

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): **October 23, 2024**

iBio, Inc.

(Exact name of registrant as specified in charter)

Delaware

(State or other jurisdiction of incorporation)

001-35023

(Commission File Number)

26-2797813

(IRS Employer Identification No.)

**11750 Sorrento Valley Road, Suite 200
San Diego, California 92121**

(Address of principal executive offices and zip code)

(979) 446-0027

(Registrant's telephone number including area code)

N/A

(Former Name and Former Address)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of 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(b) 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, \$0.001 par value per share	IBIO	NYSE American

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 checkmark 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 7.01. Regulation FD Disclosure.

iBio, Inc. (the “Company”) has updated its corporate presentation. A copy of the updated corporate presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in this Item 7.01 and in the corporate presentation attached as Exhibit 99.1 to this Current Report on Form 8-K shall not be deemed to be “filed” for purposes of Section 18 of the Securities Act of 1934, as amended, or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information contained in this Item 7.01 and in the corporate presentation attached as Exhibit 99.1 to this Current Report on Form 8-K shall not be incorporated by reference into any filing with the Securities and Exchange Commission made by the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

The corporate presentation attached as Exhibit 99.1 to this Current Report on Form 8-K includes “safe harbor” language pursuant to the Private Securities Litigation Reform Act of 1995, as amended, indicating that certain statements contained therein are “forward-looking” rather than historical.

The Company undertakes no duty or obligation to update or revise the information contained in this Current Report on Form 8-K, although it may do so from time to time if its management believes it is appropriate. Any such updating may be made through the filing of other reports or documents with the Securities and Exchange Commission, through press releases or through other public disclosures.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

The following exhibits are furnished with this Current Report on Form 8-K:

<u>Exhibit No.</u>	<u>Description</u>
99.1	Corporate Presentation of iBio, Inc., dated October 2024
104	Cover Page Interactive Data File (the cover page XBRL tags are embedded within the inline XBRL document)

SIGNATURES

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

Date: October 23, 2024

IBIO, INC.

By: /s/ Marc A. Banjak
Name: Marc A. Banjak
Title: Chief Legal Officer

Tomorrow's Precision Antibody Therapeutics Powered by Machine Learning

October 2024



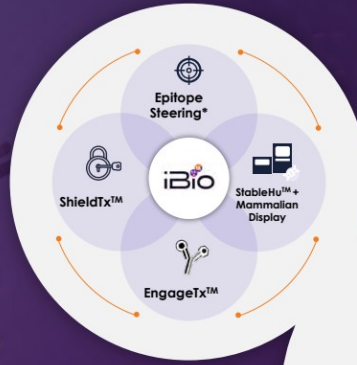
Forward-looking Statements

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.

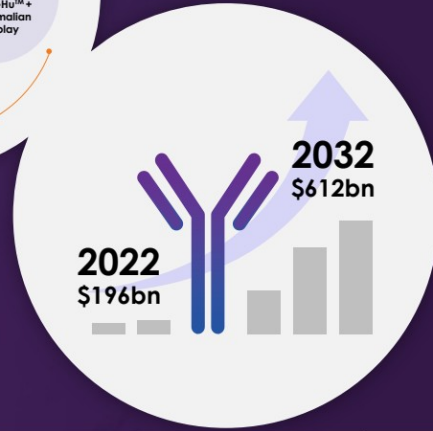




iBio Machine Learning Engine



Antibody Market Potential



Next Generation Antibody company utilizing our proprietary Machine Learning Antibody Engine to create first-in-class and best-in-class drugs for hard-to-drug molecules



Evolution of iBio: From CDMO to Machine-Learning (ML) Enabled Antibody Discovery

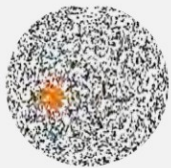


Innovating with Intelligence: Unleashing Our AI-Driven Antibody Discovery



Challenges of Antibody Discovery and Development Requires Integration of Individual Point Solutions

Pursuit of Novel Biology & Targets



- Approved mAbs only target small cluster of all potential drug targets
- 40% of all approved mAbs bind to only 10 targets²

Design mAbs with Complex MoA



- Vast majority of approved mAbs simply block protein interaction
- mAbs with complex Mechanisms of Action (MoAs) are rare (agonistic, cell-activating, ...)

Compress Time From Discovery to IND



- Typical times from Discovery to IND 5-6 years¹
- Lengthy trial and error process adds significant time to Hit ID
- Iterative, single dimension Lead Optimization (LO) is time consuming

Increase Low Overall Success Rate

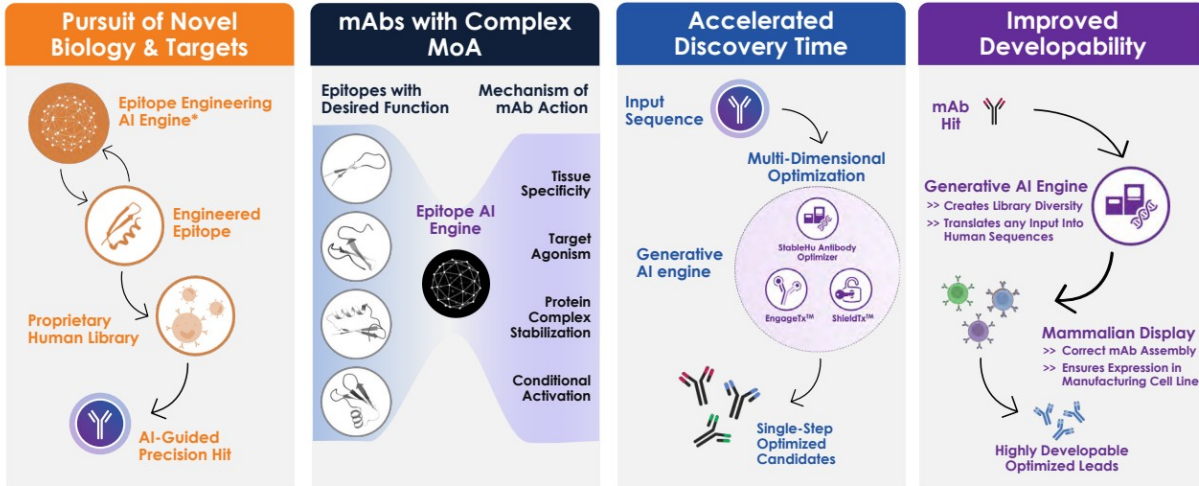


- Low success rate overall
- Poor developability of development candidates (DC) significantly contributes to failure rate



1. Ingelheim, B. Drug Discovery at Boehringer Ingelheim. *Boehringer Ingelheim* (2019).
2. Lyu et al., *Antibody Therapeutics*, September 2022

iBio's Generative AI-Driven Tech Stack - Integrated Solution for Antibody Discovery & Development



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

Our Generative AI Platform: Endorsed by Leading Partners



R&D Partnerships

Eli Lilly

R&D Agreement

Undisclosed
>\$1Bn Market Cap mAb Company

R&D Agreement, Option to License Antibodies Against Two Hard-to-Drug Targets

Undisclosed
>\$500M Market Cap mAb Company

MTA*; POC Established; Engaged in Talks for Follow-On Agreement

Undisclosed
Privately Held mAb Company

MTA* to Establish POC

Strategic Collaborations

AstraBio

Exclusive License and Collaboration to Develop 4 targets in Obesity and Cardiometabolic Disease with Option to License 3 Targets.

NIH (NIAID)

Completed R&D Collaboration to Develop Lassa Fever Vaccine

Pipeline Asset Sales

Otsuka

PD-1 Agonist Asset Acquired by Otsuka; \$52.5M Potential Milestone Payments



*Material Transfer Agreement

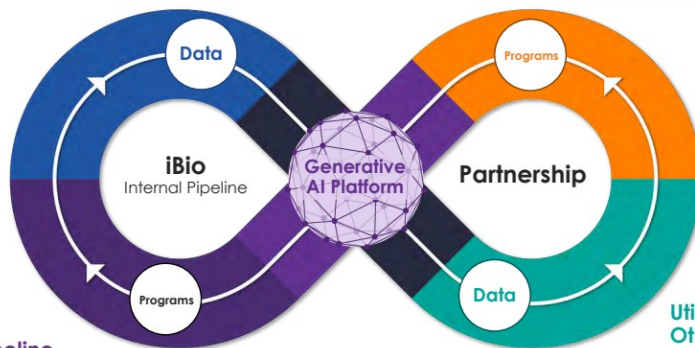
Seizing Future Opportunities: A Growing Pipeline and Strategic Collaborations Driving Platform Development

Rapidly Evolving Obesity/Cardiometabolic Pipeline

- Strong Focus on Validated Biology
- Generative AI Platform to Engineer Best-In-Class Molecules

Through Partnerships Unlocking Hard-to-Drug Targets in Other Disease Areas

- Inflammation and Immunology (i.e. Agonistic mAbs)
- Neurology (i.e. Ion Channels)



Monetizing Existing Immuno-Oncology Pipeline

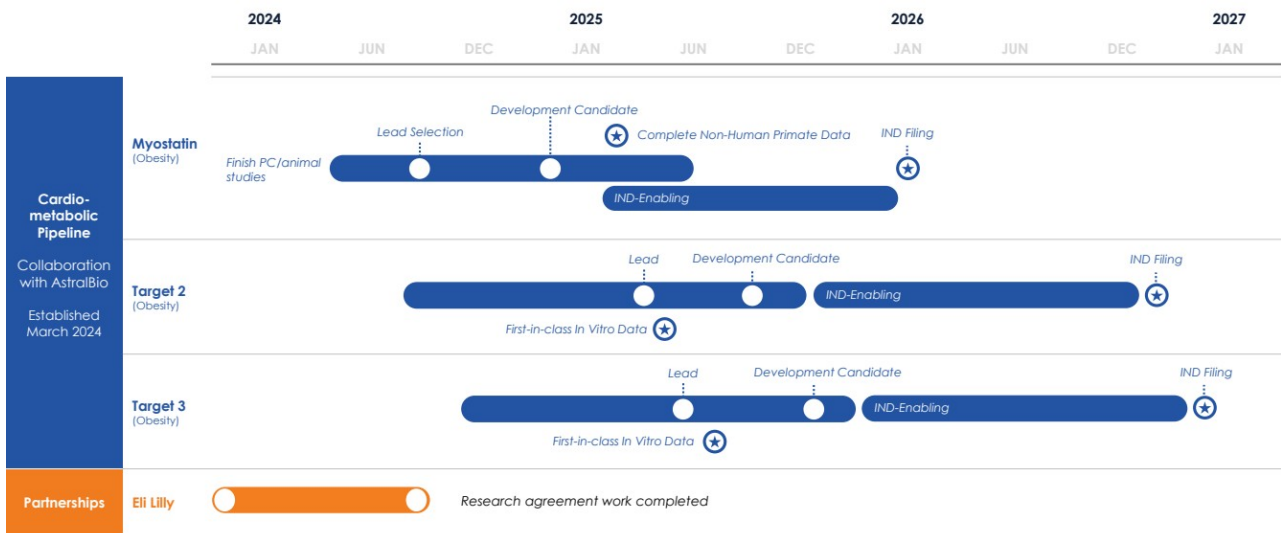
- Created and optimized with our generative AI platform
- Focus on out-licensing of preclinical pipeline assets
- Opportunistic advancement of candidates into clinical development

Utilizing the Platform for Other Modalities

- AI Engineered Epitopes as mRNA or Peptide Vaccines
- Hard-to-Drug Targets for ADC and Cell Therapy



Anticipated Collaboration Catalysts



Led by Industry Veterans, Powered by Next-Gen Scientists

Leadership Team



Martin Brenner, DVM, Ph.D.
CEO & CSO



Felipe Duran
CFO



Marc Banjak
CLO



Kristi Sarno
Senior VP BD



Leadership team with decades of experience in pharma / biotech industry and extensive deal and fund-raising expertise

Scientific team of new generation "bi-lingual" scientists, proficient in machine learning/platform development, and biology

Deep expertise in cardiometabolic disorders



iBio Summary

Company Highlights

- Patented machine learning technology solving hard to drug molecule challenges
- Numerous validating partnerships showing proof of concept
- Developing novel targets in the Obesity/Cardiometabolic space
- Best in class fast follower I/O pipeline ready for partnering

Financial Highlights

- Publicly traded (NYSEA: IBIO)
- Approximately \$14.4M in cash, cash equivalents and restricted cash (30 June 2024)
- 9,137,895 shares of common stock outstanding (9 Oct 2024)
- Texas Manufacturing Facility sale completed eliminating substantial secured debt
- Current cash provides runway through June 2025



Appendix



Technology Platform & Preclinical Pipeline

Technology Stack

iBio's Tech Stack Aims to Solve Major Challenges in Antibody Discovery & Development



Epitope Steering

Unlocking Novel Biology

Pursuit of Elusive Targets

GPCRs, Ion Channels, Protein Complexes

Complex modalities

Agonistic Antibodies, Cell Activators, Protein Complex Stabilizers



Proprietary Naïve mAb Library

Improved Speed and Developability

Fully human Ab

Reduced immunogenicity risk by clinically validated Ab frameworks

Speed

Rapid hit ID vs immunization campaigns

Improved Developability

Known sequence liabilities eliminated



StableHu & Mammalian Display

Library Diversity
ML tools create focused diversity with smaller library size

Speed

Simultaneous, Multi-Dimensional Optimization

Improved Developability

Mammalian Display with production cell lines exclusively yields expressible clones



Optimized Antibody Leads

Reduced Lead-Optimization Time
Optimization in less than **4 weeks**

Minimized Developability Risk
Mammalian Display in Manufacturing Cell Line

Potential for Improved Safety
Selective "on-tissue" action of masked antibodies

First in Class Antibodies and / or Best in Class Antibodies



iBio's Tech Stack Addresses Immuno-oncology Discovery and Development Challenges



EngageTx

2nd Gen T-cell Engager Panel

Sequence Diversity

Increased humanness and broad CD3 activity for optimized pairing with antigen arms

Hu-Cyno Cross Reactivity

Risk reduction via cyno monkey toxicity study compatibility

Range of Cytokine Release

Tailored cytokine release for expanded therapeutic window



ShieldTx

Greater Safety With Tissue Specificity

Seamlessly Integrated Ab Masking

Engineered epitopes serve dual purpose for raising and masking of Abs

Flexibility in Candidate Selection

Simultaneous co-optimization of Ab, mask and linker provides maximized flexibility in candidate selection



Enhanced Efficacy and Safety of I/O Antibody Leads

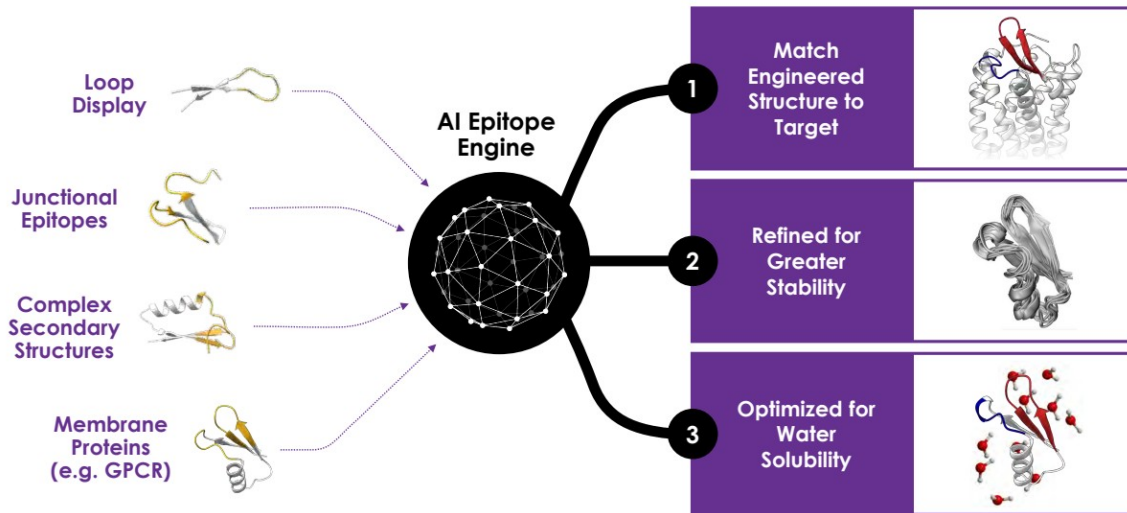
Finely tuned T-cell engagement
Adjustable T-cell engagement to fit any tumor target engager

Improved safety prediction
Cyno cross reactivity allows for better preclinical safety assessment

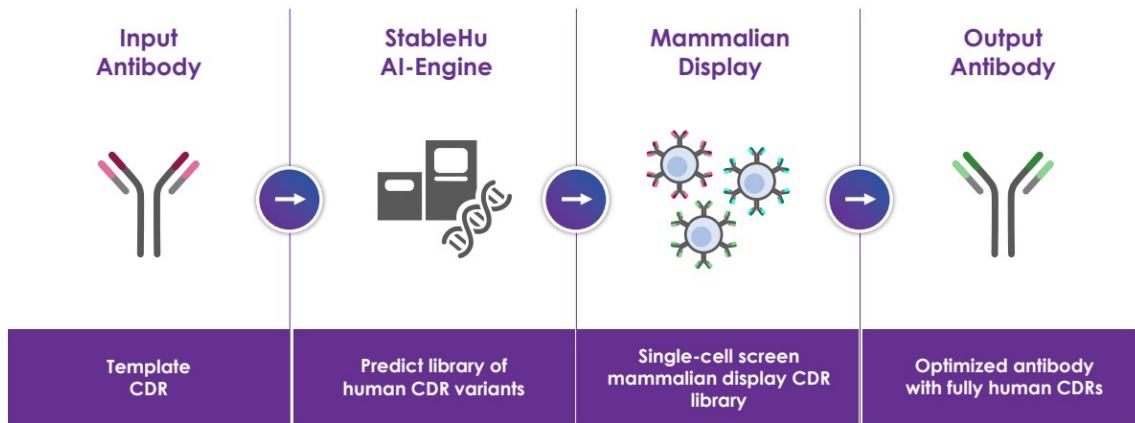
Improved Safety Profile
Tissue selective action through "smart", conditionally activated, antibodies



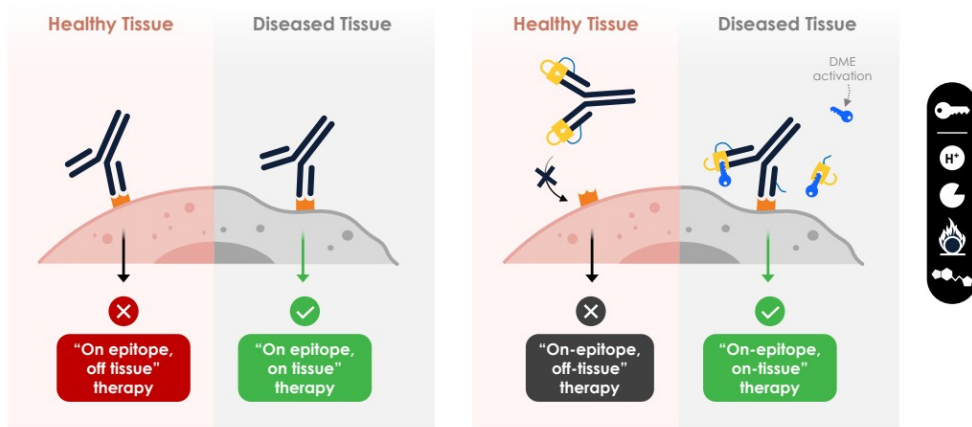
Unlocking High-Value Drug Targets: AI-Engineered Epitopes are Generalizable to a Broad Set of Complex Structural Drug Binding Sites



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



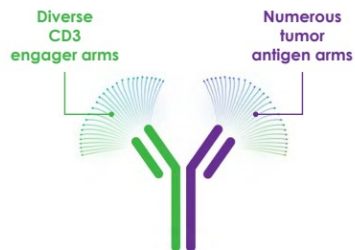
"Smart" Antibodies: ShieldTx Conditionally Activated Antibodies Strive to Improve Safety by Selectively Targeting Diseased but not Healthy Tissue



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

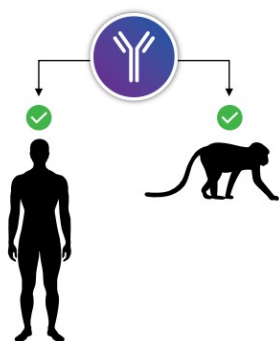
1 Sequence Diversity

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



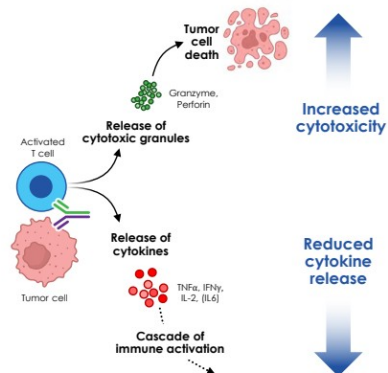
2 Hu-Cyno Cross-Reactivity

Risk reduction via cyno monkey toxicity study compatibility

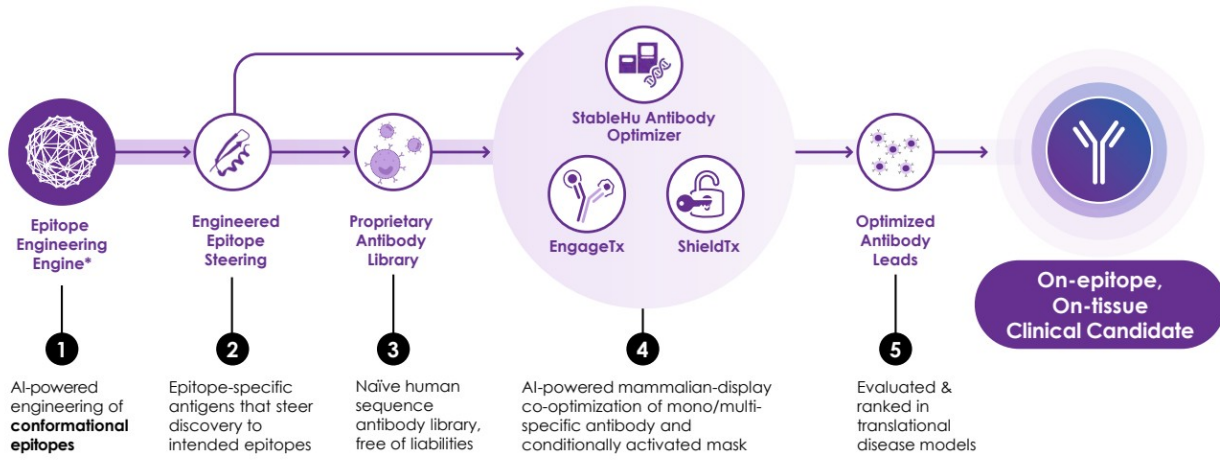


3 Range of Cytokine Release

Tailored cytokine release for expanded therapeutic window



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



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

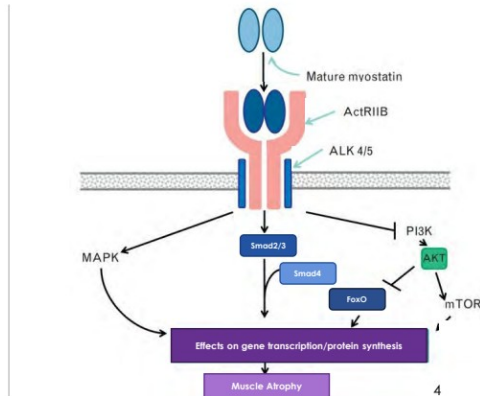
Long-Acting Anti-Myostatin

Myostatin Antagonism

Incretin-based therapies are becoming standard treatments for weight loss. However, up to 40% of the weight lost through these medications is attributed to reductions in lean muscle mass¹

Myostatin Profile

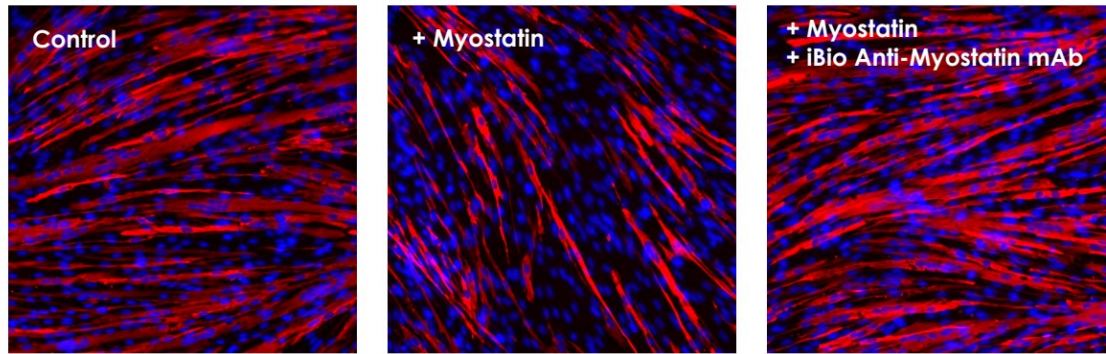
- Myostatin is produced by and acts on muscle cells to trigger muscle wasting
- Homozygous loss of function mutations lead to significant muscle hypertrophy without obvious deleterious health effects²
- Expressed as homodimer and signals through activin receptors and Smad2/3 pathway
- Beyond muscle, myostatin plays a role in the regulation of adipogenesis & leads to reduction in total body fat mass, visceral & intramuscular fat³



Enhancing the quality of weight loss by maintaining lean muscle mass during weight loss



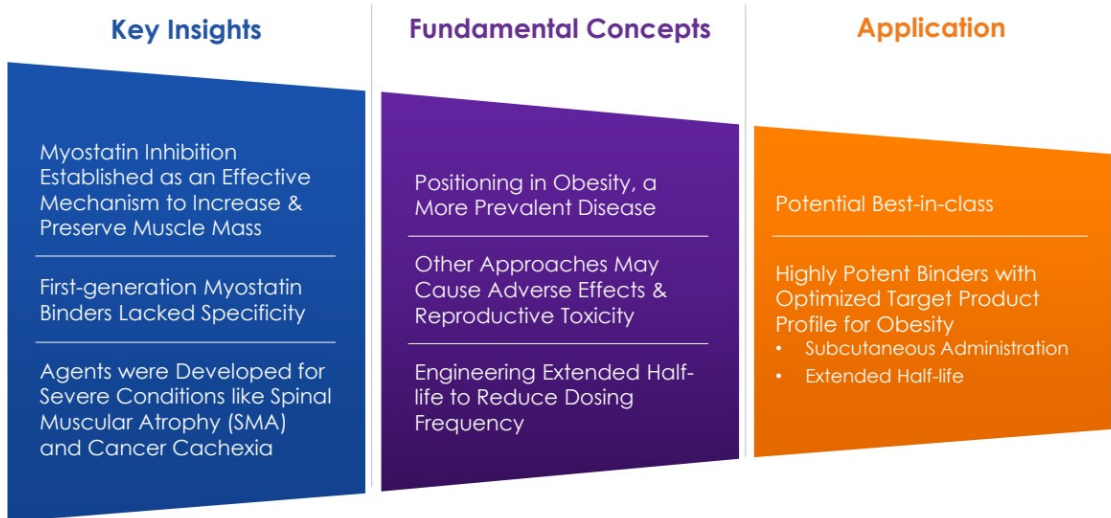
iBio Anti-Myostatin Antibody Promotes Muscle Fiber Formation in Human Muscle Progenitor Cells



Red indicates marker for muscle cell growth and development (as measured by myoblast differentiation)



Half-life Extended Myostatin Antagonist Monoclonal Antibody



Half-life Extended Myostatin Antagonist Monoclonal Antibody

Best-In-Class Profile

- Leverages Fc engineering with potentially class-leading properties
- Sequence leverages iBio's Tech Stack with a known antibody that has been in ~500 patients
 - Demonstrated activity, safety and low-volume subcutaneous feasible
- Half-life in non-human primate studies predicted ~22 days supports every 2 months to every 3 months dosing in humans

Attributes	Myostatin Development Program with AstralBio	Other Muscle Sparing Programs
Low Volume Subcutaneous Administration	✓	X
Low frequency dosing (once per 2 or 3 months)	✓	X
Avoids Reproductive Tox	✓	X
High potency	✓	✓



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

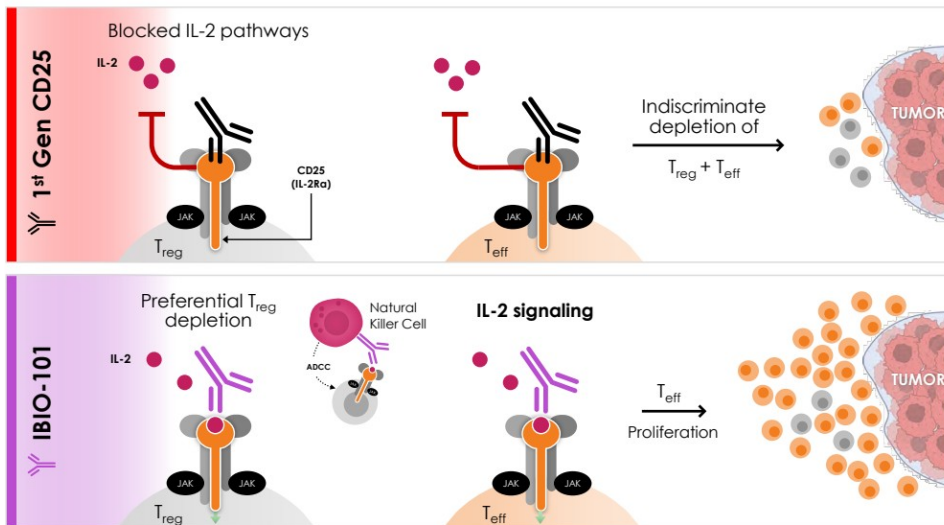
- IL-2 sparing anti-CD25 antibodies enables depletion of T_{regs} without affecting T_{effs}
- Fast-follower to Roche's RG6292 clinical molecule

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_{reg} s without Affecting Cancer Killing T_{eff} s



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

Limited efficacy

2nd gen IBIO-101 selectively targets T_{reg} s without blocking IL-2 signaling to T_{eff} s

Strong preclinical anti-tumor response



IBIO-101 Selectively Depletes Tregs

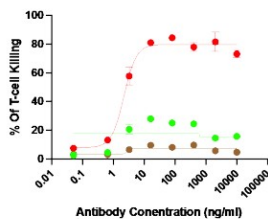
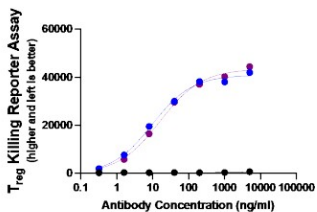
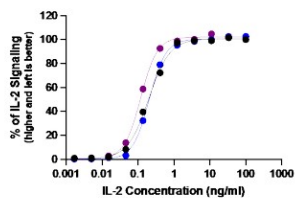
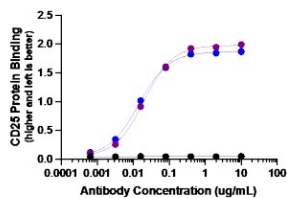


IBIO-101 potently binds recombinant CD25

while preserving IL-2 signaling

which leads to T_{reg} depletion

while sparing T_{effs}



- Negative control, EC₅₀ = no binding
- IBIO-101, EC₅₀ = 16.4 ng/ml
- RG6292 (Roche), EC₅₀ = 24.7 ng/ml

- IL-2, EC₅₀ = 0.11 ng/ml
- IBIO-101, EC₅₀ = 0.17 ng/ml
- RG6292, EC₅₀ = 0.14 ng/ml

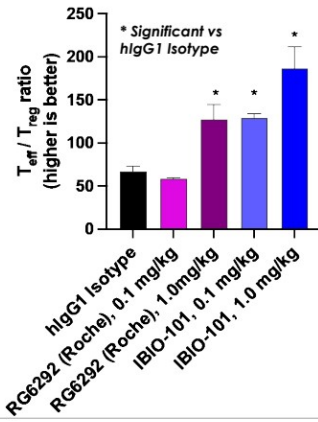
- Negative control, EC₅₀ = no cell killing
- IBIO-101, EC₅₀ = 4.7 ng/ml
- RG6292, EC₅₀ = 18.6 ng/ml

- T_{reg} killing, EC₅₀ = 7.09 ng/ml
- Activated CD4⁺ T_{eff} killing, EC₅₀ = no activity
- Activated CD8⁺ T_{eff} killing, EC₅₀ = no activity

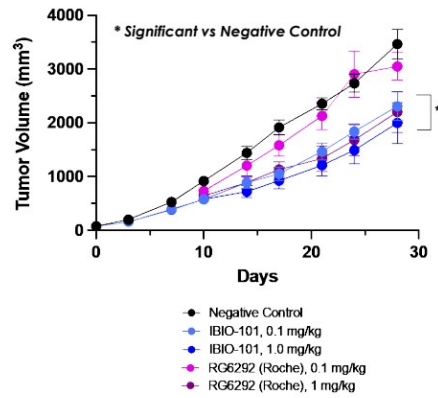


IBIO-101 Increases in T_{eff}/T_{reg} Ratio in Preclinical Studies Inhibiting Tumor Growth

Potently increases T-eff/T-reg ratio¹



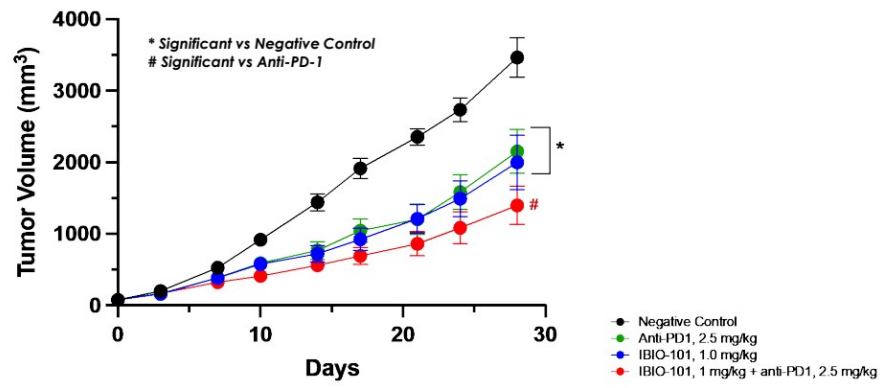
Tumor growth inhibition correlates with T-eff/T-reg ratio



¹hCD25 animal model - Data on file.

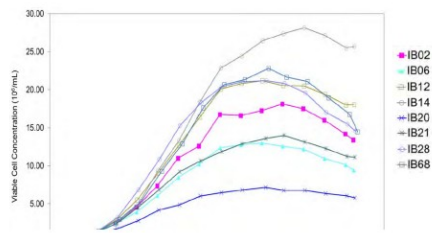
IBIO-101 in Combination With a Checkpoint Inhibitor Shows Greater Efficacy

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

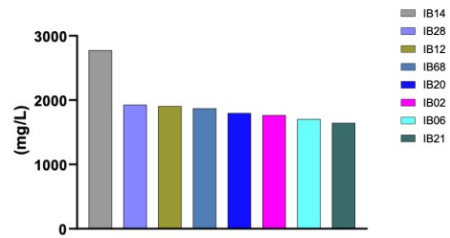


IBIO-101 is an Antibody With Favorable Characteristics for CMC Development

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

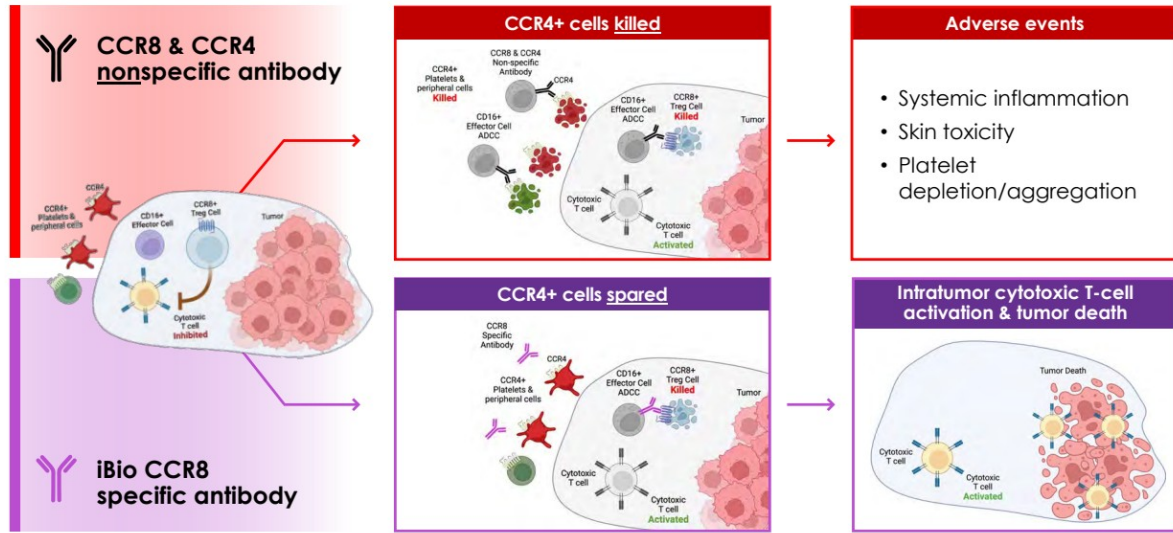
Recent Transactions & Milestones



*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

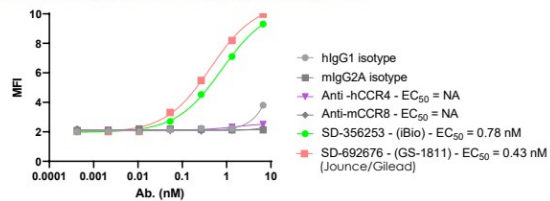
Depletion of CCR8+ Tr_{eg} cells has potential to evoke potent tumor immunity



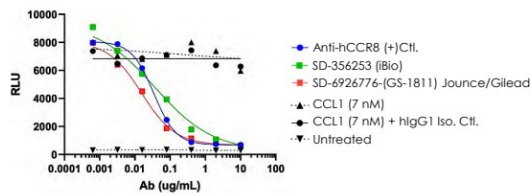
Afucosylated Anti-CCR8 Antibody Exhibits High Specificity, CCL1 Antagonism and CCR8-Specific Cell Killing

High Specificity CCR8 Cell Binding

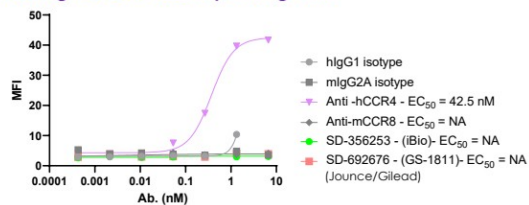
Potent binding to CCR8 overexpressing cells



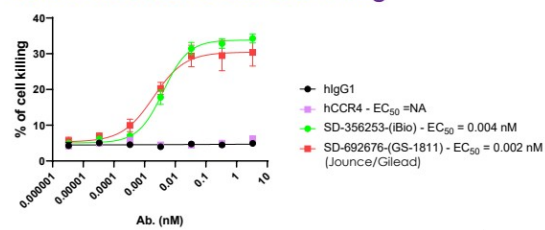
CCR8-CCL1 Antagonism



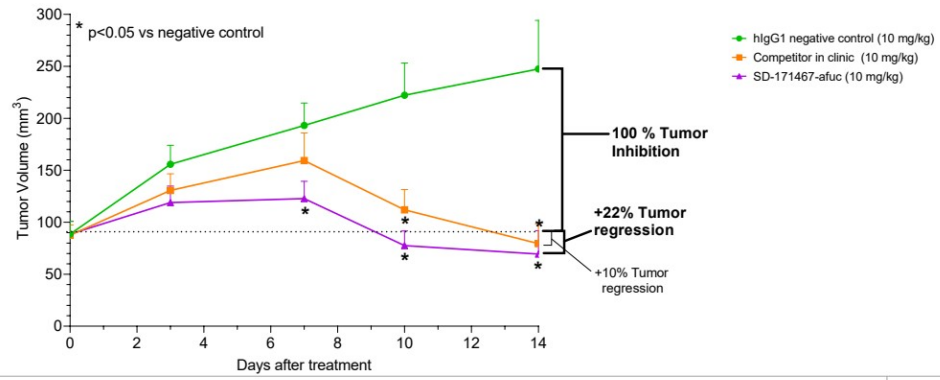
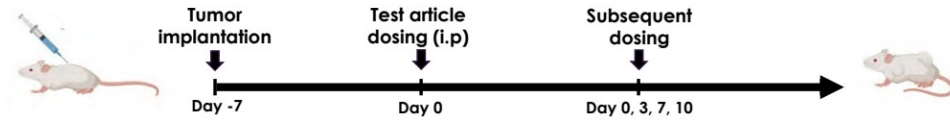
No binding to CCR4 overexpressing cells



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

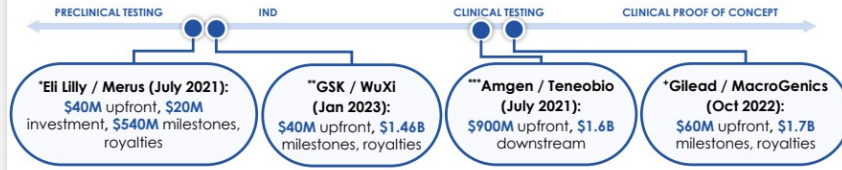
Potential Indications

- Broad solid tumor potential
- Expands therapeutic options across programs

Differentiation / Opportunity

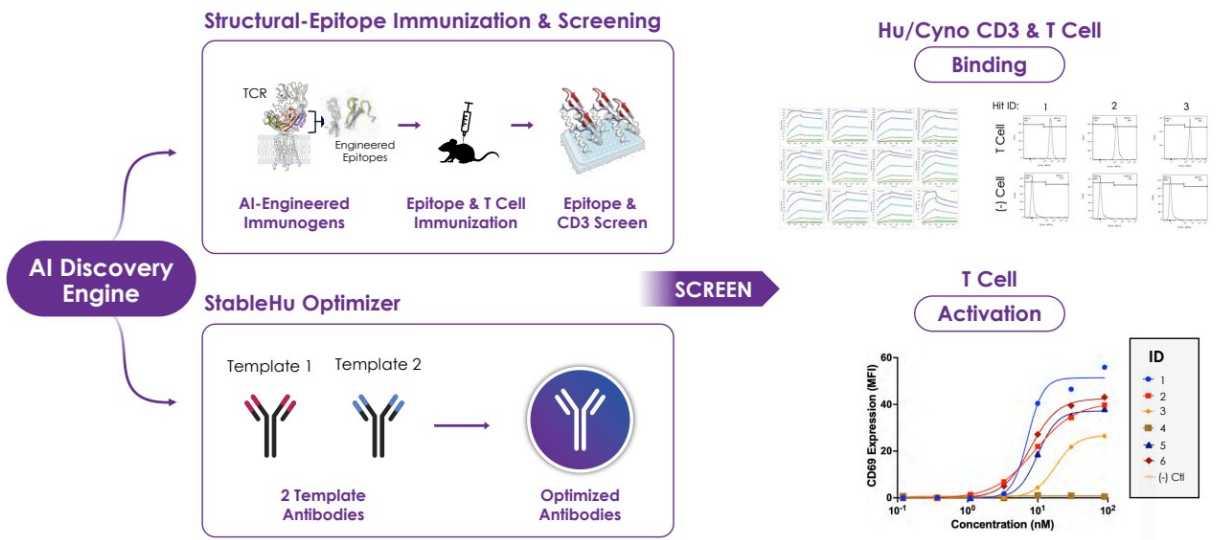
- Range of T cell activation for diverse tumor antigens
- Cyno-tox study compatibility
- StableHu optimized sequence reduces downstream risks

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

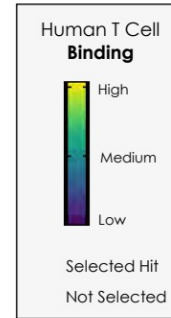
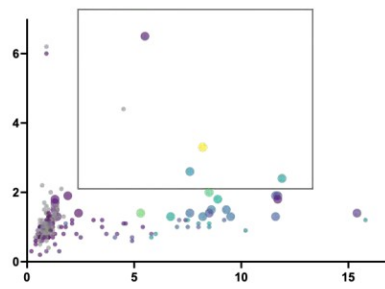
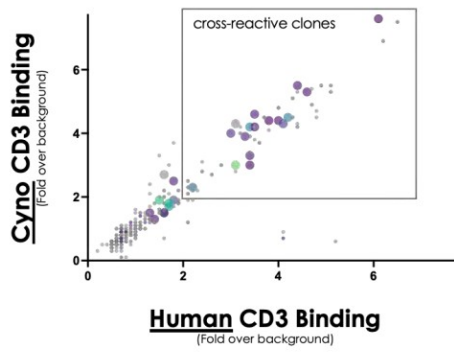


Libraries and Screens Discover Hu-Cyno CD3 Cross-Reactive Antibodies

Library
Screen:

StableHu
Mammalian-Display

Epitope-Steered
Immunization



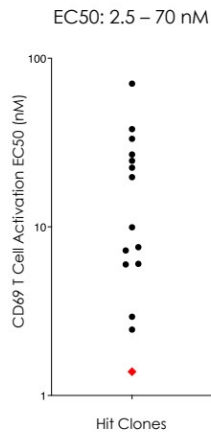
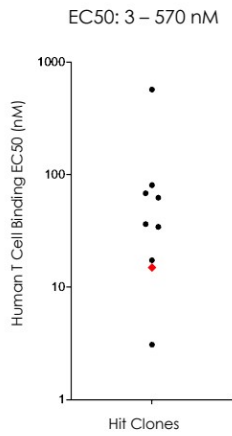
EngageTx is Selected for a Diversity of T Cell Binding and Activation

T Cell Assay:

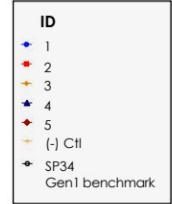
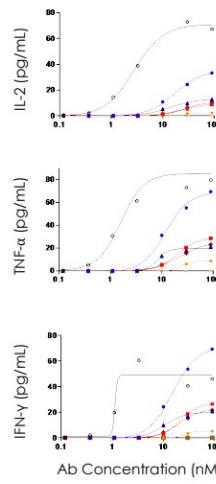
Binding

Activation

Cytokines



◆ SP34 Gen 1 benchmark



ShieldTx

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

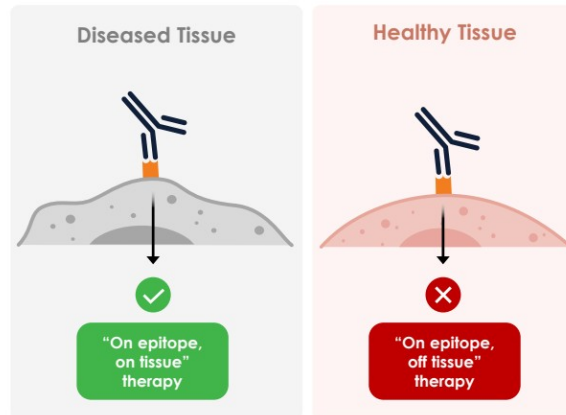
On-Target-Off-Tissue Side Effects Severely Limit The Potential of Existing And Future Antibodies

"(...) 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?

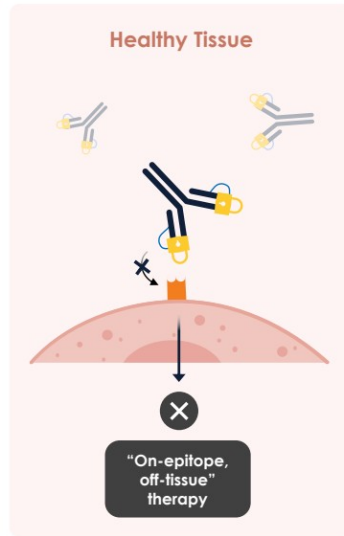
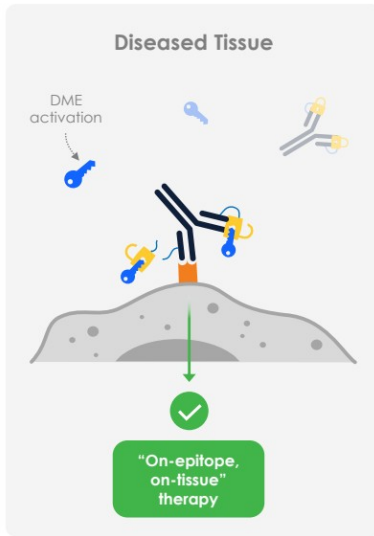


Our Engineered Epitopes Provide an Integrated Solution for Identifying And Subsequently Masking Antibodies

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



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	<i>Separate</i> antibody and mask discovery process is inefficient	<i>Co-discovery</i> of epitope-steered antibody and mask is more efficient
2 Masking performance	Separate discovery processes does <i>not</i> co-evolve an optimal antibody, mask, linker combination	<i>Co-evolution</i> of libraries of antibody, mask and linker for maximized effectiveness of masking and unmasking
3 Developability	Antibody + mask + linker combinations <i>not</i> screened for high developability in production cell lines	Mammalian-display libraries of antibody, mask and linker combinations screened for <i>developability</i> in production CHO cell lines
4 Immunogenicity	<i>Random</i> peptide or anti-idiotypic masks increase masked antibody immunogenicity risk	<i>Engineered epitope masks</i> 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

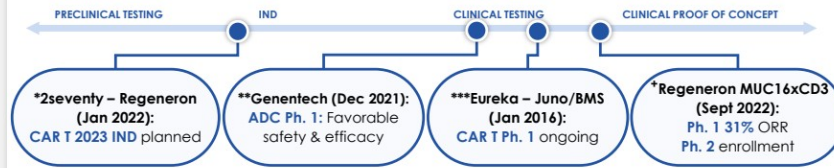
Potential Indications

- Ovarian
- Uterine
- Pancreatic

Differentiation / Opportunity

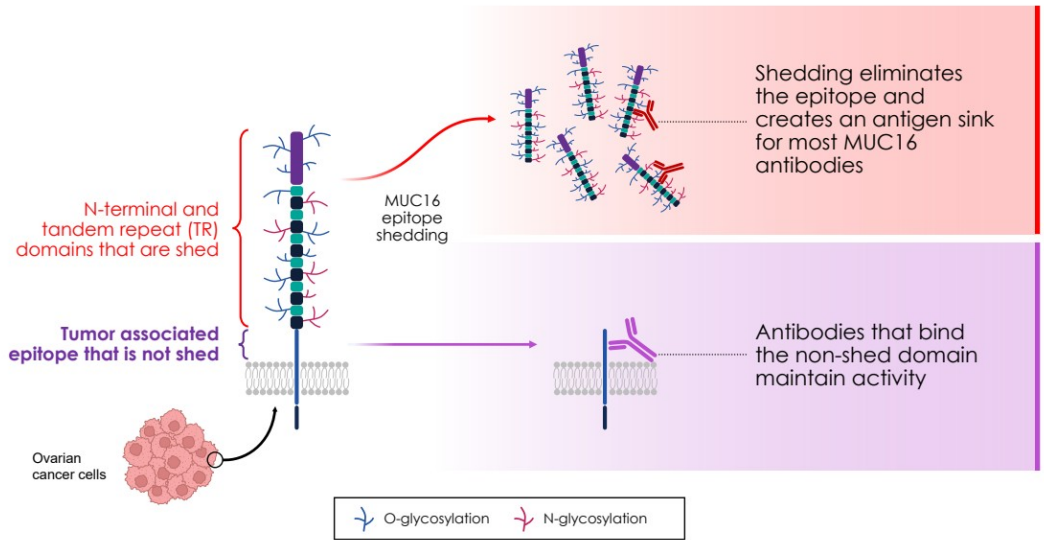
- MUC16 epitope avoids primary modes of tumor evasion
- Enabling modalities: T Cell engager, ADC, CAR-T

Recent Transactions & Milestones

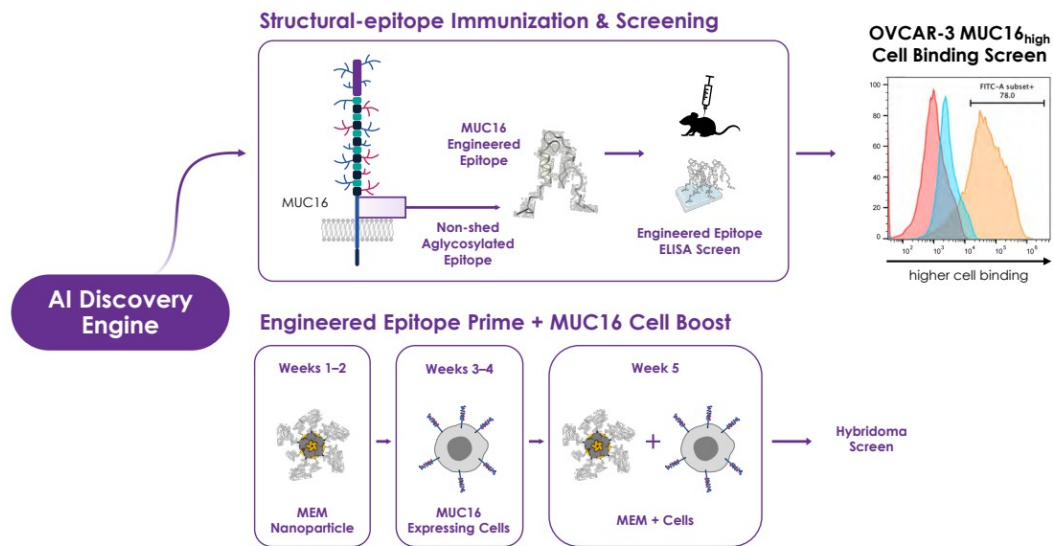


**Liu et al., An open-label phase I dose-escalation study of the safety and pharmacokinetics of DMUC4064A in patients with platinum-resistant ovarian cancer
 ***Eureka Therapeutics Announces Exclusive License Agreement between Memorial Sloan Kettering Cancer Center and Juno Therapeutics for Use of a Novel, Fully-Human MUC16 Binder in CAR T Cell Immunotherapy
 *Regeneron, Zseventy name the target of their first solid tumor CAR-T, aim for 2023 IND
 †Novel Regeneron Bispecific Antibodies Show Encouraging Anti-Tumor Activity in Two Advanced Solid Tumors

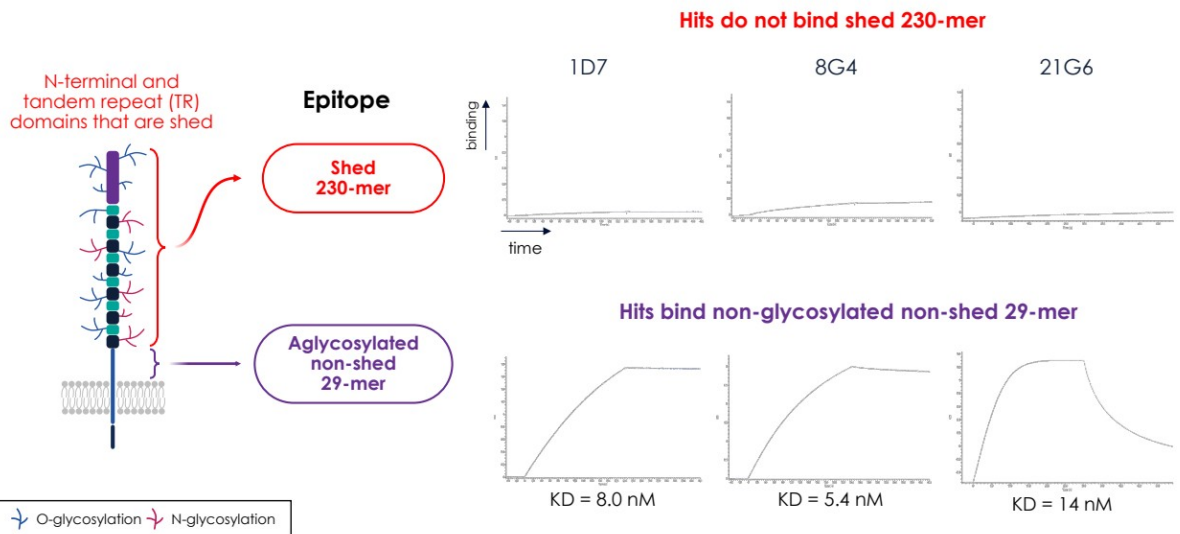
MUC16 Is Overexpressed and Shed by Tumor Cells



Immunizations Were Steered to a MUC16 Epitope that Avoids Epitope Shedding



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

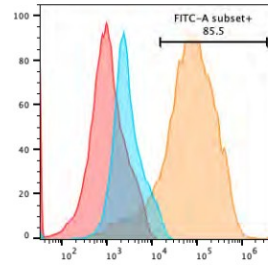
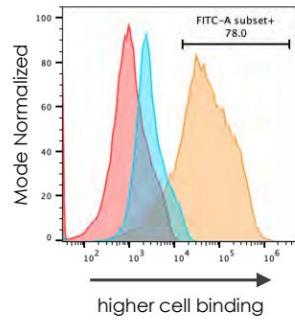


Top MUC16 Clone 8G4 Binds OVCAR-3 Cells Comparable to Regeneron Benchmark

Clone ID: 8G4
top clone

Regeneron
benchmark

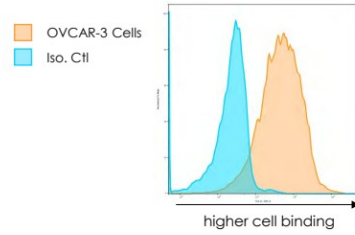
- Unstained
- Secondary Only
- OVCAR-3 Cells



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

8G4 with fully human framework reduces immunogenicity risk

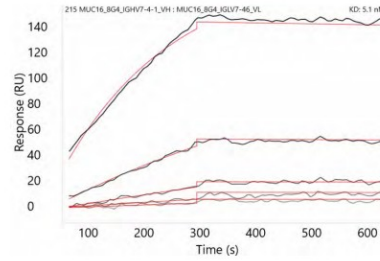
Cell binding



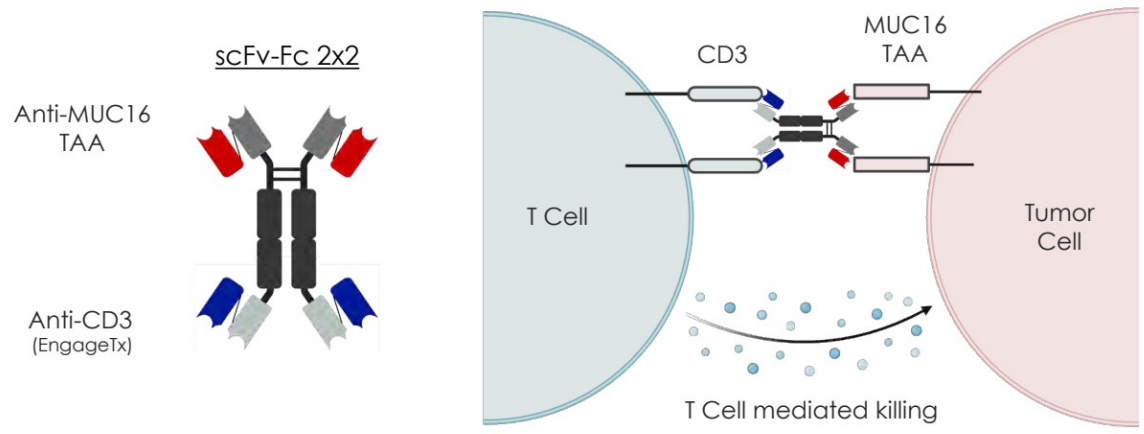
Glycosylated MUC16 membrane-proximal epitope SPR:

KD = 5.1 nM

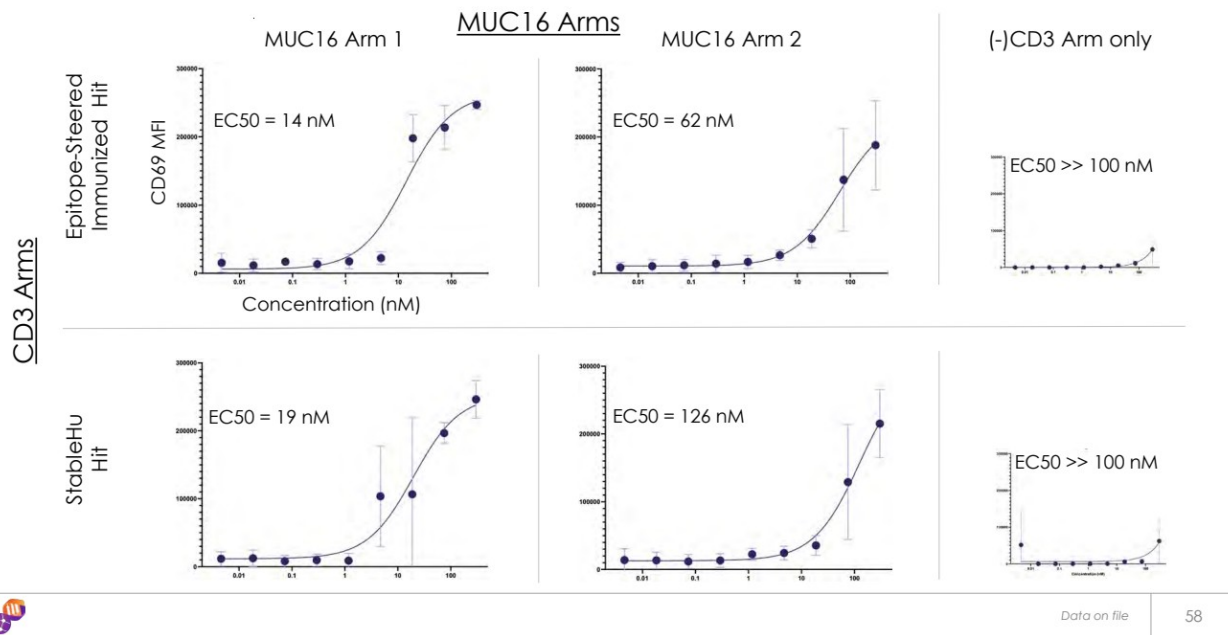
Epitope binding



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



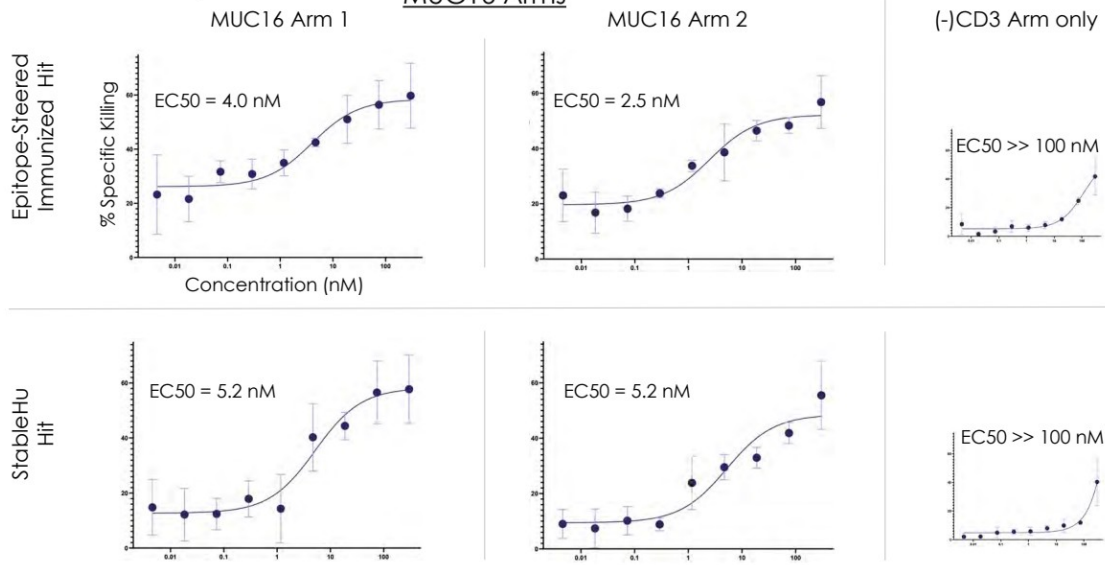
2X2 Anti-CD3 X MUC16 T Cell Engagers Stimulate T Cells in Donor PBMCs



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

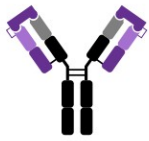
MUC16 Arms

CD3 Arms



ShieldTx Engineered Epitope Mask Conditionally Activates MUC16 and CD3 Hits

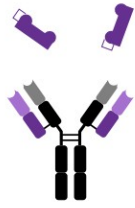
Engineered Epitope
Mask Intact



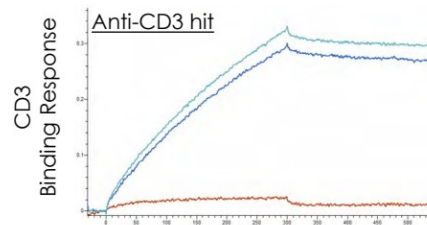
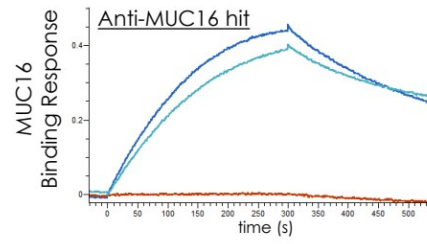
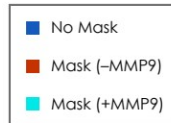
Inactive
Antibody



Mask Cleavage



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

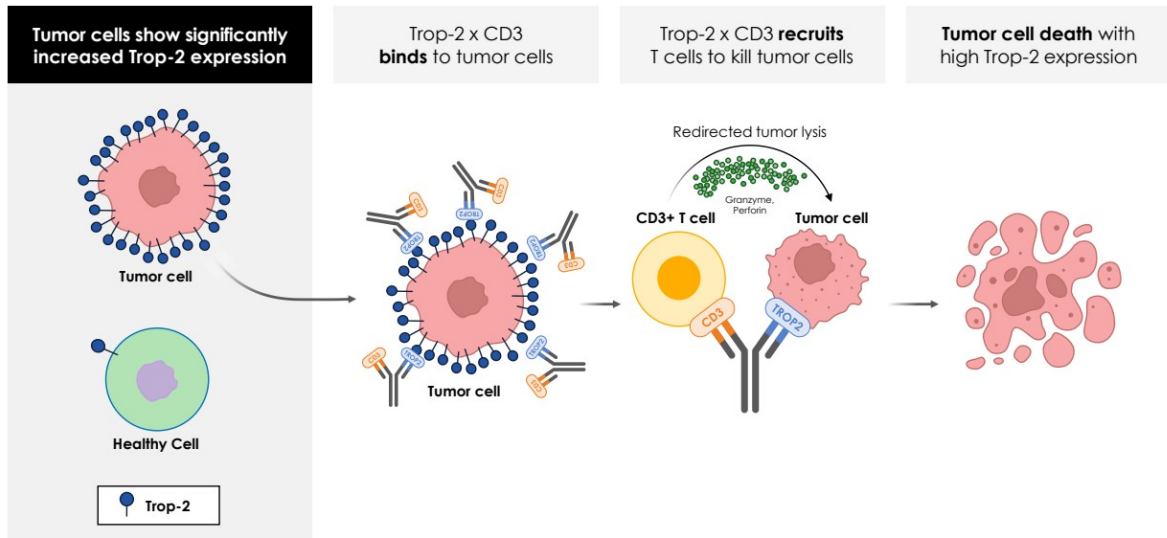
Differentiation / Opportunity

- 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

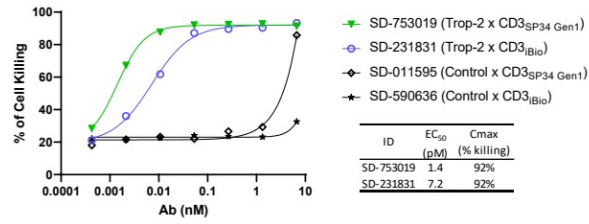


Trop-2 x CD3 Bi-Specific Antibody Selective Target Overexpress Trop-2 Cancer Cells

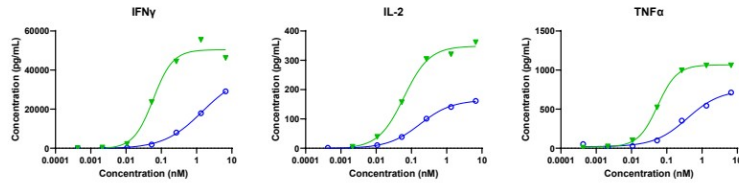


iBio's Trop-2 x CD3 Bi-Specific Antibody Potently Kills Tumor Cells with Low Cytokine Release

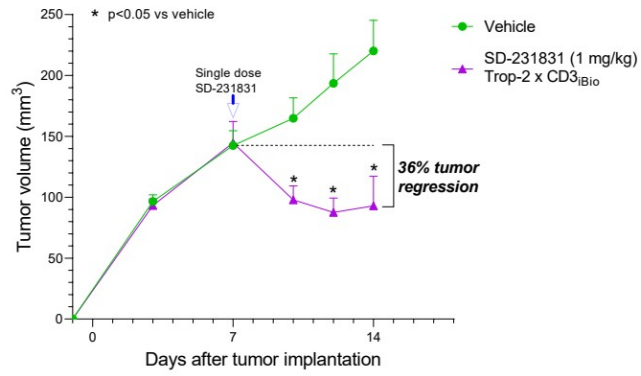
Potent Cancer Cell Killing



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.

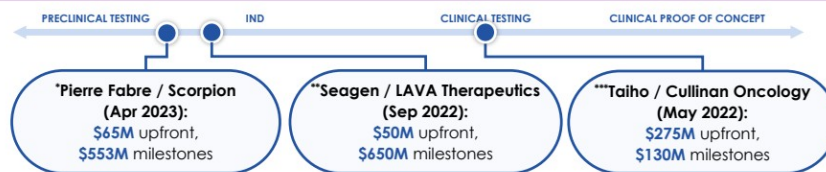
Potential Indications

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

Differentiation / Opportunity

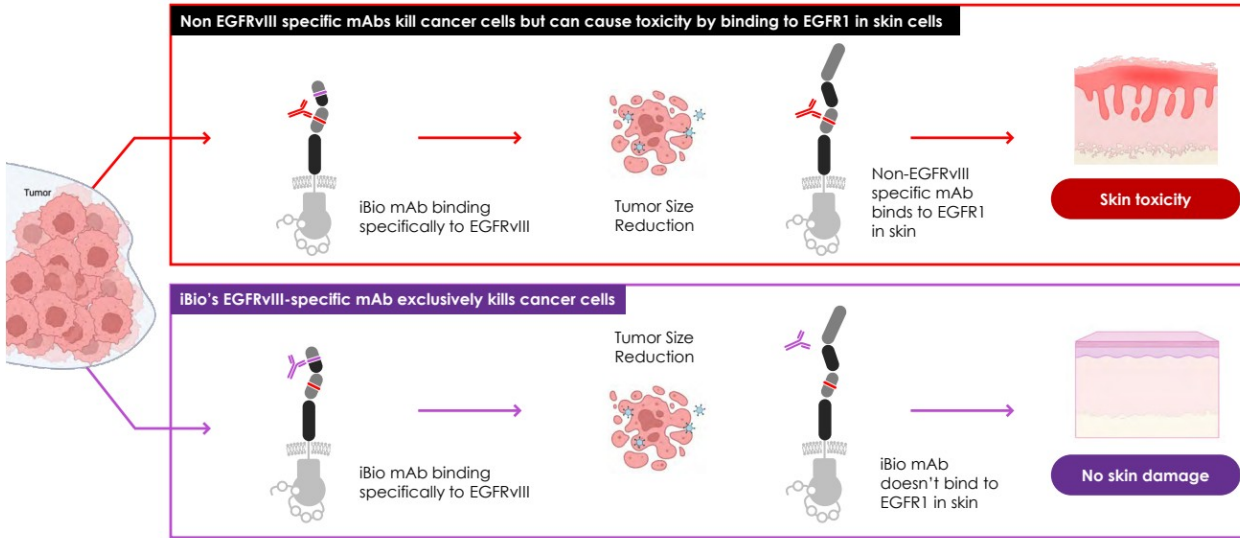
- Novel EGFRvIII high ADCC mechanism, potentially further reducing toxicity & expanding therapeutic window
- Other enabling modalities: T Cell engager, ADC, CAR-T

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/ITAS6417 (EGFR mutant mAb).

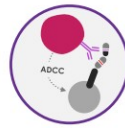
iBio's Anti-EGFRvIII mAbs Selectively Kill EGFRvIII-Positive Tumor Cells and Not EGFR1-Expressing Cells in Healthy Tissues



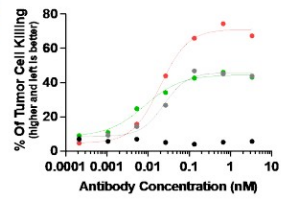
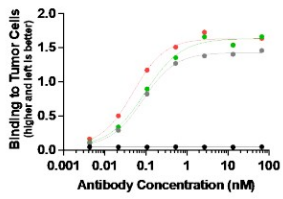
iBio's EGFRvIII-Selective mAbs Kill Tumor Cells without Affecting Healthy Cells



iBio EGFRvIII mAbs bind recombinant EGFRvIII



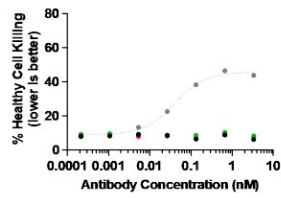
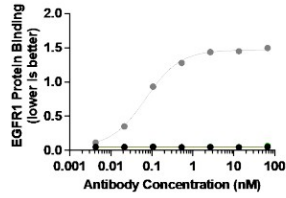
which leads to tumor cell killing



but not binding wild-type EGFR1



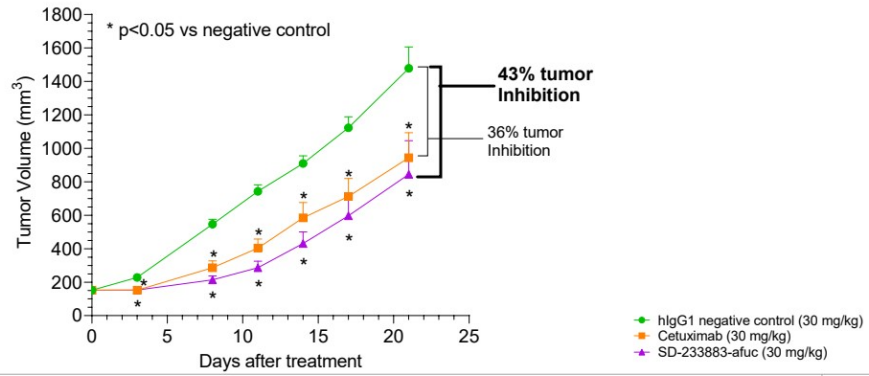
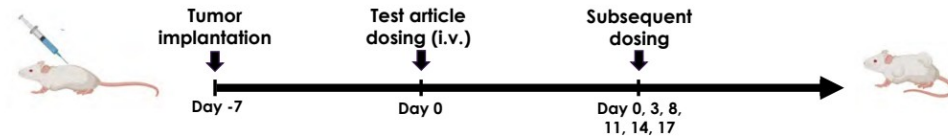
and thus not affecting healthy cells



- 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



Market-Tested Potential

Competitor Early-Stage Deals Signal Promising Opportunities

Market-Tested Potential: Immuno-Oncology Early-Stage Deals

Pre-2020	2021	2022	2023	2024
<p>SEP 2018</p> <p>CD25</p> <p>Roche / Tusk Therapeutics*: \$81M upfront, \$677M milestones</p> <p>SEP 2020</p> <p>CCR8</p> <p>Gilead / Jounce*: \$85M upfront, \$35M equity investment, \$685M milestones</p> <p>JUL 2020</p> <p>TROP-2</p> <p>AstraZeneca / Daiichi*: \$1B upfront (some deferred), \$5B milestones</p> <p>SEP 2020</p> <p>TROP-2</p> <p>Gilead / Immunomedics*: acquired for \$21B</p>	<p>FEB 2021</p> <p>PD-1 agonist</p> <p>Merck / Pandion*: acquired for \$1.85B</p> <p>JUN & DEC 2021</p> <p>CCR8</p> <p>Fibrogen / HiFiBio*: \$25M option fee, \$35M option exercise, \$1.1B milestones</p> <p>JUL 2021</p> <p>CD3</p> <p>Eli Lilly / Merus*: \$40M upfront, \$20M investment \$540M milestones</p> <p>JUL 2021</p> <p>CD3</p> <p>Amgen / Teneobio*: \$900M upfront, \$1.6B milestones</p> <p>DEC 2021</p> <p>ShieldTx</p> <p>Sanofi / Amunix* acquired for \$1B, \$225M milestones</p>	<p>MAY 2022</p> <p>EGFRvIII</p> <p>Taiho / Cullinan Oncology*: \$275M upfront, \$130M milestones</p> <p>AUG 2022</p> <p>PD-1 agonist</p> <p>Gilead / Mirobio*: acquired for \$405M</p> <p>SEP 2022</p> <p>EGFRvIII</p> <p>Seagen / LAVA Therapeutics*: \$50M upfront, \$650M milestones</p> <p>OCT 2022</p> <p>CD3</p> <p>Gilead / MacroGenics*: \$60M upfront, \$1.7B milestones</p> <p>NOV 2022</p> <p>ShieldTx</p> <p>Regeneron / Cytomx* \$30M upfront, \$2B milestones</p>	<p>JAN 2023</p> <p>CD3</p> <p>GSK / WuXi Biologics*: \$40M upfront, \$1.46B milestones</p> <p>JAN 2023</p> <p>CCR8</p> <p>Gilead / Jounce*: \$67M for remaining stake in CCR8 program</p> <p>APR 2023</p> <p>TROP-2</p> <p>BioNTech / Duality Biologics*: \$170M upfront, \$1.5B milestones</p> <p>APR 2023</p> <p>EGFRvIII</p> <p>Pierre Fabre / Scorpion*: \$65M upfront, \$553M milestones</p> <p>JUN 2023</p> <p>CCR8</p> <p>Coherus / Surface Oncology*: acquired for \$65M</p>	<p>DEC 2023</p> <p>CD25</p> <p>Neoleukin / Neurogene*: all-stock transaction</p> <p>JAN 2024</p> <p>TROP-2</p> <p>Biohaven / Pyramid*: acquired for \$55M</p> <p>MAR 2024</p> <p>TROP-2</p> <p>Merck / Harpoon*: acquired for \$680M</p> <p>APR 2024</p> <p>MUC16</p> <p>Regeneron / 2Seventy Bio: multi-asset purchase for \$5M upfront w/milestone</p>



* Acquisition / Merger
* License or collaboration