UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): August 12, 2025

ABSCI CORPORATION
(Exact name of registrant as specified in its charter)

Delaware	**001-40646**	**85-3383487**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

18105 SE Mill Plain Blvd
Vancouver, WA 98683
(Address of principal executive offices, including zip code)

(360) 949-1041
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	ABSI	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02. Results of Operations and Financial Condition.

On August 12, 2025, Absci Corporation (the "Company") announced its financial results for the second quarter ended June 30, 2025. A copy of the press release is being furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information contained in Item 2.02 of this Current Report on Form 8-K, together with Exhibit 99.1 hereto, is being furnished and shall not be deemed to be "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section and shall not be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 8.01. Other Events.

From time to time, the Company presents and/or distributes slides and presentations to the investment community to provide updates and summaries of its business. On August 12, 2025, the Company released a presentation which includes certain internal pipeline program updates, which is available on the "News & Events" section of the Company's website. A copy of this presentation is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated by reference herein.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

99.1	Press Release issued by the Company on June 12, 2025, furnished herewith.
99.2	Absci Corporate Presentation Summer 2025

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Absci Corporation

Date: August 12, 2025

By: /s/ Shelby Walker

Shelby Walker

Chief Legal Officer

Absci Reports Business Updates and Second Quarter 2025 Financial and Operating Results

Strengthened balance sheet raising approximately $64 million in gross proceeds in July 2025; cash, cash equivalents, and short-term investments now sufficient to fund operations into the first half of 2028

Expanded ongoing collaboration with Almirall, with election of a second target focused on dermatological indications

VANCOUVER, Wash. and NEW YORK, August 12, 2025 – Absci Corporation (Nasdaq: ABSI), a clinical-stage biopharmaceutical company advancing breakthrough therapeutics with generative AI, today reported financial and operating results for the quarter ended June 30, 2025.

"The past few months have been a period of strong execution for Absci, and we are positioned to build on this momentum," said Sean McClain, Founder and CEO. "ABS-101 is advancing through clinical trials, ABS-201 is on track to enter the clinic early next year, and we recently announced a key milestone in our collaboration with Almirall. With a strengthened balance sheet and runway into the first half of 2028, we are well positioned to deliver on our mission."

Recent Highlights

- Completed an underwritten public offering of common stock raising gross proceeds of approximately $50 million, and raised an additional approximately $14 million through Absci's at-the-market facility in July 2025.
- Expanded ongoing AI Drug Discovery collaboration with Almirall with election of a second target focused on dermatological indications. The election follows the successful delivery of AI *de novo* designed, functional antibodies by Absci against a difficult-to-drug target — the first target nominated under the collaboration. The collaboration, originally announced in November 2023, combines Absci's Integrated Drug Creation™ platform with Almirall's dermatology expertise to accelerate the development of novel therapeutics for chronic and debilitating skin diseases. In addition to product royalties, Absci is eligible to receive up to approximately $650 million in upfront fees, R&D, and post-approval milestone payments across the two programs if all milestones are successfully completed.

- Continuing to advance all internal asset programs, with Phase 1 interim readout for ABS-101 (anti-TL1A) anticipated later this year and potential Phase 1/2a interim efficacy readout for ABS-201 (anti-PRLR) anticipated in the second half of 2026.
- Progressing on key initiatives in strategic collaboration with AMD, with objective of scaling Absci's AI Drug Creation platform using AMD Instinct™ accelerators and ROCm™ software. In January 2025, concurrent with this collaboration, AMD also made a $20 million strategic equity investment in Absci.

Internal Pipeline Updates, Anticipated Program Progress, and 2025 Outlook

- **ABS-101 (potential best-in-class anti-TL1A antibody):** The ongoing Phase 1 (ACTRN12625000212459p) randomized, double-blind, placebo-controlled, first-in-human study of single ascending doses of ABS-101 will evaluate safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) in healthy volunteers. The primary endpoint is safety and tolerability, with PK, PD, and immunogenicity serving as secondary endpoints. The Phase 1 interim data readout is expected in the second half of 2025.
- **ABS-201 (potential best-in-class anti-PRLR antibody):** ABS-201 is a potential best-in-class anti-PRLR antibody in development for androgenetic alopecia, an indication with significant unmet clinical need and a large potential patient population of approximately 80 million individuals in the U.S. alone. Absci has nominated a development candidate with a preclinical profile suggesting high affinity and potency, favorable safety and immunogenicity, extended half life for convenient infrequent dosing, and excellent developability and manufacturability. ABS-201 has the potential to offer a more efficacious, convenient, durable, and safe option as compared to current standard of care. Absci anticipates initiation of a Phase 1/2a clinical trial for ABS-201 in early 2026, with potential for an interim efficacy readout in the second half of 2026.
- **ABS-301 (potential first-in-class antibody for undisclosed immuno-oncology target):** ABS-301 is a fully human antibody designed to bind to a novel target discovered through Absci's Reverse Immunology platform. Absci has presented data for this program showing that expression of ABS-301's target suggests broad potential in squamous cell carcinomas and beyond. For this program, Absci has optimized an antibody lead with high affinity and potency, and has successfully completed the first *in vivo* target validation study. The findings from the study demonstrate that signaling through the pathway drives a potent anti-tumor response, providing strong rationale for advancing into *in vivo* efficacy studies with ABS-301. These results support continued preclinical development and further exploration of ABS-301's therapeutic potential.
- **ABS-501 (potential best-in-class novel AI-designed anti-HER2 antibody):** For this program, Absci has identified antibody leads using its zero-shot *de novo* AI technology with the following

characteristics: novel epitope interactions, increased or equivalent affinity to *trastuzumab* in preclinical settings, efficacious against a *trastuzumab*-resistant xenograft tumor, and good developability.

- **Drug Creation Partnerships:** Absci continues to make further progress on its existing drug creation partnerships and anticipates signing one or more partnerships, including with a Large Pharma company, in 2025.

Absci continues to focus its investments and operations on advancing its internal pipeline of programs, alongside current and future partnered programs, while achieving ongoing platform improvements and operational efficiencies. In July 2025, Absci raised an additional approximately $64 million in gross proceeds from an underwritten public offering of common stock and strategic utilization of the company's at-the-market facility. Based on the company's current plans, Absci now believes its existing cash, cash equivalents, and short-term investments will be sufficient to fund its operations into the first half of 2028.

Second Quarter 2025 Financial Results

Revenue was $0.6 million for the three months ended June 30, 2025 compared to $1.3 million for the three months ended June 30, 2024.

Research and development expenses were $20.5 million for the three months ended June 30, 2025 compared to $15.3 million for the three months ended June 30, 2024. This increase was primarily driven by advancement of Absci's internal programs, including direct costs associated with external preclinical and clinical development, and an increase in personnel costs and stock compensation expense.

Selling, general, and administrative expenses were $8.5 million for the three months ended June 30, 2025 compared to $9.3 million for the three months ended June 30, 2024. This decrease was primarily due to a decrease in stock compensation expense.

Net loss was $30.6 million for the three months ended June 30, 2025, as compared to $24.8 million for the three months ended June 30, 2024.

Cash, cash equivalents, and short-term investments as of June 30, 2025 were $117.5 million, compared to $134.0 million as of March 31, 2025. In July 2025, Absci raised an additional approximately $64 million in gross proceeds, including $50 million through an underwritten public offering of common stock, and approximately $14 million through the company’s at-the-market facility.

Webcast Information

Absci will host a conference call to discuss its second quarter 2025 business updates and financial and operating results on Tuesday, August 12, 2025 at 4:30 p.m. Eastern Time / 1:30 p.m. Pacific Time. A webcast of the conference call can be accessed at investors.absci.com. The webcast will be archived and available for replay for at least 90 days after the event.

About Absci

Absci is advancing the future of drug discovery with generative design to create better biologics for patients, faster. Our Integrated Drug Creation™ platform combines cutting-edge AI models with a synthetic biology data engine, enabling the rapid design of innovative therapeutics that address challenging therapeutic targets. Absci's approach leverages a continuous feedback loop between advanced AI algorithms and wet lab validation. Each cycle refines our data and strengthens our models, facilitating rapid innovation and enhancing the precision of our therapeutic designs. Alongside collaborations with top pharmaceutical, biotech, tech, and academic leaders, Absci is advancing its own pipeline of AI designed therapeutics. These include ABS-101, a potentially best-in-class antibody to treat inflammatory bowel disease (IBD), as well as other indications, and ABS-201, a groundbreaking innovation in hair regrowth with the potential to redefine treatment possibilities for androgenetic alopecia, commonly known as male and female pattern baldness. Absci is headquartered in Vancouver, WA, with an AI Research Lab in New York City, and Innovation Center in Switzerland. Learn more at www.absci.com or follow us on LinkedIn (@absci), X (@Abscibio) and YouTube.

Forward-Looking Statements

Certain statements in this press release 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," "pursues," "anticipates," "plans," "believes," "forecast," "potential," "goal," "estimates," "extends," "expects," and "intends," or similar expressions. We intend these forward-looking statements, including statements regarding our expectations related to business operations, portfolio strategy, financial performance, and results of operations, our expectations and guidance related to the success of our partnerships, the gross use of cash, cash equivalents, and short-term investments, including revised guidance, our projected cash usage, needs, and runway, our expectations regarding the signing and number of additional partners and number of programs included in such partnerships, our technology development efforts and the application of those efforts, including for generalizing our platform, accelerating drug development timelines, improving the economics of drug discovery by lowering costs, and increasing the probability of success for drug development, our ability to execute with our partners to create differentiated antibody therapeutic candidates in an efficient manner, create and execute a successful development and commercialization strategy related to such candidates with current or future partners, and design and develop differentiated therapeutics to treat disease with unmet need, our ability to market our platform technologies to potential partners, and our internal asset programs, including our clinical development strategy, the progress and timing for various stages of development including advancement to lead stage, completion of pre-clinical studies, 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 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 obtaining and maintaining necessary approvals from the FDA and other regulatory authorities, replicating in clinical trials promising or 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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press@absci.com
absci@methodcommunications.com

Absci Corporation

Unaudited Condensed Consolidated Statements of Operations

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
(In thousands, except for share and per share data)	**2025**	**2024**	**2025**	**2024**
Partner program revenue	$ 593	$ 1,270	$ 1,772	$ 2,168
Operating expenses				
Research and development	20,458	15,261	36,822	27,497
Selling, general and administrative	8,528	9,346	18,000	18,090
Depreciation and amortization	3,000	3,384	6,072	6,800
Total operating expenses	31,986	27,991	60,894	52,387
Operating loss	(31,393)	(26,721)	(59,122)	(50,219)
Other income (expense)				
Interest expense	(56)	(150)	(135)	(326)
Other income, net	1,011	2,121	2,469	3,832
Total other income, net	955	1,971	2,334	3,506
Loss before income taxes	(30,438)	(24,750)	(56,788)	(46,713)
Income tax benefit (expense)	(131)	—	(127)	(12)
Net loss	$ (30,569)	$ (24,750)	$ (56,915)	$ (46,725)
Net loss per share: Basic and diluted	$ (0.24)	$ (0.22)	$ (0.45)	$ (0.44)
Weighted-average common shares outstanding: Basic and diluted	127,592,948	112,934,086	126,035,844	106,163,709

Absci Corporation

Unaudited Condensed Consolidated Balance Sheets

(In thousands, except for share and per share data)	June 30, 2025	December 31, 2024
ASSETS		
Current assets:		
Cash and cash equivalents	$ 38,024	$ 41,213
Restricted cash	16,209	15,947
Short-term investments	79,434	71,212
Accounts receivable, net	700	—
Prepaid expenses and other current assets	3,037	5,459
Total current assets	137,404	133,831
Operating lease right-of-use assets	3,457	3,968
Property and equipment, net	24,063	29,167
Intangibles, net	43,198	44,883
Restricted cash, long-term	1,054	1,054
Other long-term assets	716	705
TOTAL ASSETS	$ 209,892	$ 213,608
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 8,206	$ 3,529
Accrued expenses	5,715	6,842
Contingent consideration	12,750	12,750
Long-term debt	1,986	2,733
Operating lease obligations	1,705	1,608
Financing lease obligations	7	78
Deferred revenue	954	1,116
Total current liabilities	31,323	28,656
Long-term debt, net of current portion	161	1,257
Operating lease obligations, net of current portion	3,553	4,429
Other long-term liabilities	1,482	133
TOTAL LIABILITIES	36,519	34,475
STOCKHOLDERS' EQUITY		
Preferred stock	—	—
Common stock	13	12
Additional paid-in capital	739,565	688,726
Accumulated deficit	(566,516)	(509,601)
Accumulated other comprehensive income (loss)	311	(4)
TOTAL STOCKHOLDERS' EQUITY	173,373	179,133
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY	$ 209,892	$ 213,608

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 2025

```
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

Forward-Looking Statements
Certain statements in this presentation that are not historical facts are considered forward-looking within the meaning of 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," and "intends," or similar expressions. We intend these forward-looking statements, including statements regarding our strategy, our expectations regarding the clinical, therapeutic and market potential of product candidates discovered and developed through our platform; the potential advantages of our technology and the assets in our internal pipeline; our ability to achieve catalysts in our preclinical and clinical development programs, such as the initiation of IND-enabling studies and Phase 1 clinical development and the receipt of clinical data; the anticipated timing of such events; the expected evolution of our portfolio over time; guidance regarding cash, cash equivalents and our projected cash runway, our future operations, internal research and technological development activities, estimated speed and cost advantages of leveraging our AI drug creation platform; our expectations regarding the status and progress of our existing partnerships and our plans for potential new partnerships; our expected operational efficiencies, research and technology development collaboration efforts, growth plans, prospects, plans and objectives of management, 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 the development of our technology as well as the assets in our internal pipeline, our ability to secure milestone payments and royalties, and our ability to effectively conduct research, drug discovery and development activities with respect to our internal programs and to collaborate with our partners or potential partners with respect to their research, drug discovery and development activities; 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.

Market and Statistical Information
This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other industry data. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. We have not independently verified the data generated by independent parties and cannot guarantee their accuracy or completeness.

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A PROVEN AI × BIO PLATFORM

PURPOSE BUILT TEAM
10+ approved drugs by our scientists + AI talent from OpenAI, Google, Tesla, NVIDIA.

INTEGRATED DATA FLYWHEEL
77 k ft² automated lab generating hundreds of millions of sequence-function datapoints since 2020

LEADING AI MODELS
De novo AI models now unlock first-in-class biology by cracking tough epitopes—from HIV's caldera to ion channels

PIPELINE MOMENTUM
Anticipate two clinical-stage assets within 12 months

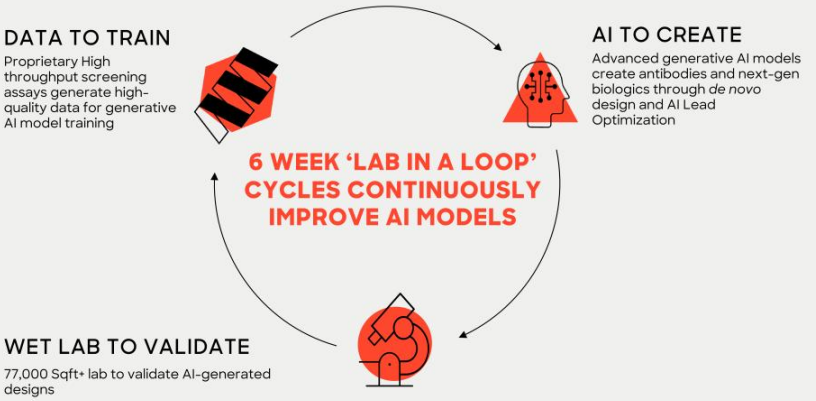
PIPELINE WITH NEAR-TERM CATALYST

ABS-101 (anti-TL1A)
Phase 1 clinical trial initiated in May 2025. Interim readout expected 2H2025

ABS-201 (anti-prolactin receptor)
IND-enabling studies on track for anti-PRLR antibody targeting androgenetic alopecia—Anticipated Phase 1/2a start early 2026, with interim efficacy expected 2H2026.

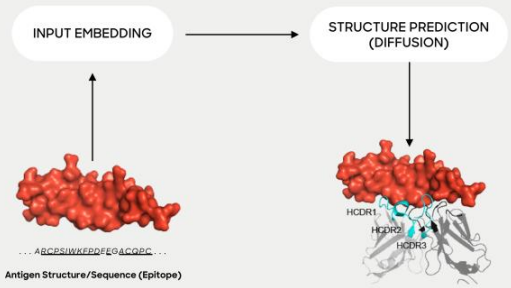
EARLY PIPELINE
Advancing early-stage oncology and I&I programs including ABS-301, ABS-501, and TL1A bi-specific

Since 2020 Absci has been amassing high-quality data at scale for AI model training and validation



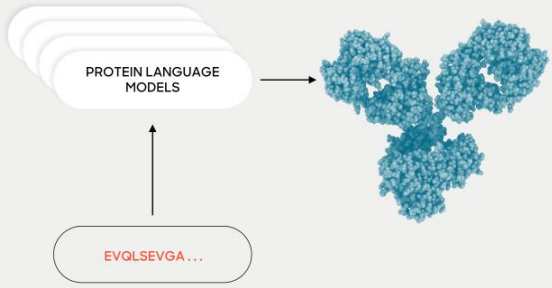
Leadership in AI *de novo* design of antibody-based therapeutics

DE NOVO ANTIBODY DESIGN



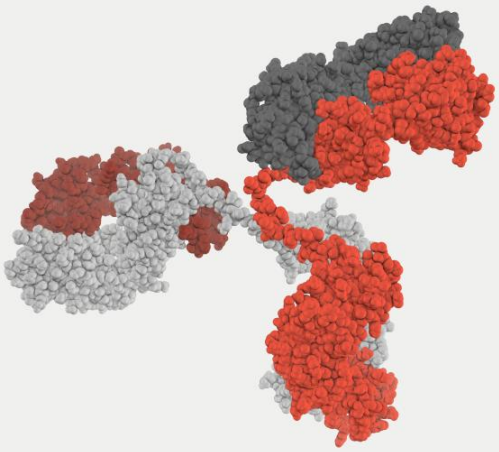
- *de novo* antibody design model creates epitope-specific binders given a target structure
- Designed in framework of choice or multiple frameworks

AI LEAD OPTIMIZATION



- Co-optimization enables improvement of antibody attributes while maintaining developability
- Precise engineering of molecule pharmacology

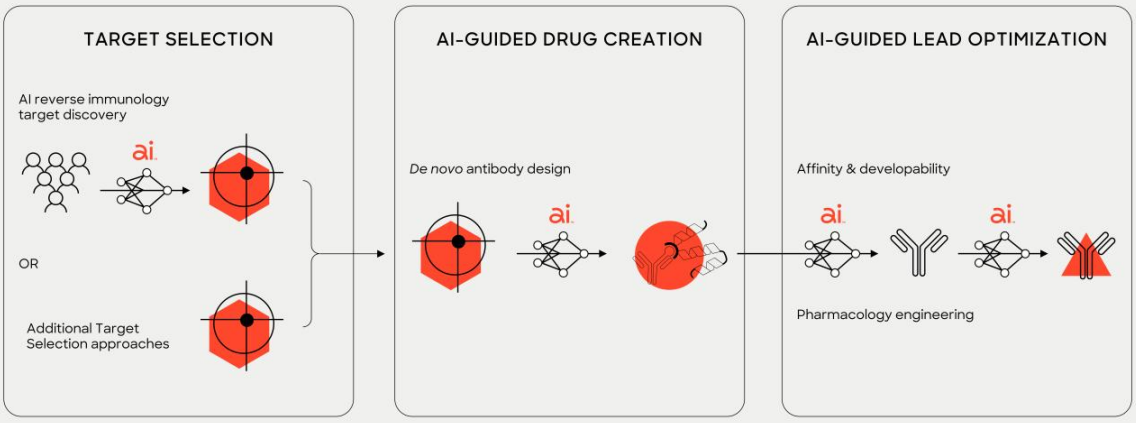
We use AI to create novel & differentiated therapeutics



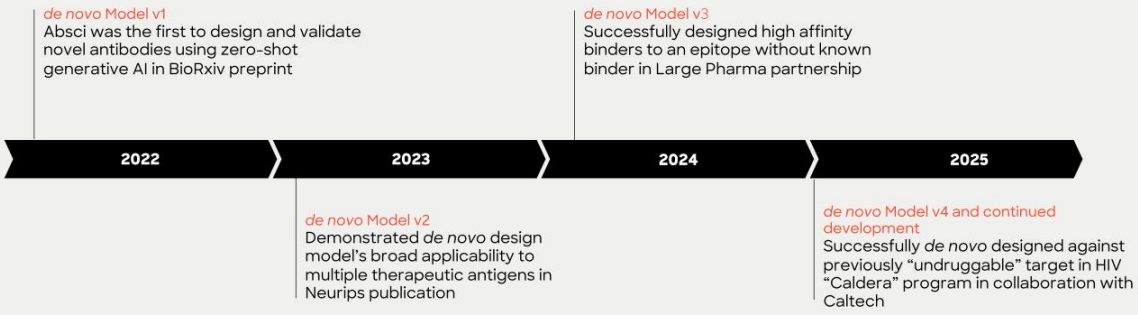
- EPITOPE-SPECIFIC DESIGN + EPITOPE INTERFACE OPTIMIZATION
- ENHANCED POTENCY AND MOA
- ABILITY TO ADDRESS DIFFICULT TARGET CLASSES, E.G. GPCRS
- ENABLING FEATURES: MULTI-VALENCY, pH-DEPENDENT BINDING
- BROAD IP: 100S TO 10,000S OF FUNCTIONALLY VALIDATED SEQUENCES ENABLED BY PROPRIETARY WET-LAB VALIDATION

INTEGRATED DRUG CREATION PLATFORM™

Leveraging AI throughout the end-to-end drug discovery process



Since publishing the first work in AI *de novo* antibody design, Absci has continued to rapidly progress and lead the field



de novo Model v1
Absci was the first to design and validate novel antibodies using zero-shot generative AI in BioRxiv preprint

de novo Model v2
Demonstrated *de novo* design model's broad applicability to multiple therapeutic antigens in Neurips publication

de novo Model v3
Successfully designed high affinity binders to an epitope without known binder in Large Pharma partnership

de novo Model v4 and continued development
Successfully *de novo* designed against previously "undruggable" target in HIV "Caldera" program in collaboration with Caltech

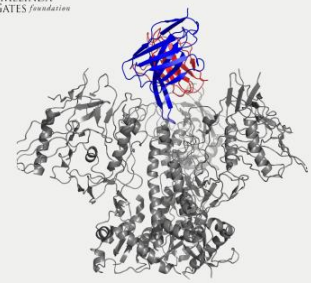
Platform Case Studies

DE NOVO ANTIBODY DESIGN

DE NOVO ANTIBODY DESIGN PROGRAM IN COLLABORATION WITH CALTECH FUNDED BY THE GATES FOUNDATION

VIEW THE FULL CASE STUDY

Caltech BILL & MELINDA GATES foundation

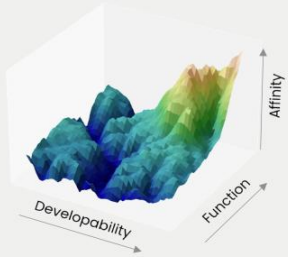


- **Goal:** create universally neutralizing HIV antibody by binding conserved epitope within "caldera" region of HIV gp120
- Absci's *de novo* design platform can successfully address difficult to drug target epitopes

AI LEAD OPTIMIZATION

AI LEAD OPTIMIZATION FOR PH SENSITIVITY WHICH MAY REDUCE TOXICITY AND/OR IMPROVE EFFICACY OF THERAPEUTIC mAbs

VIEW THE FULL CASE STUDY



Model searches a massive space of ~10^{19}, identifying functional and developable antibodies in one step.

- **Goal:** Co-optimize antibodies for pH sensitive binding to increase efficacy and reduce
- Absci's lead optimization platform enables molecules with differentiated pharmacology

OUR PEOPLE

"Multilingual" team with expertise in AI and drug creation

LEADERSHIP TEAM

Sean McClain
Founder, CEO & Director

Andreas Busch, PHD
Chief Innovation Officer

Zach Jonasson, PHD
Chief Financial Officer & Chief Business Officer

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SVP, Chief AI Officer

Shelby Walker, JD
Chief Legal Officer

Karin Wierinck
Chief People Officer

Christian Stegmann, PHD
SVP, Drug Creation

Christine Lemke, DVM
SVP, Portfolio & Growth Strategy

Penelope
Chief Morale Officer

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EXPERTISE & BACKGROUND FROM

OpenAI · Google · NVIDIA · Harvard University · Stanford University · MIT · Meta · Takeda · X · AstraZeneca · Broad Institute · Bayer · Pfizer · Bristol Myers Squibb · Novo Nordisk · Philips · Microsoft · amazon

WELL-POSITIONED TO DELIVER

Absci's Talent and Infrastructure for Better Biologics Faster

~150 Unlimiters with deep experience in AI, drug discovery, immunology, and synthetic biology

Leading AI team with expertise from: NVIDIA, Google, MIT, Microsoft Research, Harvard University, OpenAI, X, Stanford University

Biologics drug discovery expertise from: Bayer, Takeda, Pfizer, AstraZeneca, Novo Nordisk, Broad Institute, Shire, University of Oxford

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

>$600M Capital raised to date

AI PIPELINE

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

KEY HIGHLIGHTS

ABS-101
Ph1 study initiated with interim data readout expected 2H25.

ABS-201
Category defining PRLR antibody for androgenetic alopecia. Ph1/2ª study anticipated early 2026 with interim PoC readout expected 2H2026.

ABS-301
Potential first-in-class asset discovered through Reverse Immunology Platform

ABS-501
Candidate ID phase for novel HER2 program designed using *de novo* AI

PARTNERSHIPS

Track Record of Industry-Leading Partnerships

AI Drug Creation™

AstraZeneca · almirall · MERCK · OWKIN · TWIST BIOSCIENCE · precisionlife · Memorial Sloan Kettering Cancer Center · UCLA · Caltech

- 25+ PARTNERED PROGRAMS TO DATE
- 4 NAMED INTERNAL PROGRAMS
- ADDITIONAL PROGRAMS IN EARLY DEVELOPMENT

Data & compute

AMD · ORACLE · NVIDIA · Aster Insights · Saint John's Health Center, Providence · University of Oxford

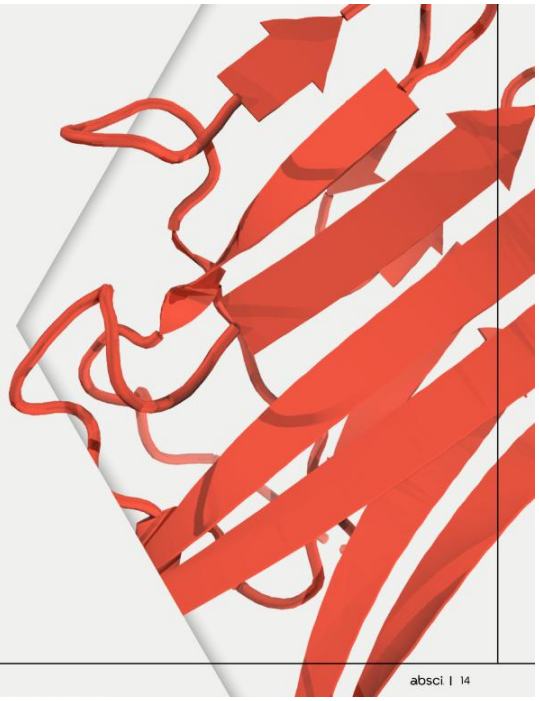
- SCALING COMPUTE
- IMPROVING MODELS
- INCREASING EFFICIENCIES

Leading AI platform driving numerous near-term value inflection points

ABS-101
Phase 1 Study initiated - May 2025
Phase 1 Interim Data Readout - anticipated 2H 2025
Phase 1b/2a Study initiation - anticipated 1H 2026

ABS-201
Ph1/2a Study Initiation - anticipated early 2026
Potential POC Readout - expected 2H 2026

PARTNERSHIPS
Anticipate signing one or more partnerships, including with a Large Pharma in 2025



INTERNAL PIPELINE

Absci's progress in Drug Creation

Continued advancement of lead assets

ABS-101

Phase 1 Program initiated in May 2025

- New preclinical data supporting superior immunogenicity profile
- Phase 1 Interim data readout expected 2H 2025

ABS-201

IND-enabling activities on-track for PRLR (prolactin receptor) program with anticipated initiation of Ph1/2a studies in early 2026

Discovery of next assets

ABS-301

Progress of first-in-class asset discovered through Absci's Reverse Immunology Platform

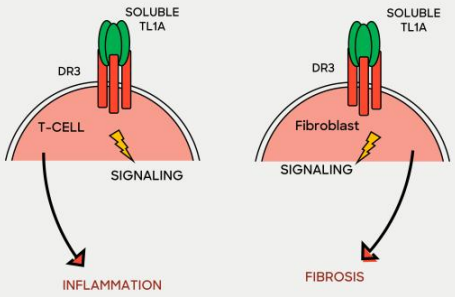
ABS-501

Nomination of a potential best-in-class HER2 asset

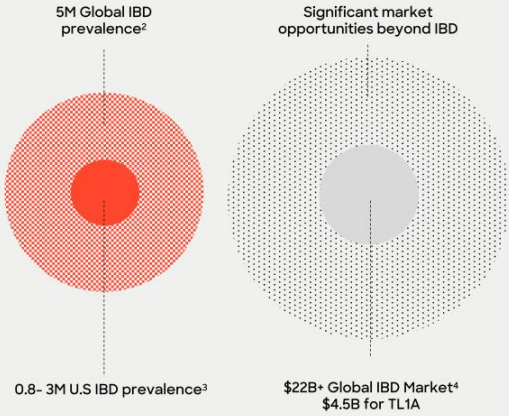
ABS-101 TL1A

Validated mechanism of action in large underserved market

TL1A: DR3 SIGNALING CLINICALLY SHOWN TO INDUCE PRO-INFLAMMATORY RESPONSES[1]



POTENTIAL RELEVANCE IN WIDE RANGE OF AUTOIMMUNE INDICATIONS



[1] Adapted from Takedatsu 2008 doi: 10.1053/j.gastro.2008.04.037
[2] Wang 2023 http://dx.doi.org/10.1136/bmjopen-2022-065186
[3] 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.
[4] Evaluate Pharma Oct 2023.

ABS-101 TL1A

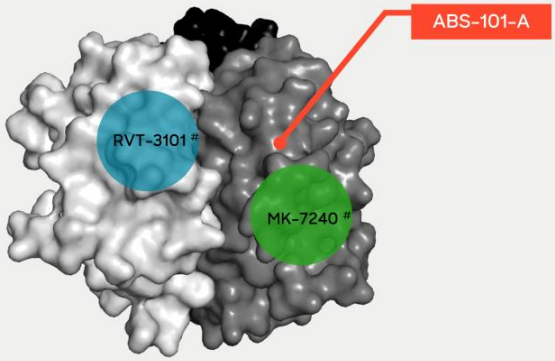
Potential best-in-class TL1A mAb designed using generative AI

- Higher affinity and potency
- Bind monomer and trimer TL1A
- High bioavailability
- Expected low immunogenicity
- Favorable developability
- High convenience based on half-life extension and sub-Q dosing

ABS-101 TL1A

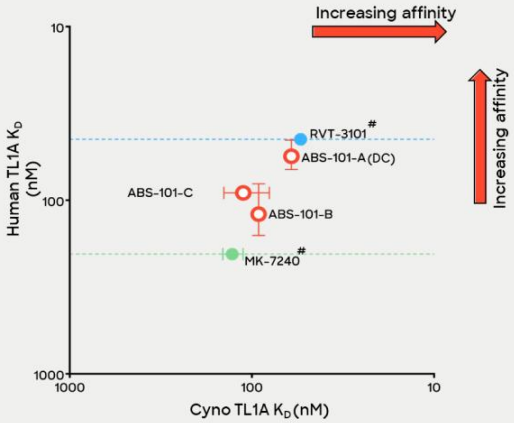
Successful application of AI platform to generate high affinity variants

Epitope bins on TL1A*



› Absci AI-designed and optimized leads span multiple unique epitopes on a single TL1A subunit.

HIGH AFFINITY mAbs WITH PRESERVED CROSS-REACTIVITY



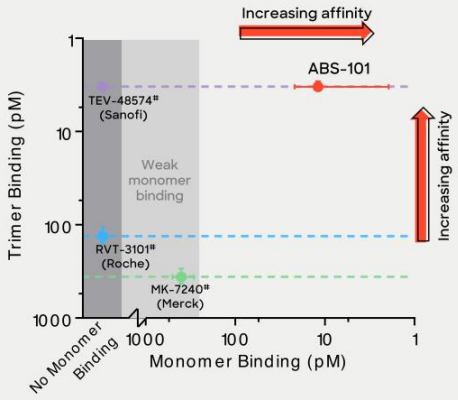
*Estimated performance of a putative clinical competition molecule generated for in house comparison

ABS-101 TL1A

AI-designed candidate with high affinity and potential for superior potency

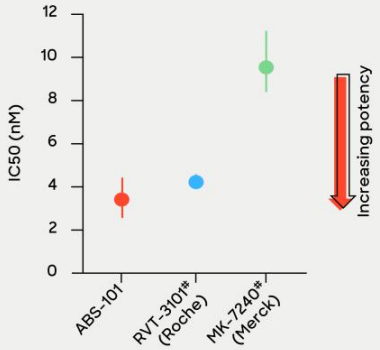
HIGH AFFINITY mAbs WITH BINDING TO BOTH THE TL1A MONOMER AND TRIMER

AFFINITY BY BIOLAYER INTERFEROMETRY (BLI)



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

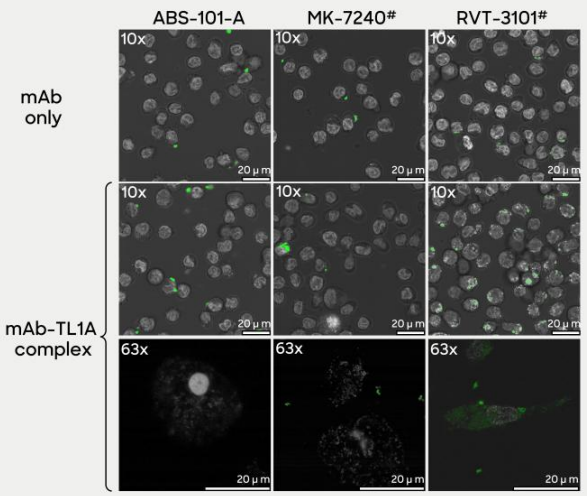
APOPTOSIS INHIBITION ASSAY IN TF-1 CELLS



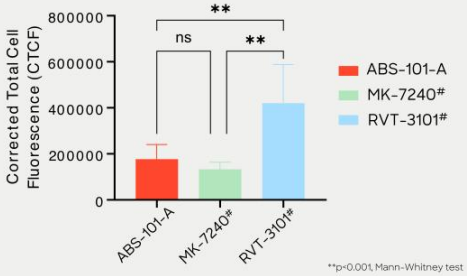
*Estimated performance of a putative clinical competition molecule generated for in house comparison

ABS-101 TL1A | IMMUNOGENICITY ASSESSMENT

Internalization of mAb:TL1A complexes potentially contributes to immune activation and formation of ADA



mAb:TL1 COMPLEX INTERNALIZATION IN THP-1 CELLS



**p<0.001, Mann-Whitney test

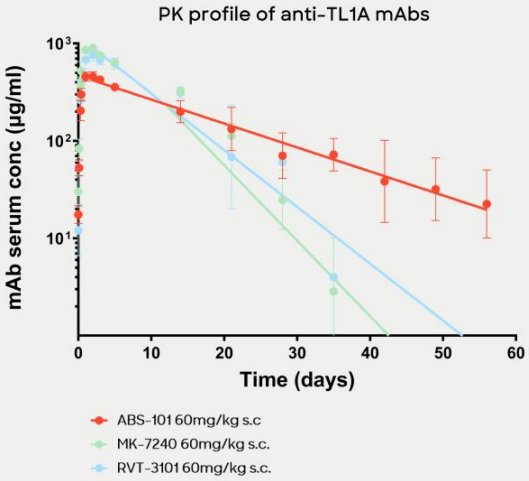
- ABS-101 and MK-7240# show reduced TL1A complex internalization versus RVT-3101#

*Estimated performance of a putative clinical competition molecule generated for in house comparison

Reference, doi: 10.1053/j.gastro.2019.08.009

ABS-101 TL1A | NHP COMPARATIVE PK

NHP Pharmacokinetics & CMC data confirm compelling ABS-101 competitive profile



NHP-PK & PRELIMINARY 13-WEEK NHP GLP-TOX

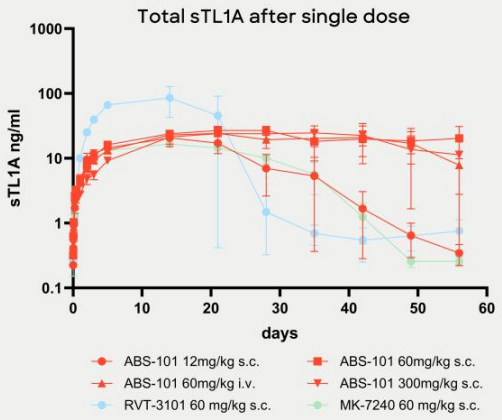
- 2-3x extended half-life in NHPs over clinical competitors to support Q8W-Q12W dosing interval
- ABS-101 shows enhanced biodistribution in NHPs, compared to antibodies in clinical development based on in silico modelling
- High subcutaneous bioavailability in NHPs at ~80%
- Preliminary 13-week GLP-tox shows no treatment-related adverse findings during in-life phase and necropsy

CMC - HIGH CONCENTRATION FORMULATION

- Optimal developability profile allowed successful development of high-concentration formulation at 200mg/mL suitable for subcutaneous injection

ABS-101 TL1A | NHP COMPARATIVE PD

ABS-101 NHP data confirm sustained prolonged targe engagement versus clinical competitors



ABS-101 SHOWS DOSE-DEPENDENT AND SUSTAINED TARGET ENGAGEMENT

- Data confirm engagement of soluble TL1A (sTL1A) in non-human primates.
- Target engagement is dose-dependent with a ceiling effect.
- ABS-101's extended half-life translates into sustained target engagement compared to first generation TL1A antibodies at comparable dose and route of administration.

ABS-101 TL1A

AI-designed for potentially optimal therapeutic profile

ATTRIBUTE	ABS-101	MK-7240 (MERCK, PROMETHEUS)	RVT-3101 (ROCHE, ROIVANT)	TEV-48574 (SANOFI, TEVA)
High affinity/potency	++	–	+	+
Trimer TL1A binding	++	+	++	++
Monomer TL1A binding	++	+	–	–
Low Immunogenicity potential	+	+	–	NA
Bioavailability/ Biodistribution	++	+	–	NA
Sub-Q injection	+	+	+	–
Q8W to once quarterly dosing	++	–	–	––

ABS-101 TL1A

Phase 1 Clinical Trial Initiated in May 2025 with interim readout expected 2H2025

DISCOVERY

AI-designed Development Candidate

- ✓ High affinity
- ✓ High potency
- ✓ Long half-life
- ✓ Favorable manufacturability

CMC/PRECLINICAL

IND-enabling studies to evaluate:

- ✓ GMP manufacture of sub-Q formulation at high concentration
- ✓ Favorable PK and long half-life
- ✓ High Bioavailability in NHPs
  - Low ADA
- ✓ 13-week GLP tox: No treatment-related adverse findings during in-life phase and necropsy observed.

MAY 2025

Phase 1 double-blind, placebo-controlled trial initiated in Australia

2H 2025

Phase 1 interim data readout expected

INTERNAL PIPELINE

Absci's progress in Drug Creation

Continued advancement of lead assets

ABS-101

Continued progress of TL1A asset with FiH in 1H 2025

- New preclinical data supporting superior immunogenicity profile
- Phase 1 Interim data readout in 2H 2025

ABS-201

IND-enabling activities on-track for PRLR (prolactin receptor) program with anticipated initiation of Ph1/2a studies in early 2026

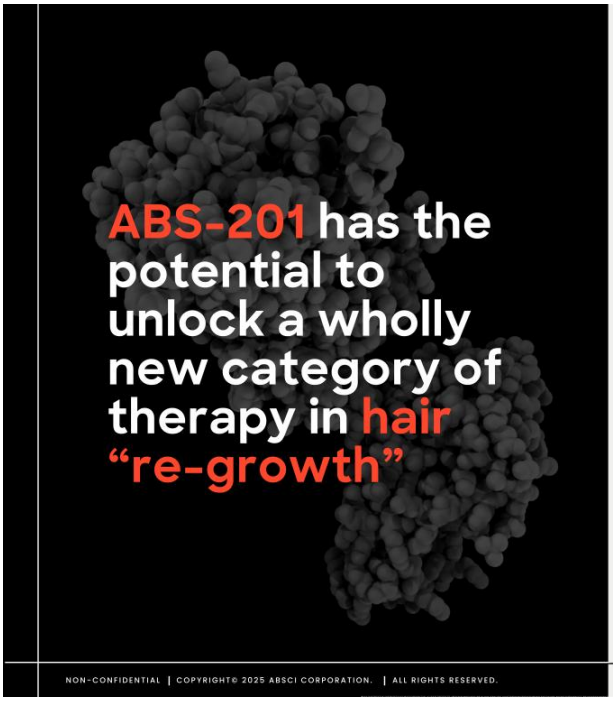
Discovery of next assets

ABS-301

Progress of first-in-class asset discovered through Absci's Reverse Immunology Platform

ABS-501

Nomination of a potential best-in-class HER2 asset



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

CLINICAL AND COMMERCIAL UNMET NEED

- Significant unmet clinical need for androgenetic alopecia
- Large market: approximately 80 million patients in U.S.; highly motivated patient population

SCIENTIFIC RATIONALE

- Strong target validation (efficacy & safety) for treatment of androgenetic alopecia
- Mode of action conserved across many species
- Supportive pharmacological profile of ABS-201

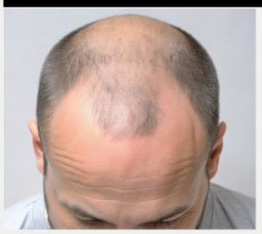
DEVELOPMENT PATH

- Straightforward clinical development path with potential for early Proof of Concept
- Low competition, potentially first to U.S. market

ABS-201 PRLR

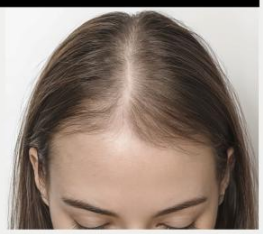
Underserved patient population looking for therapeutic innovation

~80 MILLION AMERICANS LIVE WITH ANDROGENETIC ALOPECIA



MALE ANDROGENETIC ALOPECIA

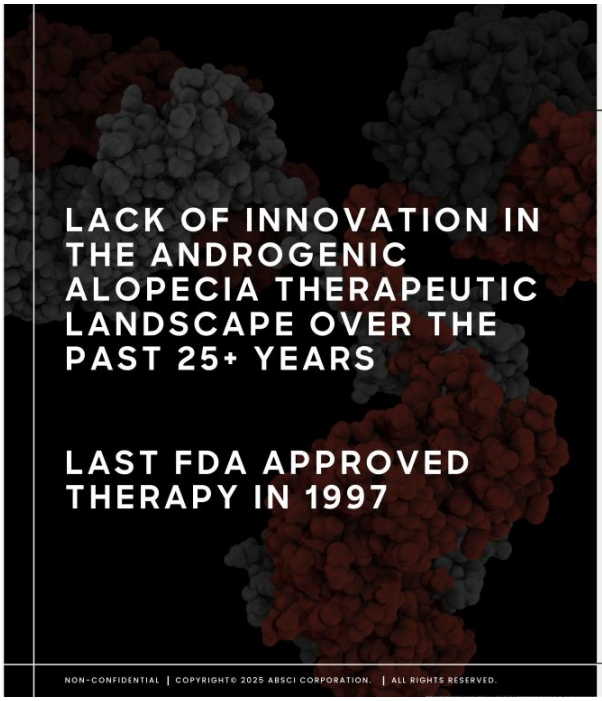
- ~50M men in the U.S.
- Only 2 FDA approved therapies



FEMALE ANDROGENETIC ALOPECIA

- ~30M women in the U.S.
- Only 1 FDA approved therapy for women

- **Growing patient population with limited therapeutic options and concerns of adverse side-effects**
- **Last FDA approved therapy for Androgenetic alopecia 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

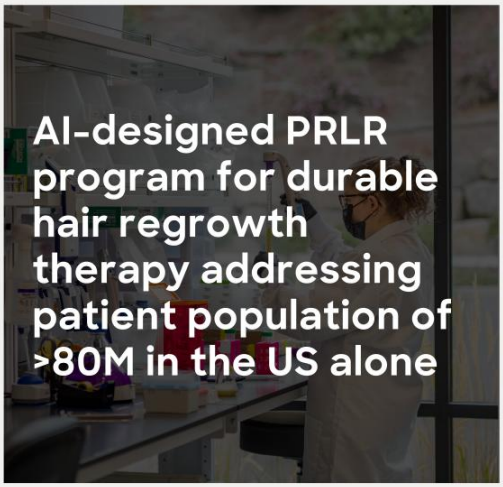


Patients and clinicians need better treatment options for “hair re-growth”

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

ABS-201 PRLR

Potential best-in-class PRLR antibody for treating androgenic alopecia

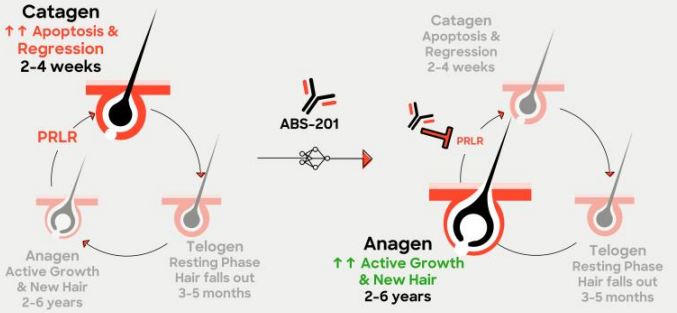


- High affinity and potency
- Excellent developability profile → high-concentration formulation and great stability
- Anticipated low immunogenicity
- Extended half-life and expected longer dosing intervals
- Clinical development strategy expected to enable PoC in H2-2026
- Potential to be first to market in the U.S.

ABS-201 PRLR | PROPOSED DIRECT MODE OF ACTION

PRLR inhibition as a safe innovative alternative to current treatment options

Proposed direct impact of ABS-201 on Hair Cycle Stages



ABS-201 has the potential to:

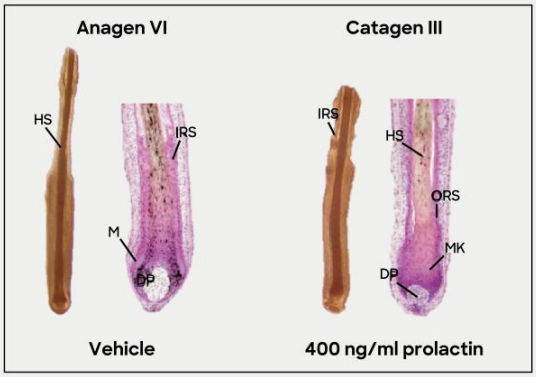
- Shift the balance in hair cycle stage towards anagen phase[1,2] with:
  - active and new hair growth
  - prevention of telogen effluvium
- Promote a long-lasting effect after treatment cessation
- Restore hair pigmentation[2]

[1] doi: 10.1016/S0002-9440(10)64295-2
[2] doi: 10.2353/ajpath.2006.050468

ABS-201 PRLR

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[1] characterized by:

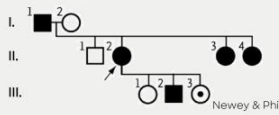
- Condensed shape of the dermal papilla (DP)
- Diminishment of the hair matrix volume
- Apparent cessation of pigmentation
- Inhibition of hair shaft elongation

[1]doi: 10.2353/ajpath.2006.050468

ABS-201 PRLR

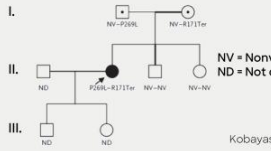
PRLR inhibition anticipated to be safe & well tolerated as supported by human genetics

Dominant negative PRLR loss-of-function



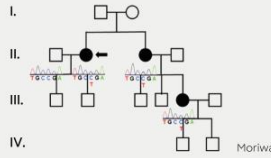
Newey & Phil , 2013 NEJM

Compound heterozygous PRLR loss-of-function



Kobayashi, 2018 NEJM

Dominant negative PRL loss-of-function



Moriwaki, 2021 JCEM

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

ABS-201 PRLR

Translational Model validates PRLR Target

TOP HEAD VIEW OF STUMPTAILED MACAQUE'S SHOWING PHENOTYPIC CHANGE OVER TIME

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

Disclosure from competitor

TREATMENT WITH AN ANTI-PRLR MAB PROMOTES AND SUSTAINS LONG-TERM HAIR GROWTH IN NHP

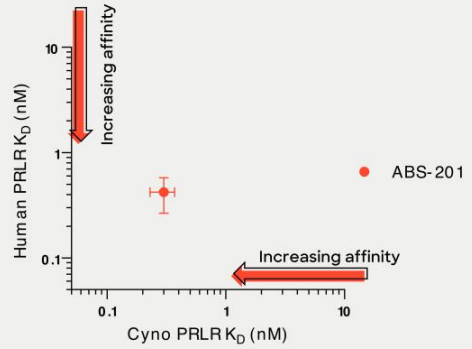
- Hair density & thickness improved with short treatment duration in primate model of androgenic alopecia
- Hair growth remains several years post cessation
- Hair re-growth observed for both male and female animals

ABS-201 PRLR | *IN VITRO* PROFILE

ABS-201 candidates are high affinity and potent binders

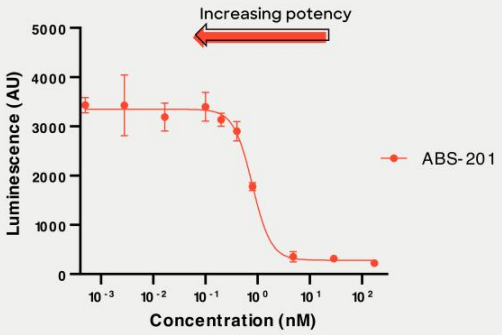
HIGH AFFINITY ANTI-PRLR mAbs WITH CYNO CROSS-REACTIVITY

ABS-201 leads show nM - sub nM affinity to human PRLR



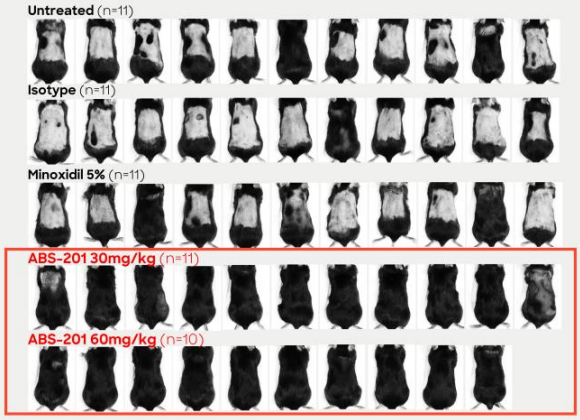
AI-OPTIMIZED HIGH AFFINITY LEADS TRANSLATE TO HIGH CELLULAR POTENCY

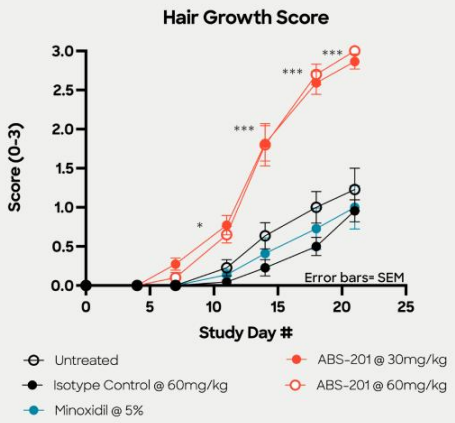
PathHunter - *in vitro* PRLR reporter functional assay



ABS-201 | *IN VIVO* EFFICACY

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





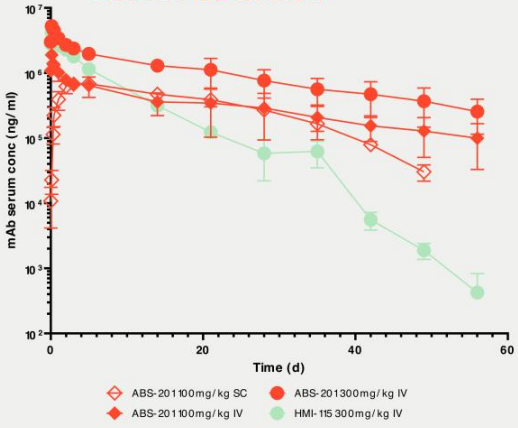
Administration: mAbs i.p. biweekly; Minoxidil topical daily

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

ABS-201 PRLR

56 day interim NHP pharmacokinetic data confirms ABS-201 is well positioned for AGA market

SINGLE DOSE COMPARATIVE PK PROFILE IN NHPs



Datapoints of animals with positive ADA rates impacting PK were excluded at corresponding timepoints onwards

NHP-PK 56 DAY RESULTS

- >3x extended half-life in NHPs compared to HMI-115
- High subcutaneous bioavailability in NHPs at >90%
- In silico prediction of Q8W-Q12W dosing intervals in humans
- Manufacturability & Developability profile enables the potential for future high concentration formulation targeting >150mg/mL

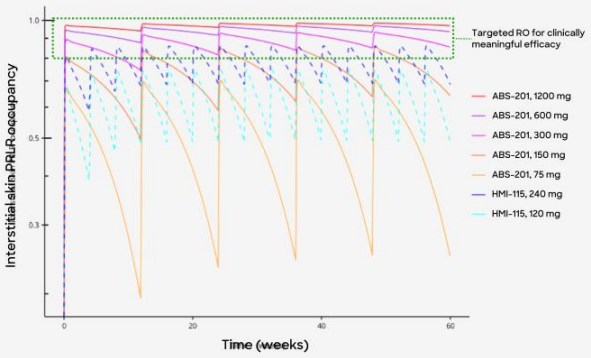
Based on PK/PD modeling, ABS-201 is expected to likely require **only 2-3 doses over a 6-month treatment period**, compared to HMI-115, which would likely require 6-12+* doses in the same period, assuming the AGA indication is pursued.

*assumption on HMI-115: 60mg/mL formulation and Q2W or Q4W dosing interval

ABS-201, PRLR | *IN SILICO* MODELING

Modelling shows superiority of ABS-201 vs HMI-115 on PK & Receptor Occupancy

ABS-201 vs HMI-115 in humans Q12W skin receptor occupancy (RO)*



ABS-201 refers to the development candidate (DC) ABS-201-A
*Assumptions: 100% bioavailability after short term infusion, 0.2 skin exposure coefficient, 2.6 x 10^{-2} nM interstitial PRLR concentration

PRELIMINARY IN SILICO MODELLING

- >3x extended half-life in NHPs predicted to translate in humans to **Q8W-Q12W** dosing intervals
- PK profile predicted to translate into higher interstitial skin concentrations resulting in higher receptor occupancy. This supports our expectations of higher **clinical efficacy.**

ABS-201 | PROFILE

Superior profile of ABS-201

DESIRED ATTRIBUTE	HMI-115	ABS-201
AFFINITY	+	++
IN VITRO POTENCY	++	++
HIGH SOLUBILITY	–	++
STABILITY	–	+
EXTENDED ½-LIFE	–	++
BIOAVAILABILITY	?	++
PATENT LIFE	–	++

Expected improved efficacy and patient convenience based on:

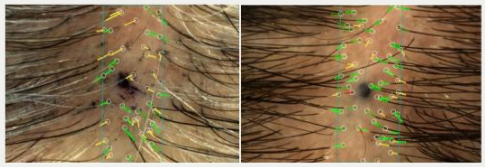
- Excellent Manufacturability & Developability enables future **high concentration formulation** targeting 200mg/ml (ABS-201) vs. ~60mg/ml (HMI-115)
- Excellent absolute bioavailability profile in NHPs (>90%) to enable **subcutaneous (SC) injection**
- > 3x extended half-life vs HMI-115 in NHPs to enable **longer dosing intervals** - Q8W/Q12W vs. Q2W/Q4W

BENCH TO BEDSIDE

Straightforward path for ABS-201 clinical development

CLINICAL TRIALS FOR HAIR TREATMENTS ARE EXPECTED TO BE STRAIGHTFORWARD

- Ease of patient recruitment
- High level of KOL Interest
- Ability to conduct multi-center trials
- Non-invasive trial conduct



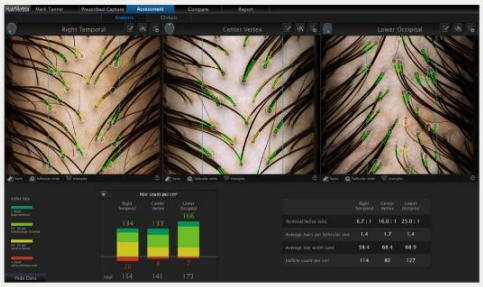
WELL DEFINED ENDPOINTS WITH VALIDATED MEASURES

Primary Endpoints: Quantitative measurements with follicular dermatoscope (trichoscopy)

- Terminal Hair Growth
- Total Hair Count
- Total hair density (per cm2)

Secondary Endpoints:

- Patient Reported Outcomes as measured by validated scales accepted by the FDA (HairDex; Hair Specific Skindex-29 (FPHL); The Men's Hair Growth Questionnaire (MHGQ)); Women's Hair Growth Questionnaire (WHGQ)
- Re-pigmentation



Leading Scientific Advisory Board of Hair Experts

Over Half a Million alopecia patients treated each year by these KOL practice networks

DR. ANTHONY ROSSI
Memorial Sloan Kettering Cancer Center

DR. KEN WASHENIK
Bosley Medical Group

DR. MARIA K. HORDINSKY
Univ. of Minnesota

DR. DAVID GOLDBERG
Schweiger Dermatology

DR. RODNEY SINCLAIR
Sinclair Dermatology

DR. DORIS DAY
Day Dermatology & Aesthetics

DR. MATT L. LEAVITT
Advanced Dermatology and Cosmetic Surgery

DR. MEENA SINGH
Skin and Hair Center

DR. SUZANNE KILMER
Laser & Skin Surgery Center of Northern California

DR. GLYNIS ABLON
Ablon Skin Institute

DR. CHESAHNA KINDRED
Kindred Hair & Skin Center

DR. NEIL S. SADICK
Sadick Dermatology

INTERNAL PIPELINE

Absci's progress in Drug Creation

Continued advancement of lead assets

ABS-101

Continued progress of TL1A asset with FiH in 1H 2025

- New preclinical data supporting superior immunogenicity profile
- Phase 1 Interim data readout in 2H 2025

ABS-201

IND-enabling activities on-track for PRLR (prolactin receptor) program with anticipated initiation of Ph1/2a studies in early 2026

Discovery of next assets

ABS-301

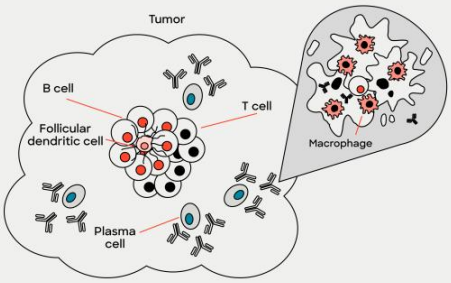
Progress of first-in-class asset discovered through Absci's Reverse Immunology Platform

ABS-501

Nomination of a potential best-in-class HER2 asset

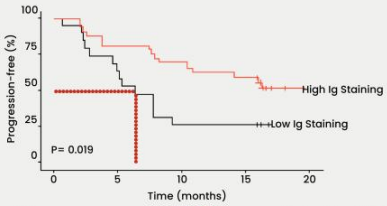
TARGET DISCOVERY

Tertiary Lymphoid Structures (TLS): The focus of Absci's Reverse Immunology approach



Tertiary lymphoid structures (TLS) are centers of immune activity, such as 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].

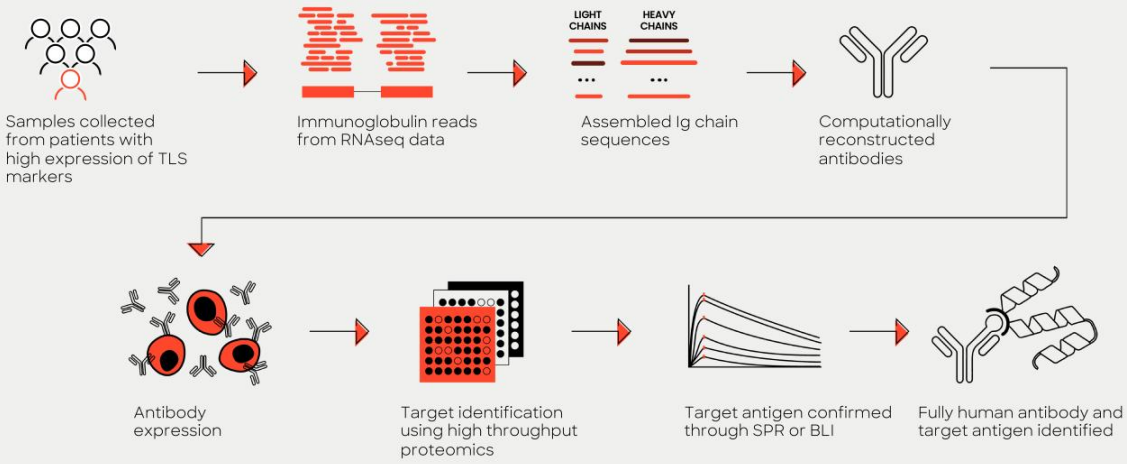


The presence of TLS is associated with longer progression-free survival and better response to immune checkpoint inhibitors[2,3].

- 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] doi: 10.3389/fimmu.2018.01952 [2] doi: 10.1016/j.immuni.2022.02.001 [3] doi: 10.1038/s41586-019-1922-8

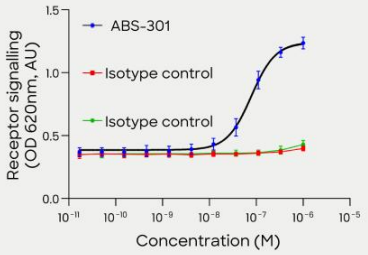
ABS-301 | Reverse Immunology platform identifies the antigens targeted by endogenous antibodies produced in tumor lymphoid structures (TLS)



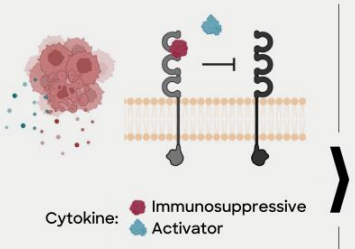
Reference. doi: 10.1101/2021.02.06.430058

ABS-301 | A patient-derived antibody discovered by reverse immunology blocks an immunosuppressive cytokine

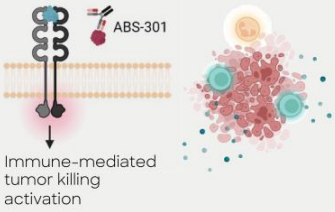
ABS-301 rescues pro-inflammatory signaling through inhibition of immunosuppressive cytokine



Target biology and proposed ABS-301 mechanism of action



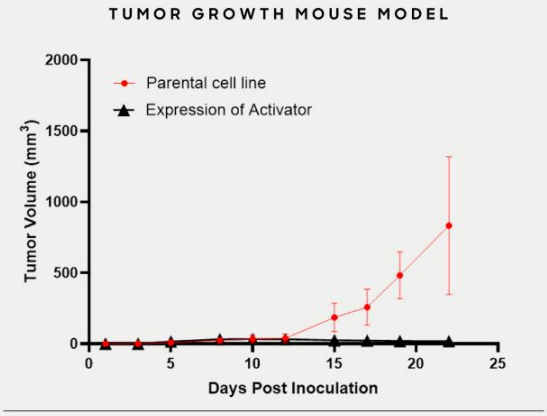
Target cytokine is suggested to maintain an immunosuppressive environment through signaling inhibition



Restoring signaling by blocking immunosuppressive cytokine which may promote immune-mediated tumor cell killing

ABS-301

In vivo Target Validation: Pathway Activation Drives Potent Anti-Tumor Response



Key Findings:

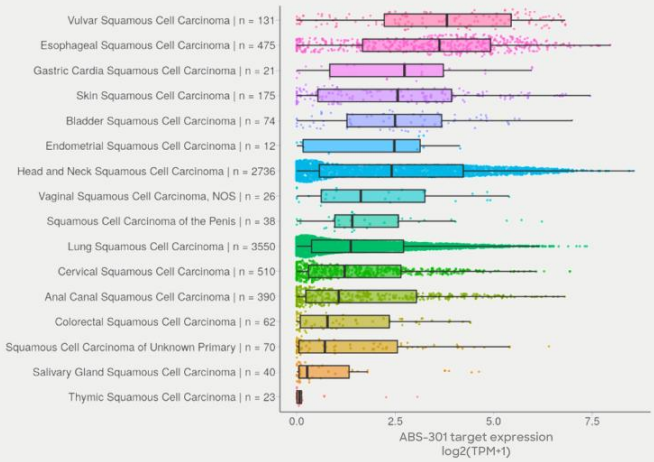
- Activation of the ABS-301-targeted pro-inflammatory pathway triggers a robust anti-tumor immune response.

Study Overview:

- Mouse melanoma cells were genetically modified to activate the ABS-301-targeted pro-inflammatory pathway via Activator expression.
- Tumor progression was assessed in immunocompetent mice injected with either engineered cells or unmodified parental cells.

ABS-301

Expression of ABS-301's target suggests broad potential in squamous cell carcinomas

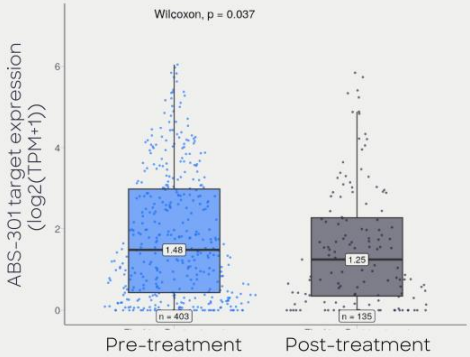


Distribution of ABS-301 target expression across squamous cell carcinoma cohorts.

Values shown are log2(TPM+1) normalized. Multiple biopsies from a patient are included in the analysis.
Source: Tempus

ABS-301 | Expression in Lung Squamous Cell Carcinoma (LUSC): no change with treatment and strong negative correlation with CD8+ T cell infiltration

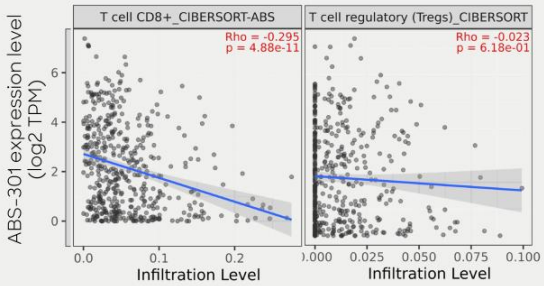
Sustained target expression in LUSC



Source: Tempus

In LUSC, univariate analysis of ABS-301 expression indicate only a minor change in expression between pre- and post-treatment suggesting opportunity for combination therapy.

CD8+ Infiltration negatively correlated with target expression in LUSC



Source: TCGA

ABS-301 target expression shows a strong negative correlation with CD8+ T cell infiltration with a minimal effect on Treg infiltration supporting immunosuppressive activity of target *in vivo*.

ABS-301 | Broad potential in immuno-oncology

Based on literature and potential competitive molecules, the following indications could be of interest:

Indication		US Prevalence	Estimated 5-year survival rate*	US Sales in 2030
NSCLC		Calculated: ~202K in 2023	28%	$27B
	SCC	30% of NSCLC cases Calculated: ~61K	24%	Calculated Sales: $8.1B
Head and Neck SCC		~54K in 2022	68.5%	Calculated Sales: $2.3B
Esophageal Cancer		~21K in 2022	20%	$1.5B
	SCC	~20% of cases Calculated: ~4.2K		Calculated Sales: $0.3B
Cervical Cancer		~14K in 2023		$0.6B
	SCC	90% of cases Calculated: ~13K	67%	Calculated Sales: $0.6B
Skin Cancer, non-melanoma		Incidence = ~3,300K	95-100%	$1.0B
	SSC	Incidence = ~700K	95%	Calculated Sales: $0.2B

*dependent on stage of diagnosis
References provided in appendix

INTERNAL PIPELINE

Absci's progress in Drug Creation

Continued advancement of lead assets

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IND-enabling activities on-track for PRLR (prolactin receptor) program with anticipated initiation of Ph1/2a studies in early 2026

Discovery of next assets

ABS-301

Progress of first-in-class asset discovered through Absci's Reverse Immunology Platform

ABS-501

Nomination of a potential best-in-class HER2 asset

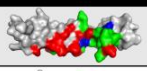
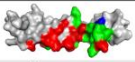
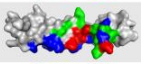
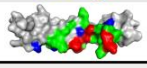
ABS-501, HER2 | Deploying *de novo* AI model on HER2 led to discovery of antibodies displaying molecular interactions distinct from trastuzumab

Zero shot *de novo* AI discovery on HER2

- Hits with edit distance of up to 12 amino acids in HCDR3 region (13 aa, search space of 20^{13}) were screened
- Selected 50 hits with <10 nM affinity were expressed as mAbs for binding affinity determination
- Top 11 antibodies were characterized *in vitro* and 3 leads evaluated *in vivo*

bioRxiv 2023.01.08.523187; doi: https://doi.org/10.1101/2023.01.08.523187

AI-designed antibodies: same epitope, different HER2 contact preferences

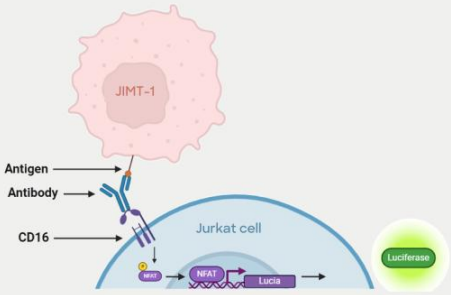
Variant #	Edit distance	K_D (nM)	Epitope mapping view	Loop 581-590
Trastuzumab	0	1.07		
1	7	4.16		
3	7	9.75		
4	2	6.66		

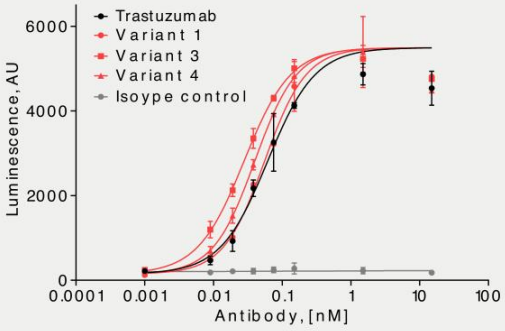
Not critical
Partial
Critical

ABS-501, HER2 | AI-designed antibodies demonstrate measurable enhancement of ADCC activity compared to trastuzumab

ADCC assay principle

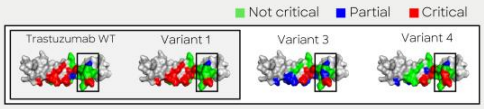
Luciferase signal driven by NFAT transcription factor positively correlates to ADCC activation against JIMT-1



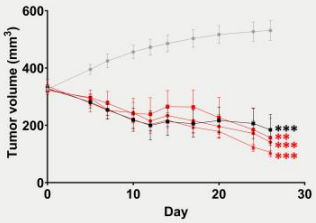


	Trastuzumab	Variant 1	Variant 3	Variant 4
EC50 (nM)	0.062	0.056	0.028	0.040
R squared	0.93	0.97	0.97	0.95
P value	N/A	Not significant	<0.0001	0.0015

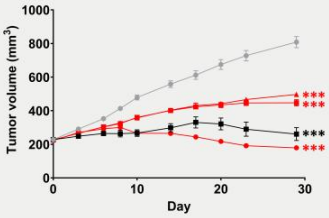
ABS-501, HER2 | AI-designed antibodies suppress growth of trastuzumab-sensitive & resistant HER2+ breast tumors



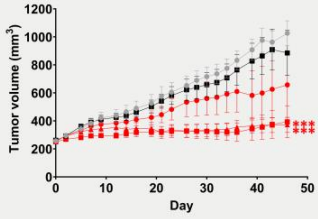
Mouse xenograft model using **EFM192A** (HER2+ BC; **Tz sensitive**)



Mouse xenograft model using **MDA-MB-361** (HER2+ BC; **Tz sensitive**)



Mouse xenograft model using **JIMT-1** (HER2-amp BC; **Tz resistant**)



● Isotype control ● Trastuzumab ● Variant 1 ■ Variant 3 ▲ Variant 4

Trastuzumab-sensitive EFM192A and MDA-MB-361 tumors respond to both trastuzumab (Tz) & AI-designed antibodies

JIMT-1 tumors are trastuzumab resistant but sensitive to variants 3 and 4

Xenograft studies conducted by Dr. Dennis Slamon's team at UCLA

2-way ANOVA ** P<0.001 and ***P<0.0001 vs isotype control

ABS-501, HER2 | AI-designed antibodies create opportunities to address unmet medical need

Currently exploring breast cancer as opportunity: alternative to or post Enhertu®

- Despite Enhertu's good efficacy, leading oncologists are only moderately satisfied due to toxicity (e.g. interstitial lung disease); less toxic therapy and effective treatment post-Enhertu are key unmet needs.

"Post-Enhertu is really where the action is right now in the field. I think the first company that comes up with something that has significant benefit in Enhertu progressive disease is going to win." - KOL

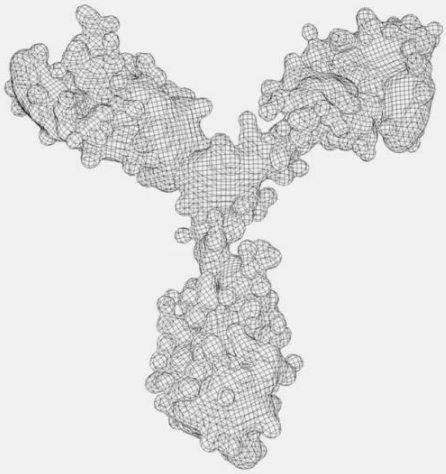
Multiple paths possible for therapeutic development:

- Modality switch or combination opportunities under consideration to address unmet medical needs

Later-line treatment regimens for HER2-positive cancer:
- Monotherapy
- Combination therapy with targeted small molecules

Enhancing efficacy and expanding indications (e.g. Enhertu resistance):
- Antibody-drug conjugates (ADCs)
- Multi-specific antibodies

Leading AI models to create novel & differentiated therapeutics



ADDRESS COMPLEX AND PREVIOUSLY "HARD TO DRUG" TARGETS

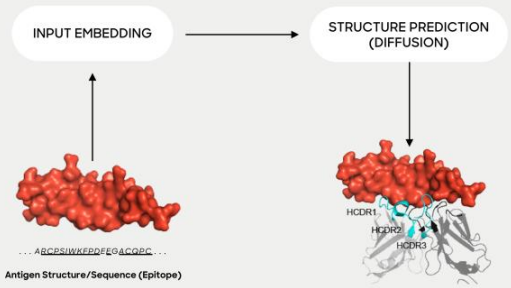
- Bind Specific extracellular domains
- Target Specific conformations
- Address difficult target classes e.g. GPCRs

INTRODUCE PRECISE CONTROL OVER ANTIBODY DESIGN

- "Smart" biologics
- Enhanced Potency & MOA
- Engineer selectivity, minimizing off target toxicity
- Agonism vs. Antagonism

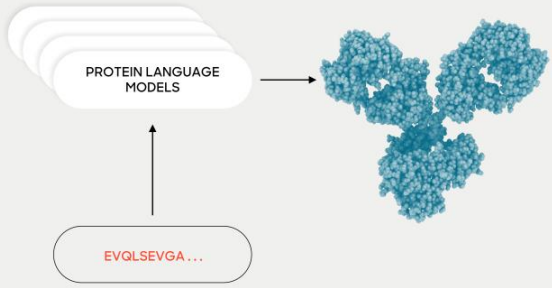
Leadership in AI *de novo* design of antibody-based therapeutics

DE NOVO ANTIBODY DESIGN



- *de novo* antibody design model creates epitope-specific binders given a target structure
- Designed in framework of choice or multiple frameworks

AI LEAD OPTIMIZATION



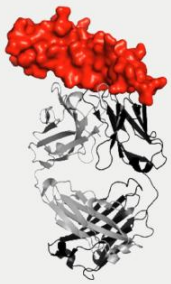
- Co-optimization enables improvement of antibody attributes while maintaining developability
- Precise engineering of molecule pharmacology

Our AI platforms are enabled by our 6-week 'lab-in-the loop' active learning cycles

AI PLATFORMS

DE NOVO **ANTIBODY DESIGN**

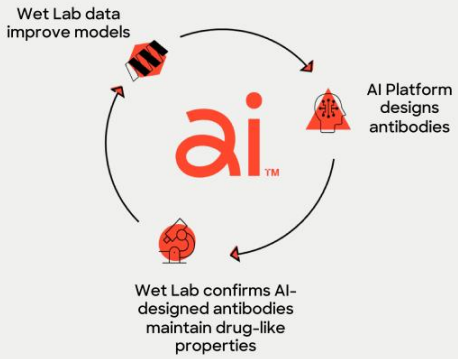
***de novo* design of epitope-specific antibodies** against targets without requiring a known binder



LEAD OPTIMIZATION

AI guided lead optimization enables tunable pharmacology

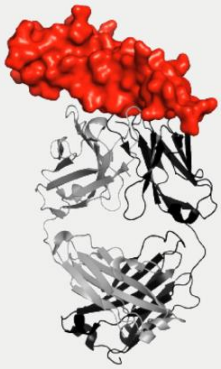
LAB-IN-THE-LOOP



DE NOVO ANTIBODY DESIGN

AbsciDesign comprises two categories of AI models for *de novo* antibody design

AbsciGen:
antibody<>antigen complex structure and sequence design



Design 1
HCDR1: GFNIKDTY
HCDR2: IYPTNGYT
HCDR3: SRWGGDGFYAMDY

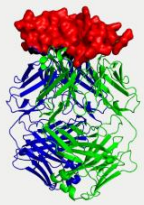
LCDR1: QDVNTA
LCDR2: SAS
LCDR3: QQHYTTPPT

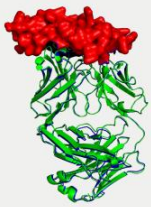
▪
▪
▪

Design N
HCDR1: GFNIKDTW
HCDR2: IYPSNGYT
HCDR3: ARWGGDGFYAMDY

LCDR1: QDVNTA
LCDR2: SAS
LCDR3: QQHYTTPPT

AbsciBind:
antibody design scoring and filtering





Antigen
AbsciGen
AbsciBind

AbsciBind
Low Rank

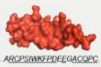
RMSD = 5.3 Å
Confidence = 0.64

AbsciBind
High Rank

RMSD = 2.3 Å
Confidence = 0.95

The AbsciDesign AI platform delivers *de novo* antibodies via an end-to-end design-validation workflow

STEP 1.
Define design parameters



...ARGPSWKFPDEFGACGPC...

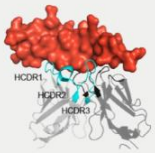
Antigen Structure/Sequence (Epitope)

HFWR1: EVQLE.....GSLSCAAS
HFWR2: IHWVR.....LEWVAR
HFWR3: RYRF.....SLEDTAVYYC
HFWR4: WGQGTLVTVSS

LFWR1: DIQMT...RVTITCRAS
LFWR2: VAWYQ...KLLIY
LFWR3: FLLQFE...DFATYYC
LFWR4: FGQGTKVEIK

Heavy/Light Framework Sequences

STEP 2.
Fine-tune and deploy AbsciGen and AbsciBind to generate hundreds of thousands of variants and filter to a subset that are likely binders



Design 1
HCDR1: GFNIKDTY
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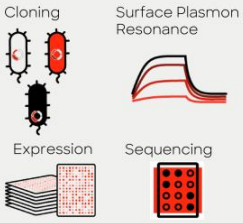
HCDR3: SRWGGDGFYAMDY
LCDR1: QDVNTA
LCDR2: SAS
LCDR3: QQHYTTPPT

⋮

Design N
HCDR1: GFNIKDTW
HCDR2: IYPSNGYT
HCDR3: ARWGGDGFYAMDY
LCDR1: QDVNTA
LCDR2: SAS
LCDR3: QQHYTTPPT

Heavy/Light CDR Sequences

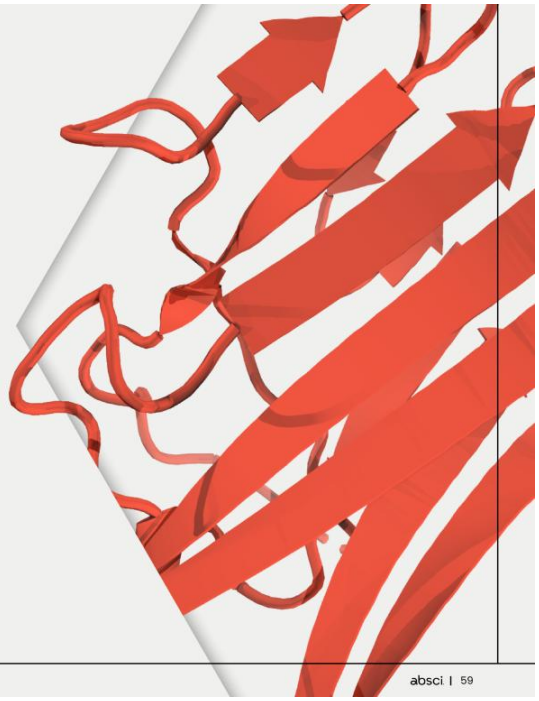
STEP 3.
Wet lab screening and model performance validation



CASE STUDY

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

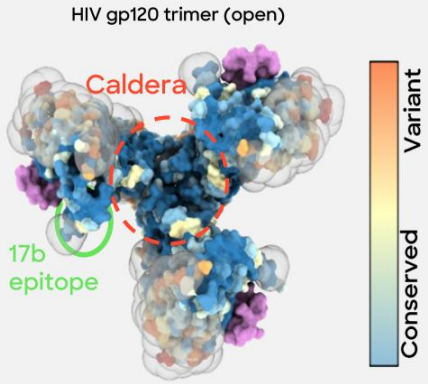
Caltech absci BILL & MELINDA GATES *foundation*



DE NOVO DESIGN

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.



DE NOVO DESIGN

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

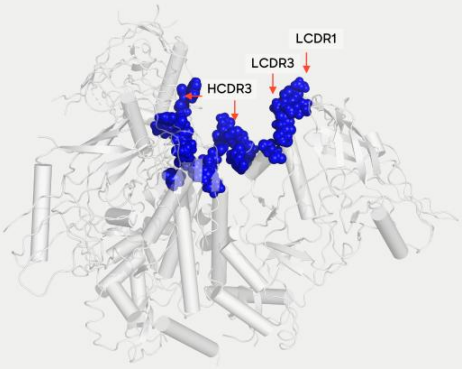
Model inputs:

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

Design of CDRs:

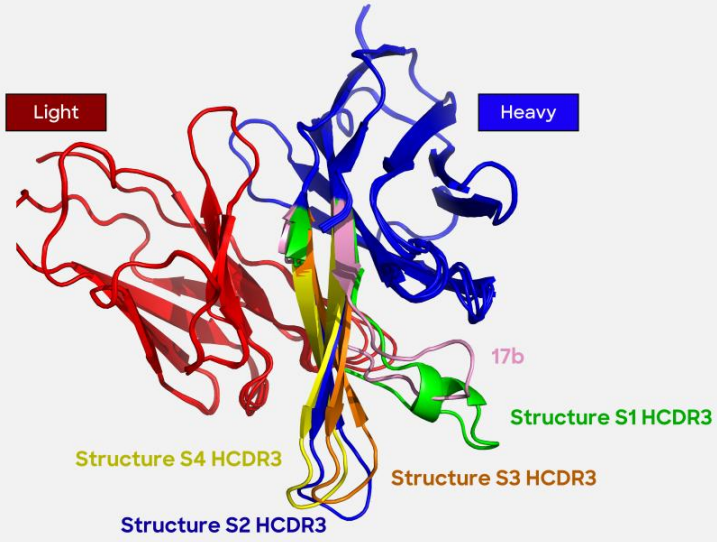
- Condition the model to design long HCDR3s to reach into open caldera region (>20 residues)
- Designed HCDR2 and LCDR3 to bind to HIV surface

HIV Env trimer (open)

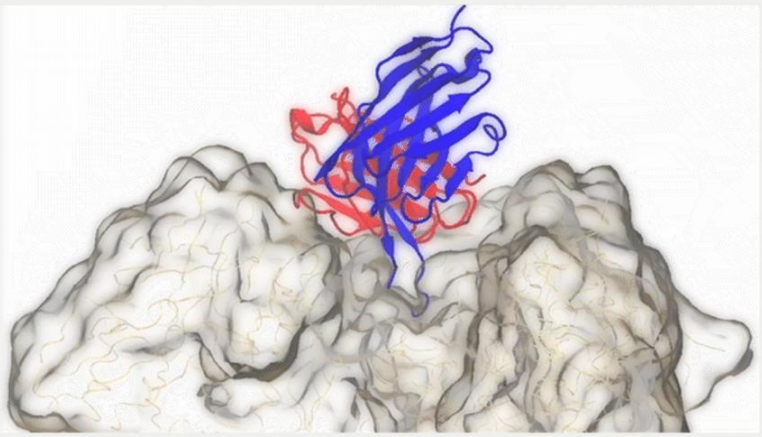


DE NOVO DESIGN

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

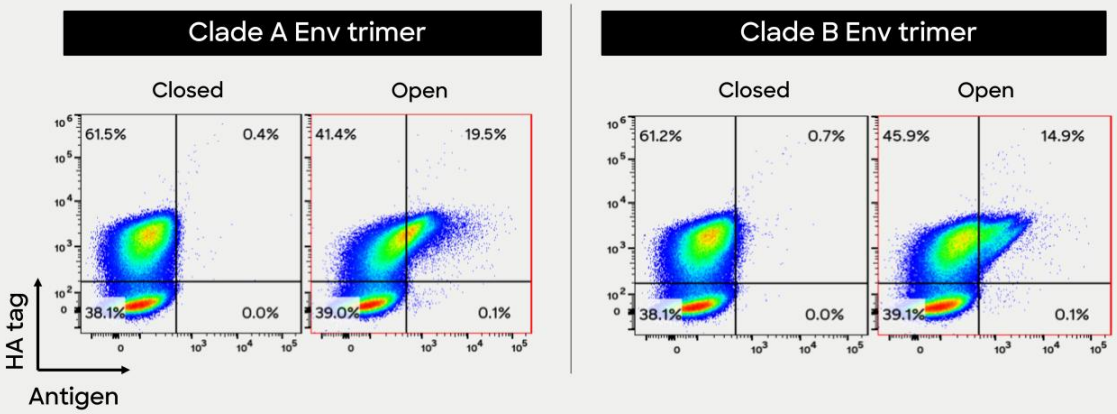


Applied molecular dynamics simulation to *de novo* designed antibodies



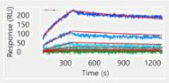
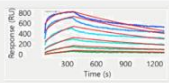
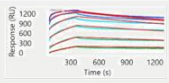
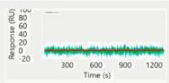
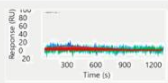
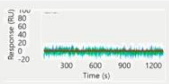
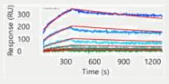
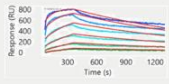
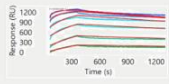
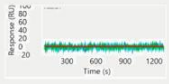
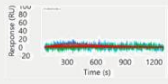
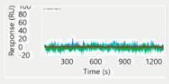
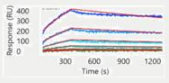
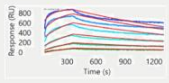
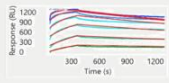
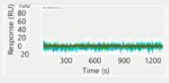
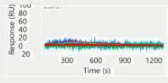
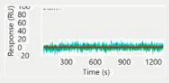
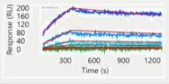
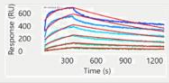
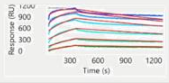
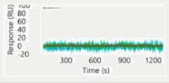
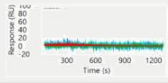
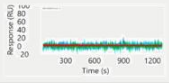
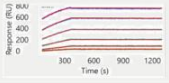
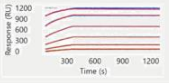
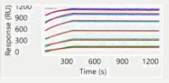
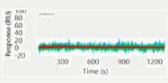
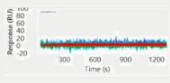
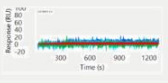
DE NOVO DESIGN

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



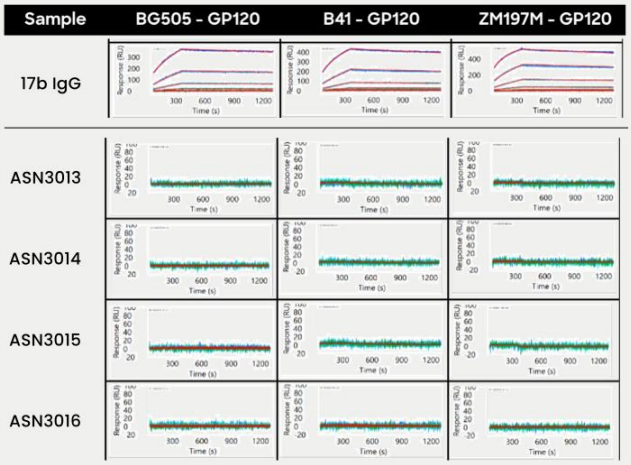
DE NOVO DESIGN

SPR data demonstrate binding characteristics consistent with binding of caldera

Sample	BG505 – open (+CD4)	B41 – open (+CD4)	ZM197M – open (+CD4)	BG505 – closed (–CD4)	B41 – closed (–CD4)	ZM197M – closed (–CD4)
ASN3013						
ASN3014						
ASN3015						
ASN3016						
17b IgG						

DE NOVO DESIGN

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



Hypothesis:

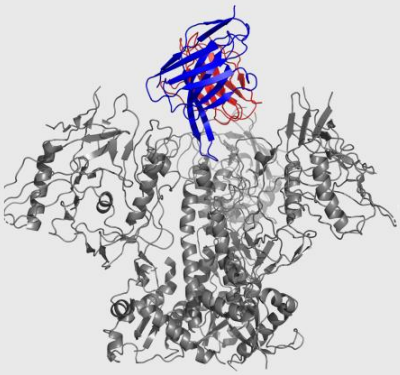
If the designed mAbs are binding to the caldera region we should not observe binding to monomeric GP120 since the caldera is only present in the Env trimer

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 DE NOVO DESIGN

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



SUMMARY

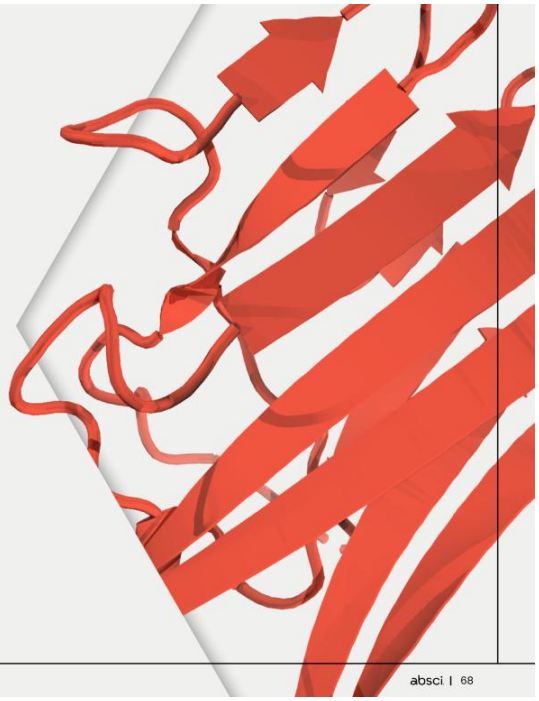
- *de novo* design model created a novel and diverse antibody which binds multiple clades of HIV indicating successful targeting of the caldera epitope
- Screening cascade enabled selection of differentially binding variants

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

CASE STUDY

AI Optimization for pH sensitivity



CASE STUDY -AI LEAD OPTIMIZATION for pH SENSITIVITY

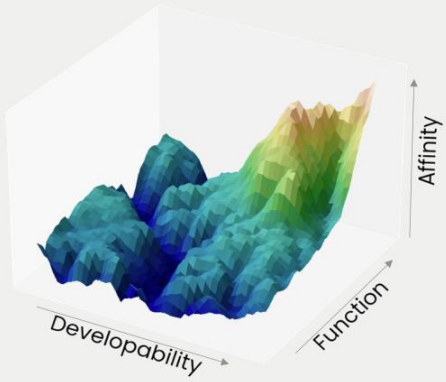
AI lead optimization platform for 'smart biologics'

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 ~10^{19}, a million times larger than traditional methods, identifying functional, developable antibodies in one step.

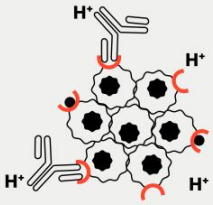


CASE STUDY - AI LEAD OPTIMIZATION for pH SENSITIVITY

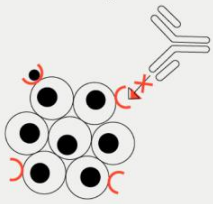
pH sensitivity may reduce toxicity and/or improve efficacy of therapeutic mAbs

TUMOR SPECIFICITY IMPROVES EFFICACY AND REDUCES "ON-TARGET OFF-TUMOR" TOXICITIES

Binding occurs in the acidic pH of the tumor microenvironment



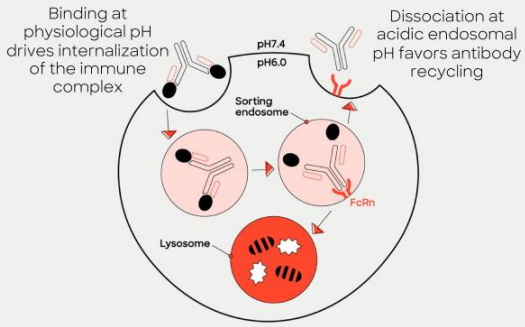
No binding occurs in the neutral pH surrounding healthy cells



DISSOCIATION IN THE ENDOSOME DRIVES ANTIBODY RECYCLING AND EFFICIENT CLEARANCE OF SOLUBLE TARGETS

Binding at physiological pH drives internalization of the immune complex

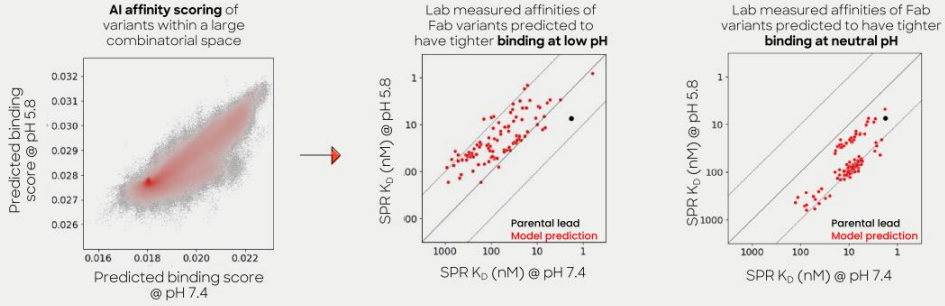
Dissociation at acidic endosomal pH favors antibody recycling



CASE STUDY - AI LEAD OPTIMIZATION for pH SENSITIVITY

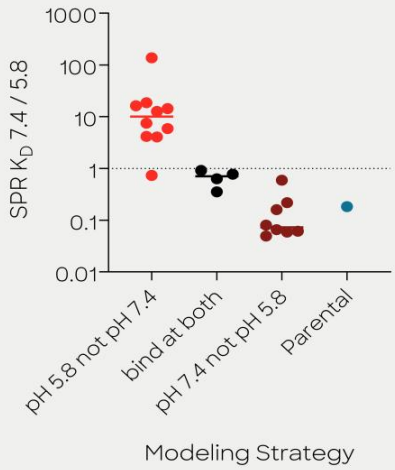
Models identify pH sensitive Fab variants from the same lead for either indication

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



CASE STUDY - AI LEAD OPTIMIZATION for pH SENSITIVITY

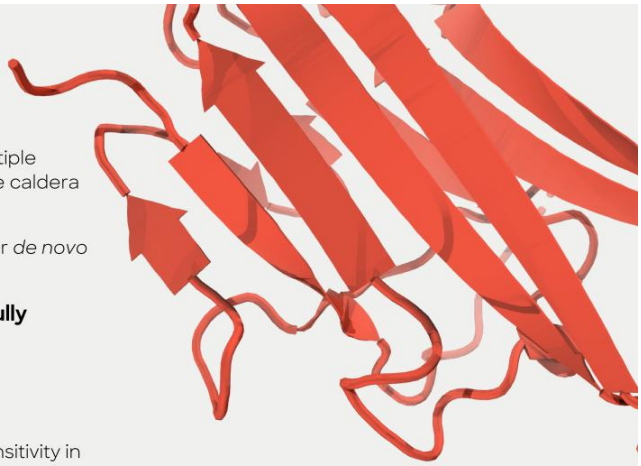
Hits reformatted as mAbs show desired binding profiles



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

[1] Data provided in appendix

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

absci®

Better biologics for patients, faster