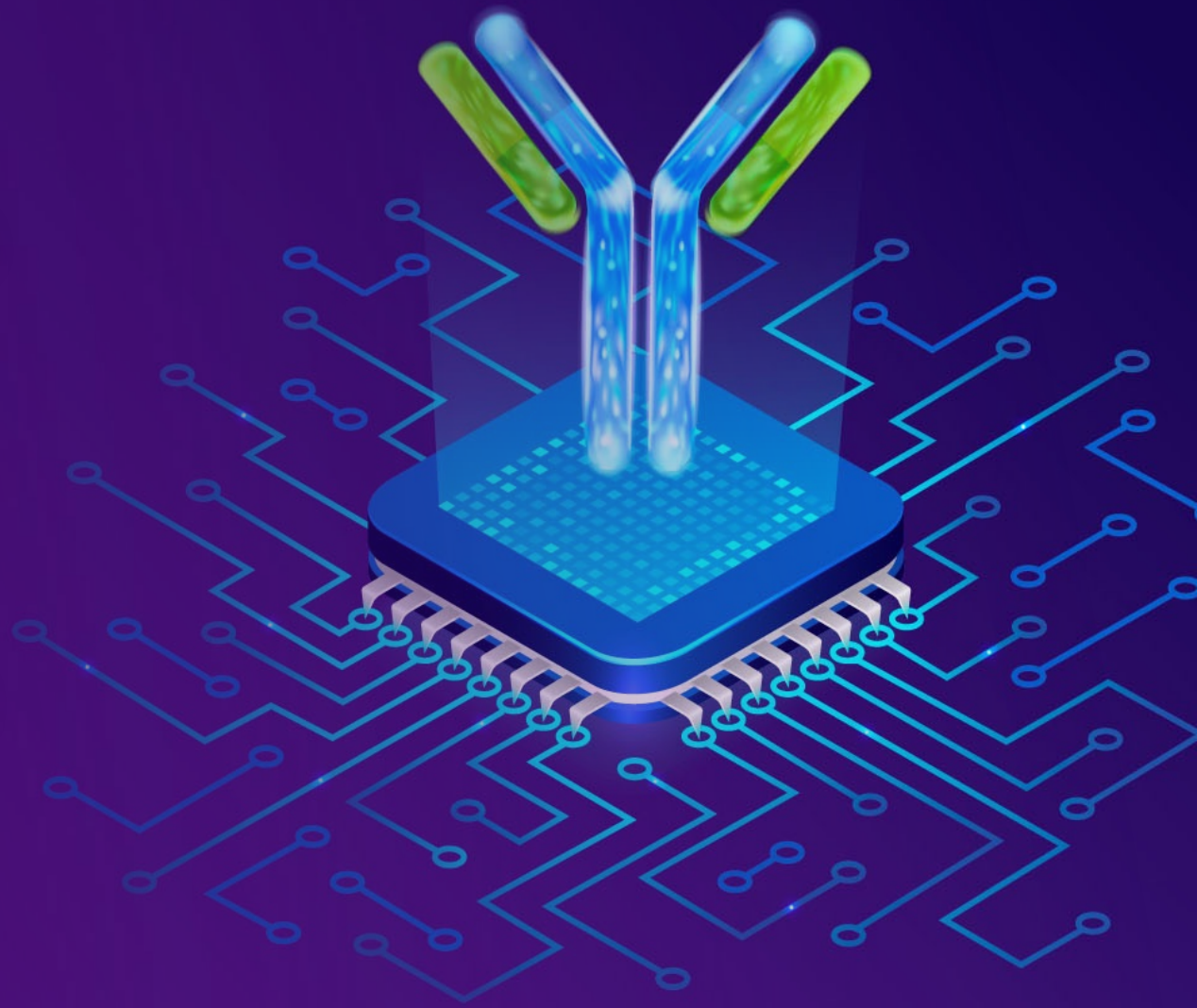
Tomorrow's Precision Antibody Therapeutics Powered by Machine Learning

January 2024

Forward-looking Statements

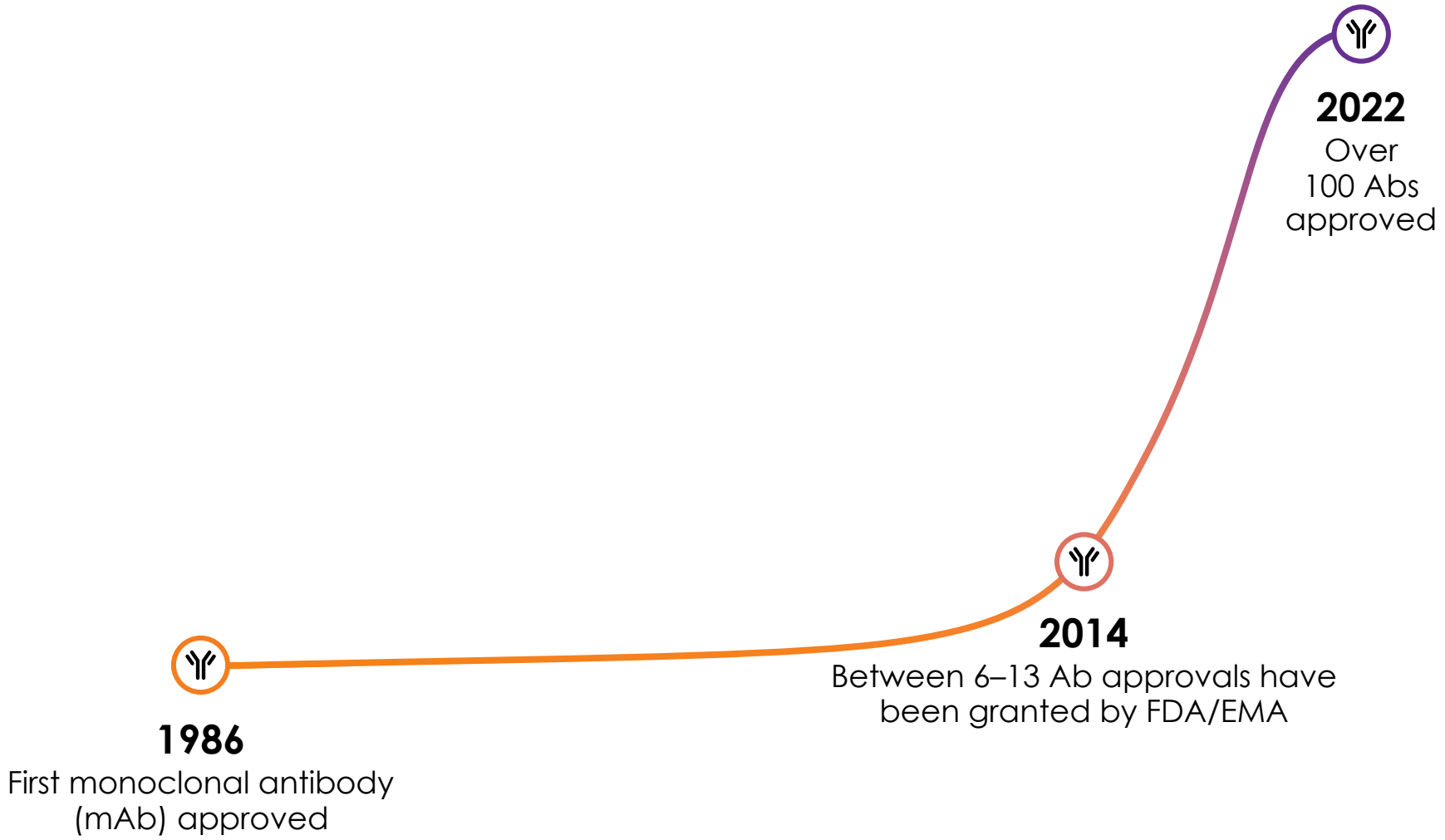
Certain statements in this presentation constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as "may," "might," "will," "should," "believe," "expect," "anticipate," "estimate," "continue," "predict," "forecast," "project," "plan," "intend" or similar expressions, or statements regarding intent, belief, or current expectations, are forward-looking statements. These forward-looking statements are based upon current estimates. While iBio, Inc., a Delaware corporation (including its consolidated subsidiaries, "iBio," the "Company," "we," "us" or "our") believes these forward-looking statements are reasonable, undue reliance should not be placed on any such forward-looking statements, which are based on information available to us on the date of this presentation. These forward-looking statements are subject to various risks and uncertainties, many of which are difficult to predict that could cause actual results to differ materially from current expectations and assumptions from those set forth or implied by any forward-looking statements. Important factors that could cause actual results to differ materially from current expectations include, among others, the Company's ability to obtain regulatory approvals for commercialization of its product candidates, or to comply with ongoing regulatory requirements, regulatory limitations relating to its ability to promote or commercialize its product candidates for specific indications, acceptance of its product candidates in the marketplace and the successful development, marketing or sale of products, its ability to attain license agreements, the continued maintenance and growth of its patent estate, its ability to establish and maintain collaborations, its ability to obtain or maintain the capital or grants necessary to fund its research and development activities, competition, its ability to retain its key employees or maintain its NYSE American listing, and the other factors discussed in the Company's most recent Annual Report on Form 10-K and the Company's subsequent filings with the SEC, including subsequent periodic reports on Forms 10-Q and 8-K. The information in this presentation is provided only as of today, and we undertake no obligation to update any forward-looking statements contained in this presentation on account of new information, future events, or otherwise, except as required by law. This presentation, and any oral statements made in connection with this presentation, shall not constitute an offer to sell, or the solicitation of an offer to buy, or a recommendation to purchase any equity, debt or other securities of the Company, nor, in connection with any securities offering by the Company, will there be any sale of these securities in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of such state or jurisdiction.

We are developing antibodies for the next generation of difficult targets and modes of action with the goal of engineering high developability and enhanced safety into our molecules



** U.S. Patent No. 11,545,238*

We Believe Our Technology Can Unlock the Next Phase in a Maturing Antibody (Ab) Market



Today's Ab Market

$196B

(USD)

https://www.globenewswire.com/news-release/2023/09/06/2738625/0/en/Monoclonal-Antibodies-Market-is-expected-to-reach-USD-612-2-Billion-by-2032-growing-at-a-CAGR-of-12-3-from-2022-to-2032.html
*Lyu, X. et al. The global landscape of approved antibody therapies. Antibody Therapeutics **5**, 233–257 (2022).*

Vast Areas of the Human Surfaceome Remain Untapped by Antibodies

Approved Antibodies[3]

162

Current Antibody Targets[3]

91

40% of approved antibodies bind to only 10 targets

Current Estimates of The Potential Target Space

2,886

In silico predicted cell surface proteins[1]

>6,500

membrane and secreted proteins[2]

1 Bausch-Fluck et al., PNAS, October 2018
2 Charles River, Retrogenix Human Protein Library
3 Lyu et al., Antibody Therapeutics, September 2022

Today's Ab Market Challenge: Complex Targets, Safety & Developability Issues

The era of low-hanging fruit is over-saturated

Existing techniques do not address increasing target complexity and modes of actions

ADCs and bispecifics have proven successful but revealed off-tissue safety concerns

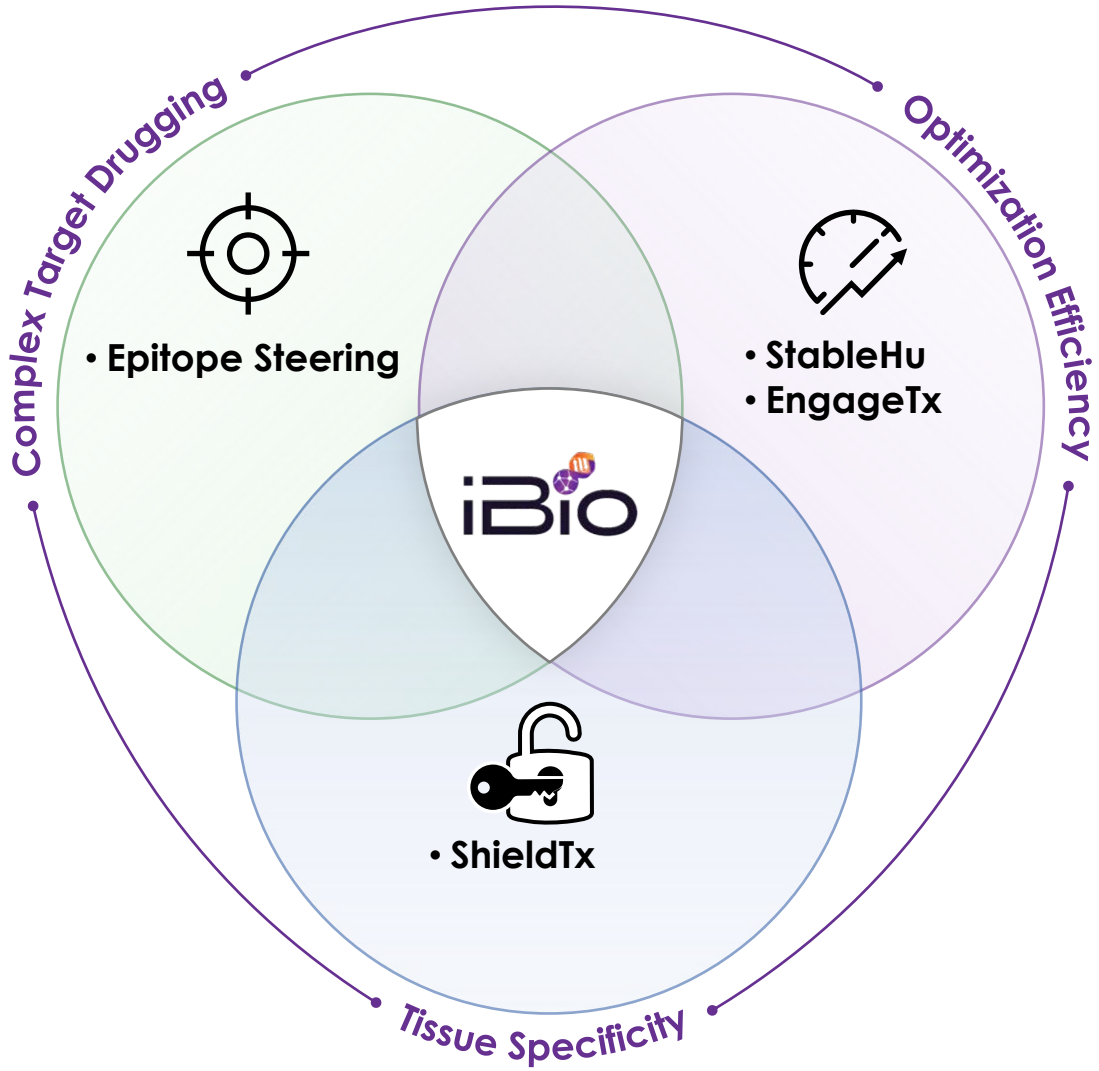
Antibody developability has surfaced as critical hurdles

iBio's Technology Platform Aims to Solve Today's Key Issues of mAb Discovery and Development

Epitope Steering Technology reliably unlocks antibodies for challenging targets

StableHu™ and mammalian display technologies synergize to slash mAb optimization to under 4 weeks and create the **EngageTx™** T-cell engager panel

ShieldTx™: Our latest technology advancement: Engineered epitopes enabling antibodies to discern and act selectively in diseased tissue

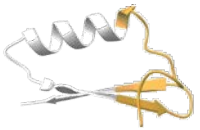


Unlocking High-Value Drug Targets: AI-Engineered Epitopes are Generalizable to a Broad Set of Complex Structural Drug Binding Sites

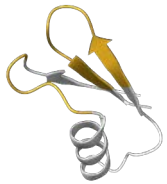
Loop Display

Junctional Epitopes

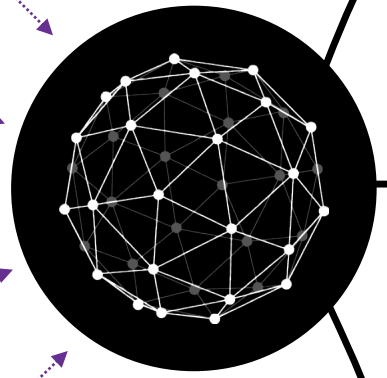
Complex Secondary Structures



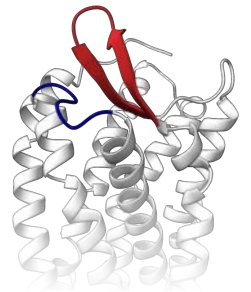
Membrane Proteins (e.g. GPCR)



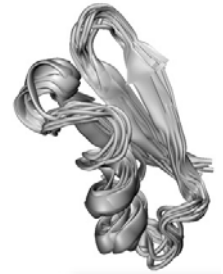
AI Epitope Engine



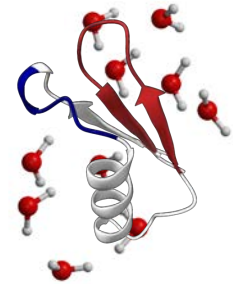
1 Match Engineered Structure to Target



2 Refined for Greater Stability



3 Optimized for Water Solubility



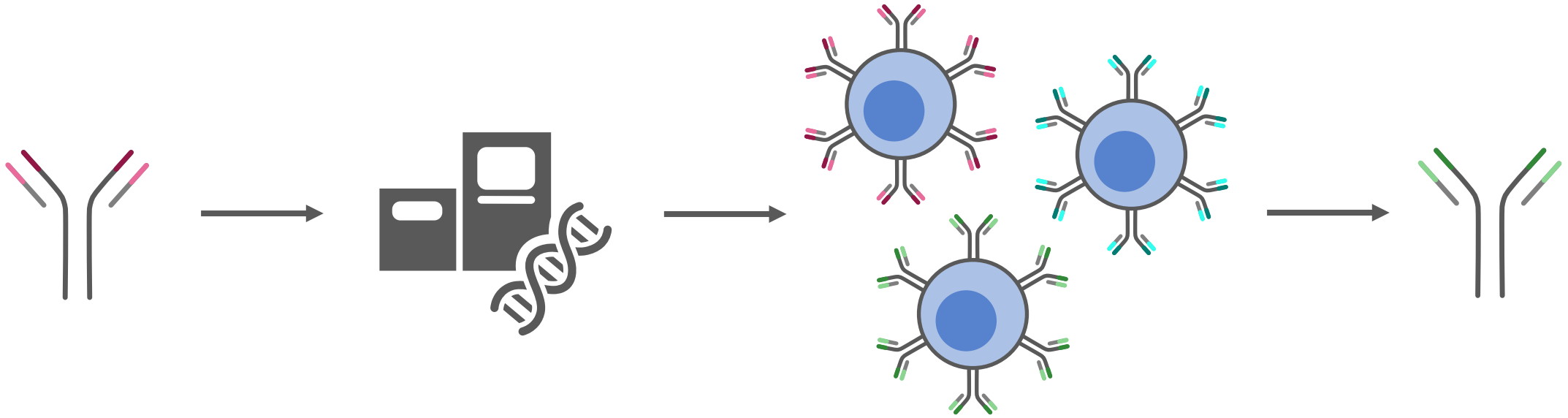
Accelerate Success: StableHu Antibody Optimization & Mammalian Display Screening Propel Faster, Cost-Effective Antibody Development

Input Antibody

StableHu AI-Engine

Mammalian Display

Output Antibody



Template CDR

Predict library of human CDR variants

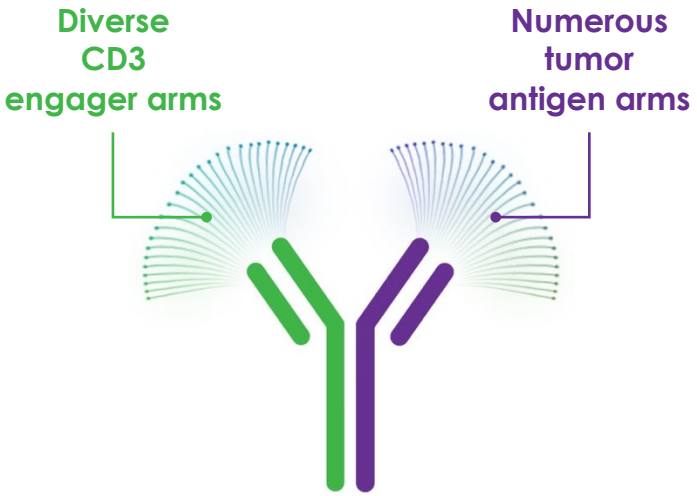
Single-cell screen mammalian display CDR library

Optimized antibody with fully human CDRs

EngageTx, a CD3-Based T-Cell Engager Panel, Addresses 3 Key Challenges: Cytokine Release, NHP Cross-Reactivity and Immunogenicity Risk

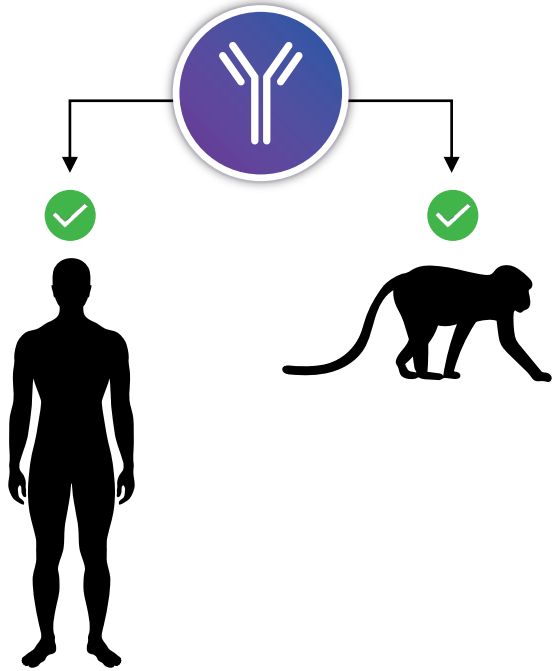
1 Sequence Diversity

Increased humanness and broad CD3 activity for optimized paring with tumor antigen arms



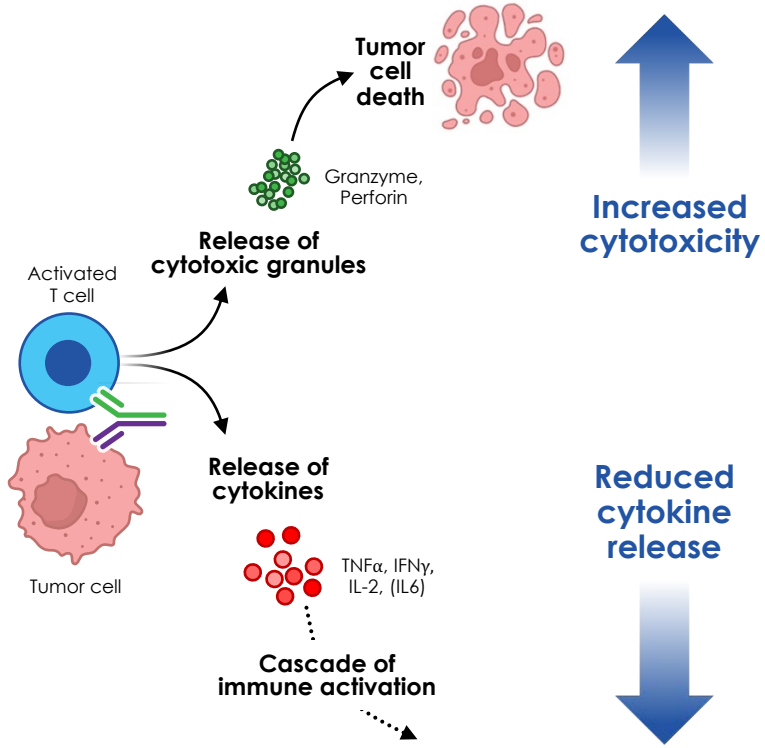
2 Hu-Cyno Cross-Reactivity

Risk reduction via cyno monkey toxicity study compatibility

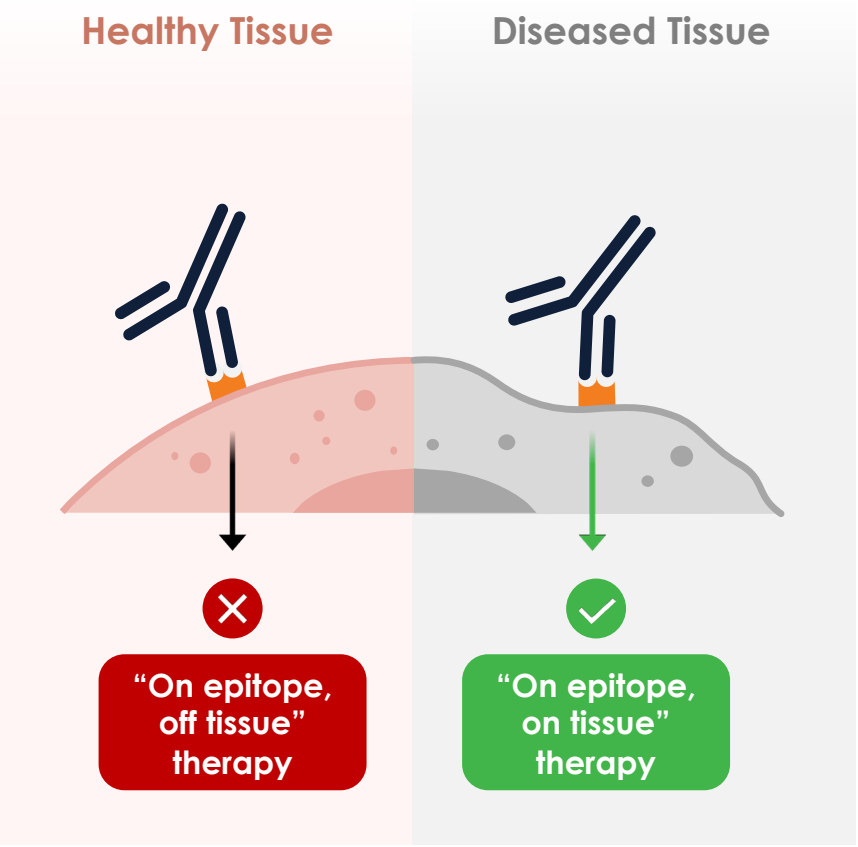


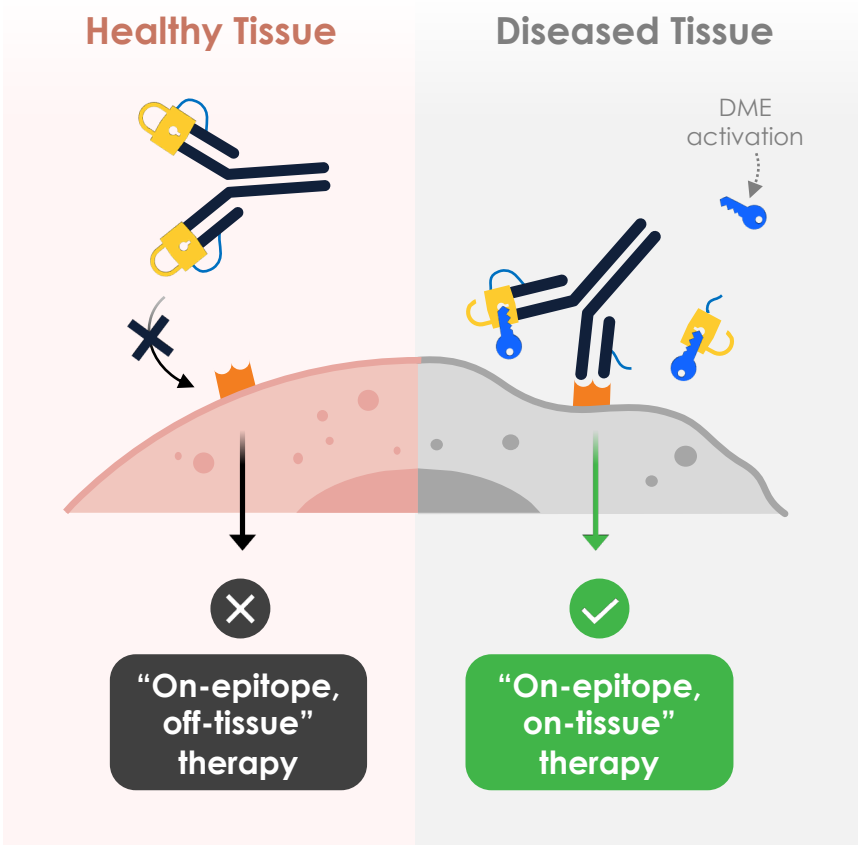
3 Range of Cytokine Release

Tailored cytokine release for expanded therapeutic window

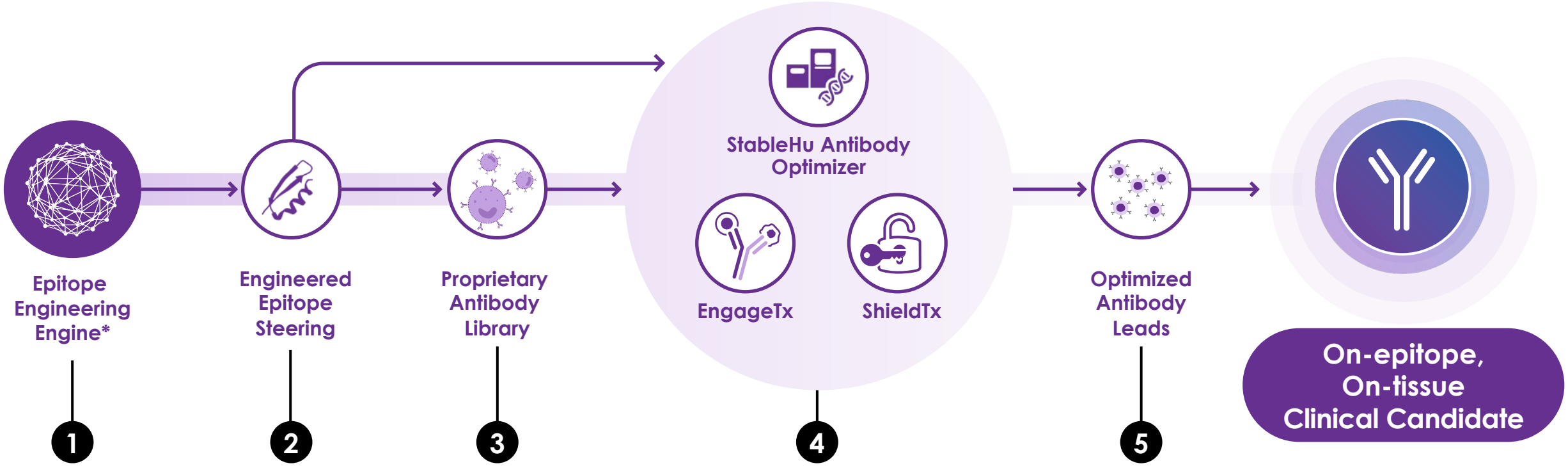


“Smart” Antibodies: ShieldTx Conditionally Activated Antibodies Strive to Improve Safety by Selectively Targeting Diseased but not Healthy Tissue





iBio's Platform Tackles Discovery Challenges for the Next Era of Antibodies



AI-powered engineering of **conformational epitopes**

Epitope-specific antigens that steer discovery to intended epitopes

Naïve human sequence antibody library, free of liabilities

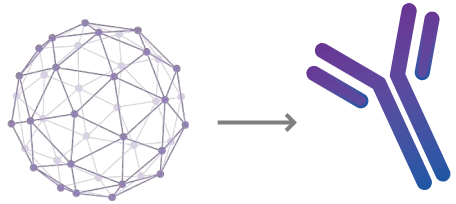
AI-powered mammalian-display co-optimization of mono/multi-specific antibody and conditionally activated mask

Evaluated & ranked in translational disease models

** U.S. Patent No. 11,545,238 (issued January 3, 2023)*

Capitalizing on AI: We Believe Our Platform Powers a Focused, Capital Efficient Business Plan

AI Discovery Platform



Strategic Partnerships

- Potential for short- and long-term milestone payments and/or royalties

Third Party Collaboration

- Potential for upfront technology access fee and milestones plus royalties for multiple targets

Proprietary Pipeline

- Advancing a select few "fast followers"
- Potential licensing and asset sales for other molecules

Partners and Collaborators Trusting in iBio's Ability to Solve Today's Drug Discovery Challenges

Strategic Partnerships

Partner existing molecules or discovery projects against new targets

Third Party Collaborations

Exclusive licensing for non-core therapeutic areas to 3rd parties (vaccines, etc.)

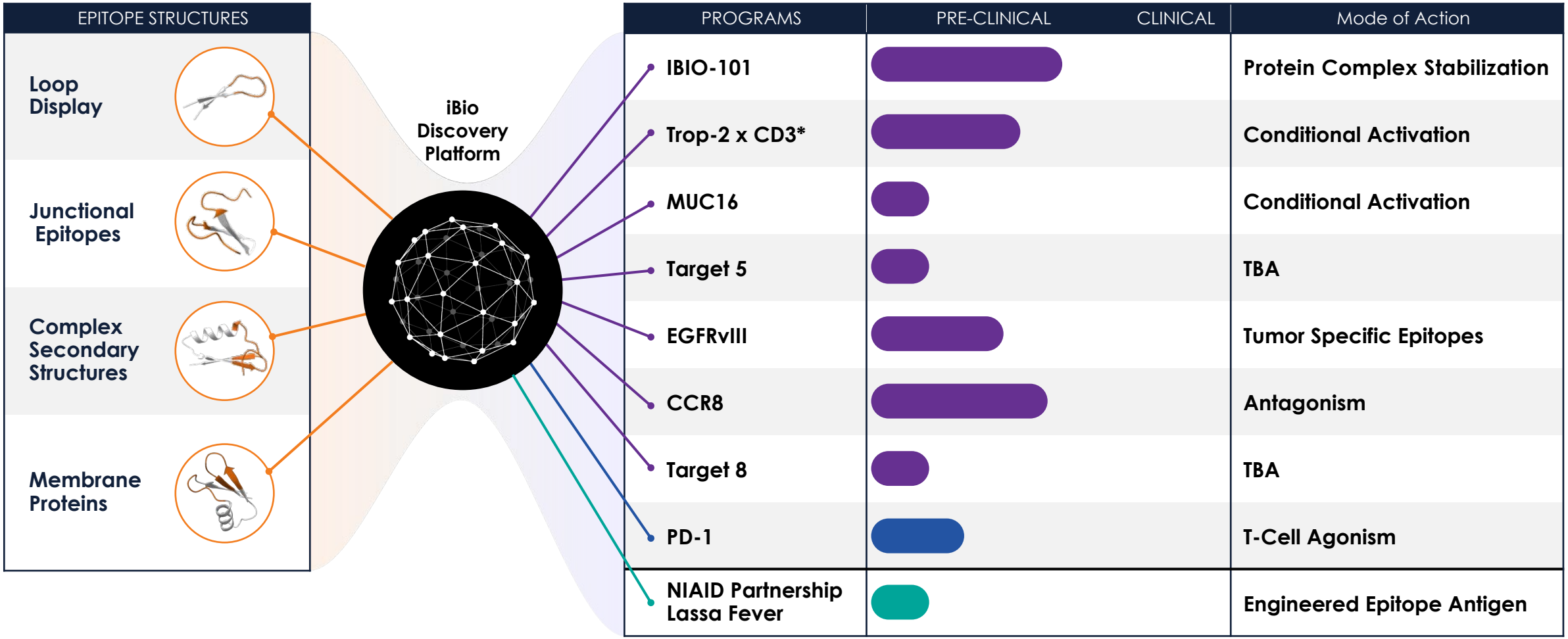
Collaborations

NIH

Eli Lilly

… and more

Catalyzing Innovation: Technology Stack Spurs Rapid Preclinical Pipeline Growth and Maturation



Oncology Autoimmune Vaccine

*Developed with Engage Tx bispecific platform

Market-Tested Potential: Competitor Early-Stage Deals Signal Promising Opportunities for Our Pipeline

Pre-2019

SEP 2018

IBIO-101 (CD25)

Roche / Tusk Therapeutics*:
$81M upfront,
$677M milestones

2020

SEP 2020

CCR8

Gilead / Jounce+:
$85M upfront,
$35M equity investment,
$685M milestones

JUL 2020

TROP-2

AstraZeneca / Daiichi+:
$1B upfront (some deferred),
$5B milestones

SEP 2020

TROP-2

Gilead / Immunomedics*:
Acquired for **$21B**

2021

FEB 2021

PD-1 agonist

Merck / Pandion*:
Acquired for **$1.85B**

JUN & DEC 2021

CCR8

Fibrogen / HiFiBio+:
$25M option fee,
$35M option exercise,
$1.1B milestones

JUL 2021

CD3

Eli Lilly / Merus+:
$40M upfront, **$20M** investment
$540M milestones

JUL 2021

CD3

Amgen / Teneobio*:
$900M upfront,
$1.6B milestones

DEC 2021

ShieldTx

Sanofi / Amunix*
Acquired for **$1B**, **$225M** milestones

2022

MAY 2022

EGFRvIII

Taiho / Cullinan Oncology+:
$275M upfront, **$130M** milestones

AUG 2022

PD-1 agonist

Gilead / Mirobio*:
Acquired for **$405M**

SEP 2022

EGFRvIII

Seagen / LAVA Therapeutics+:
$50M upfront, **$650M** milestones

OCT 2022

CD3

Gilead / MacroGenics+:
$60M upfront, **$1.7B** milestones

NOV 2022

ShieldTx

Regeneron / Cytomx+
$30M upfront, **$2B** milestones

2023

JAN 2023

CD3

GSK / WuXi Biologics+:
$40M upfront,
$1.46B milestones

JAN 2023

CCR8

Gilead / Jounce+:
$67M for remaining stake in CCR8 program

APR 2023

EGFRvIII

Pierre Fabre / Scorpion+:
$65M upfront,
$553M milestones

JUN 2023

CCR8

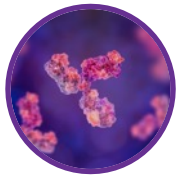
Coherus / Surface Oncology*:
Acquired for **$65M**

** Acquisition / Merger*
+ License or collaboration

iBio Company Highlights

AI-driven discovery tech stack

- Patented epitope-engineering technology
- StableHu antibody optimizer coupled with mammalian display
- EngageTx next generation bi-specific antibody platform
- ShieldTx antibody masking fully integrated in technology stack



Pipeline of difficult to find biologics

- Pipeline of 8 preclinical programs of hard to drug targets
- Targets in focus of major immuno-oncology (I/O) companies with significant deal flow
- Promising early CMC development data for lead asset IBIO-101

Layered Business Model

- Strategic partnerships
- Proprietary pipeline
- Exclusive platform licensing for specific disease areas outside of I/O

Financial

- Ticker: IBIO (NYSE-A); 3,655,036 shares outstanding as of 12/6/23*
- Reduced costs by ~68% post CDMO divestment from FY 23 Q1 to Q4
- Majority of debt secured by property for sale in Bryan, TX

- *Inclusive of pre-funded warrants and assuming no exercise of any common warrants issued in Dec 2023 offering.*

Technology Platform & Preclinical Pipeline

IBIO-101

IL-2 Sparing Anti-CD25

IBIO-101 for Regulatory T-Cell (T_{reg}) Depletion

Target Mechanism

Depletion of immunosuppressive T_{regs} via antibody dependent cellular cytotoxicity (ADCC), without disrupting activation of effector T-cells (T_{effs}) in the tumor microenvironment

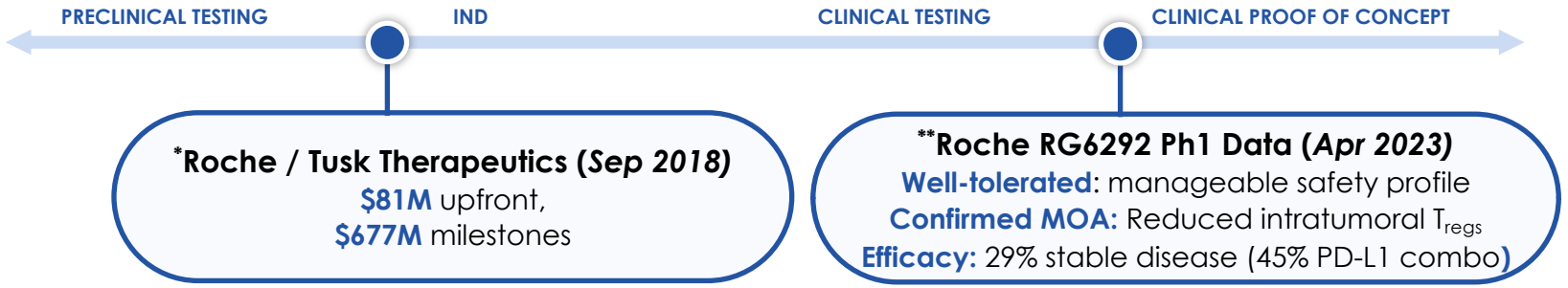
Potential Indications

- Solid tumors
- Hairy cell leukemia
- Relapsed mult. myeloma
- Lymphoma
- Head & neck cancer

Differentiation / Opportunity

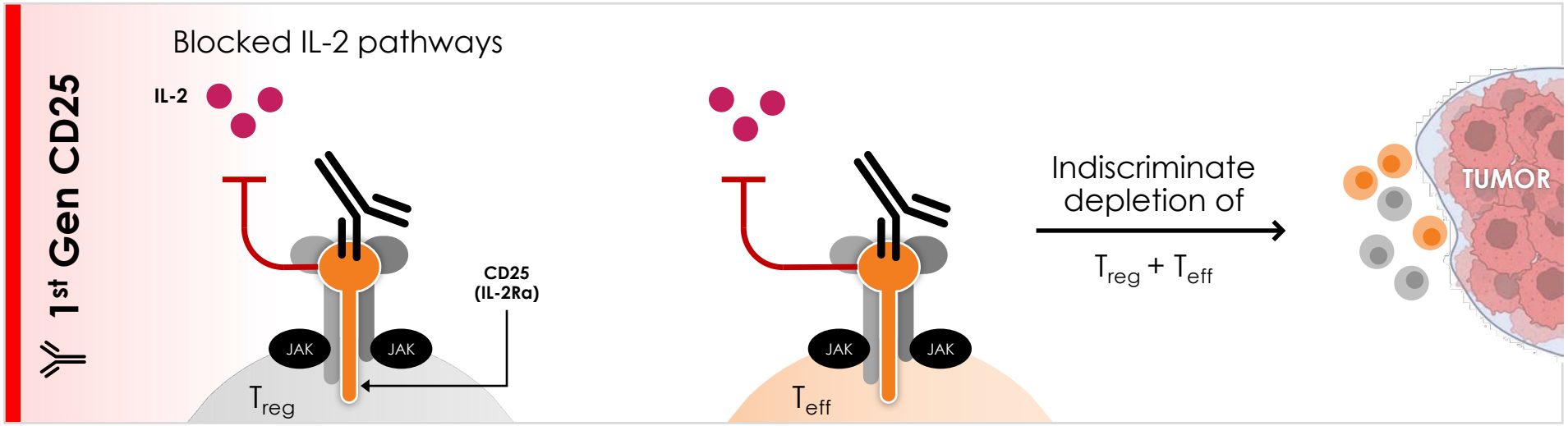
- IL-2 sparing anti-CD25 antibodies enables depletion of T_{regs} without affecting T_{effs}
- Fast-follower to Roche's RG6292 clinical molecule

Recent Transactions & Milestones



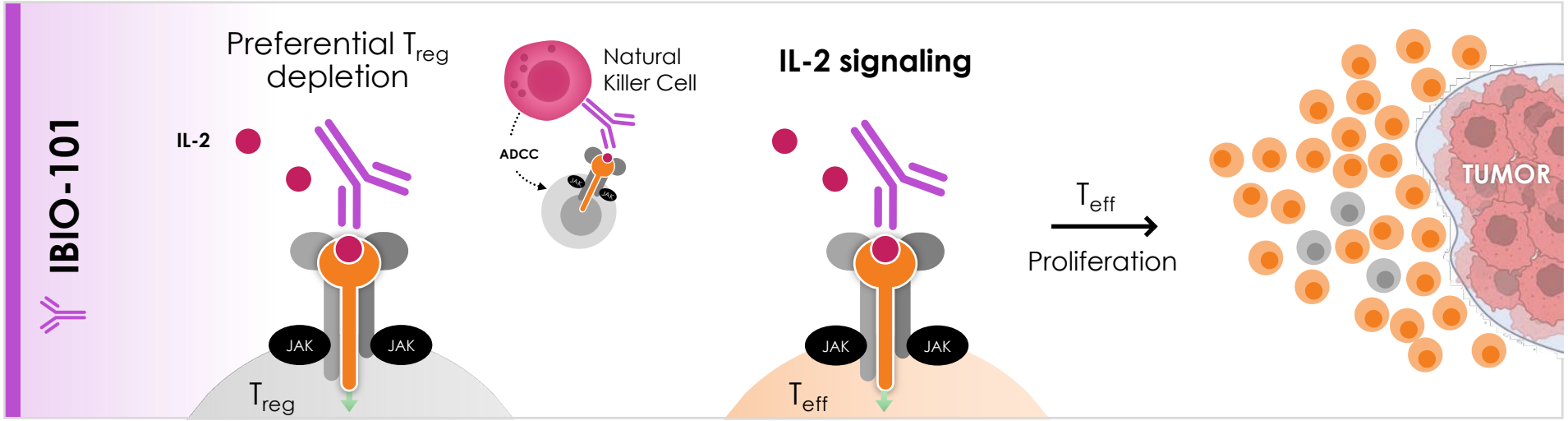
*Roche acquisition of Tusk Therapeutics completed for €70M upfront, acquiring worldwide rights to anti-CD25 program. Values converted to dollars as reported in public press releases
**Data presented by Roche at AACR 2023

IBIO-101 Reduces Tumor Growth in Preclinical Studies by Selectively Depleting Immunosuppressive T_{regs} without Affecting Cancer Killing T_{effs}



1st gen CD25 mAbs depleted immuno-suppressive T_{reg} and immuno-stimulatory T_{eff}

Limited efficacy

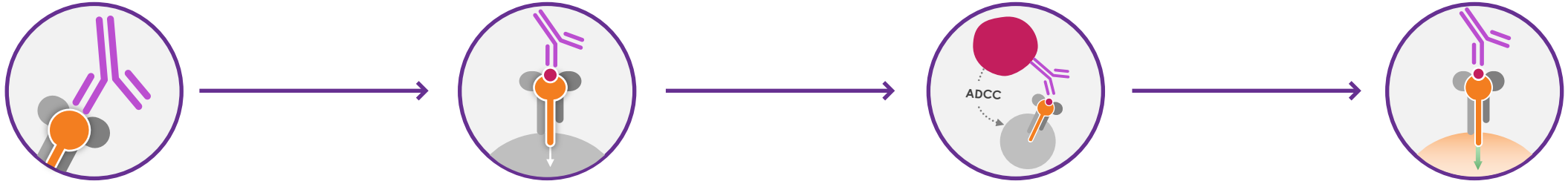


2nd gen IBIO-101 selectively targets T_{regs} without blocking IL-2 signaling to T_{effs}

Strong preclinical anti-tumor response

Data on file. Treg = Regulatory T Cells; Teff = Effector T Cells; ADCC = Antibody Dependent Cellular Cytotoxicity

IBIO-101 Selectively Depletes Tregs

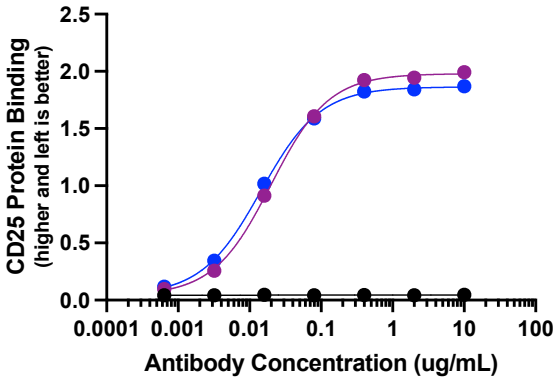


IBIO-101 potently binds recombinant CD25

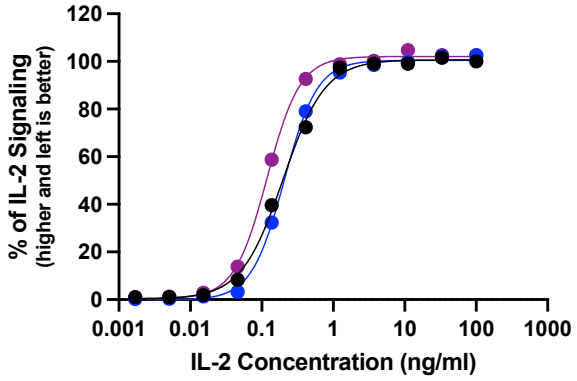
while preserving IL-2 signaling

which leads to T_{reg} depletion

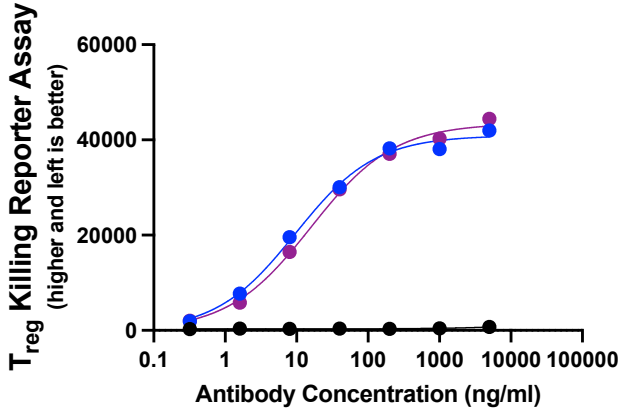
while sparing T_{effs}



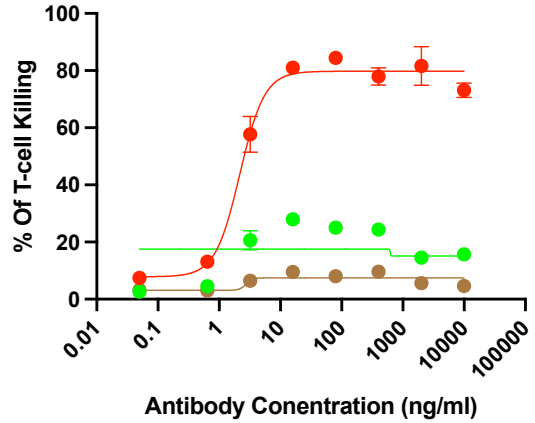
- Negative control, EC_{50} = no binding
- IBIO-101, EC_{50}= 16.4 ng/ml
- RG6292 (Roche), EC_{50}= 24.7 ng/ml



- IL2, EC_{50}= 0.11 ng/ml
- IBIO-101, EC_{50}= 0.17 ng/ml
- RG6292, EC_{50} = 0.14 ng/ml



- Negative control, EC_{50} = no cell killing
- IBIO-101, EC_{50}= 4.7 ng/ml
- RG6292, EC_{50} = 18.6 ng/ml

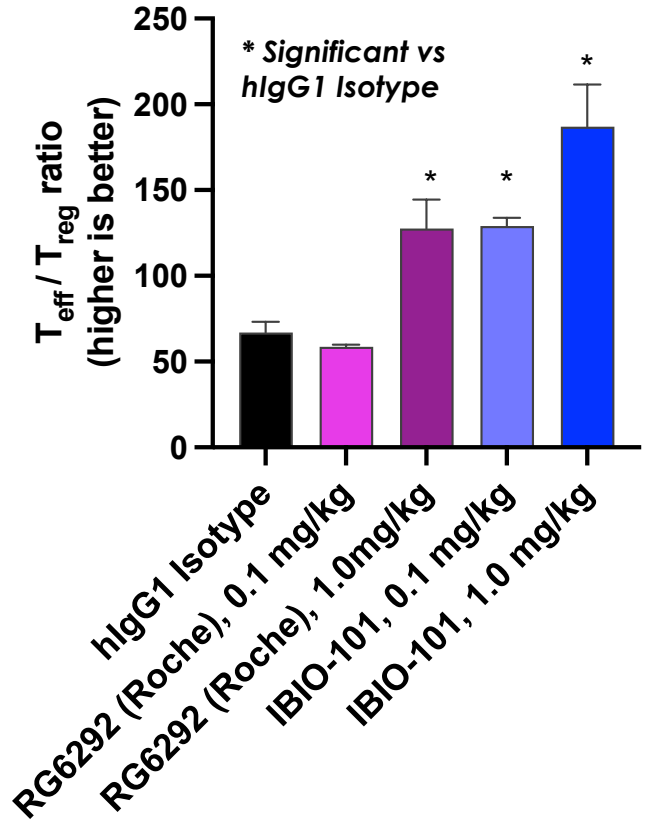


- T_{reg} killing, EC_{50}= 7.09 ng/ml
- Activated $CD4^+$ T_{eff} killing, EC_{50}= no activity
- Activated $CD8^+$ T_{eff} killing, EC_{50}= no activity

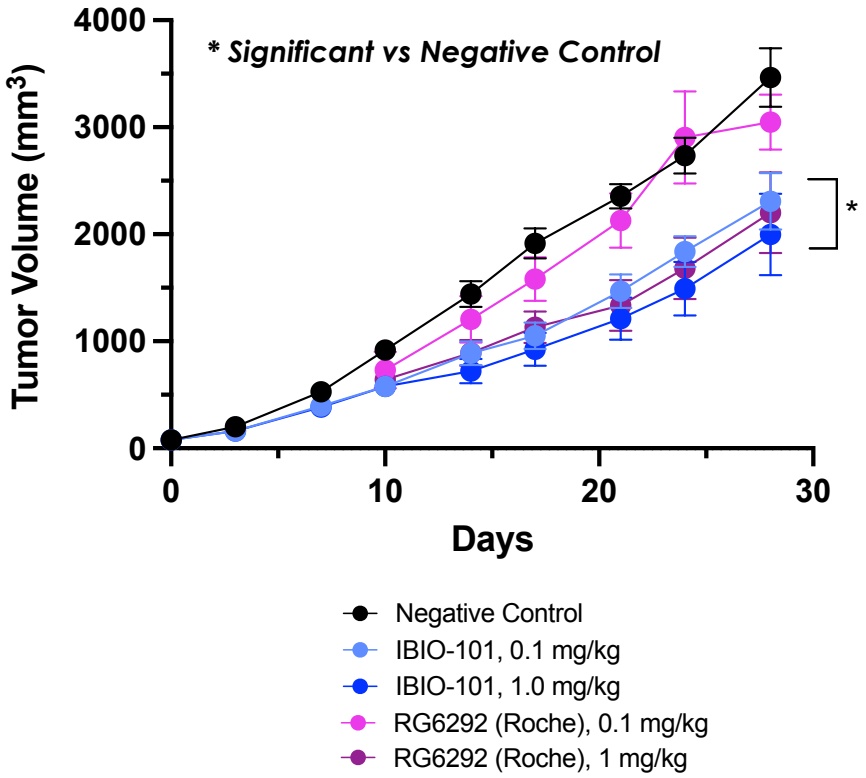
RG6292 is Roche's monoclonal antibody that targets CD25 (IL-2Ra). IBIO-101 data on file.

IBIO-101 Increases in T_{eff}/T_{reg} Ratio in Preclinical Studies Inhibiting Tumor Growth

Potently increases T-eff/T-reg ratio[1]



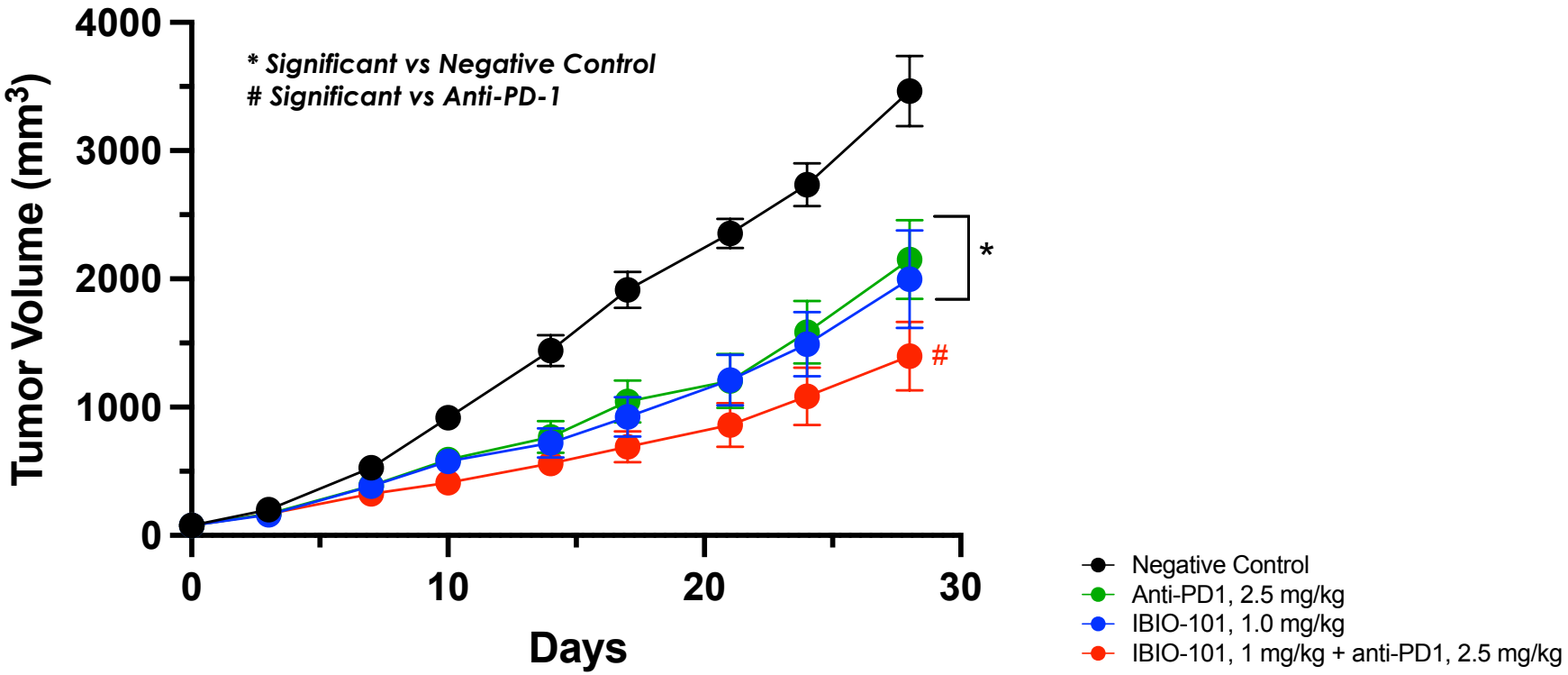
Tumor growth inhibition correlates with T-eff/T-reg ratio



[1]hCD25 animal model - Data on file.

IBIO-101 in Combination With a Checkpoint Inhibitor Shows Greater Efficacy

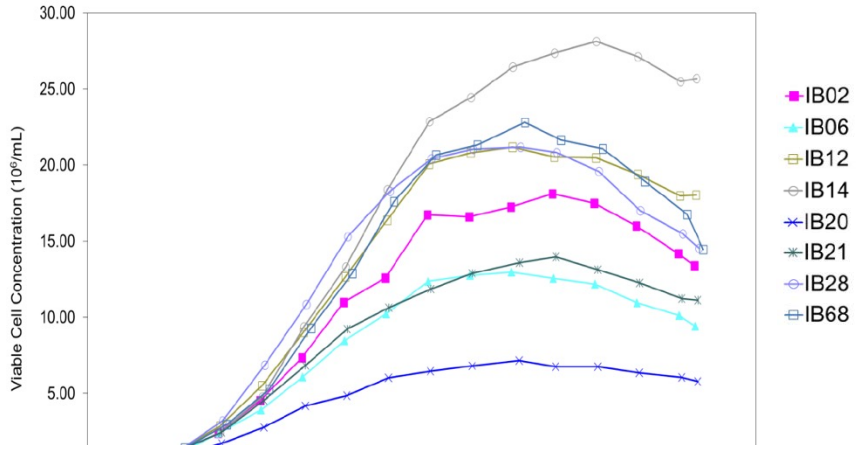
IBIO-101 + PD-1 Checkpoint Inhibitor In PreClinical Studies Enhances Tumor Suppression



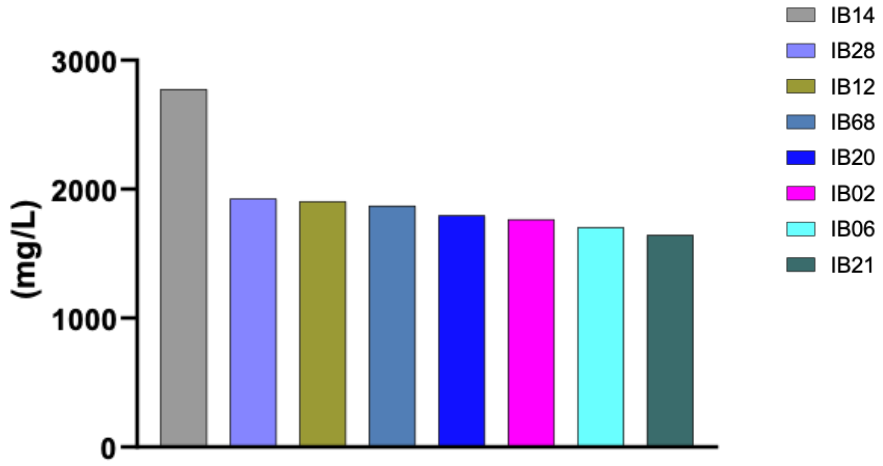
*hCD25 animal model - Data on file.

IBIO-101 is an Antibody With Favorable Characteristics for CMC Development

Potential for Master Cell Bank (MCB) Development From 8 Promising Cell Lines



Unoptimized Cell Lines Already Show Promising IBIO-101 Yields



- Identified manufacturing partner to produce IBIO-101 for Phase 1&2 clinical trials
- Discovered suitable cell lines for manufacturing MCB
- Established IBIO-101 CMC methodology for producing high yield, high purity, stable product under cGMP conditions

Anti-CCR8

High ADCC Anti-CCR8 for the Depletion of T-regulatory Cells

CCR8 for Tumor-Infiltrating T_{reg} Depletion

Target Mechanism

Tumor-infiltrating Tregs highly express CCR8. iBio program targets depletion of highly immunosuppressive CCR8+ Tregs in tumor microenvironment via an ADCC mechanism.

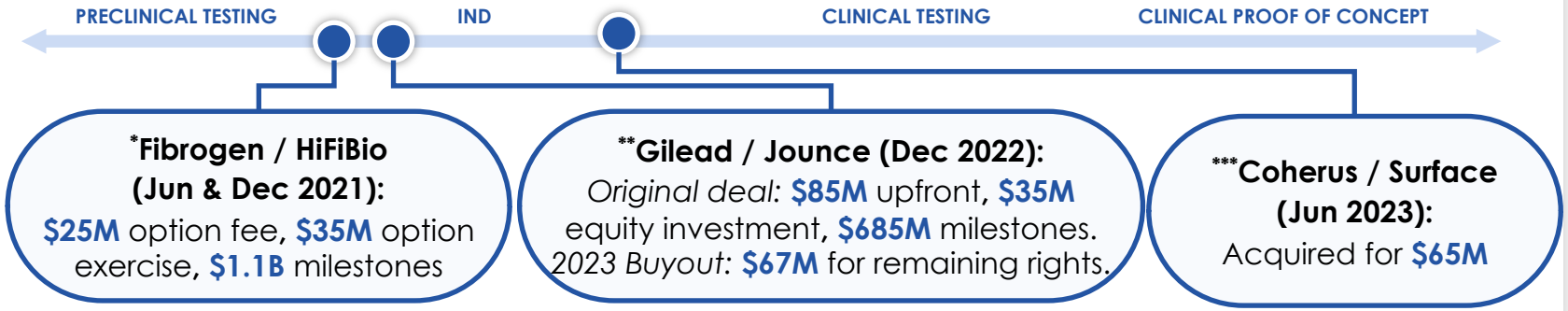
Potential Indications

- Broadly applicable in solid tumors
- Prospective combination therapy

Differentiation / Opportunity

- Selective binding to CCR8 over its close homolog, CCR4

Recent Transactions & Milestones

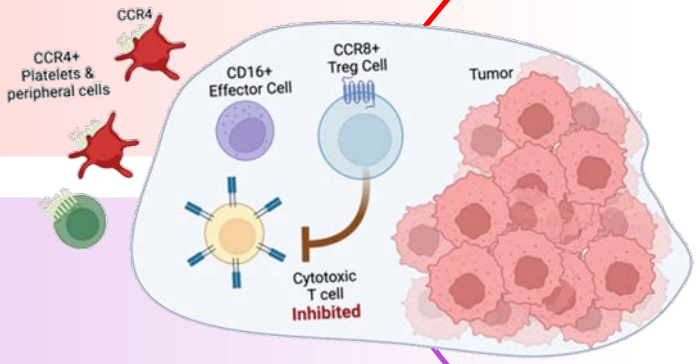


*Fibrogen / HiFiBio: Fibrogen purchased option to multiple programs in June 2021, then exercised the option for excl. license to CCR8 program in Dec. 2021.
**Gilead / Jounce: Exclusive worldwide license to anti-CCR8 antibody.
*** Coherus / Surface Oncology: acquisition, announced in June 2023, adds two clinical assets, including a phase 2 anti-IL-27 and a phase 1/2 anti-CCR8 for oncology.

CCR8+ T_{reg} Cells Are Tumor Infiltrating and Highly Immunosuppressive

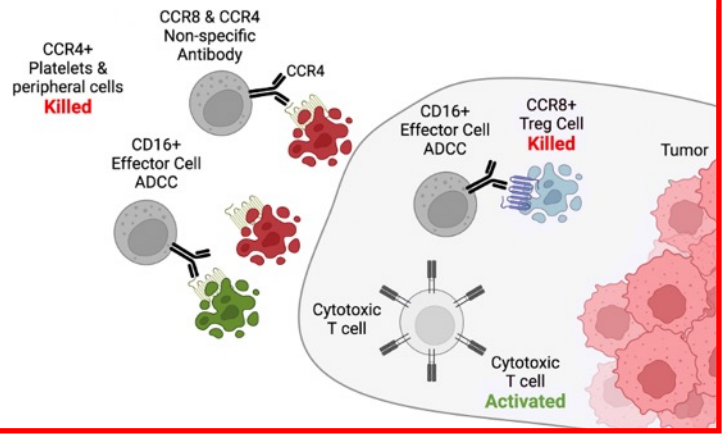
Depletion of CCR8+ Treg cells has potential to evoke potent tumor immunity

CCR8 & CCR4 nonspecific antibody

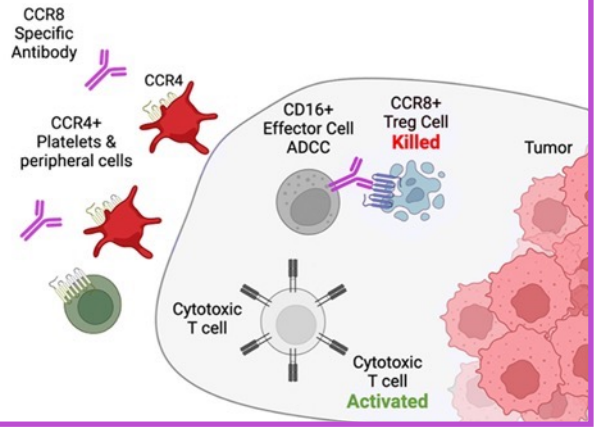


iBio CCR8 specific antibody

CCR4+ cells killed



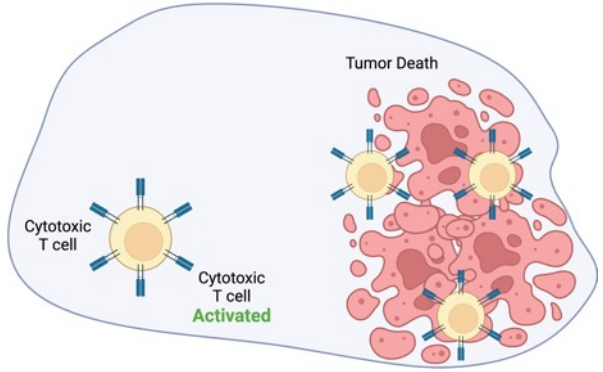
CCR4+ cells spared



Adverse events

- Systemic inflammation
- Skin toxicity
- Platelet depletion/aggregation

Intratumor cytotoxic T-cell activation & tumor death

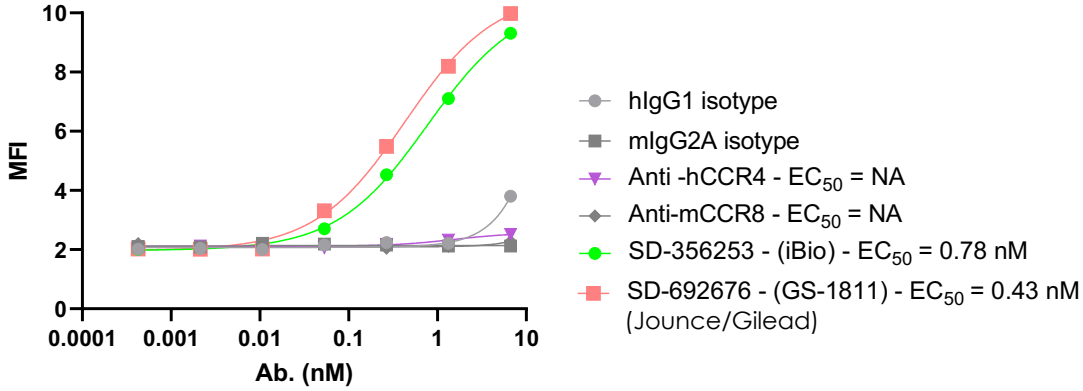


Zheng, et al. Cell 169.7 (2017): 1342-1356; Whiteside, et al. Immunology 163(4) (2021): 512-520; Kidani, et al. PNAS 119(7) (2022): e2114282119

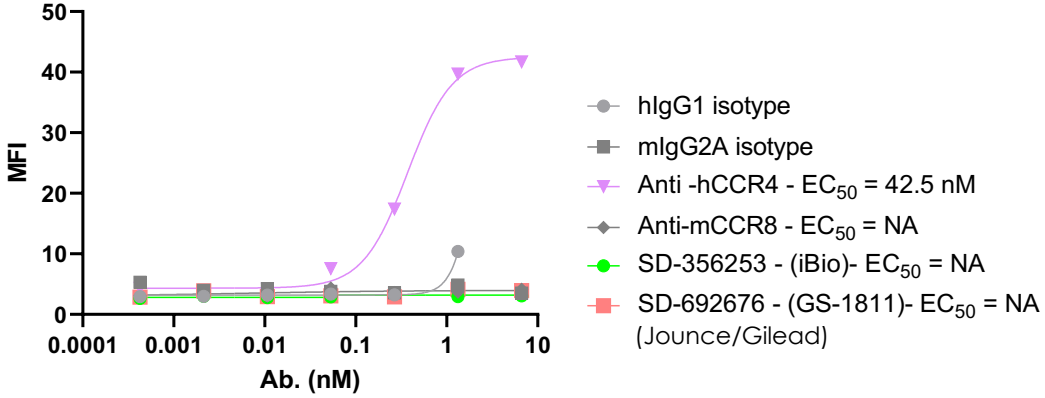
Afucosylated Anti-CCR8 Antibody Exhibits High Specificity, CCL1 Antagonism and CCR8-Specific Cell Killing

High Specificity CCR8 Cell Binding

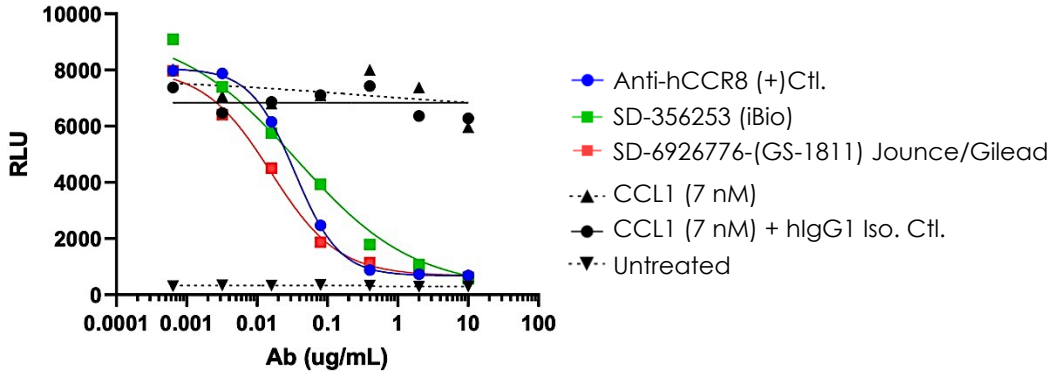
Potent binding to CCR8 overexpressing cells



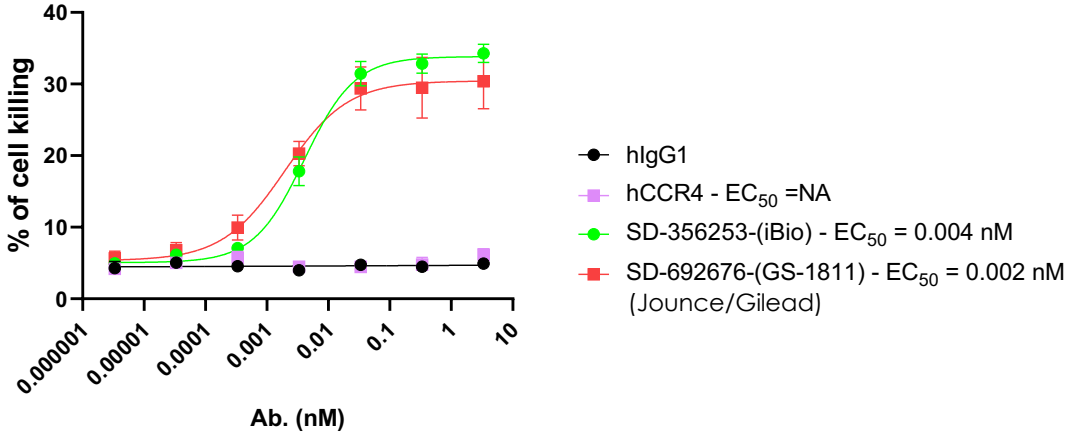
No binding to CCR4 overexpressing cells



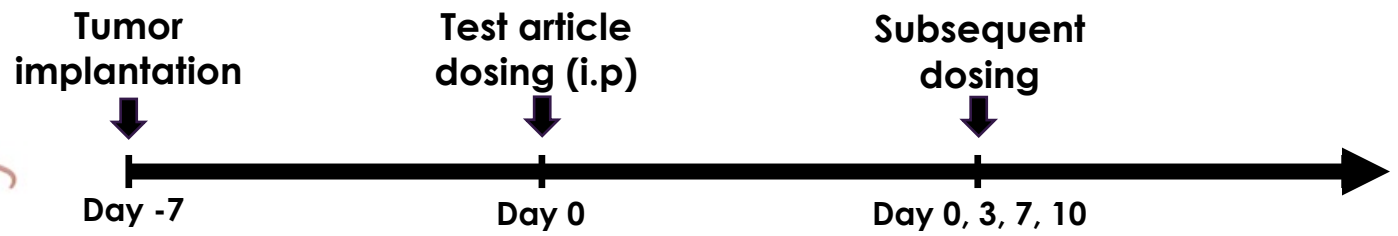
CCR8-CCL1 Antagonism

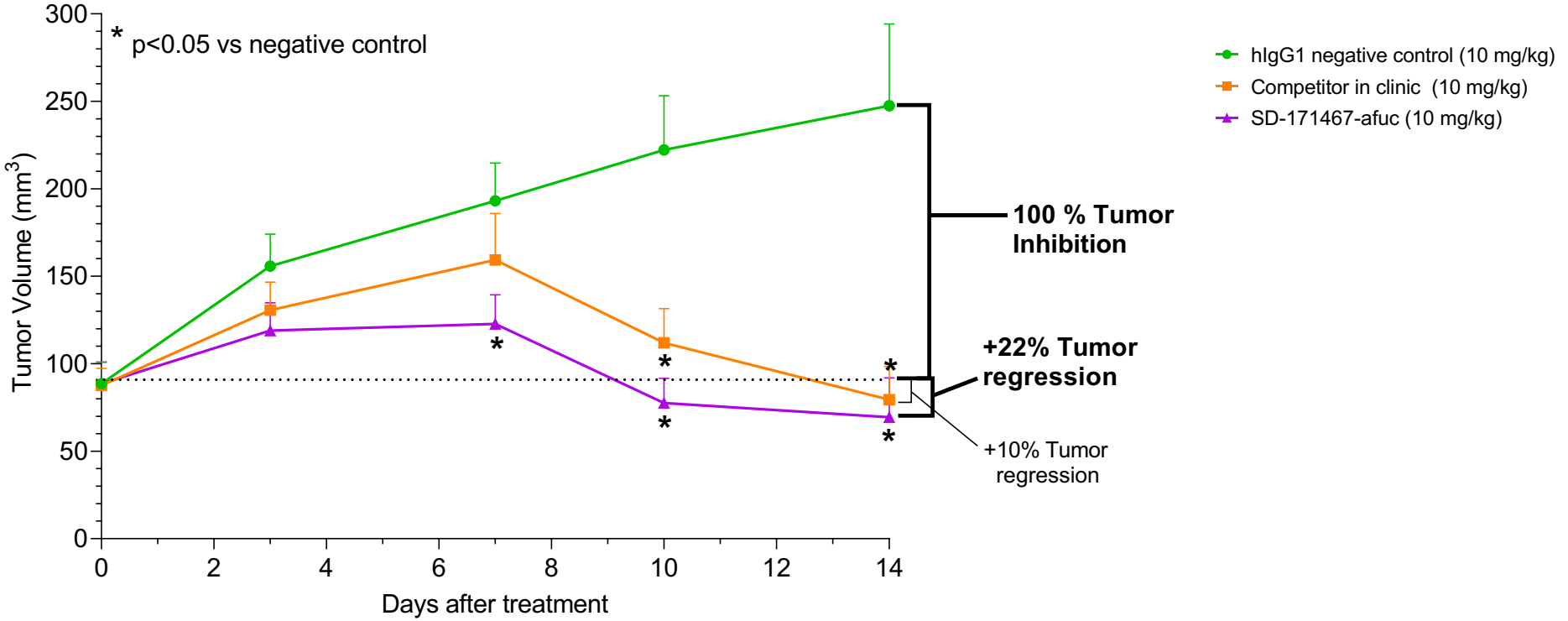


PBMC-Induced CCR8 Cell Killing



iBio's CCR8-Specific High ADCC Antibody Induces Tumor Regression in a Transgenic Human CCR8 Mouse Model





Unlocking the Power of Bi-Specific Antibodies with EngageTx, Our Versatile CD3 mAb Panel

Wide Range of Affinities, NHP Cross Reactivity, High Developability

Next Generation Anti-CD3 T Cell Engagers

Target Mechanism

T-cell-redirecting bispecific antibodies are a new therapeutic class that simultaneously targets CD3 on T cells and tumor antigens, inducing T cell mediated tumor cell killing

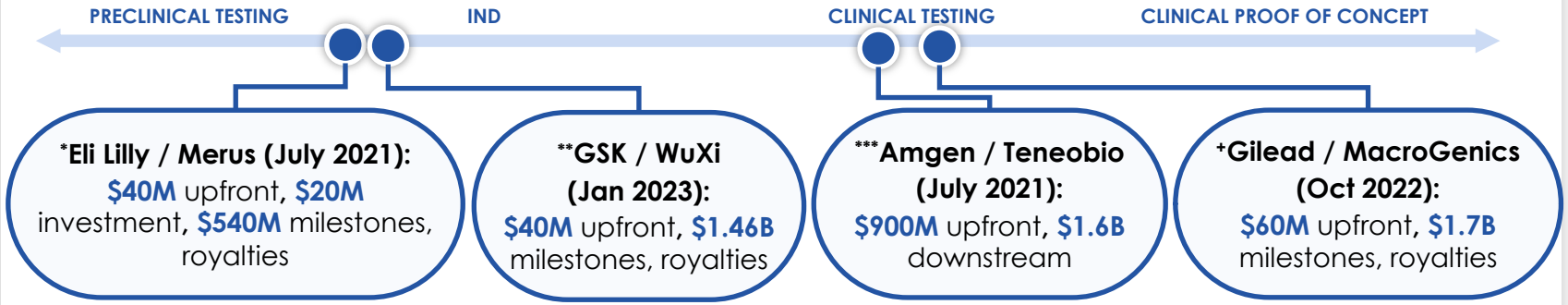
Potential Indications

- Broad solid tumor potential
- Expands therapeutic options across programs

Differentiation / Opportunity

- Range of T cell activation for diverse tumor antigens
- Cyno-tox study compatibility
- StableHu optimized sequence reduces downstream risks

Recent Transactions & Milestones



*Eli Lilly / Merus: Fibrogen Research collaboration using Merus' proprietary platform to develop up to three CD3-engaging T-cell re-directing bispecific antibody therapies.
** GSK WuXi: License of WuXi's preclinical CD3 bi-specific, plus 3 earlier stage programs
***Amgen / Teneobio: Teneobio was developing a heavy-chain only platform as well as its CD3 engager technology. TNB-585, the lead program, was in phase 1.
+ Gilead / MacroGenics: Gilead granted option to MGD024, a phase 1 CD3 bi-specific, plus collaboration on two additional research programs.

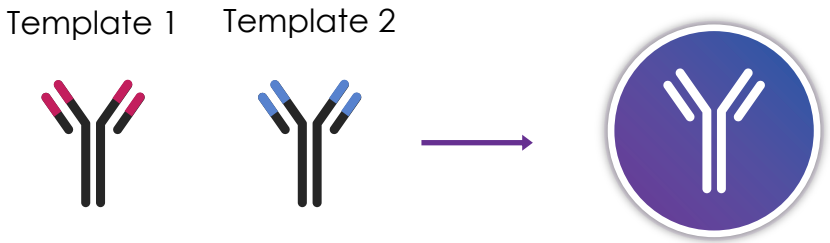
Dual Approaches to a Diverse Panel of Anti-CD3 Antibodies

AI Discovery Engine

Structural-Epitope Immunization & Screening

AI-Engineered Immunogens → Epitope & T Cell Immunization → Epitope & CD3 Screen

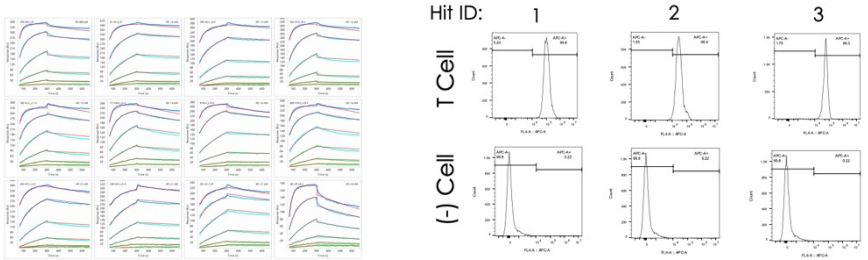
StableHu Optimizer



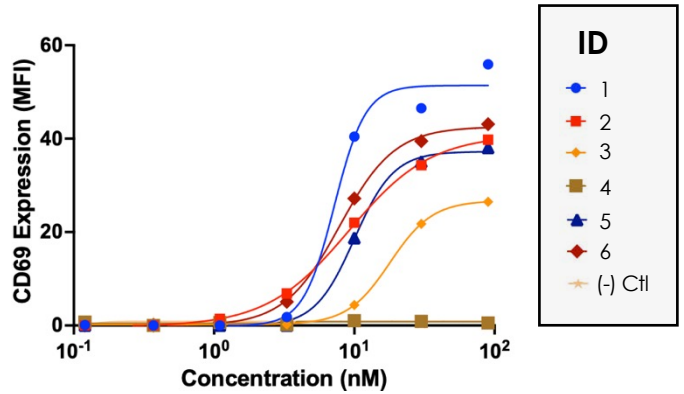
2 Template Antibodies → Optimized Antibodies

SCREEN

Hu/Cyno CD3 & T Cell Binding



T Cell Activation

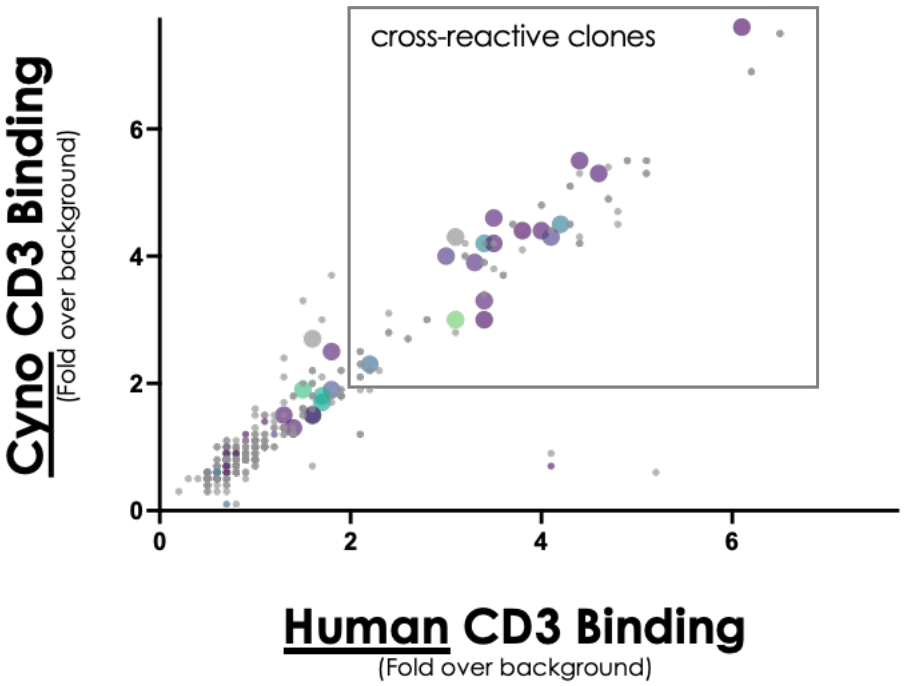


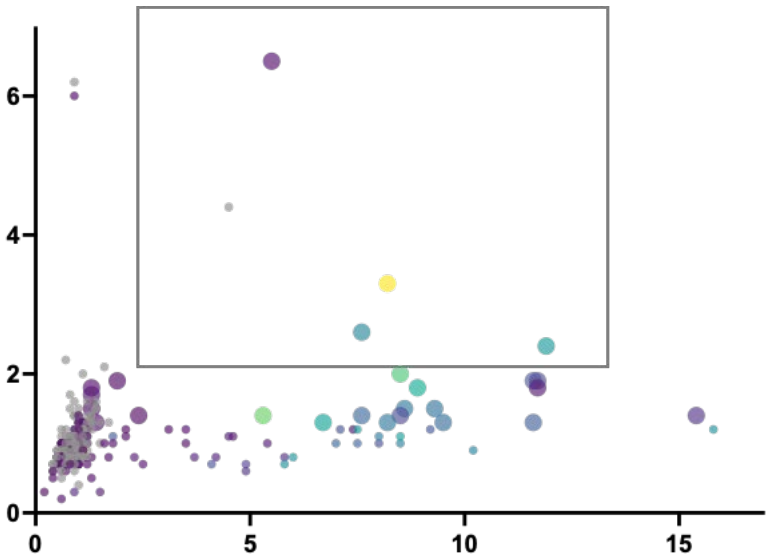
Libraries and Screens Discover Hu-Cyno CD3 Cross-Reactive Antibodies

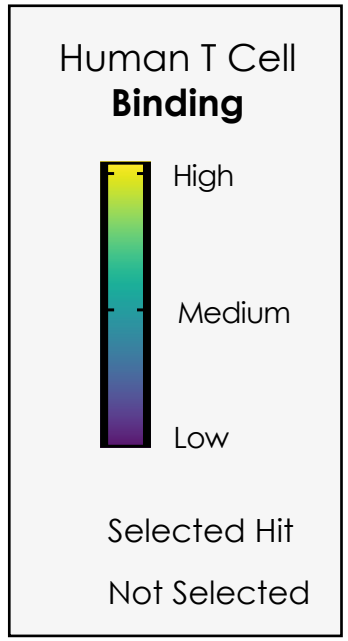
Library Screen:

StableHu **Mammalian-Display**

Epitope-Steered **Immunization**



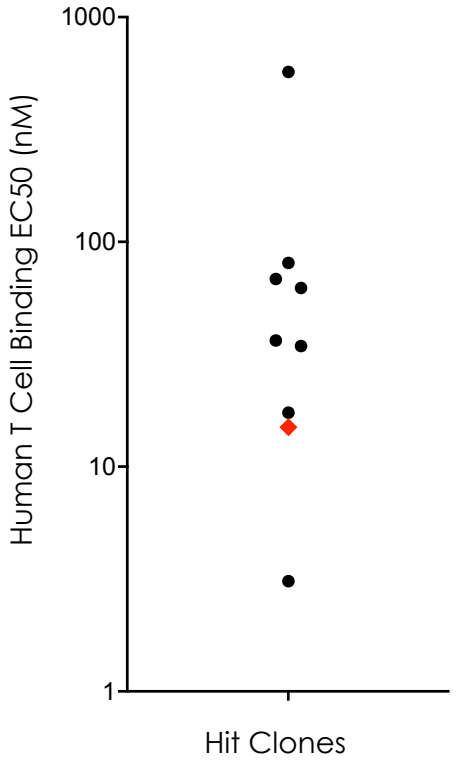




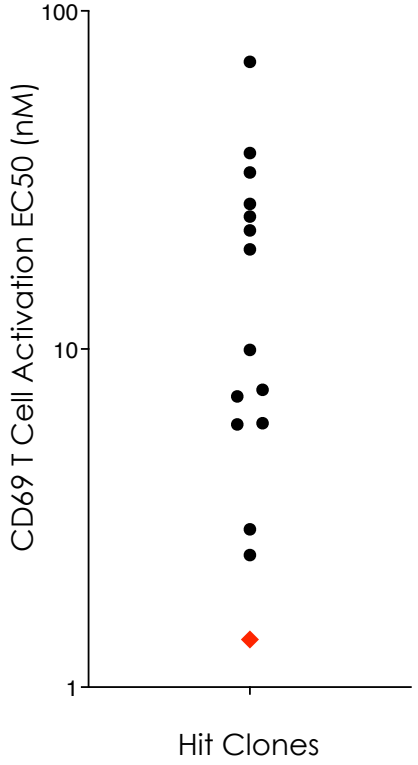
EngageTx is Selected for a Diversity of T Cell Binding and Activation

T Cell Assay: **Binding** **Activation** **Cytokines**

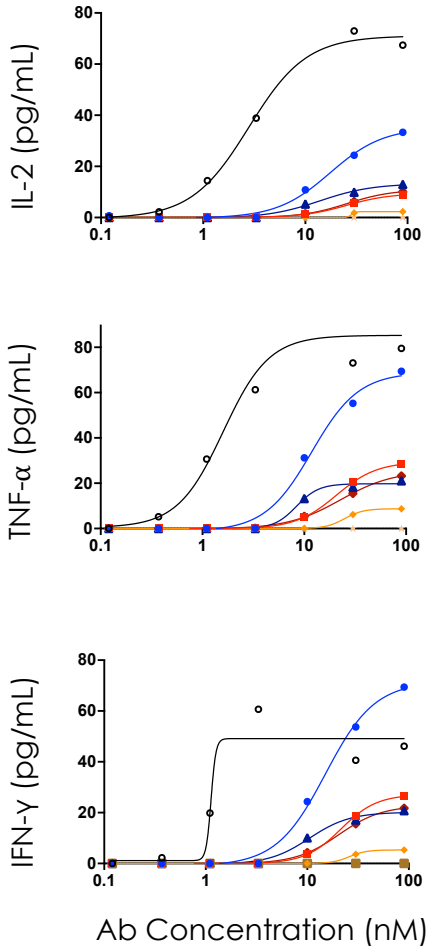
EC50: 3 – 570 nM



EC50: 2.5 – 70 nM



SP34 Gen 1 benchmark



ShieldTx

Antibody masking technology for delivering on-epitope, on-tissue clinical candidates with enhanced safety and developability

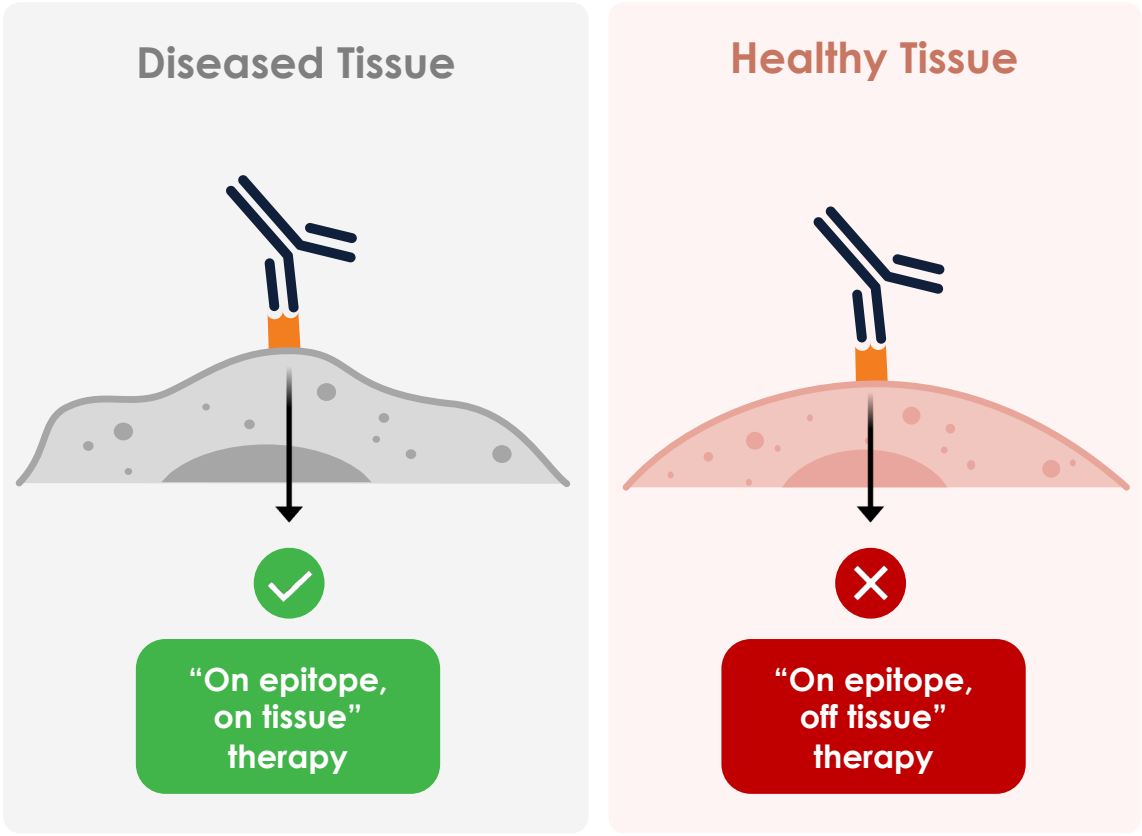
On-Target-Off-Tissue Side Effects Severely Limit The Potential of Existing And Future Antibodies

"(…) targeting antibody delivery to selected organs and tissues (…) represents a major unmet challenge that if ultimately solved may rewrite medical textbooks" - Paul J. Carter and Arvind Rajpal, Cell, 2022.

Even exquisitely specific antibodies fail in clinical trials by doing exactly what they are asked to do – hit the target. The problem often lies in the target being also expressed on *healthy* tissue.

Many potential targets remain unexplored as a drug target for fear of on-epitope off-tissue side effects.

The challenge: how do we achieve disease tissue specificity while avoiding healthy tissue expressing the same epitope?

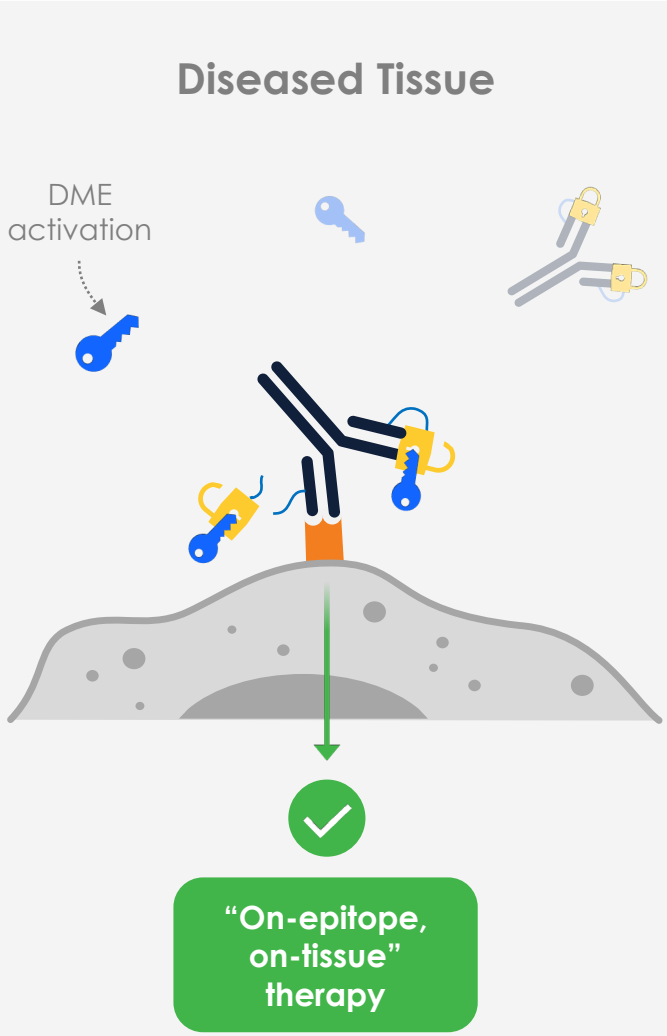


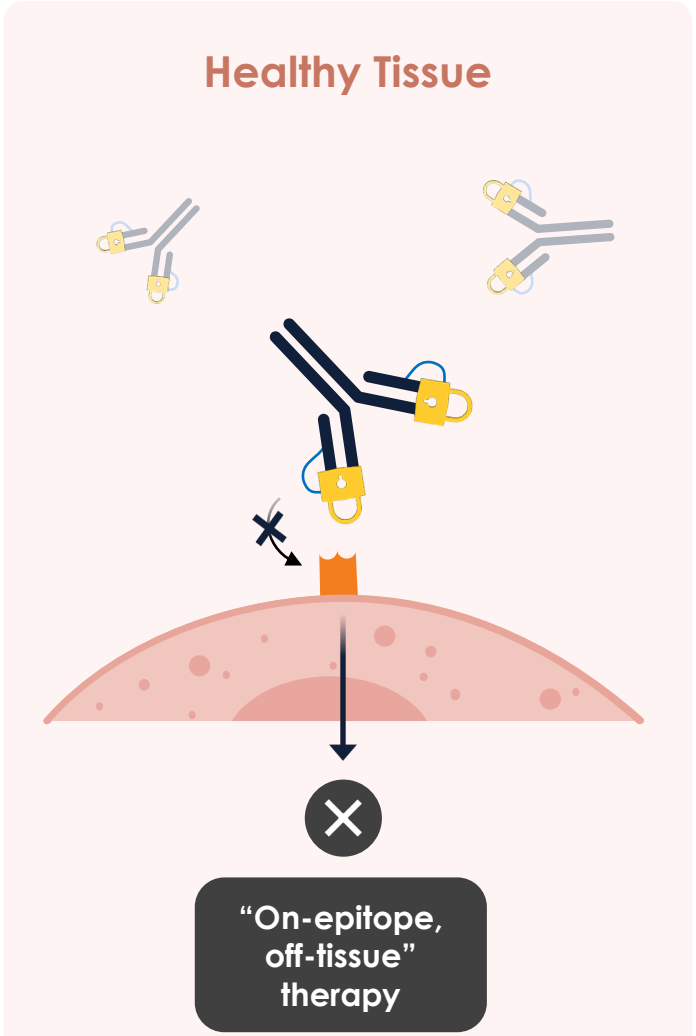
Our Engineered Epitopes Provide an Integrated Solution for Identifying And Subsequently Masking Antibodies

Antibodies are activated by the removal of the mask in the diseased tissue.

Masks can be removed by tumor-specific enzymes, pH, redox state, and disease-specific metabolites.

The technology can be employed for other indications i.e. inflammatory and auto-immune diseases.





Antibodies remain inactive in healthy tissue

DME: Disease Micro Environment

Masked Antibodies are a Proven Concept and iBio's Platform has the Potential to Solve Key Remaining Challenges

		THE PROBLEM	OUR SOLUTION
1	**Discovery process**	*Separate* antibody and mask discovery process is inefficient	*Co-discovery* of epitope-steered antibody and mask is more efficient
2	**Masking performance**	Separate discovery processes does *not co-evolve* an optimal antibody, mask, linker combination	*Co-evolution* of libraries of antibody, mask and linker for maximizes effectiveness of masking and unmasking
3	**Developability**	Antibody + mask + linker combinations *not screened* for high developability in production cell lines	Mammalian-display libraries of antibody, mask and linker combinations *screened for developability* in production CHO cell lines
4	**Immunogenicity**	*Random* peptide or anti-idiotype masks increase masked antibody immunogenicity risk	*Engineered epitope masks* are designed with intention to maximize the natural sequence of the epitope and minimize immunogenicity

Conditionally Activated Anti-MUC16 x CD3 Bispecific Antibodies Targeting the Non-Shed MUC16 Region

Leveraging iBio's Epitope Steering, ShieldTx, and EngageTx Technologies

MUC16 Potentially for Ovarian and Other Cancers

Target Mechanism

Bind a membrane-proximal MUC16 epitope

Membrane-proximal binding avoids epitope elimination by tumors

Bind a non-glycosylated epitope to avoid altered glycosylation on tumors

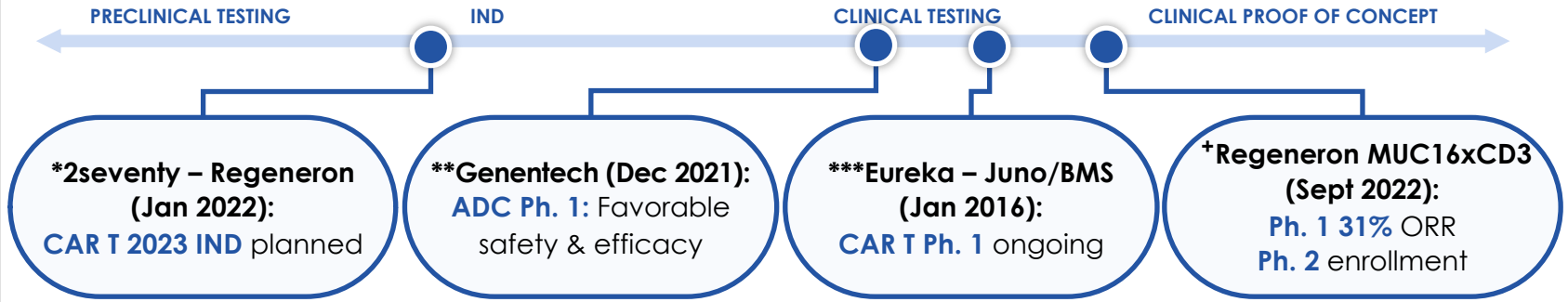
Potential Indications

- Ovarian
- Uterine
- Pancreatic

Differentiation / Opportunity

- MUC16 epitope avoids primary modes of tumor evasion
- Enabling modalities: T Cell engager, ADC, CAR-T

Recent Transactions & Milestones



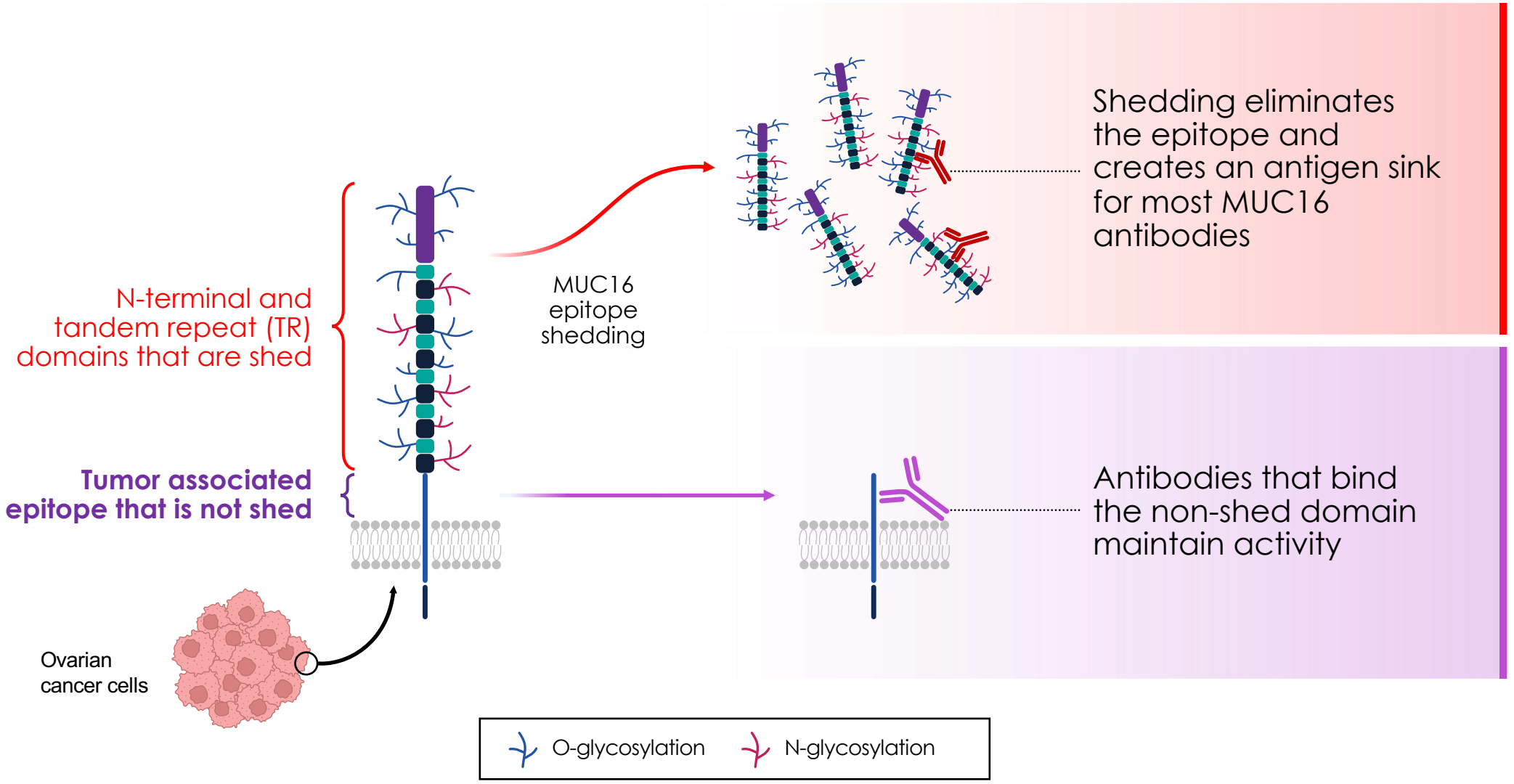
*Regeneron, 2seventy name the target of their first solid tumor CAR-T, aim for 2023 IND

** Liu et al., An open-label phase I dose-escalation study of the safety and pharmacokinetics of DMUC4064A in patients with platinum-resistant ovarian cancer

***Eureka Therapeutics Announces Exclusive License Agreement between Memorial Sloan Kettering Cancer Center and Juno Therapeutics for Use of a Novel, Fully-Human MUC16 Binder in CAR T Cell Immunotherapy

+Novel Regeneron Bispecific Antibodies Show Encouraging Anti-Tumor Activity in Two Advanced Solid Tumors

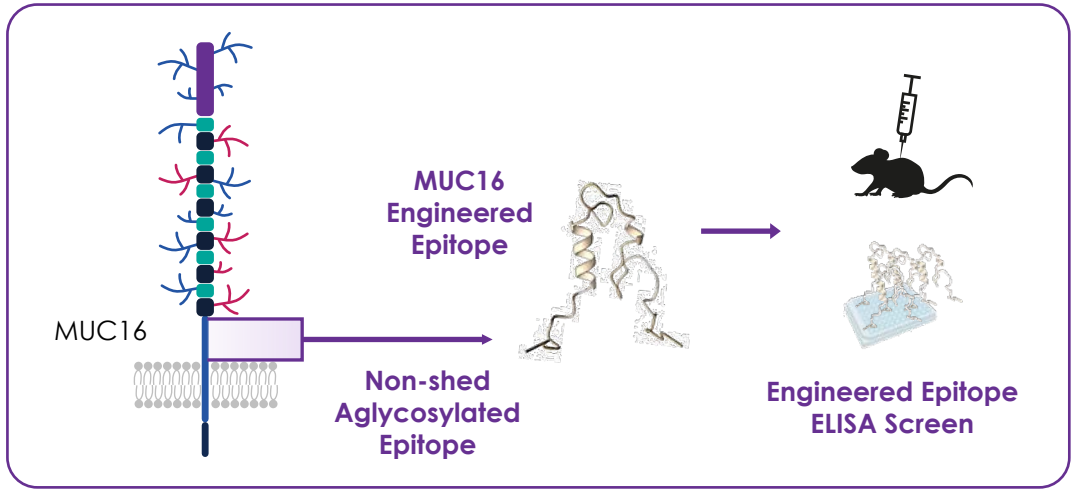
MUC16 Is Overexpressed and Shed by Tumor Cells



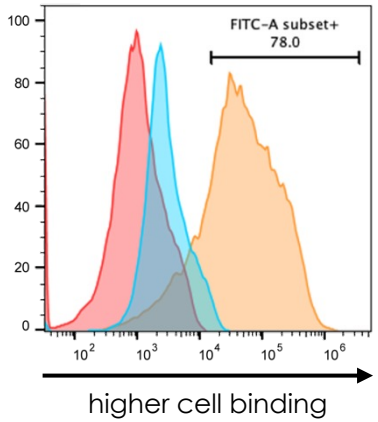
Immunizations Were Steered to a MUC16 Epitope that Avoids Epitope Shedding

AI Discovery Engine

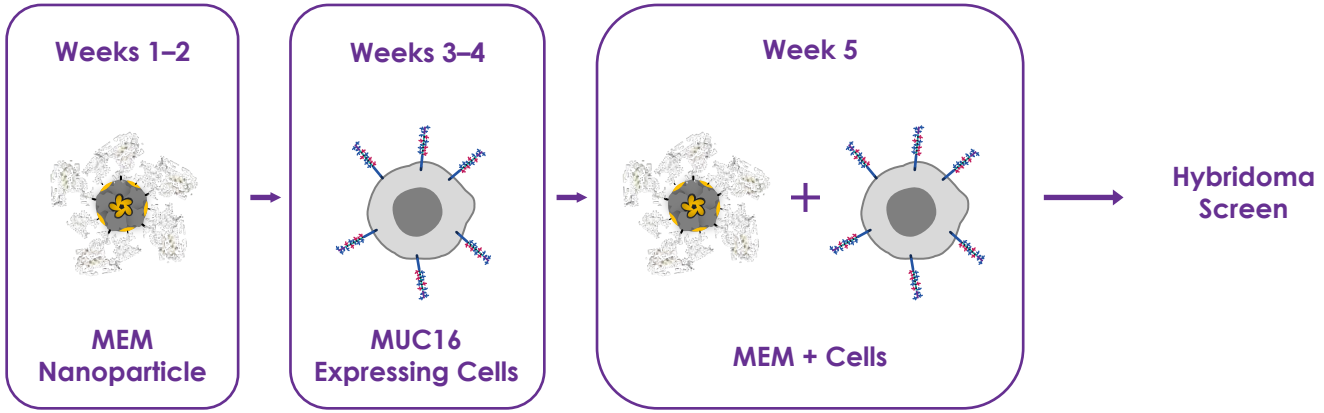
Structural-epitope Immunization & Screening



OVCAR-3 MUC16$_{high}$ Cell Binding Screen

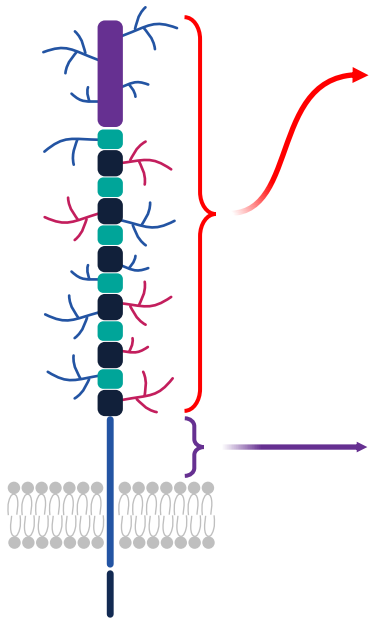


Engineered Epitope Prime + MUC16 Cell Boost



Top Three Hit Clones Bind the Non-Glycosylated MUC16 Epitope Closest to the Membrane

N-terminal and tandem repeat (TR) domains that are shed



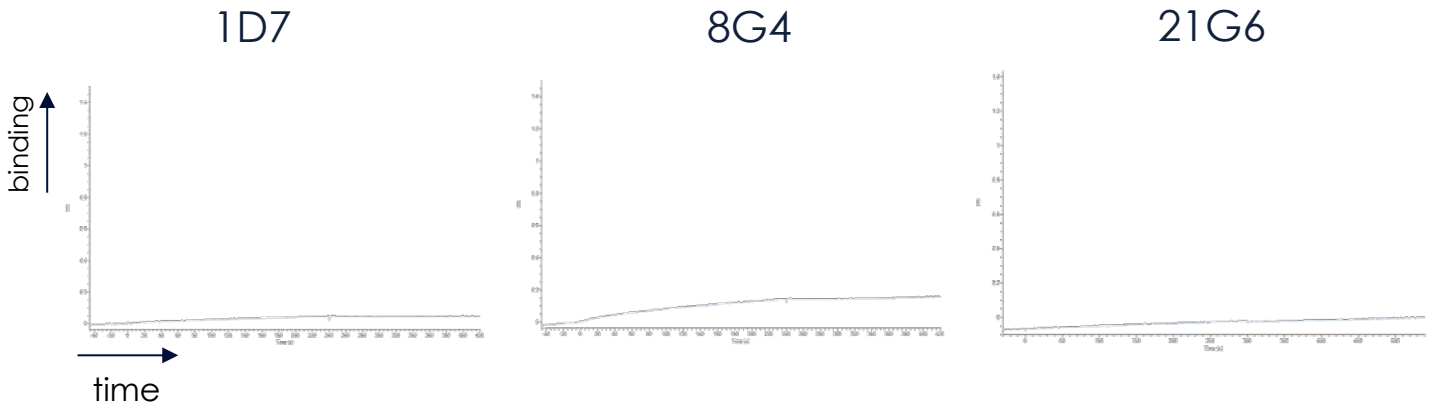
Epitope

Shed 230-mer

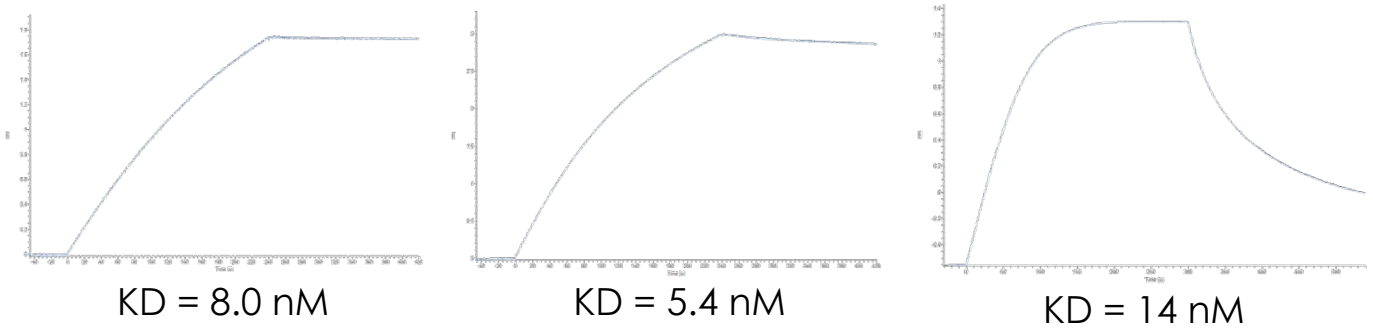
Aglycosylated non-shed 29-mer

O-glycosylation N-glycosylation

Hits do not bind shed 230-mer



Hits bind non-glycosylated non-shed 29-mer



KD = 8.0 nM KD = 5.4 nM KD = 14 nM

Top MUC16 Clone 8G4 Binds OVCAR-3 Cells Comparable to Regeneron Benchmark

Clone ID:

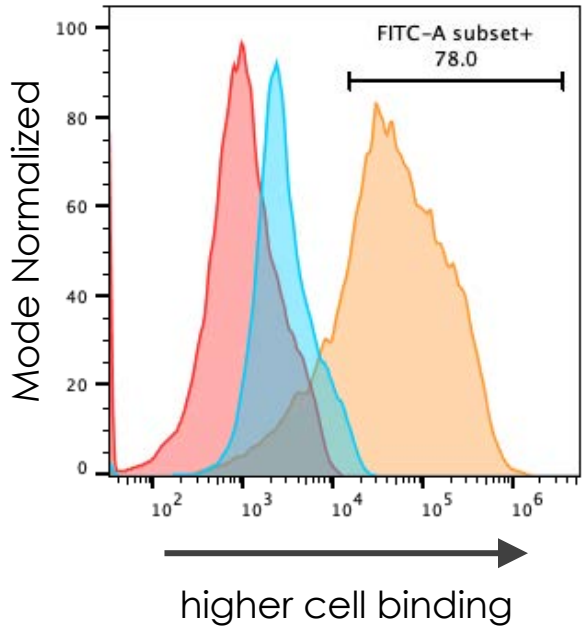
8G4
top clone

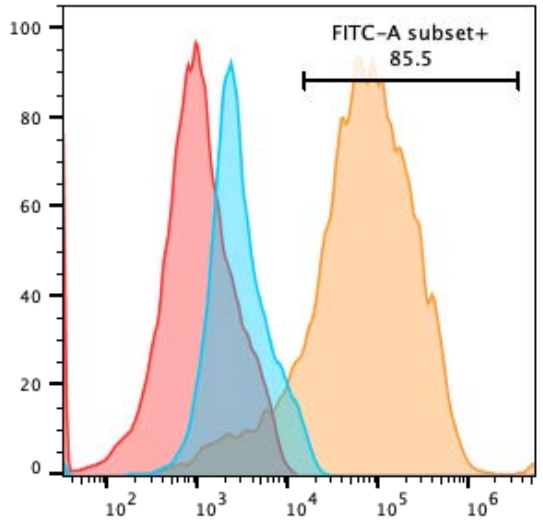
Regeneron
benchmark

Unstained

Secondary Only

OVCAR-3 Cells

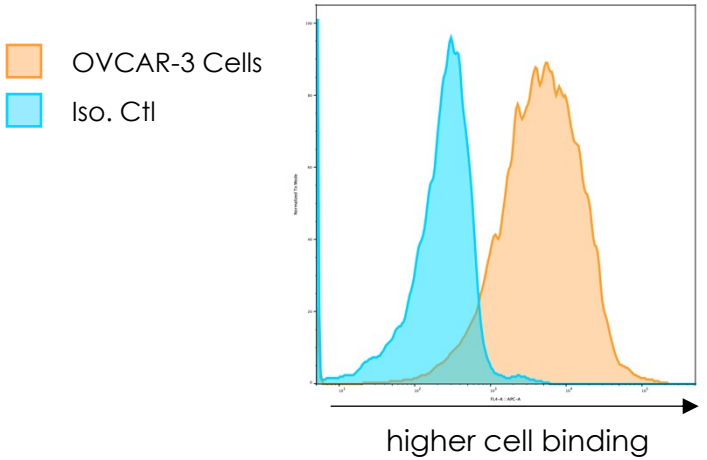




8G4 Clone Maintains OVCAR-3 Cell and MUC16 Epitope Binding in a Fully Human Framework

8G4 with fully human framework reduces immunogenicity risk

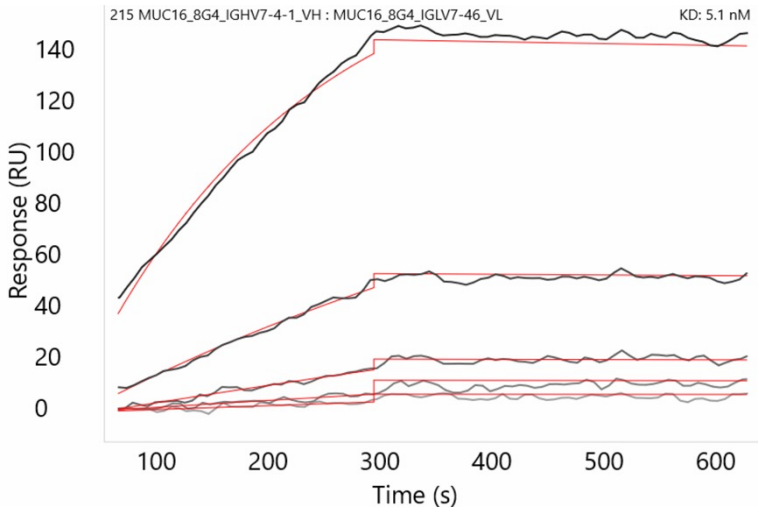
Cell binding



Glycosylated MUC16 membrane-proximal epitope SPR:

KD = 5.1 nM

Epitope binding

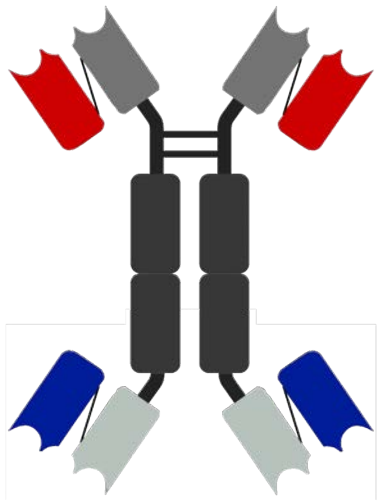


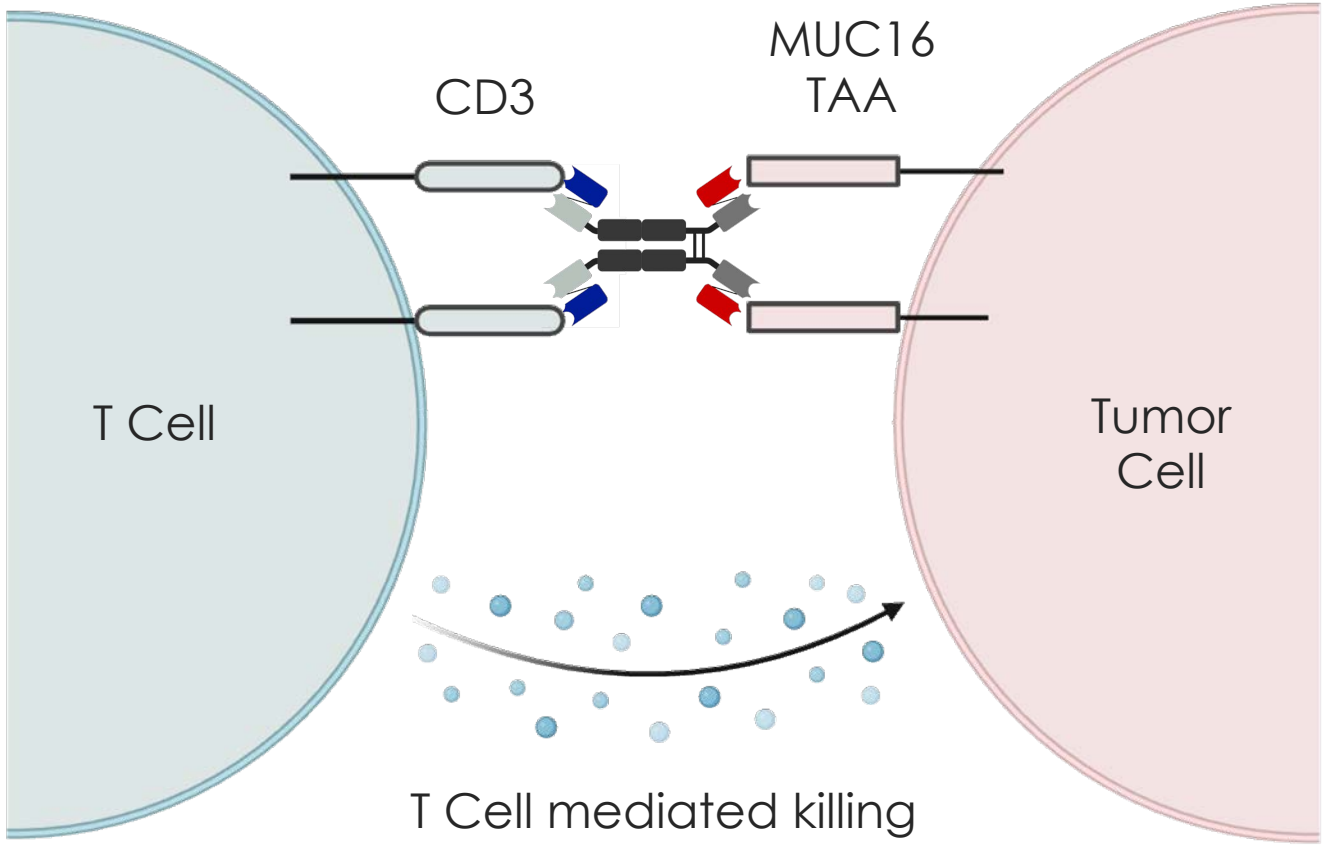
Efficient Expression with 2x2 Format: Anti-CD3 x MUC16 Bispecific T-Cell Engagers

scFv-Fc 2x2

Anti-MUC16 TAA

Anti-CD3 (EngageTx)

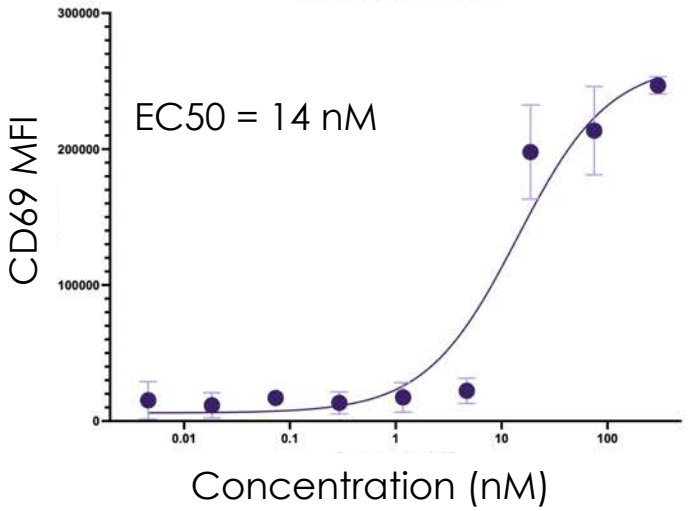
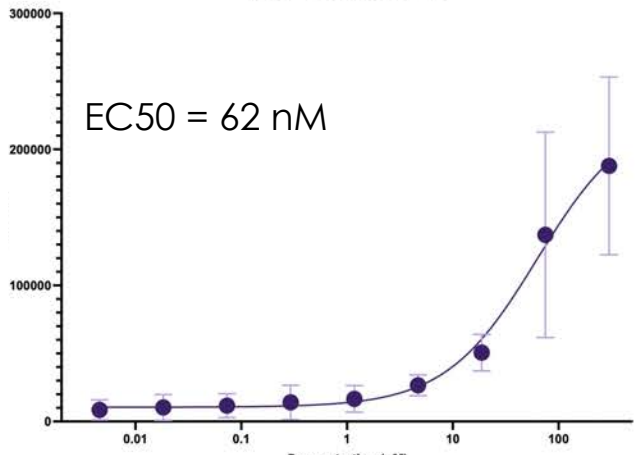
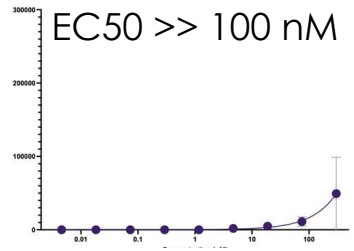
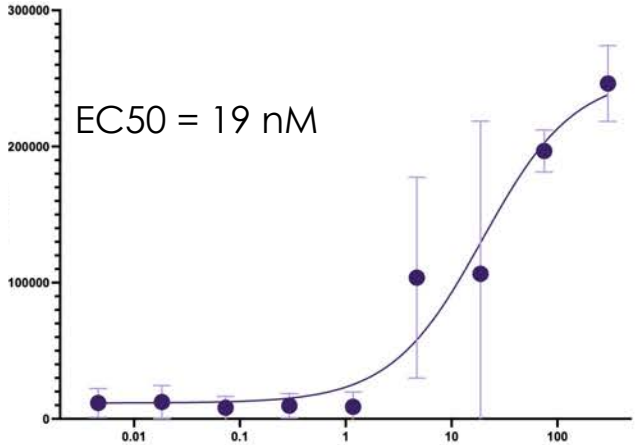
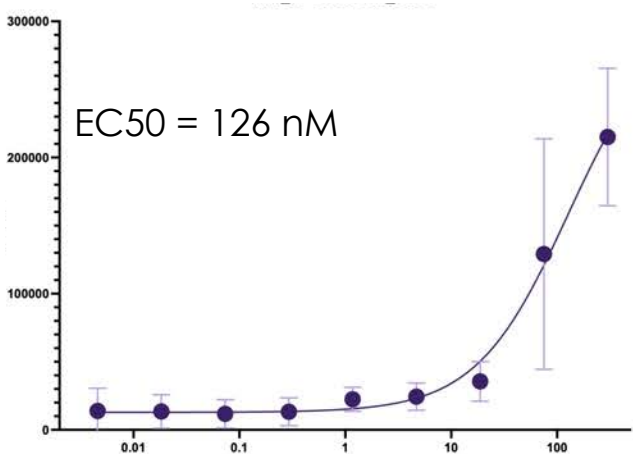
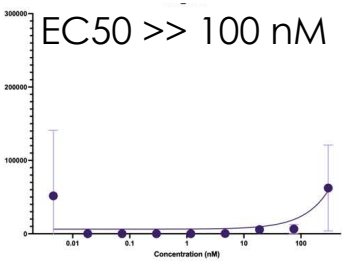




2X2 Anti-CD3 X MUC16 T Cell Engagers Stimulate T Cells in Donor PBMCs

MUC16 Arms

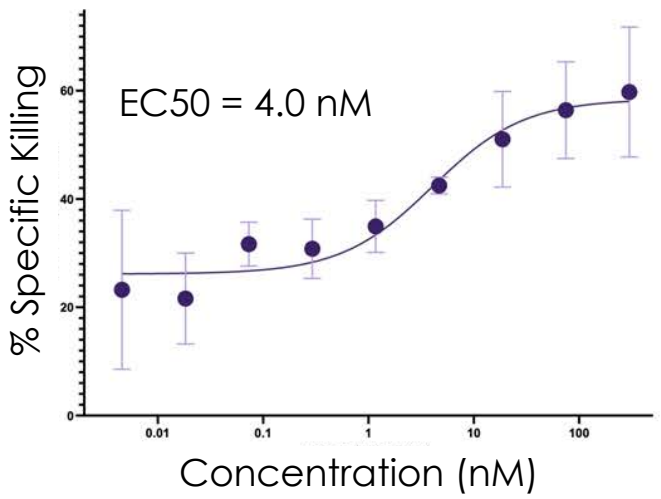
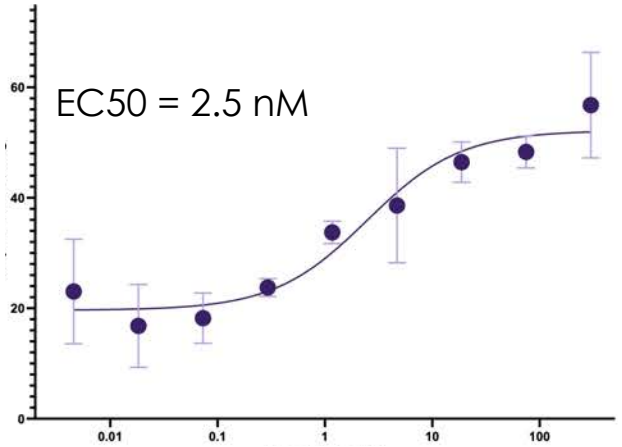
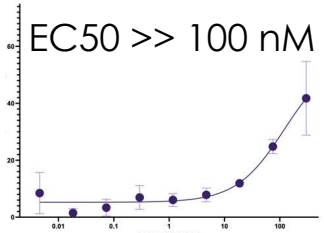
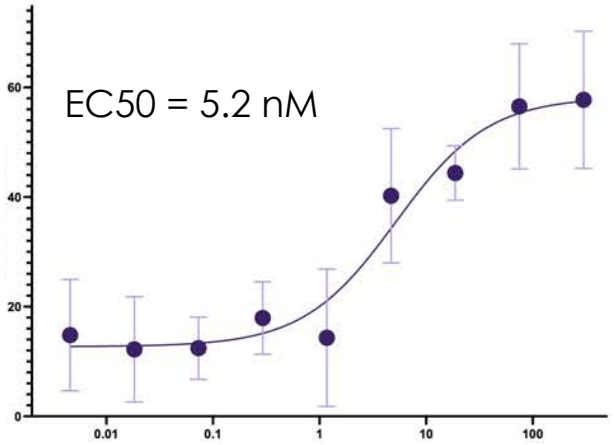
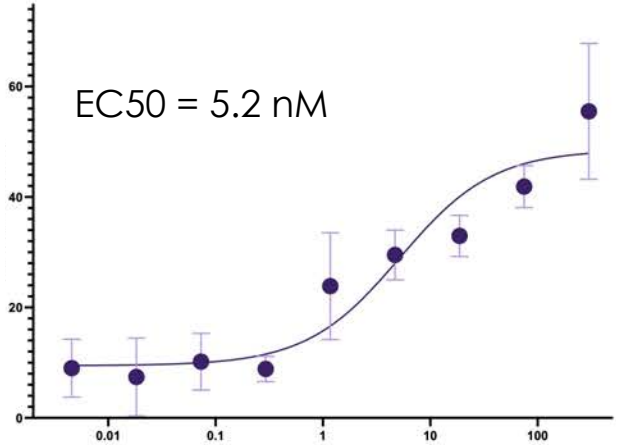
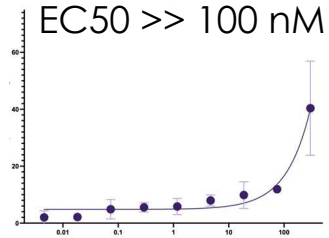
CD3 Arms

	MUC16 Arm 1	MUC16 Arm 2	(-)CD3 Arm only
Epitope-Steered Immunized Hit			
StableHu Hit			

2X2 Anti-CD3 X MUC16 T Cell Engagers Kill OVCAR-3 Ovarian Cancer Cells

MUC16 Arms

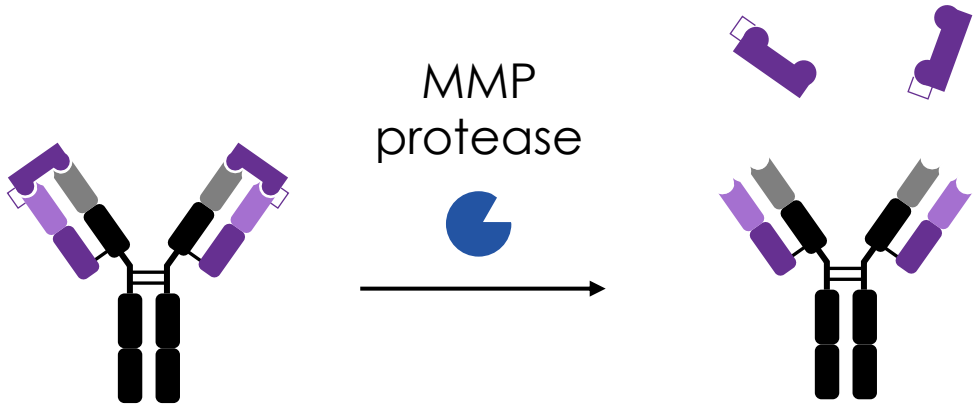
CD3 Arms

	MUC16 Arm 1	MUC16 Arm 2	(-)CD3 Arm only
Epitope-Steered Immunized Hit			
StableHu Hit			

ShieldTx Engineered Epitope Mask Conditionally Activates MUC16 and CD3 Hits

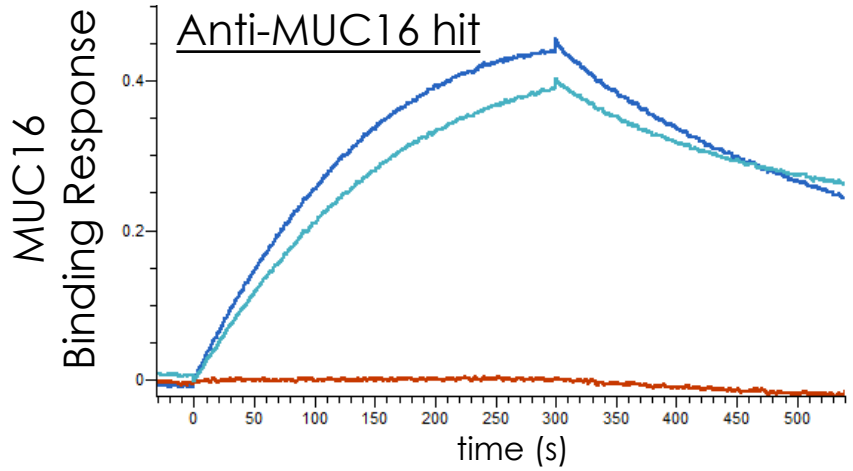
Engineered Epitope Mask Intact

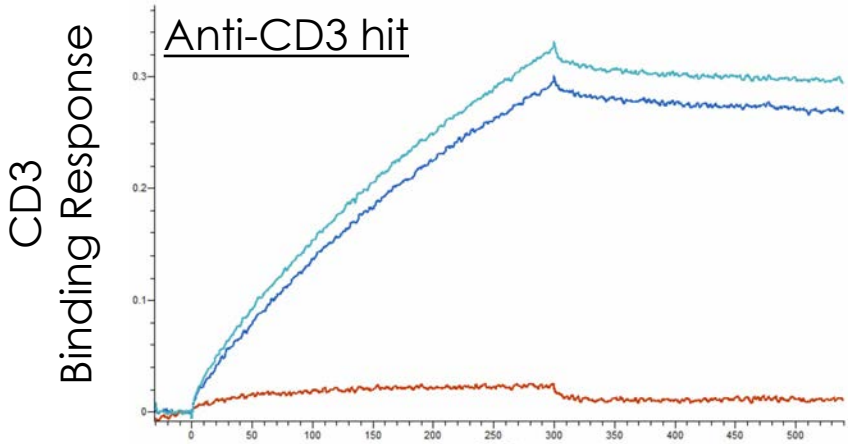
Mask Cleavage

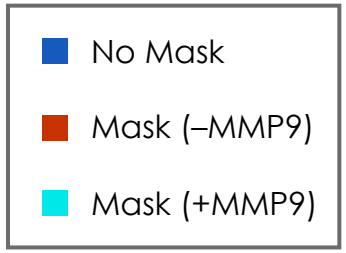


Inactive Antibody

Active Antibody







Anti-Trop-2 x CD3

Bi-Specific Antibody against Tumor-Specific Trop-2 Cancer Cells

Trop-2 x CD3 Bi-Specific Antibody Potentially for Head & Neck and Other Cancer

Target Mechanism

Select killing cancer cells that up-regulate Trop-2 expression while improving safety margin in reducing cytokine release syndrome (CRS)

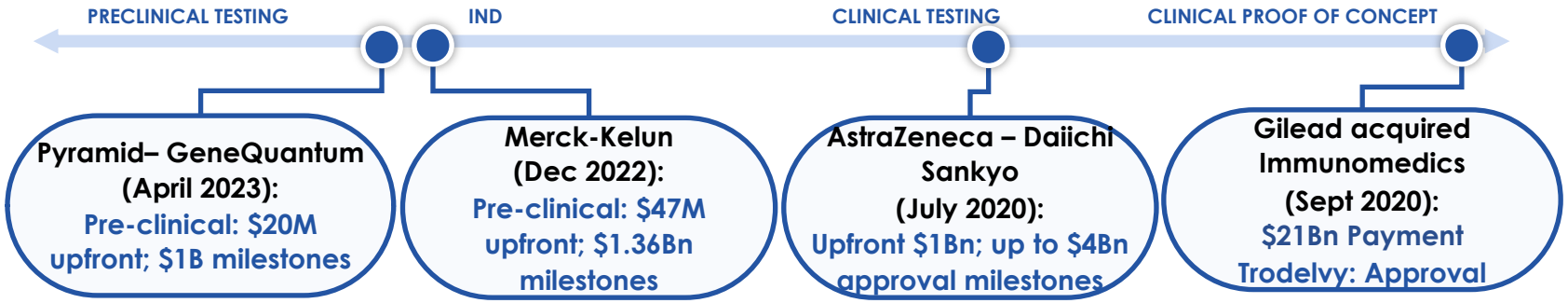
Potential Indications

- Head & neck cancer
- Lung cancer
- Ovarian cancer
- Breast cancer
- Pancreatic cancer

Differentiation / Opportunity

- Novel Trop-2 epitope with extreme high affinity to target
- Trop-2 binder with mouse/cyno/human cross reactive enables early safety profile optimization
- Optimal iBio CD3 engager with low CRS and cyno/human cross reactive

Recent Trop-2 ADC Transactions & Milestones



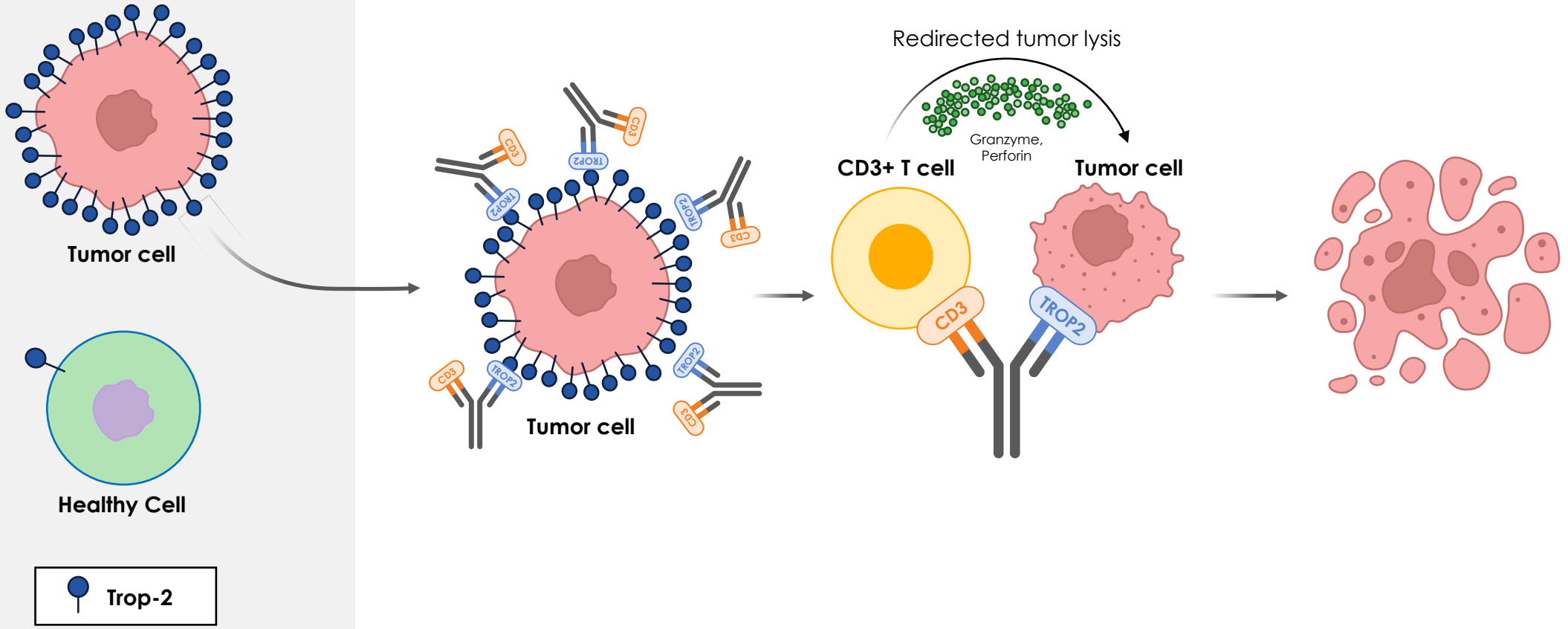
Trop-2 x CD3 Bi-Specific Antibody Selective Target Overexpress Trop-2 Cancer Cells

Tumor cells show significantly increased Trop-2 expression

Trop-2 x CD3 **binds** to tumor cells

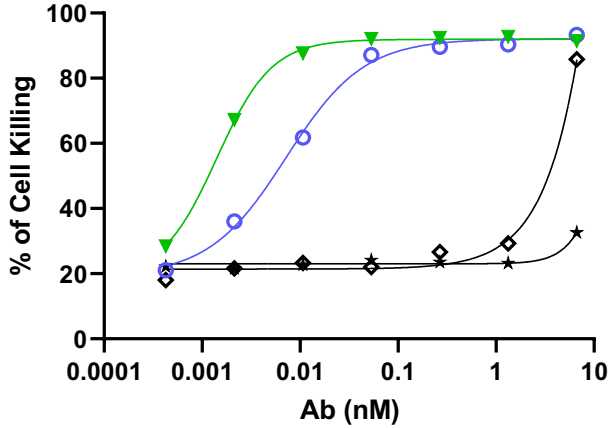
Trop-2 x CD3 **recruits** T cells to kill tumor cells

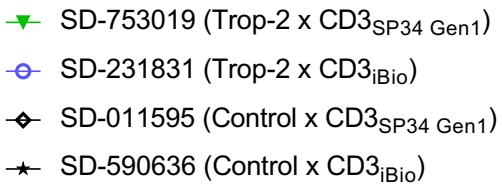
Tumor cell death with high Trop-2 expression



iBio's Trop-2 x CD3 Bi-Specific Antibody Potently Kills Tumor Cells with Low Cytokine Release

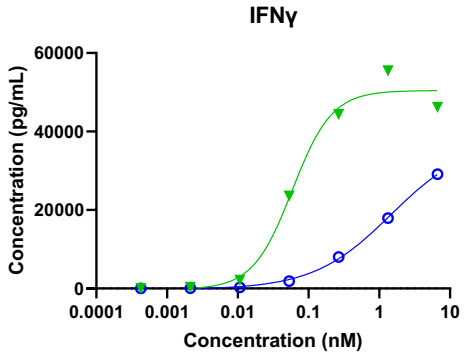
Potent Cancer Cell Killing

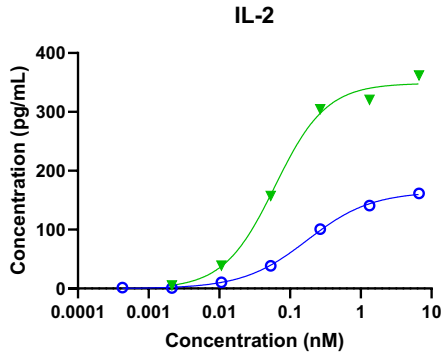


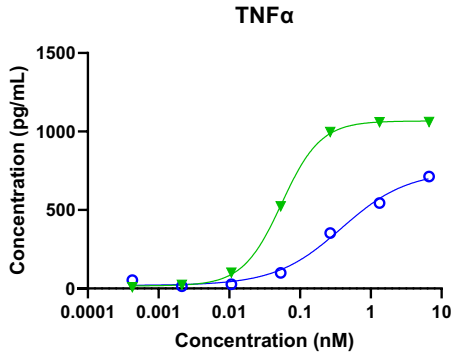


ID	EC_{50} (pM)	Cmax (% killing)
SD-753019	1.4	92%
SD-231831	7.2	92%

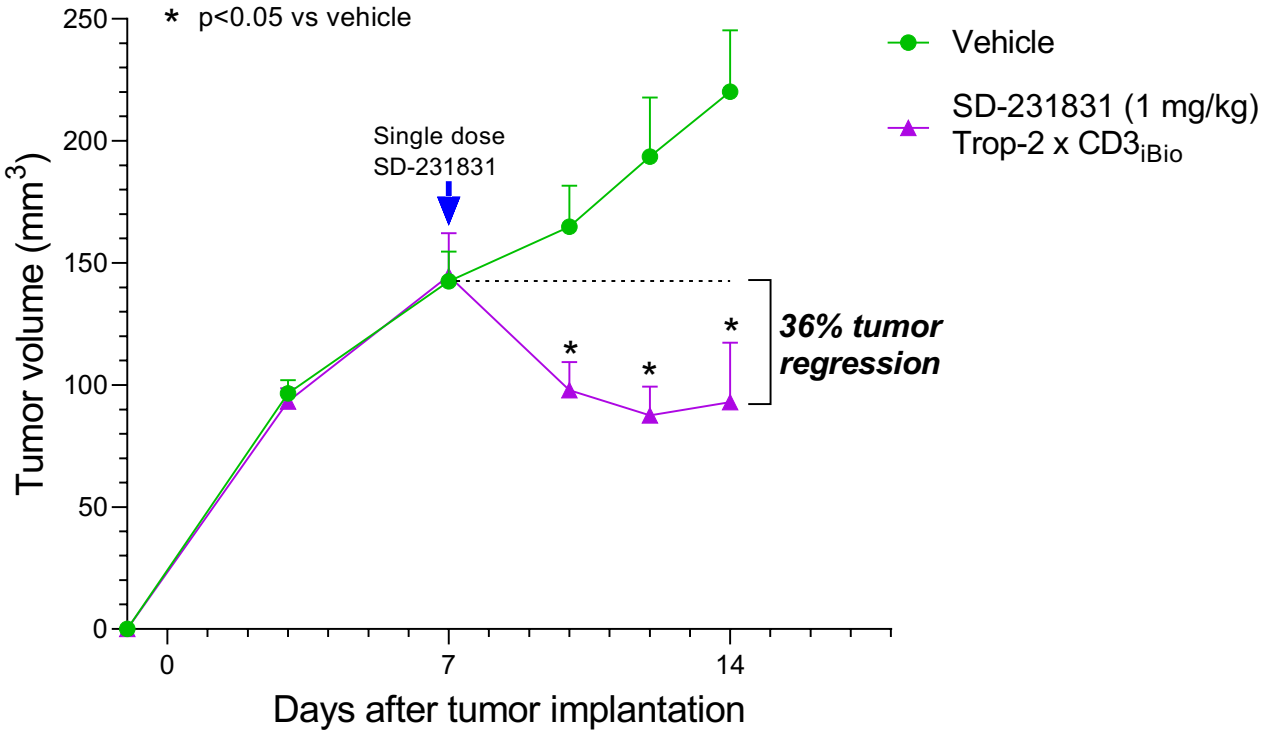
Minimal Cytokine Release







A Single Dose of iBio's Bispecific Trop-2 x CD3 Antibody Induces Tumor Regression in a Humanized Mouse Cancer Model



Anti-EGFRvIII

High ADCC mAb Against Tumor-Specific EGFRvIII Cells

EGFRvIII Potentially for Glioblastoma and Other Cancers

Target Mechanism

Binding a tumor-specific mutation of EGFR variant III with an afucosylated antibody for high ADCC.

EGFRvIII is constantly "switched on" which can lead to the development of a range of different cancers.

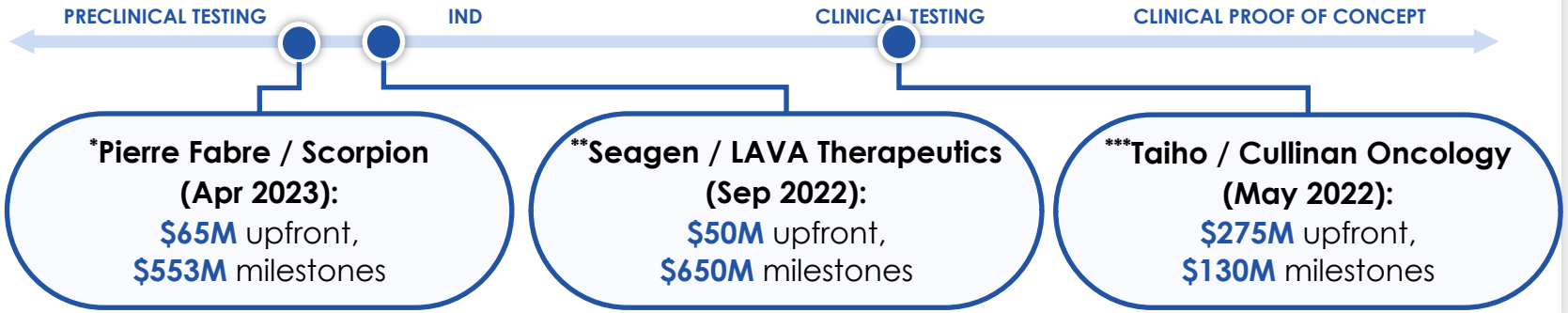
Potential Indications

- Glioblastoma
- Head & neck cancer
- Non-small cell lung cancer

Differentiation / Opportunity

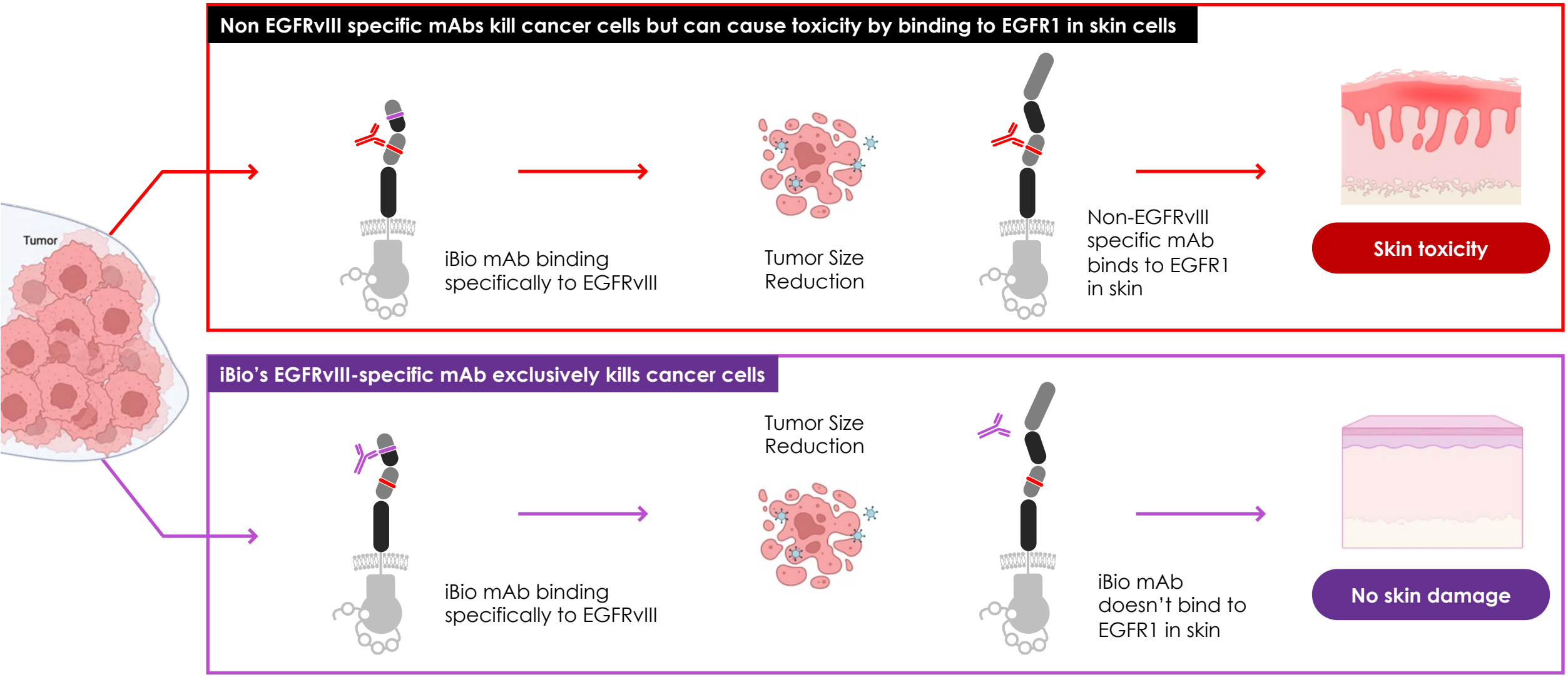
- Novel EGFRvIII high ADCC mechanism, potentially further reducing toxicity & expanding therapeutic window
- Other enabling modalities: T Cell engager, ADC, CAR-T

Recent Transactions & Milestones

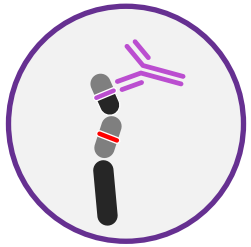


** Pierre Fabre / Scorpion: Scorpion licensed two preclinical-stage programs to Pierre Fabre which are targeted to specific EGFR mutations in lung cancer.*
***Seagen transaction with LAVA Therapeutics was an exclusive license to LAVA-1223 (EGFR program), plus additional projects using Lava's platform.*
****Taiho transaction to acquire Cullinan Oncology's subsidiary, Cullinan Pearl, which has worldwide rights outside of Japan to CLN-081/TAS6417 (EGFR mutant mAb).*

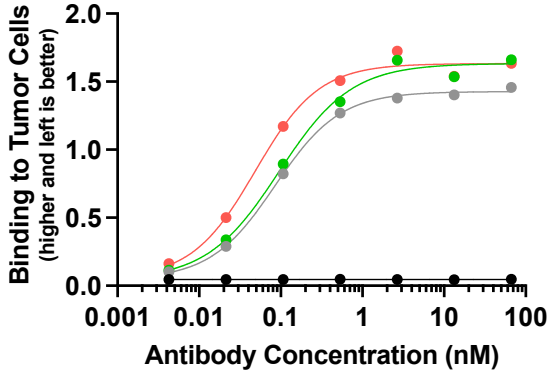
iBio's Anti-EGFRvIII mAbs Selectively Kill EGFRvIII-Positive Tumor Cells and Not EGFR1-Expressing Cells in Healthy Tissues



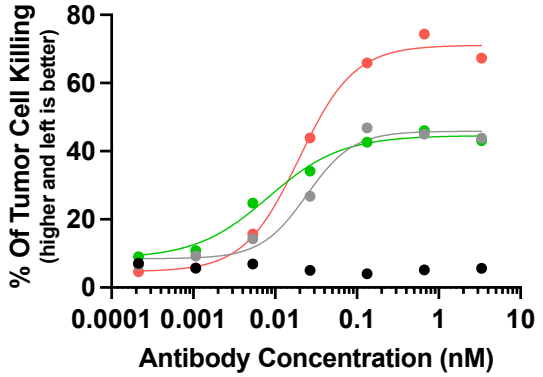
iBio's EGFRvIII-Selective mAbs Kill Tumor Cells without Affecting Healthy Cells

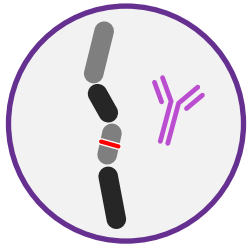


iBio EGFRvIII mAbs bind recombinant EGFRvIII

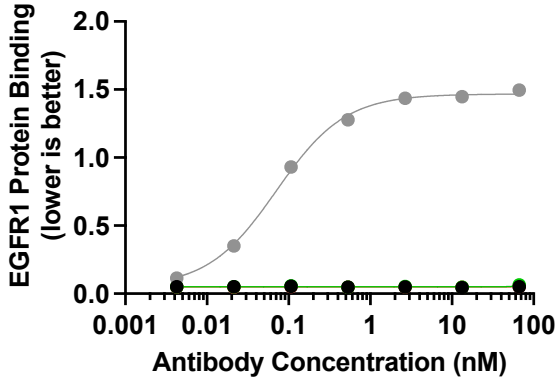


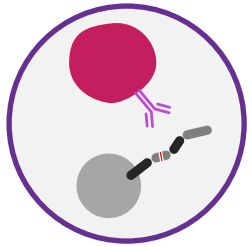
which leads to tumor cell killing



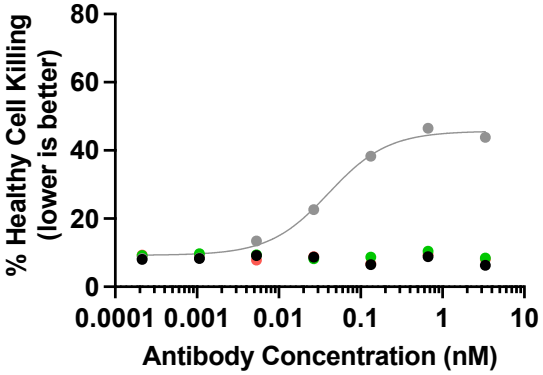


but not binding wild-type EGFR1



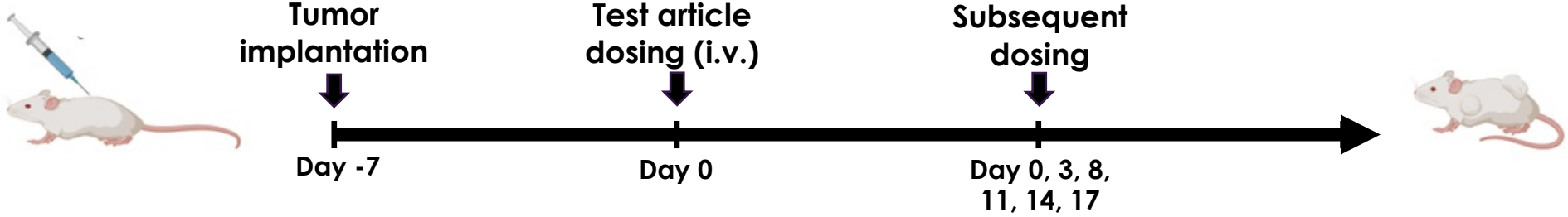


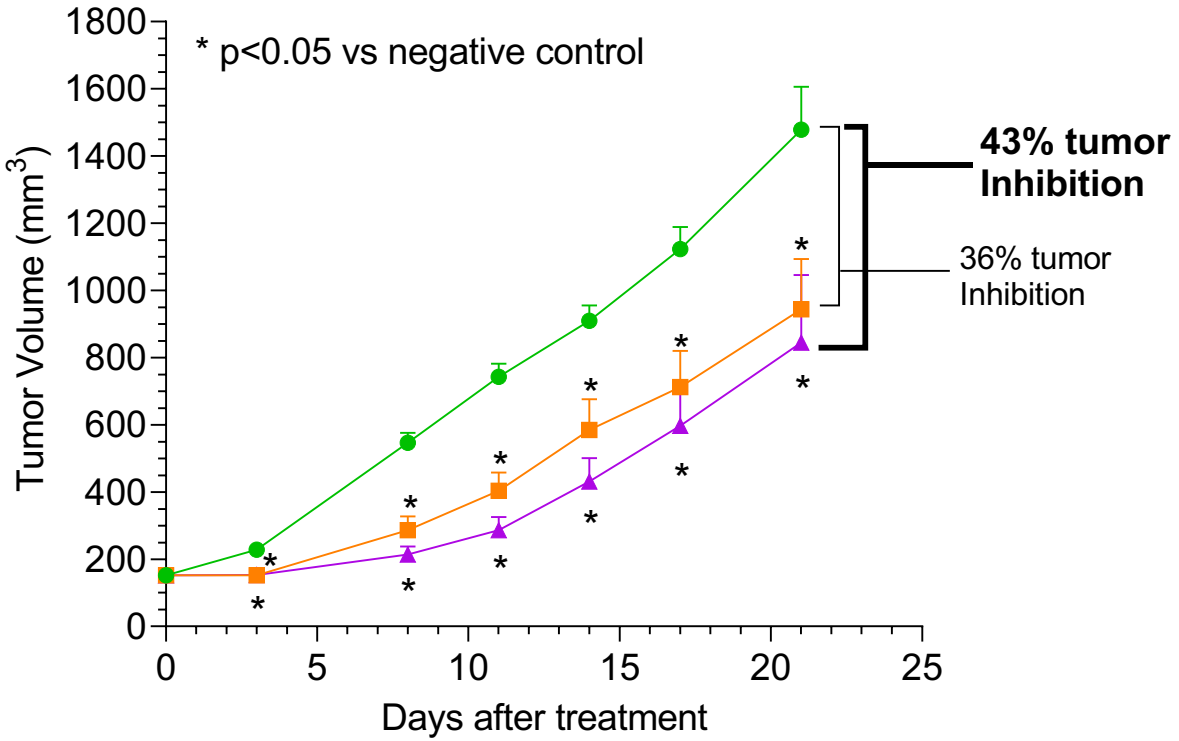
and thus not affecting healthy cells



- Negative control, EC_{50} = no binding
- Cetuximab, EC_{50} = 0.018 nM
- SD-233883, EC_{50} = 0.008 nM
- SD-710726, EC_{50} = 0.020 nM

iBio's EGFRvIII-Specific High-ADCC Antibody Inhibits Tumor Growth in an EGFRvIII Tumor Xenograft Mouse Model





PD-1 Agonist

Supports Restoration of Homeostasis for Inflammatory Diseases

PD-1 Agonist Potentially to Alleviate Inflammatory Disease

Target mechanism

Selectively agonize PD-1 without antagonizing the natural PD-1:PD-L1 anti-inflammatory interaction

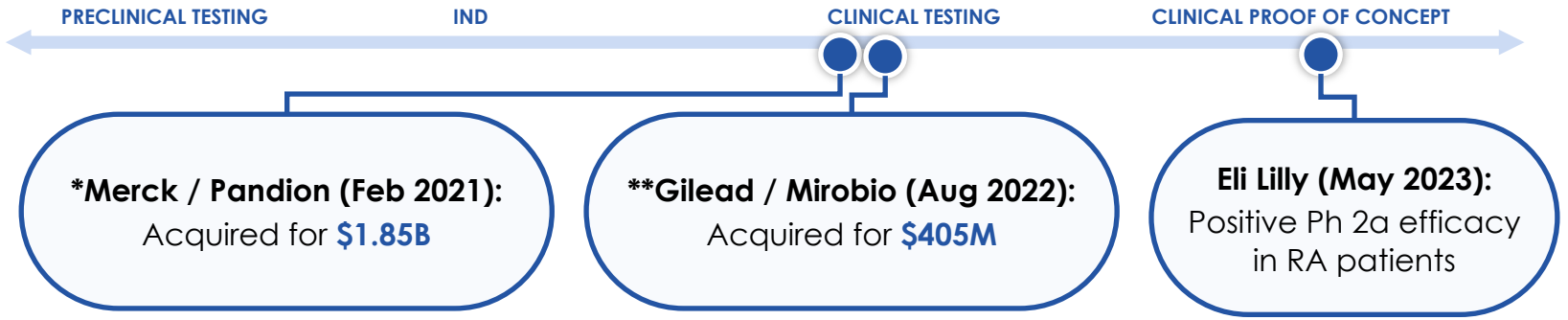
Potential indications

- Rheumatoid arthritis
- Broad application in treating inflammatory disease

Differentiation / opportunity

- Potent PD-1 agonism vs. benchmarks with in vitro reporter and primary cell assays

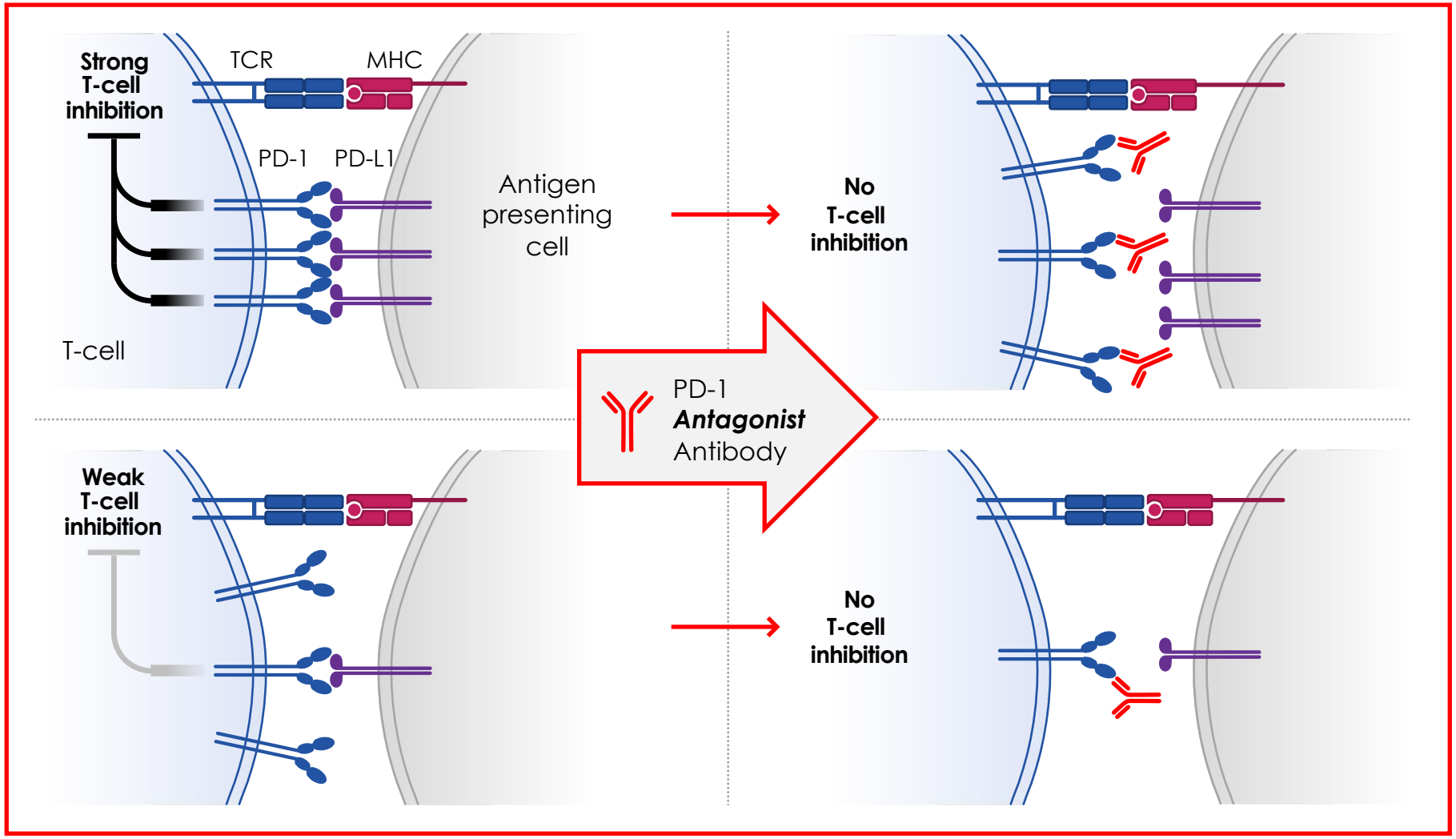
Recent Transactions & Milestones



- *Merck / Pandion: At the time of acquisition, Pandion pipeline including an IL-2 fusion drug in phase 1a, as well as group of preclinical PD-1 agonists.*

*** Gilead / Mirobio: Mirobio pipeline at time of deal included a phase 1 BTLA (checkpoint) agonist as well as preclinical programs which included a PD-1 agonist.*

Antagonizing PD-1 with PD-L1 Blocking Worsens Autoimmunity and Systemic Inflammation

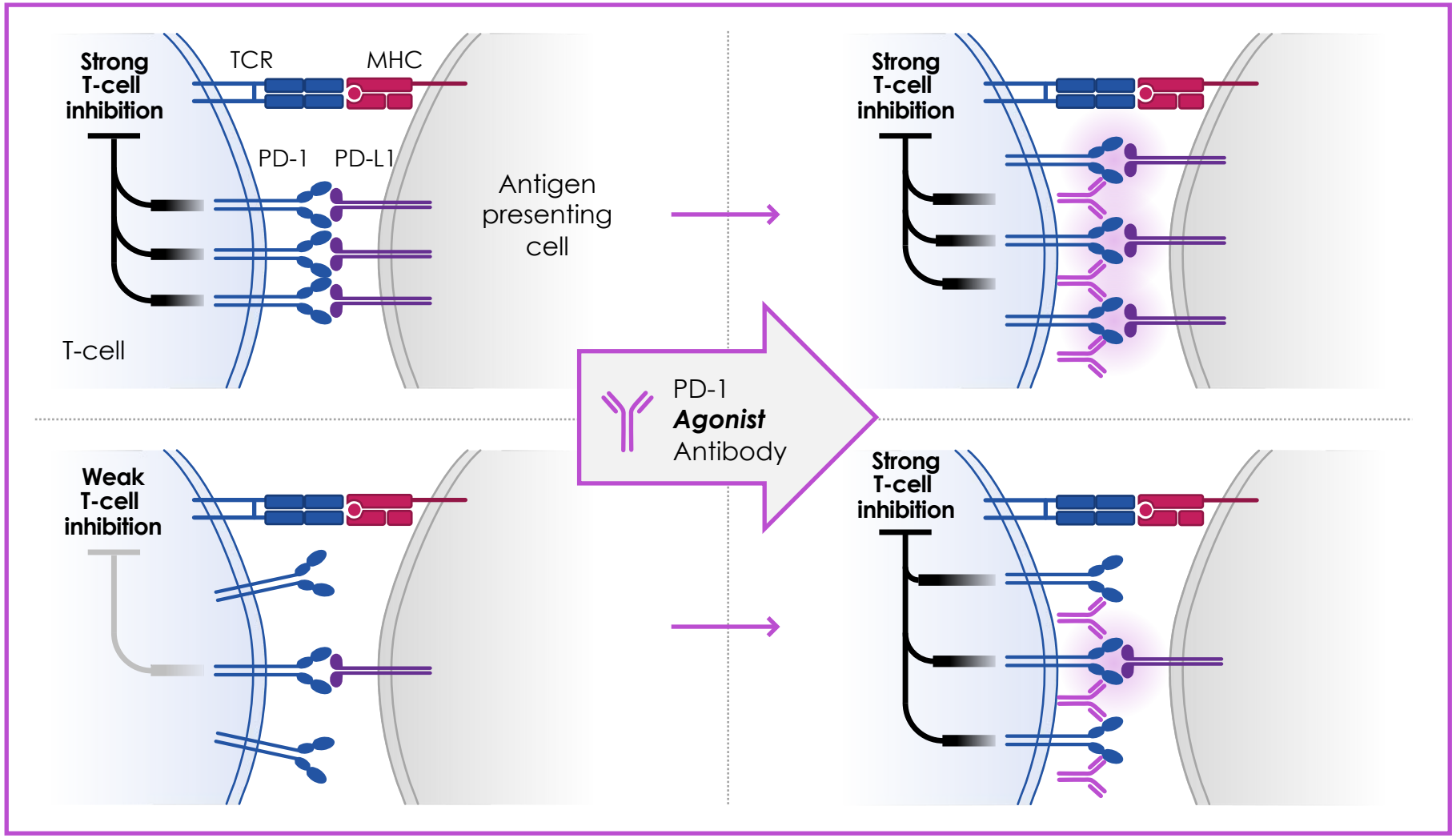


Autoimmunity

Worsened

Increased & systemic inflammation

Agonizing PD-1 Without Blocking PD-L1 Restores Activated T-Cell Suppression



Autoimmunity

Improved

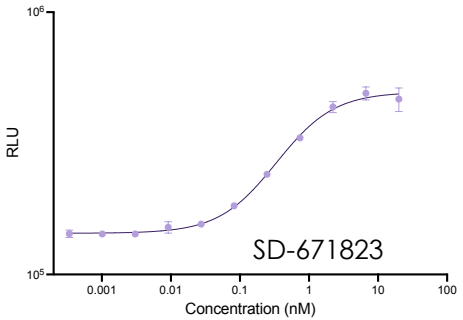
Healthy Tissue
Low-inflammation preserved

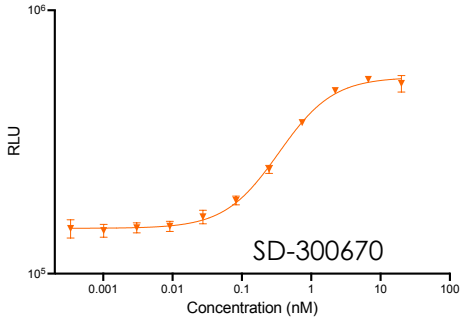
Diseased Tissue
Reduced inflammation

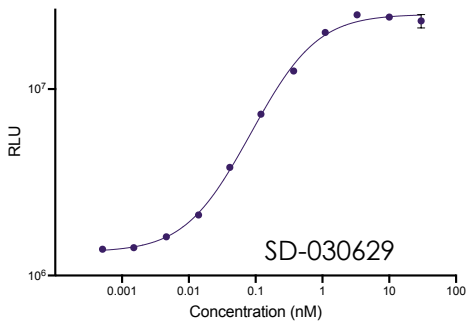
In vitro PD-1 Agonism Equals or Surpasses Benchmarks and PD-L1

PD-1 Agonist Antibodies

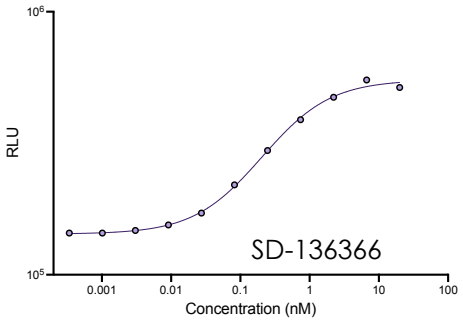
Bivalent

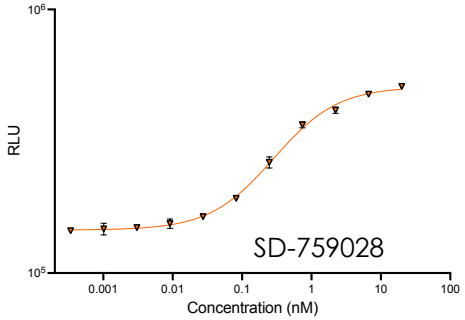


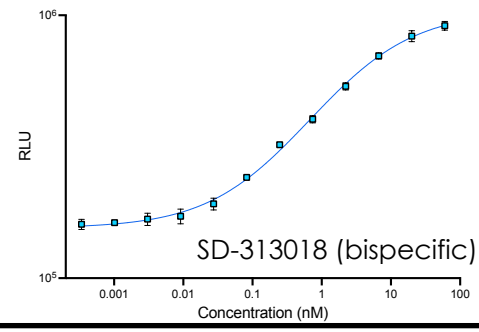




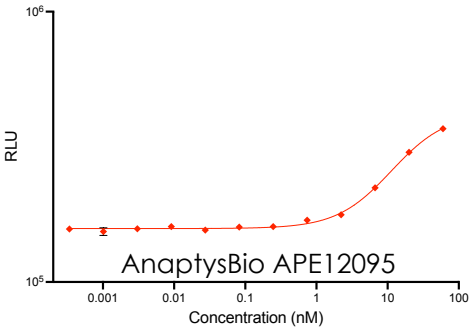
Tetravalent

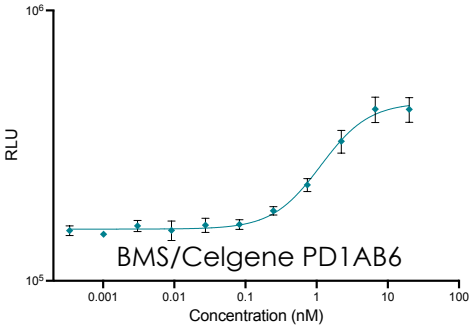


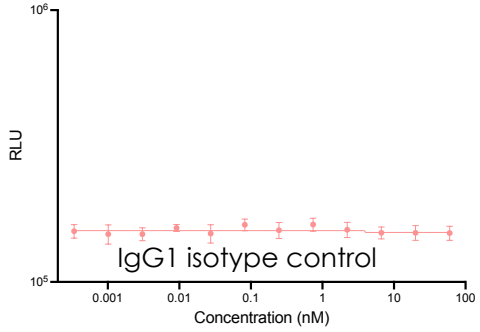




Benchmark Antibodies

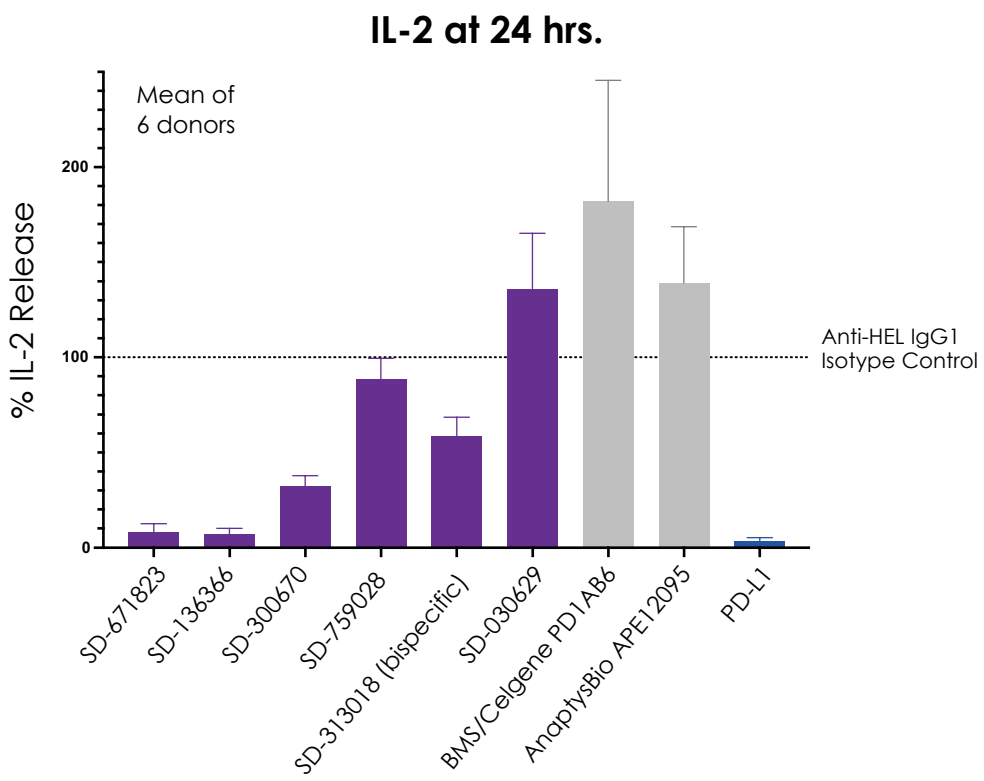


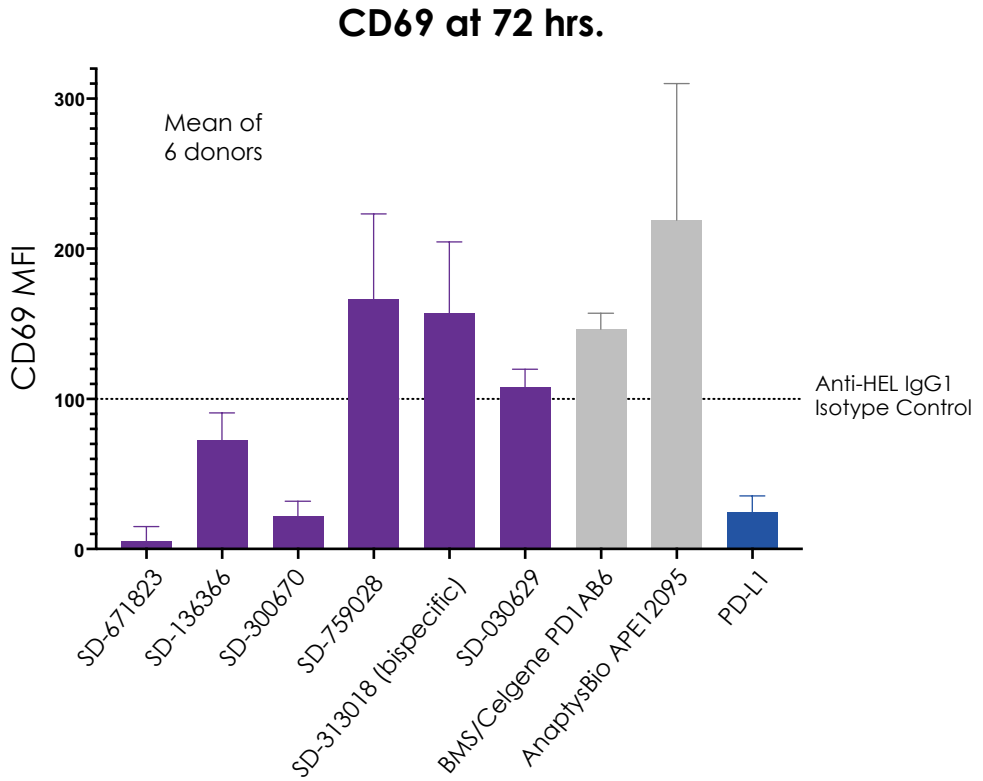




Ab ID	EC50 (nM)
SD-671823	0.88
SD-300670	0.31
SD-030629	0.36
SD-136366	0.28
SD-759028	0.52
SD-313018 (bispecific)	0.30
AnaptysBio APE12095	17.4
BMS/Celgene PD1AB6	0.76
IgG1 isotype control	inactive

Primary T-Cell Suppression Equals or Surpasses Benchmarks and PD-L1





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