SAb BIOTHERAPEUTICS

Leveraging Genetically Engineered Ungulates to Produce Novel Human Biotherapeutic

Large Animal Genetic Engineering Summit, June 2022

Forward Looking Statements

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Unless otherwise specified, information is current at the date hereof, unless specifically noted.

Novel DiversitAb™ Platform for Developing Highly-Differentiated Immunotherapies

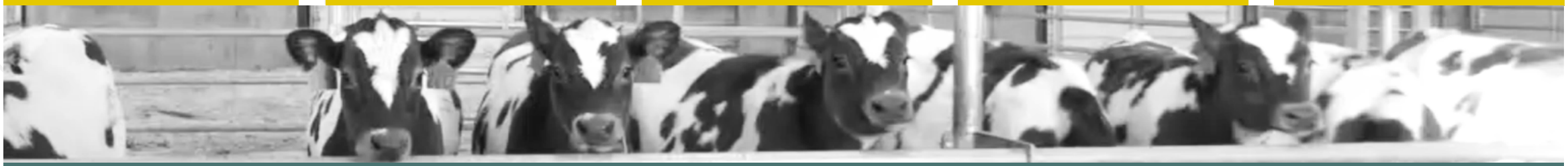
Robust, growing clinical-stage pipeline spanning multiple therapeutic areas

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

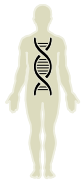
Established proof-of-concept through US Government funded programs & partnerships totaling ~$200MM

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

DiversitAb™ Proprietary Platform Technology



Human DNA
Human genes for antibody production

Human Chromosomes
Chromosomes isolated for antibody production

Human Artificial Chromosome (HAC)
Constructed vector for carrying human antibody production genes

HAC in CHO Cell
HAC vector replicated in hamster CHO cell

Microcell-Mediated Chromosome Transfer (MMCT)

HAC Bovine Fibroblast Cell
HAC vector inserted in Ig knockout bovine cell line

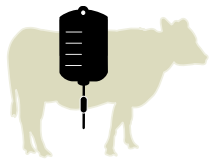
Chromatin Transfer (Cloning)

Embryo Transfer
Embryo inserted into qualified recipient cow to gestate calf

Tc Bovine™
Transchromosomic bovine genetically designed to produce human antibodies

Hyperimmunization
Tc Bovine inoculated with target disease antigen to generate antibodies

Human Antibody Production
Bovine produce human antibodies to disease target that circulate in the blood stream



Plasmapheresis
Antibodies are collected in the form of plasma

Purification
Purification process isolates antibodies from plasma

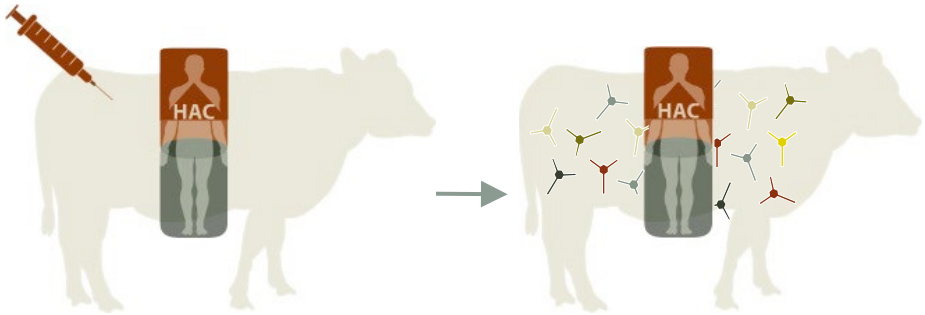
Human Antibodies
Purified and formulated human polyclonal antibodies

Testing
Each lot of material is tested to ensure safety and potency

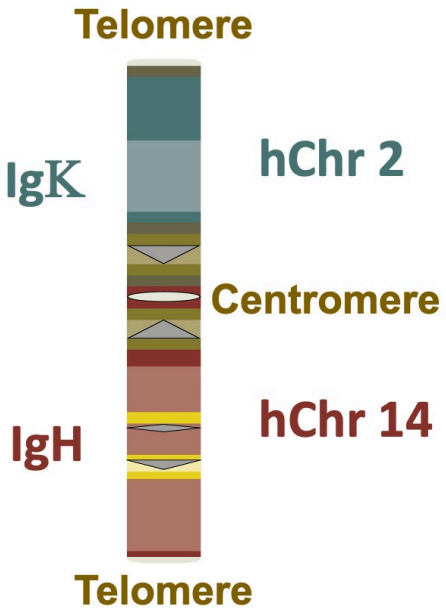
Immunotherapy
Therapeutic for treatment of human patient

A Natural Way to Produce Human Polyclonal Antibodies

Tc Bovine™ contain all the human immunoglobulin genes



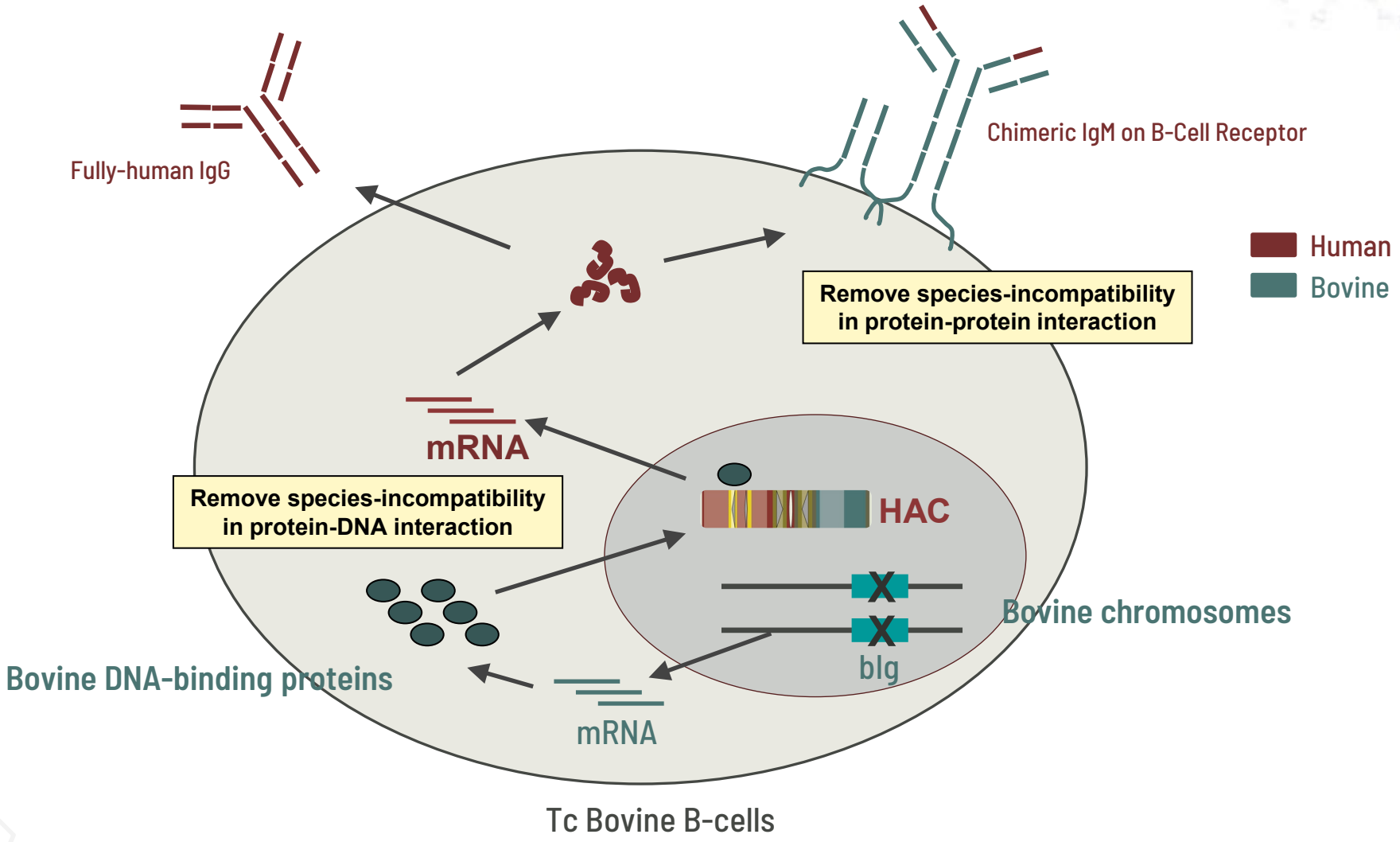
Human artificial chromosome (HAC) contains the entire human immunoglobulin loci (IgH + Igκ)



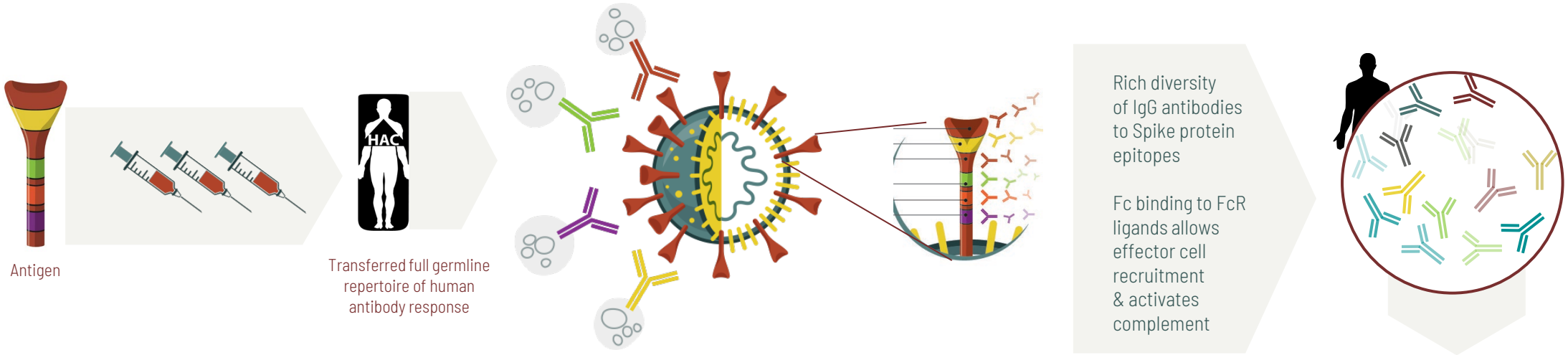
Tc Bovine

- 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 chromsomes.
- HAC present in the Tc Bovine allows for the highest production of human antibody repertoire most similar to humans.

Human Antibody Production in Bovine B-Cell



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



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)

Polyclonals: Broader Spectrum Efficacy Valuable in Range of Indications

FDA: CENTER FOR **DRUG** EVALUATION & RESEARCH (CDER)

Characterized Monoclonal Antibody

mAb

Clones of a single antibody bind to a specific epitope

Monoclonal Approach

- Highly-targeted with specific activity
- Iterative Ab identification and selection process
- Selected and cloned *in vitro*
- May promote escape mutants via selective pressure
- Resistance may develop as pathogen/target mutates
- Current cocktail trend to address resistance

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

Plasma-Derived Polyclonal Antibodies

pAbs

Natural mixture of many antibodies bind to multiple epitopes

Polyclonal Approach

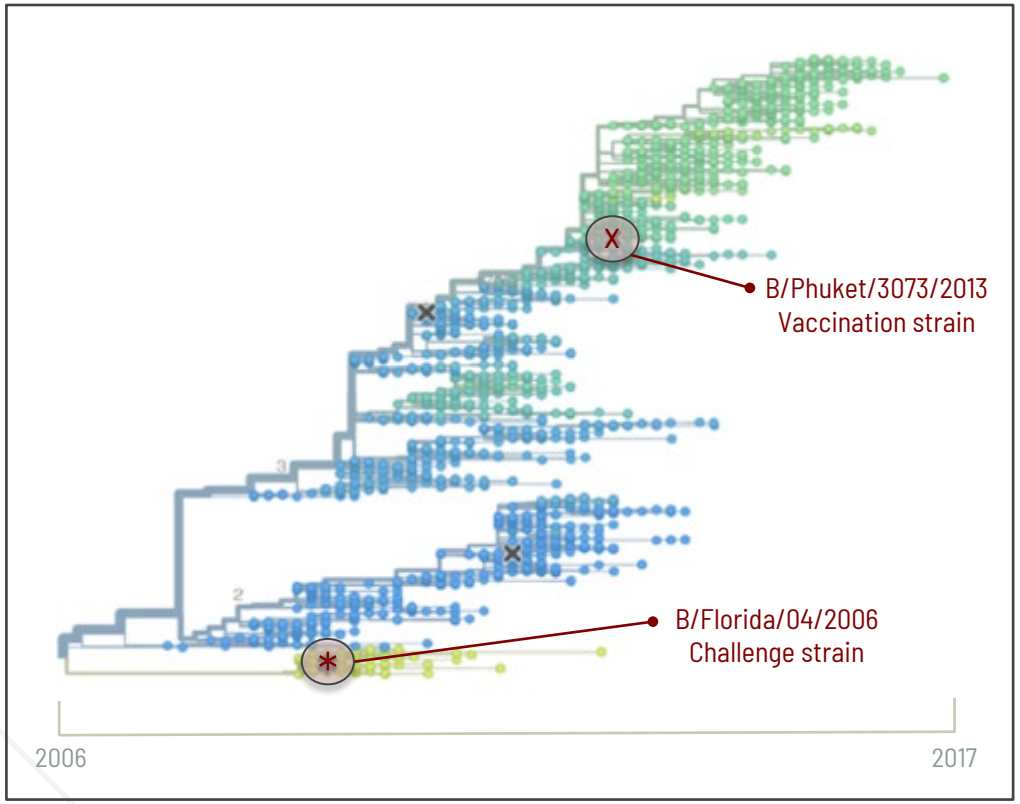
- Diversity of antibodies with multiple modalities
- Naturally selected and produced *in vivo*
- Effective against escape mutants
- Reduced possibility of resistance
- Activates cellular immunity
- Synergistic properties not duplicated by mono- or oligoclonals

Efficacy Against Mutational Drift

Adaptive & Cross Reactive to Mutating Strains

Highly-Mutational Influenza Virus

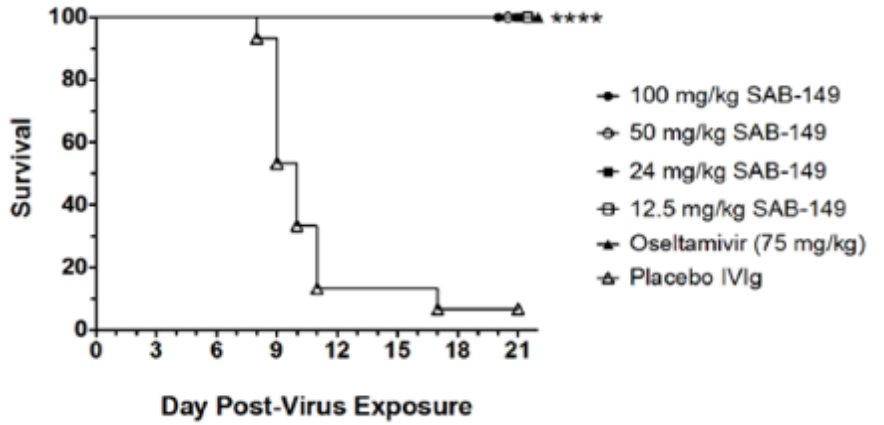
BYAM PHYLOGENIC TREE



SOURCE: NEXTFLU AT HTTPS://NEXTFLU.ORG/VIC/12Y/

100% Protection at All Dose Levels in Influenza Mouse Challenge

Antibodies produced to **B/Phuket/3073/2013** protected against **B/Florida/04/2006**



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
Clostridium 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
Zika	100% 100% 100%	mouse (lethal) hamster (lethal) non-human primate (viral clearance)	Public Health Agency of Canada, Utah State University Harvard University

*Current DoD interest

Human Clinical Trial Experience

Clinical Trial Proof of Concept

CLINICAL TRIAL	INDICATION	COLLABORATORS
Phase 1b	Mycoplasma hominis	Brigham and Women's Hospital, Harvard
Phase 1	MERS-CoV	Naval Medical Research Center; NIH NIAID
Phase 1	Type A and B Influenza	Naval Medical Research Center; University of South Dakota
Phase 2a	Type A and B Influenza	Naval Medical Research Center; University of South Dakota
Phase 1	SARS-CoV2	DoD; BARDA; University of Pittsburgh
Phase 1b	SARS-CoV2	DoD; BARDA; University of Pittsburgh
Phase 2	SARS-CoV2	DoD; BARDA; DAIDS NIH NIAID; University of Pittsburgh
Phase 3	SARS-CoV2	DoD; BARDA; DAIDS NIH NIAID; University of Pittsburgh

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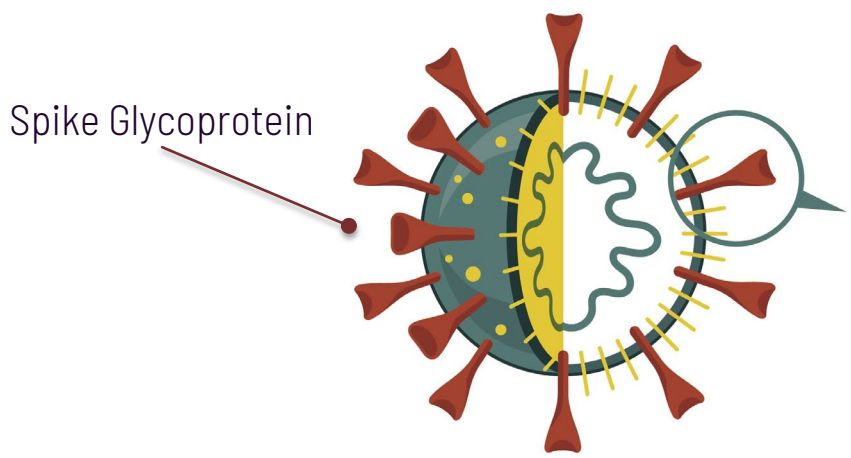
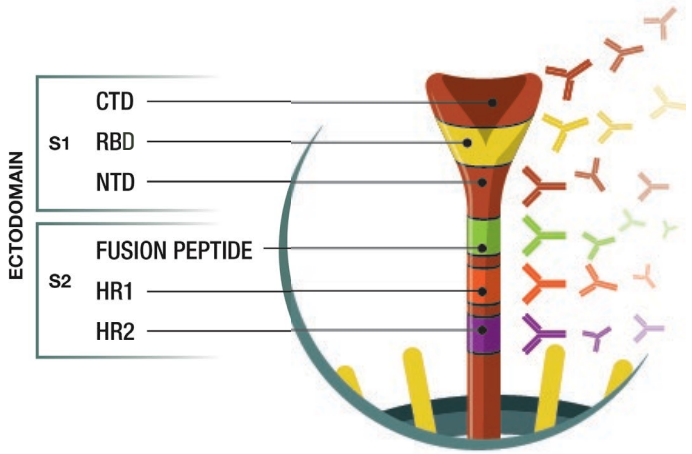
SAB-185 Anti-SARS-CoV2

SAB-185: Specifically Targeted Human Immune Response

MOA of Novel Polyclonal Antibody Raised Against SARS-CoV-2 Spike Protein





Multiple blocking and neutralizing antibody species bind to **single** epitope

Multiple blocking and neutralizing antibodies with uniquely determined and multifactorial paratopes bind to single multi-conformational antigen epitope

Diversity of antibodies and uniquely combinatorial paratopes drives effector functions including antibody and complement dependent cellular cytotoxicity

Spike Glycoprotein

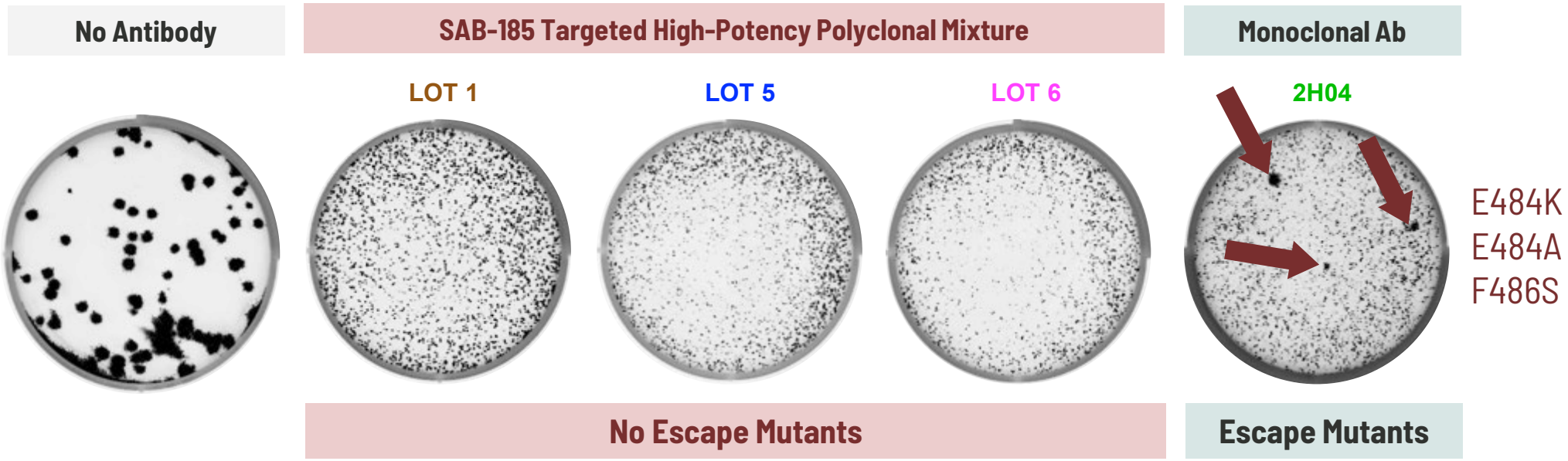
Receptor binding domain in S1 spike protein binds to ACE-2 receptor on human cells; then undergoes a conformational change to allow the S2 spike protein domain to fuse with the cellular membrane leading to infection of the cell

SAB-185 Polyclonal Spike Protein MOA

Antibodies bind multiple conformations of SARS-CoV-2 extracellular spike protein epitope and appears to prevent most all conformations of the infectious determinant spike protein from interacting with ACE-2 receptors on host cells, allowing effector cells to phagocytize virus and eliminate/lyse infected cells via complement

Addresses Escape Mutants: SAB-185 Superior to Monoclonal Antibody

Selection for VSV-SARS-CoV-2 Wild Type Escape Mutation



WASHINGTON UNIVERSITY SCHOOL OF MEDICINE–ST. LOUIS; 15 JAN 2021

Mutational Drift and Shift of COVID Variants

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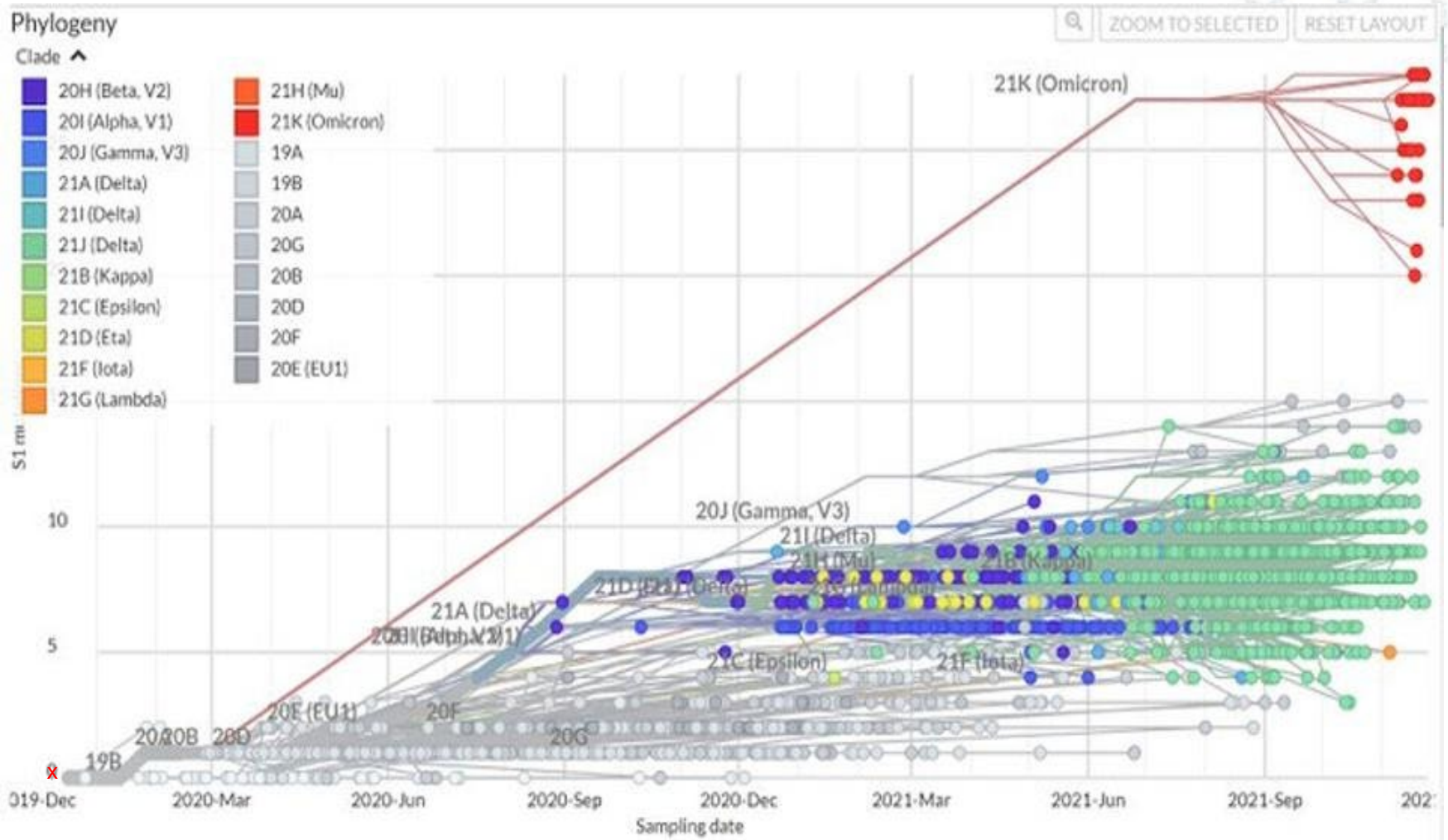
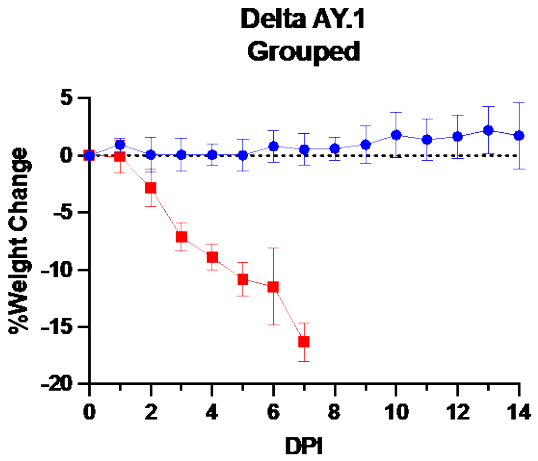


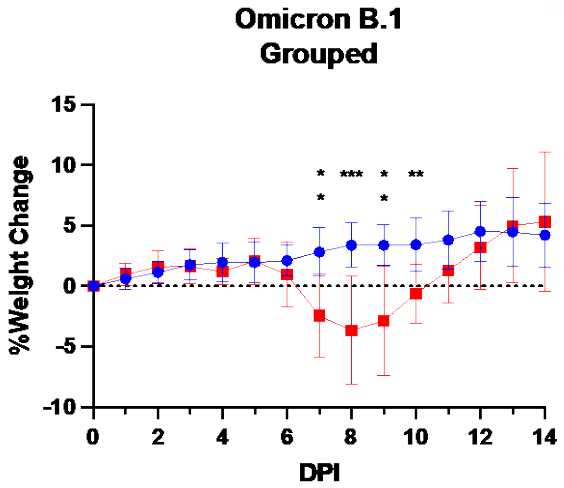
BA.1
BA.2
BA.3

Haseltine W. Birth Of The Omicron Family: BA.1, BA.2, BA.3. Each As Different As Alpha Is From Delta. Online Forbes Article

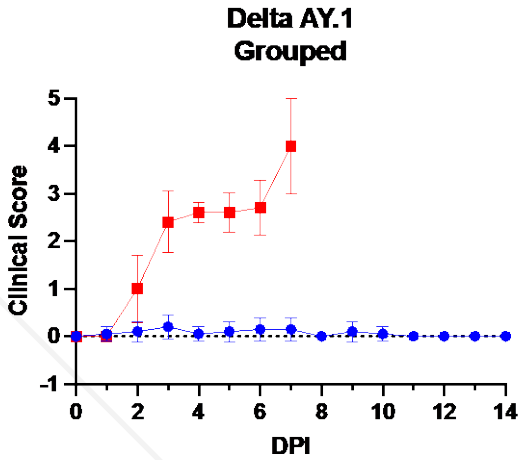
SAB-185 Provides 100% protection against Delta and Omicron in an in-vivo hACE2 Hamster model

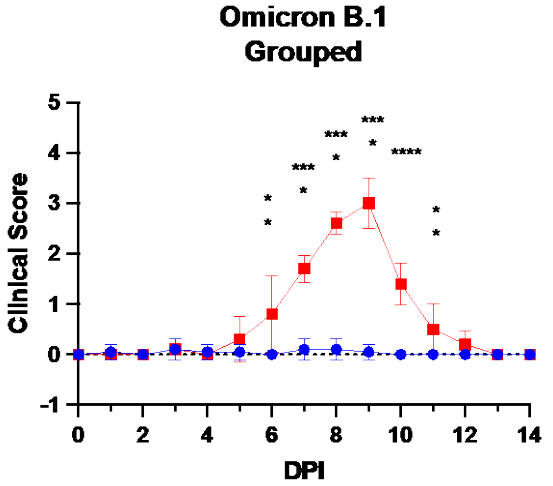


Note: Control demonstrated 100% mortality in the ACE2 Hamster Model against Delta



Note: Control demonstrated 0% mortality in the ACE2 Hamster Model against Omicron





PERFOMRED BY WILLIAM KLIMSTRA's LAB AT UNIVERSITY OF PITTSBERGH; hACE2 HAMSTER MODEL DEVELOPED BY WANG LAB AT USU

Phase 2 Data from NIH ACTIV-2 Trial Confirms SAB-185 Met Virology Endpoints for Graduation to Phase 3

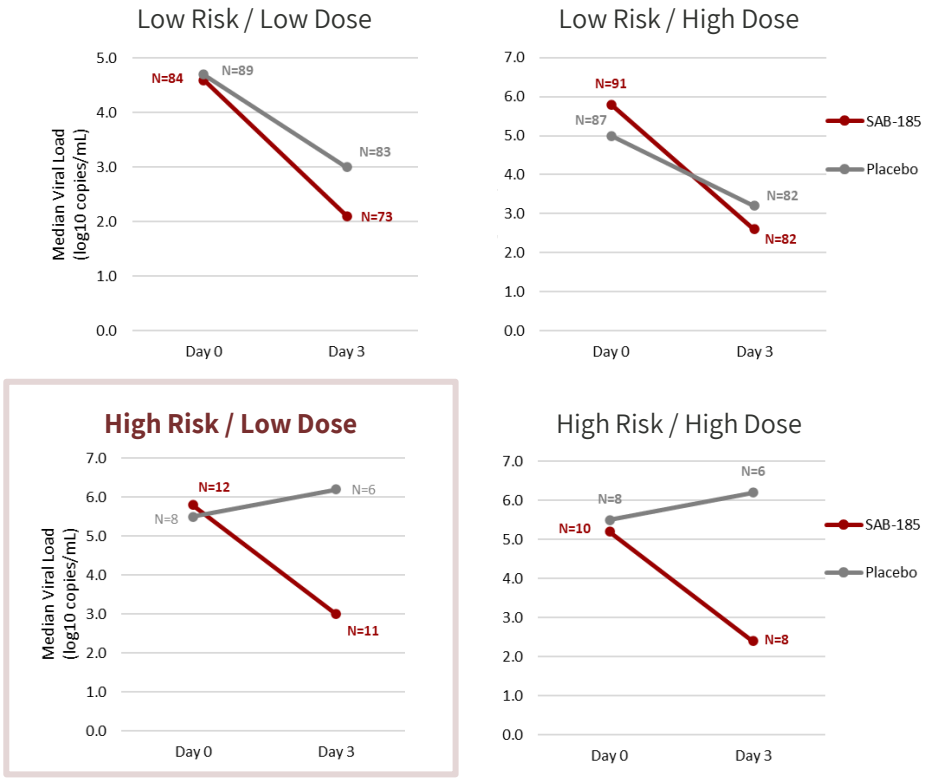
Viral load reductions of ≥0.5 log_{10} for both lower and higher dose at Day 3

INTERIM ANALYSIS

	LOW-DOSE (3,840 UNITS/KG)	HIGH-DOSE (10,240 UNITS/KG)
Difference from PBO for RNA level (log_{10} copies/ml)	**1.48**	0.67
Minimum RNA level difference (log_{10} copies/ml)	**0.5**	0.5
Minimum Posterior Probability	**0.6***	0.6*
Actual Posterior Probability	**0.91**	0.75

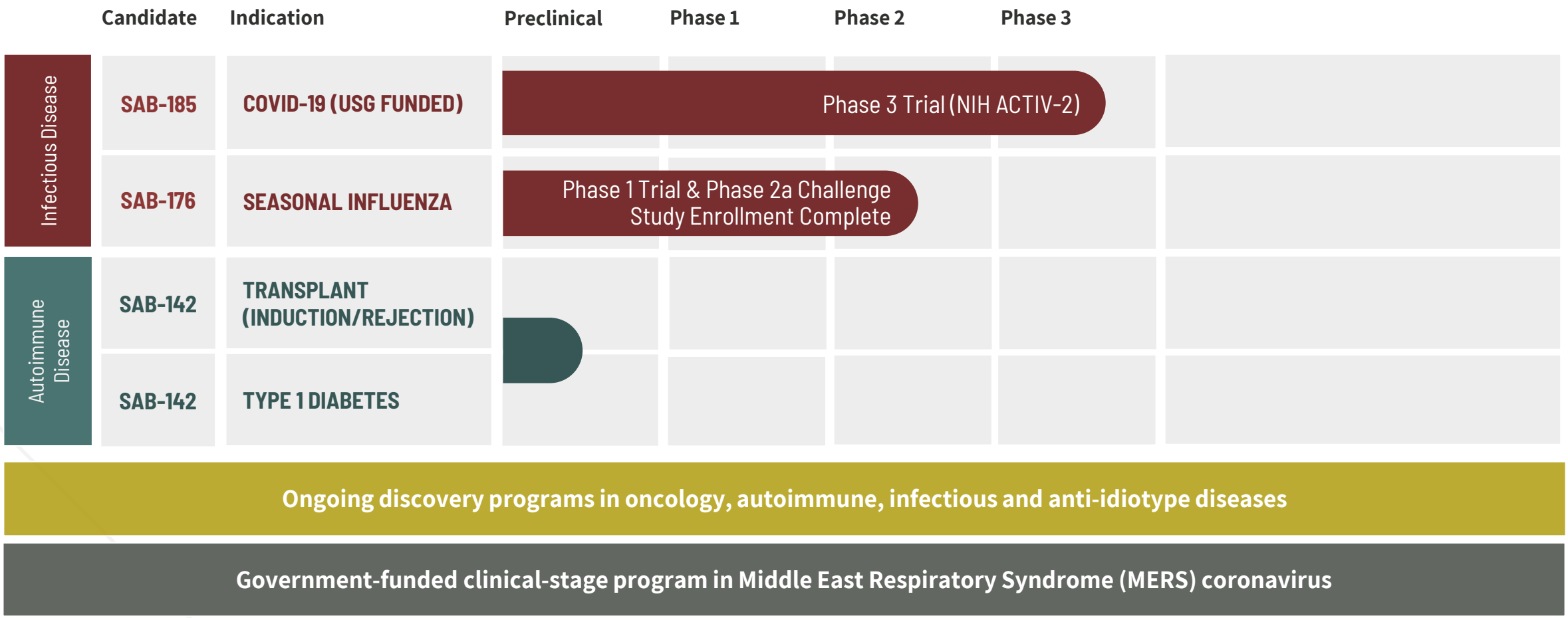
* The choice of 0.6 for this Bayesian probability indicates that there is a 3 to 2 odds of the agent being better than placebo by the desired amount (≥0.5 log_{10} /ml) for the outcome measure.

Sub-analysis** of viral load reduction shows **pronounced impact** in small subset of high-risk patients given either lower or higher dose



** Results shown are not statistically significant

Robust Pipeline with Broad Therapeutic Reach



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Tc Goats™ - Expanding The Human Immunotherapeutic Platform for Personalized Medicine

Genetic Engineering Science Applied Across

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UtahState University

- SAB Capra, LLC. is a wholly-owned subsidiary of SAB Biotherapeutics, Inc.
- Advancing novel antibody production platform leveraging transgenic goats
- Functionality of the HAC proven in a second species (ruminant ungulate)
- Generated H7N9-specific human polyclonal antibodies from Tc Goat (caprine) platform. Scientific Reports, 2019
- SAB Capra Phase 2 STTR Grant (NIH/NIAID): in collaboration with Utah State University
- Total funding $1,501,157 ($926,194 to SABC, $574,963 to USU)
- Two years: 18 Apr 2019 – 31 Mar 2021
- Two times of 12-month no cost extension granted—new end date 31 Mar 2023
- Genetic optimization in our Tc Bovine was done in 10 years while the goat optimization was done in 2 years.

Demonstrated Fully Human IgG in Tc Goat

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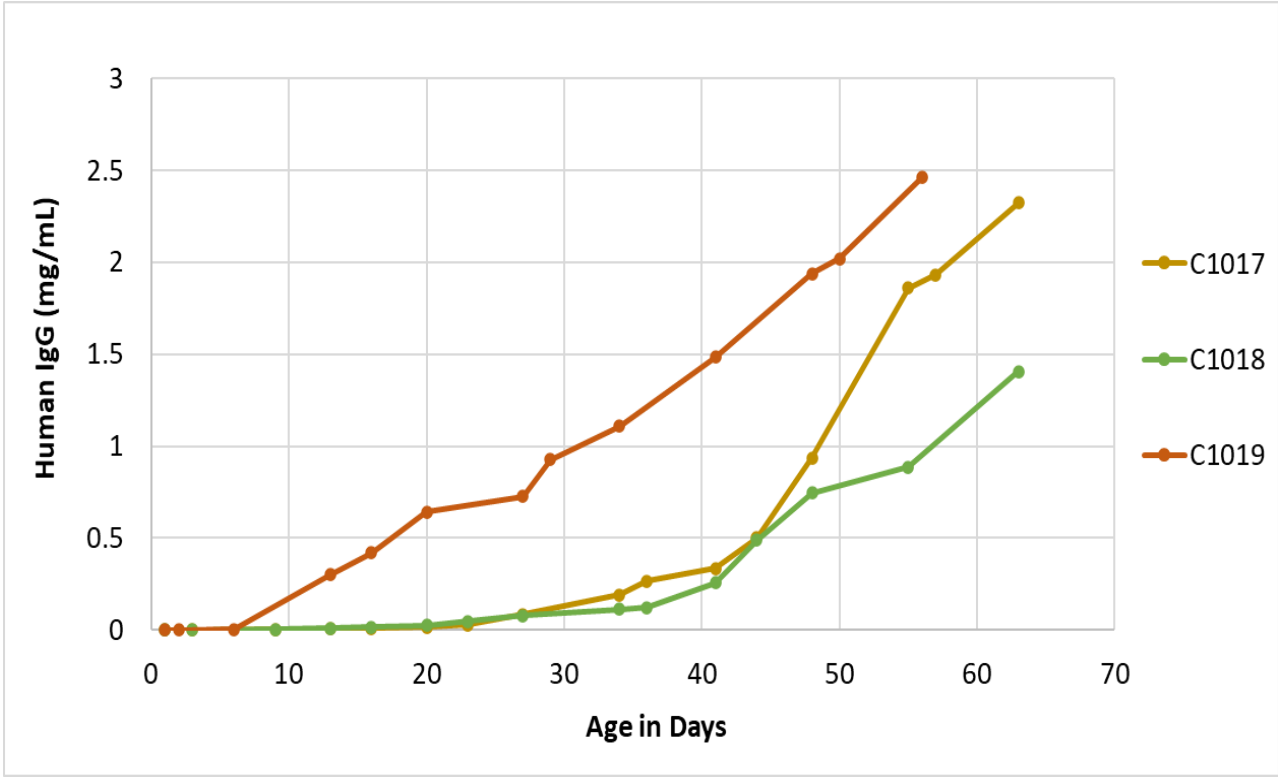
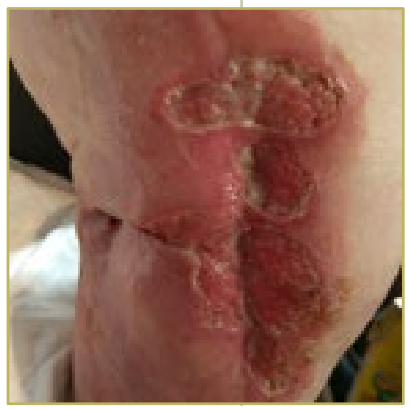
Human IgG in Tc Capra Kids



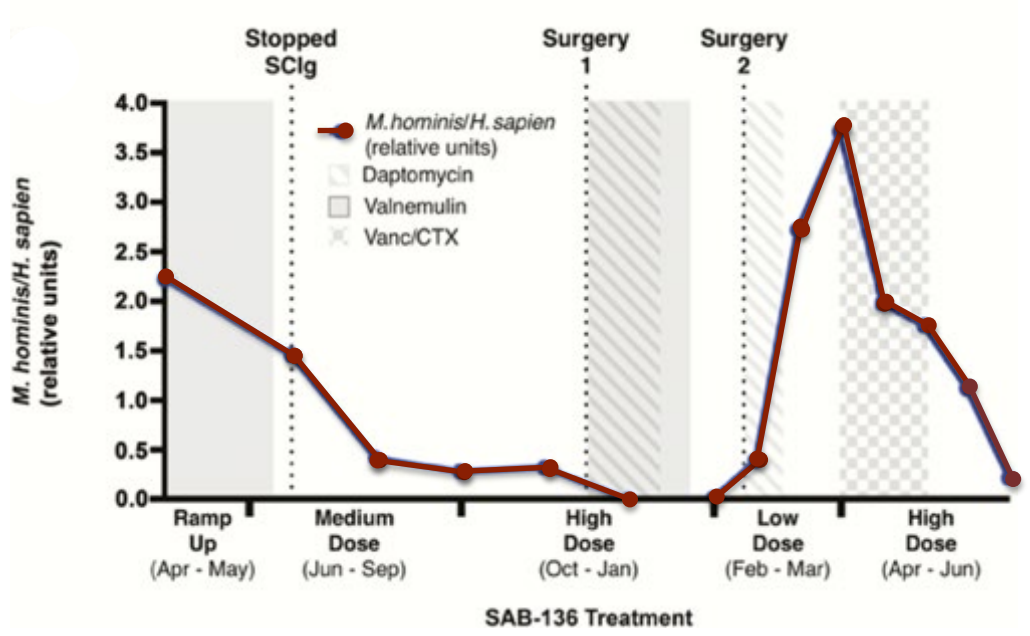
Positioned for Personalized Medicine

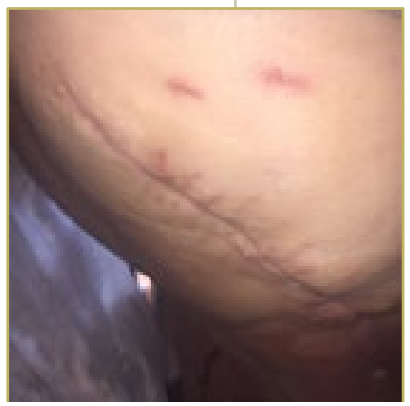
Confirms Feasibility of Multi-dosing

High-dose therapy resulted in improved clinical parameters associated with reduced *M. hominis* burden following two subsequent infections



Open wound persisted ~7 years prior to treatment





Same area following treatment with SAB -136

BRIGHAM AND WOMEN'S HOSPITAL

HARVARD MEDICAL SCHOOL

JARED N SILVER, CAMERON D ASHBAUGH, JACOB J MILES, HUA WU, GREGORY T MARECKI, JOYCE K HWANG, JIN-AN JIAO, MARK ABRAMS, EDDIE J SULLIVAN, DUANE R WESEMANN, DEPLOYMENT OF TRANSCHROMOSOMAL BOVINE FOR PERSONALIZED ANTIMICROBIAL THERAPY, CLINICAL INFECTIOUS DISEASES, VOLUME 66, ISSUE 7, 1 APRIL 2018, PAGES 1116–1119

Advancing the Tc Platform for Continued Advancement of Human Health

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UtahState University

- Developing targeted human polyclonal antibodies for use in personalized medicine
- Tc Goat platform production ready for producing diagnostics and testing reagent applications.
- Accommodating smaller volume markets, lower cost of development and maintenance, and accelerated scaling (shorter gestation, multiple births)