SAb BIOTHERAPEUTICS

ADVANCING POWERFUL NEW CLASS OF IMMUNOTHERAPEUTIC ANTIBODIES

R&D Day
13 OCTOBER 2021

Legal Disclaimer

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Big Cypress, SAB and their respective directors, executive officers, other members of management, and employees, under SEC rules, may be deemed to be participants in the solicitation of proxies of Big Cypress stockholders in connection with the Proposed Business Combination. Investors and stockholders may obtain more detailed information regarding the names and interests in the Proposed Business Combination of Big Cypress' directors and officers in Big Cypress' filings with the SEC including the Registration Statement to be filed with the SEC by Big Cypress, which will include the proxy statement of Big Cypress for the Proposed Business Combination, and such information and names of SAB's directors and executive officers will also be in the Registration Statement filed with the SEC by Big Cypress, which will include the proxy statement of Big Cypress for the Proposed Business Combination.

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

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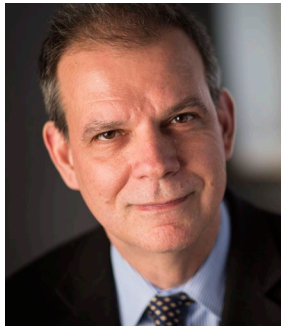
Today's Speakers

KOL SPEAKERS



Arturo Casadevall, MD, PhD
The Alfred and Jill Sommer Professor and Chair
W. Harry Feinstone Department of Molecular
Microbiology & Immunology, Bloomberg Distinguished Professor
JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH
JOHNS HOPKINS SCHOOL OF MEDICINE

Michael Haller , MD, MS-CL
Professor and Chief Pediatric Endocrinology
Silverstein Family Eminent Scholar
Pediatric Endocrinology
UNIVERSITY OF FLORIDA
COLLEGE OF MEDICINE

SAB BIOTHERAPEUTICS MANAGEMENT

Eddie J. Sullivan, PhD
PRESIDENT & CEO / CO-FOUNDER

Tom Luke, MD
CHIEF MEDICAL OFFICER

Christoph Bausch, PhD, MBA
CHIEF SCIENCE OFFICER

Novel DiversitAb™ Platform for Developing Highly-Differentiated Immunotherapies

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Robust, growing clinical-stage pipeline spanning multiple therapeutic areas with multiple near-term catalysts

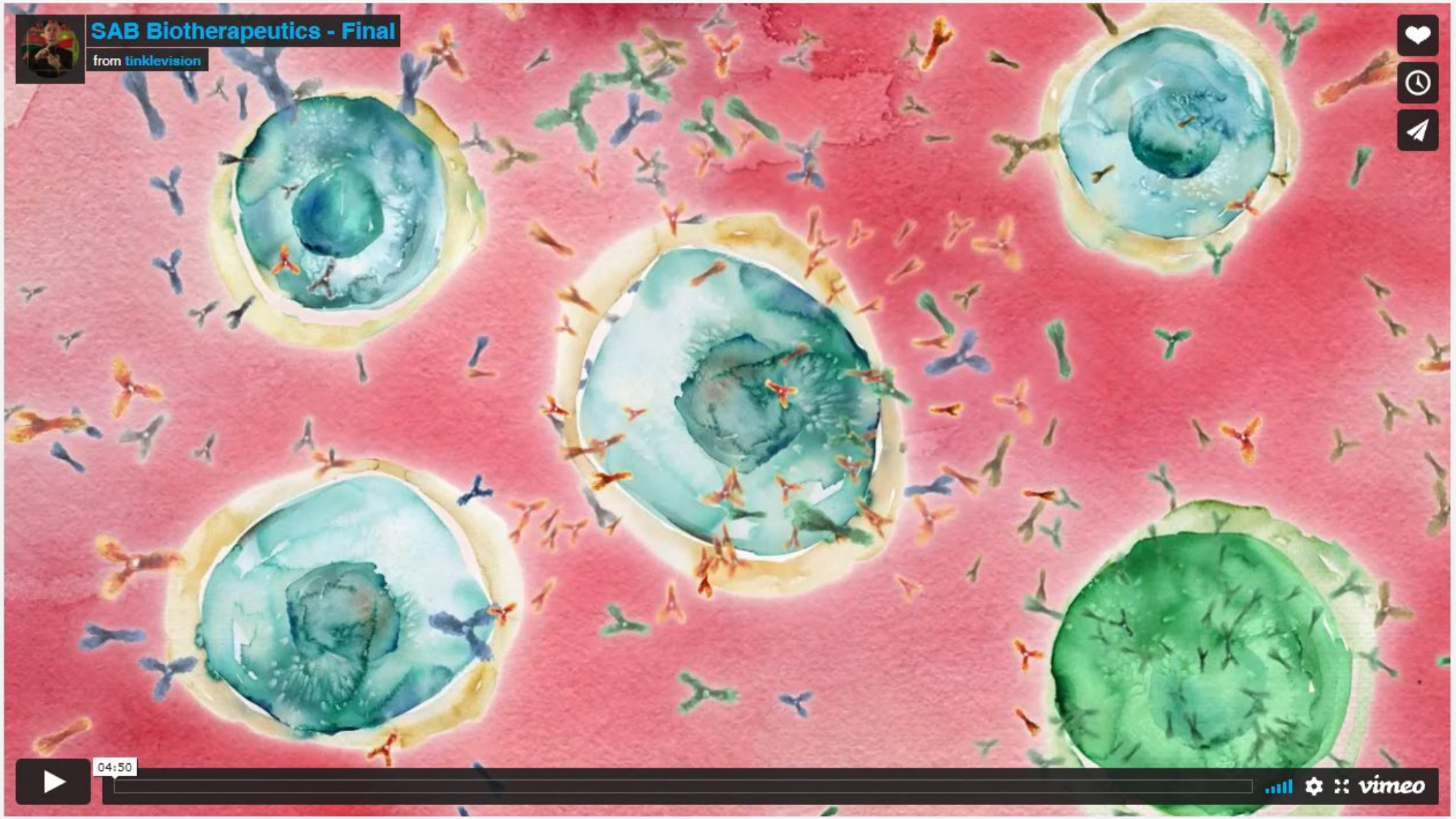
Vertical integration enables rapid, scalable development of multi-targeted products

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 ~$300MM

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

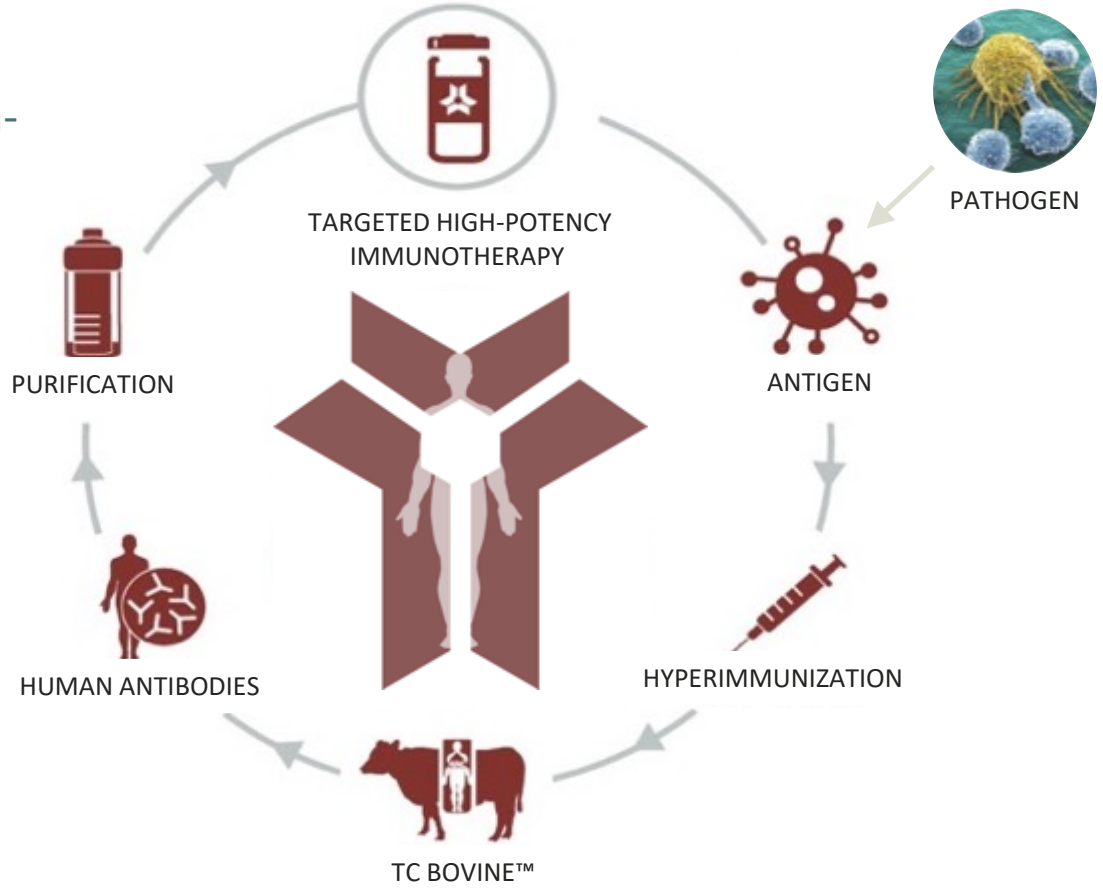


Video: SAB Biotherapeutics - Final (vimeo.com)

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



Versatile Antibody Platform with Ability to Capture Multiple Markets

Human Antibody Discovery & Development Engine, New Source for IgG, Therapeutic Production

Represents Multibillion-Dollar Market Opportunity

Polyclonal Antibody Development	–Human, targeted, high-potency –Multivalent, multi-targeted	• **Robust pipeline across multiple therapeutic areas** • **Potential to capture mAb, hIVIG, animal pAb markets and address unmet needs**
Human Immunoglobulin	–Offers large scale, consistently managed donor pool, genetically representing single human donor	• ***In vivo* data demonstrating comparability to approved SC product and potential benefits over human-derived**
Reagent Antibodies (Diagnostics)	–Fully human –Rapid development –Specifically targeted	• **Current worldwide standard for Ebola and MERS** • **Low volume and high margin, unique capability**
Monoclonal Antibody Discovery	–Larger volume of antibodies –Greater diversity; higher affinity –Robust (ruminant) immune response	• **Multiple ongoing global pharma collaborations**

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DiversitAb™: Multi-Dimensional Immunotherapies from Tc Bovine-Derived Human Antibody Platform

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Combinatorial mechanisms target diverse causes common to many human diseases

Polyclonal	*Activates full cell effector function and complement*	**Exceeds Targeted Neutralization**
Multi-valent	*Designed to bind to multiple targets, strains, or mutations*	**Specifically-Targeted Antibodies**
Hyperimmunization	*Drives higher titers with elevated potency, avidity, improved function*	**Cross-Reactive & High Potency**
Strain Change	*Potential to introduce identically-produced new strain or antigen*	**Seasonal Therapeutic/ Emerging Variants**
Admin. Route	*Expanding IV base formulations to IM, SC and inhaled forms*	**Clinical Flexibility & Patient Ease**

Multi-Pronged Business Strategy Powered by Novel Proprietary Platform

Opportunity to Create New Class of Immunotherapies

DiversitAb Platform

- **RAPID PROOF-OF-CONCEPT**
  (90 days to CGMP)
- **NATURAL HUMAN ANTIBODIES**
  (without human donors or serum)
- **MULTI-VALENT CAPABILITIES**
  (by nature, & by design–multiple targets in one product)
- **TARGET AGNOSTIC**
  (virus, bacteria, toxin, allergen)
- **SCALABLE, REPLICABLE, CONSISTENT PRODUCTION**

Product Development of Pipeline Assets:
Best-in-Class, First-in-Class & Unmet Needs

- **Demonstrated clinical safety and efficacy**
- **Proof-of-platform with highly-mutating infectious disease**
- **Robust pipeline with broad therapeutic reach**

Industry Partnering & Research Collaborations:
Monoclonal Discovery & Polyclonal Development/Production

- **Multiple ongoing collaborations with global pharma**
- **Opportunities in monoclonal discovery, human immune globulins and therapeutic innovation**

US Gov. Rapid Response Biodefense & Public Health Security:
Emerging Infectious Disease & Biothreats

- **$200M+ awarded for rapid & pandemic response**
- **Recognized as only therapeutic platform to address priority pathogens by World Health Organization**
- **Demonstrated *in vivo* efficacy to >12 targets**

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Robust Pipeline with Broad Therapeutic Reach

	Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3
Infectious Disease	SAB-176	SEASONAL INFLUENZA	Phase 1 and Phase 2a Challenge enrollment complete			Phase 1 full data readout; Phase 2a topline data expected 4Q2021
	SAB-185	COVID-19 (USG FUNDED)	Phase 3 (ACTIV-2) ongoing			NIH NIAID led
Autoimmune Disease	SAB-142	TYPE 1 DIABETES	Additional studies (IND-Enabling) expected to begin 1Q2022			
	SAB-142	TRANSPLANT (INDUCTION/REJECTION)	Additional studies (IND-Enabling) expected to begin 1Q2022			
	SAB-181	HUMAN IMMUNE GLOBULIN (IgG)	Pre-IND meeting discussion expected 4Q2021			

Government-funded clinical-stage program in Middle East Respiratory Syndrome (MERS) coronavirus

Ongoing discovery programs in oncology, infectious and idiopathic diseases

Multiple Catalysts through YE2022

✓	✓	✓	○	○	○	○
Proof-of-concept established for DiversitAb™ Platform	**SAB-176** for seasonal influenza Phase 2a Challenge Trial fully enrolled	**SAB-185** for COVID-19 Phase 1, 1b, 2 fully enrolled; graduated to Phase 3 in ACTIV-2 adaptive trial at interim analysis	**SAB-176** for seasonal influenza Phase 1 data readout and Phase 2a Challenge Trial topline data expected in **4Q2021**	**SAB-142** for Type 1 Diabetes and Transplant additional studies (IND-Enabling) expected to begin **1Q2022**	**SAB-181** for IgG pre-IND meeting expected in **4Q2021**	**SAB-162** oncology proof-of-concept data expected in **1H2022**

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The Power of Polyclonal Antibodies

Tom Luke, MD

CHIEF MEDICAL OFFICER

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

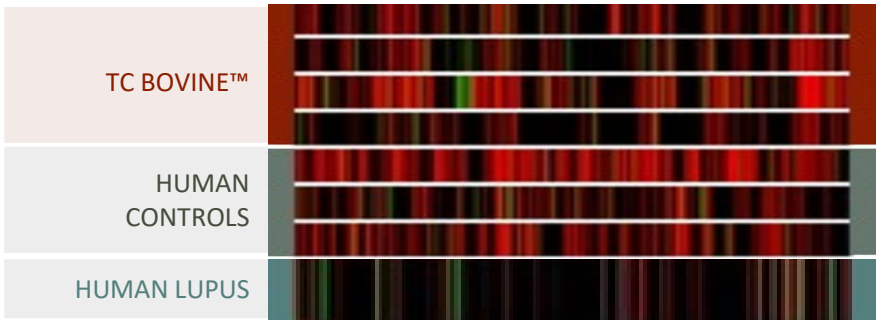
Polyclonal Approach

- 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

Fully-Human & Functional Antibodies

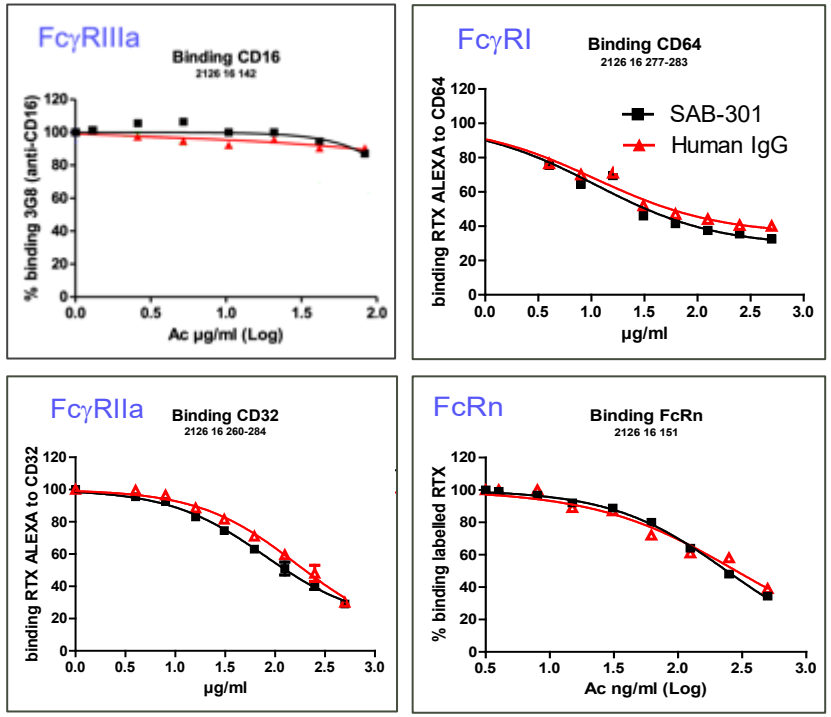
Rich Antibody Diversity

VDJ repertoire usage mimics human-derived diversity in variable region



Highly-Functional Fc Region

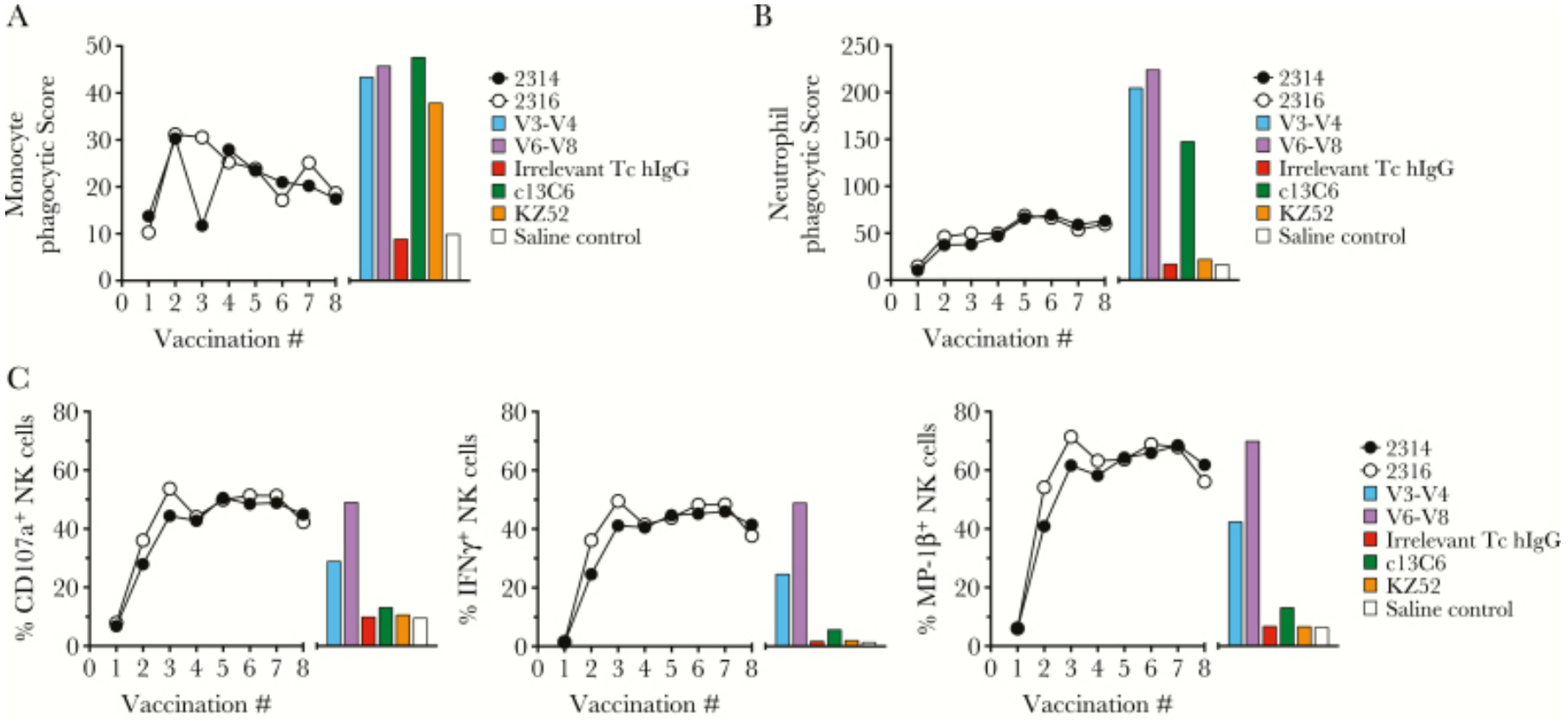
Matches full activation of effector cells and functional glycosylation / post translational modification



Activation of Effector Function

Human effector cell phagocytosis and degranulation activation

MONOCYTES, NEUTROPHILS, NATURAL KILLER CELLS

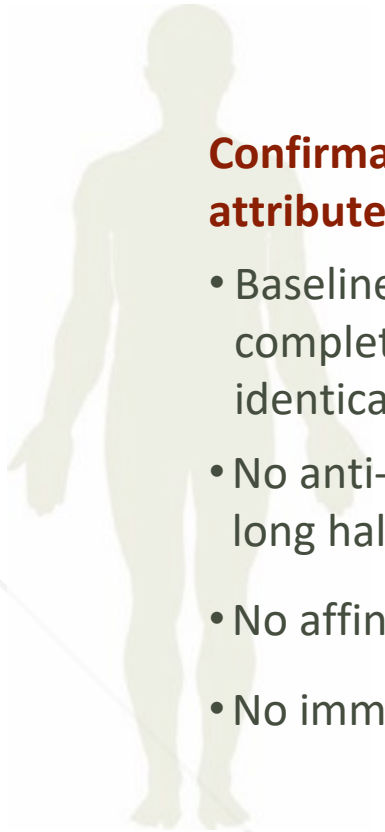


Integrated Research Facility, NIAID

Clinically-Demonstrated Proof-of-Platform

Completed Government-Funded Phase 1 Clinical Trial

MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS (MERS-COV)



Confirmation of human antibody attributes & behavior

- Baseline pharmacokinetics (PK) analysis completed with half-life of 28.5 days; identical to human-derived IgG
- No anti-drug antibodies detected despite long half-life
- No affinity ligand immunogenicity
- No immunogenicity to bovine plasma proteins

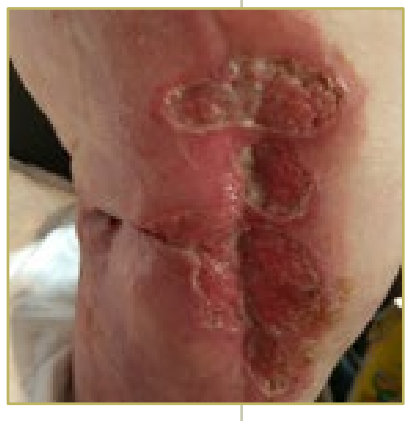
Well-tolerated with no drug-related SAE's

- 38 healthy volunteers
- 6 cohorts, IV, escalating dose
- Dose range: 1.5 mg/kg to 50 mg/kg

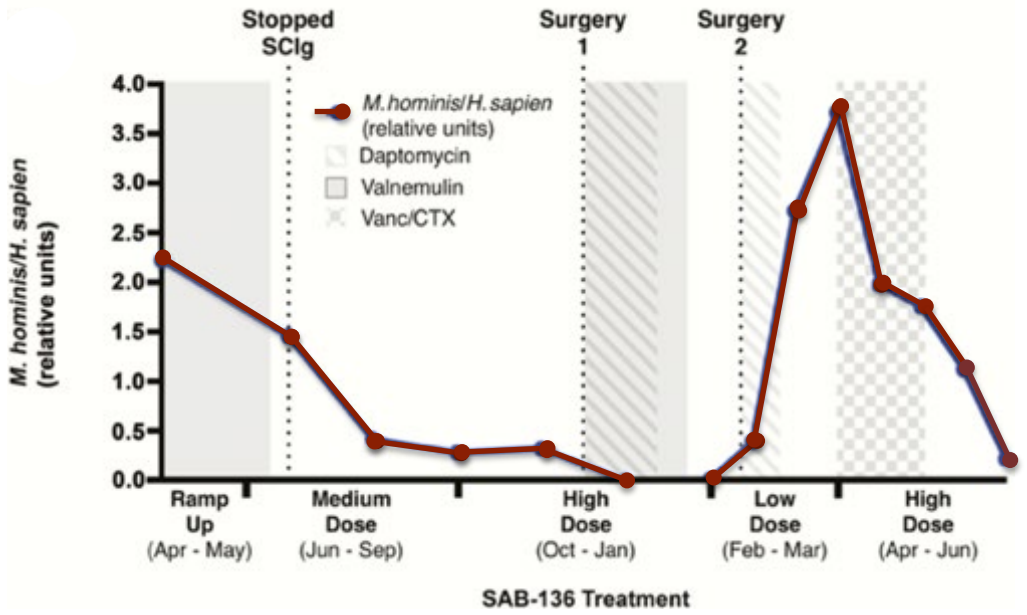
Demonstrated Human Safety and Efficacy

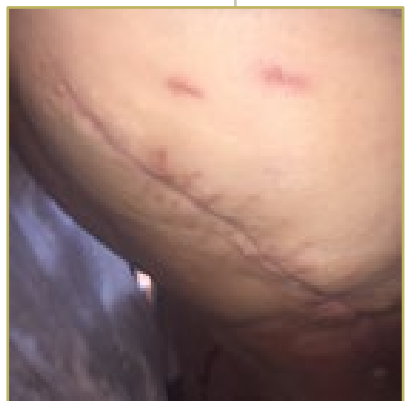
Confirms Feasibility of Multi-dosing

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

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KOL PRESENTATION:

Antibody therapies against Infectious Diseases past, present and future

Arturo Casadevall, MD, PHD

Bloomberg Distinguished Professor

JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH

Antibody therapies against Infectious Diseases past, present and future

Arturo Casadevall MD, PhD

Johns Hopkins Bloomberg School of Public Health

Thomas Shastid Experience with Diphtheria and antitoxin

Thomas Shastid

GOYA'S 'LAZARILLO DE TORMES' (1819)

I FOUND THE BOY VERY ILL, THE WHOLE BACK OF HIS THROAT BEING LIKE A WHITE VELVET. I HAD NEVER USED THE NEW REMEDY BEFORE, BUT DETERMINED TO TRY IT TO SAVE THE BOY'S LIFE. I INJECTED A SMALL QUANTITY UNDER THE SKIN OF THE STOMACH AND WATCHED THE THROAT. I CAN ONLY COMPARE THE MARVELOUS RESULT TO THE DISAPPERANCE OF SNOW BENEATH A HOT SUN. AFTER THE SECOND DOSE EVERY TRACE OF THE MEMBRANE DISAPPEARED, AND THE BOY SOON RECOVERED"

Thomas Shastid experience in small Illinois town in 1890s

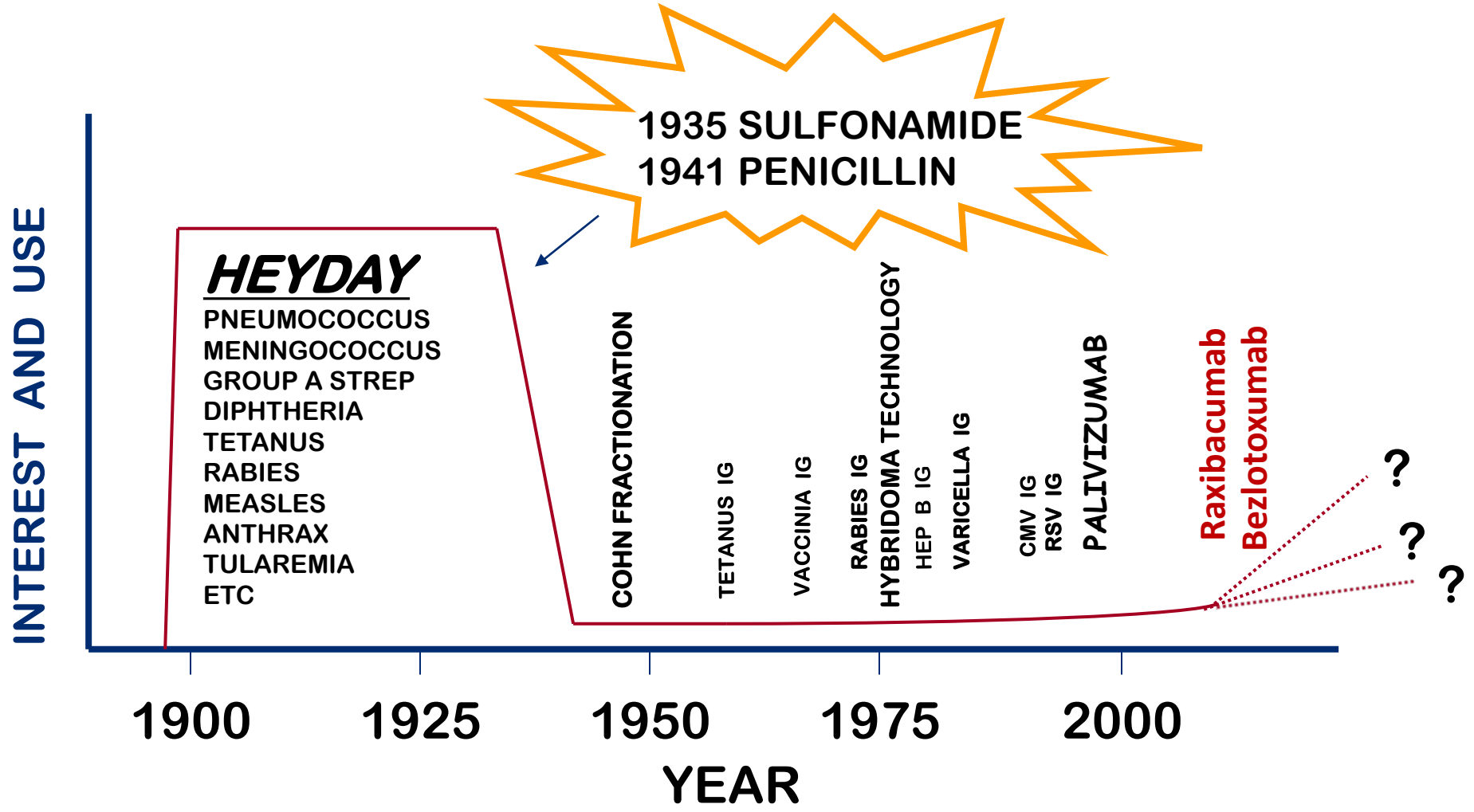
1901 First Nobel Prize in Medicine or Physiology

Emil Adolf von Behring (1854-1917)

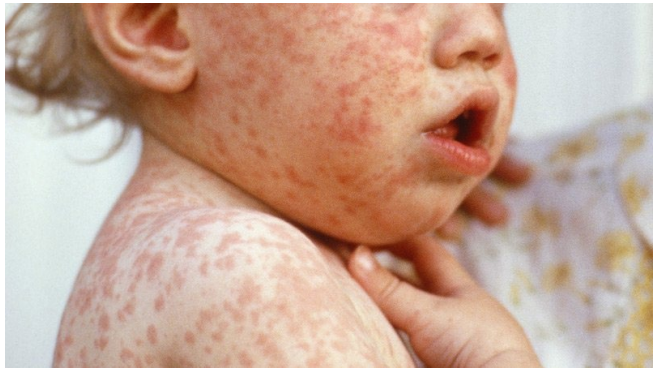
“for his work on serum therapy, especially its application against diphtheria, by which he has opened a new road in the Domain of medical science and thereby placed in the hands of the physician a victorious weapon against illness and deaths"

Child treated with Serum Scientific American 1894

A timeline for Antibody therapy for infectious diseases



Convalescent Serum (Plasma) used in past epidemics



THE USE OF CONVALESCENT HUMAN SERUM IN INFLUENZA PNEUMONIA—A PRELIMINARY REPORT.*

L. W. McGuire,
Lieutenant Commander, M. C., U. S. N.,
and
W. R. Redden,
Lieutenant, j. g., M. C., U. S. N., U. S. Naval Hospital, Chelsea, Mass.

1918

Use of Convalescent Measles Serum to Control Measles in a Preparatory School

J. ROSWELL GALLAGHER, M.D.
School Physician, The Hill School, Pottstown, Pa.

1934

American Journal of Diseases of Children
VOLUME 71 JANUARY 1946 NUMBER 1

MUMPS
Use of Convalescent Serum in the Treatment and Prophylaxis of Orchitis

COMMANDER ALWIN C. RAMBAR (MC), U.S.N.R.

1946

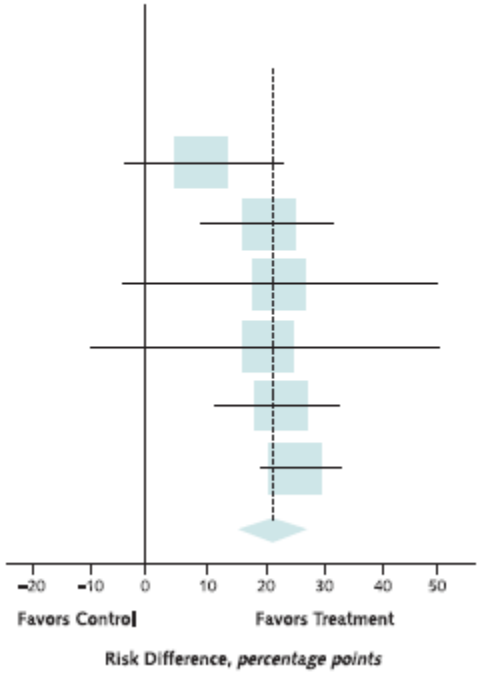
Meta Analysis of 1918 Epidemic Serum Data

Annals of Internal Medicine | REVIEW

Meta-Analysis: Convalescent Blood Products for Spanish Influenza Pneumonia: A Future H5N1 Treatment?

Figure 2. Absolute risk differences in mortality among patients treated with convalescent blood products and controls.

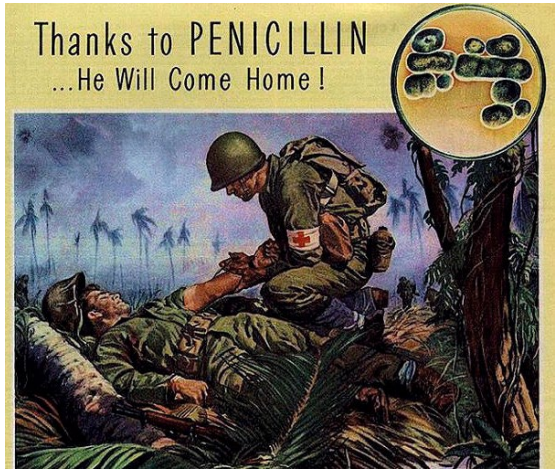
Study (Reference)	Mortality Rate, *n/n (%)*		Risk Difference (95% CI), *percentage points*
	Treatment Group	Control Group	
Stoll (17)	25/56 (45)	201/379 (53)	8 (–6 to 22)
O'Malley and Hartman (18)*	3/46 (7)	28/111 (25)	19 (8 to 29)
Ross and Hund (19, 20)	6/28 (21)	9/21 (43)	21 (–5 to 47)
Kahn (21)	12/25 (48)	12/18 (67)	19 (–11 to 48)
Gould (22)	2/30 (7)	82/290 (28)	22 (11 to 32)
McGuire and Redden (23, 24)*	6/151 (4)	120/400 (30)	26 (21 to 31)
Overall	54/336 (16)	452/1219 (37)	21 (15 to 27)



Luke et al Ann Int Med 2006

Abandonment of Antibody Therapies to Treat Infectious Diseases 1940-1950

Antimicrobial therapy replaces serum therapy for Bacterial Diseases



Concerns about serum-associated hepatitis Lead to abandonment of convalescent sera

Correspondence

Hepatitis after Prophylactic Serum

SIR,—A recent outbreak of poliomyelitis has aroused controversy as to the value of convalescent serum. In the *Journal* of September 10 (p. 588) Mr. G. R. Girdlestone advocates its use, and regrets the statement of Drs. Donald Paterson and MacDonald Critchley in the *Times* of August 8 that the disease does not yield to any known treatment applied within the first few days of onset.

On June 1, 1937, seven children housed in one block of a large institution for mental defectives were inoculated with convalescent measles serum to protect them from the disease with which they had recently been in contact. Each child received 4.5 c.cm. of the serum, which came from the same batch and which was obtained from a well-known reputable firm.

After an interval varying between seventy-eight and eighty-three days these seven children developed jaundice and became gravely ill. No other child in the institution at that time had jaundice. The disease in its early stages or in its milder forms appeared to be indistinguishable from common infective hepatitis (infectious catarrhal jaundice), but of the seven cases three developed rapidly increasing signs of liver failure terminating in death. Material derived from post-mortem examination of the fatal cases showed a condition of acute atrophy of the liver. (Photomicrographs of sections of the liver in two of the cases are enclosed.)

British Medical Journal Sept 24, 1938

Serum therapy experience establish the three principles of antibody therapy for Infectious Diseases

1. **The Specificity Principle** - ***effective antibody preparations for the prevention and therapy of infectious diseases must contain antibody specific to the microbe targeted***
2. **The Quantitative Principle** – ***effective antibody preparations for the prevention and therapy of infectious diseases must contain sufficient antibody to microbe targeted to mediate protection.***
3. **The Temporal Principle** - ***antibody preparations are most effective when given prophylactically or early in the course of disease.***

From Flexner J. Exp. Med 1913 on the Treatment of meningococcal meningitis

Mortality according to the Period of Injection of the Serum.

Period of injection.	No. of cases.	Recovered.	Died.	Per cent. recovered.	Per cent. died.
1st to 3d day	199	163	36	81.9	18.1
4th to 7th day	346	252	94	72.8	27.2
Later than 7th day	666	423	243	63.5	36.5
Totals	1,211	838	373	69.2	30.8

CP Efficacy in Several Epidemics

Pathogen (Year)	Study type	Mortality Reduction	Reference
Influenza (1918)	Meta Analysis	-20%	Luke et al. 2005
Junin Virus (1979)	RCT	-93%	Maiestegui et al. 1979
SARS-CoV (2003)	Case Series	-73%	Cheng et al. 2005
2009 H1N1 (2009)	RCT	-63%	Hung et al 2011
Ebola Virus	RCT	-18% (before adjustment) -8% NS	Griensven et al 2016
Seasonal flu	RCT	0	Beiger et al. 2019
SARS-CoV-2 (2020)	Meta Analysis	About -35%	Joyner et al. 2020

Post Morten on two negative trials

ORIGINAL ARTICLE

Evaluation of Convalescent Plasma for Ebola Virus Disease in Guinea

J. van Griensven, T. Edwards, X. de Lamballerie, M.G. Semple, P. Gallian, S. Baize, P.W. Horby, H. Raoul, N. Magassouba, A. Antierens, C. Lomas, O. Faye, A.A. Sall, K. Fransen, J. Buyze, R. Ravinetto, P. Tiberghien, Y. Claeys, M. De Crop, L. Lynen, E.I. Bah, P.G. Smith, A. Delamou, A. De Weggheleire, and N. Haba, for the Ebola-Tx Consortium*

Problem with Quantitative principle

Used plasma with unknown amounts of specific antibody and subsequent studies showed many potential donors in the area had no significant antibody to Ebola virus

Anti-influenza immune plasma for the treatment of patients with severe influenza A: a randomised, double-blind, phase 3 trial

*John H Beigel, Evgenia Aga, Marie-Carmelle Elie-Turenne, Josalyn Cho, Pablo Tebas, Carol L Clark, Jordan P Metcalf, Caroline Ozment, Kanakatte Raviprakash, Joy Beeler, H Preston Holley Jr, Stephanie Warner, Carla Chorley, H Clifford Lane, Michael D Hughes, Richard T Davey Jr, on behalf of the IRC005 Study Team**

Problem with temporal principle?

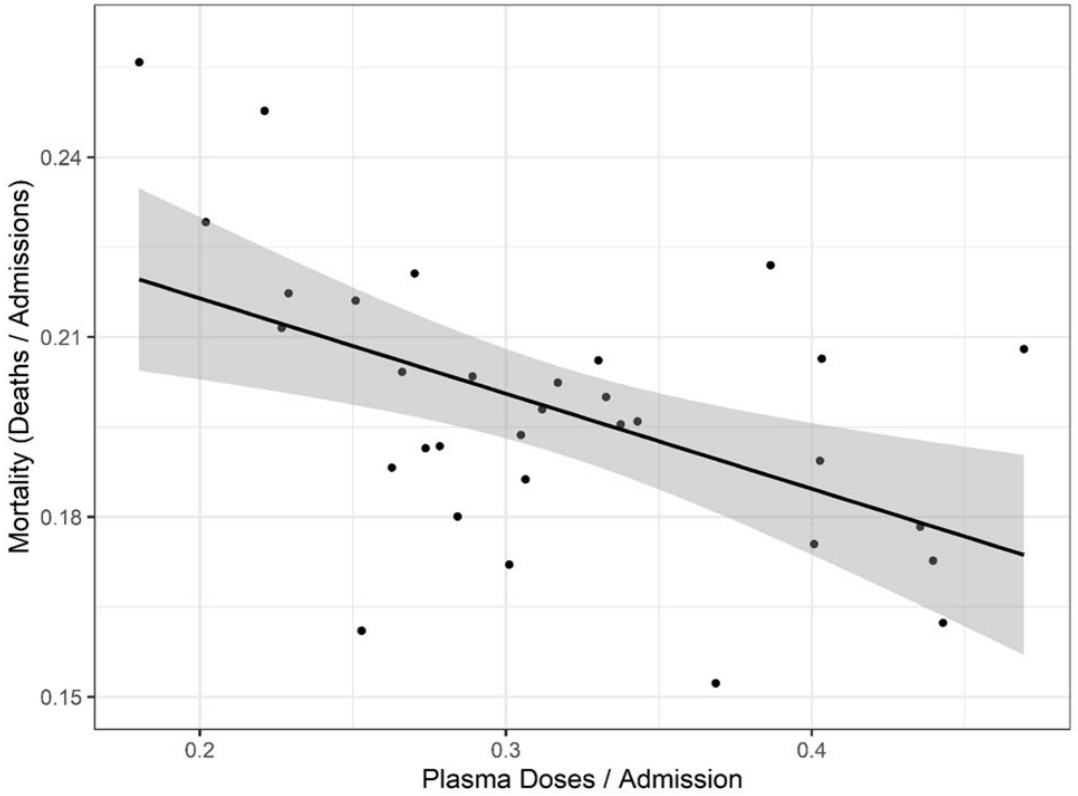
~44% were in ICU with advanced disease

Problem with Quantitative principle?

High titer sera was > 1:80

2020-2021: COVID-19 Brings Greatest Deployment of Antibody Therapy against One Disease

- > 500,000 patients treated with Convalescent Plasma
- Several mAb therapies successfully deployed
- Horse immunoglobulins used against SARS-CoV-2
- Antibody therapies shown to be effective in reducing hospitalization and mortality

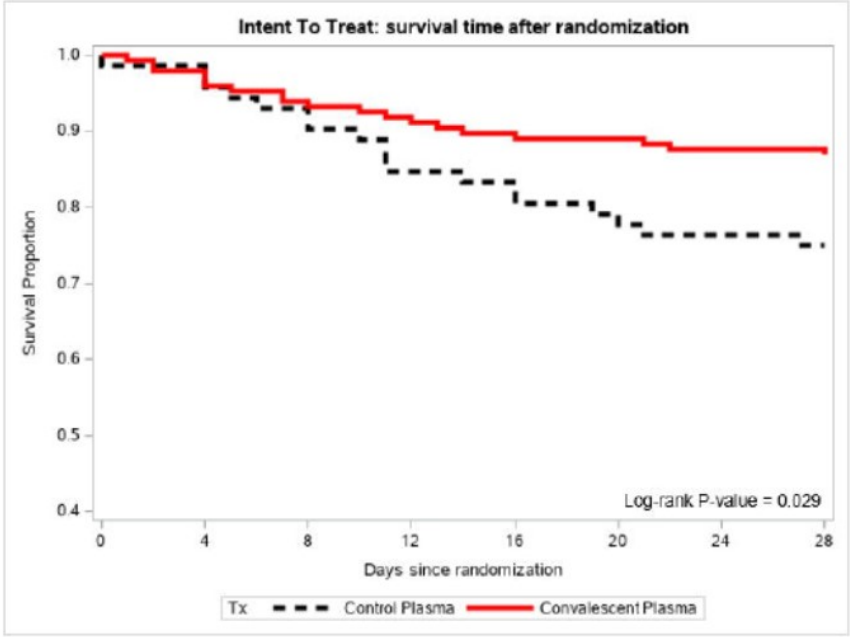


Casadevall et al eLife 2021

Is Convalescent Plasma Effective?
The 7 lines of evidence

1. **Mechanism of action.** Antibody to SARS-CoV-2 spike protein can mediate viral neutralization. Other mechanisms of action such as ADCC and complement action also operative. **(YES!)**
2. **Animal studies show efficacy of human convalescent plasma. (YES!)**
3. **EAP Data Analysis** – suggests lower mortality with early use of high titer plasma (used by FDA in EUA recommendation) **(YES!)**
4. **> 10 Observational studies:** Mt. Sinai NYC, Methodist Houston, Hackensack NJ, Italy, Iran, etc. report large reductions in mortality if given early – before ICU. **(YES!)**
5. **> 10 Randomized controlled trials** – all suboptimal in some way but most provide some encouragement. **(MIXED)**
6. **Experiments of nature**. Convalescent plasma has dramatic effects patients with congenital immune suppression (X-linked agammaglobulimia) **(YES!)**
7. **Population data**. Inverse correlation between plasma use and mortality in USA. **(YES!)**

O'Donnell et al. Columbia-Brazil RCT: Double-blinded placebo controlled trial



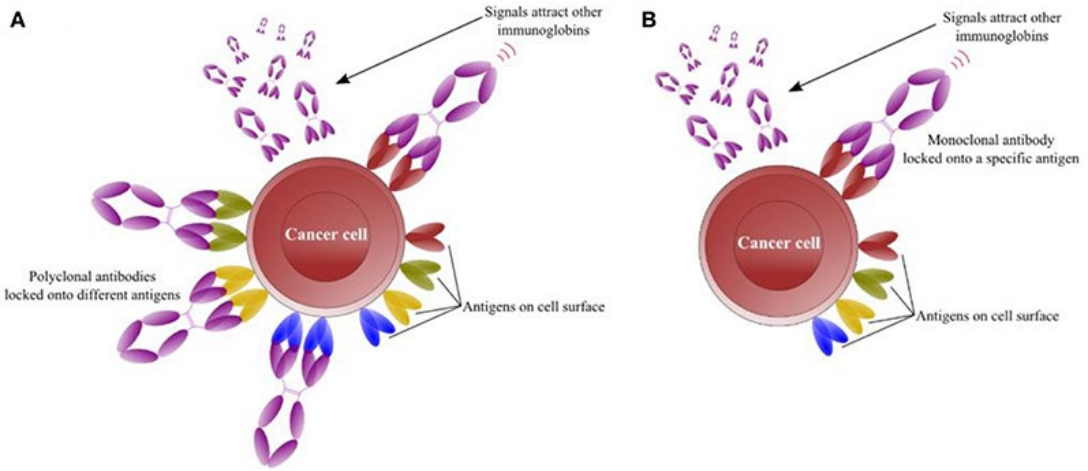
Time since randomization (days)		0	4	8	12	16	20	24	28
Control plasma	At risk	73	71	67	61	60	57	55	50
	Died	1	3	7	11	14	16	17	18
Convalescent Plasma	At risk	150	144	137	134	131	130	128	122
	Died	0	6	10	13	16	16	16	19

O'Donnell JCI 2021

Monoclonal vs. Polyclonal Preparations

	Monoclonal	Polyclonal
Specificity	Narrow	Broad
Activity/protein	**High**	**Low**
Virus Escape	High	Low
Cost	High	Low
Development Time	~ 1 year	~2-3 months
Source	Cells	Humans, Cows

Y



Front. Microbiol., 28 March 2017

Promise and Perils of mAb Therapies

LETTER TO THE EDITOR

Bamlanivimab + etesevimab therapy induces SARS-CoV-2 immune escape mutations and secondary clinical deterioration in COVID-19 patients with B-cell malignancies

Monoclonal antibody therapies are effective in reducing progression of disease in COVID-19 Patients but can select for resistant variants. This Study describes five patients in whom monoclonal Therapy led to resistance and they were recued by Convalescent plasma.

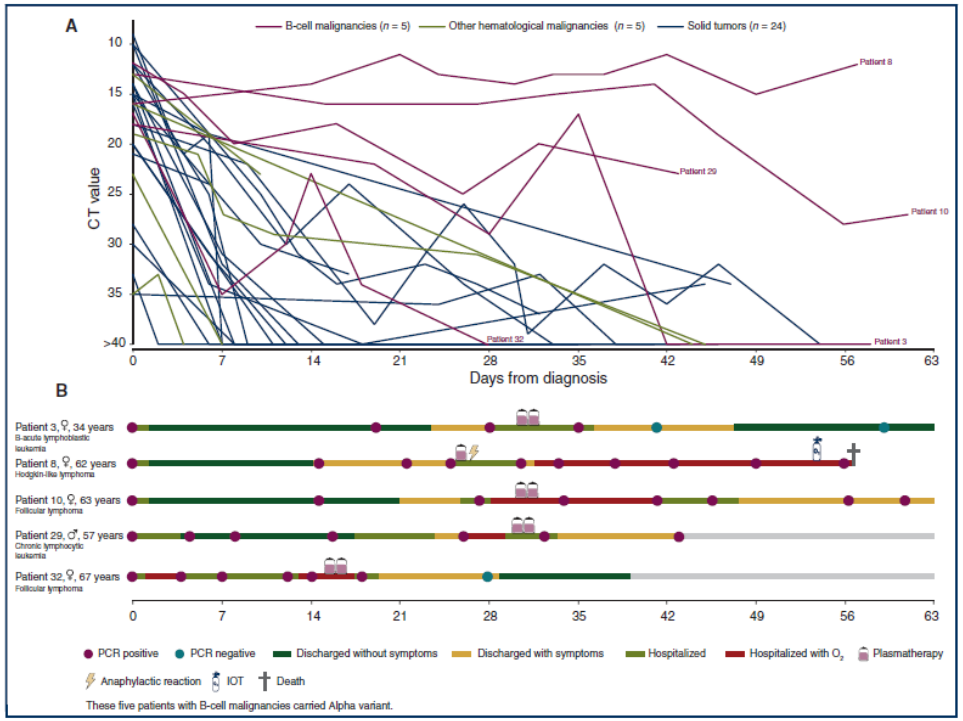


Figure 1. CT and clinical evolution in patients according to cancer type.
CT, cycle threshold; IOT, orotracheal intubation.

The future of antibody therapies against infectious diseases

- Antibody therapies are thriving in oncology and rheumatology but very underdeveloped for the treatment of infectious disease.
- COVID-19 has shown the efficacy, importance and feasibility of rapid development of antibody-based therapies
- Physicians and the public are now highly aware of the potential of antibody therapies against infectious diseases.
- The field of infectious diseases is the only area of medicine where the situation today is worse than in the past due to antimicrobial resistance.
- Areas of great promise include drug resistant organisms, infectious diseases in immunocompromised hosts and pathogens for which we have no drugs.
- Prediction: The 21st century will see the large-scale redeployment of antibody-based therapies in infectious diseases.

SAb BIOTHERAPEUTICS

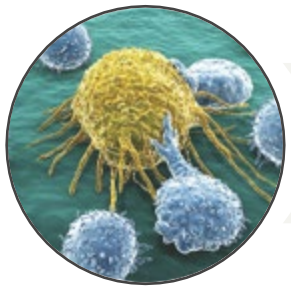
DiversitAb Platform

Christoph Bausch, PhD, MBA

CHIEF SCIENCE OFFICER

Genetically-Engineered Therapeutic Engine Leveraging Natural Human Immune Response

Mimics way that nature synergistically targets human disease complexity



Antigen(s)

Bacteria (whole killed), viruses, toxins, pDNA, cell, human tissues (internally / externally sourced)

Tc Bovine™

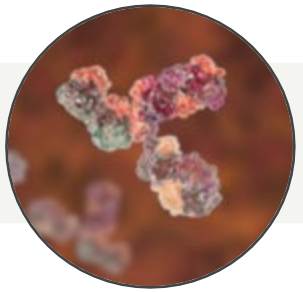
Transchromosomic bovine genetically engineered to produce fully human antibodies

Hyperimmunization

Tc Bovine inoculated with target antigen to generate immune response, driving titers beyond protective levels

Plasmapheresis

Antibodies collected in plasma



Purified Human Antibodies

Antibodies isolated through purification

Human Immunotherapy

Treatment or Prophylaxis

UPSTREAM PROCESS

DOWNSTREAM PROCESS (INDUSTRY STANDARD)

CONSISTENT AND SCALABLE PRODUCTION

Transferred full germline repertoire of human antibody response

*MATSUSHITA H, SANO A, WU H, WANG Z, JIAO J-A, KASINATHAN P, ET AL. (2015) SPECIES-SPECIFIC CHROMOSOME ENGINEERING GREATLY IMPROVES FULLY HUMAN POLYCLONAL ANTIBODY PRODUCTION PROFILE IN CATTLE. PLOS ONE 10(6): E0130699. DOI:10.1371/JOURNAL.PONE.0130699

Consistent, Replicable Platform

In Vivo Efficacy Demonstrated Across a Broad Range of Targets

TARGET	EFFICACY	MODEL(S)
Anthrax	100%	mouse (lethal)
Alphaviruses	100% 100%	mouse (lethal aerosol) non-human primate (viral clearance)
Clostridium Difficile	100% 87%	hamster (quad anti-toxin) mouse
Dengue	100%	non-human primate
Ebola*	90% 100%	mouse (lethal challenge) non-human primate (lethal challenge)
Hantavirus	80-100% 100%	hamster (lethal) non-human primate (viral clearance)
Influenza	100% 100%	mouse mouse
MERS-CoV	100%	mouse
Zika	100% 100% 100%	mouse (lethal) hamster (lethal) non-human primate

*IND-Enabled

BARDA

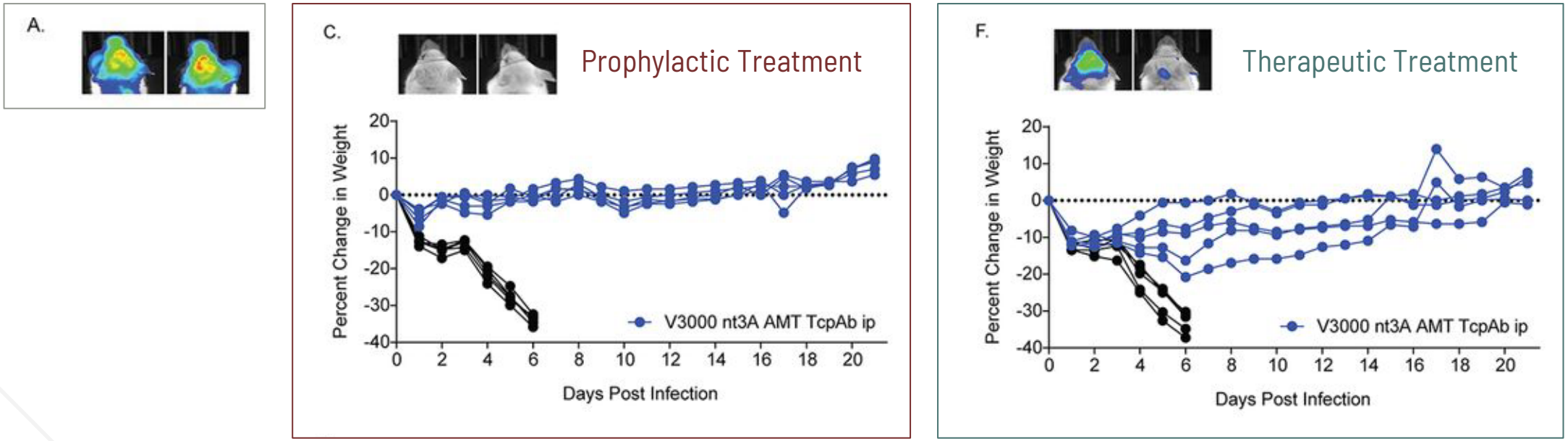
NIH National Institute of Allergy and Infectious Diseases

USAMRIID United States Army Medical Research Institute of Infectious Diseases

Demonstrated Prophylactic & Therapeutic Efficacy *In Vivo*

SAB-131 Protects Against Lethal Challenge

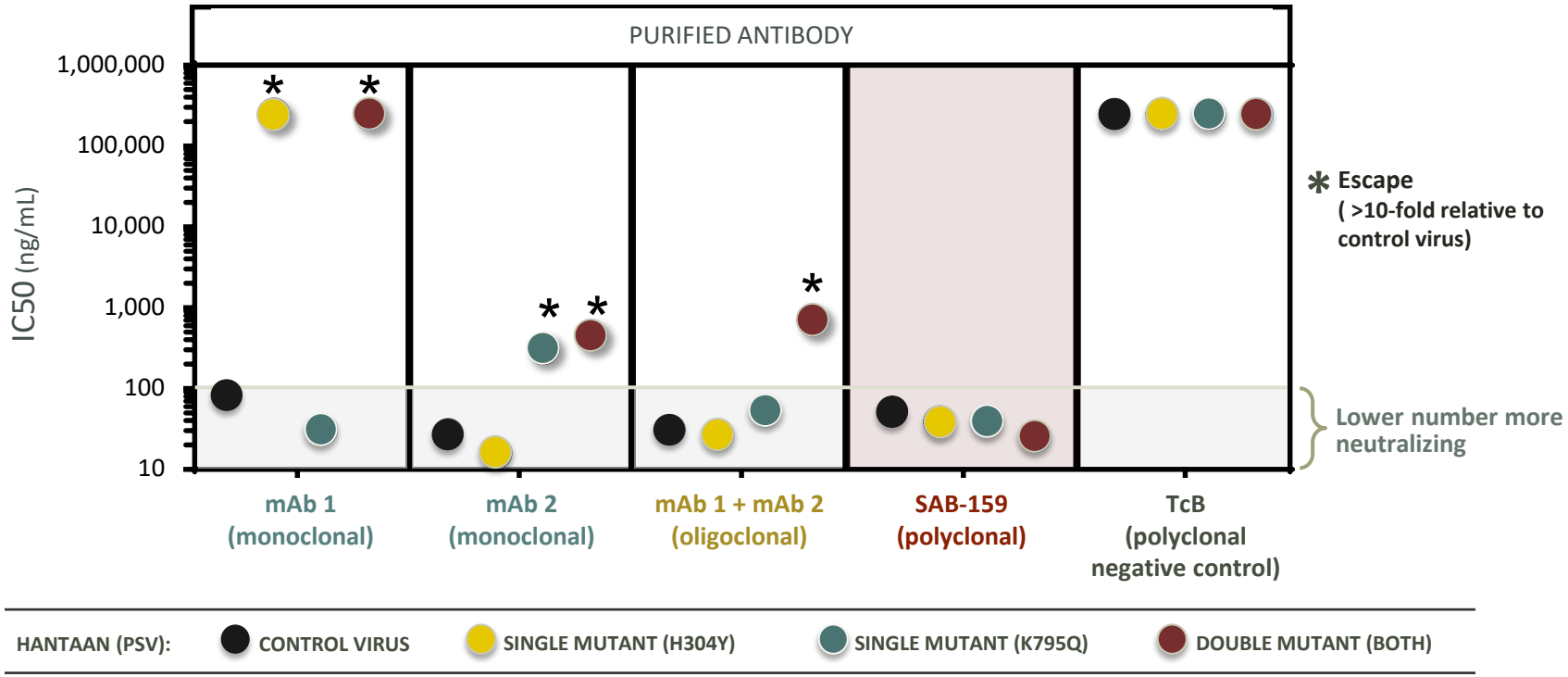
5mg/kg Dose in Venezuelan Equine Encephalitis (VEE) Virus Lethal Mouse Challenge Model



CHRISTINA L. GARDNER, CHENGQUN SUN, THOMAS LUKE, KANAKATTE RAVIPRAKASH, HUA WU, JIN-AN JIAO, EDDIE SULLIVAN, DOUGLAS S. REED, KATE D. RYMAN, WILLIAM B. KLIMSTRA . (2017) ANTIBODY PREPARATIONS FROM HUMAN TRANSCHROMOSOMIC COWS EXHIBIT PROPHYLACTIC AND THERAPEUTIC EFFICACY AGAINST VENEZUELAN EQUINE ENCEPHALITIS VIRUS 91(14): E00226-17.

Neutralization of Monoclonal Cocktail Escape Mutations

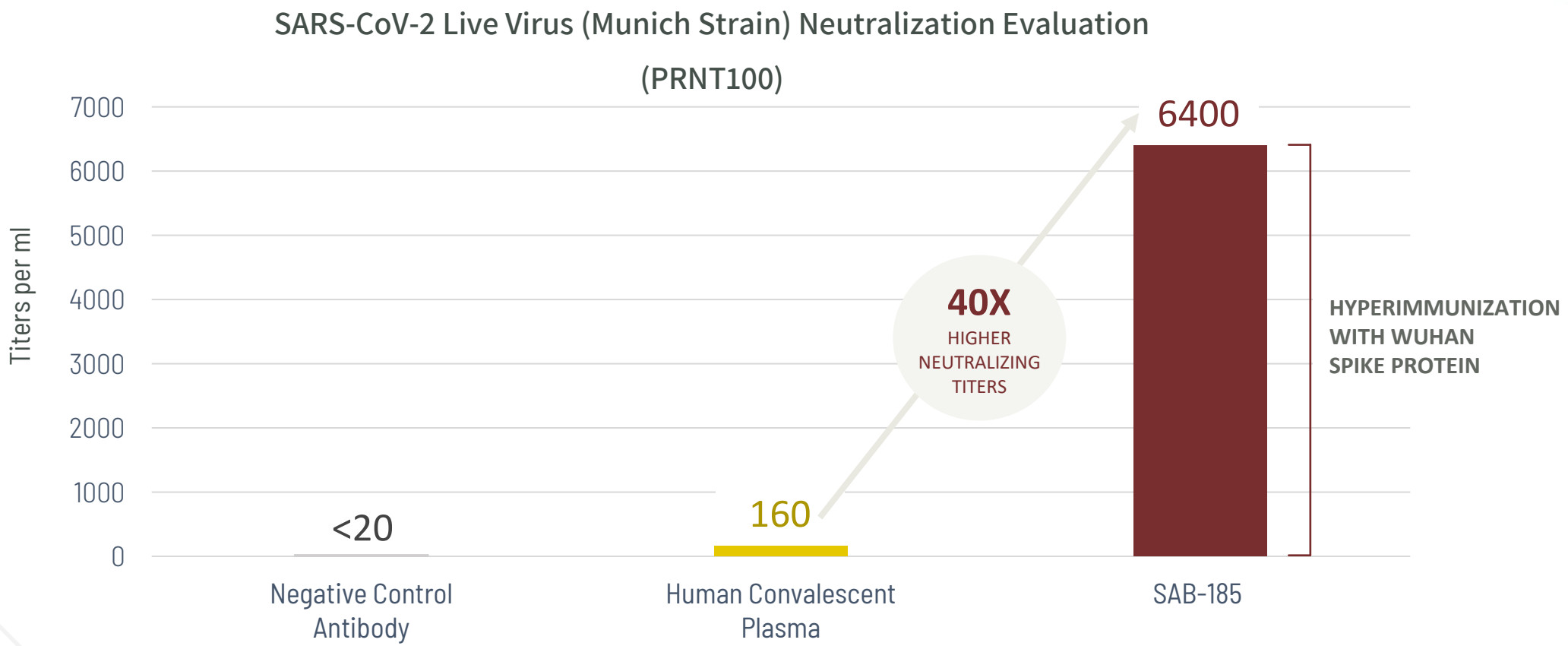
Polyclonal SAB-159 Neutralizes mAb Escape Mutants



PERLEY CASEY C., BROCATO REBECCA L., WU HUA, BAUSCH CHRISTOPH, KARMALI PRIYA P., VEGA JEREL B., COHEN MELANIE V., SOMERVILLE BRANDON, KWILAS STEVEN A., PRINCIPE LUCIA M., SHAMBLIN JOSHUA, CHIVUKULA PADMANABH, SULLIVAN EDDIE, HOOPER JAY W. ANTI-HFRS HUMAN IGG PRODUCED IN TRANSCHROMOSOMIC BOVINES HAS POTENT HANTAVIRUS NEUTRALIZING ACTIVITY AND IS PROTECTIVE IN ANIMAL MODELS, FRONTIERS IN MICROBIOLOGY,VOLUME 11, 2020, PAGE 832

Pipeline Programs

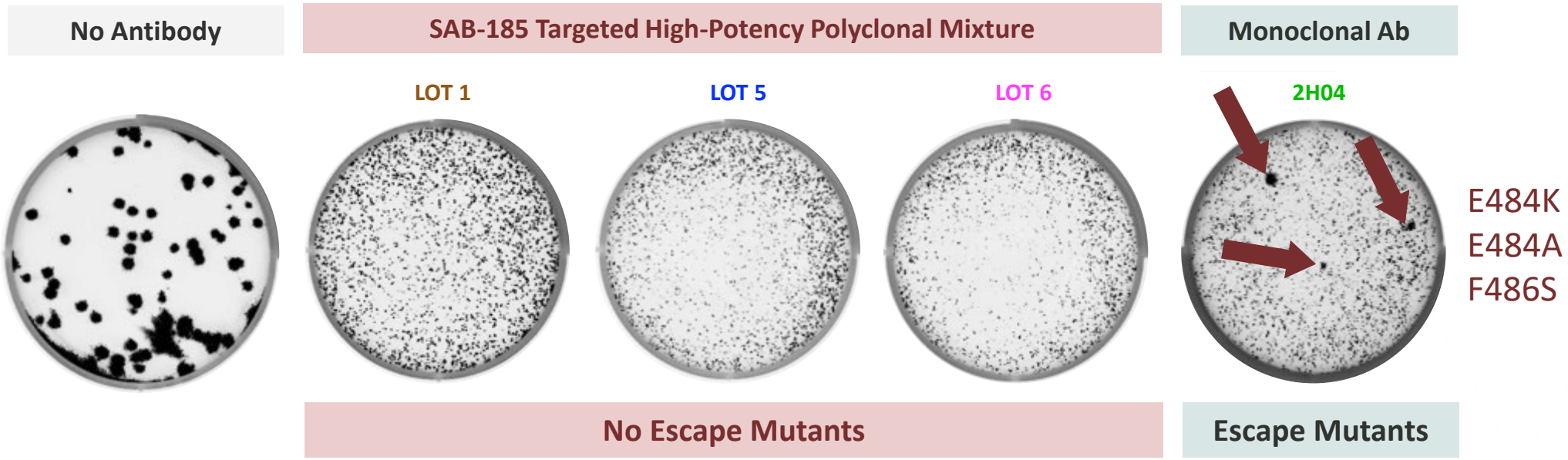
Highly-Potent: SAB-185 Exceeds Titers of Human Convalescent Plasma by 40X



WILLIAM B. KLIMSTRA. PH.D. DEPARTMENT OF IMMUNOLOGY ; MEMBER, CENTER FOR VACCINE RESEARCH; THE UNIVERSITY OF PITTSBURGH

Addresses Escape Mutants: SAB-185 Superior to Monoclonal Antibody

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



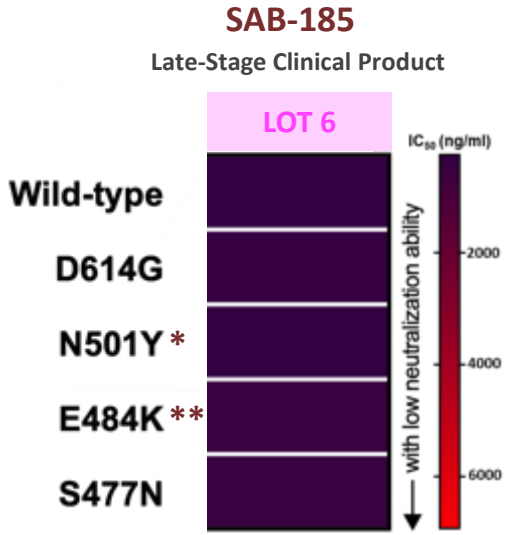
WASHINGTON UNIVERSITY SCHOOL OF MEDICINE–ST. LOUIS; 15 JAN 2021

SAb BIOTHERAPEUTICS

SAB-185 Demonstrated High Neutralization Potency Against Mutants in Circulating Strains

In vitro Neutralization Potency Against VSV-SARS-CoV-2 Mutants

VARIANTS	WT IC50 (ng/ml)	Mutation IC50 (ng/ml)	IC50 ratio (Mu:WT)*
B.1.617.1 [Kappa]	48.09	120.9	2.6
B.1.617.1 (-T95I) +V382L+D1153Y	48.09	120.9	2.6
B.1.617.2 [Delta]	49.68	138.9	2.8
B.1.617.2 + K417N	77.20	272.8	3.6
C.37 [Lambda]	78.22	74.4	1.0
B	80.94	279.0	3.4
B.1.523	80.10	229.3	3.0
B.1.525 [Eta]	80.94	279.4	3.5



* UK variant & South Africa variant '501.V2'
** E484K (South Africa variant '501.V2'

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

<5 NO SIGNIFICANT IMPACT **5-10** MILD IMPACT **10-50** MODERATE IMPACT **50** COMPLETE LOSS

*The average IC50 ratio of Mu/WTD614G

UNITED STATES FOOD AND DRUG ADMINISTRATION , CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER), WEISS LABORATORY, AUGUST 2021.

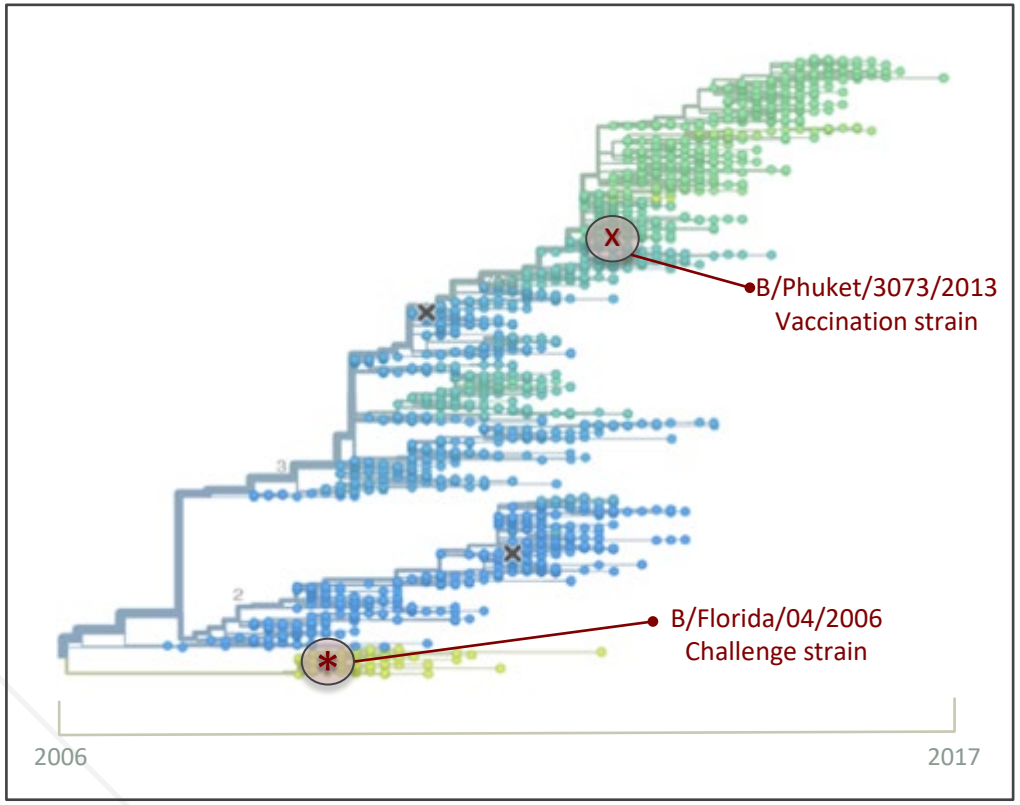
SAb BIOTHERAPEUTICS

Efficacy Against Mutational Drift

Adaptive & Cross Reactive to Mutating Strains

Highly-Mutational Influenza Virus

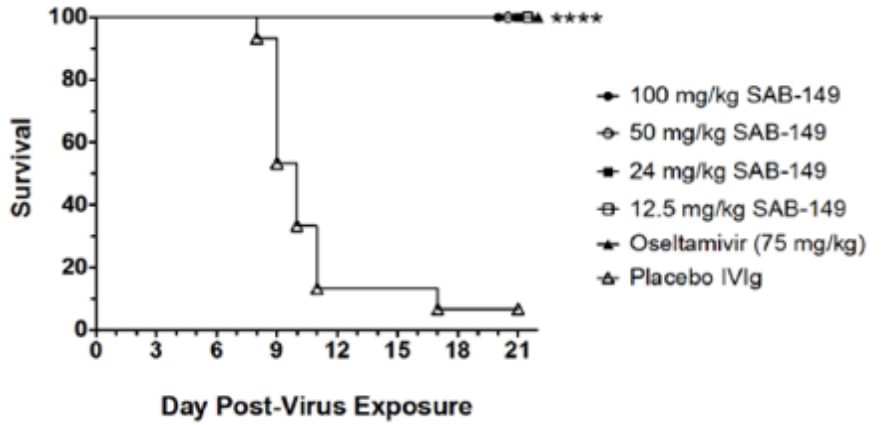
BYAM PHYLOGENIC TREE



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

100% Protection at All Dose Levels in Influenza Mouse Challenge

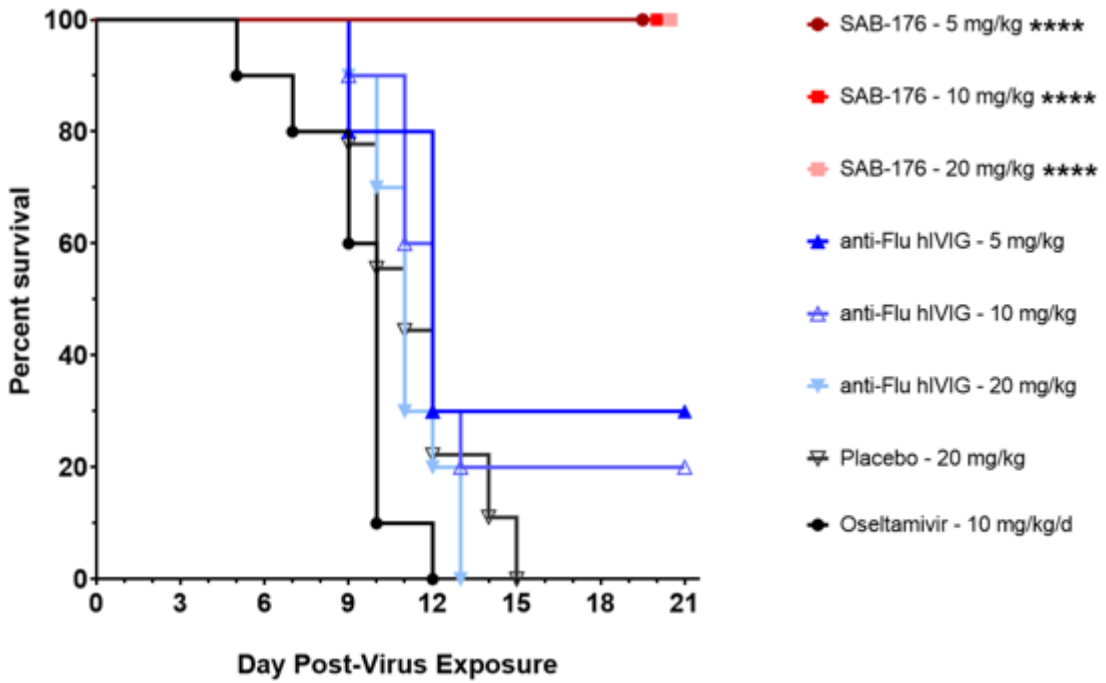
Antibodies produced to B/Phuket/3073/2013 protected against B/Florida/04/2006



Overcomes Resistance: SAB-176 Demonstrated *In Vivo* Efficacy Against Oseltamivir-Resistant Viruses

Single dose of SAB-176 at 5mg/kg provided 100% protection from mortality
Mice treated with anti-Flu hIVIG at 20mg/kg had 0% survival

In-vivo Oseltamivir Resistant pH1N1 Mouse Challenge Study
Intraperitoneal Treatment



JUNE 2019

SAB-142: Potential Breakthrough Applicable to Many Autoimmune Diseases

Superior to Widely-Used Animal Serum-Derived Immune Globulins ATGAM & Thymoglobulin

Limitations of approved animal serum-derived ATG products:

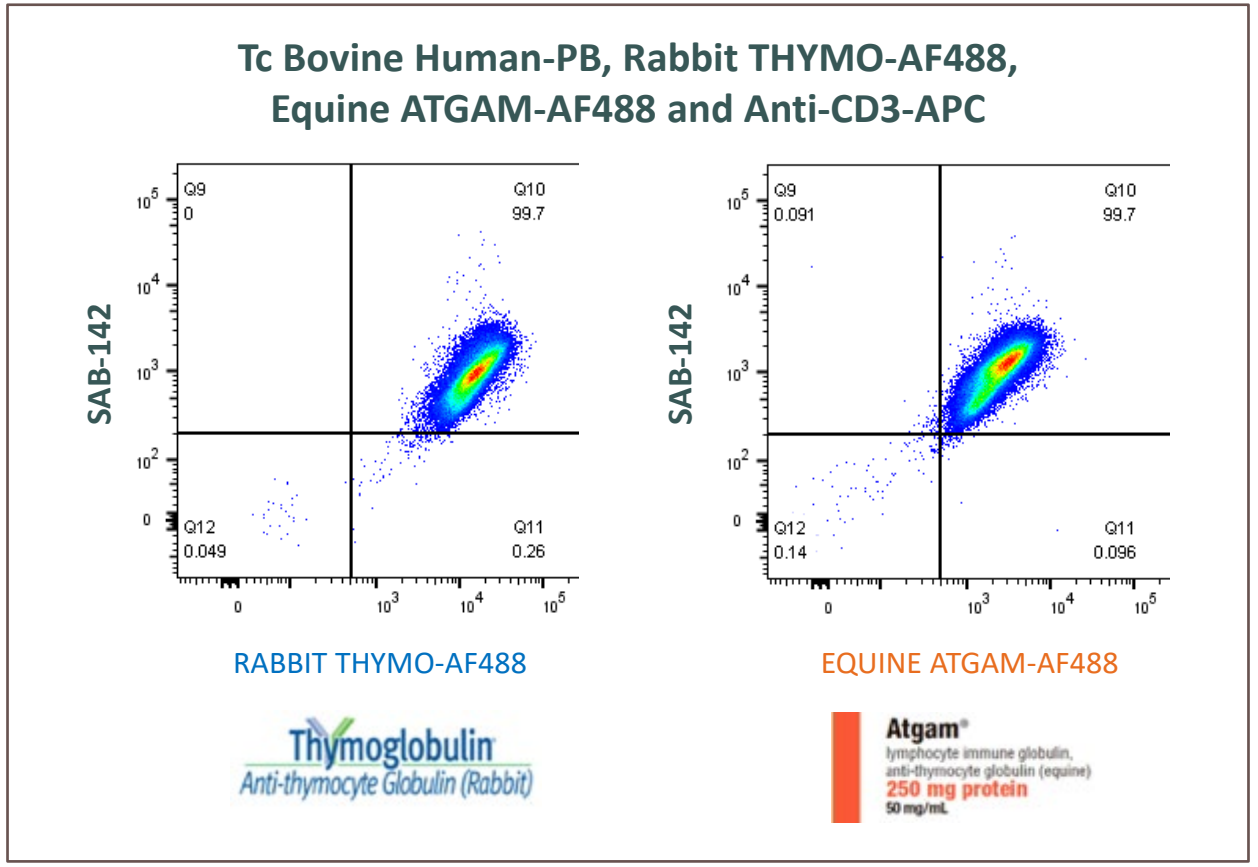
- Serum sickness and development of anti-drug antibodies (ADA) have limited use
- Rates of serum sickness are >30% so repeat dosing is not recommended
- Physicians reserve use for transplant induction or rejection – but not both
- These issues limit use in new indications such as delaying/preventing onset of type 1 diabetes

Human alternative could have **significant efficacy, safety, and dosing advantages** over ATG animal products

In the **established transplant market**, a fully-human ATG with reduced risk of serum sickness AEs could **rapidly penetrate and expand existing use**

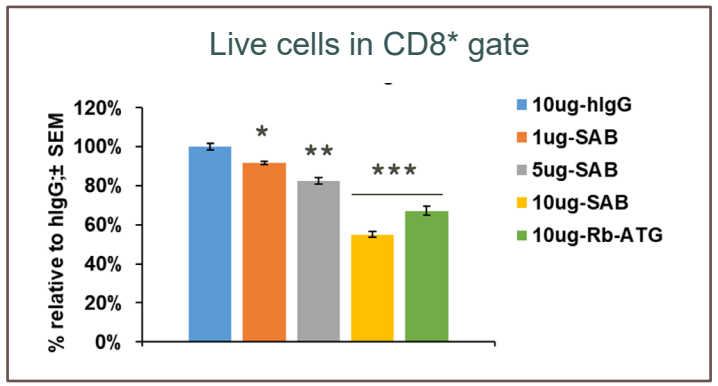
Significant market potential in delaying or preventing new-onset type 1 diabetes based on Phase 2 clinical trial results of rabbit ATG

SAB-142: Comparable Mode of Action to Approved Products

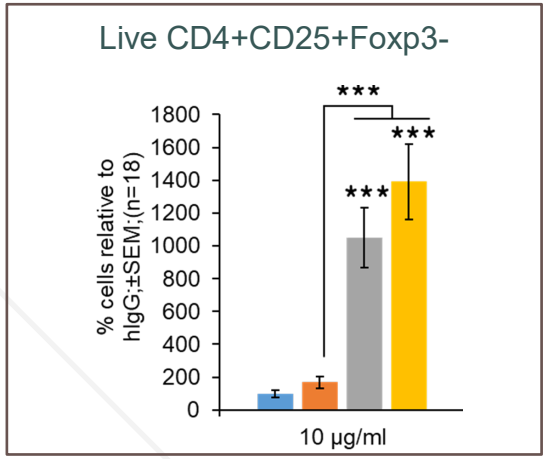


SAB-142: Similar Activity to Approved Rabbit ATG Targets CD8 and Protects T-Regulatory Cells

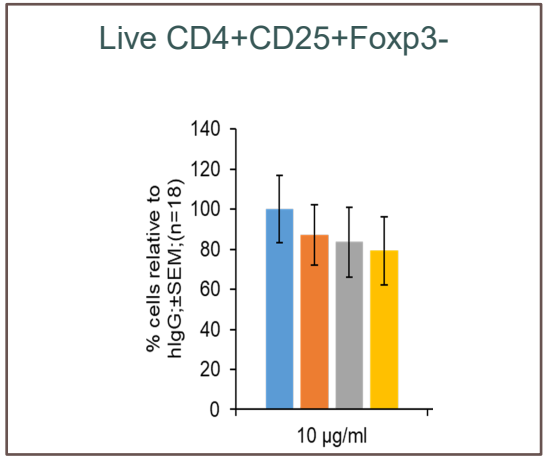
CD8 T Cells



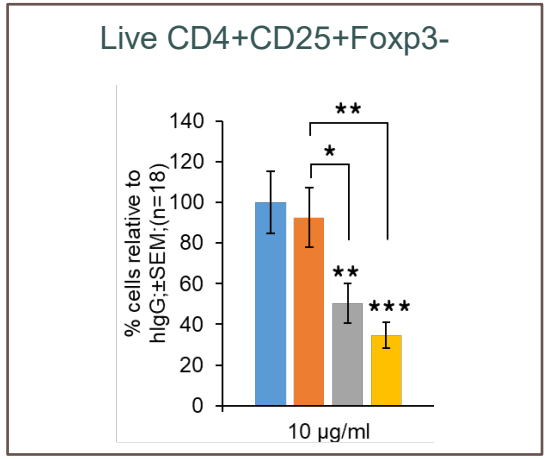
Treg Cells

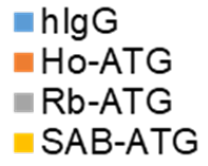


Activated CD4 T Cells



Naïve CD4 T Cells





SAb BIOTHERAPEUTICS

KOL PRESENTATION:

Low Dose Anti-Thymocyte Globulin (ATG) in Type 1 Diabetes

Michael Haller , MD, MS-CL

Professor and Chief Pediatric Endocrinology, Silverstein Family Eminent Scholar

Pediatric Endocrinology

UNIVERSITY OF FLORIDA COLLEGE OF MEDICINE

Low Dose Anti-Thymocyte Globulin (ATG) in Type 1 Diabetes

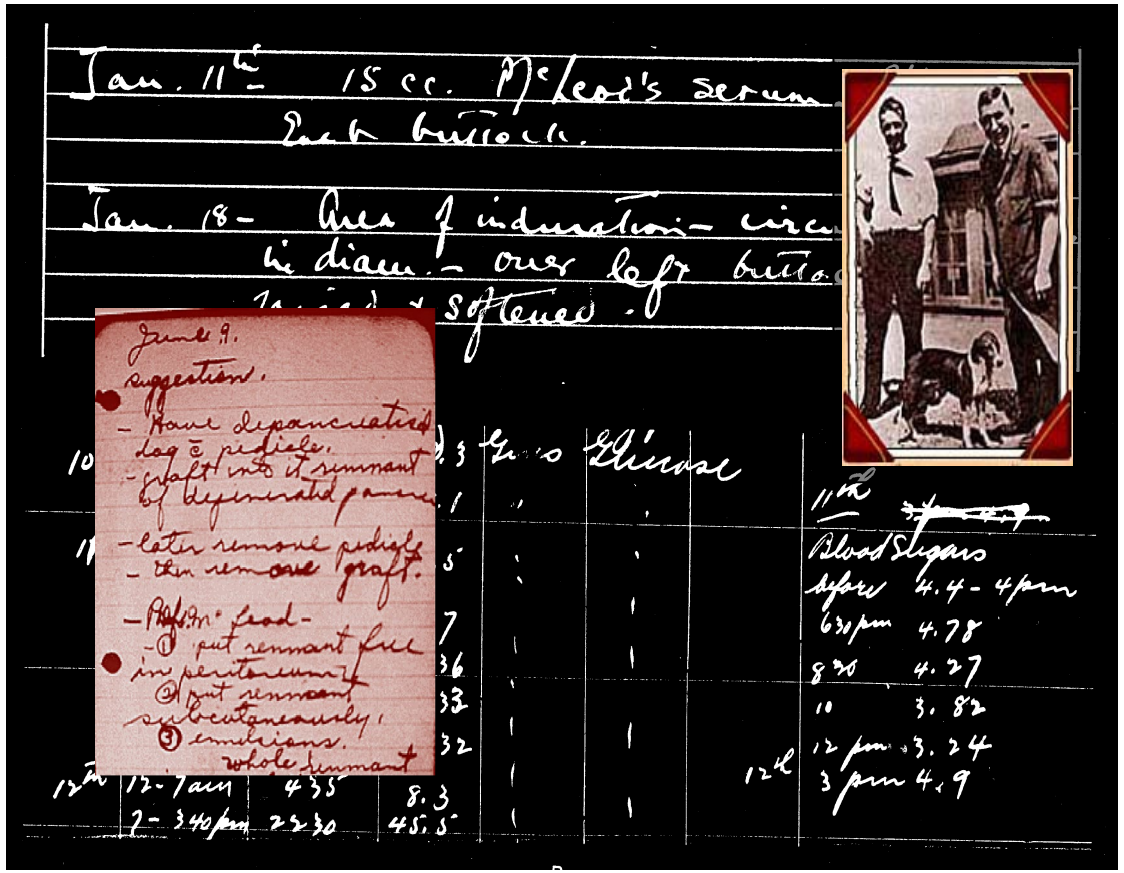
Michael J. Haller, MD
Professor and Chief
Pediatric Endocrinology
University of Florida

UFHealth
Shands Children's Hospital

What is the scope of the problem?

- **Type 1 diabetes – 1 in 300 children**
- **1 in 7 health care dollars attributable to diabetes and downstream costs**
- **No FDA approved therapeutics outside of….insulin**
- **Complex Disease requiring polyclonal “combination” therapy approach”**
- **Need induction and maintenance therapies**

The Major Therapeutic Breakthrough for Type 1 Diabetes - 1921

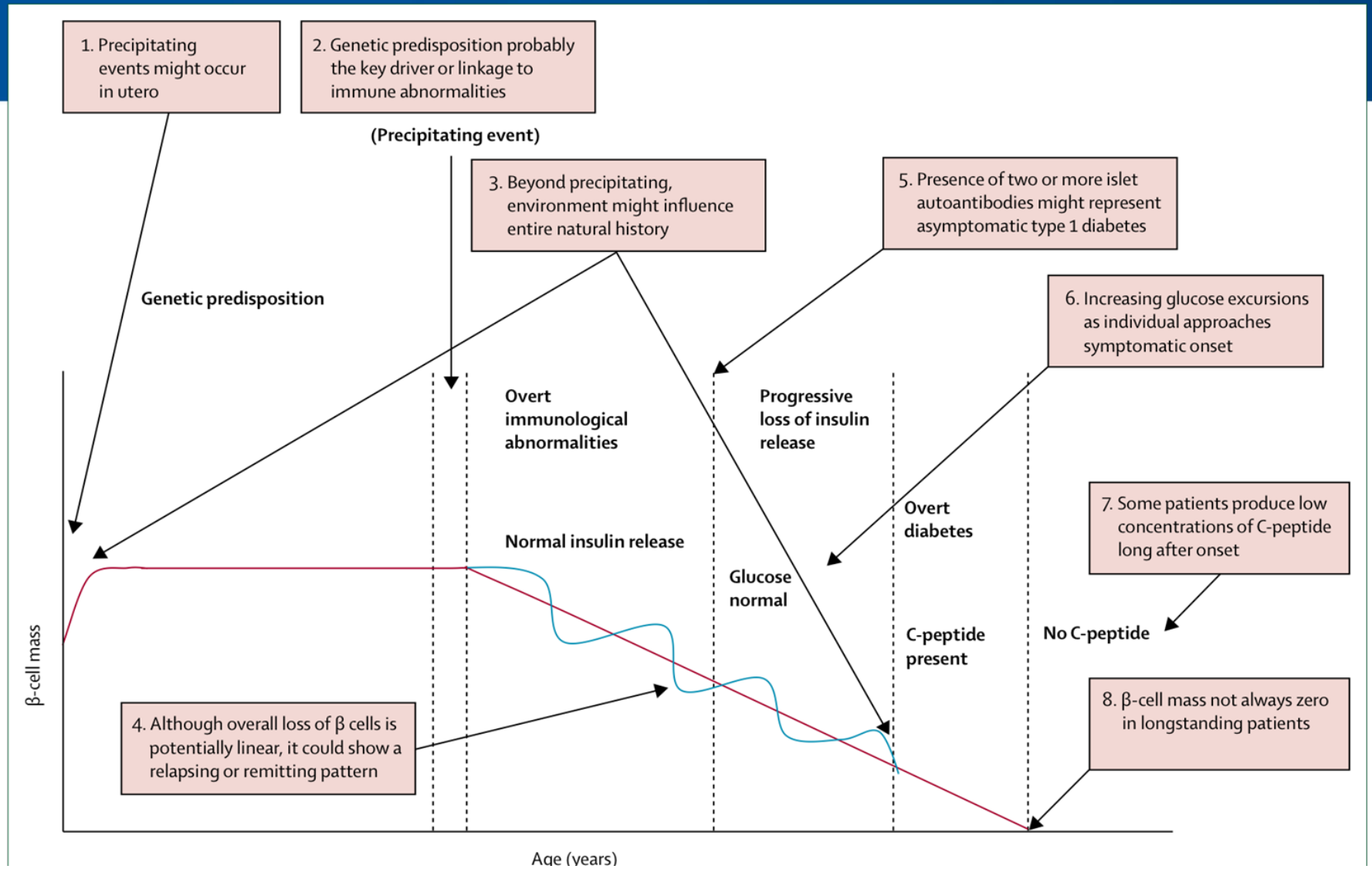


Thick brown muck" lowered glucose from 520 to 120 mg/dl

7.5ml into each buttock

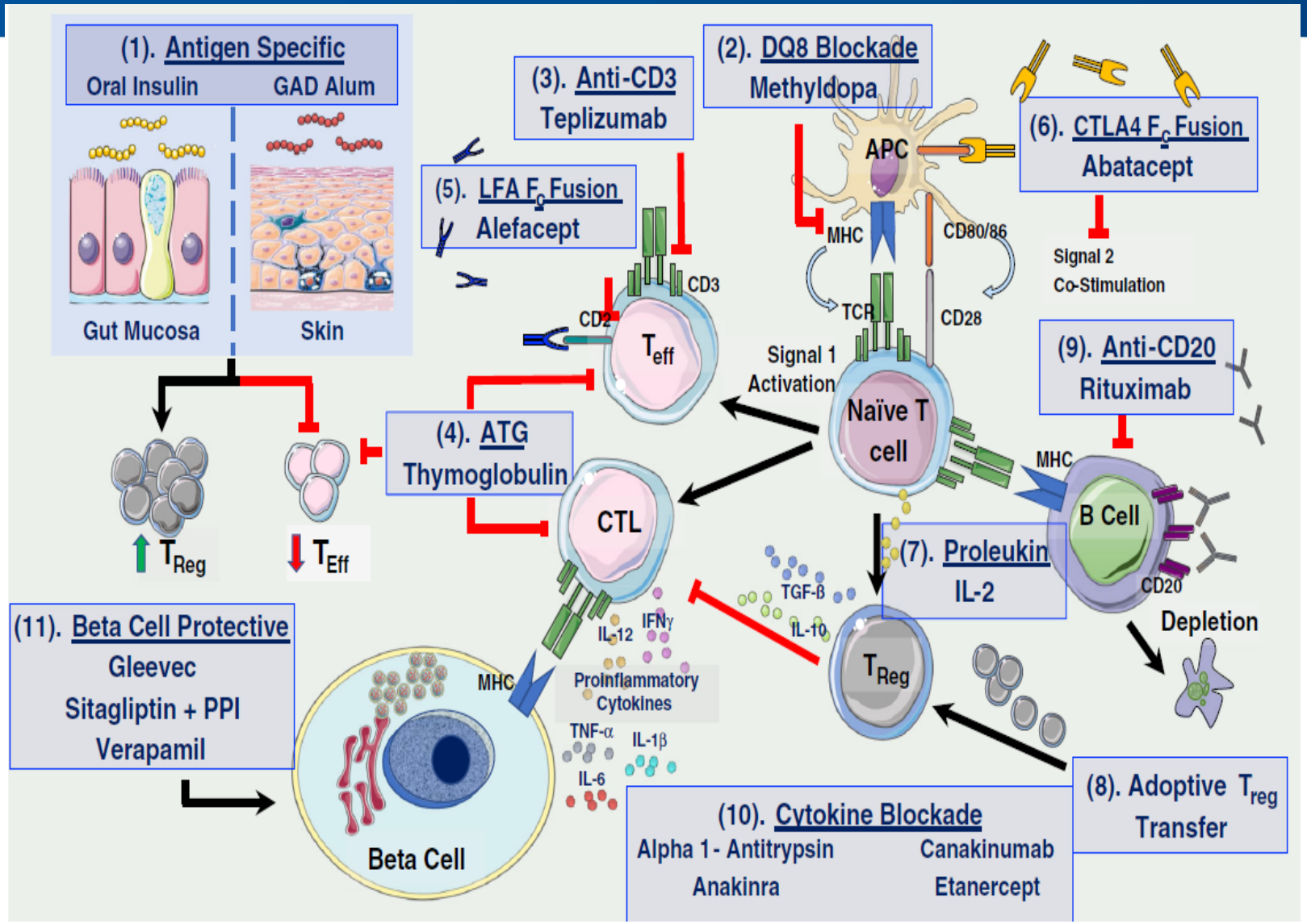
100 years Later, 1921-2021…

Type 1 Diabetes Pathogenesis



Atkinson, M; Eisenbarth, G.S.; Michels, A. Lancet, 2014

Multiple therapeutic targets in a complex disease …..Ideal for a “Clean” Polyclonal Agent



“Failures”

IL2+Rapamycin (ITN-led)	Adverse effect
Mycophenylate+Anti-CD25	No effect
GAD	No effect
Canakinumab Anti-IL1-β	No effect
Metabolic Control Study	No effect

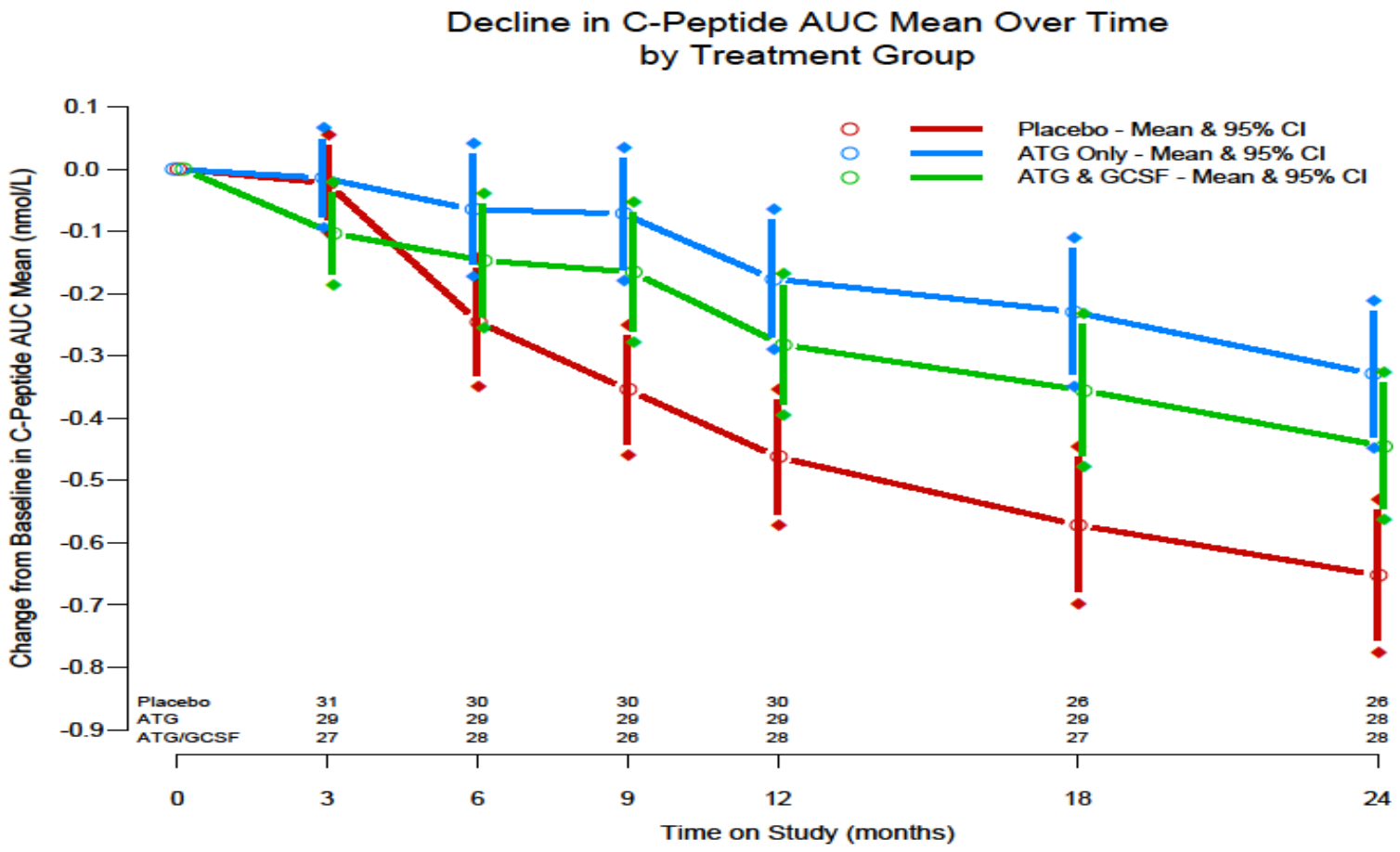
“Successes”

❑ **Rituximab Anti-CD20**	**Transient effect**
❑ **Abatacept CTLA4-Ig**	**Transient effect**
❑ **Teplizumab Anti-CD3 (ITN-led)**	**Transient effect**
❑ **Teplizumab (prevention)**	**Delay of onset in Stage 2**
❑ ***Thymoglobulin 6.5mg/kg (ITN-led)**	**Positive effect in age 22-35**
❑ ***Thymoglobulin 2.5mg/kg**	**2-year preservation of C-peptide and A1c reduction across all study ages**

*Rabbit ATG from Sanofi – NOT SAB-142 Humanized TG Bovine

2 Years: Low-Dose ATG
Preserved C-Peptide in New Onset T1D

*Rabbit ATG from Sanofi – NOT SAB-142 Humanized TG Bovine



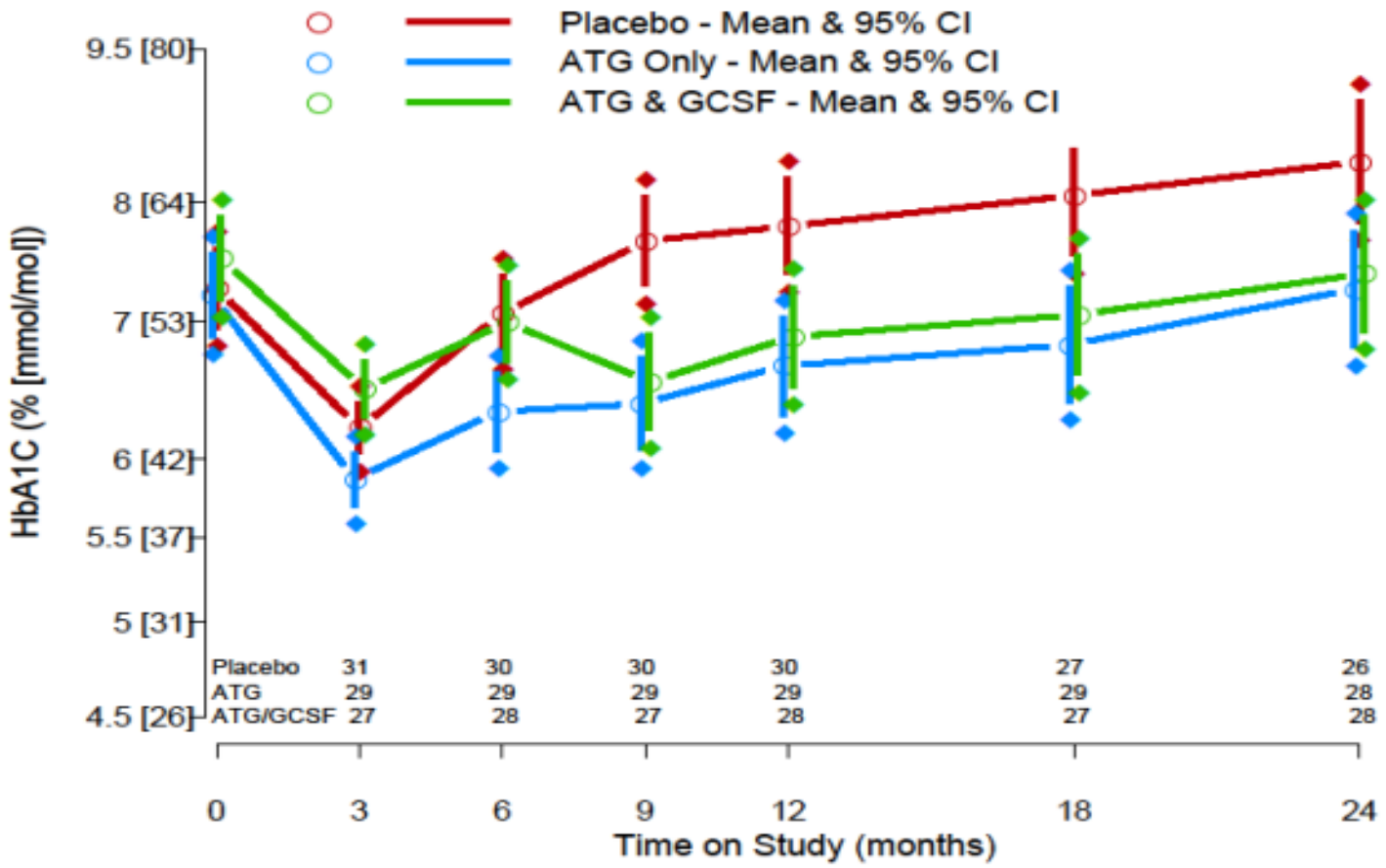
p=0.00005
ATG vs Placebo

Placebo

Haller et al. Diabetes. 2019. Jun;68(6):1267-1276

2 Years: Low-Dose ATG
Reduced HbA1c in New Onset T1D

*Rabbit ATG from Sanofi – NOT SAB-142 Humanized TG Bovine



Placebo

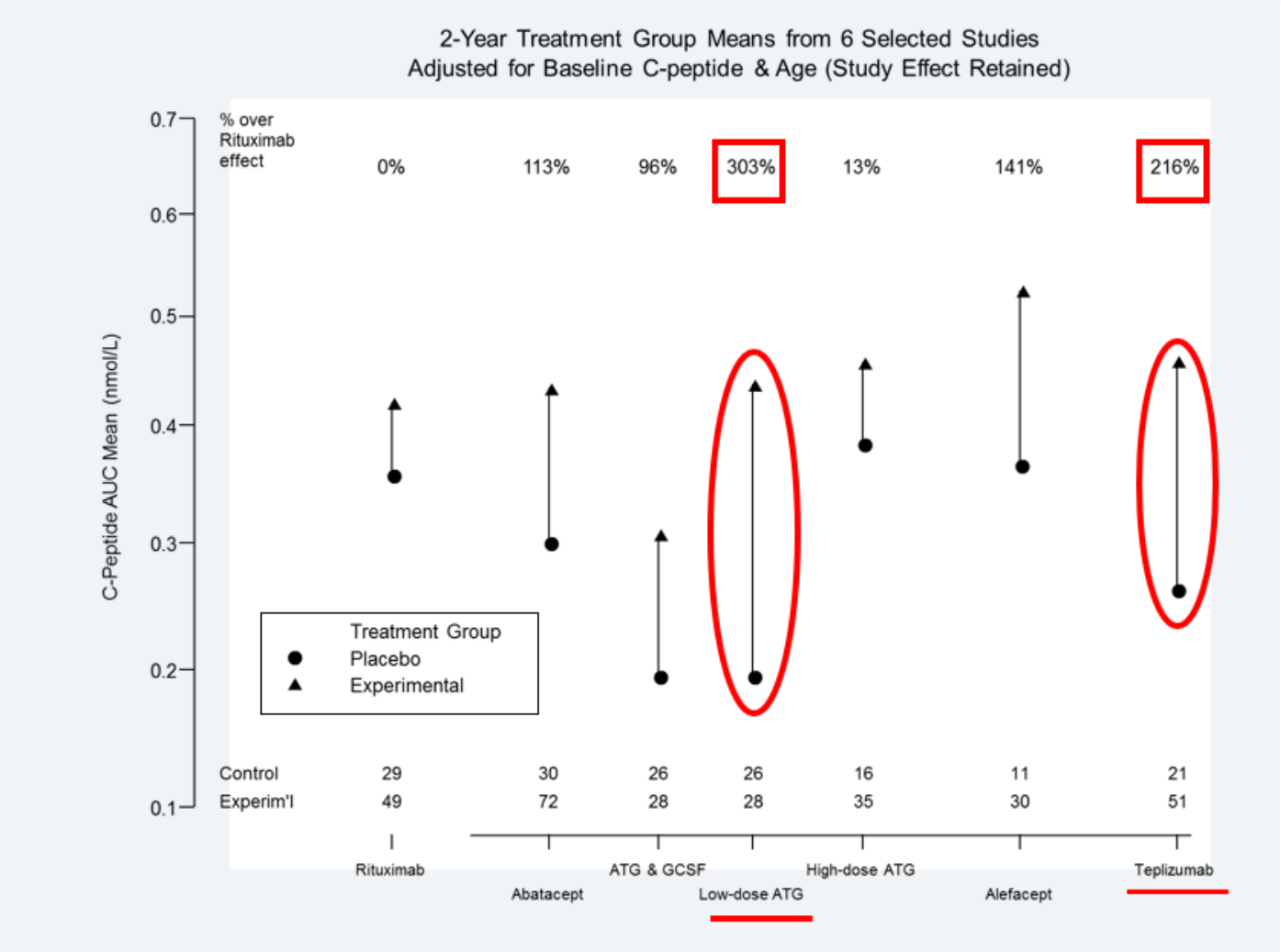
p=0.011 ATG vs Placebo

Haller et al. Diabetes. 2019. Jun;68(6):1267-1276

Outcomes of T1D Studies

	N	Age (yrs)	Regimen	Primary Outcome (AUC C-peptide)	p
Abatacept	112	6–36	10mg/kg IV day 1, 14, 28, then monthly x 2 years	2hr MMTT at 2 years	0.0022
Rituximab	87	8–40	375mg/m^2 IV day 1, 8, 15, 22	2hr MMTT at 1 year	0.03
ATG (± G-CSF) – Low Dose	89	12–45	ATG 2.5mg/kg IV over 2 days (± G-CSF 6mg SQ x 6 q2 week)	2hr MMTT at 1 year	0.0003 (ATG only)
Alefacept (T1DAL)	49	12–35	15mg IM weekly x 12, repeated 12 weeks later	2hr MMTT at 1 year	0.065
Teplizumab (AbATE)	77	8–30	Median dose ~11.6mg IV over 14 days ± repeat at 1 year	4hr MMTT at 2 years	0.002
ATG – High Dose (START)	52	12–35	6.5mg/kg IV over 4 days	2hr MMTT at 1 year	0.591

Cross Trial Comparison – 2 Years



Effect of Low-dose ATG superior at 2 years

Rabbit ATG from Sanofi – NOT SAB-142 Humanized TG Bovine

Diabetes Technol Ther. 2020 Dec;22(12):948-953

Low Dose ATG Prevention: Starting Q1 2022

- ❑ **Stage 2 T1D = Ab+ / Dysglycemic**
- ❑ **Age 8 and up**
- ❑ **Single course low-dose ATG (2.5mg/kg)**
- ❑ **Rabbit ATG from Sanofi**
- ❑ **2 IV infusions on back to back days**
- ❑ **1:1 Randomization**
- ❑ **97 Subjects**

Type 1 Diabetes TrialNet

Low Dose ATG – Clinical Therapy?

- ❑ **Patients asking for clinical therapy = No**
- ❑ **Pilot ATG/GCSF = No…no…no**
- ❑ **TrialNet ATG = no (1 yr), no (18 mo), maybe (2 yr)**

- ❑ **Access to Drug – FDA Approved**
- ❑ **No….no…no…no…no**

….Maybe….Maybe…..Lets Discuss

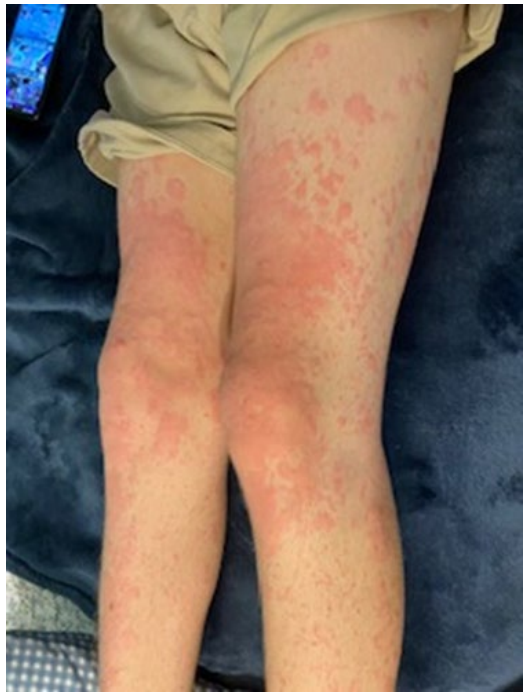
….*OK, but*

Low Dose ATG – Open Label Prevention

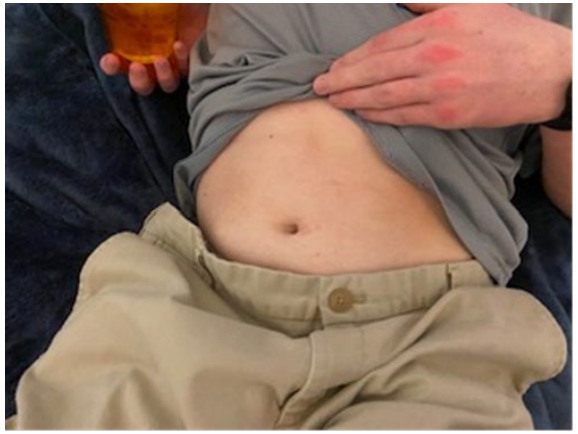
- ❑ **2 Children with Multiple Antibodies and Dyglycemia**
- ❑ **No study available for them/ likely to progress to T1D**
- ❑ **Both have a Parent who is in Health Care and with T1D**
- ❑ **Approached Me (not recruited)**
- ❑ **Treated April 2019 and July 2019**

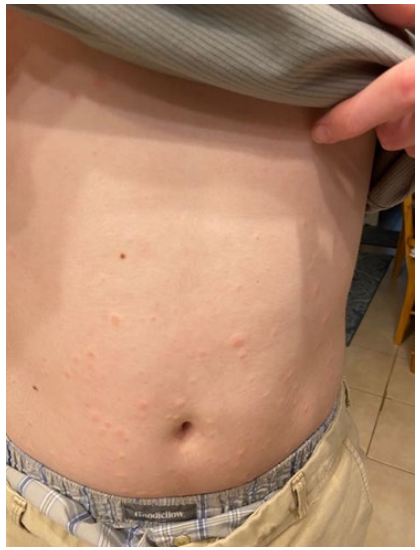
- ❑ **Neither have progressed to T1D as of Today…. 2+ years**

Serum Sickness in 2/3 of Rabbit ATG (Sanofi)
NOT SAB-142



- ❑ 3-4 days of malaise, fever, joint swelling
- ❑ Often requires steroids
- ❑ Worsens diabetes management (days)
- ❑ Reduces capacity to give ATG again (though common in aplastic anemia)

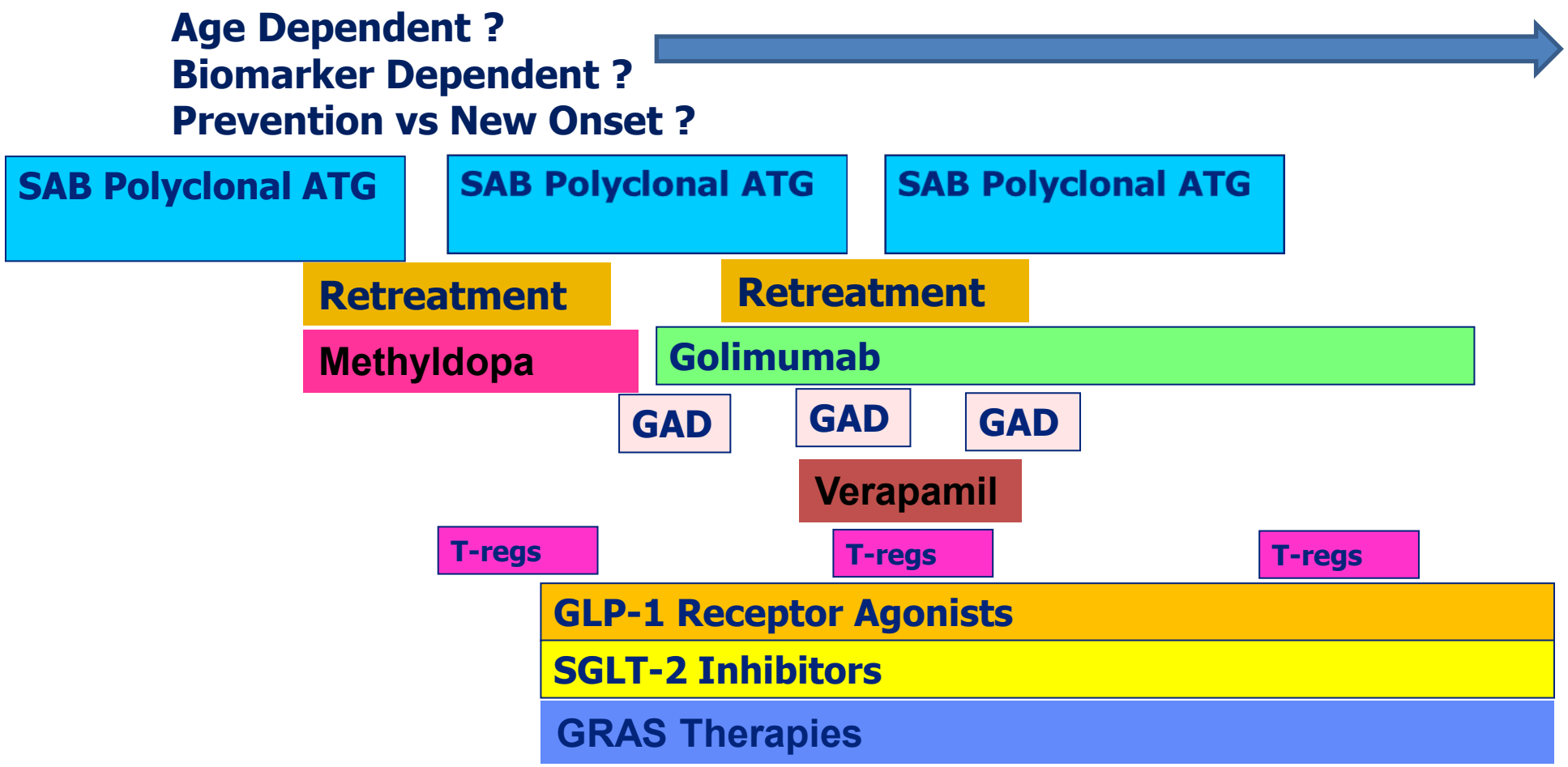




Why SAB Polyclonal ATG (SAB-142) ?

- **Eliminate Serum Sickness**
- **Re-treatment without risk**
- **More potent in vitro than current ATG**
- **Likely to entirely replace current polyclonal immunosuppressive (Thymoglobulin) if similarly effective**
- **Kidney Transplant / Autoimmune Disease / Cancer Therapy**
- **Large untapped market**

Next Approaches



UFHealth
Shands Children's Hospital

Acknowledgements

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Clinical Trials

Tom Luke, MD

CHIEF MEDICAL OFFICER

SAB-185: Clinical Development Plan

	Phase 1: Healthy Volunteers	Phase 1b: COVID-19 Positive Ambulatory Patients	Phase 2/3 Pivotal Treatment Trial: NIH NIAID ACTIV-2 Adaptive Platform	
STUDY DESIGN	• Randomized, double-blind, placebo-controlled • Single and multiple ascending dose study • Administered intravenously • 28 healthy participants in four cohorts • 10, 25, 25 x 2, 50 mg/kg	• Randomized, double-blind, placebo-controlled • Ascending dose study • Administered intravenously • 21 non-hospitalized patients with mild or moderate COVID-19 in three cohorts • 10, 25, 50 mg /kg	• Randomized, blinded, superiority • 220 participants (110 low dose, 110 high dose) vs 110 control • COVID-19 disease symptoms <7 days	• Randomized, unblinded, active comparator control, non-inferiority • 600 participants (SAb-185 low dose) vs 600 active comparator • COVID-19 disease + one risk factor and symptoms ≤ 7 days
ENDPOINTS	• Primary: Safety • Secondary: pharmacokinetics, pharmacodynamics, anti-drug antibodies	• Primary: Safety • Secondary: pharmacokinetics, pharmacodynamics, anti-drug antibodies, virology, symptoms/signs	• Co-Primary: 1–Safety, 2–Reduce duration of COVID-19 symptoms through 28 days, 3–Proportion of negative SARS-CoV-2 NP swabs at one or more days 3, 7 or 14, as compared to placebo • Secondary: Multiple	• Co-Primary: 1–Safety, 2–Composite endpoint of either hospitalization due to any cause or death due to any cause through day 28. • Secondary: Multiple

SAB-176: Clinical Development Plan

	Phase 1: Healthy Volunteers	Phase 2a H1N1 Challenge Study: Healthy Volunteers	Planned Phase 2b/3 Adaptive Design Bone Marrow and Hematologic Malignancy Volunteers	
STUDY DESIGN	• Randomized, double-blind, placebo-controlled • 27 healthy volunteers • Single ascending dose study • 1, 10, 25 and 50 mg/kg	• 60 total participants • Two cohorts of 30 randomized to SAB-176 (25 mg/kg) or normal saline control (30:30) • Challenge strain: H1N1 California (pandemic)	• 100 participants • Bone marrow and hematologic malignancy participants with Type A or B influenza diagnosis and symptoms ≤ 4 days • SAB-176 and SOC vs SOC • Single dose : 25 mg/kg	• 100+ participants (TBD) • Bone marrow and hematologic malignancy participants with Type A or B influenza diagnosis and symptoms ≤ 4 days • SAB-176 and SOC vs SOC • Single dose: 25 mg/kg
ENDPOINTS	• Primary: Safety • Secondary: Pharmacokinetics, pharmacodynamics, anti-drug antibodies	• Primary: Safety and viral load reduction • Secondary: Sign/symptom reduction	• Primary: Elimination of virus, hospitalization and ICU days and death • Secondary: Prevention of recrudescent influenza or new influenza infection over 120 days, others	• Primary: TBD • Secondary: multiple

Q&A Session

R&D Day
13 OCTOBER 2021

Thank you