Transchromosomic Bovine-Derived Fully Human Polyclonal Antibodies: A Platform for Military Infectious Disease Countermeasures

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Disclosure

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

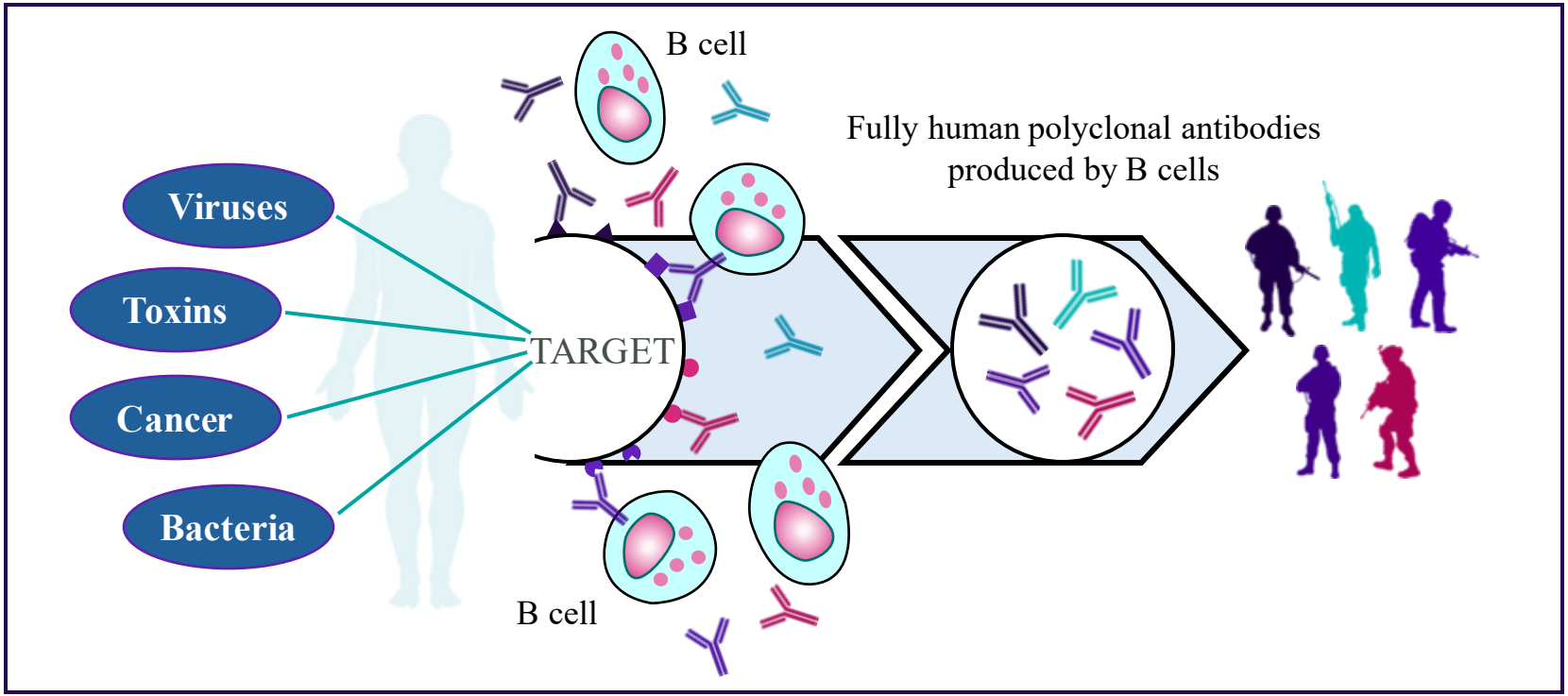
Learning Objectives

Objective 1: Describe the transchromosomic bovine platform and its capability to rapidly produce fully human polyclonal antibodies against militarily relevant pathogens and toxins.

Objective 2: Interpret preclinical/clinical efficacy and safety evidence for Tc bovine-derived polyclonal antibodies across Ebola, MERS, SARS-CoV-2, and influenza.

Objective 3: Discuss strategic advantages of polyclonal vs. monoclonal platforms for military biodefense against endemic, epidemic, and biowarfare threats.

Fully-Human Polyclonal Antibody Production by B cells in Human and Transchromosomic Bovine



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

Objective 2

Interpret preclinical and clinical evidence supporting the efficacy and safety of Tc bovine-derived polyclonal antibodies across multiple pathogen targets including Ebola, MERS, SARS-CoV-2, and influenza.

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

Ebola: SAB-136 IV Delivery NHP

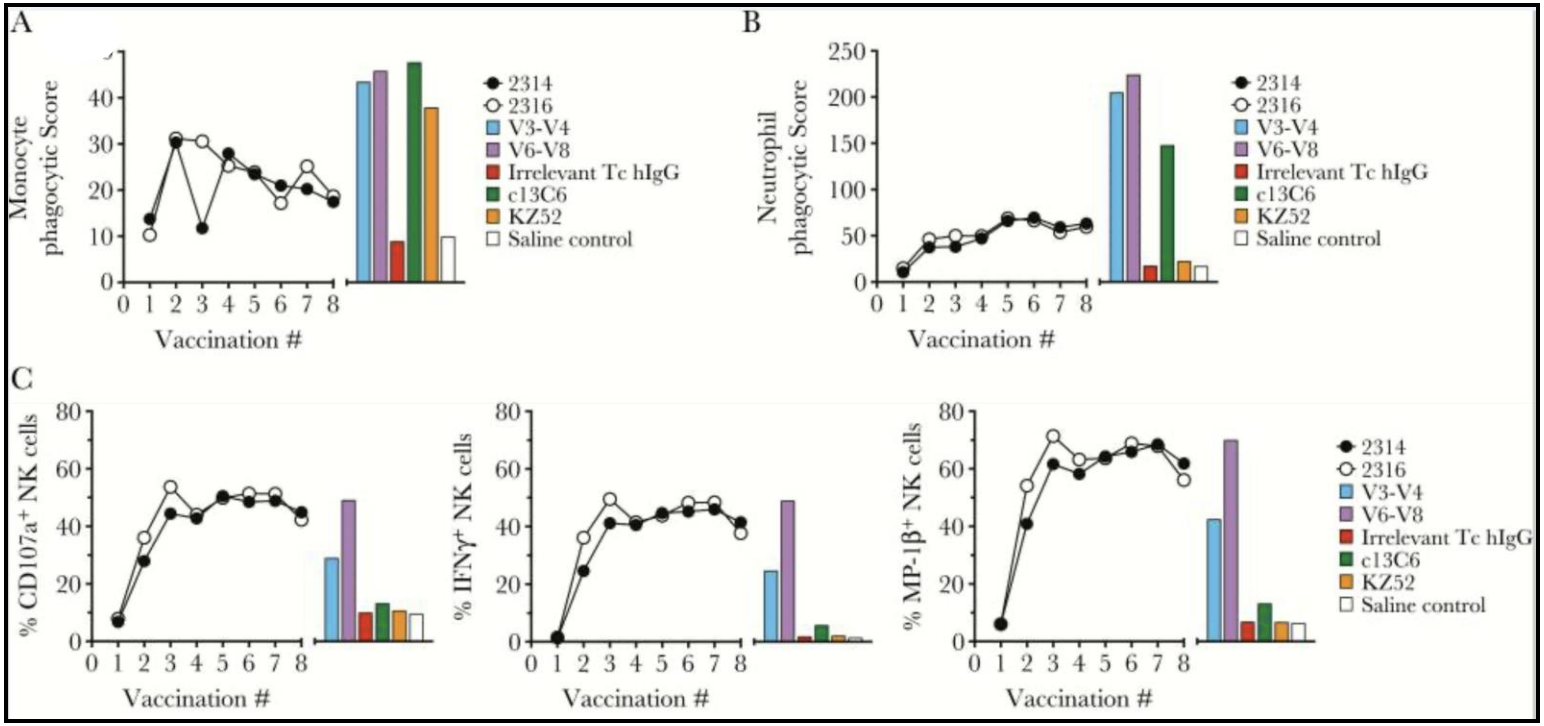
Background

- Prolonged West Africa Ebola outbreak drove rapid response.
- Anti-Ebola IgG (SAB-139) was purified from Tc-bovine plasma after hyperimmunization with Ebola Makona (Zaire) glycoprotein nanoparticle vaccine.
- Characterized across *in vitro* production, research, and clinical-grade assays.

Ebola: SAB-136 IV Delivery NHP

- Potently activates NK cells, monocytes, and PBMCs; high-binding avidity (surface plasmon resonance).
- (V6-V8) form shows more potent NK cell degranulation vs. (V3-V4) or the anti-Ebola c13C6 & KZ52 monoclonal Abs.
- Alpha-gal levels comparable to human IVIg; IgG1 subclass predominant.
- 100% survival when dosed at 1 or 3 days post-infection, versus 0% in controls (rhesus macaques).

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



MERS-CoV: Phase 1 SAB-301

Background

- MERS: severe respiratory illness, ~35% mortality; high exposure risk for US forces stationed in the Middle East.
- SAB-301 showed high neutralizing titers and prophylactic/ therapeutic efficacy in Ad5-hDPP4 receptor–transduced mice.
- Phase 1 double-blind, placebo-controlled, single-dose escalation trial conducted at the NIH Clinical Center.

MERS-CoV: Phase 1 SAB-301

- 38 participants randomized to 1–50 mg/kg SAB-301 or saline, IM route (20 and 50 mg/kg cohorts randomized 8:2).
- Well-tolerated across all doses, generally mild AEs; one serious AE (hospital admission, suicide attempt) at 50 mg/kg.
- Dose-response observed in MN titers against the Jordan N3 strain.
- SAB-301 safe and well-tolerated up to 50 mg/kg in healthy participants.

SARS-CoV-2

Background

- Tc bovines primed with pDNA, boosted with Wuhan-strain Spike protein → SAB-185
- *In vitro* neutralization and efficacy in hACE2 transgenic Syrian hamsters across Munich, Alpha, Beta, Gamma, Δ144-146, Delta, and Omicron variants
- ACTIV-2 Phase 2/3: high-risk adults (≤7 days symptom onset), randomized 1:1 to SAB-185 (3840 units/kg) versus casirivimab/imdevimab (1200 mg)
- Primary endpoint: all-cause hospitalization/death + grade ≥3 TEAEs through Day 28; secondary: time to sustained symptom resolution

SARS-CoV-2: Results

- **Omicron was resistant to casirivimab/imdevimab and had a much lower hospitalization/death rate than previous strains.**
- Halted for futility (insufficient power) after 255 pre-Omicron strains and 392 Omicron strain subjects enrolled.
- Hospitalization/death rates similar between arms.
- No significant difference in grade ≥3 TEAEs.
- Time to symptom resolution shorter with SAB-185, Omicron only: 18 versus >25 days (P=0.006).

Influenza: Phase 1 SAB-176 IM Delivery

Background

- SAB-176: Tc bovine tetravalent anti-influenza Ig (HA target, Type A/B).
- Prior data: safe IV up to 50 mg/kg; efficacious at 25 mg/kg IV post-intranasal H1N1 challenge (hVIVO).
- IM route tested for rapid field/tactical administration — first-in-man safety/tolerability study at NMRC.

Influenza: Phase 1 SAB-176 IM Delivery

- 28 participants randomized to 75–1500 mg/kg SAB-176 or saline (5/2), IM route.
- Well-tolerated across all doses, generally mild AEs; no serious AEs or dose-limiting toxicity.
- Dose-response trend observed in MN titers against influenza strains.
- Safe/well-tolerated up to 1500 mg/kg; IM route enables use in austere settings as an IV alternative.

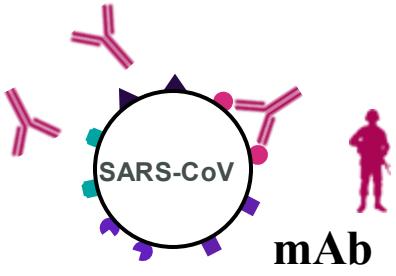
Objective 3

Discuss the strategic advantages of polyclonal antibody platform technologies over monoclonal approaches for military biodefense preparedness against endemic, epidemic, and biowarfare threats.

Monoclonals vs Polyclonal Antibodies

Regeneron
Casirivimab
Imdevimab

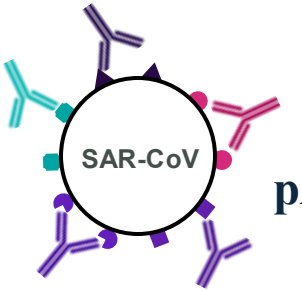
Eli Lilly
Bebtelovimab
Bamlanivimab
Etesevimab



mAb

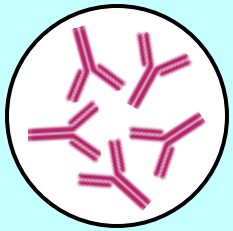
Versus

SAB Biotherapeutics
SAB-185



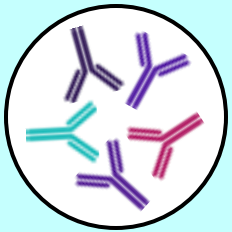
pAb

Monoclonal Approach



- Antibody from single clone
- Single epitope binding site
- Limited recruitment of innate and effector cell functions.
- No/limited efficacy against mutants

Polyclonal Approach



- Mixture of Abs to one or more antigens
- Multiple epitope binding sites
- Broad spectrum recruitment of innate and effector cells functions.
- Effective against mutants (resistance)

Advantages of Tc Bovine Human Polyclonal Antibodies (hpAb)

Manufacturing

- Responsive large-scale production of fully human pAbs.
- Consistent source - Tc animals produce at high volume for years.
- Established regulatory pathway for FDA CBER approval.

Biological Activity

- Multi-protein/epitope targeting versus a monoclonal Ab single epitope.
- Broad neutralization and engagement of effector cell functions (ADCC, ADNP, ADMP, NK functions).
- No neutralizing antibodies or serum sickness versus monoclonals and wild-type animal immunoglobulins.

Pre-Clinical/Clinical Validation

- Safe and efficacious in small mammals, NHPs, and humans.

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Industry

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