

GENERATIVE AI

# DRUG CREATION

Corporate Presentation  
August 2026

absci<sup>®</sup>

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# From Code to Clinic

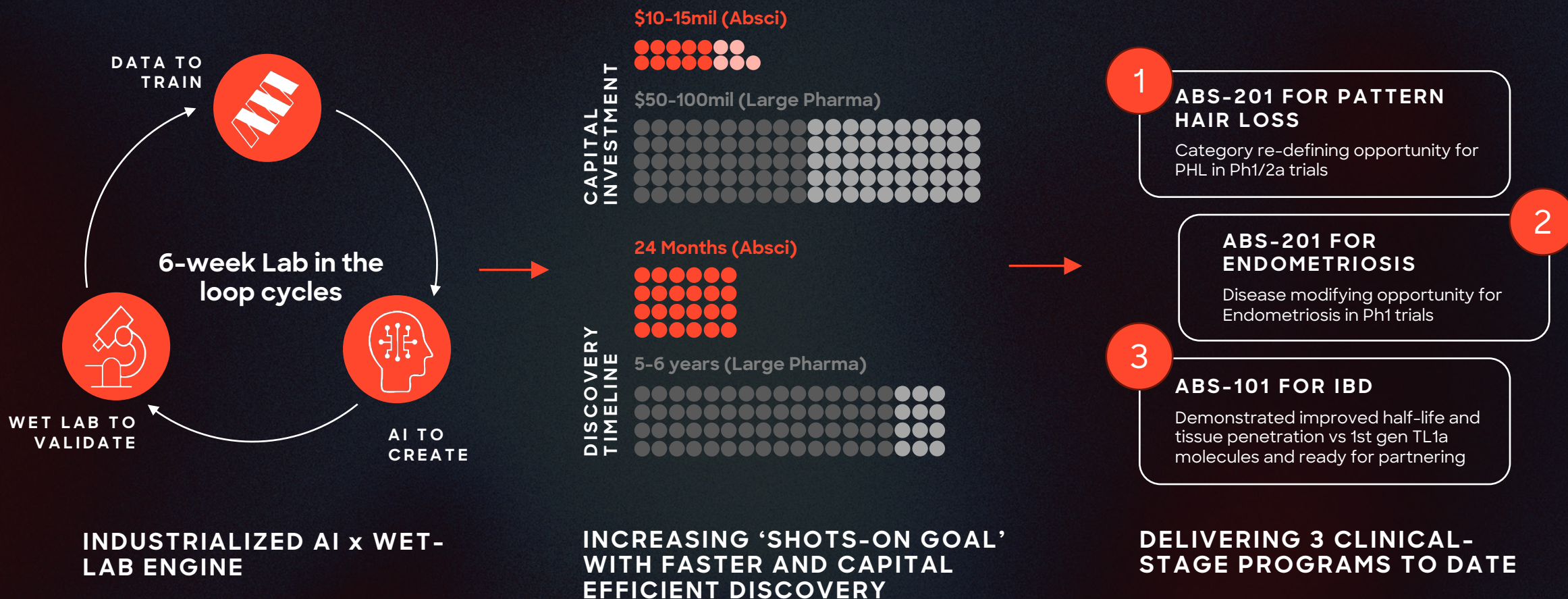
## 1. AI NATIVE PLATFORM

- Interdisciplinary Team with 10+ approved drugs and AI expertise
- Integrated Lab-in-the-Loop leveraging 77k ft<sup>2</sup> automated wet-lab
- Leading AI platform for *de novo* design and AI optimization of antibody-based therapeutics

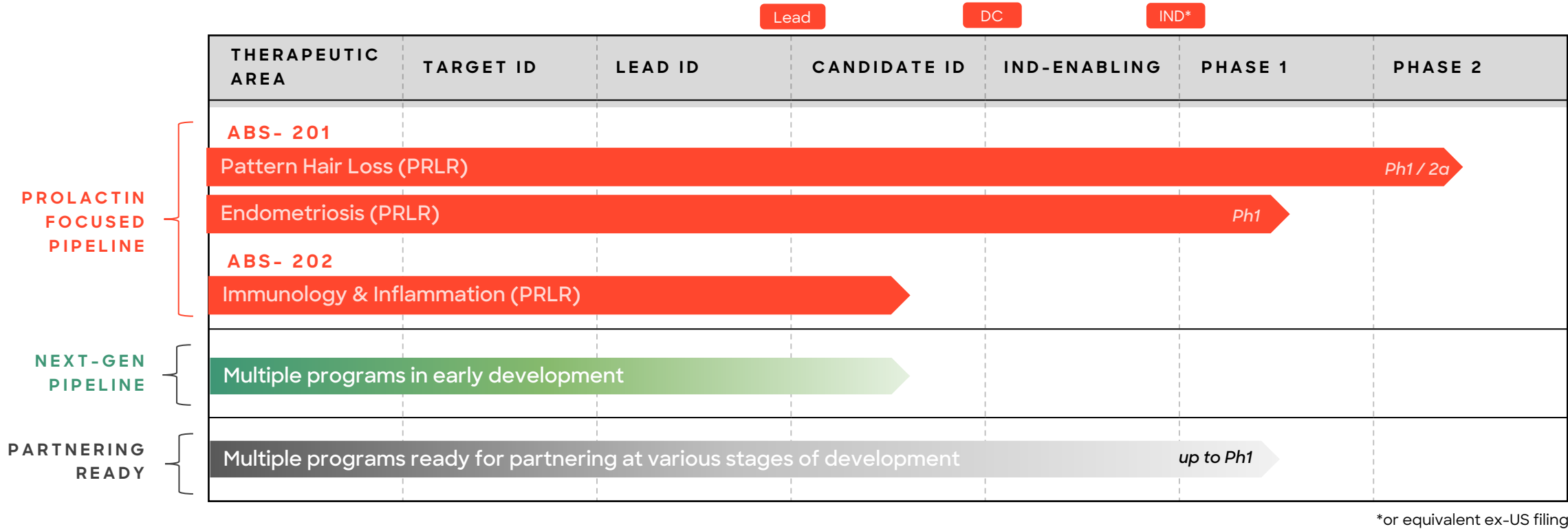
## 2. DIFFERENTIATED PIPELINE

- ABS-201 (anti-prolactin receptor)
  - Pattern Hair Loss (PHL): Ongoing Ph1/2a HEADLINE trial with interim POC readout 2H 2026
  - **Endometriosis (Endo)**: Indication expansion into endometriosis with anticipated Ph2 initiation in 4Q2026 with PoC readout as early as 2H 2027
- **Preclinical pipeline** focused on metabolism and I&I

# Industrializing Drug Discovery



# Advancing and expanding our pipeline of novel & differentiated assets designed using AI



# ABS-201 has the potential to unlock a wholly new category of therapy in hair “re-growth”

1. Significant clinical and commercial unmet need in Pattern Hair Loss
2. Strong scientific rationale, with validated target, de-risked Mode of Action, and pharmacology
3. Straightforward development path with objective endpoints



# Underserved patient population looking for therapeutic innovation

~80 million Americans live with  
Pattern Hair Loss (PHL)



**MALE PHL**

~50M men in the U.S.

Only 2 FDA approved drug  
therapies

**FEMALE PHL**

~30M women in the U.S.

Only 1 FDA approved drug  
therapy for women

Growing patient population with limited  
therapeutic options and concerns of  
adverse side-effects

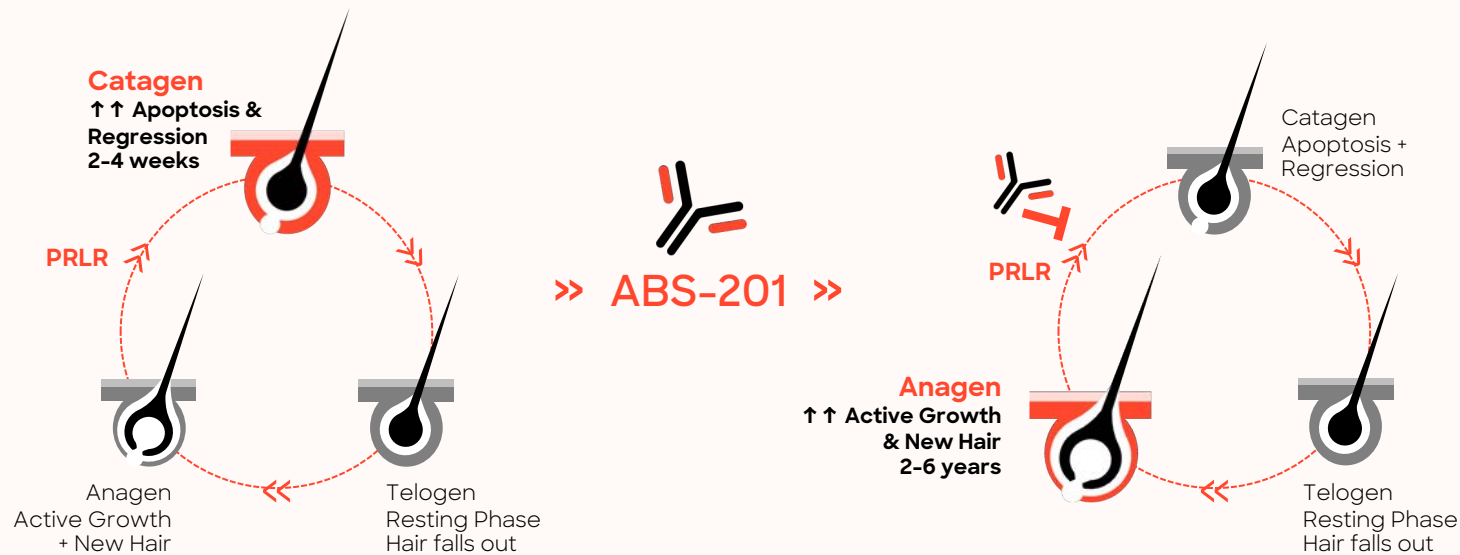
Last FDA approved therapy for Pattern Hair  
Loss was in the 1990s

Patients and clinicians need better treatment  
options for “hair re-growth”

- › Hair re-growth, not just slowing of hair loss
- › Safe and minimal side effects
- › Durable effect
- › Convenient administration frequency
- › FDA approved

# PRLR inhibition for Pattern Hair Loss is an innovative alternative to current treatment options

## PROPOSED DIRECT IMPACT OF ABS-201 ON HAIR CYCLE STAGES

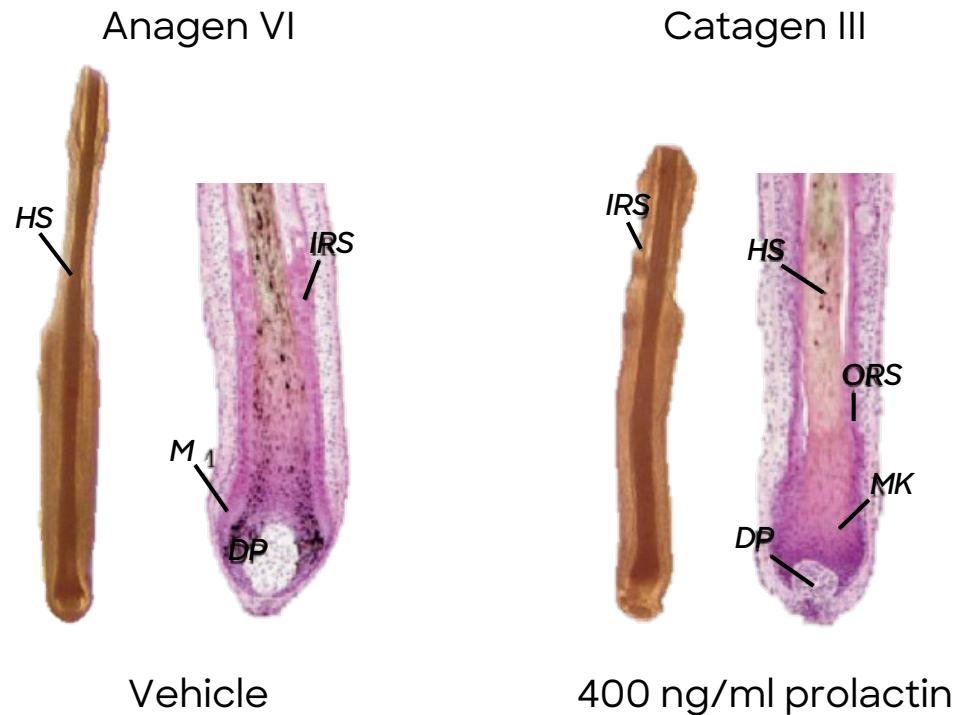


## ABS-201 HAS THE POTENTIAL TO:

- Shift the balance in hair cycle stage towards anagen phase<sup>1,2</sup> with:
  - Active and new hair growth
  - Prevention of telogen effluvium
- Promote a long-lasting effect after treatment cessation
- Block cessation of pigmentation, which may lead to the restoration of hair pigmentation<sup>2</sup>

# Prolactin impacts on organ-cultured human hair follicles

Prolactin drives hair follicle regression in human ex vivo culture

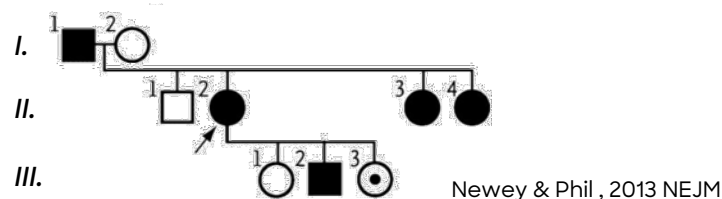


Prolactin prematurely induces a catagen-like stage in organ-cultured human hair follicles<sup>1</sup> characterized by:

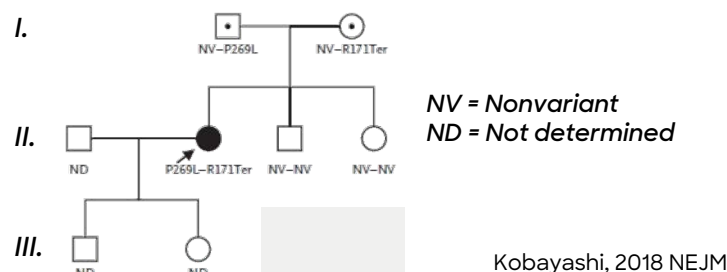
- › Condensed shape of the dermal papilla (DP)
- › Diminishment of the hair matrix volume
- › Apparent cessation of pigmentation
- › Inhibition of hair shaft elongation

# PRLR inhibition anticipated to be safe & well tolerated as supported by human genetics

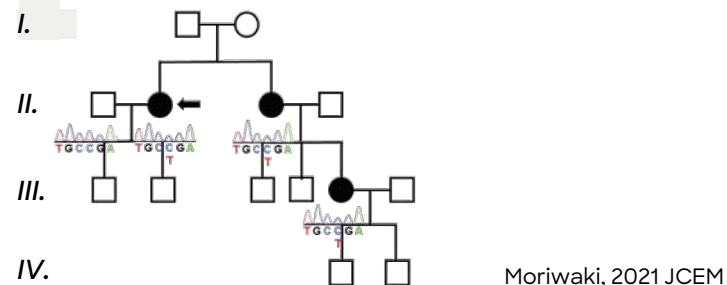
Dominant negative  
PRLR loss-of-function



Compound heterozygous  
PRLR loss-of-function



Dominant negative  
PRL loss-of-function



Reduced/Loss of PRL or PRLR Signaling

- › Postpartum agalactia
- › Otherwise in good health:
  - No apparent impact on fertility
  - No report on erectile dysfunction in male
  - Normal breast development and menses in females
  - Normal serum electrolytes and hormone levels (except elevated PRL in PRLR mutation carrier)
  - No reported abnormalities of other hypothalamic-pituitary axes

## Top head view of Stumptailed Macaque's showing phenotypic change over time

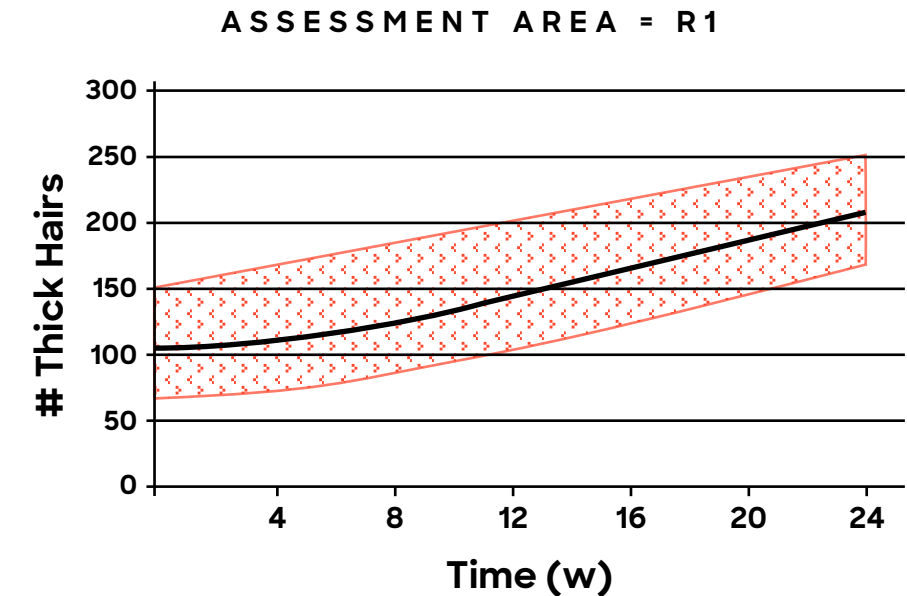


40mg/kg s.c. Q2W for 28 weeks

Study commissioned by Absci CIO Andreas Busch while at Bayer.  
Disclosure from competitor

- Hair density & thickness improved with short treatment duration in primate model of Pattern Hair Loss
- Hair growth remains and improves several years post cessation

## Terminal hair count "Thick Hairs" in prior bald areas



- Hair regrowth observed for both male and female animals (>100 hairs/cm<sup>2</sup> increase in bald area at week 28 of treatment\*)

# ABS-201 shows superior efficacy vs 5% topical minoxidil in 21d hair regrowth model

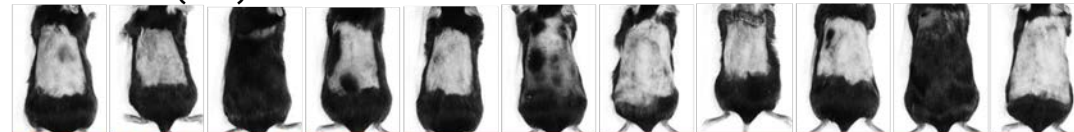
Untreated (n=11)



Isotype (n=11)



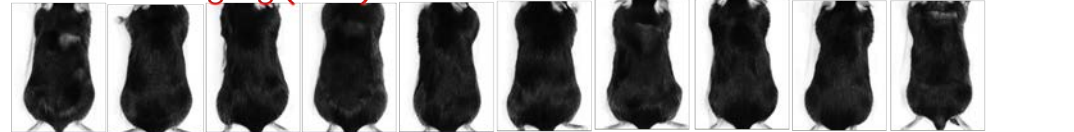
Minoxidil 5% (n=11)



ABS-201 30mg/kg (n=11)

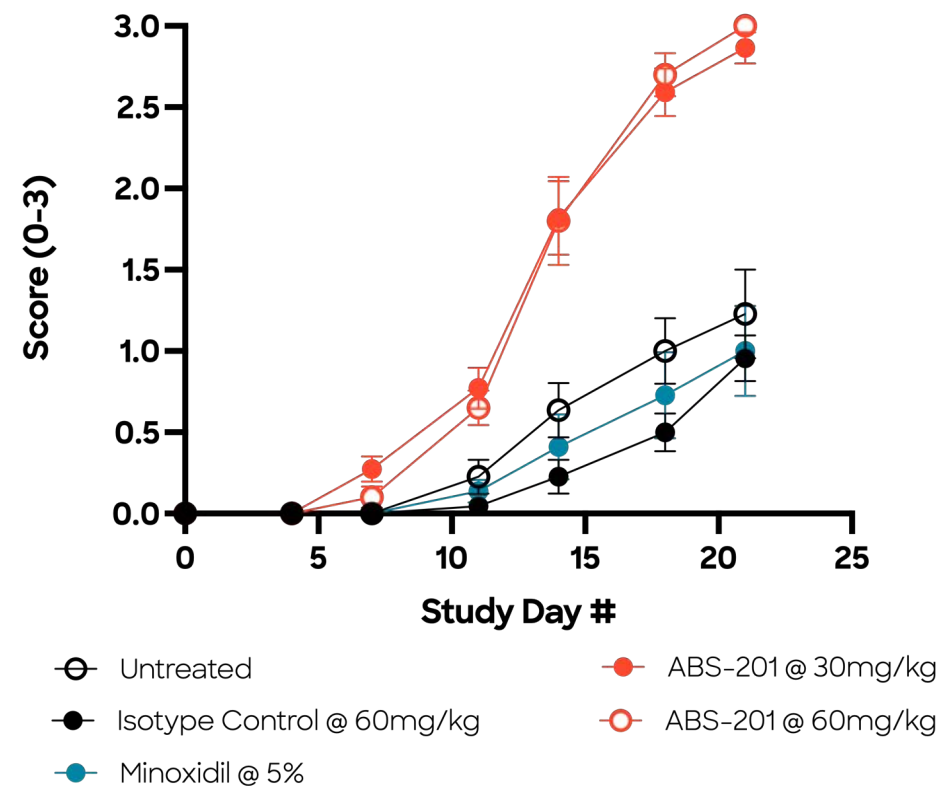


ABS-201 60mg/kg (n=10)



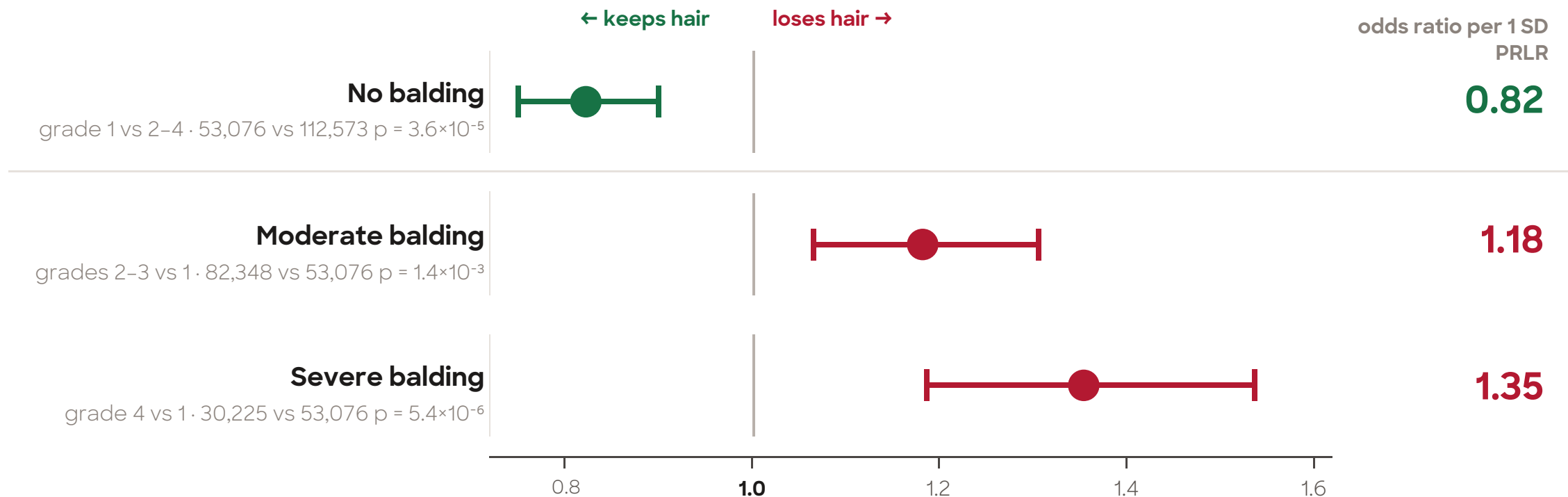
Administration: mAbs i.p. biweekly; Minoxidil topical daily

Hair Growth Score



ABS-201 vs minoxidil/untreated/isotype \*\*p<0.05; \*\*\*p<0.0001 - 2way ANOVA

# Men without PHL carry genetically lower PRLR levels; severity of PHL scales with PRLR expression



- **Dose-response:** odds ratios climbs across the severity spectrum.
- More PRLR, more hair loss – **ABS-201 blocks PRLR signaling**

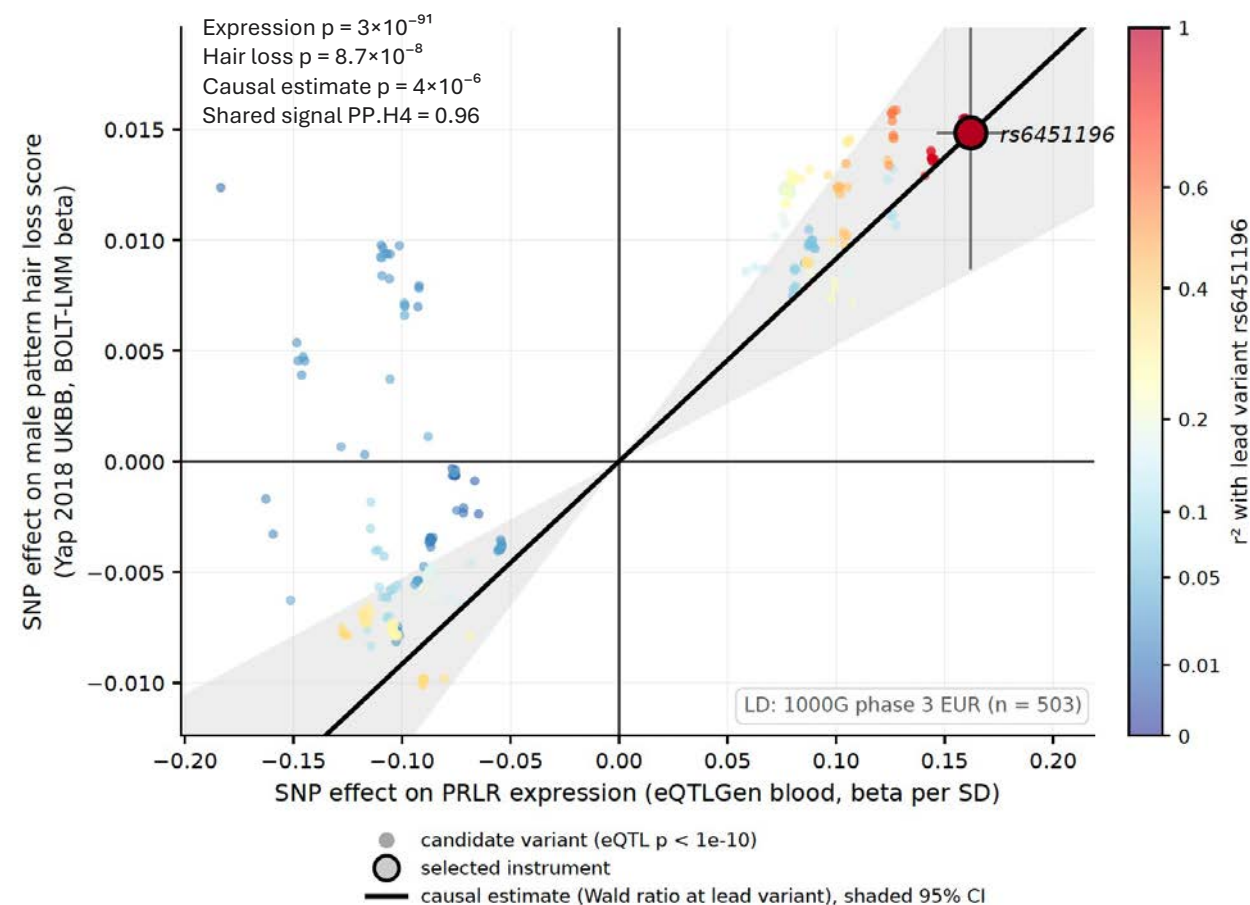
## Notes:

- SNP rs6451196, 1.35 is per standard deviation; between the most extreme genotypes, G/G and A/A, it is 1.10.
- Each row is a separate logistic contrast between the grades shown, from 165,649 UK Biobank men (self-reported 1-4 scale: no, slight, moderate, severe). Rows 2 and 3 share the grade-1 reference, so the rows are not independent.

# cis-MR + colocalization supports a causal relationship for PRLR in Pattern Hair Loss

- More PRLR, more proportional balding.
- The neighboring genes show no association with PHL
- The PRLR expression and hair loss signals share the same underlying genetic signal, further supports PRLR blockade as a therapeutic target.

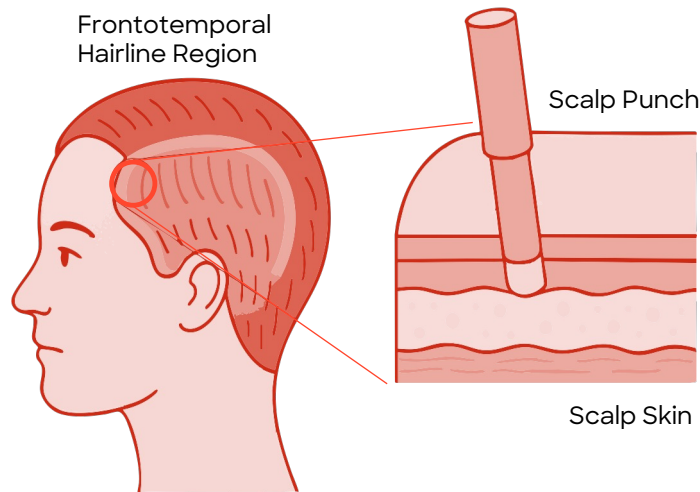
## PRLR cis-MR colocalization plot



### Notes

- **Instrument:** rs6451196 – 1 of 312 candidates (eQTL  $p < 1 \times 10^{-10}$ , clumped at  $r^2 < 0.001$ )
- **Data:** eQTLGen PRLR cis-eQTL (n = 31,644) · Yap 2018 hair loss (205,327 UK Biobank men) · 1000G phase 3 EUR (n = 503) for LD
- **Causal estimate:** Wald ratio +0.0915[+0.0526, +0.1305] score units per SD,  $p = 4.2 \times 10^{-6}$ . Strongest hair-loss association at the locus:  $p = 8.7 \times 10^{-8}$
- **Colocalization:** PP.H4 = 0.961
- Largely the same UK Biobank men and balding scale as the previous slide, analyzed here as a continuous score – odds ratios are on that slide

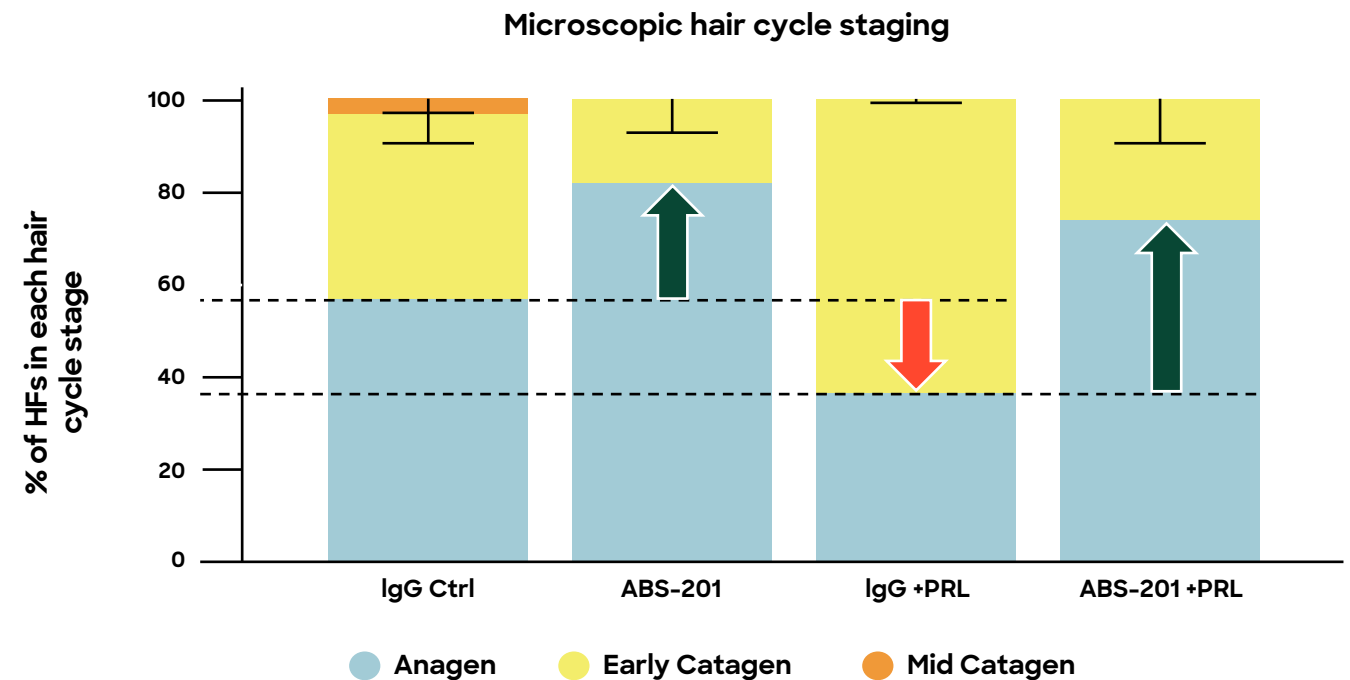
# ABS-201 in human ex vivo culture study supports MOA in human scalp follicles

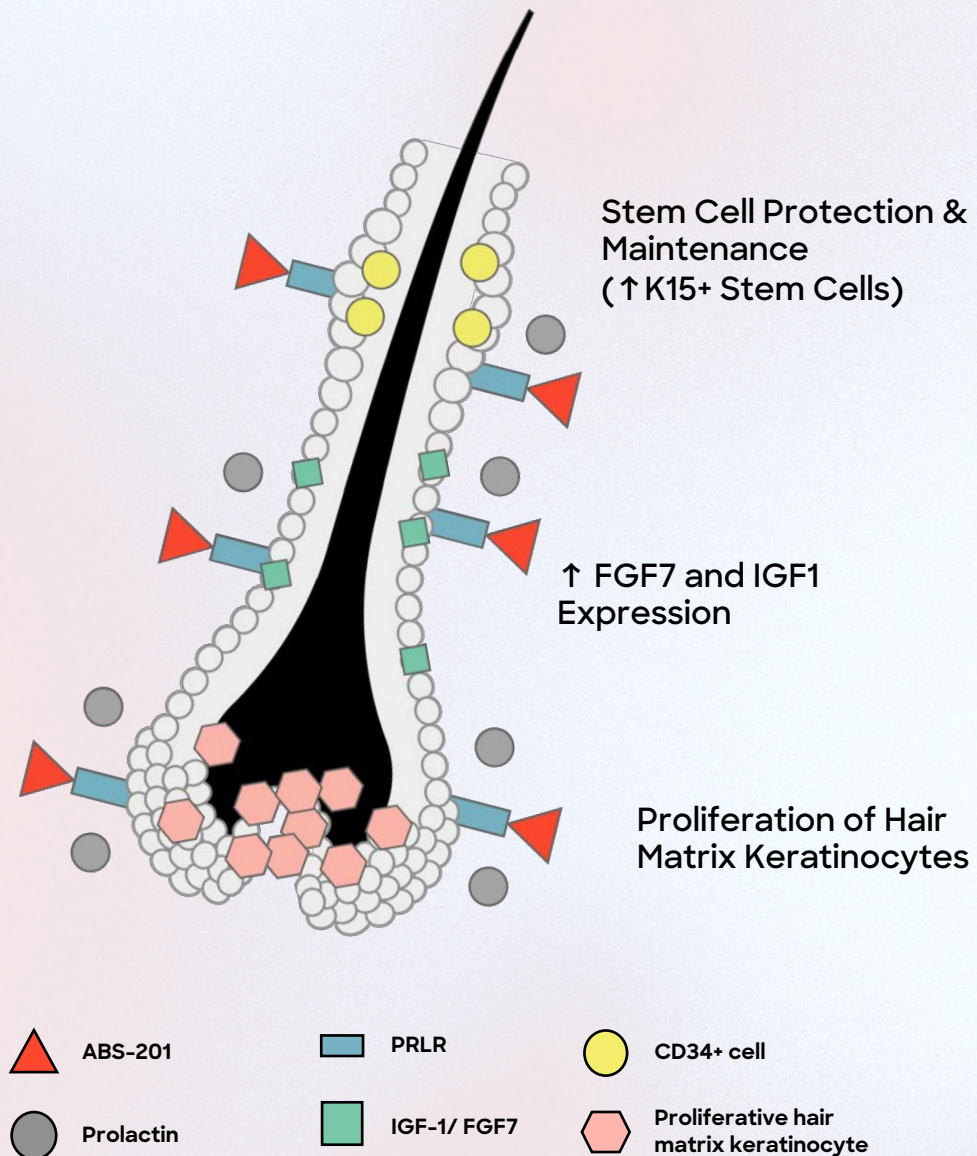


## MODEL SYSTEM:

- Frontotemporal male scalp skin is the most Pattern Hair Loss affected skin region
- Organ culture is the most relevant human preclinical hair research tool ex vivo

**ABS-201 significantly prolongs anagen/inhibits catagen and stimulates hair matrix proliferation**





## Additional ABS-201 ex vivo study found:

- Prolonging anagen phase and blocking catagen, thereby inhibiting telogen effluvium
- Protecting and promoting hair follicle stem cells and restoring CD34+ progenitor cells
- Stimulating key hair growth factors (IGF1, FGF7)
- Decreasing catagen driver TGFβ-2
- Increasing hair shaft and hair shaft keratin production

# Phase 1/2a trial designed to provide readouts on safety, tolerability, and PoC in PHL

## HEADLINE

### Design Elements:

- Double-Blind, Placebo-controlled, FIH
- Multi-site study in Australia
- Dose range ensures predicted >90% RO

### Population:

- Up to 227 male & female healthy participants
- SAD; n= 32 healthy volunteers
- MAD; n= 147 AGA subjects (Norwood Scale IIIv-V)
- Optional PHL cohorts in SAD/MAD; n= 48
- 3:1 randomization

### Endpoints:

- **Primary:** Safety & Tolerability
- **Secondary:**
  - PK/PD
  - Efficacy readouts include target area hair count, width, and darkness (pigmentation)



### Single Ascending Dose

Cohort 1  
150mg IV  
n=8

Cohort 2  
450mg IV  
n=8

Cohort 3  
900mg IV  
n=8

Cohort 4  
1800mg IV  
n=8

- Initiated December 2025
- All planned SAD cohorts dosed
- Interim SAD data shows study medication appears well tolerated, with favorable safety data across all blinded SAD cohorts
- Half life of at least 65 days



### Multiple Ascending Dose (26 weeks)

Cohort 1  
300mg SC  
n=49

Cohort 2  
600mg SC  
n=49

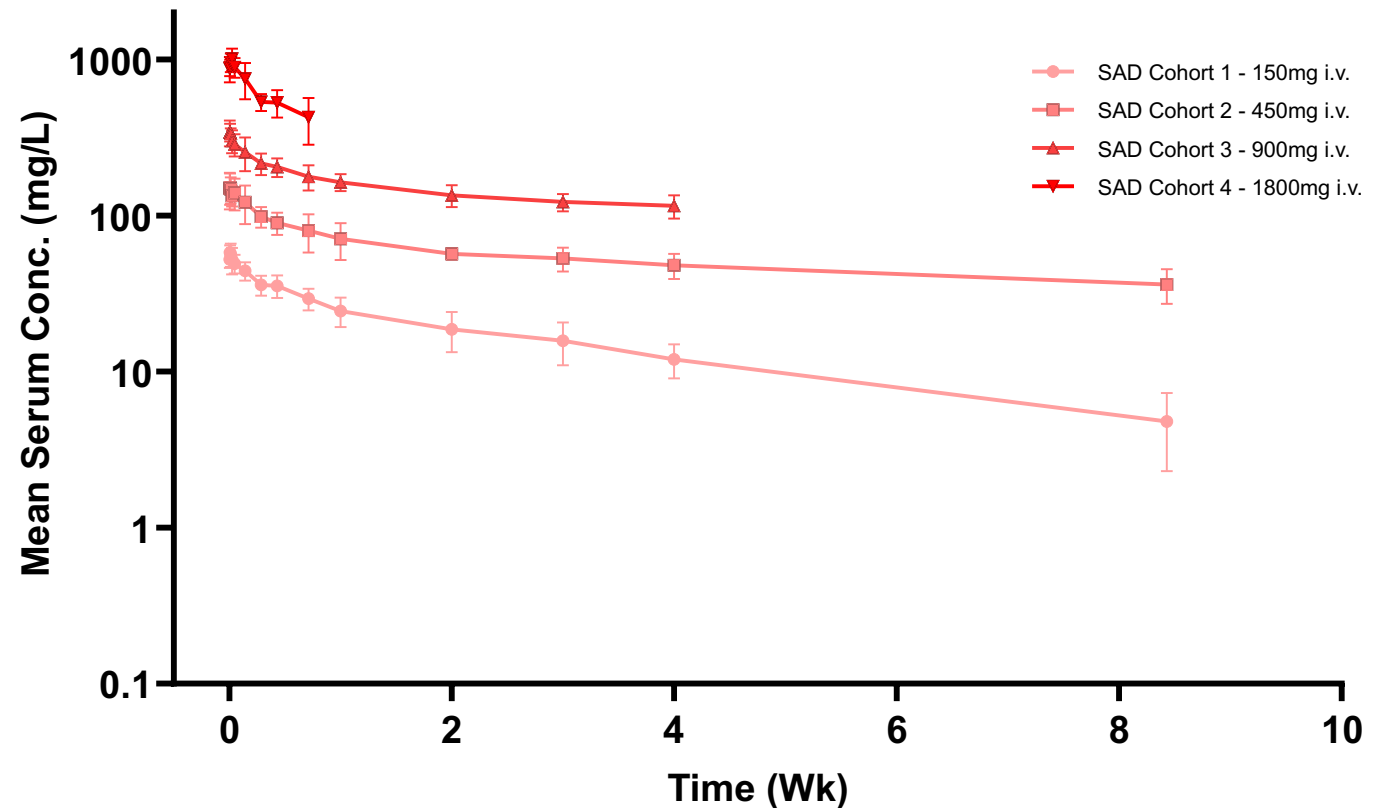
Cohort 3  
1200mg SC  
n=49

- MAD design enabling **PoC for AGA**
- **MAD Cohort 3 enrolling**
- **2H 2026:** Expected 13-week interim PoC readout
- **Early 2027:** Expected 26-week topline PoC readout

Half life of >65 days  
at doses  
overcoming TMDD

PK profile supports  
targeted dosing  
interval of 2 or 3  
injections over  
six-month period

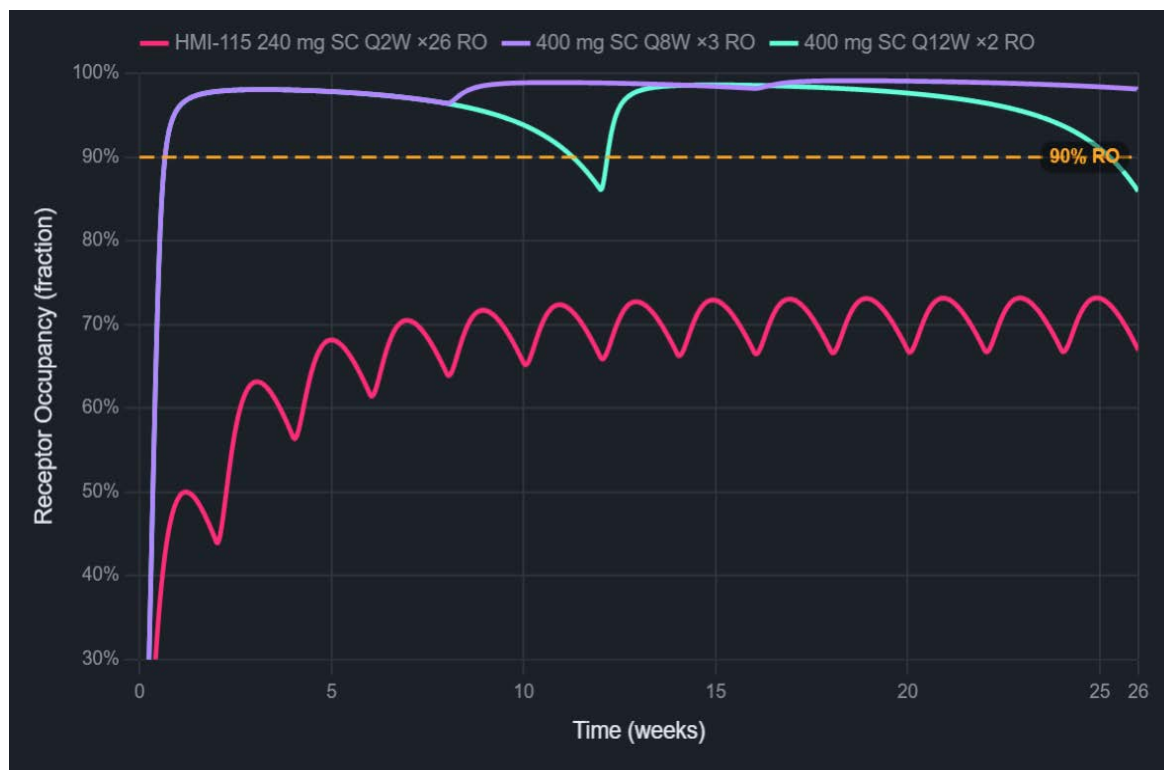
### HEADLINE Trial Interim PK Data from SAD Cohorts



Log-linear regression of geometric mean concentrations from terminal phase.  
Error bars: geometric SD interval.  
Cut-off date: June 8, 2026

# Modeling of Interim PK Data Supportive of Convenient Dosing Profile

## ABS-201 current ~70% s.c. Bioavailability



Assumptions:

- 15% - scalp skin tissue distribution
- 55% - s.c. bioavailability derived for HMI-115 based on its phase 1 data

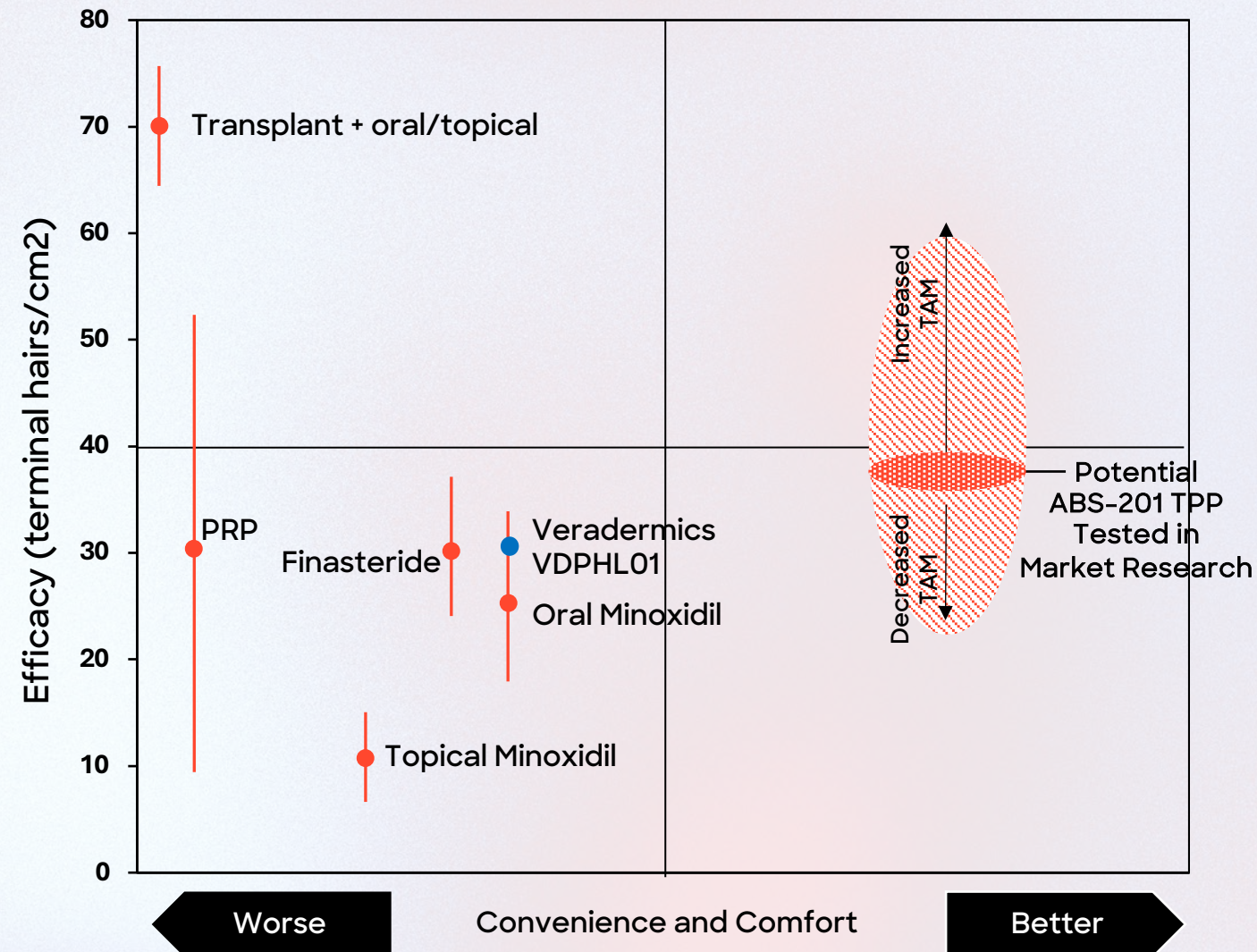
- Modeling of interim PK data from HEADLINE Trial supports the potential for 2–3 s.c. injections over six-month period (e.g., 400 mg/injection) to maintain > 90% Receptor Occupancy without cycling
- s.c. bioavailability of ~70% based on popPK modeling of early PK data
- Continued model refinement planned as further s.c. bioavailability data emerge from MAD cohorts

**Note:** The 400mg dose shown is illustrative for modeling purposes and does not represent a final, assumed dose. Dose range finding is currently ongoing in the MAD portion of the HEADLINE trial.

# ABS-201 TPP aims to offer a new treatment category in PHL based on efficacy and convenience

- Novel, targeted regenerative hair follicle mechanism
- Convenient, infrequent pulse therapy: 2-3 subcutaneous injections over six-month period
- Potential for durable efficacy: may provide 2-3 years of hair growth
- TPP tested in market research supports total addressable market >\$25B

\* Based on 2-3 injections during first 6 months for >2 years of hair growth  
 Efficacy at 24w for Vertex terminal hair count in male subjects: Oral Minoxidil (5mg/day): Panchaprateep 2020 (10.1007/s13555-020-00448-x) and Penha 2024 (doi:10.1001/jamadermatol.2024.0284); PRP: Dervishi 2019 (10.1111/jocd.13113); Finasteride and Topical Minoxidil: Gupta 2022 (doi:10.1001/jamadermatol.2021.5743 ), Transplant: based on KOL interviews.



# Consumer Research Commissioned by Absci Validates Market Potential of ABS-201

## Significant Unmet Need:

Driven by psycho-social impacts (loss of confidence, self-esteem) from PHL

## Strong Commercial Demand:

Nearly all men and roughly 90% of women are inclined to ask their doctors about ABS-201

## High Value Proposition:

Significant share of respondents willing to pay a premium for the ABS-201 TPP

## Disruptive Potential:

Over 1/3 of respondents would select ABS-201 before their current treatment, suggesting ABS-201 can effectively compete as first-line therapy

## 610 Participants:

306 Men | 304 Women

\*ALL PARTICIPANTS EXPERIENCING HAIR LOSS

UP TO  
**97%**  
MEN

UP TO  
**88%**  
WOMEN

**EXTREMELY OR VERY  
LIKELY TO ASK HCP  
ABOUT ABS-201**

**37%**  
MEN

**36%**  
WOMEN

**WOULD TRY ABS-201  
FIRST (FIRST LINE)**

**80%**  
MEN

**81%**  
WOMEN

**REPORT NEGATIVE  
PSYCHOLOGICAL  
IMPACT**

**Total PHL pts in the US**  
50M male, 30M female

**80M**

**Income ≥\$75K (US Census)**  
Pts 17-69 yo

**~39M**

**Concerned / motivated  
about hair loss**

**~26M**

**Strong interest in TPP\***

**~22 – 24M**

**Strongest interest in TPP  
with premium price-to-performance\***

**~15 – 18M**

## Patient Funnel

**>\$25B**

ESTIMATED U.S. TAM

**>\$40B**

POTENTIAL GLOBAL TAM

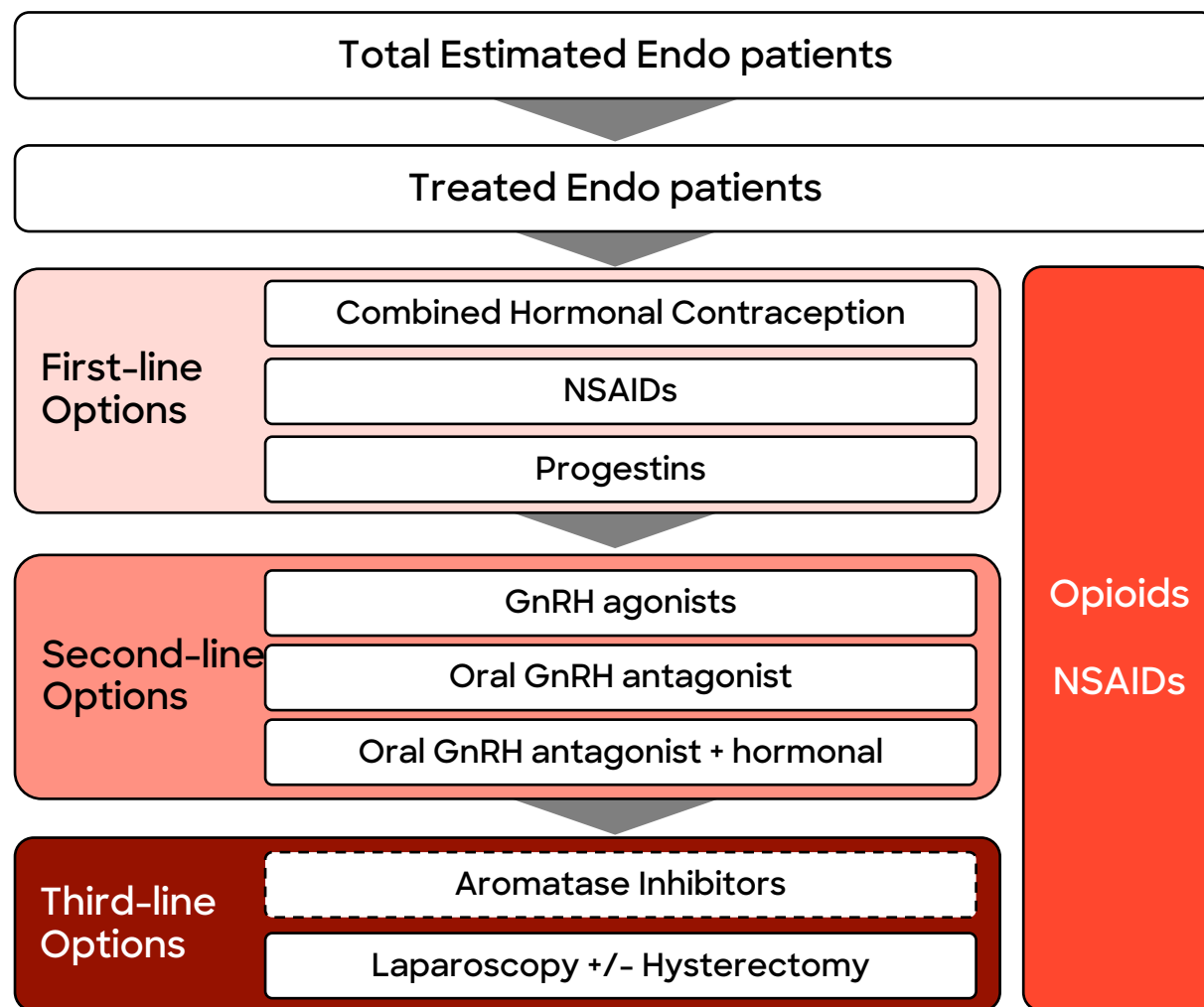
**5-9M Pts Treated/Year**  
Assuming 2-3 Year Durability

# Development of **ABS-201** in **Endometriosis**

1. Addresses Long-standing Unmet Medical Need and Poor standard of care
2. Strong Biological And Clinical Rationale: Including POC for PRLR mechanism in humans
3. Large, untapped market offers significant upside potential

# Hormonal therapies and surgical intervention make up the treatment paradigm for Endo

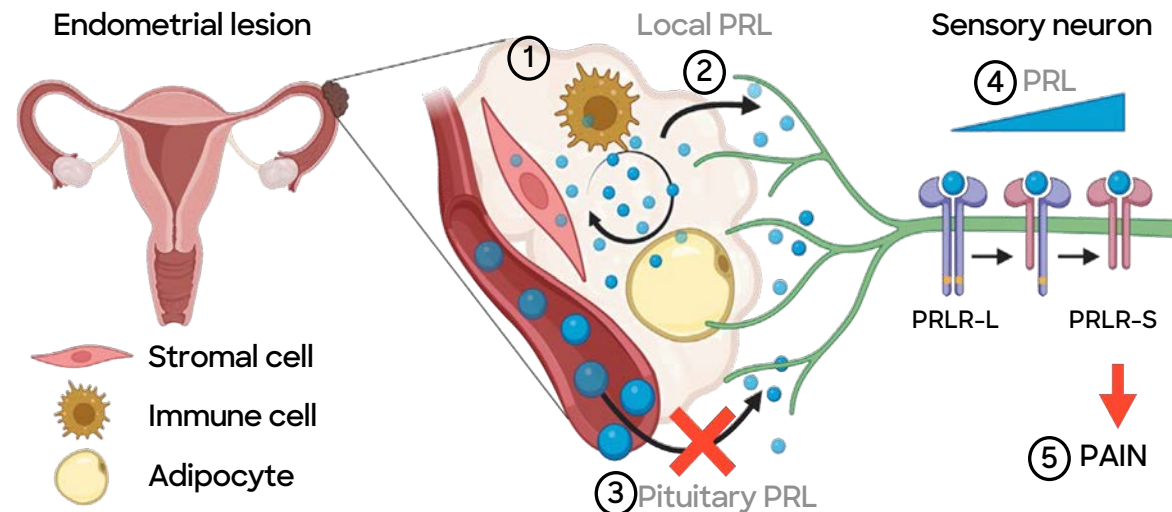
## Current Treatment Paradigm (US)



- Endo is a chronic condition with currently no medical or surgical cure
- Roughly, 75% of patients are estimated to use opioids and/or NSIADs throughout their disease course
- Up to 33% of patients do not respond to hormonal treatment alone
  - Additionally, patients will pause treatment when seeking pregnancy
- GnRH therapies are typically prescribed by Gynecologist and AE profile often limits long-term use
- Notably, aromatase inhibitors are not FDA approved for Endo, but are used off-label
- Up to 40% of Endo patients undergo a laparoscopy and 12% receive hysterectomies
- Even after hysterectomy ~15% of patients still report pain symptoms

# PRLR antagonism is a novel and differentiated MoA in Endometriosis

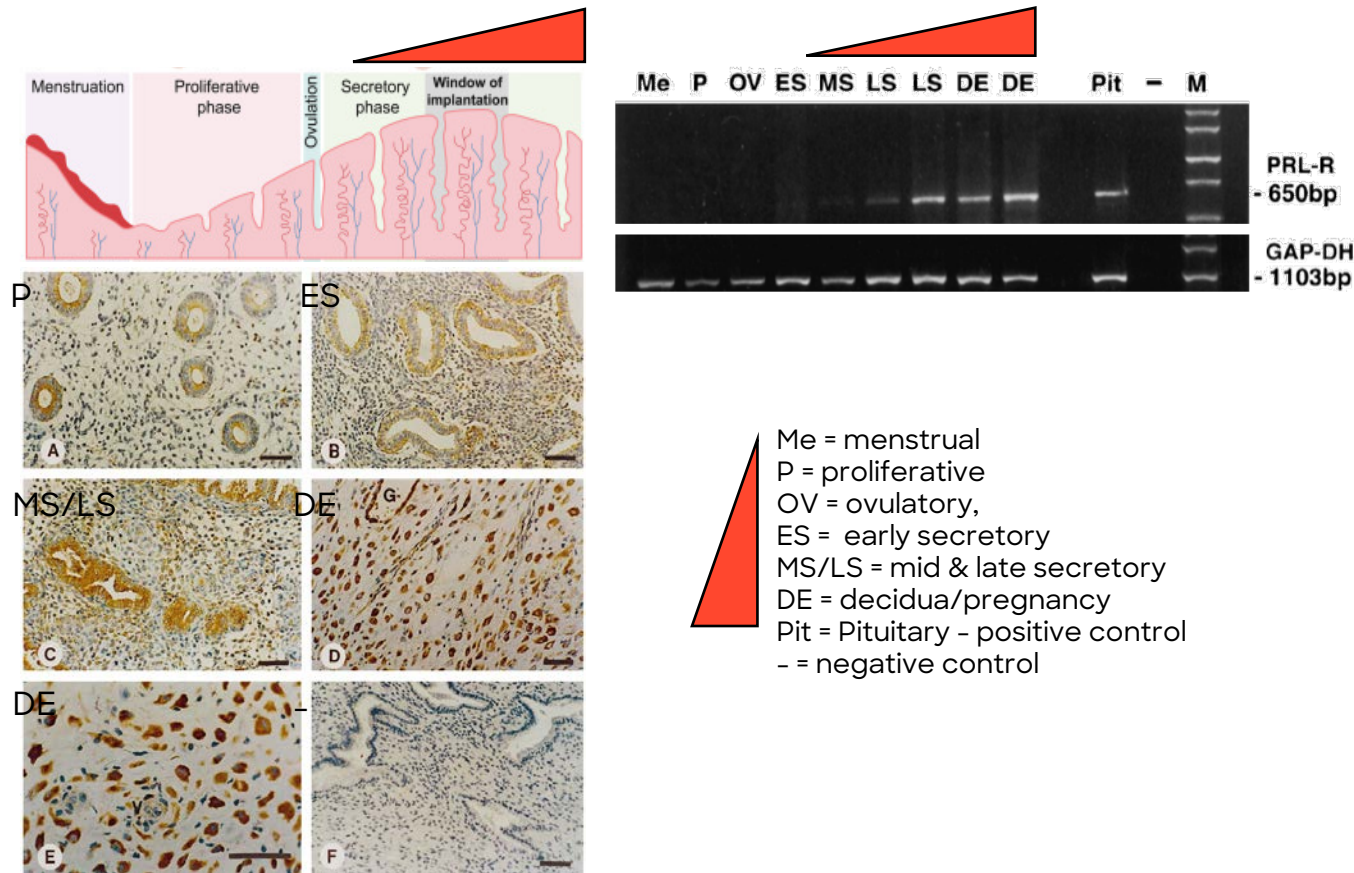
PRL and PRLR play a dual role in endometrial lesion development and pain response



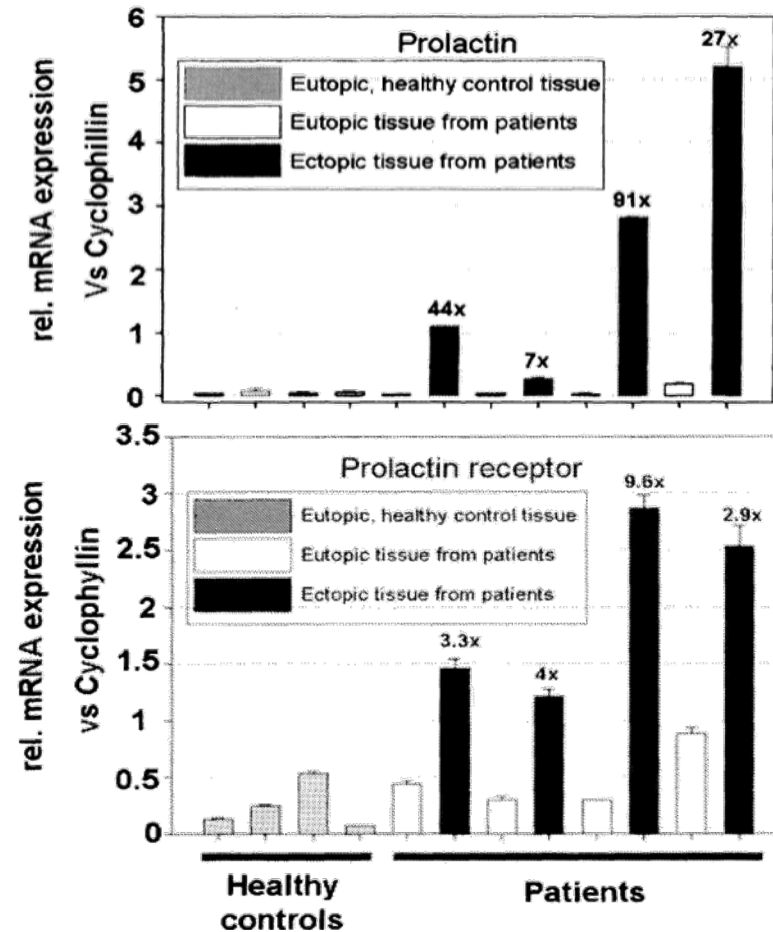
- Endometriotic lesions produce prolactin under estrogen/progesterone control.
- Excess prolactin promotes lesion growth and sensitizes pain-sensing nerves, contributing to chronic pelvic pain.
- Prolactin signaling is independent of sex-hormone pathways, offering a differentiated, non-hormonal treatment modality vs current therapies.

# PRL and PRLR increase during secretory phase in healthy tissue, and is overexpressed in endometrium of patients with endometriosis

## Localization And Temporal Expression Of Prolactin Receptor In Human Endometrium



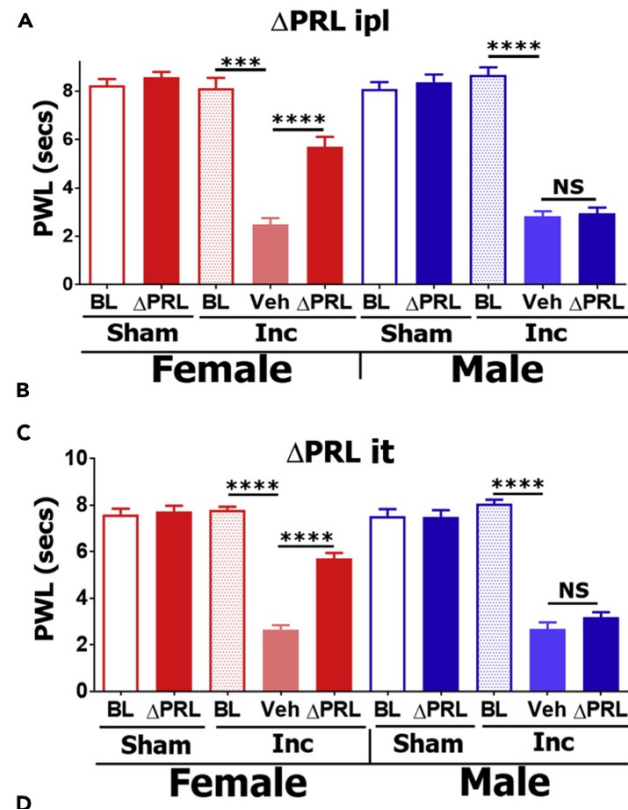
## PRL & PRLR is Elevated Ectopic Endometriotic Lesions



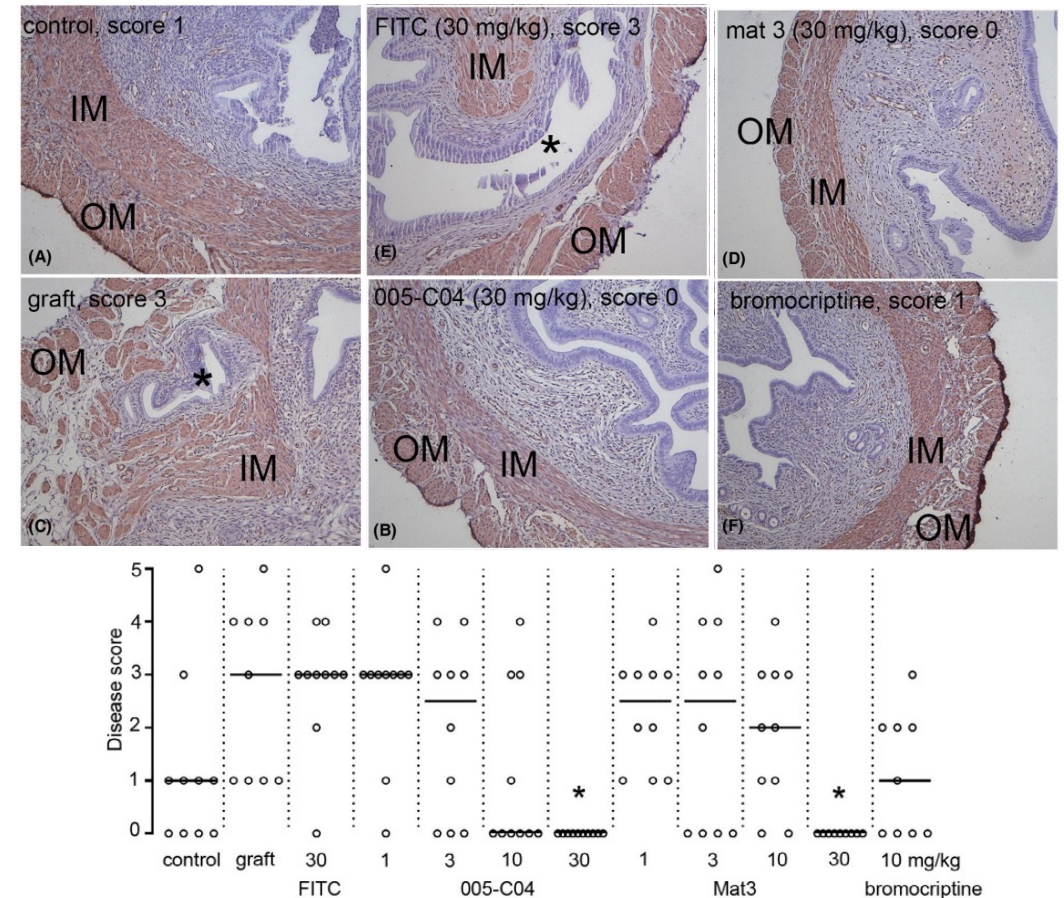
Jones et al. Journal of Clinical Endocrinology and Metabolism, 1998; Otto et al. WO 2011/069795 A4

# PRLR antagonism suppresses postoperative pain in female mice and inhibits endometriosis interna formation

Prolactin May Regulate Pain Responses via a Female-Selective Nociceptor-Specific Mechanism



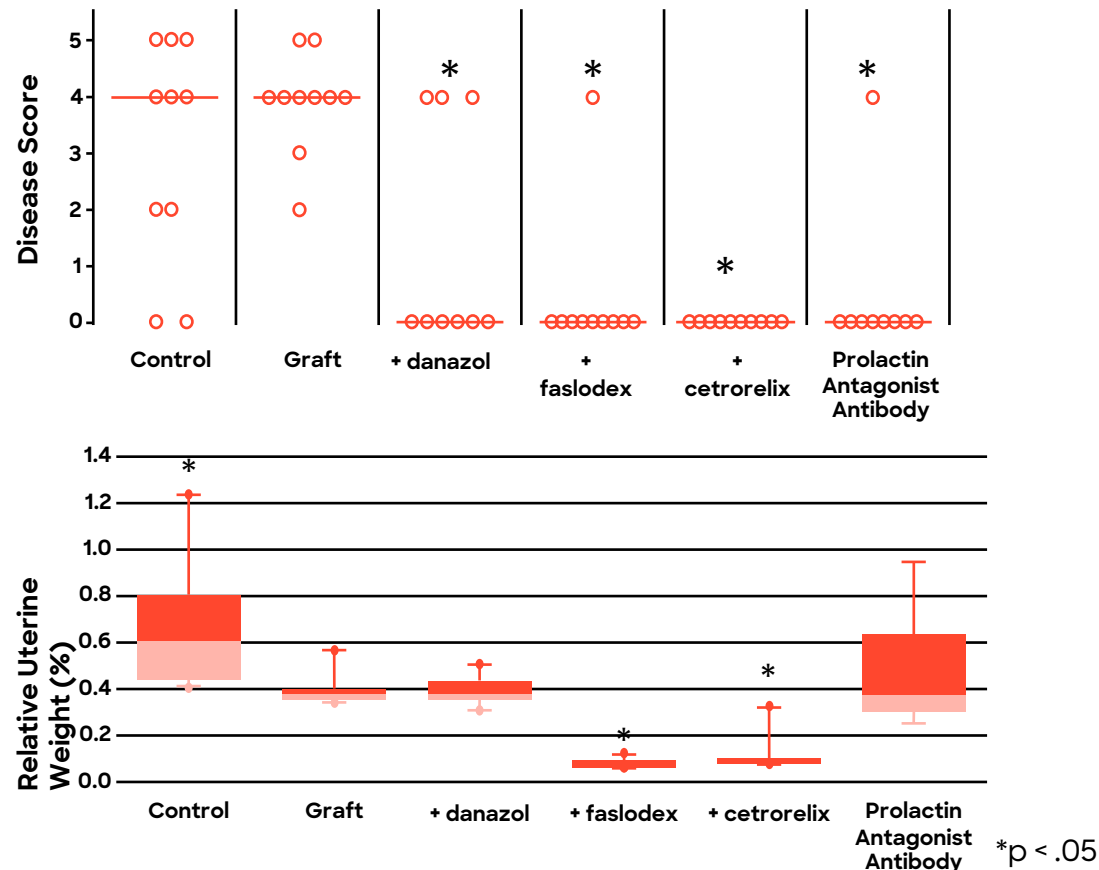
The Effects of Prolactin Receptor Blockade in a Murine Endometriosis Interna Model



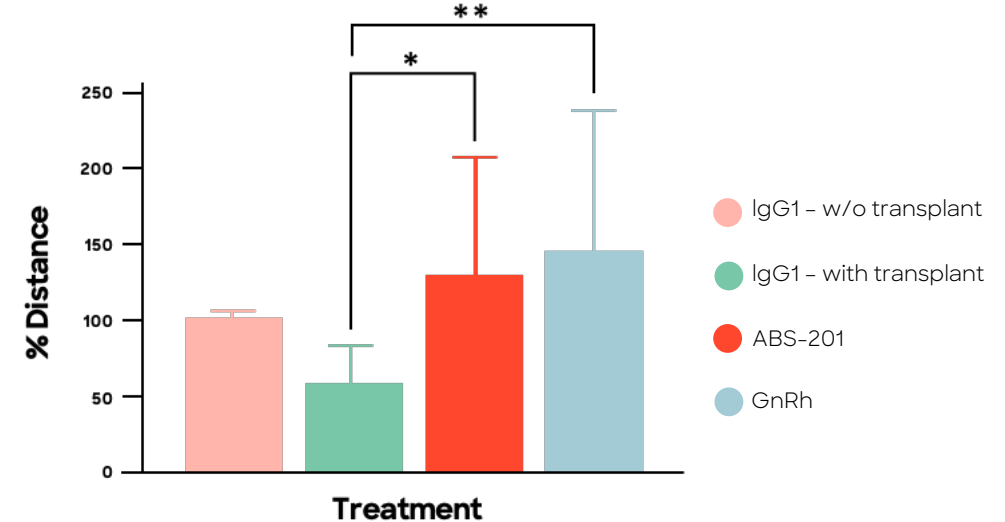
Depicted: pain incision (Inc) model for heat sensitivity &  $\Delta$ PRL administration

# PRLR antagonism reduces lesion formation and pain in endometriosis mouse model

Prolactin inhibition decreases endometrial lesion formation in female mouse interna



% Distance travelled at Week 7  
(compared to baseline)



○ ABS-201 and GnRh modulator increase distance traveled relative to placebo over time as surrogate for pain reduction

# ABS-201: a potentially differentiated profile targeting a large underserved market opportunity

NOVEL TREATMENT OPTION FOR ~9M PATIENTS  
IN THE U.S. ALONE WITH ENDOMETRIOSIS

- **Novel Mechanism:** Non-sex-steroid (peptide) hormone
- **Potential for Improved Safety Profile:** Potential improved AE profile & longer use than GnRH
- **Dual Action:** Potential on both pain and lesion growth
- **Best-in-class Potential:** Superior developability and expected half-life
- **Disease Modifying:** Potential to treat cause
- **Clinically validated:** through HMI-115 Ph2 study

Potential to generate

> \$4.5B  
at peak sales

# Clinical Strategy guided by a leading Endometriosis Advisory Board



**Hugh Taylor, MD (Chair)**  
Anita O'Keefe Young Professor  
Chair, Ob/Gyn & Reproductive  
Sciences, Yale School of  
Medicine



Joan-Carles Arce, MD, PhD  
Chief Scientific Medical  
Officer &  
Co-Founder, ReproNovo



Gaurang Daftry, MD  
Chief Scientific Officer &  
President of Physician Relations,  
Inception; Adjunct Associate  
Professor, Yale University, Mayo  
Clinic



Linda Giudice, MD, PhD  
Robert B. Jaffe, MD, Endowed  
Professor in Reproductive  
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Reproductive Sciences, UCSF



Axel Haupt, MD  
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Company



Zaraq Khan, MD  
Professor, Ob/Gyn,  
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Rob Scott, MD  
Former Chief Medical  
Officer of AbbVie; Absci  
Scientific Advisory Board  
member



Stephen Young, MD, PhD  
F. Bayard Carter Distinguished  
Professor of Ob/Gyn; Division Chief,  
Reproductive Endocrinology &  
Infertility, Duke University

# Leading AI x Bio platform driving 2 Phase 2 readouts in the next 24 months

## ABS-201 in PHL

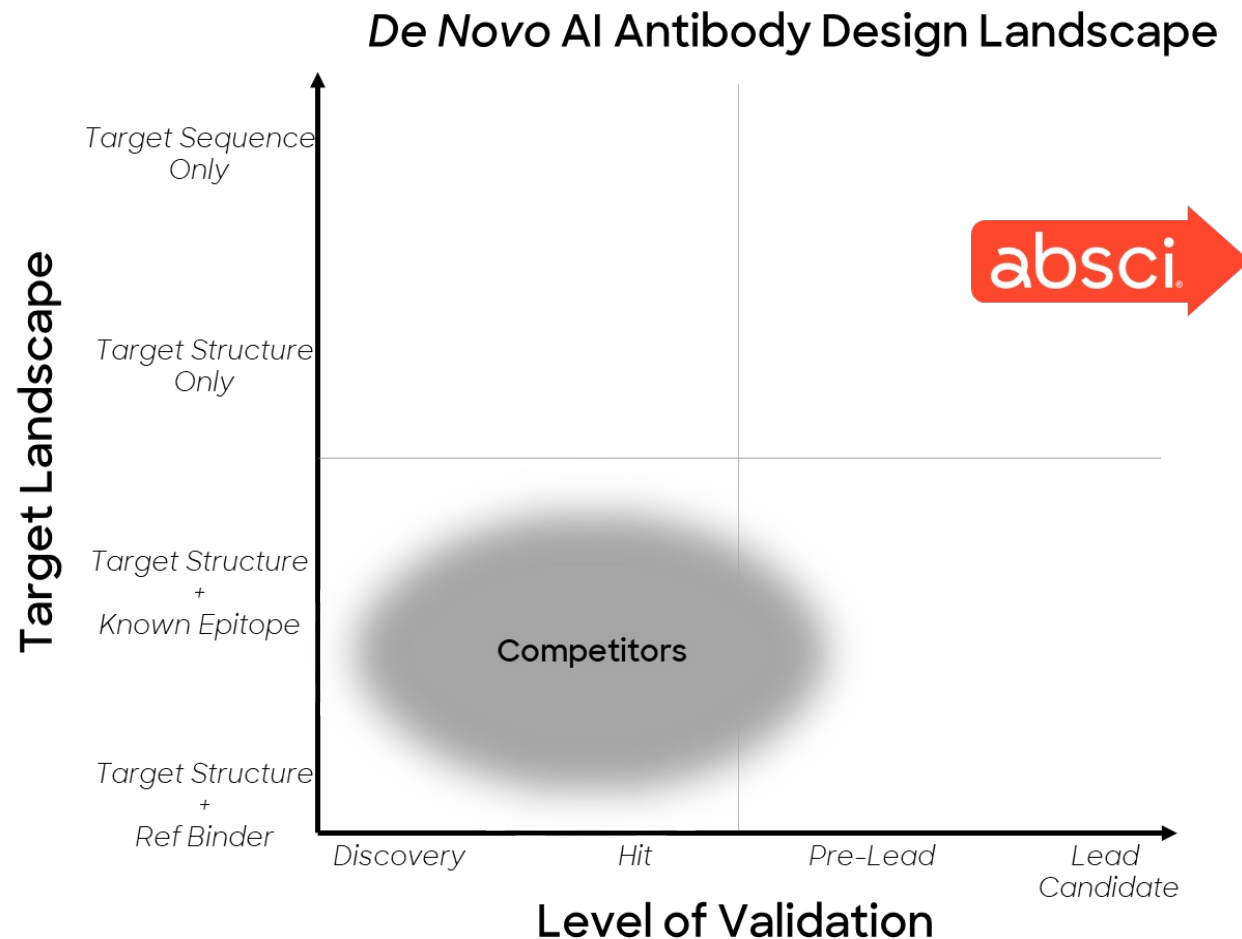
- Ph1/2a Study initiated Dec 2025
- Positive interim Safety, Tolerability, and PK readout June 2026
- Interim PoC Readout - anticipated 2H 2026

## ABS-201 in ENDO

- Ph1/2a Study initiated Dec 2025
- Phase 2 initiation expected in Q4 2026

# Powered by Absci's Leading AI Platform

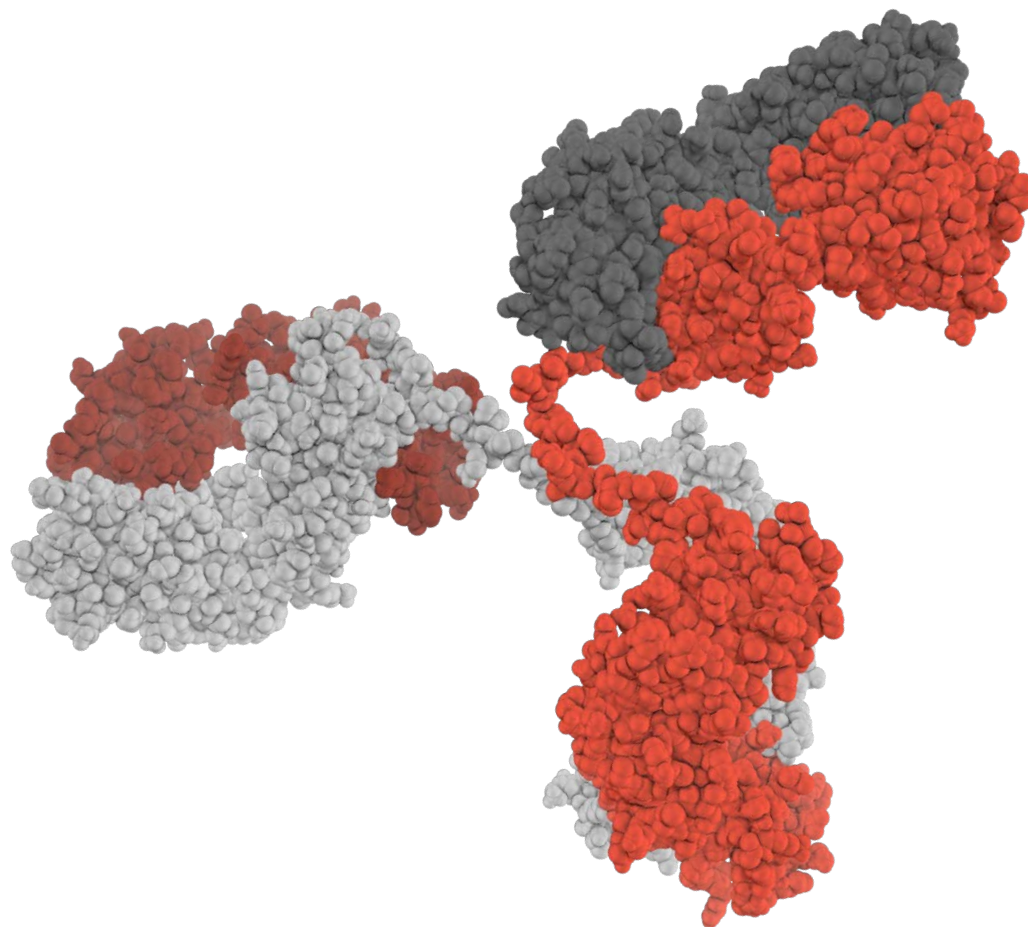
# Absci's de novo AI models deliver differentiated lead candidates against challenging targets



## ABSCI DIFFERENTIATION

- **Address challenging targets**
  - Only target structure or sequence required
- **Zero-Prior: Design against any epitope**
  - No known protein binder required
  - Interrogate multiple epitopes to achieve function (e.g. agonism)
- **Deliver mAbs that meet therapeutic criteria\***
  - Specificity
  - Developability
  - Function

# We use AI to create novel & differentiated therapeutics



- ✓ **EPITOPE-SPECIFIC DESIGN +  
EPITOPE INTERFACE OPTIMIZATION**
- ✓ **ENHANCED POTENCY AND MOA**
- ✓ **ABILITY TO ADDRESS DIFFICULT  
TARGET CLASSES, E.G. GPCRS**
- ✓ **ENABLING FEATURES: MULTI-VALENCY,  
pH-DEPENDENT BINDING**
- ✓ **POTENTIAL TO CREATE MEANINGFUL  
IP: 100S TO 10,000S OF FUNCTIONALLY  
VALIDATED SEQUENCES ENABLED BY  
PROPRIETARY WET-LAB VALIDATION**

# We create experimentally validated AI technology that enables *de novo* antibody design

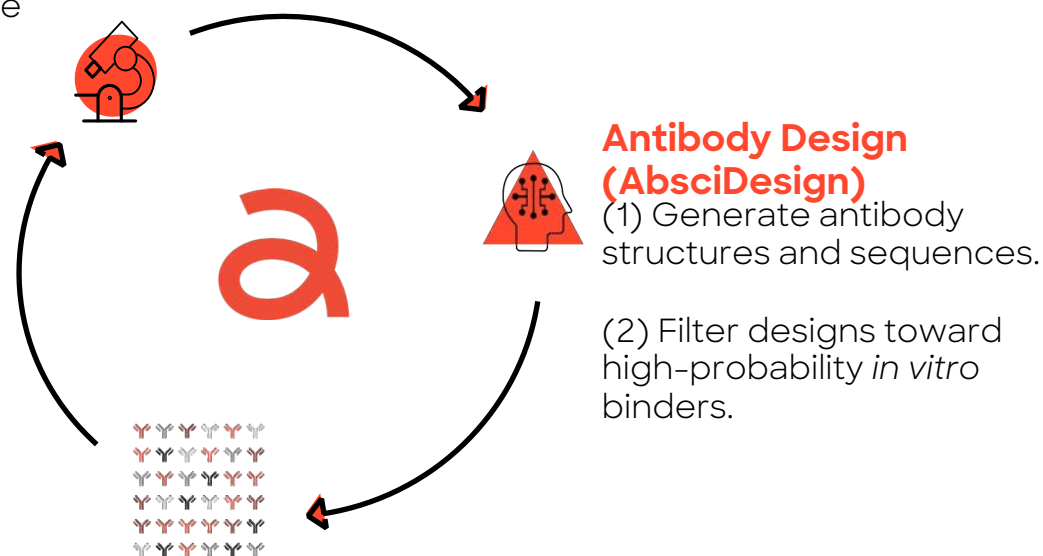
## Wet Lab Validation

**Wet Lab experiments** confirm binding, epitope-specificity, developability, and function.

**Wet Lab data** enable assessment of model performance improvements.

## Library Design

**AbsciDesign** generates “libraries” of sequences that encode putative antibody binders per disease target.



# Origin AI models design and optimize therapeutic antibodies

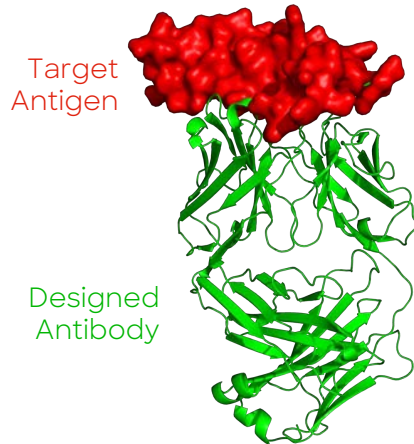
## INPUT



- 1.Target structure(s)
- 2.Epitope(s)
- 3.Antibody framework(s)
- 4.CDR lengths

## STRUCTURE & SEQUENCE DESIGN

### Structure Design



### Sequence Design

Design 1

**HCDR1:** GFNIKDTY  
**HCDR2:** IYPTNGYT  
**HCDR3:** SRWGGDGFYAMDY

**LCDR1:** QDVNTA  
**LCDR2:** SAS  
**LCDR3:** QQHYTTPPT

⋮

Design N

**HCDR1:** GFNIKDTW  
**HCDR2:** IYPSNGYT  
**HCDR3:** ARWGGDGFYAMDY

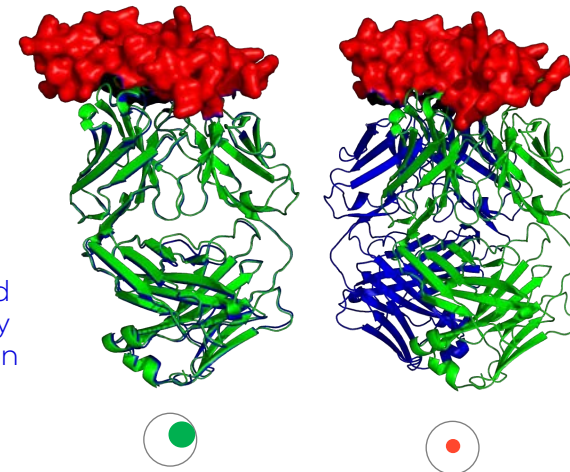
**LCDR1:** QDVNTA  
**LCDR2:** SAS  
**LCDR3:** QQHYTTPPT

## DESIGN SCORING & FILTERING

Target Antigen

Designed Antibody

Designed Antibody Prediction



- Score, rank, and filter designs to optimize for diversity and binding likelihood
- Leverage quality confidence metrics, energy metrics, and molecular dynamics simulations to evaluate designs

## OUTPUT LIBRARY

### DESIGN LIBRARY

1. DESIGN 1
2. DESIGN 2
3. DESIGN 3

⋮

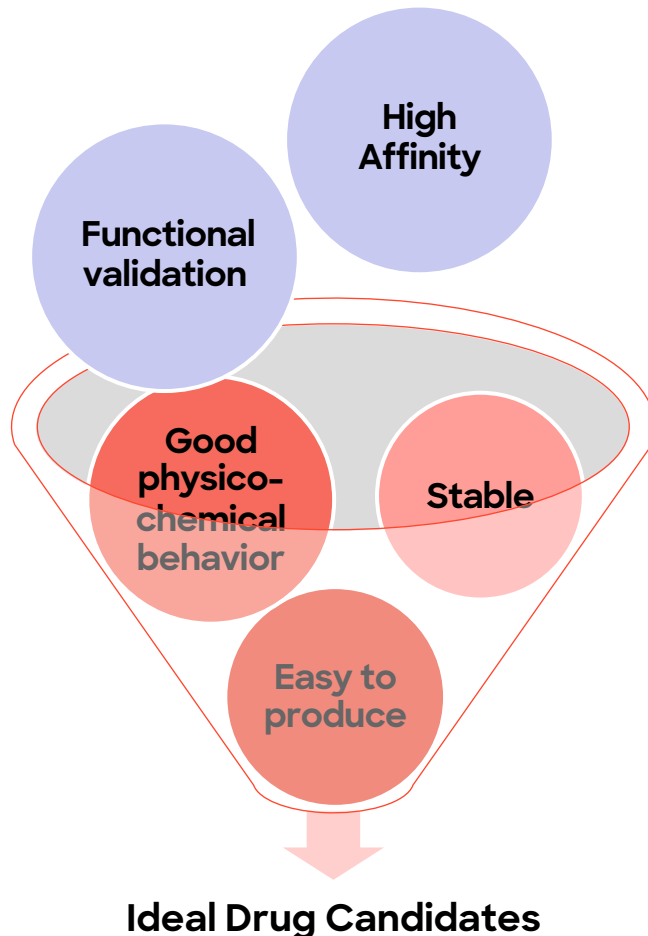
N. DESIGN N

**Output:** library of amino acid sequences encoding antibody binders to therapeutic target-of-interest

CDR = Complementarity Determining Region

H = Heavy Chain; L = Light Chain

# Lab-in-the-loop ensures AI-designed antibodies translate into drug-ready candidates



- **Screening** team confirms binding to target and affinity
- **Disease Biology** team validates functional activity
- **Analytical Development** team conducts developability assessment:
  - No self-association, hydrophobicity, or poly-reactivity
  - Appropriate melting temperature and colloidal profile, and stable upon stress conditions
- **Production team** evaluates manufacturability in CHO cells

# Introducing Origin-1: an AI platform for *de novo* antibody design against **zero-prior epitopes**



## Zero-Prior Epitope Targeting

Designed full-length mAbs against epitopes with no known protein binders or structural data in <100 designs per target



## High Structural Fidelity

Cryo-EM confirmed designs at 3.0–3.1 Å resolution with DockQ 0.73–0.83, confirming high structure design accuracy



## Functional Antagonist

AI-guided affinity maturation yielded 68x affinity gain for IL36RA, producing a functional antagonist at ~100 nM EC50

## Origin Pipeline Components:

AbsciDiff  
All-atom diffusion model



AbsciGen  
CDR sequence design

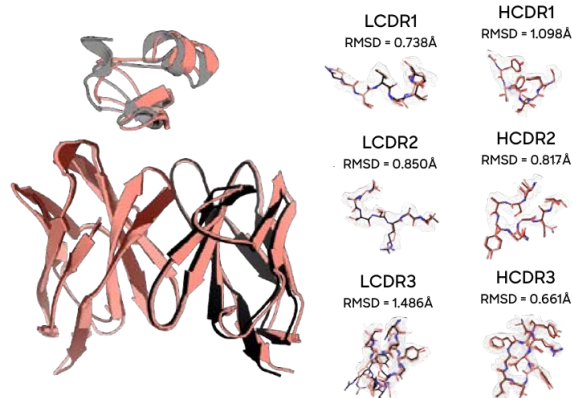


AbsciBind  
Scoring & filtering

### COL6A3

Experimental Structure  
Designed Heavy Chain  
Designed Light Chain  
Designed Antigen

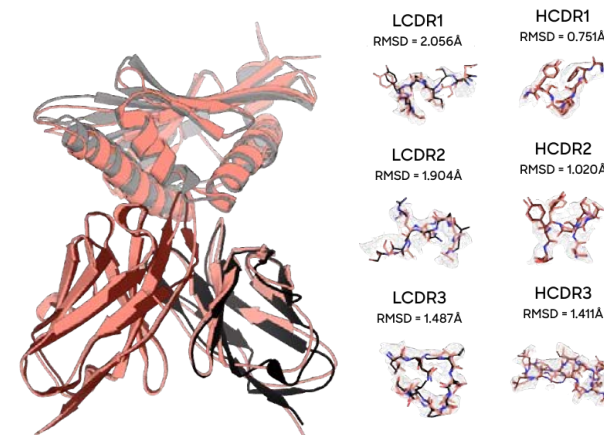
All-Atom Global RMSD = 2.56Å  
Interface RMSD = 0.95Å  
Ligand RMSD = 1.58Å  
DockQ = 0.84



### AZGP1

Experimental Structure  
Designed Heavy Chain  
Designed Light Chain  
Designed Antigen

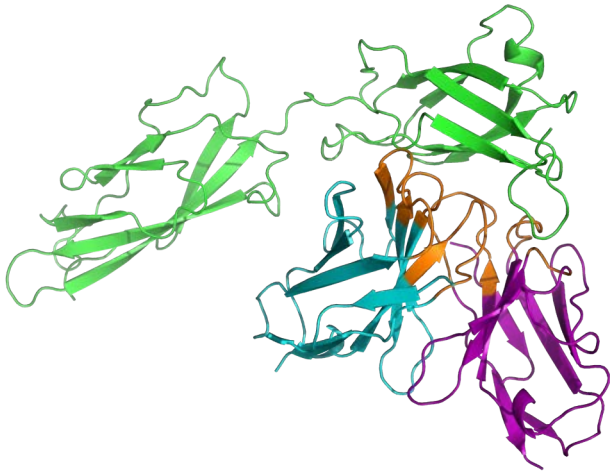
All-Atom Global RMSD = 1.79Å  
Interface RMSD = 0.96Å  
Ligand RMSD = 1.48Å  
DockQ = 0.83



<https://www.absci.com/denovo/>

# Absci's de novo AI models deliver differentiated lead candidates against challenging targets

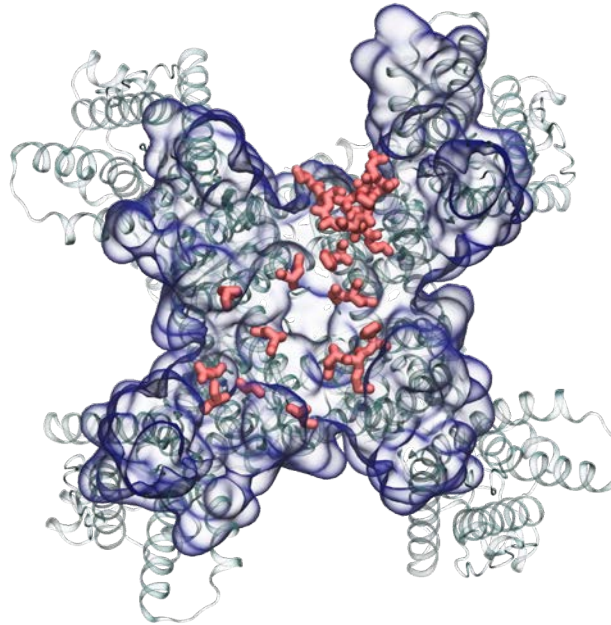
## DE NOVO ANTIBODY DESIGN AGAINST TRANSMEMBRANE TARGET EPITOPE WITH NO KNOWN BINDER



Designed seven high-affinity antibodies against partner-specified epitopes on a transmembrane antigen without a known binder.

*Pharma collaboration*

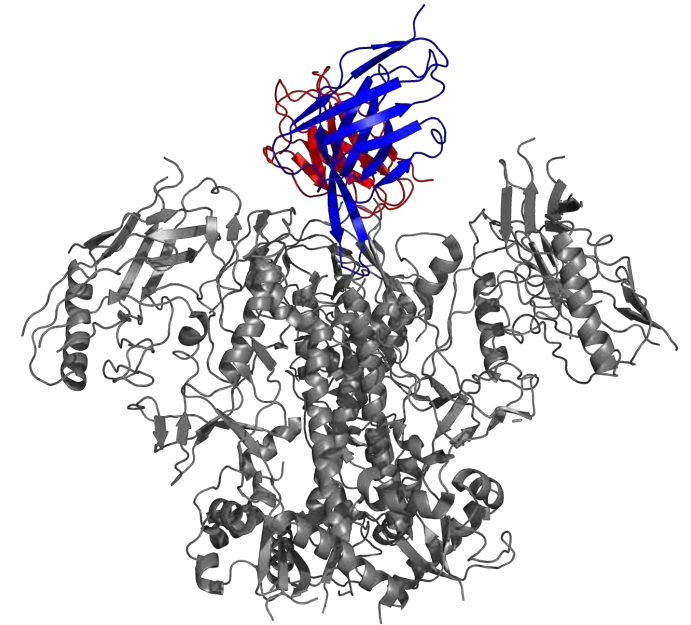
## DE NOVO ANTIBODY DESIGN AGAINST CHALLENGING ION CHANNEL



Designed a pore-blocking, functional antagonist against a tetrameric membrane-embedded ion channel.

*Pharma collaboration*

## DE NOVO ANTIBODY DESIGN AGAINST CONSERVED HIV-1 "CALDERA" EPITOPE



Designed cross-reactive, conformation-specific antibodies against the HIV-1 "Caldera" epitope.

*Caltech collaboration*

# We use high-fidelity, customized datasets with our own AI models to enrich for developable candidates

Generates **diverse**, **developable**, and **functional novel variants** within a desired target product profile (TPP):

**Precise affinity tuning** for bi-specific arms

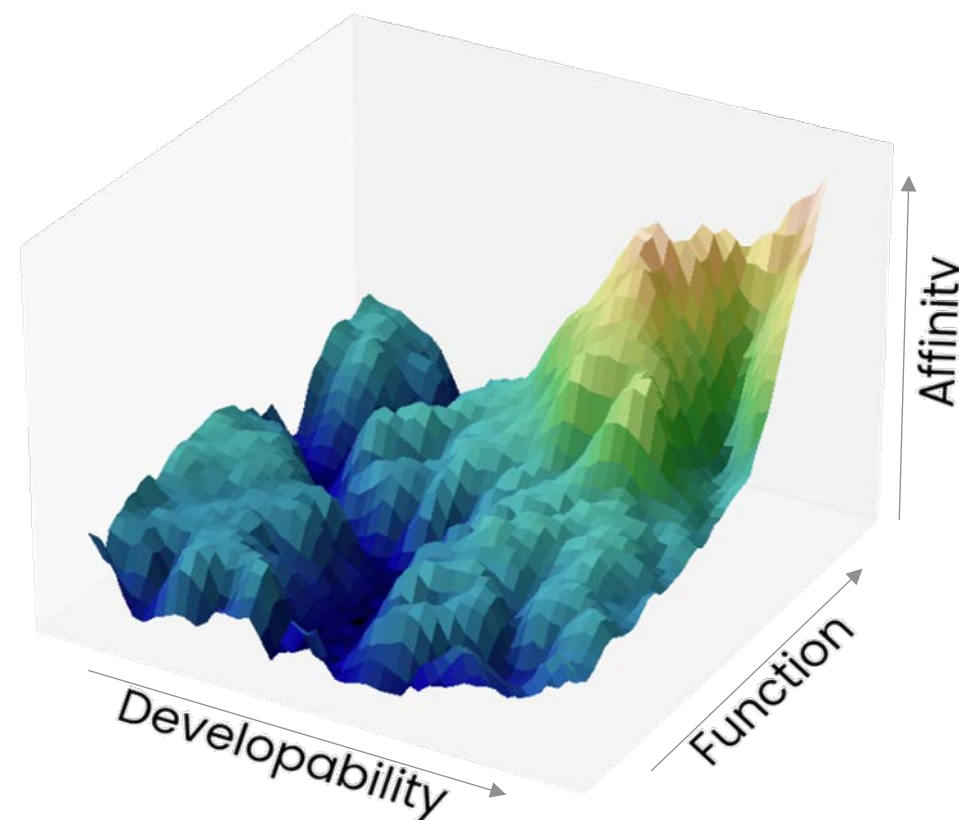
**Cross-reactive** leads to support *in vivo* testing

**Conditional** leads for optimal pharmacology

**Lab-in-the-loop** synergy provides strong model performance out to  $>10^{18}$  combinatorial space\*

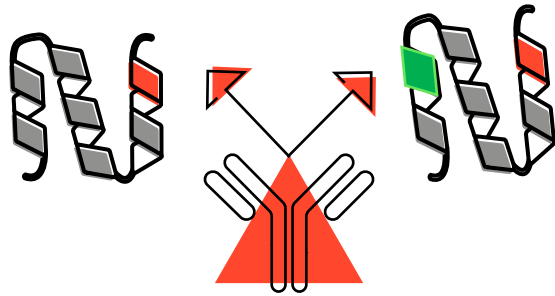
\*derived from  $\geq 10$  amino acid changes at  $\geq 24$  CDR positions sampling all residues except cysteine

**Landscape-wide scoring** enables selection of optimal sets of sequences



# Success in AI-design and optimization of multiple developability and pharmacological properties

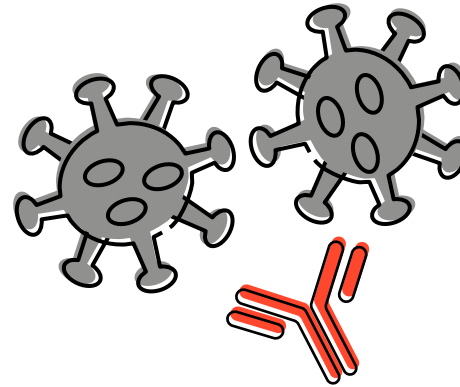
## CROSS-SPECIES OPTIMIZATION



Successful design of antibodies binding to both mouse and human antigens

- Hits identified from  $10^{19}$  combinatorial space
- Models identify hits with >175x tighter affinity and <500 pM KD to both antigens

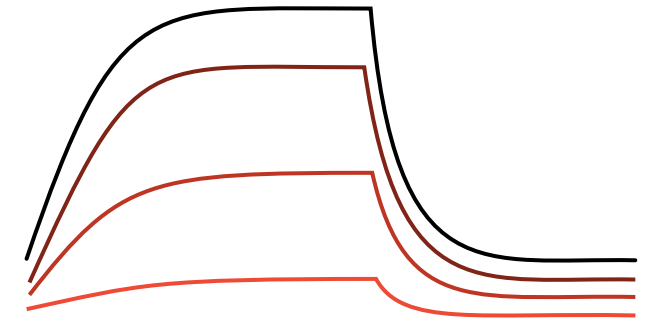
## MULTI-VARIANT SPECIFICITY



Successful design of antibodies with expanded neutralizing activity vs three SARS-CoV-2 spike variants

- Tuned models identify developable hits with higher affinity to three variants, including >50x tighter affinity to previously resistant variant
- Potent neutralization activity to all three variants

## PH-SENSITIVE BINDING



Successful design of pH-sensitive antibodies through sampling the entire relevant ionizable search space

- Hits show 20x to >100x pH sensitivity with favorable developability after one round

# Track record of industry-leading partnerships

## AI DRUG CREATION™ PARTNERSHIPS



Caltech

UCLA

## SUPPORTING COMPUTE COLLABORATIONS



ORACLE



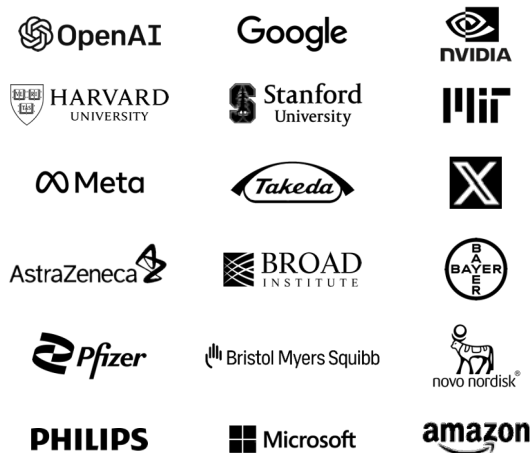
## 25+ PARTNERED PROGRAMS TO DATE

### OUR PARTNERSHIP FOCUS

- Challenging Targets / Epitopes
- Differentiated TPPs
- Mono or Multi-specific Formats

# "Multilingual" team with expertise in AI and drug creation

## EXPERTISE AND BACKGROUND FROM:



### Leadership Team:



Sean McClain  
Founder, CEO & Board  
Director



Zach Jonasson, PhD  
Chief Financial Officer  
& Chief Business Officer



Ransi Somaratne, MD  
Chief Medical Officer,  
Head of R&D



Shelby Walker, JD  
Chief Legal Officer



Christine Lemke  
SVP, Portfolio & Growth  
Strategy

### Board Of Directors:



Frans Van Houten  
Chairman of the Board  
Former CEO, Royal  
Phillips



Sean McClain  
Founder, CEO & Board  
Director



Sir Mene  
Pangalos, PhD  
Former EVP R&D  
AstraZeneca



Mary Szela  
CEO & President  
TriSalus Life Sciences



Joseph Sirosch, PhD  
Former CVP AI  
Microsoft



Dan Rabinovitsj  
VP Hardware  
Engineering, Meta



Karen McGinnis,  
CPA  
Former Chief  
Accounting Officer,  
Illumina

### Scientific Advisory Board:



Sir Mene  
Pangalos, PHD  
Co-Chair SAB  
Former EVP R&D  
AstraZeneca



Andreas Busch,  
PHD  
Co-Chair SAB  
Chief Innovation Officer



Ian McInnes, PHD  
Vice Principal and Head  
of College  
University of Glasgow



Luis Diaz, MD  
Head, Division of Solid  
Tumor Oncology  
Memorial Sloan  
Kettering Cancer  
Center



John Wherry, PHD  
Director, Institute for  
Immunology & Immune  
Health, University of  
Pennsylvania



Victor Greiff, PHD  
Associate Professor  
University of Oslo



Rob Scott, MD  
Former Chief Medical  
Officer, Abbvie

## Absci at a Glance

# 140

**EMPLOYEES**

“Multi-lingual” AI + Drug Discovery expertise AI team drawing on experience from tech leaders:



Biologics drug discovery expertise from:



# 77,000

**SQUARE FEET**

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

# 10+

**PARTNERS, INCLUDING**



# 3

**CLINICAL  
STAGE  
PROGRAMS**

In Pattern Hair Loss, Endometriosis, and I&I

# >\$750M

**CAPITAL RAISED TO  
DATE**

# Generative AI Re(Generative) Biology

## AI CASE STUDY I

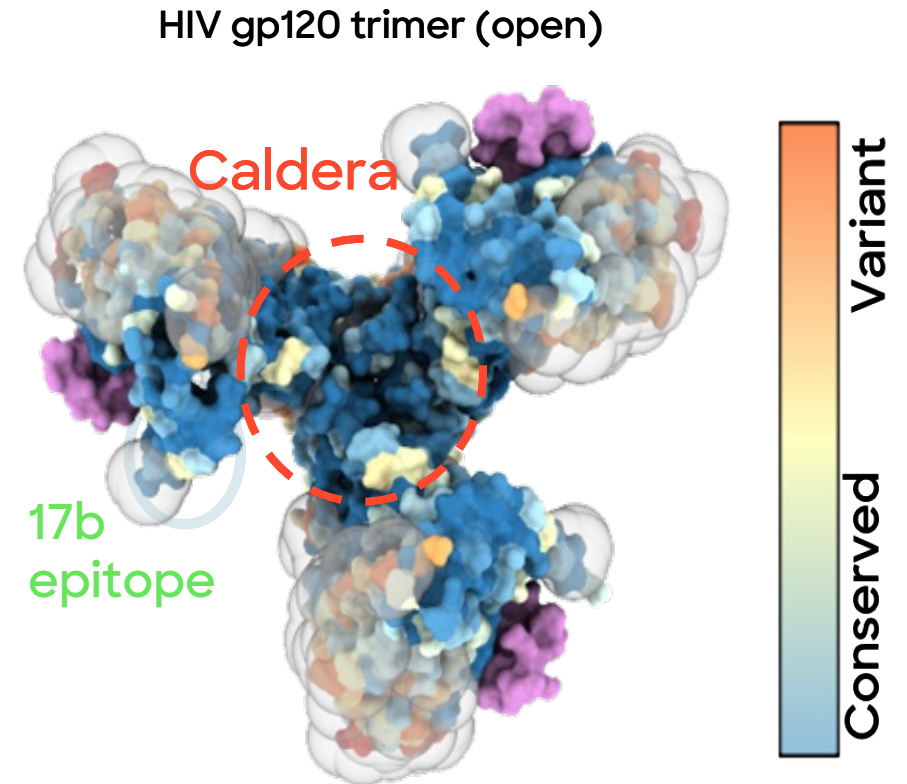
*de novo* design of an antibody that binds the  
Caldera region of HIV-1 trimer

Caltech absci. BILL & MELINDA  
GATES foundation



## ***de novo* design antibody that binds to the highly conserved caldera region of HIV gp120**

- No natural or synthetic antibody for HIV exists today because immune system cannot derive an antibody that is universally neutralizing against HIV
- Design challenge: create universally neutralizing HIV antibody by binding unique and conserved epitope within “caldera” of open conformation of gp120 to prevent HIV from entering host cells
- Numerous attempts to target this epitope have failed—previous efforts have identified antibodies, but none bind the “caldera” and none are universally neutralizing.



# HIV-Caldera: Determine inputs and design

## HIV Env Trimer Challenge :

- Highly glycosylated
- Extremely high sequence diversity among isolates
- High mutation rate at common neutralizing epitopes

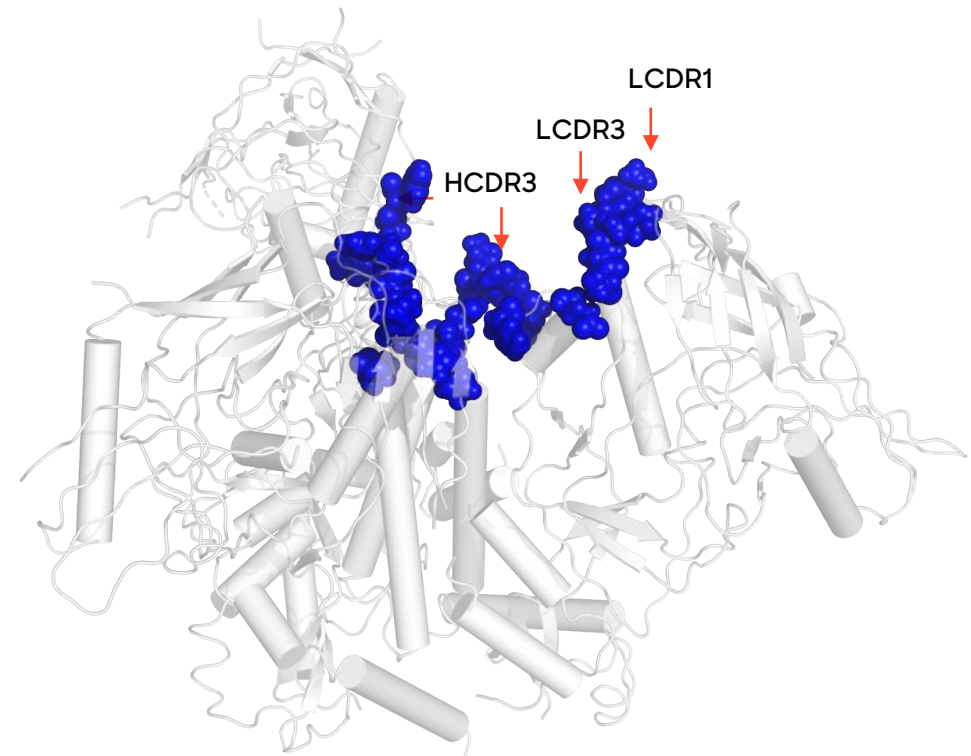
## Model inputs:

1. Antigen structure
2. Framework of 17b
3. Epitope selected conserved across HIV strains (Clades A, B, and C)

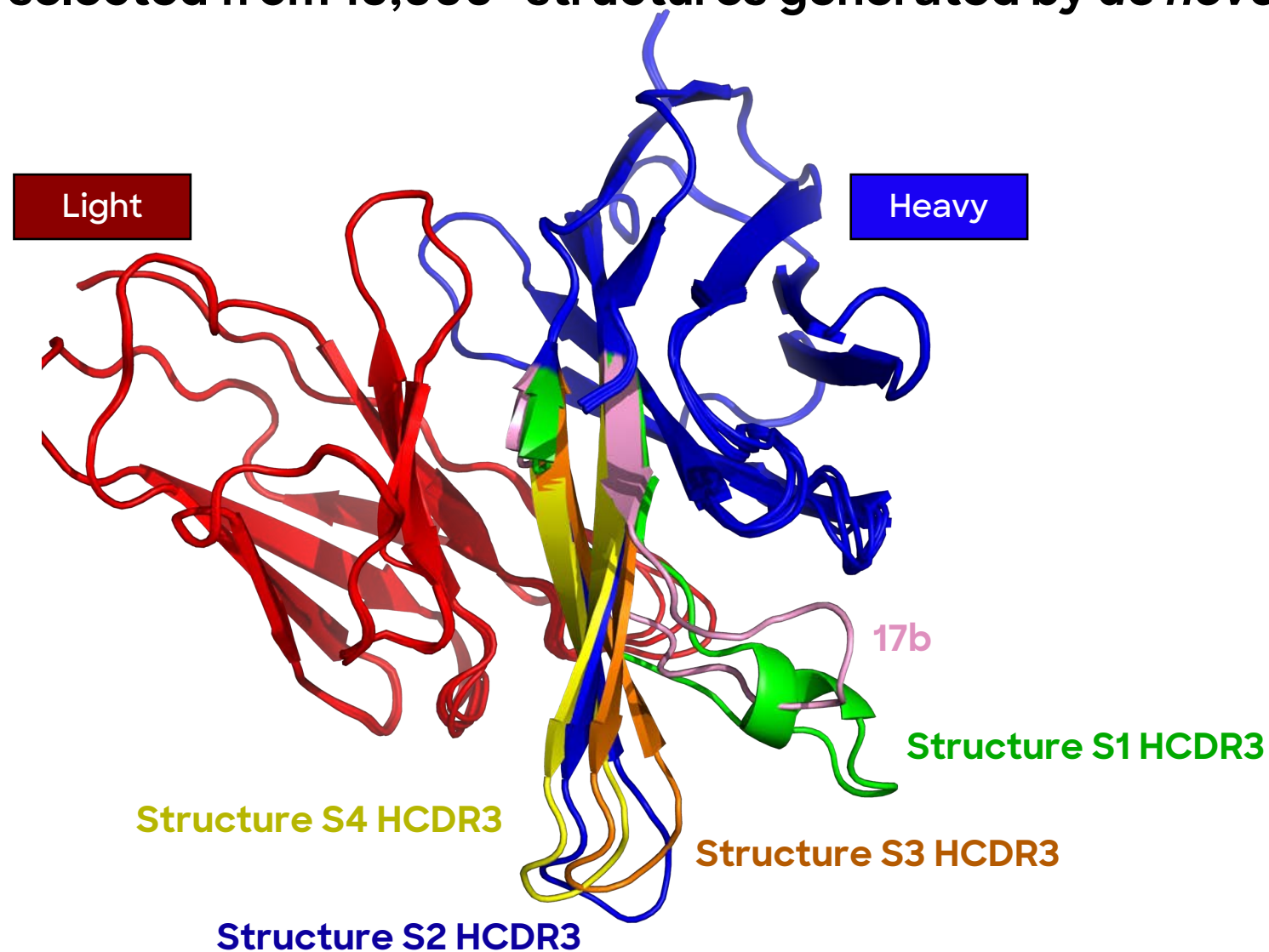
## Design of CDRs:

- Condition the model to design long HCDR3s to reach into open caldera region (>20 residues)
- Designed HCDR2 and LCDR3 to bind to HIV surface

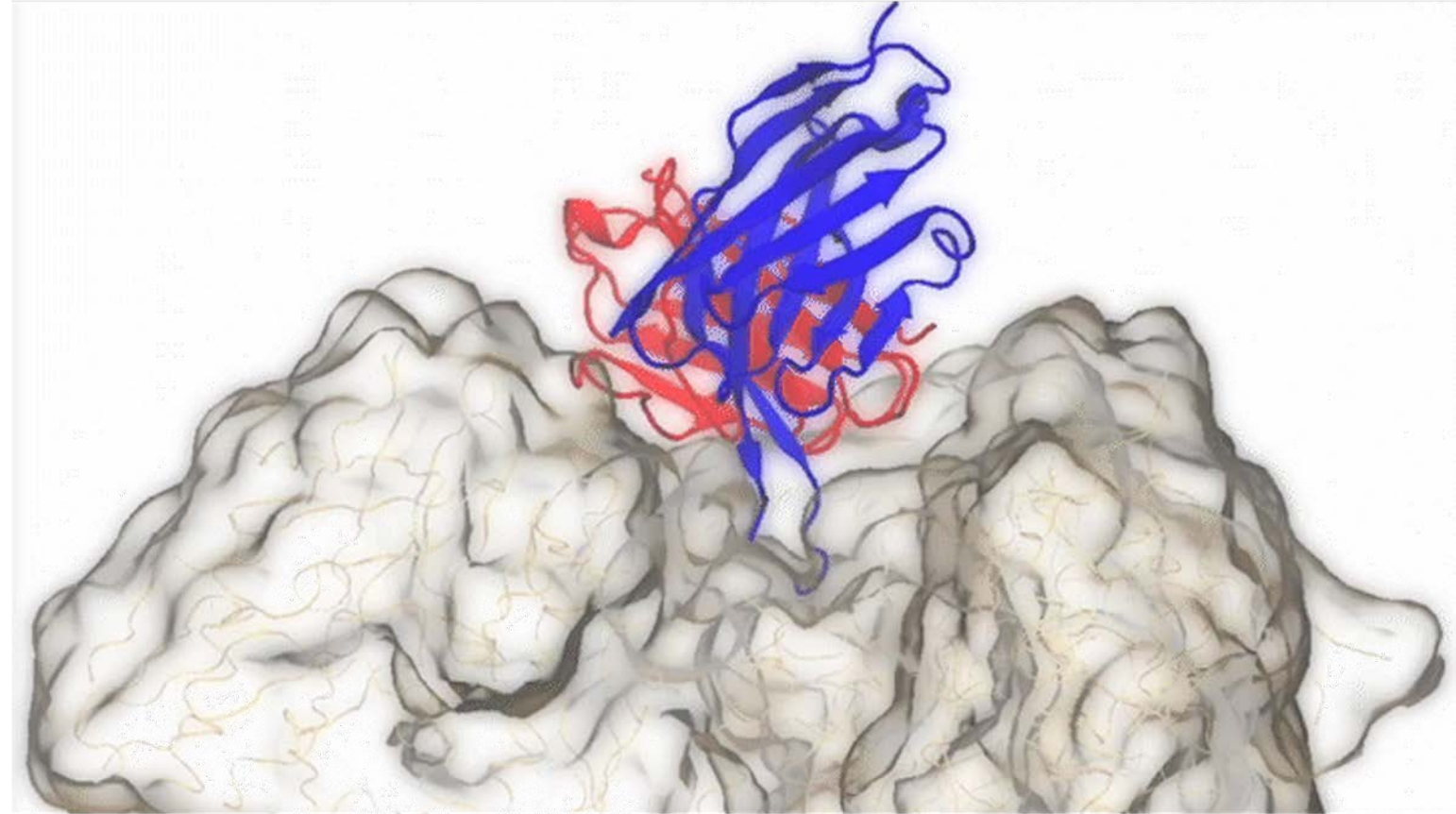
HIV Env trimer (open)



## 4 best structures selected from 10,000+ structures generated by *de novo* model

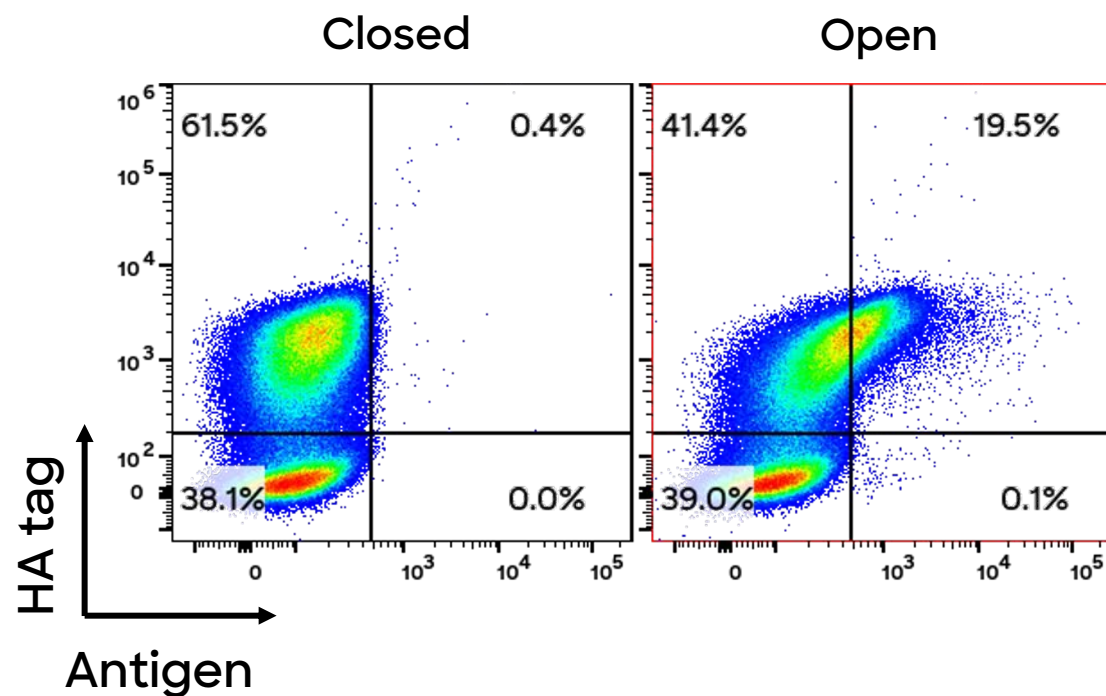


Applied molecular  
dynamics simulation  
to *de novo* designed  
antibodies

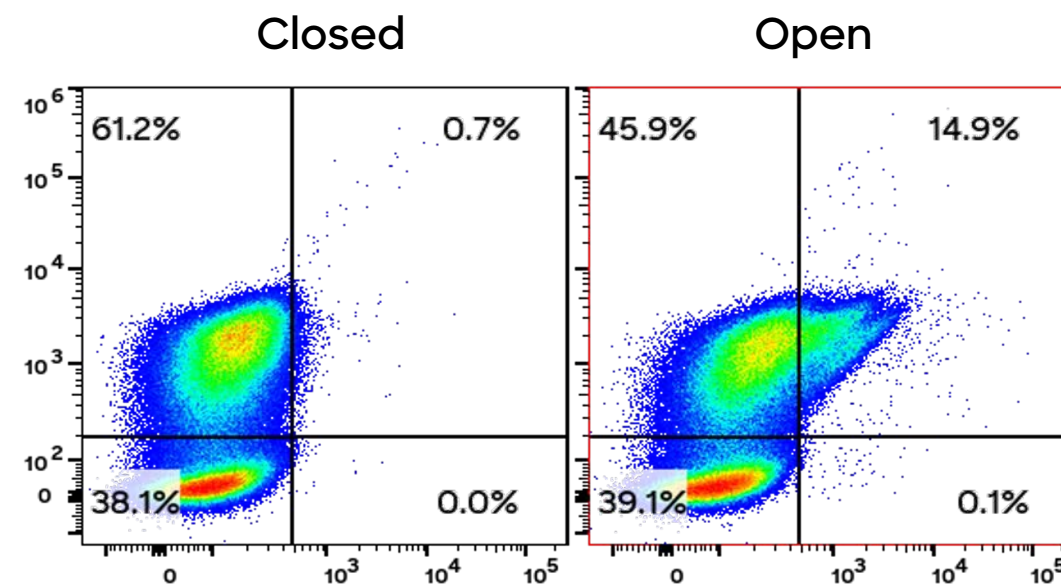


## Enriched de novo library binds open, not closed, Env trimer conformation in YSD

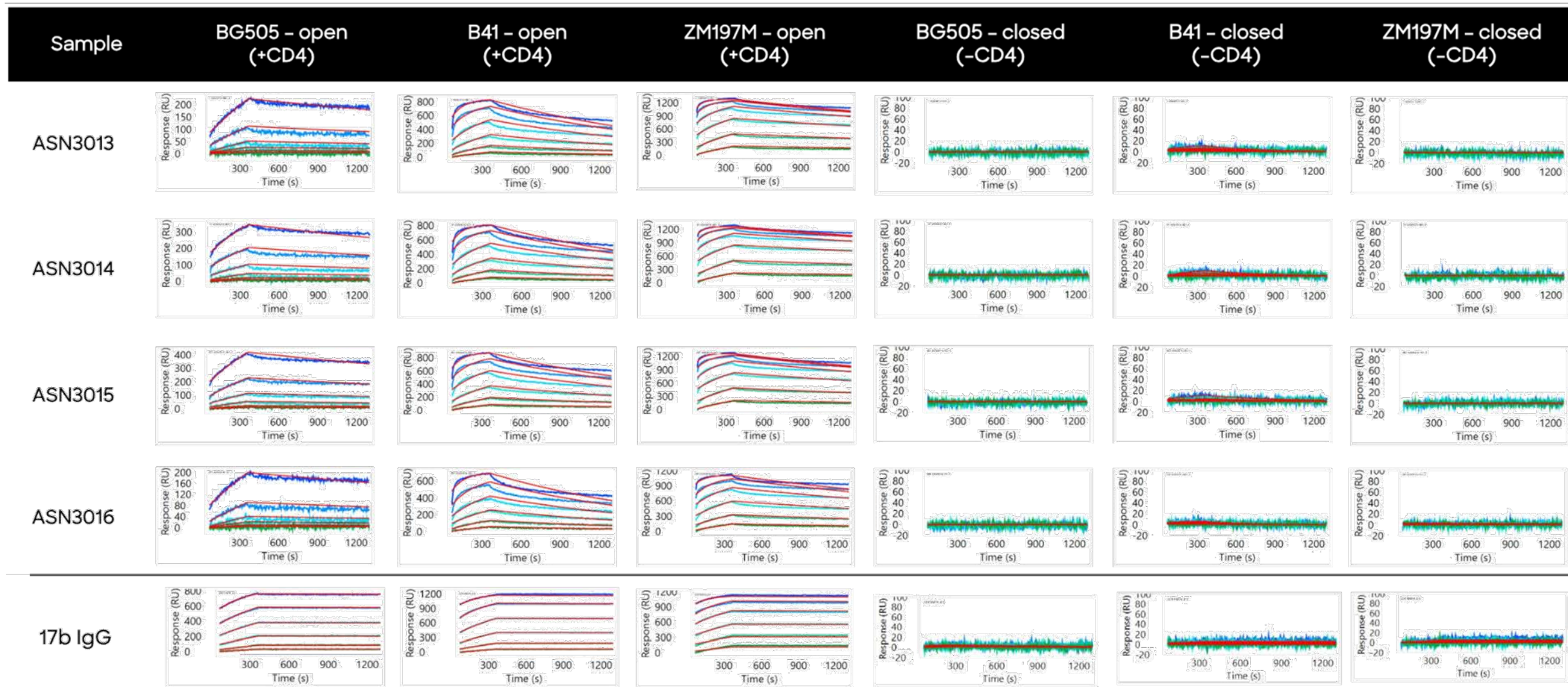
### Clade A Env trimer



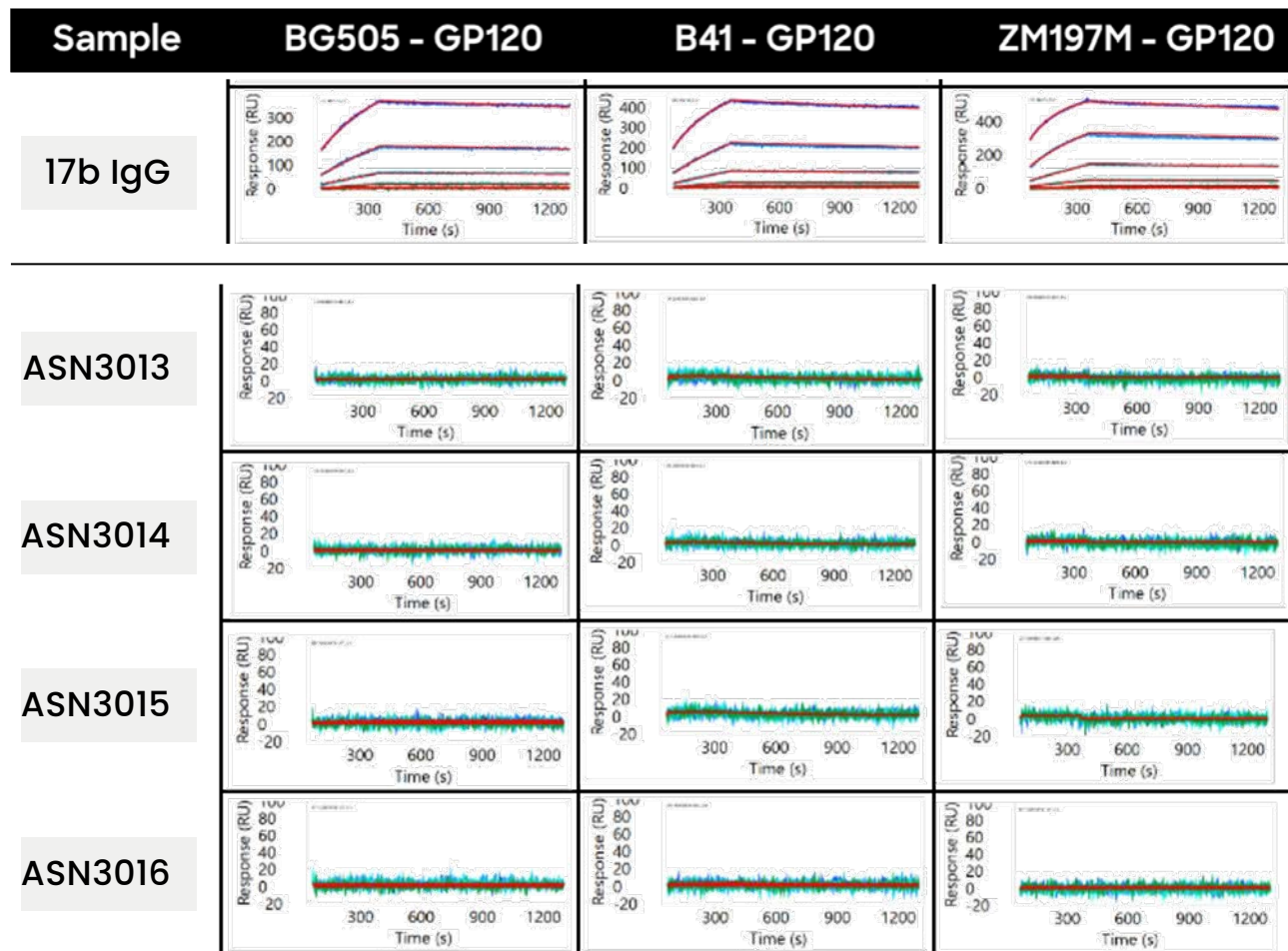
### Clade B Env trimer



# SPR data demonstrate binding characteristics consistent with binding of caldera



# HIV-Caldera: SPR demonstrates no binding of de novo designs to GP120 monomer



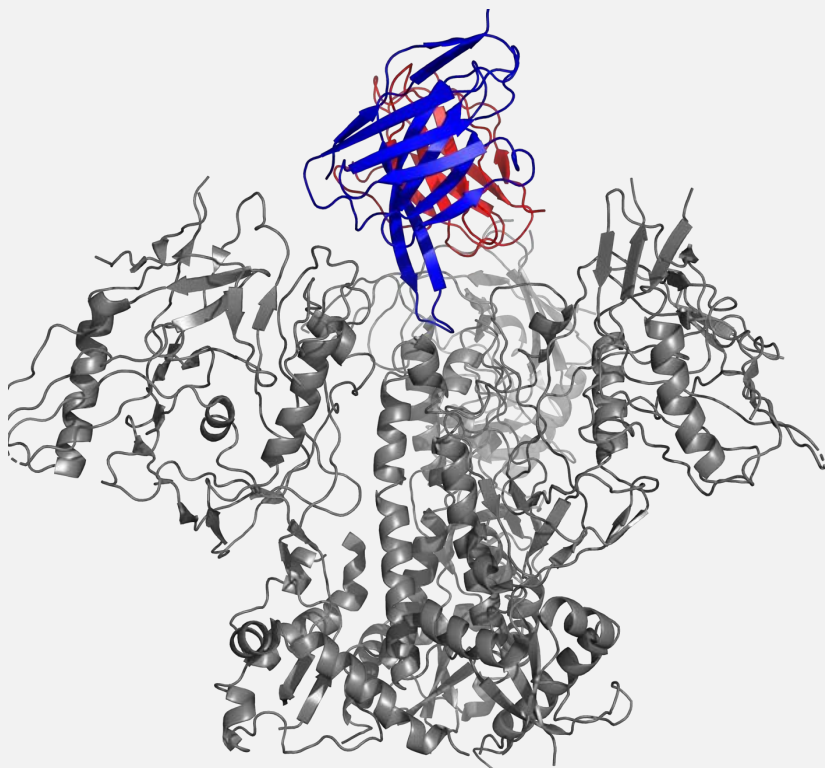
## Hypothesis:

If the designed mAbs are binding to the caldera region we should not observe binding to monomeric GP120 since the caldera is only present in the Env trimer

## Key results:

- ✓ **17b** showed high affinity binding to monomeric GP120 as expected
- ✓ **Absci mAbs** showed no binding to monomeric GP120, suggesting these binders are targeting an epitope that is only present in the Env trimer

# HIV-Caldera: demonstrating AI de novo design for challenging target



## SUMMARY

- *de novo* design model created a novel and diverse antibody which binds multiple clades of HIV indicating successful targeting of the caldera epitope
- Screening cascade enabled selection of differentially binding variants

## NEXT STEPS

- Binders from this study will be selected for affinity maturation
- Structure of *de novo* binder and epitope specificity will be experimentally solved to confirm fidelity with designed structure and targeted epitope

# AI CASE STUDY II

AI Optimization for pH sensitivity



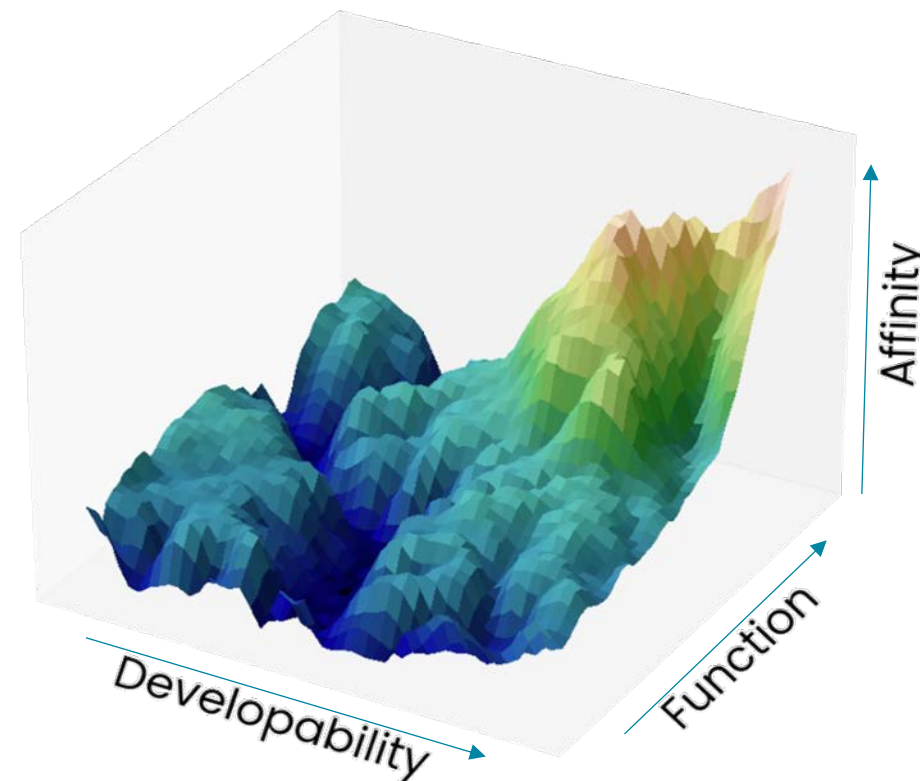
# AI lead optimization platform for 'smart biologics'

## The Challenge

The diversity of antibodies is vast, making it impossible for traditional methods to explore effectively.

## Absci Solution

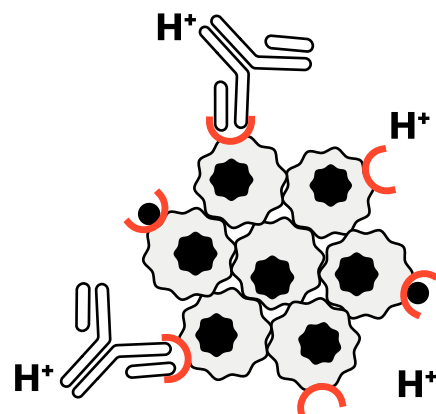
Our AI can search a space of  $\sim 10^{19}$ , a million times larger than traditional methods, identifying functional, developable antibodies in one step.



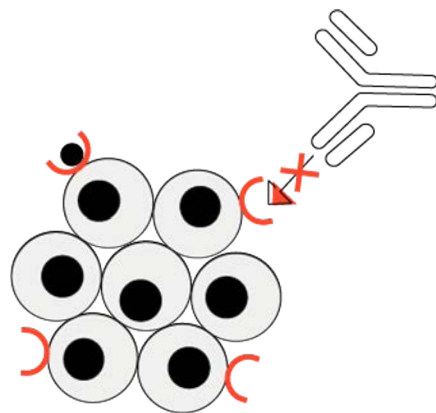
## pH sensitivity may reduce toxicity and/or improve efficacy of therapeutic mAbs

Tumor specificity improves efficacy and reduces "on-target off-tumor" toxicities

Binding occurs in the acidic pH of the tumor microenvironment



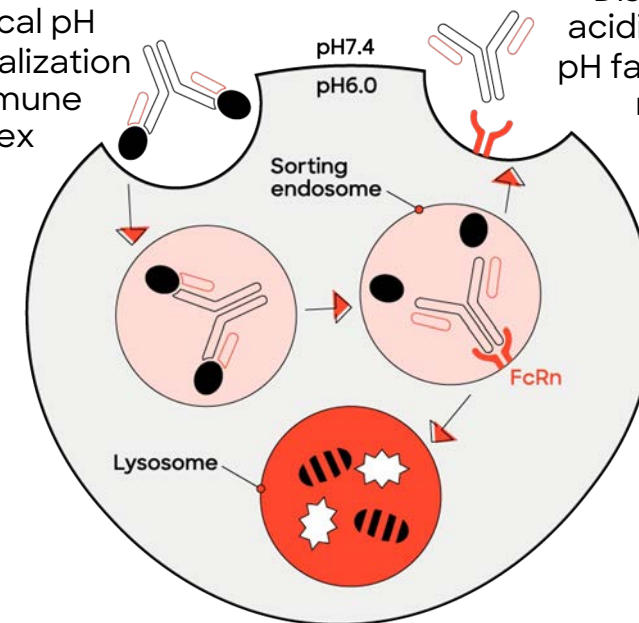
No binding occurs in the neutral pH surrounding healthy cells



Disassociation in the endosome drives antibody recycling and efficient clearance of soluble targets

Binding at physiological pH drives internalization of the immune complex

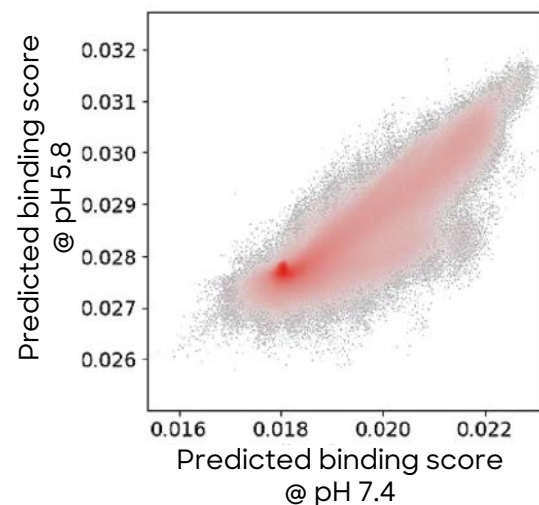
Dissociation at acidic endosomal pH favors antibody recycling



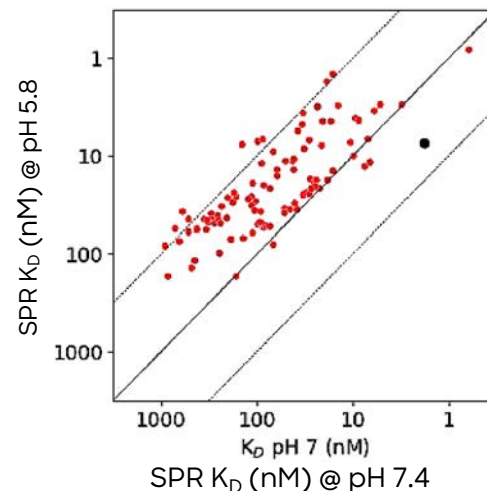
## Models identify pH sensitive Fab variants from the same lead for either indication

1. Library for model training sampled 60 positions on heavy chain framework and CDRs with up to 7 substitutions biased for ionizable residues (H, K, R, D, E)
2. Library screened for antigen binding at pH 7.4 and pH 5.8
3. Model trained and used to generate antibodies with tuned pH dependency

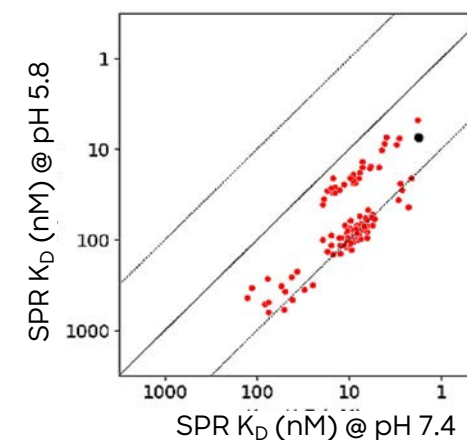
AI affinity scoring of variants within a large combinatorial space



Lab measured affinities of Fab variants predicted to have tighter binding at low pH



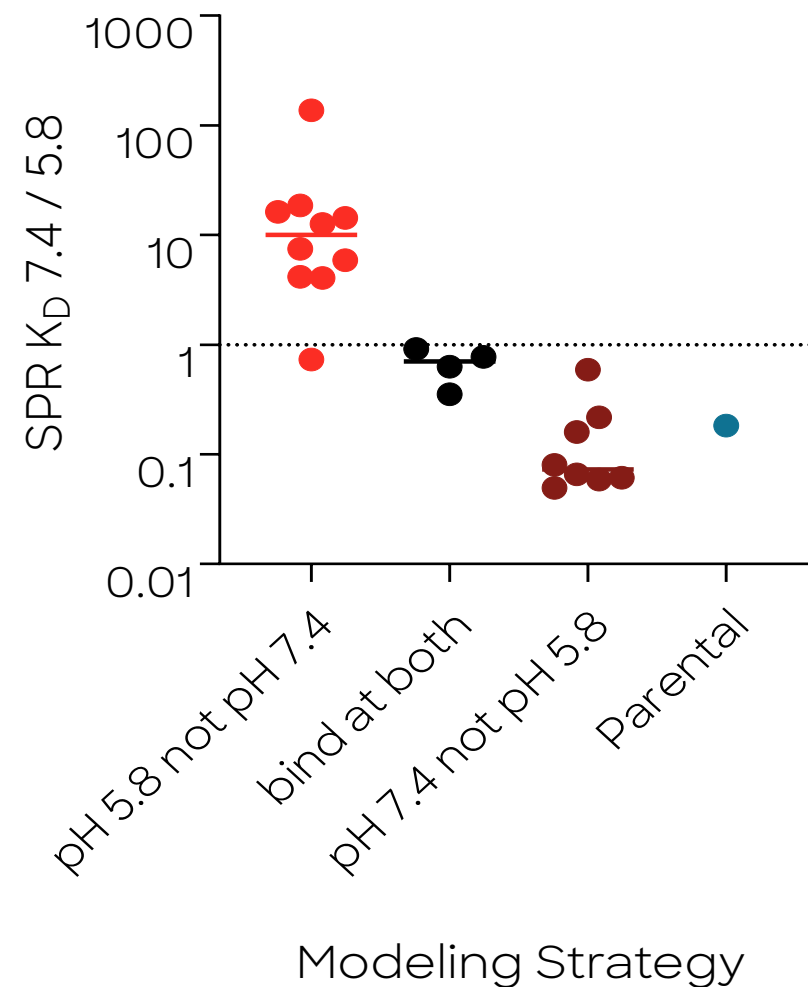
Lab measured affinities of Fab variants predicted to have tighter binding at neutral pH



# Hits reformatted as mAbs show desired binding profiles

## SUMMARY

- › AI optimized leads achieves variants with pH sensitive binding up to 100x differential
- › pH-sensitive leads had no liabilities for stability, aggregation and polyreactivity<sup>1</sup>
- › Model proposed mutations use all 6 ionizing residues in heavy chain CDRs and framework region
- › Sequences were proposed from a >10<sup>13</sup> combinatorial space



## Summarized platform case studies

### de novo Design

- › de novo design model created molecule binds multiple clades of HIV suggesting successful targeting of the caldera epitope
- › Represents second disclosed target success for our de novo platform in the 2nd half of this year

Absci's de novo design platform can successfully address difficult to drug target epitopes

### AI Optimization

- › Models identify unseen variants with 10x-20x pH sensitivity in both directions, and up to 100x differential compared to parental molecule after only one round
- › Designed leads had no liabilities indicating the ability to successfully search a fitness landscape

Absci's lead optimization platform enables molecules with differentiated pharmacology

