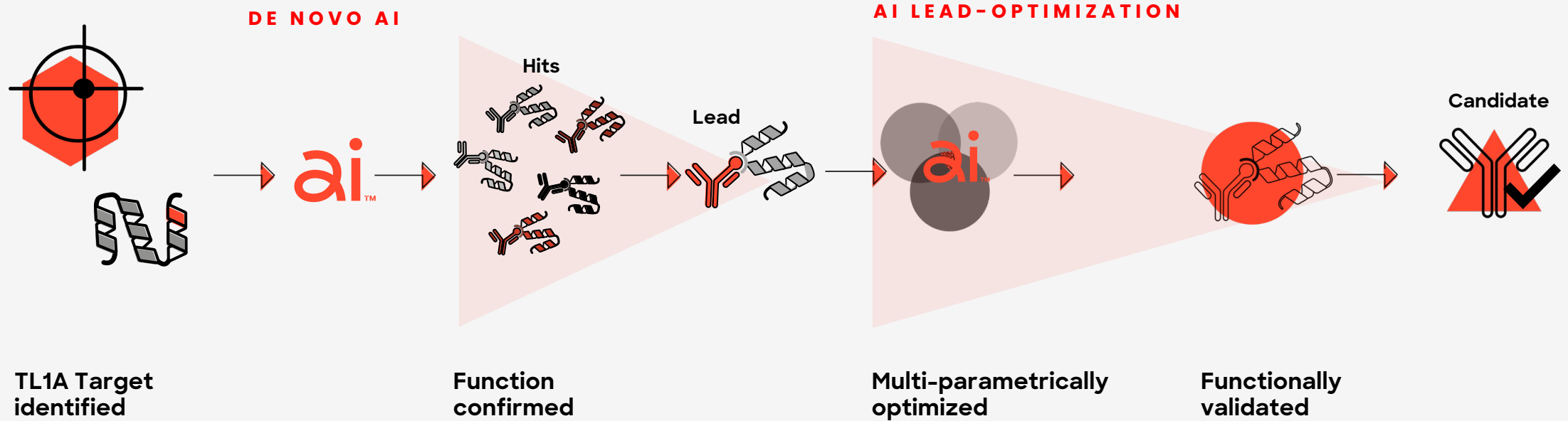
Epitope bins on TL1A\*



- ▶ Absci selected hypothesized immuno-privileged epitope for de novo model. Epitope also selected to enable both TL1A monomer and trimer binding
- ▶ De novo model performed local epitope landscaping
- ▶ AI Lead Optimization model performed further local epitope evolution
- ▶ 3 lead candidates identified with novel epitope interactions → improved affinity and potency

\* Epitope binning by BLI competition experiment  
# Estimated performance of clinical competitor reagent generated for comparison

# Potential Best-in-Class TL1A mAb Designed using Generative AI

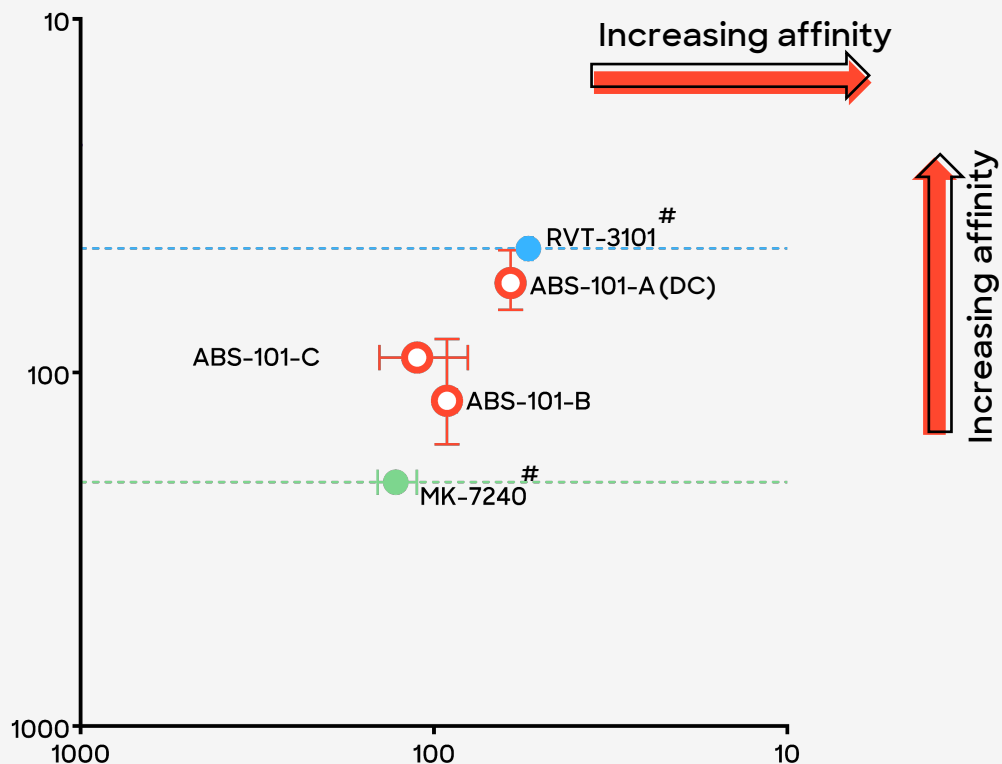


# ABS-101 TL1A DATA HIGHLIGHTS

## AI Platform Designed Advanced Leads with High Affinity and Superior Potency

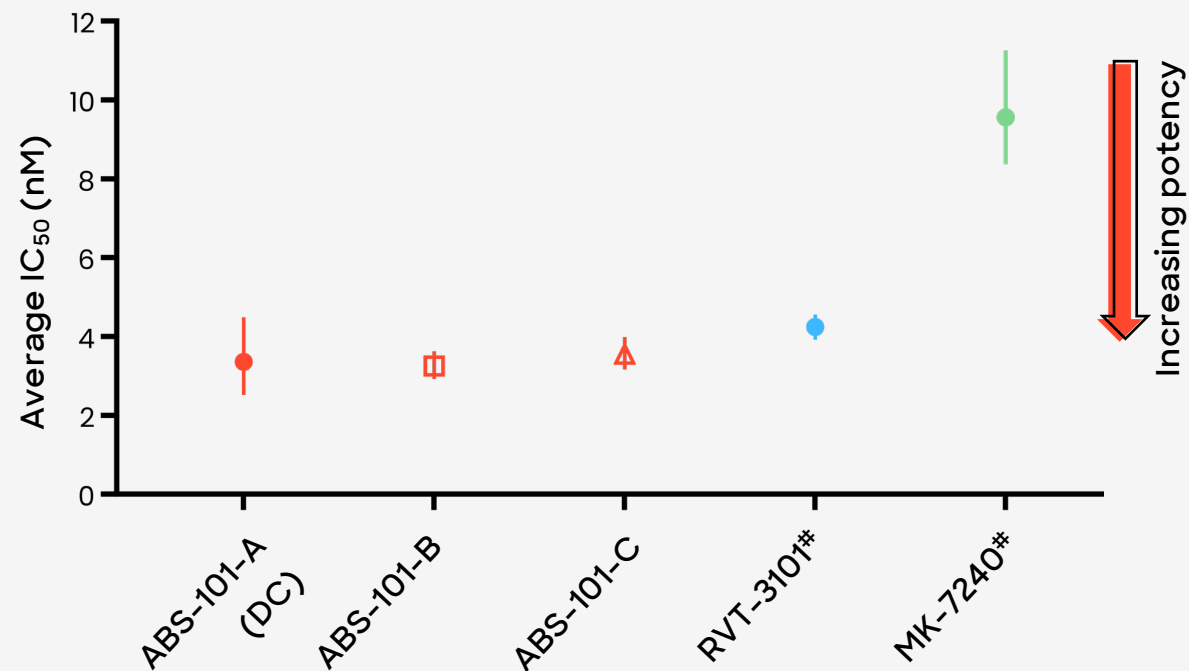
### HIGH AFFINITY mABs WITH PRESERVED CROSS-REACTIVITY

AFFINITY BY SURFACE PLASMON RESONANCE (SPR)



### AI-OPTIMIZED LOW pM AFFINITY TRANSLATES TO SUPERIOR OR EQUIVALENT POTENCY

APOPTOSIS INHIBITION ASSAY IN TF-1 CELLS

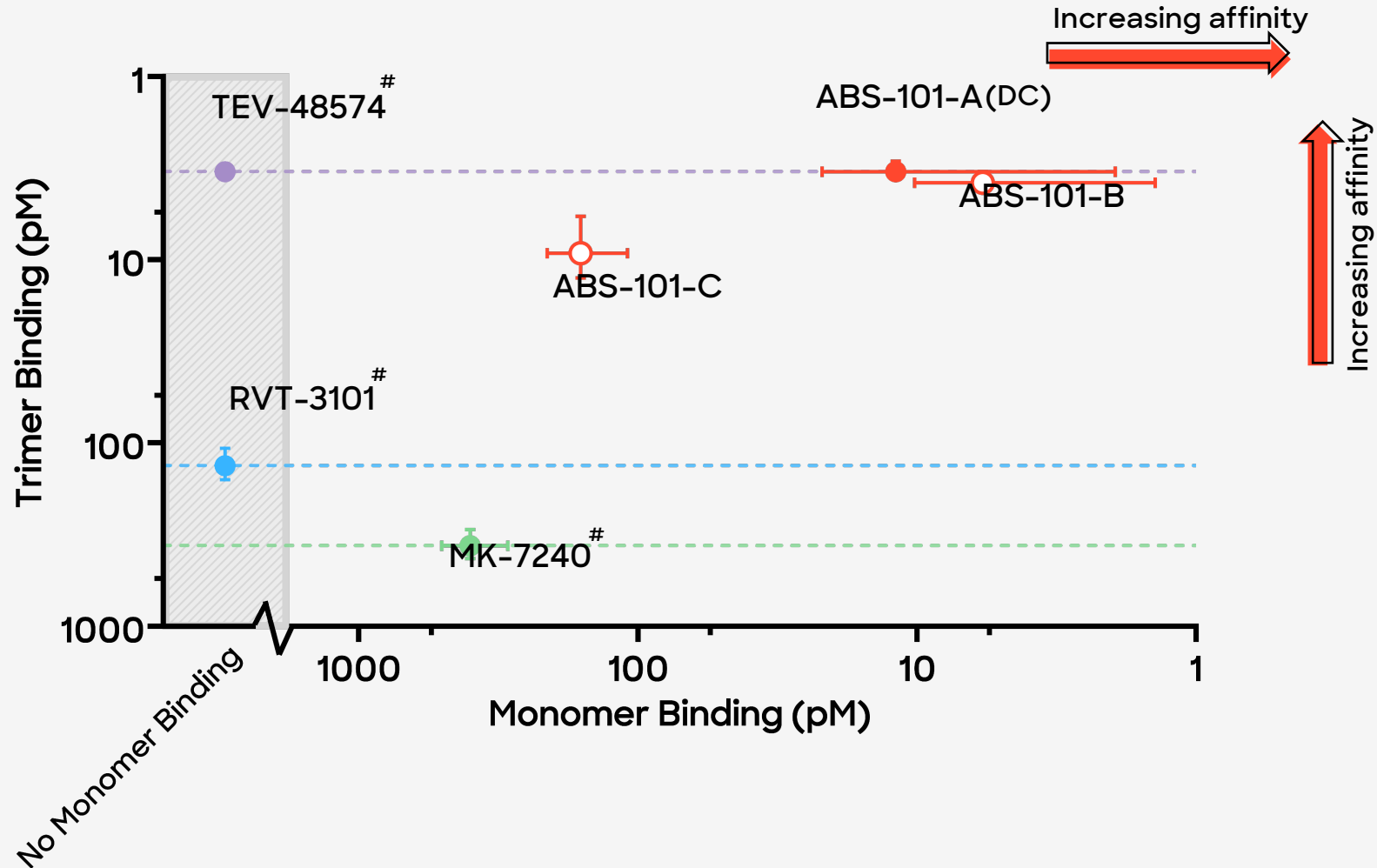


#Estimated performance of a putative clinical competitor molecule generated for in house comparison.

## ABS-101 TL1A DATA HIGHLIGHTS

# AI Epitope Selection Enables High Affinity to Both the TL1A Monomer and Trimer

## EPITOPE SELECTED ENABLED HIGH AFFINITY BINDING TO BOTH THE TL1A MONOMER AND TRIMER



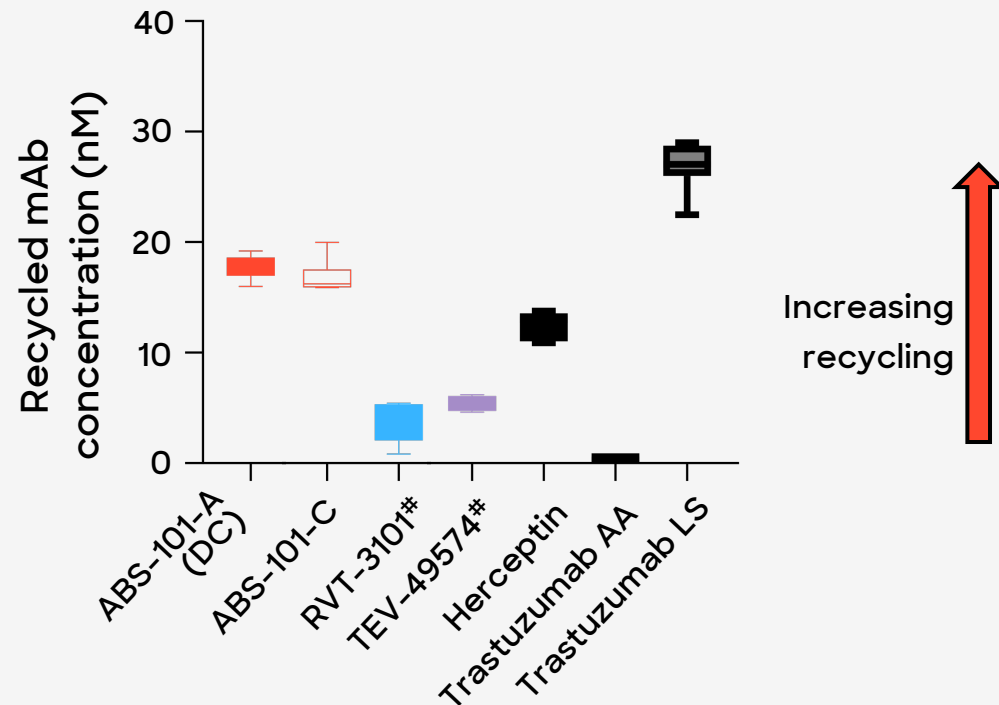
#Estimated performance of clinical competitor reagent generated for in-house comparison.

<sup>1</sup> We used BLI values for comparing monomer and trimer binding and not as absolute values due to sensitivity limits for the instrument at high affinity. SPR-based absolute affinities reported in the previous slide are considered more accurate. For samples, such as RVT-3101#, the observed difference in affinities measured by SPR and BLI are within the error expected for picomolar binders by BLI.

# Favorable in vitro Profile and PK Profile for Longer Dosing Intervals

▶ Increased recycling in *in vitro* FcRn Assay<sup>1</sup>

▶ Extended half-life in vitro compared to competitors<sup>#</sup>

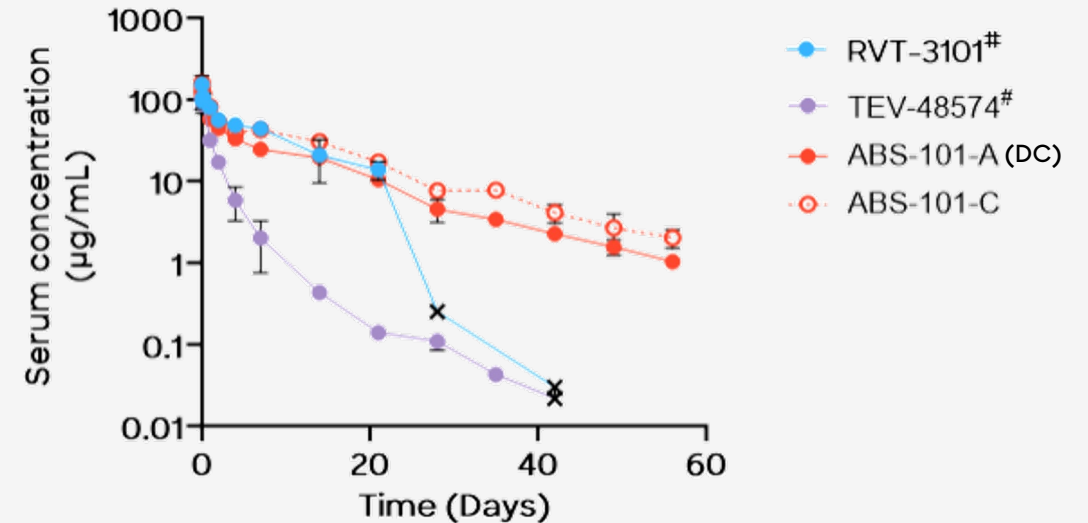


<sup>1</sup> Cell-based FcRn recycling assay in HMEC-1 cells. Grevys 2018

<sup>2</sup> Homozygous hFcRn Tg32 mouse model, single dose i.v.

<sup>#</sup>Estimated performance of a putative clinical competitor molecule generated for in house comparison

▶ PK data in Tg32 mice show lead candidates with extended half-life *in vivo* relative to RVT-3101<sup>#</sup> and TEV-48574<sup>#</sup>

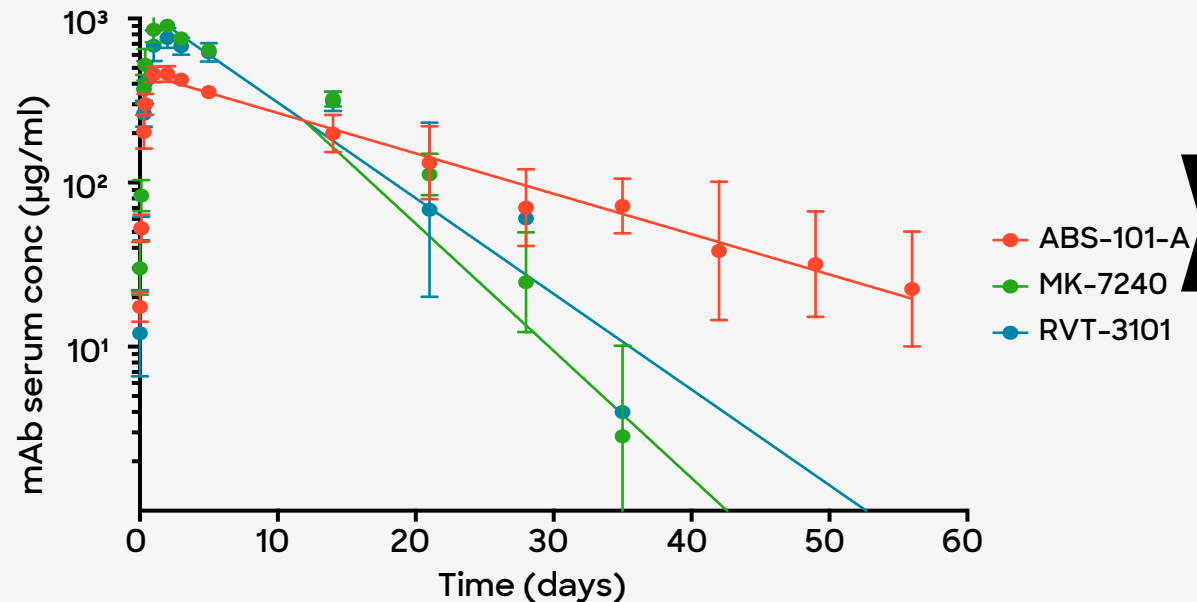


PK Parameters	ABS-101-A	ABS-101-C	RVT-3101 <sup>#</sup>	TEV-48574 <sup>#</sup>
t <sub>1/2</sub> (d)	12	14	9	5
CL (mL/hr/kg)	0.61	0.39	0.52	3.26
AUC <sub>0-∞</sub> (µg.d/mL)	688	1060	805	128
V <sub>ss</sub> (mL/kg)	198	148	121	197

## ABS-101 TLIA DATA HIGHLIGHTS

# 2-3x Extended Half-life in Non-Human Primates (NHPs) Compared to Clinical Competitors

### 2-3X LONGER HALF-LIFE IN NHPs COMPARED TO CLINICAL COMPETITORS



### 2-3X EXTENDED HALF-LIFE IN NHPs SUPPORTS POTENTIAL LONGER DOSING INTERVALS

- ▶ Extended half-life of 2-3-fold over clinical competitors to support Q8W-Q12W dosing interval.
- ▶ ABS-101 shows enhanced biodistribution in NHPs, compared to antibodies in clinical development. Potential therapeutic advantage due to faster tissue penetration, likely without the need for a loading dose.

### HIGH CONCENTRATION FORMULATION ENABLES SUBCUTANEOUS INJECTION

- ▶ Successful development of high-concentration drug substance formulation at 200mg/mL to enable subcutaneous injection.

## ABS-101 TL1A DATA HIGHLIGHTS

# AI Platform Designed ABS-101 Aims for Optimal Therapeutic Profile

ATTRIBUTE	ABS-101 PROGRAM*	MERCK (PROMETHEUS) MK-7240	ROCHE (ROIVANT) RVT-3101	SANOFI (TEVA) TEV-48574
High affinity/potency	✓	✗	✓	✓
Monomer and trimer TL1A binding	✓	✓	✗	✗
Low Immunogenicity**	✓	✓ <sup>1</sup>	✗ <sup>1,3</sup>	—
High Bioavailability	✓	✓ <sup>1</sup>	✗ <sup>1,4</sup>	—
Sub-Q injection	✓	✓ <sup>5</sup>	✓ <sup>6</sup>	✗ <sup>7</sup>
Q8W to once quarterly dosing	✓	✗ <sup>1,2</sup>	✗ <sup>1,2</sup>	✗ <sup>8</sup>

\*ABS-101 parameters projected from *in silico*, *in vitro*, and *in vivo* (NHP) metrics and modeled exposure with ½-life extension.

\*\* Low score by *in silico* immunogenicity metrics and low results in *ex vivo* T-cell assay.

<sup>1</sup> Based on Phase 2 data

<sup>2</sup> Once monthly dosing regimen

<sup>3</sup> 82% of Ph2a participants developed ADA, likely due to formation of large immune complexes. Danese et al. 2021 <https://doi.org/10.1016/j.cgh.2021.06.011>

<sup>4</sup> 45% BA at 100 mg/mL based on Ph2 data

<sup>5</sup> High dose intravenous dose, followed by high dose subcutaneous administration, based on Phase 3 protocol. Unknown if injection or infusion. NCT06052059, NCT06430801

<sup>6</sup> Expected commercial form factor

<sup>7</sup> Administered by subcutaneous infusion, not injection, based on Phase 2 protocol, NCT05499130, NCT05668013

<sup>8</sup> Based on Phase 2b protocol, NCT05668013

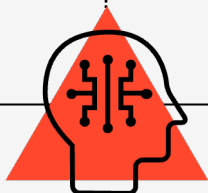
## ABS-101 TL1A DATA HIGHLIGHTS

# Projected Timeline to Potential Best-in-Class Molecule

● **JAN 2024**

AI-Designed Advanced Leads have Demonstrated:

- ✓ High Affinity
- ✓ High Potency
- ✓ Long Half-Life
- ✓ Favorable Manufacturability



● **INITIATED FEB '24**

IND-enabling studies to evaluate

- ✓ Development candidate selected Feb '24
- ✓ Sub-Q formulation
- ✓ Favorable PK and long Hal-Life
- ✓ High Bioavailability in NHPs
- Low ADA
- High Tolerability (low tox)



● **1H25**

Initiating Phase 1 Trial



● **2H25**

Phase 1 Interim Data Readout





## RECENT PARTNERSHIPS

# Over \$900M + Royalties of Deal Value in H2 2023



“This collaboration is an exciting opportunity to utilize Absci's de novo AI antibody creation platform to design a potential new antibody therapy in oncology.”

**DR. PUJA SAPRA**

AstraZeneca, SVP, Biologics Engineering & Oncology Targeted Delivery

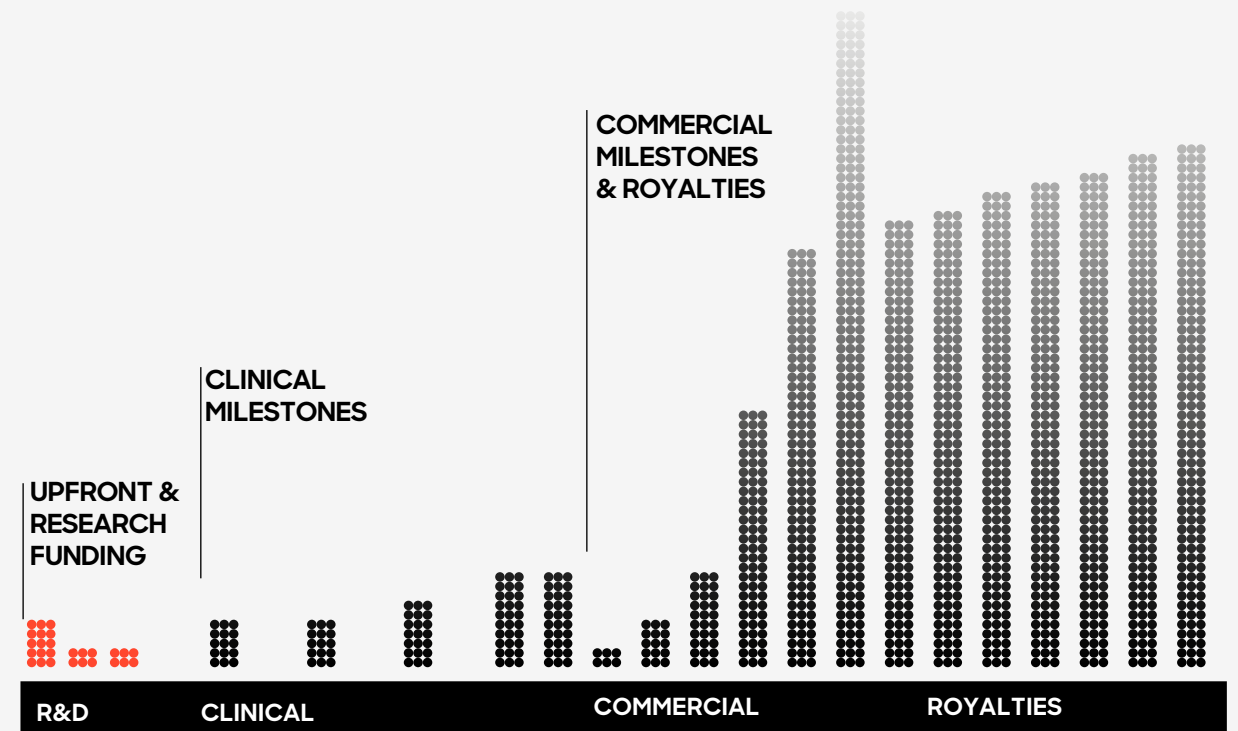


“Almirall chose Absci because their de novo platform brings truly novel innovation in solving the industry's most challenging targets facing high unmet medical need.”

**DR. KARL ZIEGELBAUER**

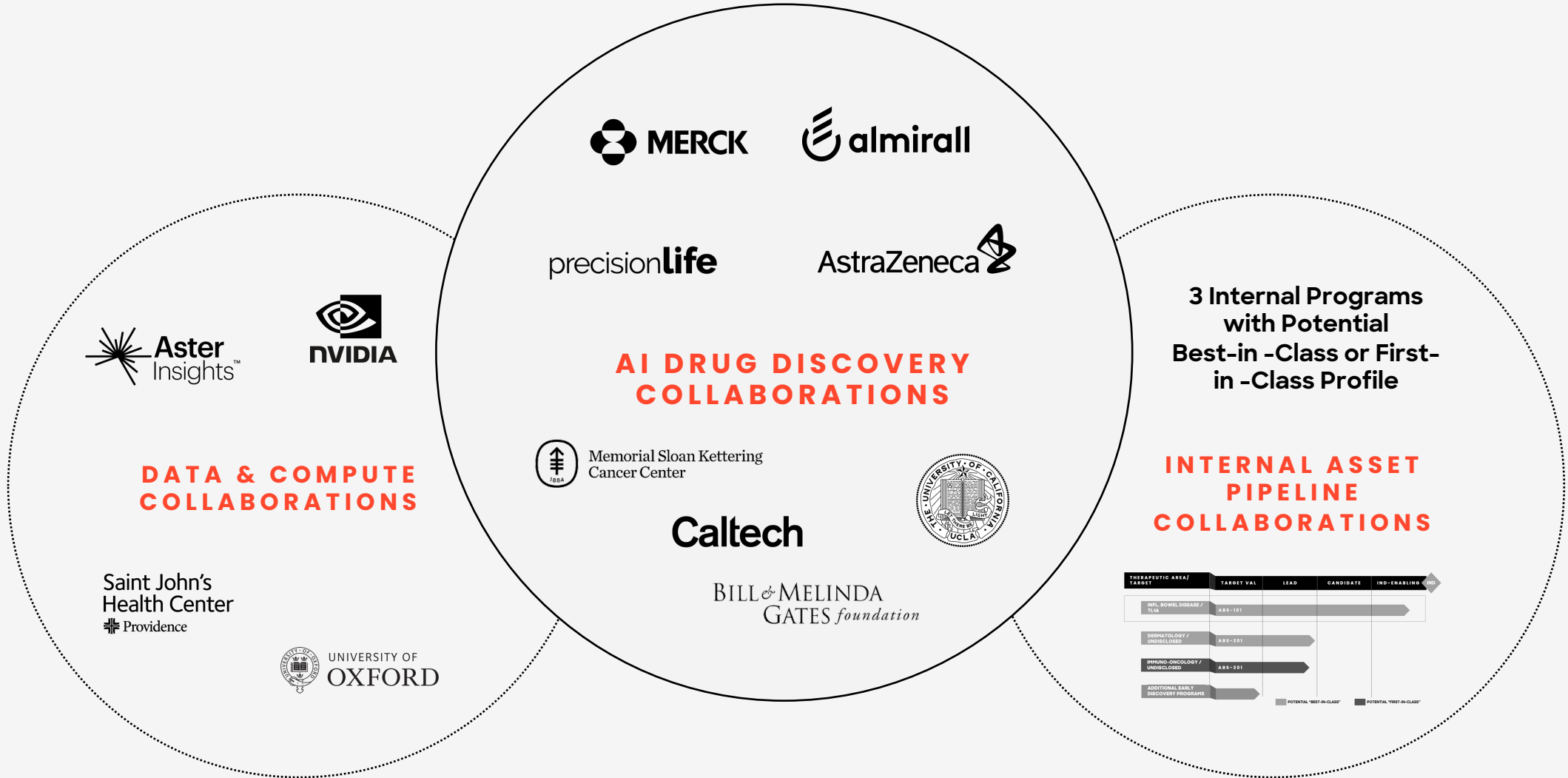
Almirall, Chief Scientific Officer and EVP of Research & Development

## ILLUSTRATIVE ECONOMIC STRUCTURE OF A SUCCESSFUL DRUG DISCOVERY PARTNERSHIP



**PARTNERSHIPS**

# Driving Growth Through Industry-Leading Collaborations



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# WORLD CLASS TEAM

## Leadership Team of Innovators Across AI and Biotech to Transform Drug Discovery

### LEADERSHIP TEAM



SEAN MCCLAIN  
Founder, CEO & Director



ANDREAS BUSCH, PHD  
Chief Innovation Officer



ZACH JONASSON, PHD  
Chief Financial Officer  
& Chief Business Officer



KARIN WIERINCK  
Chief People Officer



SHELBY WALKER, JD  
Chief Legal Officer



### BOARD OF DIRECTORS



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Former CEO,  
Royal Phillips



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Illumina



SIR MENE PANGALOS, PHD  
Former EVP R&D  
AstraZeneca



AMARO TAYLOR-WEINER, PHD  
SVP, Chief AI Officer



CHRISTIAN STEGMANN, PHD  
SVP, Drug Creation



CHRISTINE LEMKE, DVM  
SVP, Portfolio & Growth  
Strategy



JENS PLASSMEIER, PHD  
SVP, Biologics Discovery  
Technologies



PENELOPE  
Chief Morale Officer



AMRIT NAGPAL  
Managing Director,  
Redmile Group



DAN RABINOVITS, J  
Vice President  
Connectivity, Meta



JOSEPH SIROSH, PHD  
Former CTO, Compass  
VP, Amazon & Microsoft



## WELL-POSITIONED TO DELIVER

# Absci's Talent and Infrastructure for Better Biologics Faster, at Lower Cost



>160

Unlimiters with deep experience in AI, drug discovery, immunology, and synthetic biology

Leading AI team with expertise from:



Google



Microsoft Research



OpenAI



Stanford University

Biologics drug discovery expertise from:



AstraZeneca



Shire



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

>\$520M

Capital raised to date

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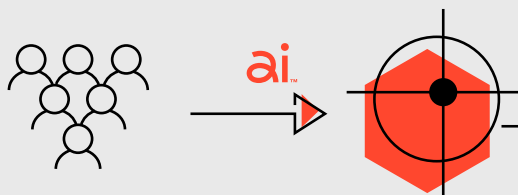
# Integrated Drug Creation™ Platform

Leveraging AI Throughout the **End-to-End** Drug Discovery Process

## TARGET DISCOVERY WITH NOVEL APPROACHES



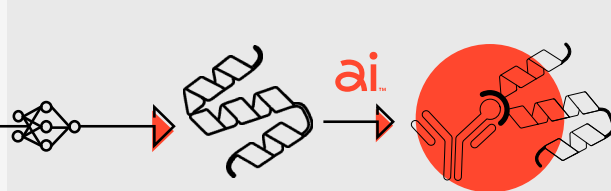
*Reverse Immunology for target discovery*



## AI-GUIDED ANTIBODY DRUG CREATION



*De novo antibodies designed by AI*



## AI-GUIDED LEAD OPTIMIZATION



*Multi-parameteric optimized antibodies*



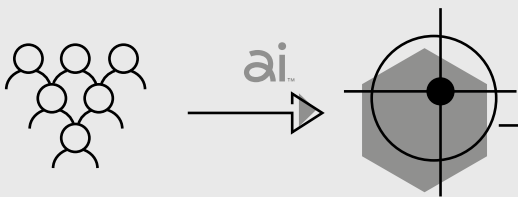
# de novo Designed Antibodies

de novo antibody design using generative AI

## TARGET DISCOVERY WITH NOVEL APPROACHES



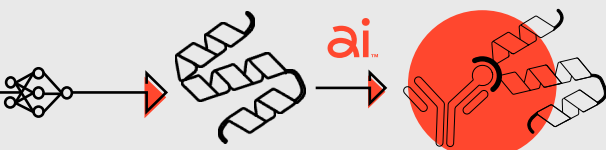
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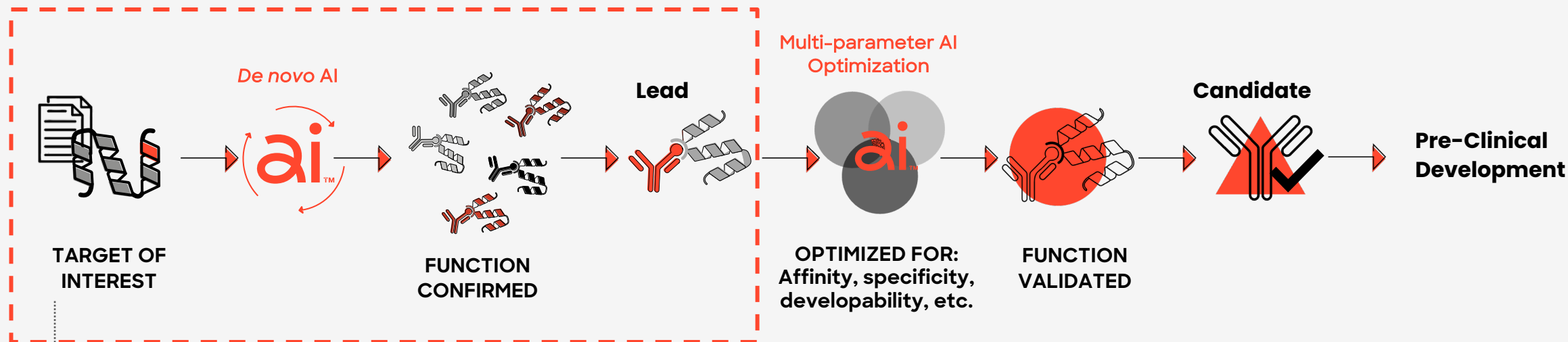
## AI-GUIDED LEAD OPTIMIZATION



*Multi-parameteric optimized antibodies*



# Generative AI Drug Creation™ Workflow



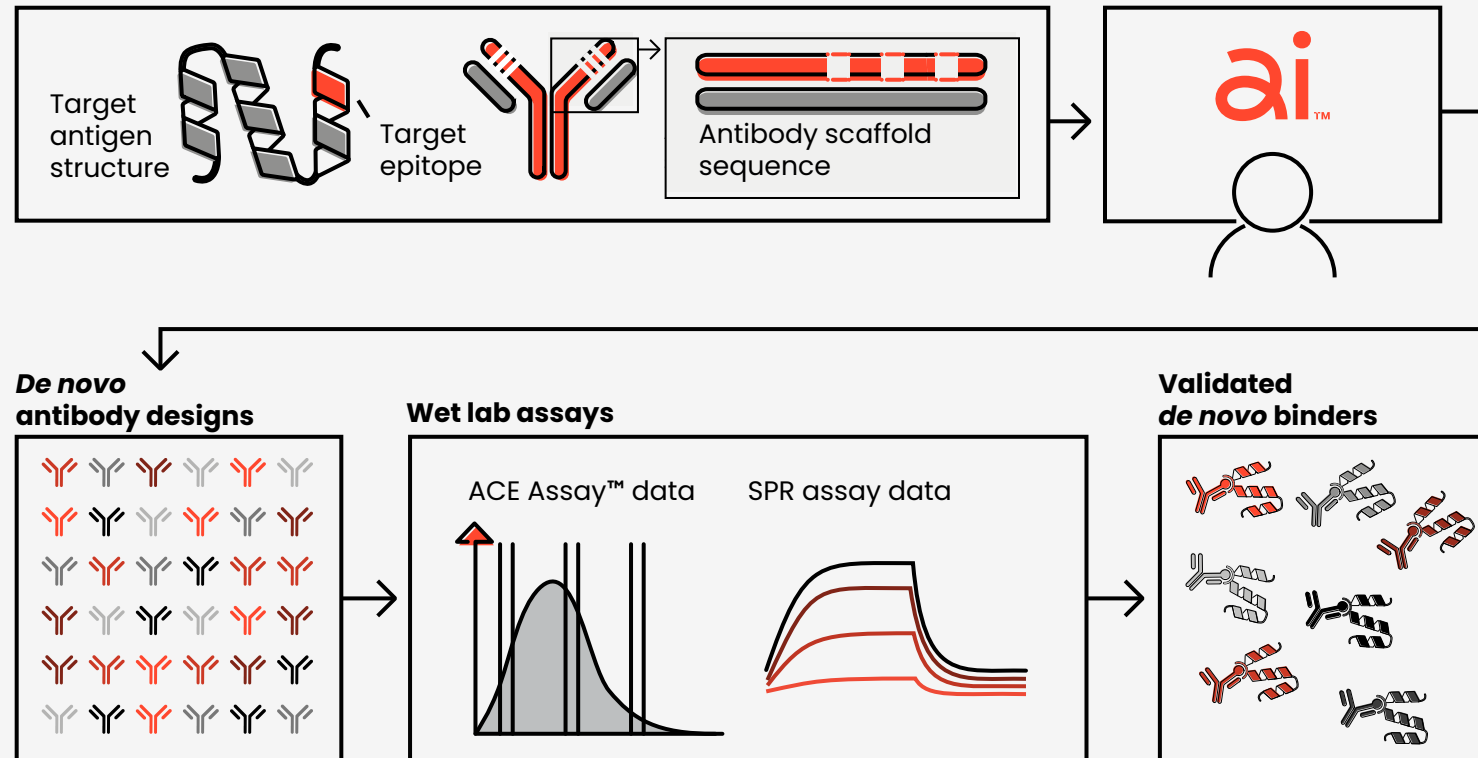
**Absci works with its partners to set the goals of partnership programs:**

- (1) Target antigen
- (2) Target antigen epitope(s) if known OR global epitope landscaping to identify optimal epitope / MOA
- (3) Drug modality, e.g. mAb, bi-specific, fusion protein
- (4) Target TPP parameters

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

Zero-Shot: Model has never seen an antibody that binds to the target or homologs

Binders were identified **straight out of the model** – no lead optimization was performed





## DE NOVO DESIGN

### Example: *de novo* design of HER2 antibodies

#### POC MODEL

Demonstration of ‘zero shot’ model by designing HCDR3 and HCDR123 for HER2

Assessed multiple parameters:

- Binding rates
- Sequence diversity
- Immunogenicity
- Functionality
- Developability

#### POC DEMONSTRATED

- 1 *De novo* models generated diverse, novel, and high affinity variants superior to baseline
- 2 Demonstrated high level of specificity
- 3 Demonstrated higher potency vs Trastuzumab *in vitro*
- 4 Achieved multi-dimensional lead optimization
  - Desired cross-species reactivity and specificity
  - Optimal developability

# DE NOVO DESIGN OF HER2 ANTIBODIES

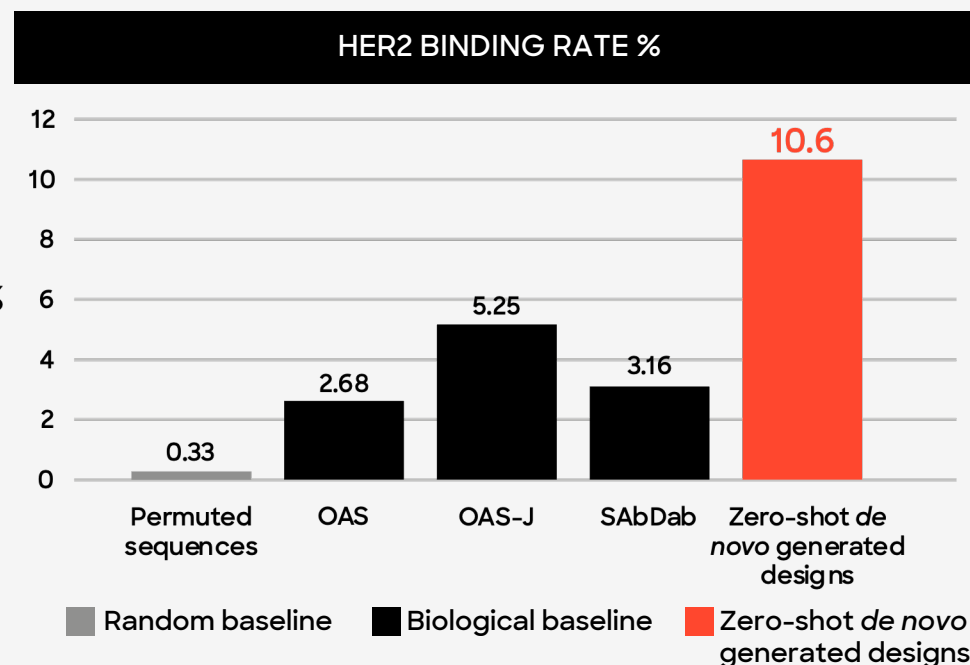
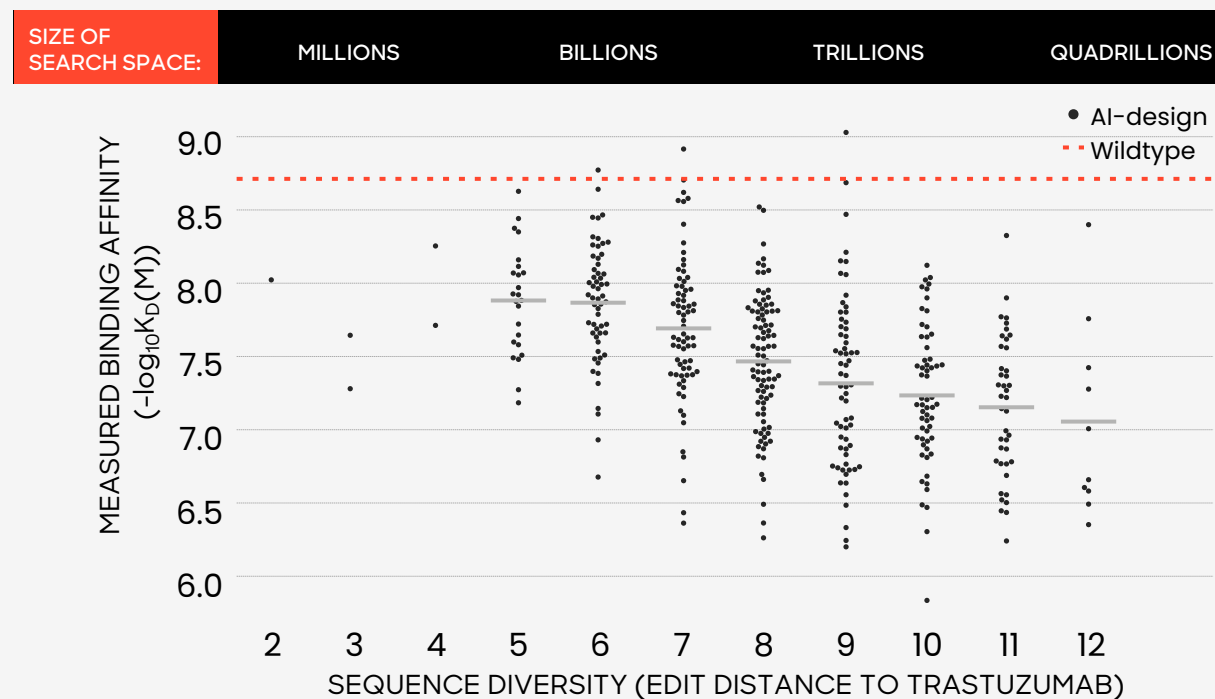
## AI Generated Diverse, Novel & High Affinity Binders that Outperforms Biological Baseline

### 1 Diverse, novel, high affinity binders

- Up to 12 mutations in a CDR region of 13 amino-acids  
(Search space of  $20^{13}$ )

### Outperforms biological baseline

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

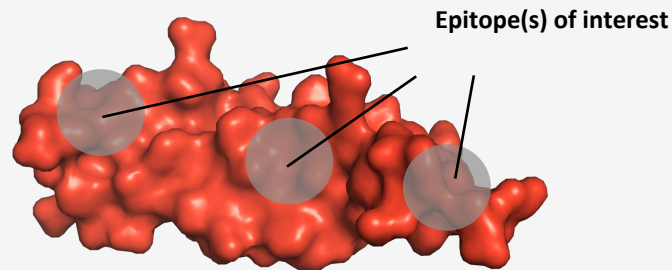


Affinity of novel binders up to 3.4 nM measured by SPR in mAb format

# De novo and Lead Optimization AI models further enable global and local epitope landscaping

Epitope landscaping and interface evolution can be used to improve affinity, potency and to potentially uncover novel Mechanisms of Action (MoAs)

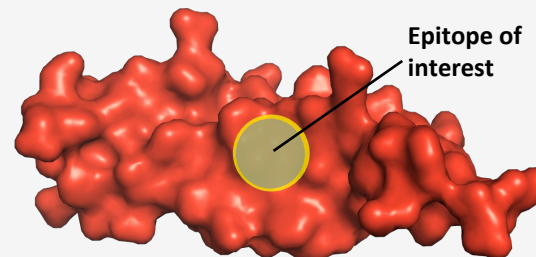
## GLOBAL EPITOPE LANDSCAPING



*de novo* AI model

*De novo* AI model allows sampling multiple epitope interfaces across the antigen to locate desired MoA

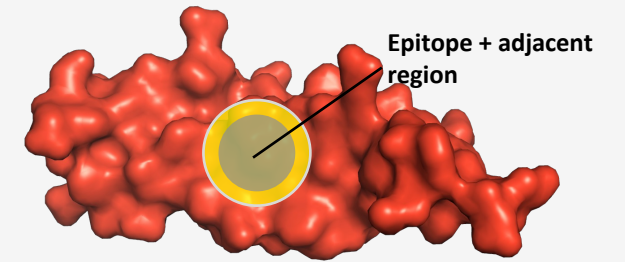
## LOCAL EPITOPE LANDSCAPING



*de novo* AI model

Once an epitope is selected the *de novo* model exhaustively samples the interface contacts with the designated epitope to further refine potency and MoA

## LOCAL INTERFACE EVOLUTION



*AI lead optimization* model

In addition to optimizing antibody variants for developability, the AI lead optimization model samples the epitope interface with its surrounding adjacent region to further improve potency and MoA

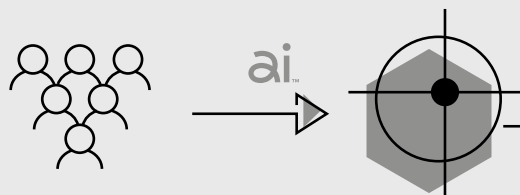
# AI-Guided Lead Optimization

From de novo design to multiparametric lead optimization using AI

## TARGET DISCOVERY WITH NOVEL APPROACHES



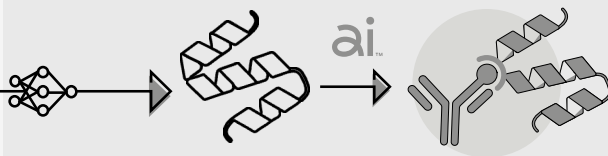
*Reverse Immunology for target discovery*



## AI-GUIDED ANTIBODY DRUG CREATION



*De novo antibodies designed by AI*



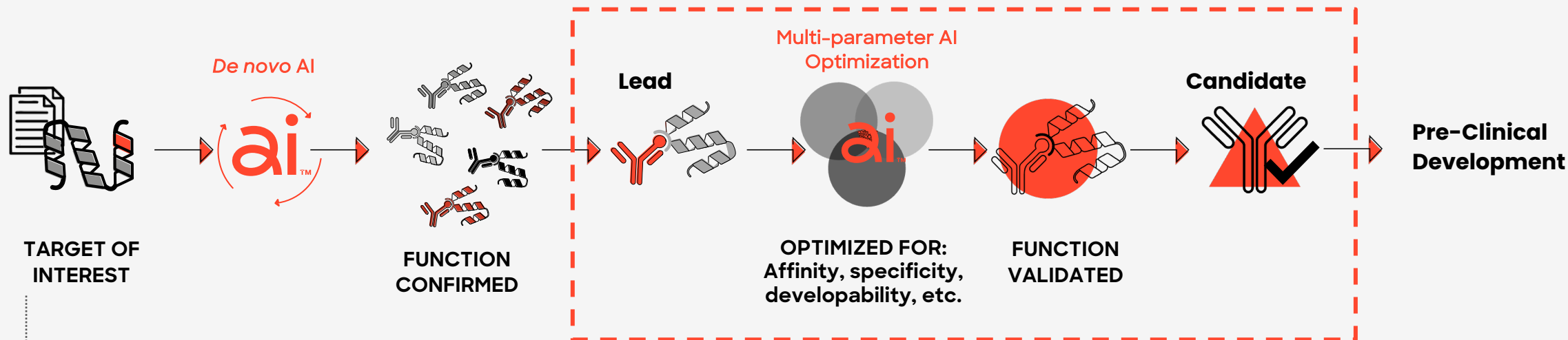
## AI-GUIDED LEAD OPTIMIZATION



*Multi-parameteric optimized antibodies*



# Generative AI Drug Creation™ Workflow



**Absci works with its partners to set the goals of partnership programs:**

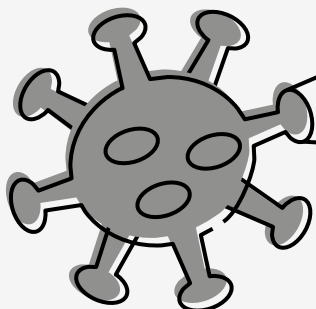
- (1) Target antigen
- (2) Target antigen epitope(s) if known OR global epitope landscaping to identify optimal epitope / MOA
- (3) Drug modality, e.g. mAb, bi-specific, fusion protein
- (4) Target TPP parameters

# AI-GUIDED LEAD OPTIMIZATION

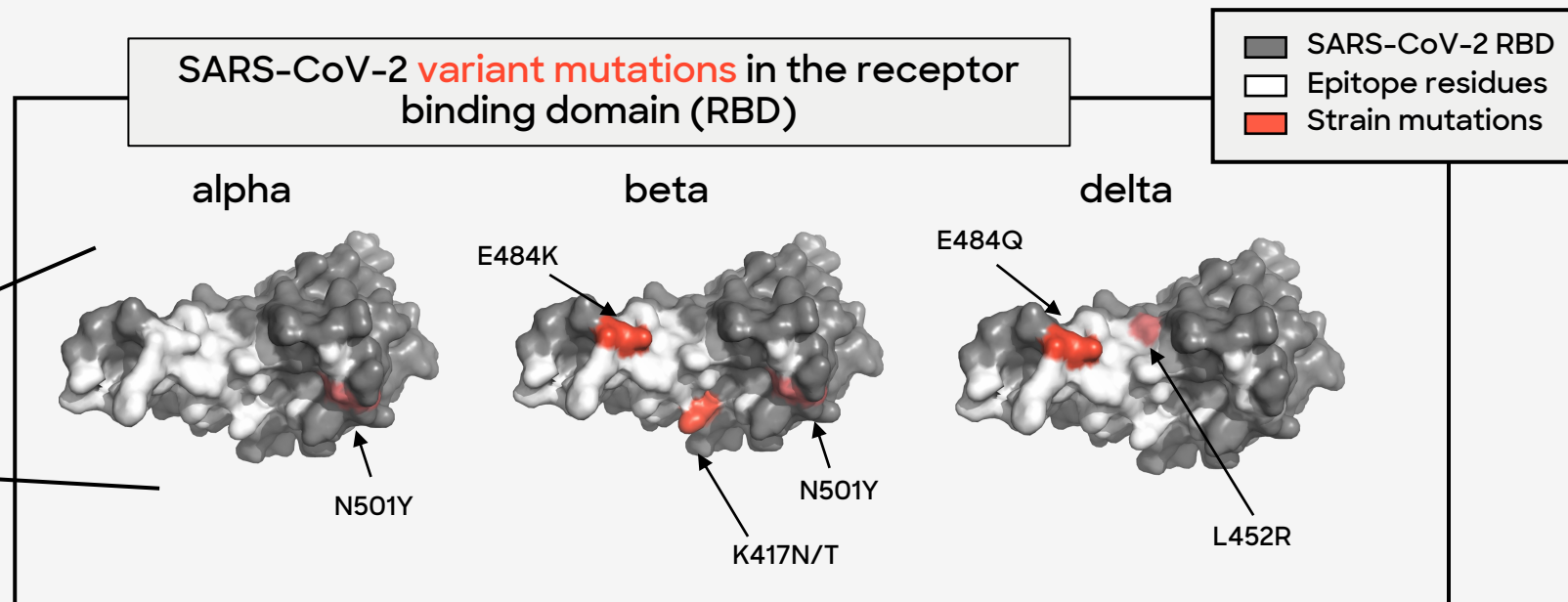
## AI multi-valent co-optimization of a broad-spectrum SARS-CoV-2 antibody

### Case study goals

Re-engineer clinically approved antibody for binding towards three SARS-CoV-2 variants



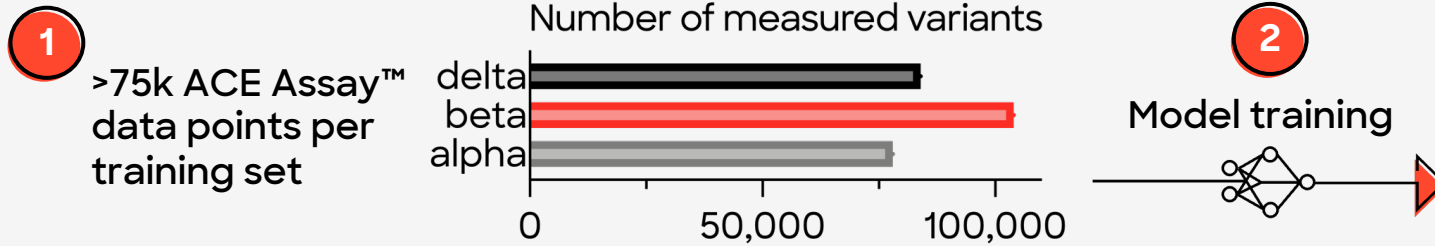
Improve binding towards beta without loss of binding towards alpha and delta



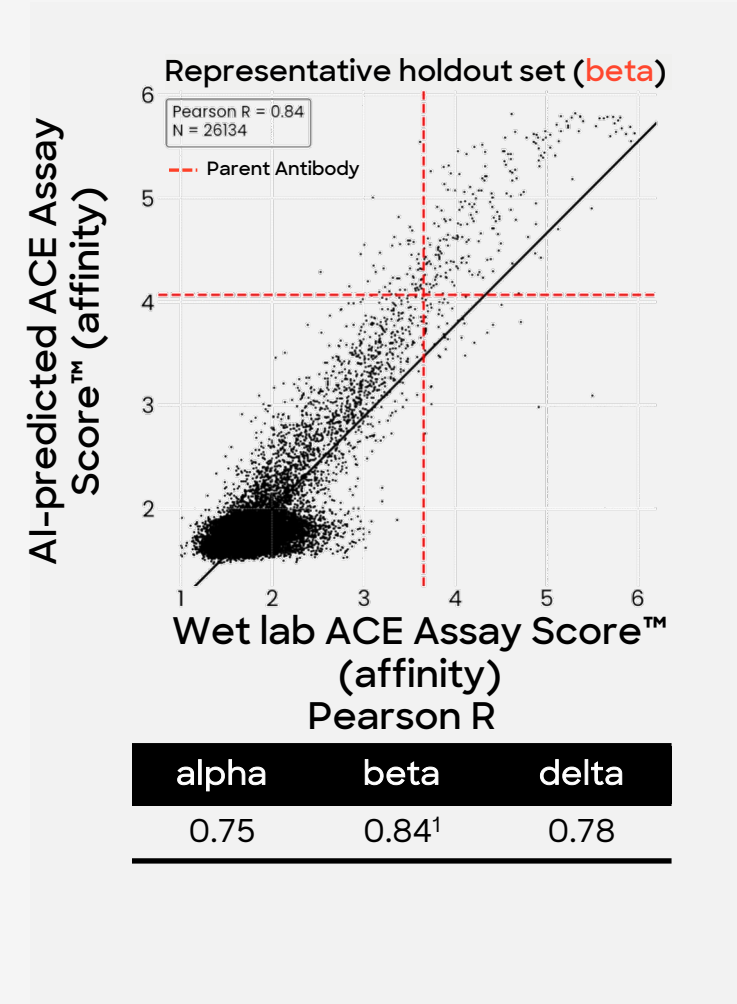
Fab	$K_d$ (nM)			
	WT RBD	alpha RBD	beta RBD	delta RBD
Parental Antibody	8.5	8.0	607	5.4

## AI-GUIDED LEAD OPTIMIZATION

# Absci's ACE Assay™ Platform Generates Large, High Quality Training Data Enabling in silico Affinity Predictions



Hold out data sets demonstrate strong model performance following training with AI-predicted affinity correlating well with experimental measurements



<sup>1</sup> High correlation between ACE Score™ and SPR-measured  $-\log_{10}$  KD values observed

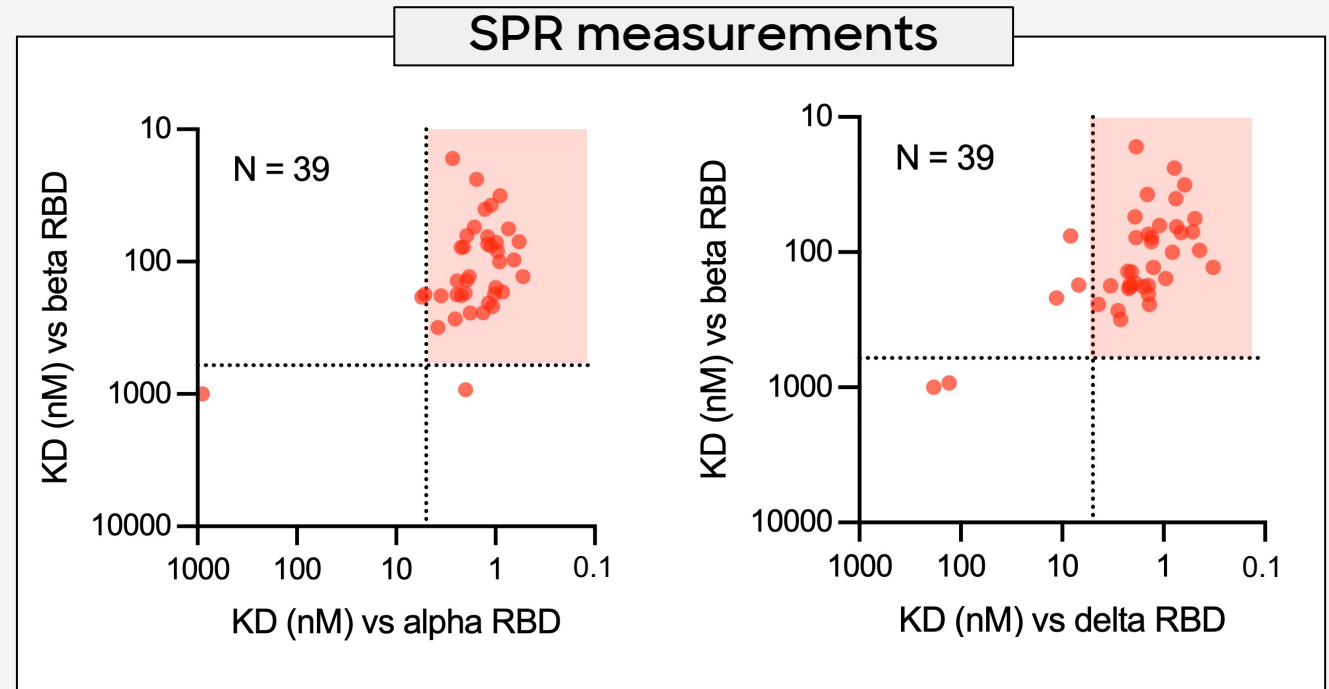
## AI-GUIDED LEAD OPTIMIZATION

# AI Model Searches Mutational Space and Top Predictions are Validated

3

Binders predicted to have the best binding towards all three SARS-CoV-2 variants are assessed in the lab by SPR

79% (31/39) of evaluated predictions exhibit higher binding affinity than parent antibody to alpha and beta and delta



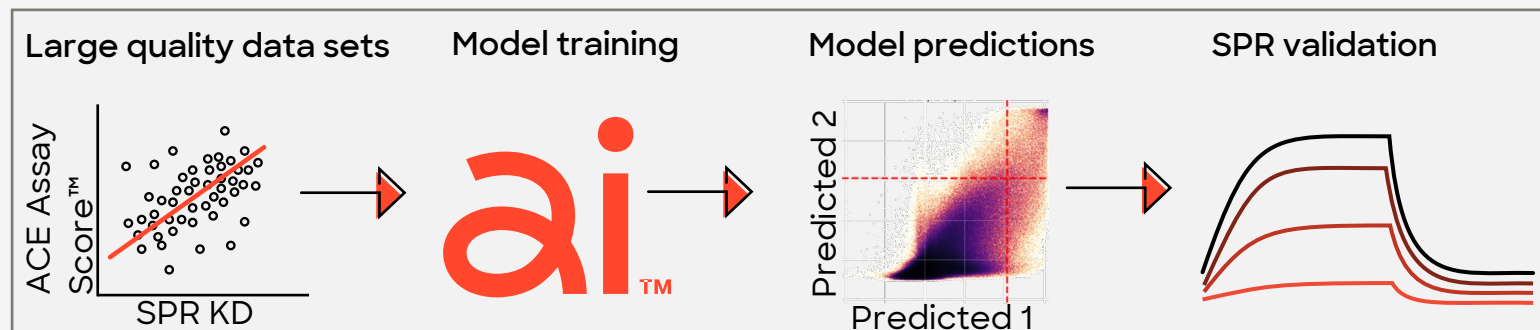
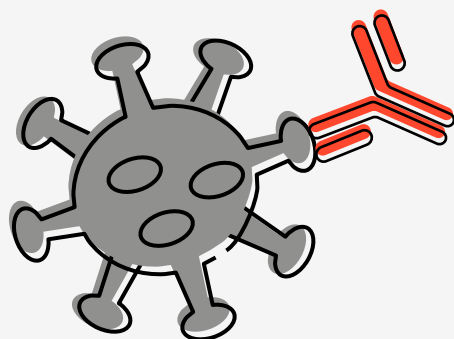


# AI-GUIDED LEAD OPTIMIZATION

## AI co-optimized binding to multiple SARS-CoV-2 variants

### Case study outcome

AI-guided lead optimization platform delivers antibodies with improved binding towards all three desired variants

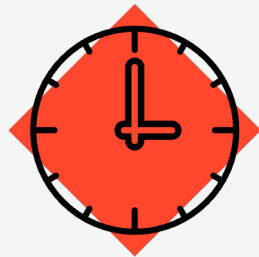


Fab	nM KD (fold improvement)		
	alpha RBD	beta RBD	delta RBD
<i>Parental antibody</i>	8.0	607	5.4
ABSCI001	2.7 (3x)	16 (37x)	1.9 (3x)
ABSCI002	1.5 (5x)	24 (25x)	0.8 (7x)
ABSCI003	0.9 (9x)	32 (19x)	0.6 (9x)
ABSCI004	1.1 (7x)	37 (16x)	1.4 (4x)
ABSCI005	1.3 (6x)	40 (15x)	0.8 (7x)

# Novel AI-designed functionalities

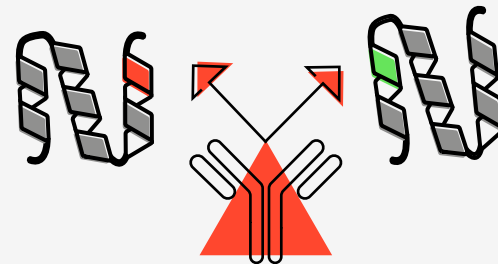
## DE NOVO DESIGN & AI-GUIDED LEAD OPTIMIZATION FOR IMPROVED THERAPEUTIC FUNCTIONALITIES

### Half-life extension



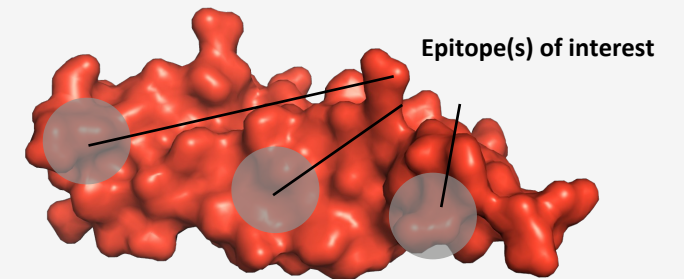
- **Extend half-life** through augmenting Fc-mediated recycling
- **Reduces dosing** intervals and lowers risk of  $C_{max}$  driven adverse events
- **Improves** pharmacokinetic profile

### Multi-valency



- **Increased efficacy** by simultaneous binding to multiple desired isoforms
- **Broad spectrum antibodies** with simultaneous binding to multiple viral variants for infectious diseases
- **Cross-species binding** for improved success rates and speed

### Epitope selection



- **Global landscaping** assess multiple epitopes of interest for the desired functionality
- **Local landscaping** evaluates a diverse set of interfaces of a specific epitope
- **Interface refinement** with lead optimization models for improved potency and / or developability

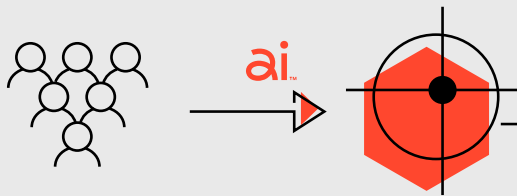
# Target Discovery

Reverse Immunology platform unifies target and antibody discovery in a single workflow enabling potential “first-in-class” biotherapeutics

## TARGET DISCOVERY WITH NOVEL APPROACHES



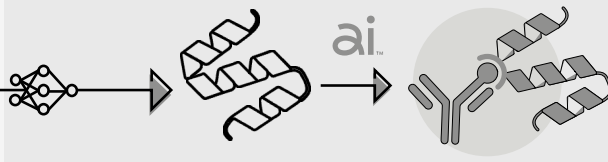
*Reverse Immunology for target discovery*



## AI-GUIDED ANTIBODY DRUG CREATION



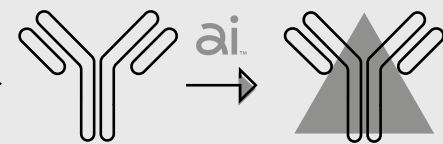
*De novo antibodies designed by AI*



## AI-GUIDED LEAD OPTIMIZATION

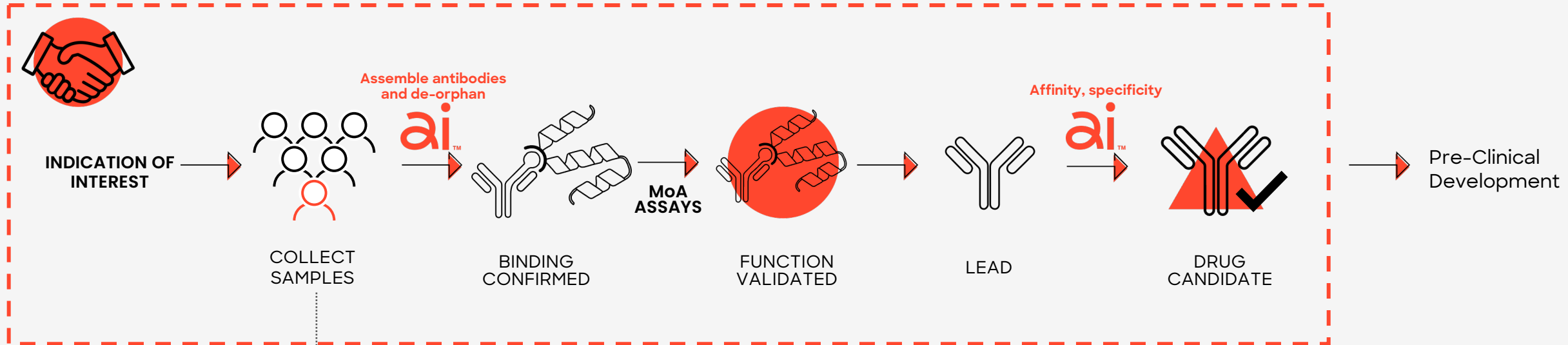


*Multi-parameteric optimized antibodies*



# TARGET DISCOVERY

## Reverse Immunology: Target and Antibody Discovery Simultaneously

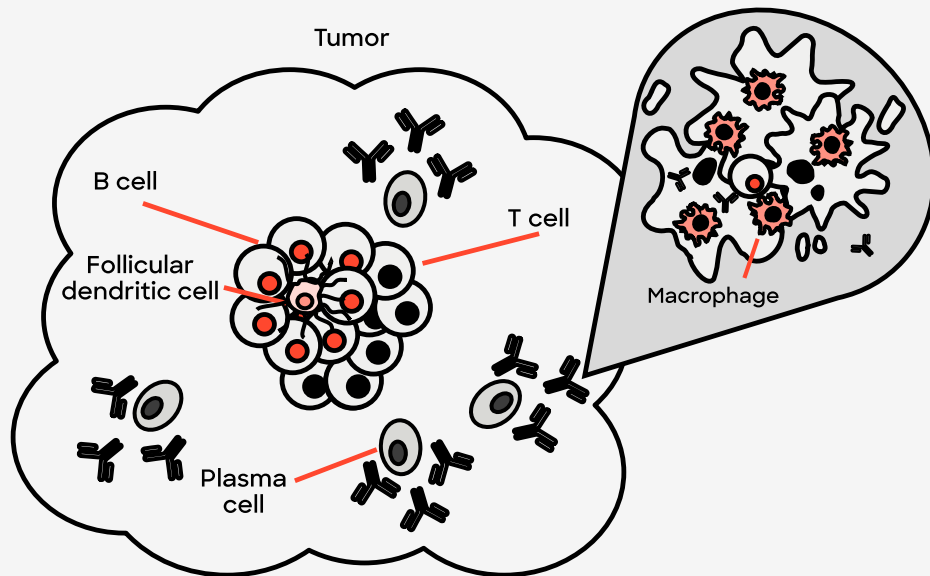


Absci partners with leading health institutions for patient samples:

- Aster Insights
- Avera Health
- Saint John's Cancer Institute
- University of Oxford, Kennedy Institute of Rheumatology

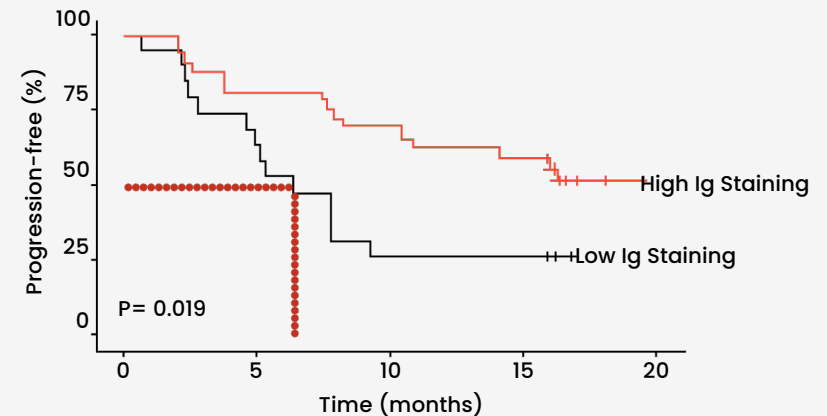
## TARGET DISCOVERY

# Tertiary lymphoid structures (TLS): the cornerstone of Absci's Reverse Immunology approach



TLS are centers of immune activity (B-cell proliferation and antibody production) that develop in chronically inflamed tissues [1].

Antibodies from TLS are specialized for local antigens and play a significant role in the progression of chronic diseases and cancer, setting them apart from the general population of antibodies in the peripheral blood [2].



The presence of **TLS** is associated with **longer progression-free survival and better response to immune checkpoint inhibitors** [2,3].

- Rapidly growing evidence illustrates correlation between **TLS-derived antibodies** in the tumor microenvironment and **positive clinical outcomes** [2].
- **TLS-derived antibodies** have been shown to be associated with apoptosis of cancer cells in patients [2].

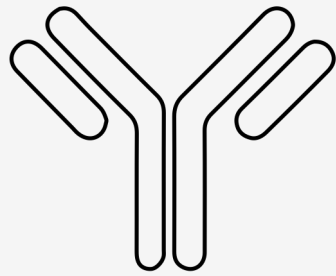
[1] Pipi et al. "Tertiary lymphoid structures: autoimmunity goes local." *Frontiers in immunology* (2018)

[2] Meylan et al. "Tertiary lymphoid structures generate and propagate anti-tumor antibody-producing plasma cells in renal cell cancer." *Immunity* (2022)

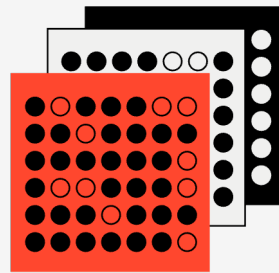
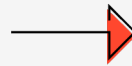
[3] Helmink et al. "B cells and tertiary lymphoid structures promote immunotherapy response." *Nature* (2020)

## TARGET DISCOVERY: ABS-301

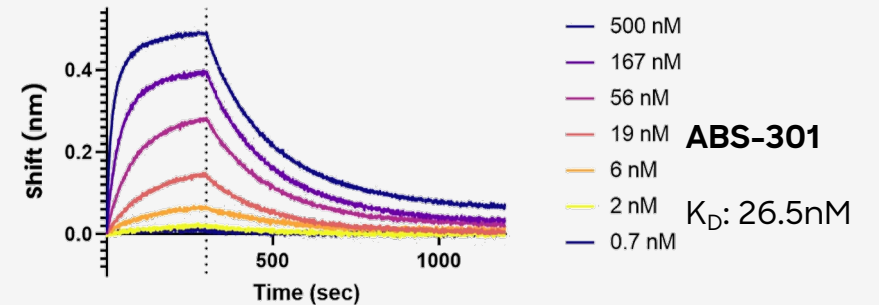
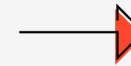
# Identification of a Novel Immunomodulatory Antibody ABS-301



Computationally reconstructed antibodies from human TLS biopsies



High-throughput proteomics screening technology covering the human proteome close to completeness



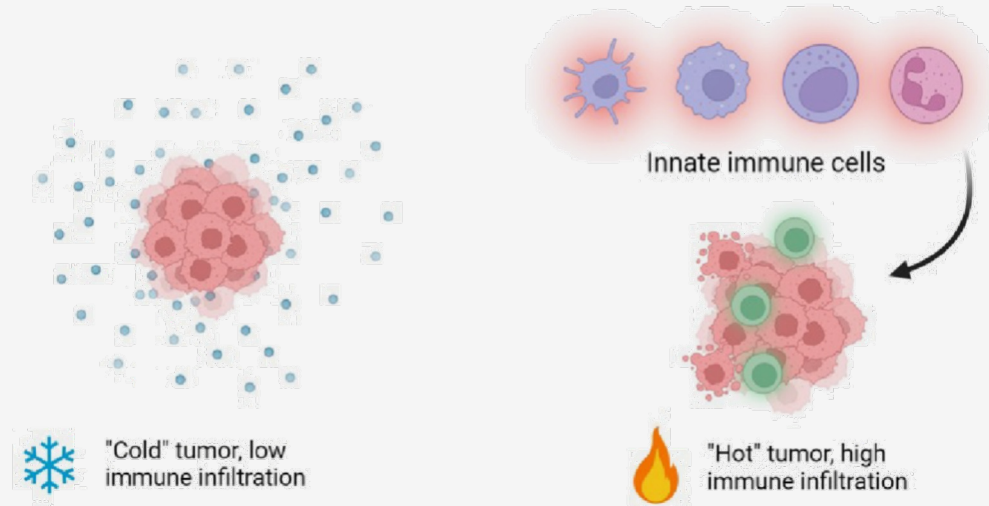
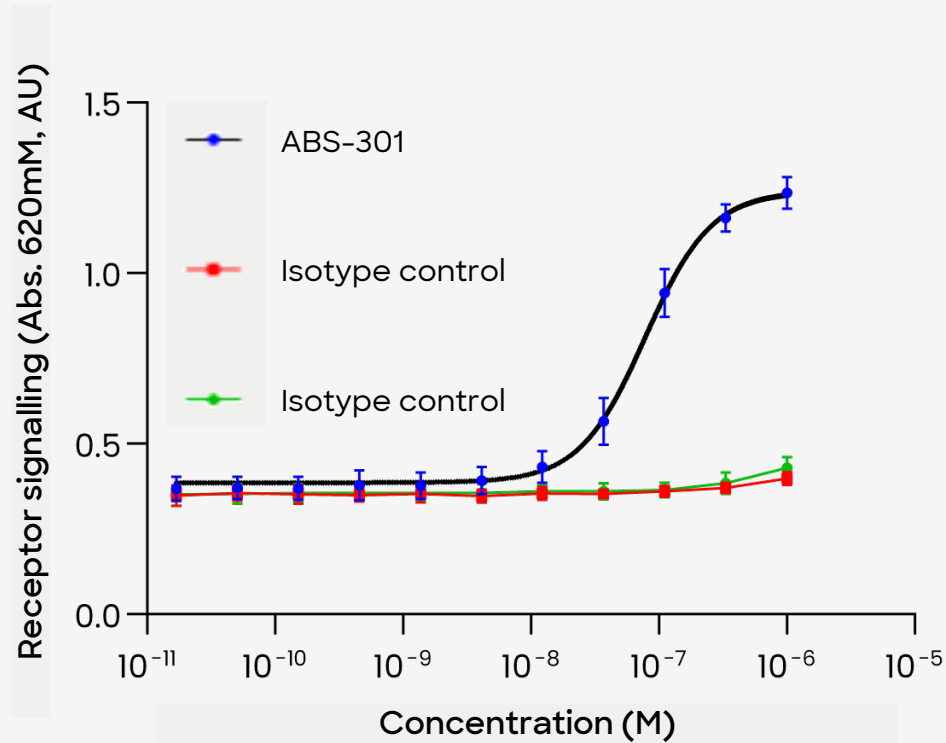
Biolayer interferometry validates potent and specific binding against a novel, undisclosed target

**ABS-301: RECONSTRUCTED PATIENT-DERIVED ANTIBODY SHOWS HIGHLY SPECIFIC AND POTENT BINDING TO A NOVEL TARGET WITH POTENTIAL IN IMMUNO-ONCOLOGY.**

## TARGET DISCOVERY: ABS-301

# ABS-301: Patient-derived Antibody Blocks a Novel Immunosuppressive Target

ABS-301 blocks a novel immunosuppressive target in human cells

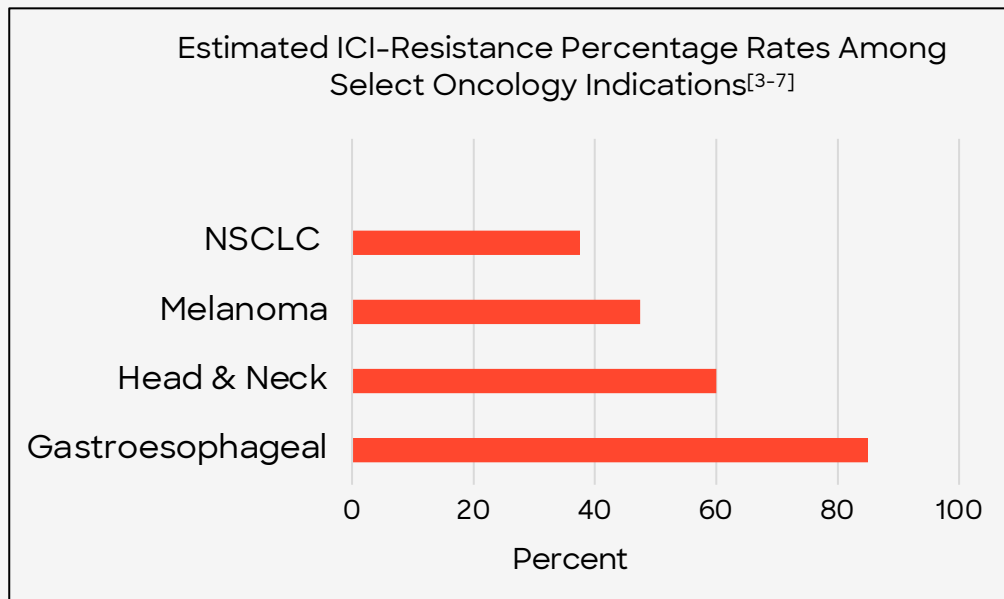


**Hypothesis:** Tumors upregulate ABS-301's target as an **immune evasion strategy** to limit immune infiltration. ABS-301 treatment in cancer may release immune suppression and permit immune cells to infiltrate the tumor, allowing for a robust anti-tumor response.

Preliminary evidence suggests that this immune escape mechanism might be **independent of known immune checkpoints** such as the PD1/PD-L1 axis.

## TARGET DISCOVERY: ABS-301

# ABS-301 has Broad Potential in Immuno-oncology



Comprehensive profiling of ABS-301's immuno-oncological potential in progress.

Indication	US Estimated New Cases in 2023 <sup>[1]</sup>	Estimated Global Therapeutics Market (2028) <sup>[2]</sup>
NSCLC	238K	\$56B
Melanoma	98K	\$14B
Head & Neck	54K	\$5B
Gastroesophageal	48K	\$3B

1. Siegel et al, CA, 2023, 73 (1), 17-48
2. Evaluate Pharma
3. Baxter et al, Br J Cancer 125, 1068-1079 (2021)
4. Lim, S.Y. et al, Nat Commun 14, 1516 (2023)
5. Zhou S et al, Front Immunol., 2023, 14:1129465
6. Huang Y et al, Cancers (Basel), 2023, 15(10):2733
7. Oualla K et al, Cancer Control, 2021, 10732748211004878



absci®



This **revolution** is  
only just beginning.