



Plasma Fractionation and Downstream Processing of Human Polyclonal Antibodies from the DiversitAb™ Platform

Plasma Product Biotechnology Conference | 2022

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Forward Looking Statements

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Novel DiversitAb™ Platform for Developing Highly-Differentiated Immunotherapies



Robust, growing clinical-stage pipeline spanning multiple therapeutic areas



Vertical integration enables rapid, scalable development of multi-targeted products



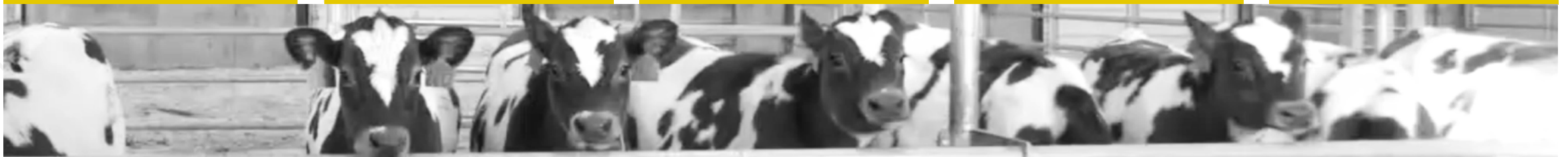
Leveraged advanced genetic engineering & antibody science to develop Tc bovine-derived fully-human polyclonal antibodies



Established proof-of-concept through US Government funded programs & partnerships totaling ~\$200MM



Strong corporate position with experienced leadership team and growing infrastructure



Innovative DiversitAb™ platform produces a new class of targeted fully-human, highly-potent polyclonal antibodies

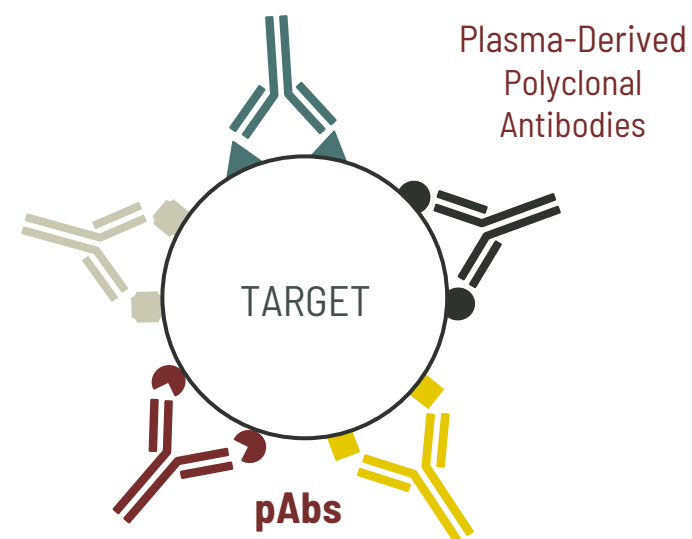
SAB Polyclonal Antibodies: Next Generation of Biologics



Key Product Differentiators:

- Multi-target capability in a single therapeutic
 - ✓ Natural multi-epitope targeted pAb selected and produced *in vivo*
 - ✓ Ability to target multiple antigens to disease
- Specifically driven high-potency antibody titers and avidity
- Naturally activates cellular immunity
- Ability to target human antigens

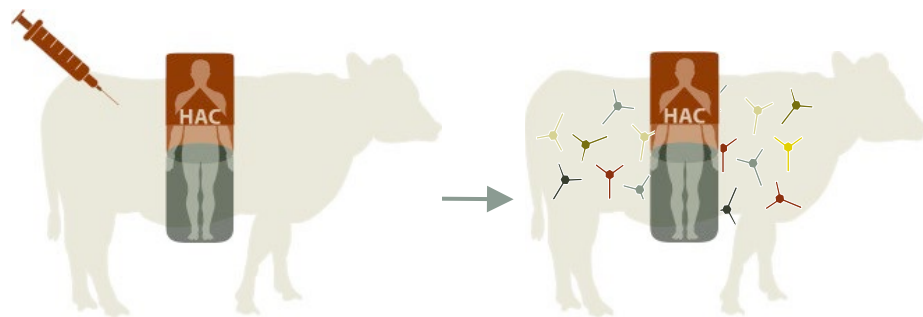
FDA: CENTER FOR **BIOLOGICS** EVALUATION & RESEARCH (CBER)



Natural mixture of many **human** antibodies that bind to multiple epitopes

A Natural Way to Produce Human Polyclonal Antibodies

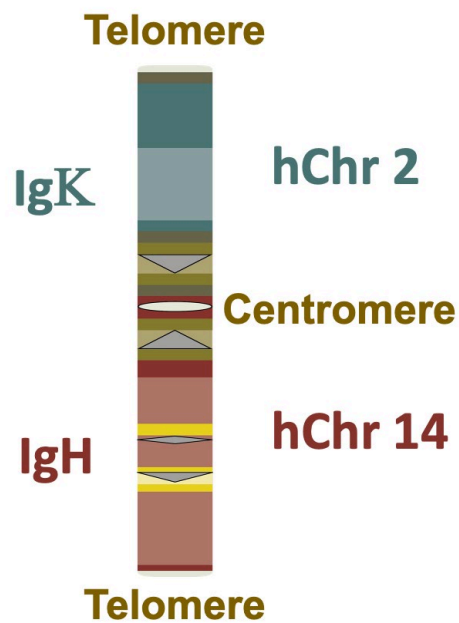
Tc Bovine™ contain all the human immunoglobulin genes



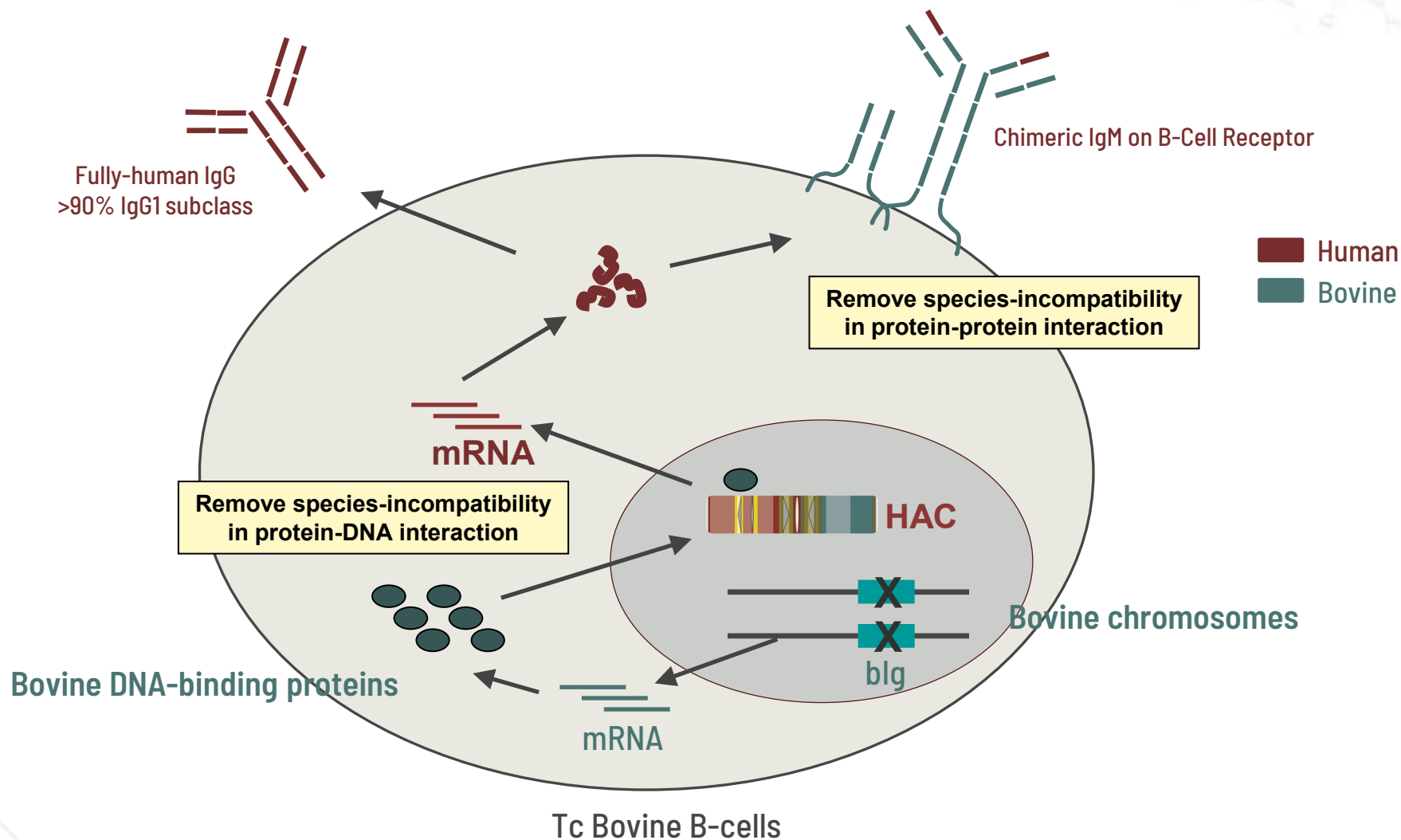
Tc Bovine

- Only transgenic animal that carries the entire human immunoglobulin (Ig) heavy and light (κ) chain loci.
- HAC is subject to mitosis along with the other 60 Tc Bovine chromosomes.
- HAC present in the Tc Bovine allows for the highest production of human antibody repertoire most similar to humans.

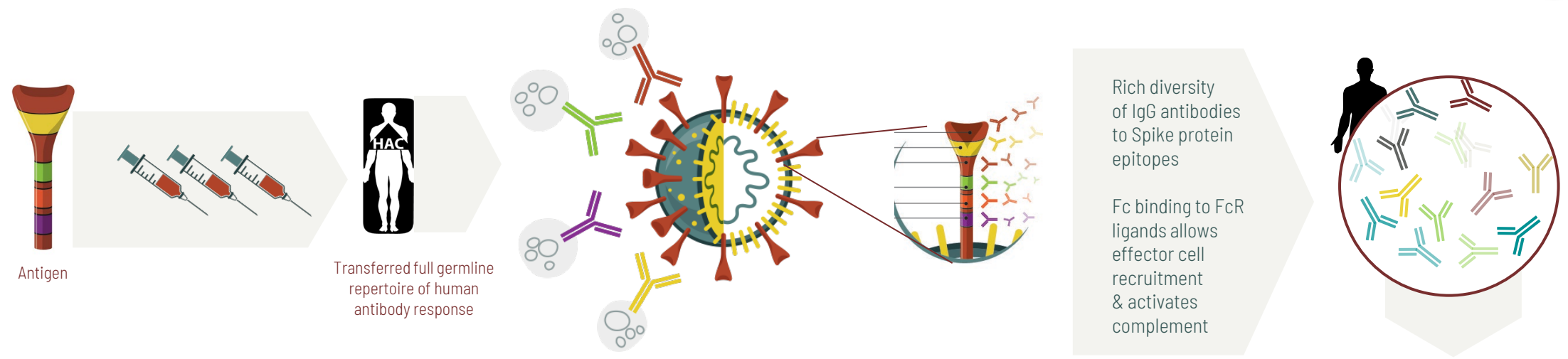
Human artificial chromosome (HAC)
 ~17Mb contains the entire unarranged VDJ human immunoglobulin loci (IgH + Ig κ)



Human Antibody Production in Bovine B-Cell



B-Cells Produce Anti-Target Fully-Human Polyclonal Antibodies



Antigen

Transferred full germline repertoire of human antibody response

Rich diversity of IgG antibodies to Spike protein epitopes

Fc binding to FcR ligands allows effector cell recruitment & activates complement

Hyperimmunization
Multiple immunizations drive titers to extremely high levels with exceptional avidity maturation and potency

B-Cells Produce Human Antibodies
Natural and somatic mutation drives very high-level B-cell clone avidity maturation in Tc Bovine

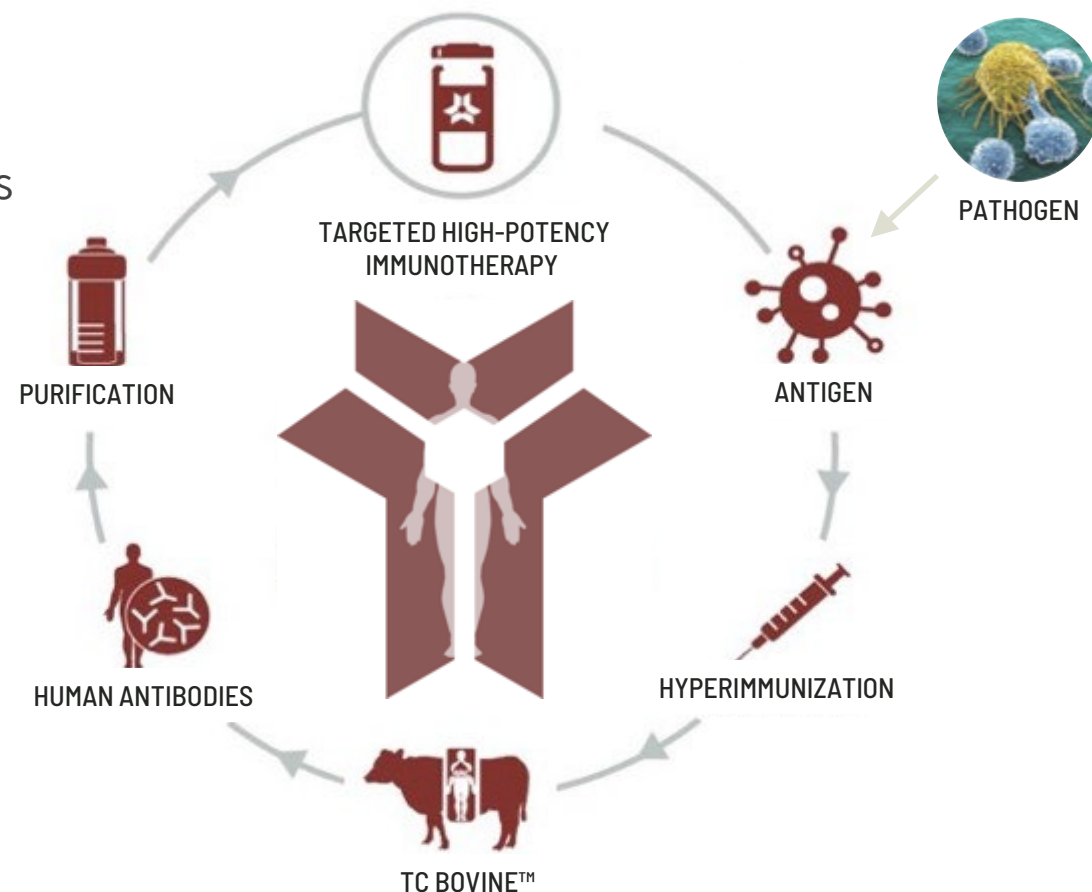
Therapeutic
Diverse mixture of anti-Target human polyclonal antibodies allowing production of a fully-human immunoglobulin (hIgG)

First of its Kind DiversitAb™ Platform



Advancing a new class of fully-human polyclonal Tc bovine-derived antibodies without the need for human serum

- Reliable, controlled, consistent production of diverse, high-titer, high-avidity, fully-human polyclonal antibodies
- Generated antibodies behave similarly to human-derived with ability to specifically target
- Proprietary immunization strategies and robust immune response drive extremely high potency
- Well-established and understood regulatory path as biologic through FDA-CBER
- Vertical integration enabling rapid, scalable development and production of multivalent products



Upstream Antibody Production



Procedures for Heterogeneity and Consistent Neutralizing Titers

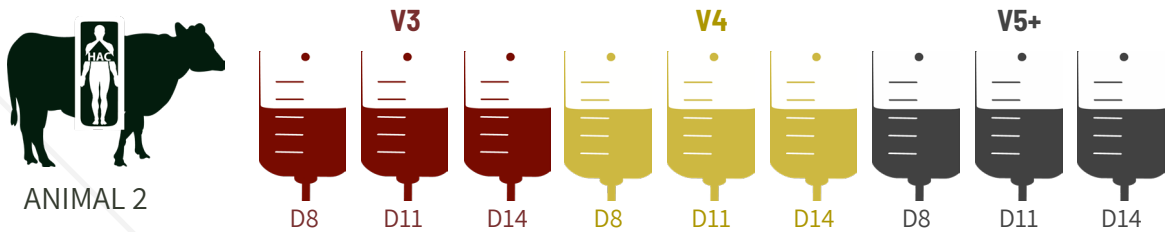
Vaccinate Every Three Weeks, One Animal = 30L Plasma/month



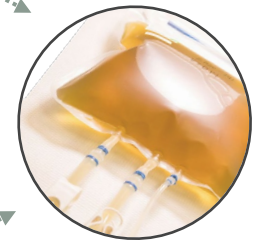
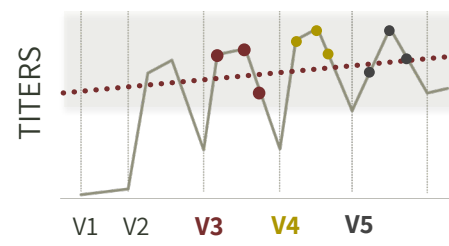
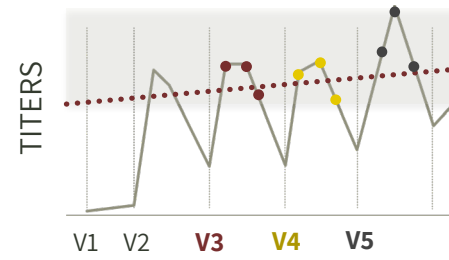
Continue Vaccinations & Collections



PLASMA COLLECTIONS



PLASMA COLLECTIONS



POOLED PLASMA

Downstream Manufacturing Process



Plasma Selection & Pooling

- Plasma selected to potency and impurity specifications
- Plasma thawed then pooled

Caprylic Acid Fractionation & Clarification

Caprylic Acid:
Precipitates bovine plasma proteins and HCP proteins

- pH adjustment
- Filter Aid – adheres insoluble proteins

Depth Filtration:
Clarifies

Effective Viral Clearance Step

- Neutralize and 0.22 filter

Chromatography

Chromatography steps include two affinity and one ion exchange

Positive Selection:
Captures human light chain

- Low pH hold for viral inactivation

Negative Selection:
Captures bovine heavy chain

TFF:
Prepare for Anion Exchange

Anion Exchange:
Anion Exchange used for polishing

Nanofiltration & Final Formulation

Nanofiltration:
Dedicated Viral Clearance Step

Final Formulation:
Concentrated and diafiltrated with Formulation Buffer

0.22um Filtered DS Bulk

Sterile filtered into bulk drug substance

Fill/finish DP

Bulk DS sterile filtered and filled into 10R glass vials.

Stoppered and capped.

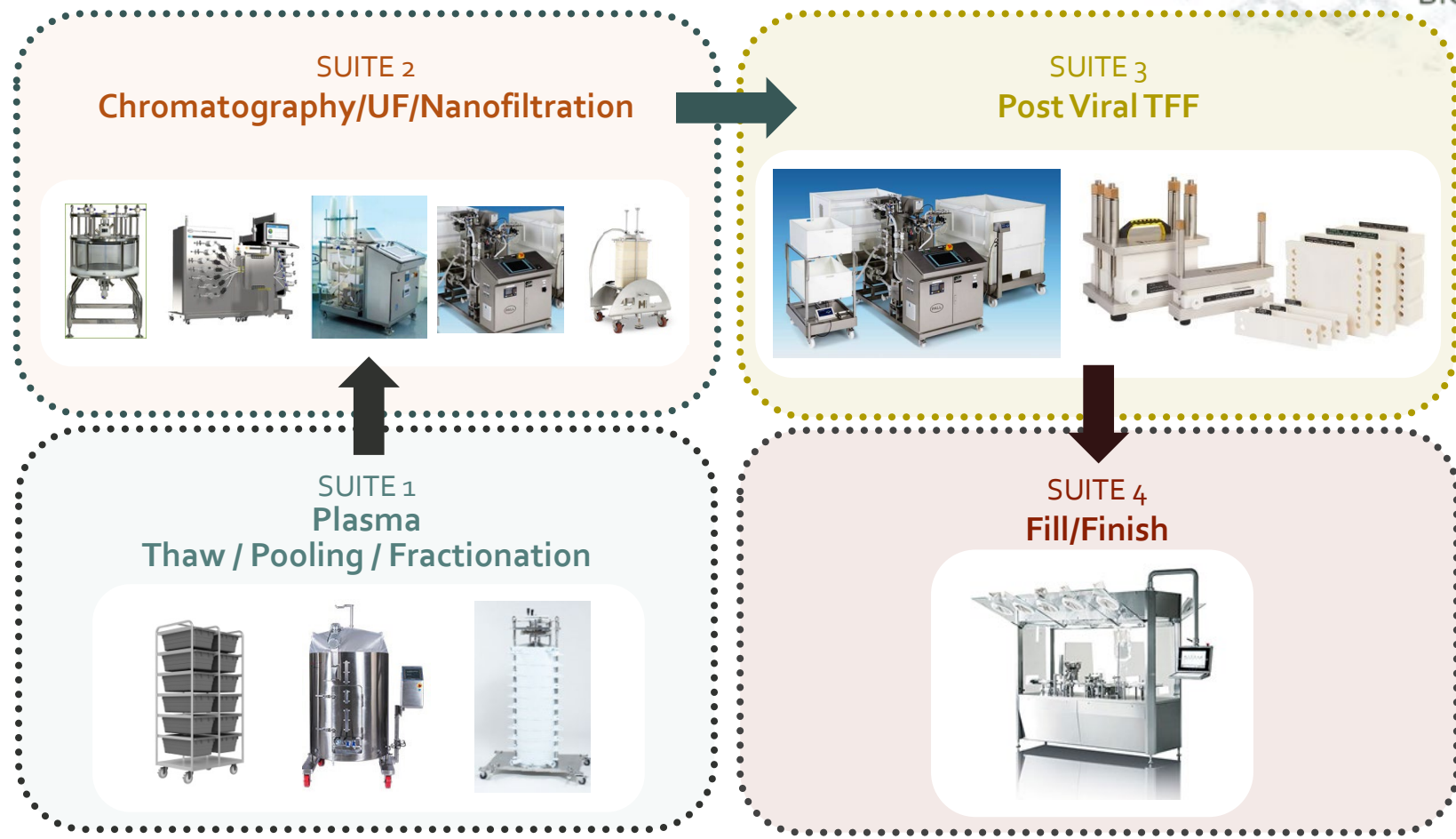
Tested and released.

Labeling & Distribution

Vials are labeled and boxed
Approved
Released



Manufacturing Step Process Overview



Scaled Infrastructure & Capacity: Laboratory & Manufacturing



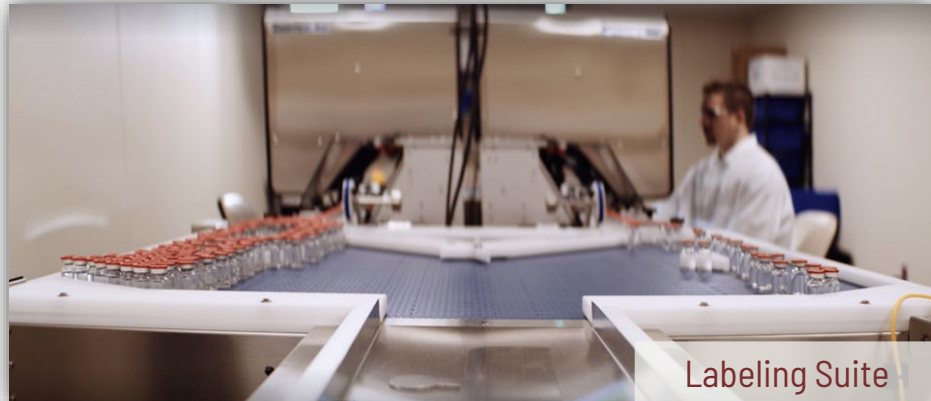
Manufacturing Facility (50L)



Manufacturing Facility (200L)



Fill Suite



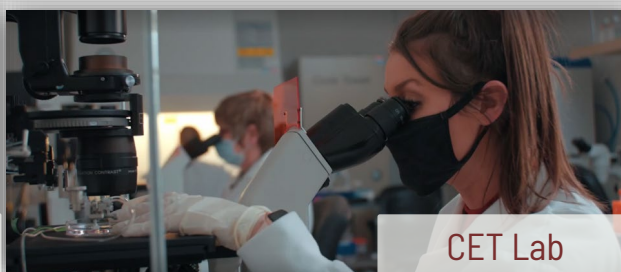
Labeling Suite



Cell Culture Lab

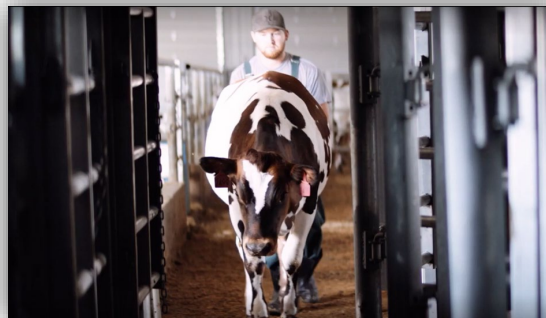


50L Suite



CET Lab

Scaled Infrastructure & Capacity: Tc Bovine & Plasma Production Facility



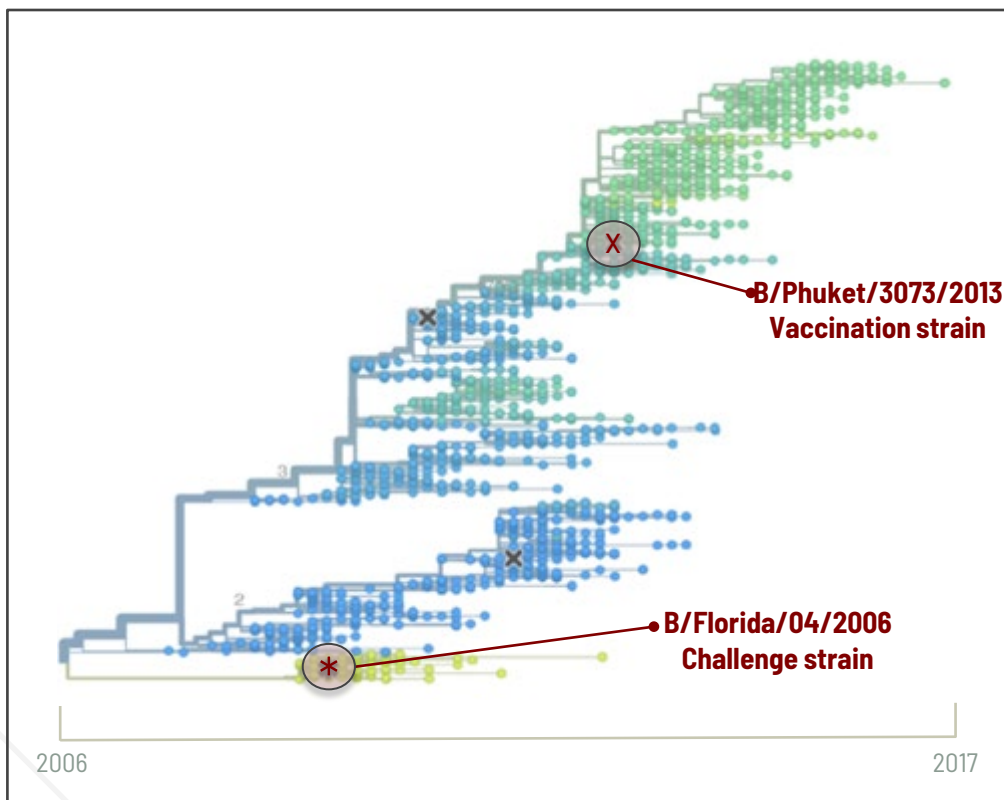
Efficacy Against Mutational Drift

Adaptive & Cross Reactive to Mutating Strains



Highly-Mutational Influenza Virus

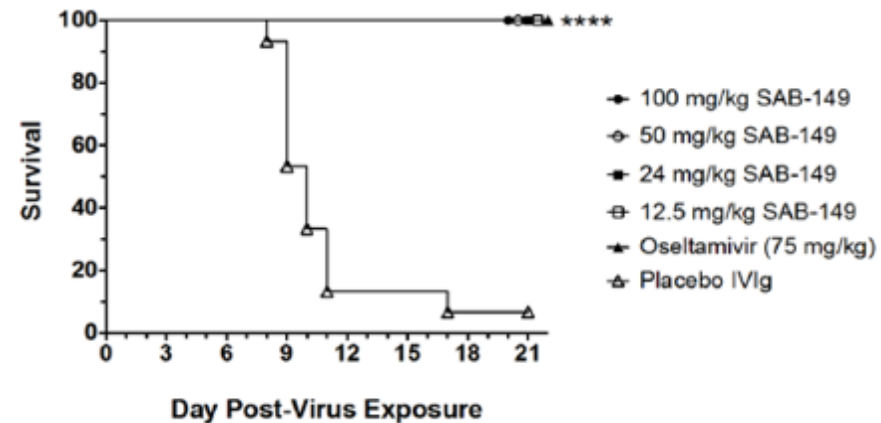
BYAM PHYLOGENIC TREE



SOURCE: NEXTFLU AT [HTTPS://NEXTFLU.ORG/VIC/12Y/](https://nextflu.org/vic/12y/)

100% Protection at All Dose Levels in Influenza Mouse Challenge

Antibodies produced to B/Phuket/3073/2013- like virus protected against B/Florida/04/2006



Highly-Potent: Exceeds Titers of Human Hyperimmune IVIG by up to 128X



SAB-176 protects against seasonal and pandemic influenza vaccine strains past & future non-vaccine strains

	Sample Started at 5mg/ml	H1N1				H3N2			B-Vic			B Yam	
		A/California/4/2009 (Pandemic Strain)	A/Michigan/45/2015	A/Brisbane/02/2018	A/Guangdong-maonan/2019	A/Singapore/INIFMH-16-0019/2016	A/Kansas/14/2017	A/Hong Kong/45/2019	B/Maryland/15/2016	B/Colorado/06/2017	B/Washington/02/2019	B/Phuket/3073/2013	B/California/12/2015
Anti-Influenza (Tc Bovine-derived quadrivalent hyperimmune)	SAB-176	1:1,024	1:512	1:512	1:512	1:512	1:512	1:256	1:256	1:256	1:128	1:256	1:128
		32X	16X	16-32X	16-32X	8-32X	16-128X	16-32X	16-32X	16-32X	16-32X	32X	16-32X
Anti-Influenza hIVIG (human-derived)	2018	1:32	1:32	1:32	1:32	1:64	1:32	1:16	1:16	1:16	1:8	1:8	1:8
	2017	1:32	1:32	1:16	1:16	1:64	1:32	1:16	1:16	1:16	1:8	1:8	1:8
	2013	1:32	1:32	1:32	1:16	1:16	1:4	1:8	1:8	1:8	1:4	1:8	1:4
Negative Control Antibody		<1	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1

Vaccine strain (season):

18-19

19-20

20-21

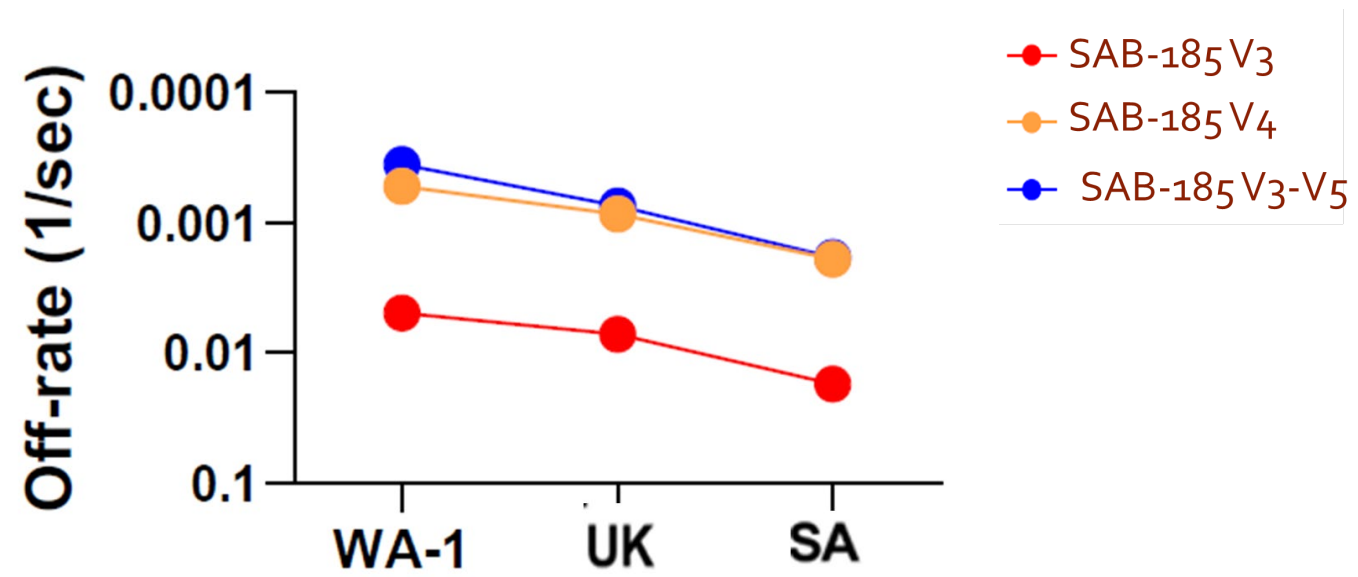
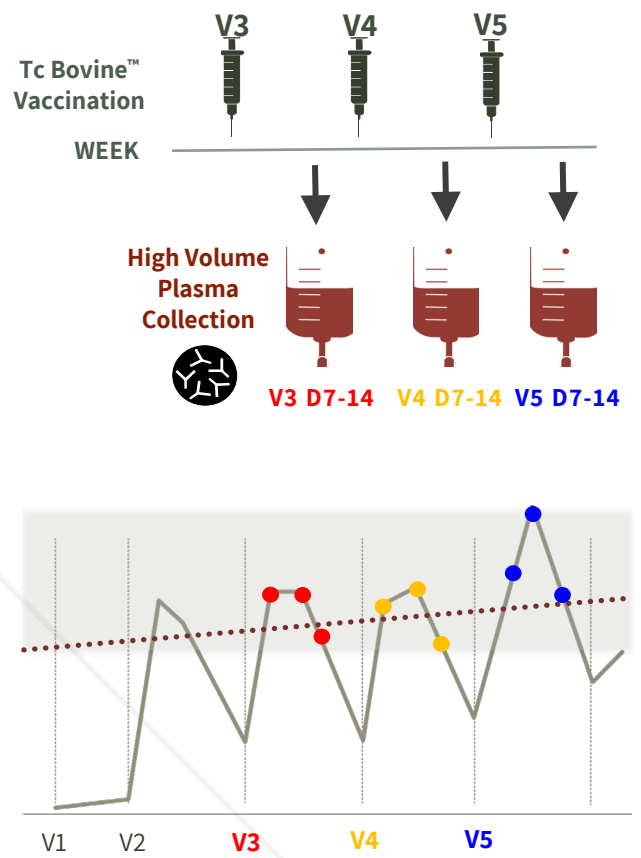
18-21

SAB-176 purified from TcB plasma vaccinated with 18-21 vaccine strain

HUBER LAB, USD, JUL 2021

High Avidity: Driven By Hyperimmunization

SAB-185 (Anti-SARS-CoV2) avidity increases with affinity maturation driven by hyperimmunization

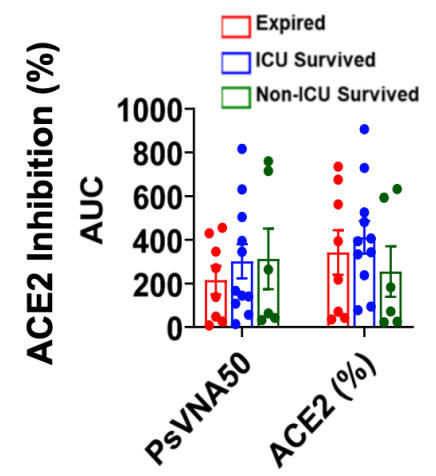


SURENDER LAB; DIVISION OF VIRAL PRODUCTS, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER) FDA 05 APR 2021
JOURNAL OF INFECTIOUS DISEASE (2022) SEP 4;226(4):655-663

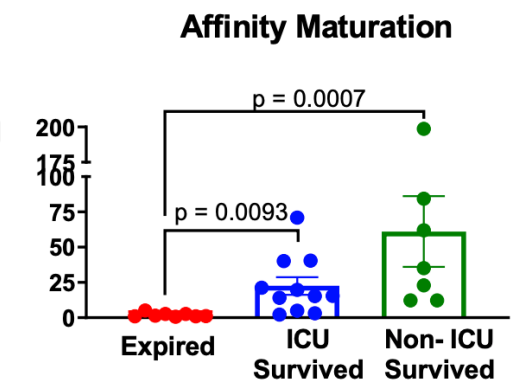
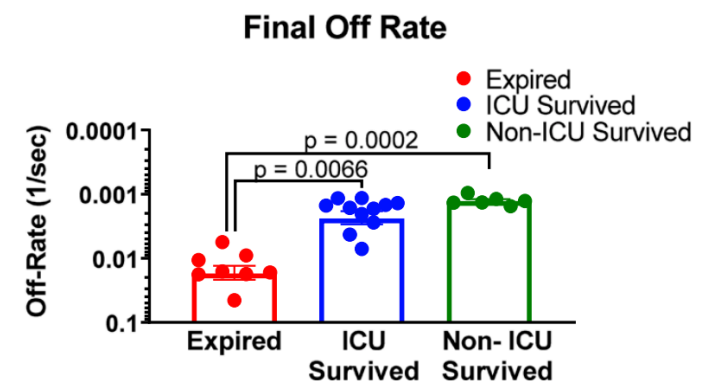


High Avidity More Closely Linked to Patient Outcomes than Neutralizing Titers

Neutralization Titers Demonstrate Discordance to Disease Severity & Outcome



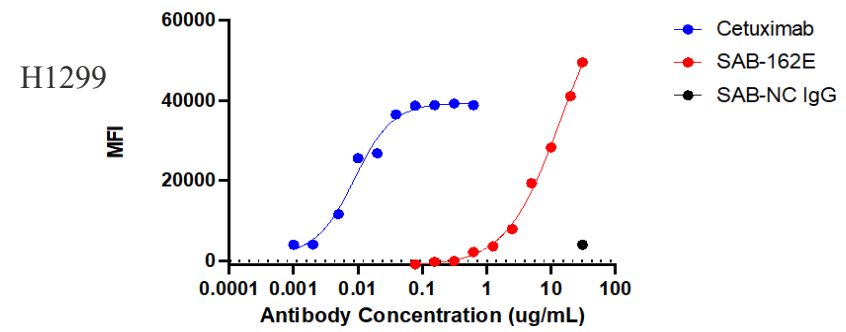
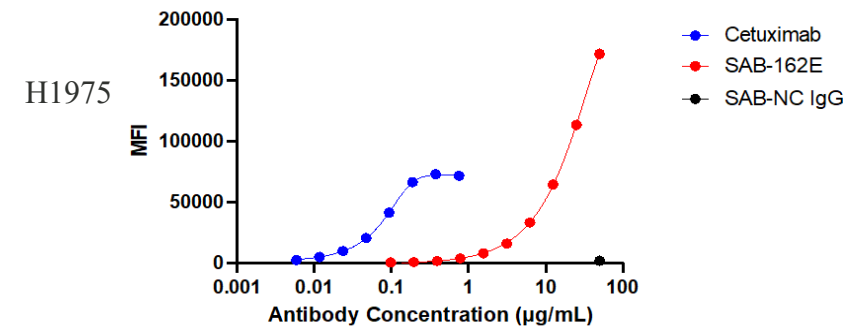
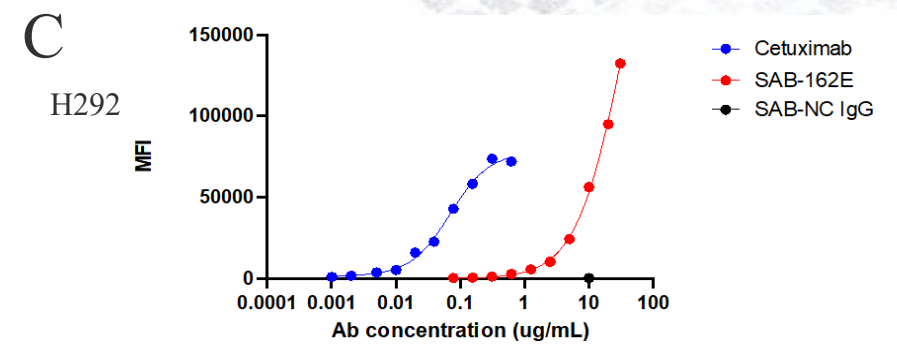
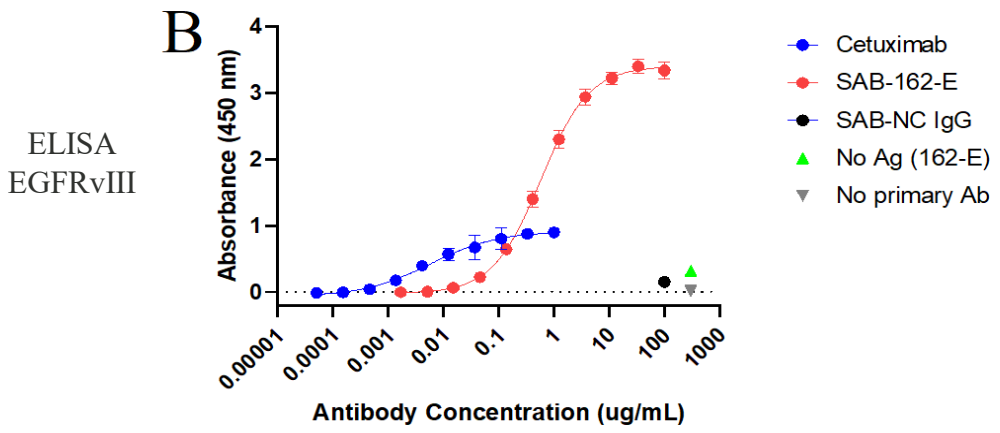
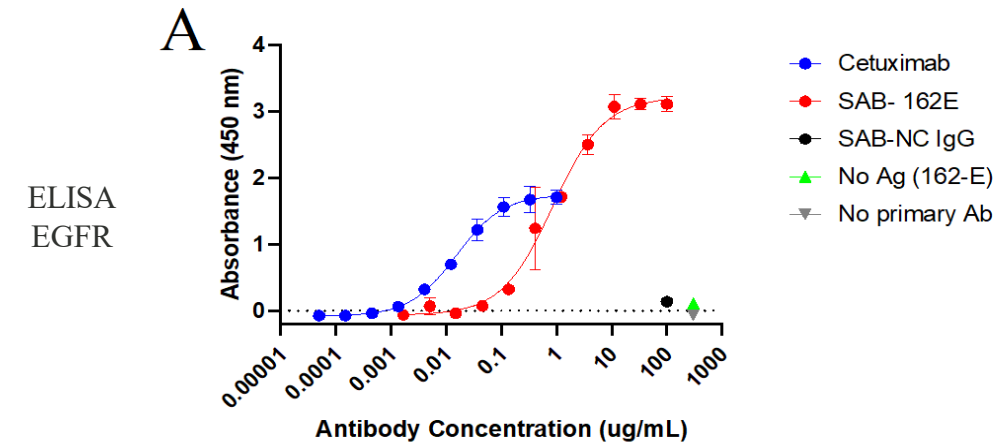
High Avidity Shows Direct Correlation to Patient Survival



Neutralizing antibody titers and hACE2 receptor inhibition activity of COVID-19 patients' plasma during hospitalization

SURENDER LAB; DIVISION OF VIRAL PRODUCTS, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER) FDA; NATURE COMMUNICATIONS (2021) 12:1221

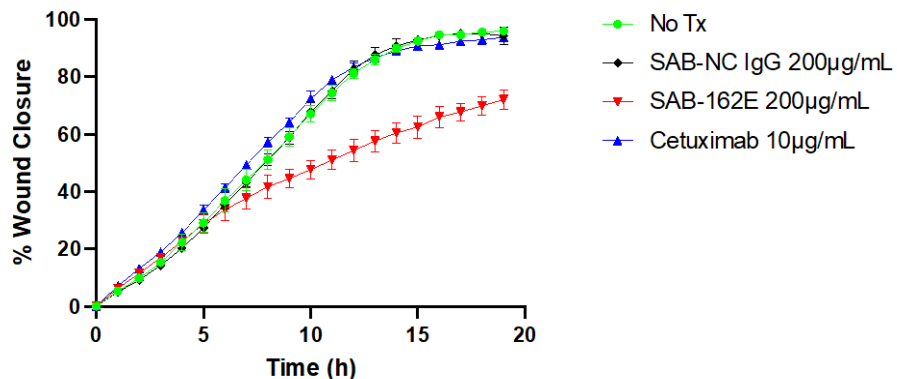
Oncology SAB-162E (Human Anti-Human EGFR pAbs) Exhibits High Binding Capability



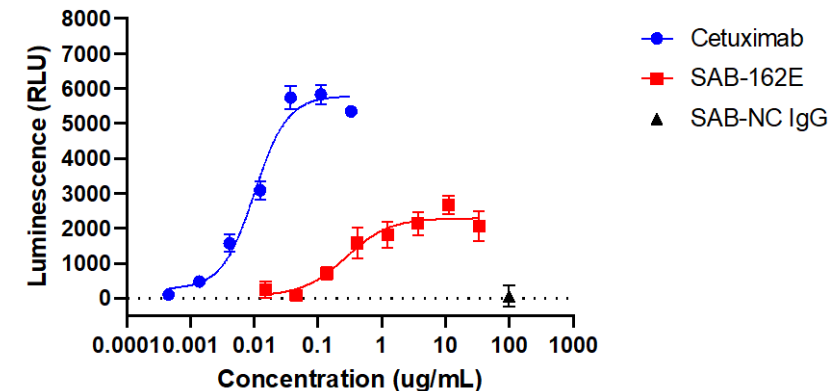
SAB-162E has Functional Properties for Addressing the Complexity of Cancer



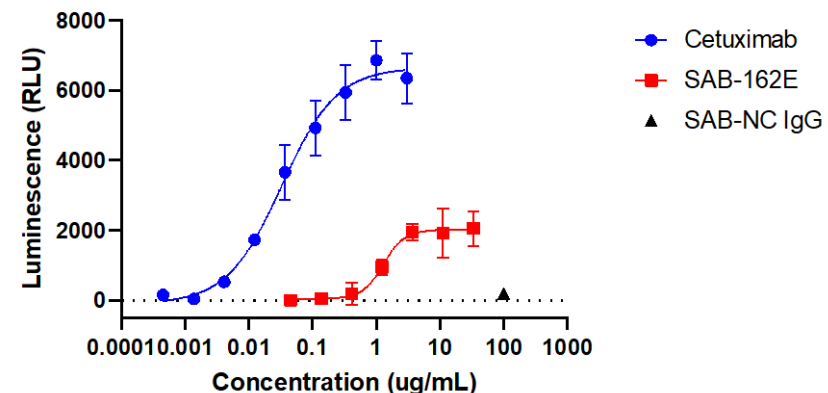
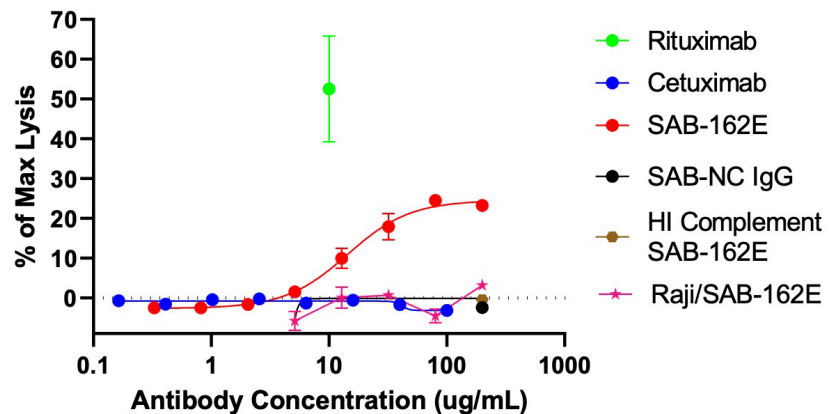
A SAB-162E inhibits cellular migration of NSCLC cells



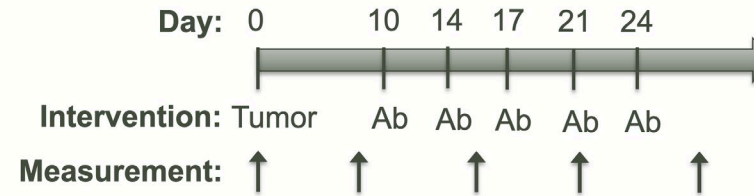
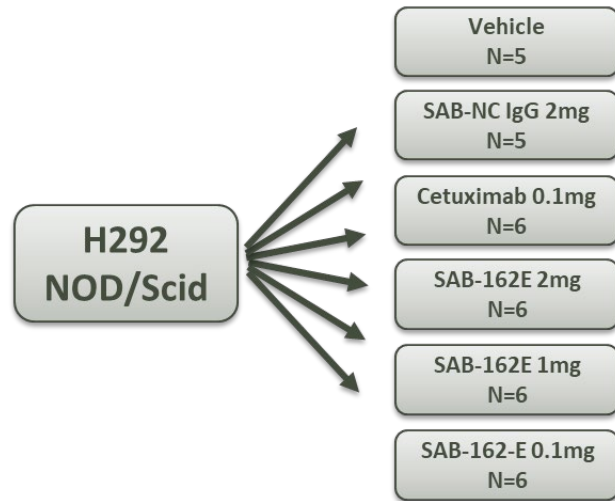
C SAB-162E activates ADCC effector function



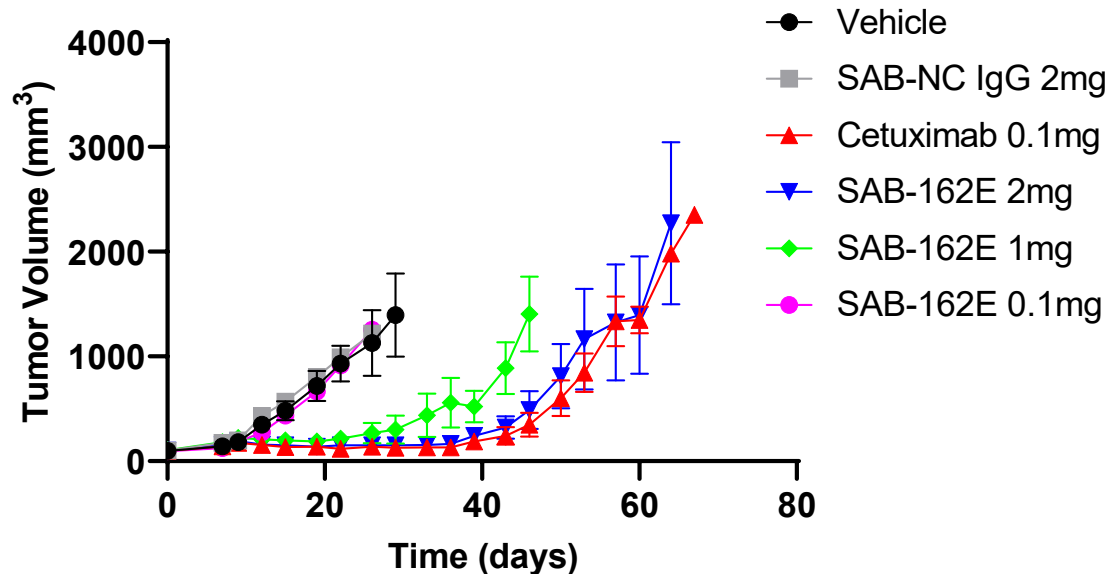
B SAB-162E activates CDC effector function



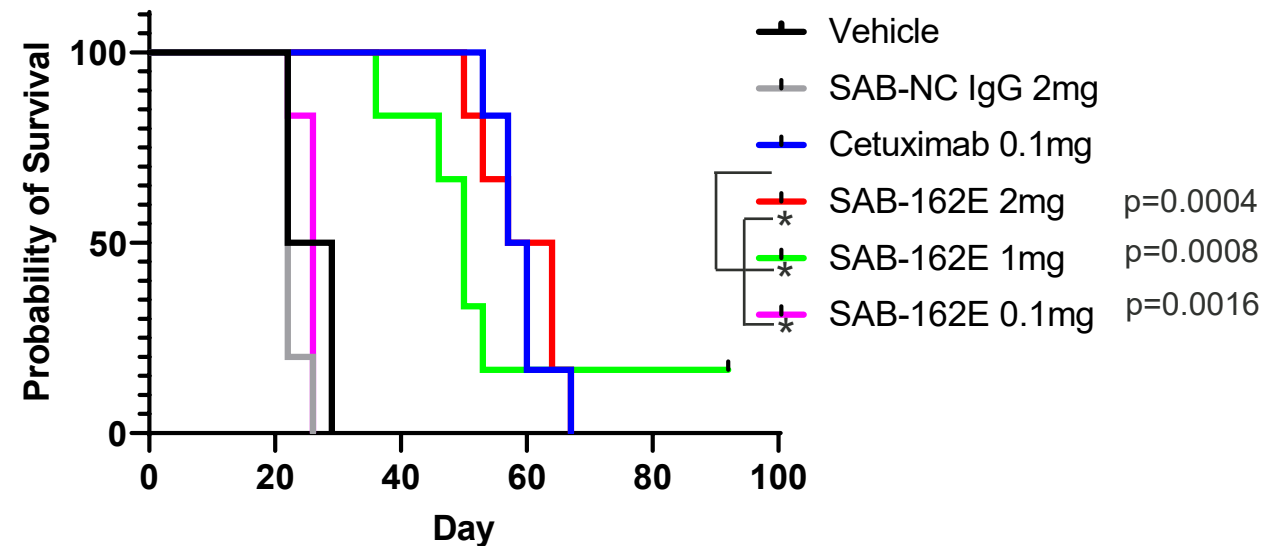
in vivo Efficacy Study for SAB-162E (NOD/SCID mice)



Average Tumor Volume



Survival





Consistent, Replicable Platform

In Vivo Efficacy Demonstrated Across a Broad Range Targets

TARGET	EFFICACY	MODEL(S)	COLLABORATORS
Anthrax	100%	mouse (lethal)	Food and Drug Administration
Alphaviruses	100% 100%	mouse (lethal aerosol) non-human primate (viral clearance)	Naval Medical Research Center, University of Pittsburgh, NIH: National Institute of Allergy and Infectious Diseases
Clostridioides Difficile	100% 87%	hamster (lethal) mouse (lethal)	Novavax
Dengue	100%	non-human primate (viral clearance)	Naval Medical Research Center
Ebola	90% 100%	mouse (lethal) non-human primate (lethal)	Naval Medical Research Center, NIH: National Institute of Allergy and Infectious Diseases, Novavax
Hantavirus	80-100% 100%	hamster (lethal) non-human primate (viral clearance)	United States Army Medical Research Institute of Infectious Diseases
Influenza	100% 100%	mouse (lethal) mouse (lethal aerosol)	National Institutes of Health, University of South Dakota, Utah State University, Naval Medical Research Center
Plague	100%	Mouse (lethal aerosolized)	United States Army Medical Research Institute of Infectious Diseases
MERS-CoV	100%	mouse (viral clearance)	Biomedical Advanced Research and Development Authority, Naval Medical Research Center, NIH: National Institute of Allergy and Infectious Diseases, Novavax
SARS-CoV2	100%	hACE2 hamster (lethal)	Biomedical Advanced Research and Development Authority, Naval Medical Research Center, University of Pittsburgh
Zika	100% 100% 100%	mouse (lethal) hamster (lethal) non-human primate (viral clearance)	Public Health Agency of Canada, Utah State University Harvard University