From Discovery to Phase 3: Advancing Transchromosomic Bovine Polyclonal Antibodies through the Military Development Pipeline

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Disclosure

- Thomas C. Luke is co-founder and owner of Poly Solutions, LLC.

Learning Objectives

Objective 1: Describe the end-to-end product development pathway for transchromosomic bovine-derived polyclonal antibodies from preclinical discovery through Phase 3 clinical trials.

Objective 2: Analyze how military partnerships with academia, NIH clinical trial networks, and industry accelerated the development of fully human polyclonal antibody countermeasures.

Objective 3: Discuss opportunities for leveraging existing DoD infrastructure and the Tc bovine platform to expand the polyclonal antibody countermeasure portfolio against current and emerging threats.

Human Antibody Production in Transchromosomic (Tc) Bovine

Therapeutic Platform Technology

Tc Bovine
Produces high-titer fully human pAbs

600-720 days

Antigen
Disease target (Bacteria, virus, toxin)

Variable

Immunization
Hyperimmunize to generate immune response

Plasma
Plasmapheresis to collect human polyclonal Abs

Human pAb
Isolate by purification process

90 days

Custom High-Potency Immunotherapy

Tc Bovine Platform Attributes

The Tc bovine platform produces **fully-human polyclonal IgG** after hyper-immunization on a timeline measured in months, not years.

Emergency Response: ~100 days from first immunization to GMP drug substance.

Antigen substrate: Recombinant protein(s), inactivated viruses, pDNA(s).

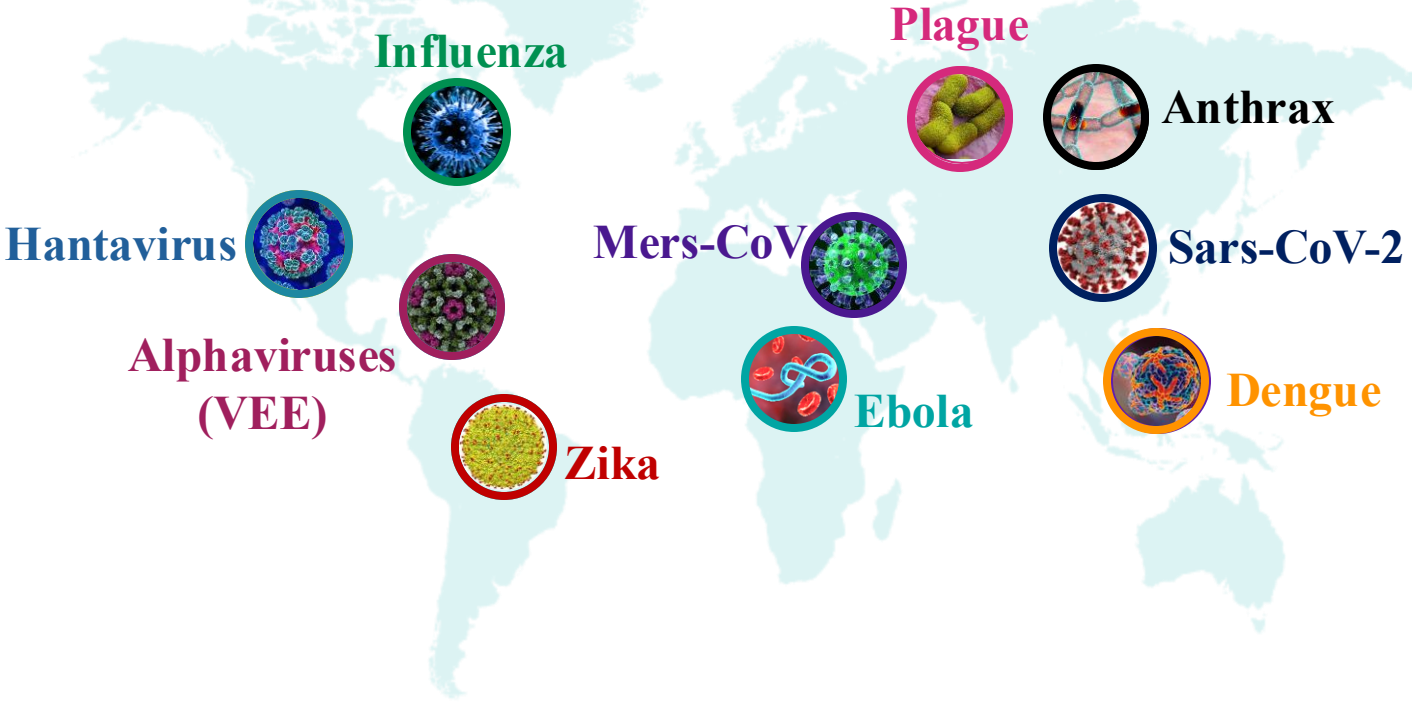
Production: 150–600 grams of purified fully-human IgG per Tc bovine per month.

Utility: Multiple military relevant pathogens advanced to CBER FDA allowed Phase 1-3 clinical trials.

Breadth: Monovalency/multivalency against viruses, bacteria, or toxins.

Administration: IV, IM, SQ or Pulmonary routes

Tc Bovine Therapeutics to Global Biothreats



In Vivo Efficacy Across a Broad Range of Pathogens

Pathogen	Efficacy/ Safety	Tested	Collaborators	Status
MERS-CoV	100% yes	mouse human safety & half-life	NMRC, NIH NIAID, NVAX, WHO, BARDA, HJF, CDC	Phase 1, 2017 Phase 2/3, TBD
Tetravalent Influenza	100% yes	mouse, ferret, NHP human challenge study	NMRC, NIH, BIOSNTR, USD, USU, hVIVO, BARDA, HJF	Phase 1, 2020 Phase 2b, 2022
Mycoplasma hominis	yes	human (safety & efficacy)	Harvard Medical School, BWH	Phase 1, 2017
SARS-CoV-2	yes	mouse, hamster, ferret human (various)	NMRC, USAMRIID, NIAID, UPITT, UIOWA, UPITT, USU, WashU, WHO, BARDA, CDC	Phase 1-3, 2020-2022
Alphavirus (VEE)	100%	mouse (lethal aerosol)	NMRC, DTRA, UPITT, HJF	Preclinical
Anthrax	100%	mouse (lethal)	USAMRIID	Preclinical
Plague	100%	mouse (lethal aerosol)	USAMRIID	
Ebola (Zaire, Sudan)	100%	non-human primate (lethal)	NMRC, NIAID, NIH, NVAX, BROAD Inst., HJF	IND-enabled
Zika	100% 100%	mouse (lethal), hamster (lethal) non-human primate	PHAC, USU, Harvard	Preclinical
Tetravalent Hantavirus	80-100%	hamster	USAMRIID	IND-enabled
Tetravalent Dengue	100%	non-human primate	NMRC, HJF	Preclinical

Coronaviruses

Threat Context

Global Pandemics

Therapeutics

MERS-CoV (SAB-301)

First-in-Man Phase 1 (2017): Safety and 28-day IgG half-life confirmed

SARS-CoV-2 (SAB-185)

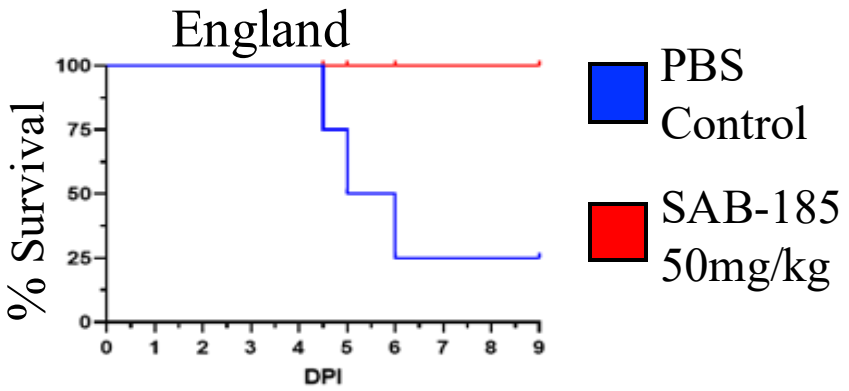
Phase 1–3 2020–2022 via ACTIV-2 network
Persistent variant coverage: Ancestral, Delta, Omicron, and others
Monoclonals rapidly failed due to resistance

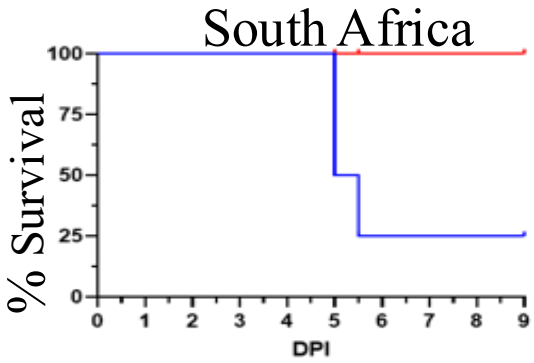
Partners

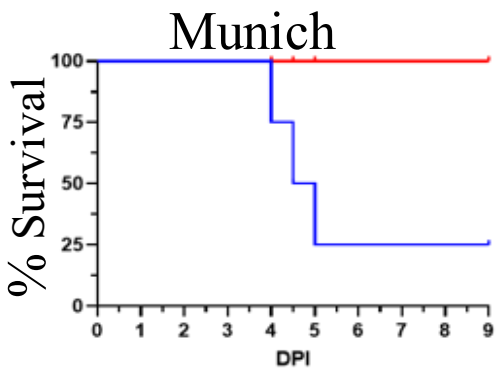
NMRC · NIAID · BARDA · USAMRIID · UPITT · USU · UIowa · WashU · KSAU-HS HJF · FDA · WHO

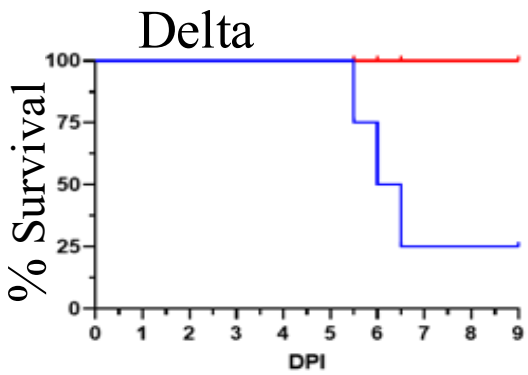
SAB-185 Demonstrated 100% Efficacy to SARS-CoV-2 Mutants *In Vivo*

SAB-185 provided 100% protection in lethal hACE-2 hamster model against challenge with SARS-CoV-2 Mutants









Hantavirus

Threat Context

Documented outbreaks among U.S. military: Korean conflict, Balkans operations, and Southwest America. Recent outbreak on cruise ship.

Therapeutic (SAB-163)

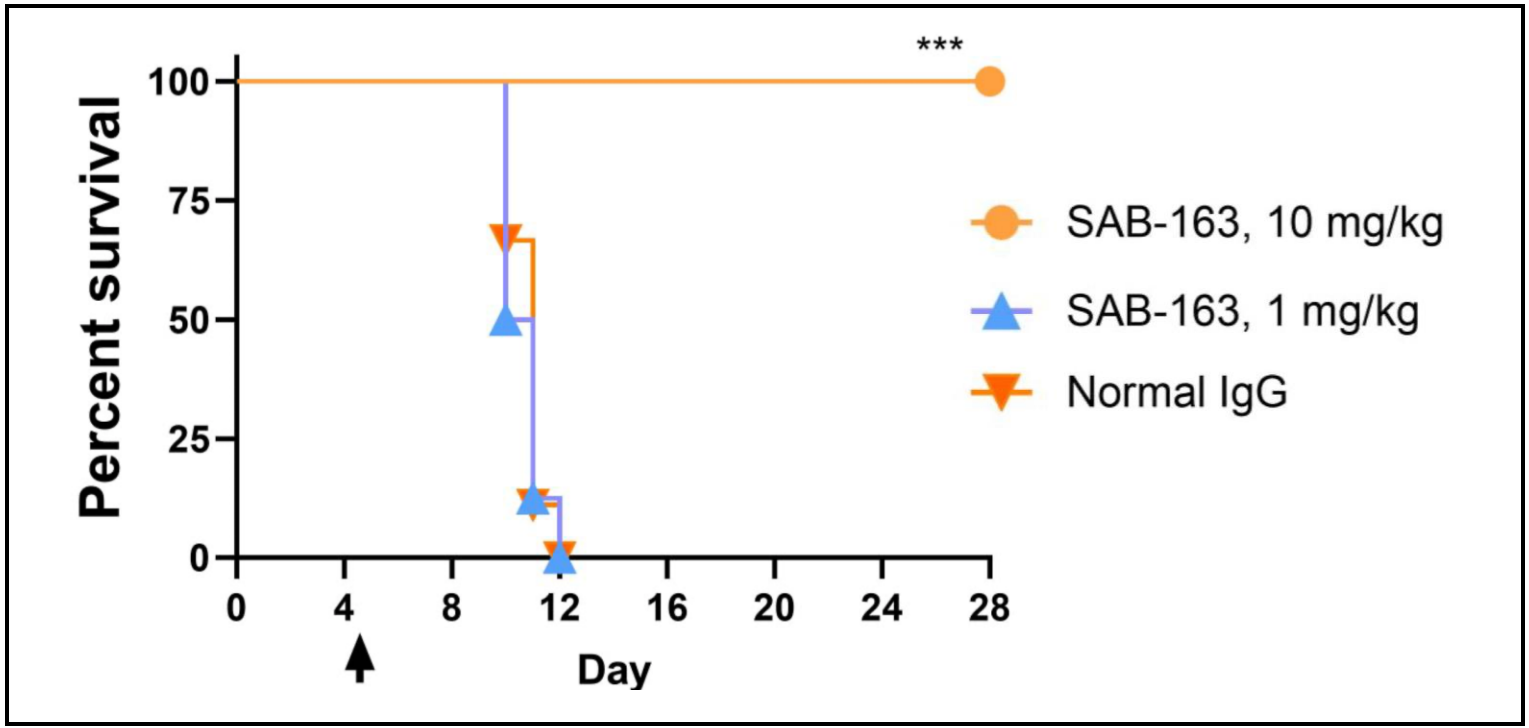
A tetravalent product covering four strains simultaneously.

(Andes · Puumala · Sin Nombre · Hantaan)

Partners

USAMRIID · NMRC · DTRA · HJF

SAB-163 at 10 mg/kg protects hamsters when administered 5 days after exposure to Andes Hantavirus



Ebola

Threat Context

Tier 1 select agent. DoD medical personnel directly exposed during 2014–2016 West Africa outbreak via aeromedical evacuation. Periodic and ongoing outbreak in Africa.

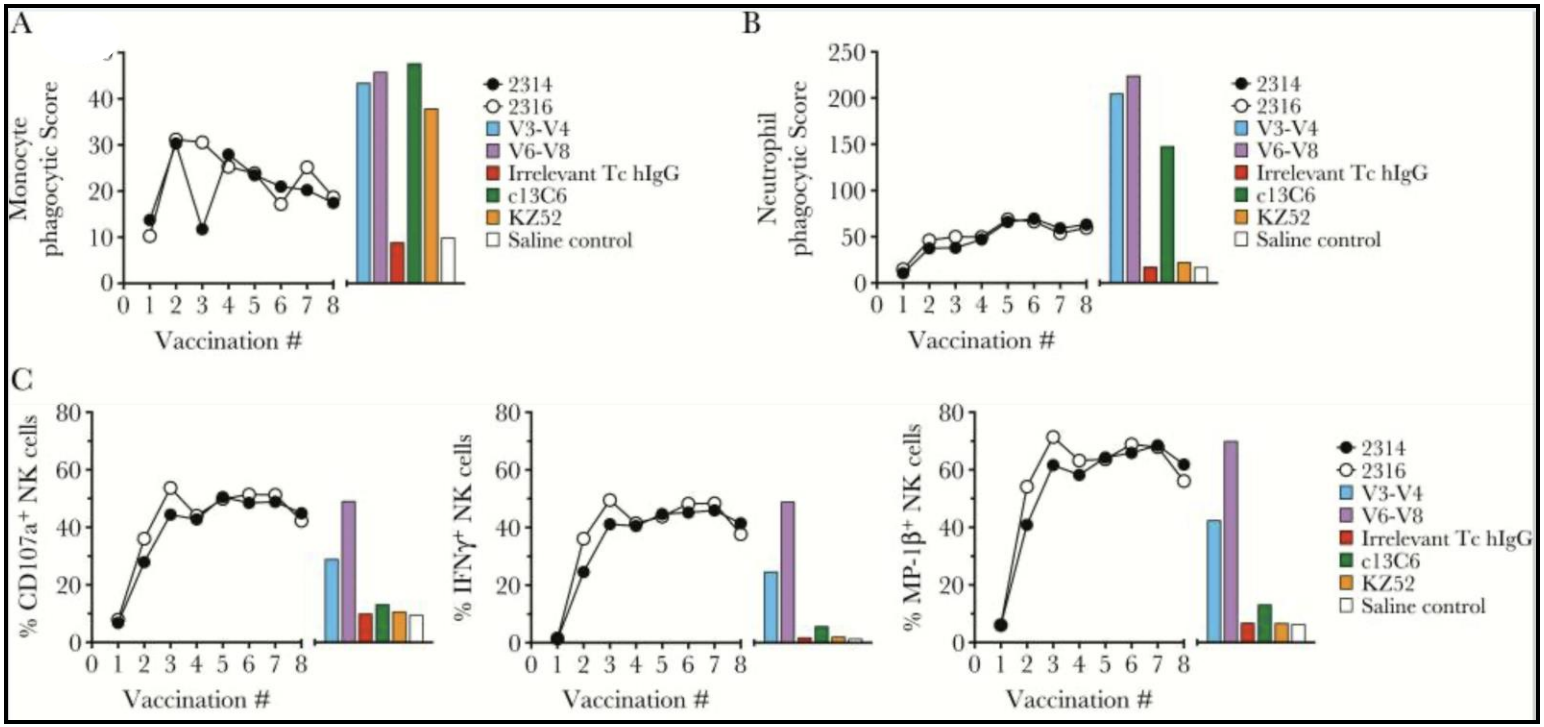
Therapeutic (SAB-139)

Bivalent Zaire/Sudan and monovalent Zaire*

Partners

NMRC · IRF-NIAID · NVAX · Broad Institute · HJF

SAB-139 Potently Activates Effector Cell Functions (ADMP, ADNP, ADCC)



Ebola Non-Human Primate Challenge

2,000x lethal dose of Ebola Makona (Zaire)
NHPs treated with SAB-139 on Day 3

Group	Animal	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D21	D28
Irrelevant Ab	1	0	0	0	0	0	0	2	Nec								
Control	2	0	0	0	0	1	3	Nec									
Challenge Delayed Group (Day 3)	9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

100% Survival in Day 3 Cohorts

# indicates symptom score; (0 = no symptoms)

Alphavirus (VEEV)

Threat Context

Venezuelan Equine Encephalitis Virus (VEEV) is a CDC Category B select agent and recognized aerosol biothreat with military exposure risk in Latin America. Epidemic and weaponized delivery potential.

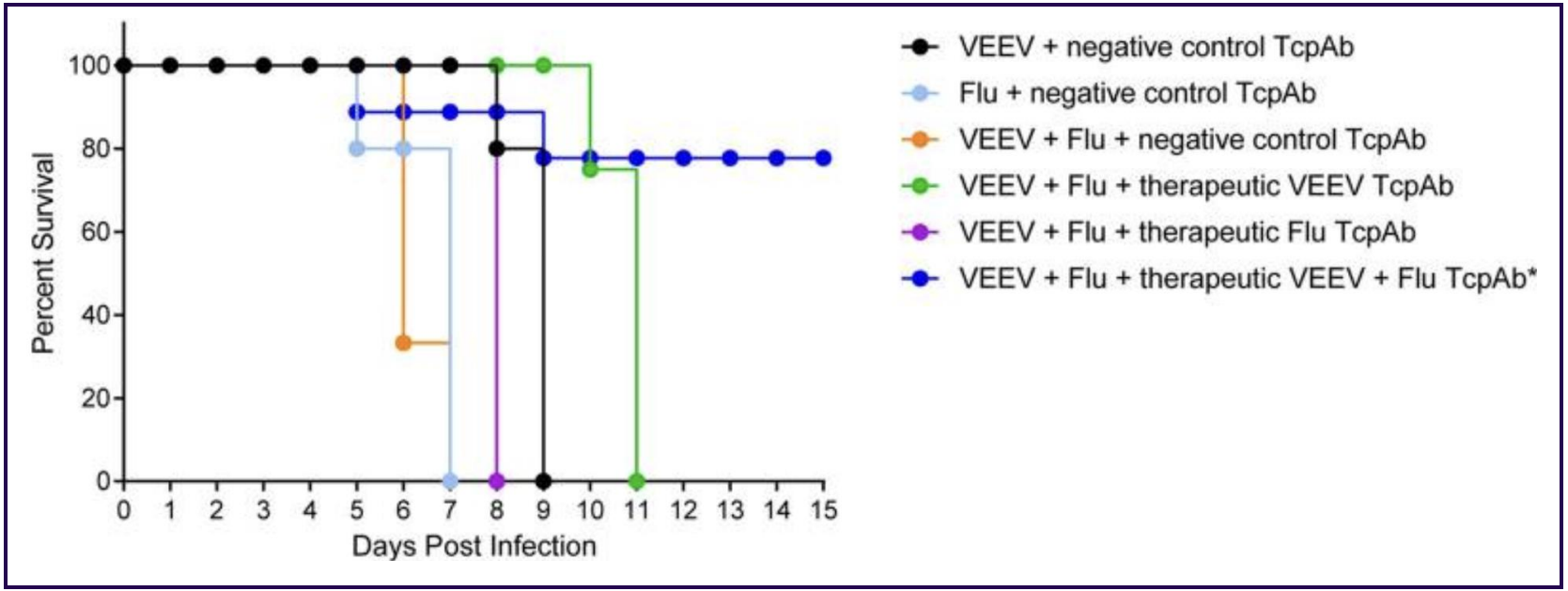
Therapeutic

Single monovalent product against VEE
Single pentavalent product against VEE, H1N1, H3N2, Type B Victoria, Type B Yamagata

Partners

NMRC · DTRA · UPITT · BARDA · HJF

Efficacy of anti-VEE/Influenza pAb against Aerosol Coinfection with VEE/H1N1



Past, Present, Future Projects and Program

Funding: Individual projects by competitive announcements or emergency response outbreaks. Some of the "DoD" pathogens have limited civilian commercial potential.

Progressing from concept to pre-clinical work to clinical trials to licensing has been/is challenging.

Interservice And Multi-Agency Cooperation: Highly effective and essential.

Partnership network: Multiple DoD Services/Federal Agencies · Academic Centers · Foreign Entities · WHO

Current and Future Efforts: Seeking collaborators and funders to continue existing projects, initiate new projects, and support a platform approach using a dedicated herd of Tc bovine for military relevant pathogen therapeutic development for EUA or licensure.

Acknowledgements

DoD / Military Medical Research

NMRC · USAMRIID · USUHS · DTRA

NIH / Federal

NIAID · BARDA · FDA · CDC

International

World Health Organization
Public Health Agency of Canada

Poly Solutions, LLC

Kristi A Egland, PhD

Academic Medical Centers

University of Pittsburgh
Washington University in St. Louis
Harvard Medical School / BWH
Broad Institute
Ragon Institute
University of Iowa
Utah State University
King Saud bin Abdulaziz, UHS

Industry

SAB Biotherapeutics · Novavax · hVIVO · BIOSNTRY