Phase 2 Efficacy and Safety of Two Novel SAB Immunotherapies Against Respiratory Disease Indications Associated with Highly Mutating Viruses

- SAB-185: A SARS-CoV-2 Immunotherapeutic
- SAB-176: A Pan Influenza Immunotherapeutic

Plasma Product Biotechnology Conference | 2022

Christoph Bausch, PhD, Chief Operating Officer

Forward Looking Statements

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DiversitAb™ Platform is Clinically Validated Across Several Targets

3 INDs & 1 CTA	**Filed in US and ex-US**
7 Clinical Trials	**Span from Phase 1 to Phase 3 across 3 indications**
Public Collaborations	**DoD, BARDA, NIH NIAID, Naval Medical Research Center, USAMRIID**
Academic Collaborations	**Brigham and Women's Hospital, Harvard, University of South Dakota, University of Pittsburgh**

Referenced Trials:

- Safety, Tolerability, and Pharmacokinetics of SAB-176 in Healthy Participants – Full Text View - ClinicalTrials.gov
- Study of SAB-176 in Healthy Adult Participants - Full Text View - ClinicalTrials.gov
- Safety, Tolerability, and Pharmacokinetics of SAB-185 in Healthy Participants – Full Text View - ClinicalTrials.gov
- Safety, Tolerability, and Pharmacokinetics of SAB-185 in Ambulatory Participants With COVID-19 - Full Text View - ClinicalTrials.gov
- ACTIV-2: A Study for Outpatients With COVID-19 - Full Text View - ClinicalTrials.gov
- Safety, Tolerability, and Pharmacokinetics of SAB-301 in Healthy Adults – Full Text View - ClinicalTrials.gov

Robust Biologic Pipeline with Broad Polyclonal Therapeutic Reach

Ongoing discovery programs in oncology, autoimmune, infectious and anti-idiotype diseases

	PRODUCT	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	COMMERCIAL
GASTROINTESTINAL	SAB-195	CLOSTRIDIOIDES DIFFICILE						
RESPIRATORY	SAB-176	PAN INFLUENZA	Phase 1 Trial & Phase 2a Challenge Study Top line results available					
IMMUNOLOGY	SAB-142	TYPE 1 DIABETES						
	SAB-142	IMMUNOLOGY						

Government-funded Phase 3 clinical-stage program

RESPIRATORY	SAB-185	COVID-19	Phase 3 Trial (NIH ACTIV-2)					

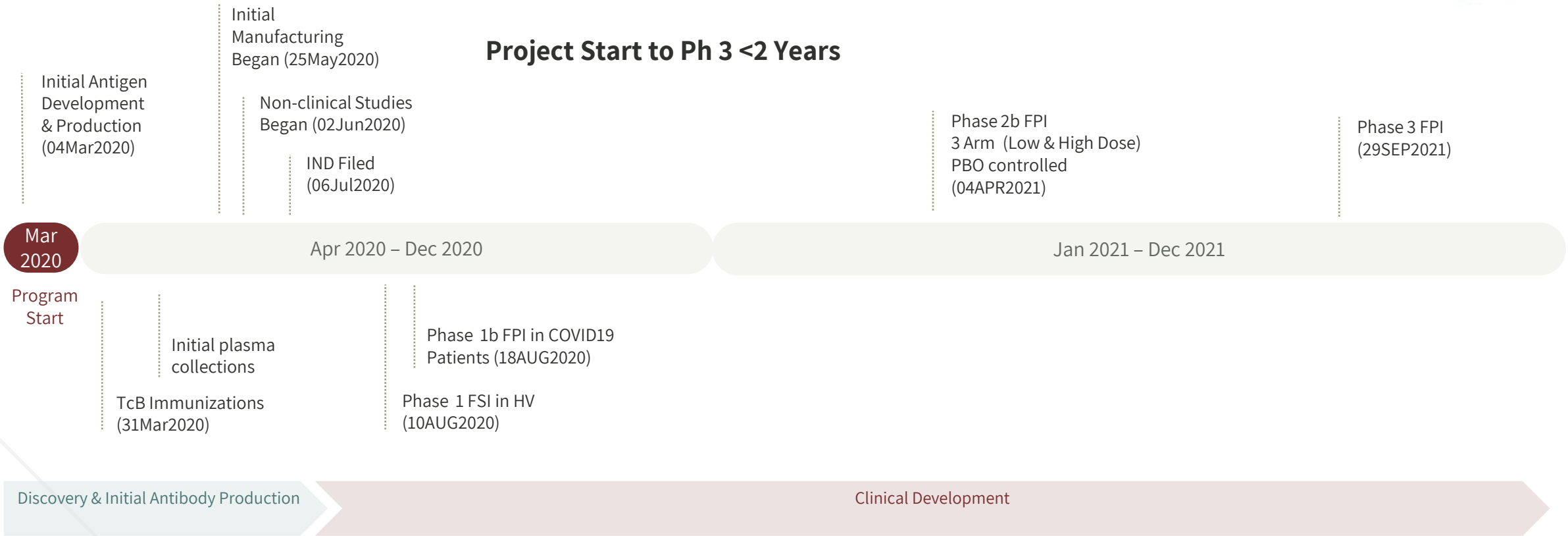
SAb BIOTHERAPEUTICS

SAB-185 Anti-SARS-CoV2

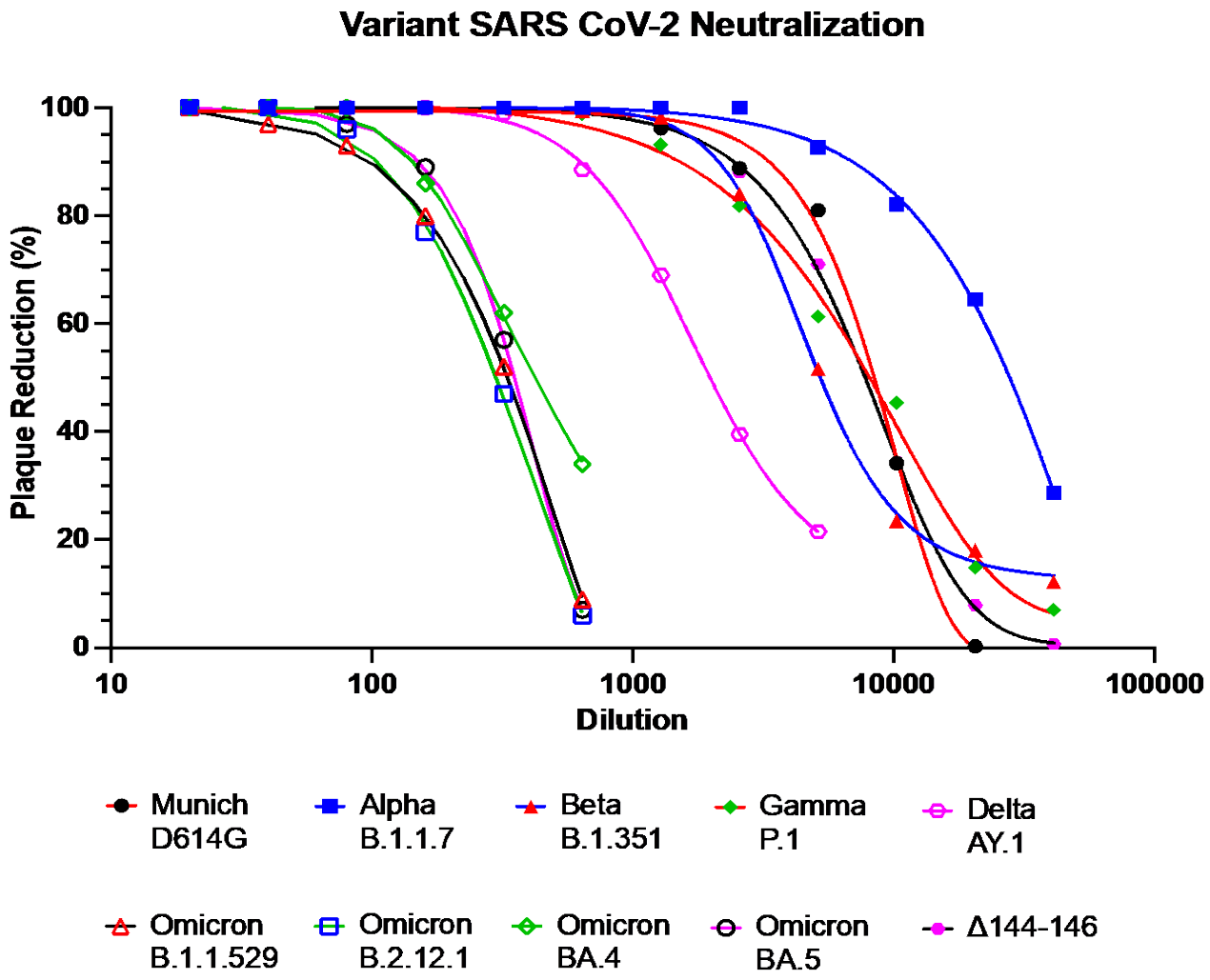
DiversitAb™ Rapid Discovery and Development Process for SAB-185

Project Start to IND Filing <125 Days, and First Subject In <160 Days

Project Start to Ph 3 <2 Years

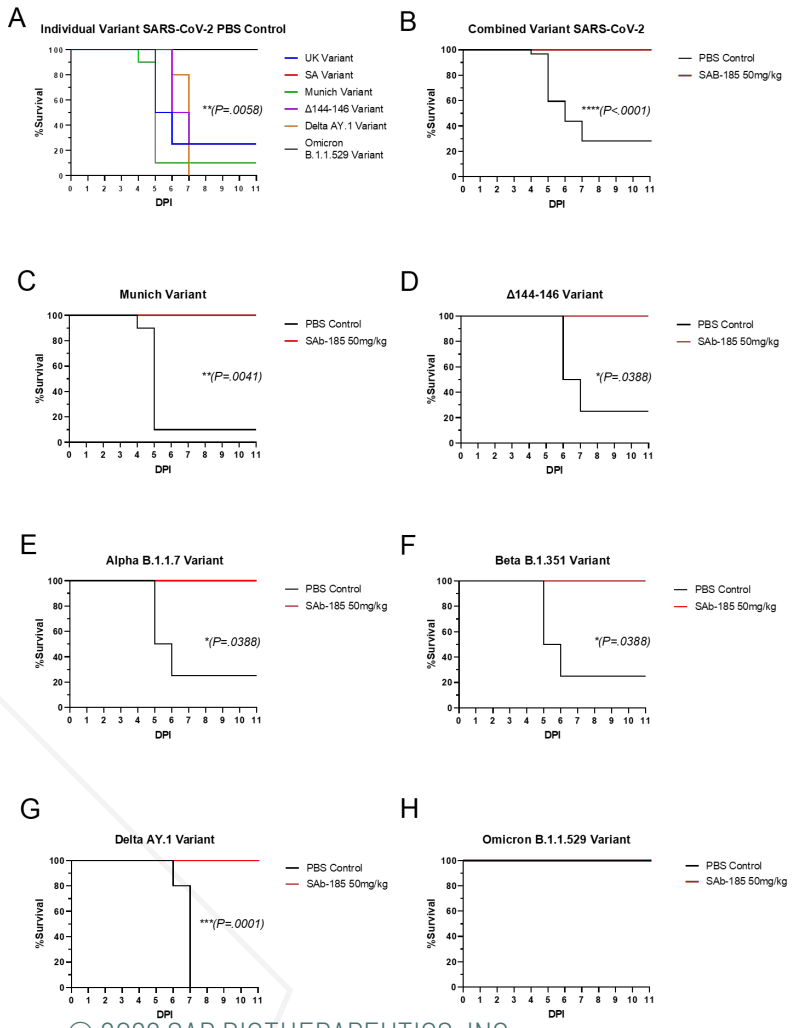


SAB-185 Neutralization Potential vs. the Munich Variant (Spike D614G) and Other Variants

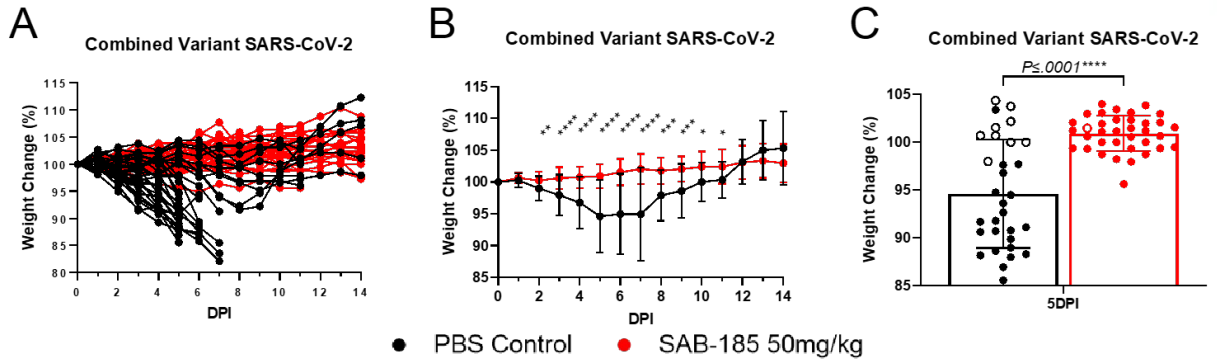


SAB-185 Protects Recombinant hACE2 Hamsters from Mortality and/or Severe Morbidity from SARS CoV-2 Variants Including Omicron

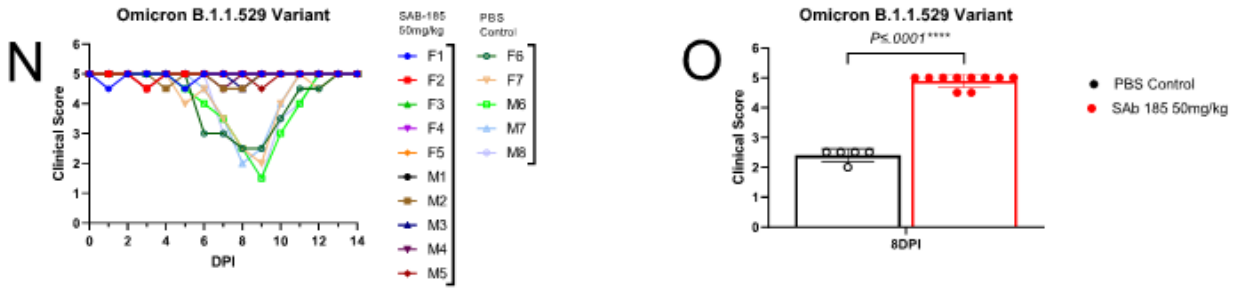
SAB-185 protection from mortality in hamsters challenged with six variant SARS CoV-2 isolates



SAB-185 protection from weight loss in hamsters challenged with six variant SARS CoV-2 isolates

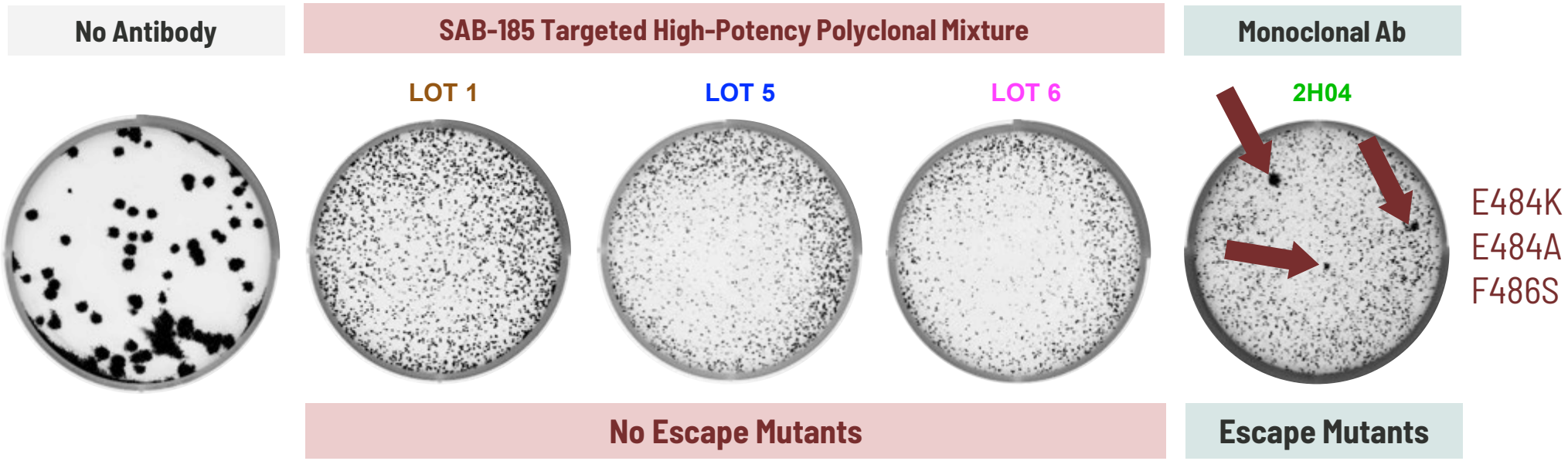


SAB-185 protection from Weight Loss in hamsters challenged with Omicron variant SA



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

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

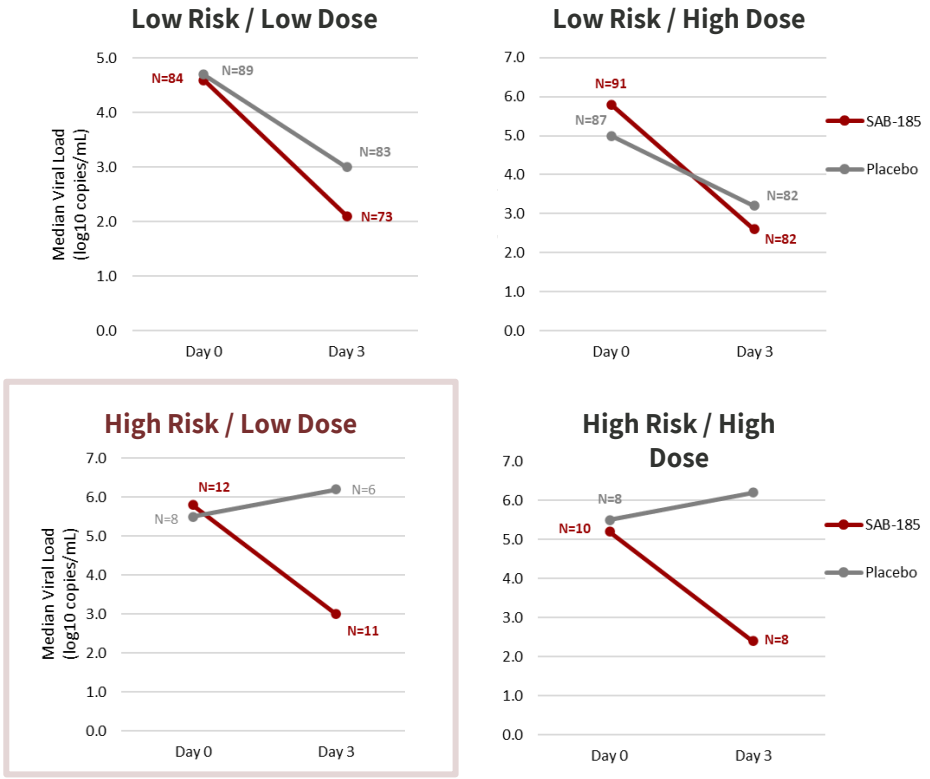
Viral load reductions of ≥0.5 log_{10} for both lower and higher dose at Day 3

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

SAb BIOTHERAPEUTICS

SAB-176 Pan Influenza Therapeutic

Targeted Product Profile and Administration Routes

Treat high-risk influenza adult patients prior to the development of severe disease:

- Adults 65 years of age and older
- Immunocompromised due to a disease or medications (autoimmune, cancer, etc.)
- Patients with respiratory, cardiovascular, kidney, metabolic, neurological disorders

- Pre- and post-exposure prophylaxis of high-risk patients and critical services personnel
  - High-risk patients in nursing homes/assisted living
  - Hospitalized
  - First responders/military/medical providers
  - Critical infrastructure operators

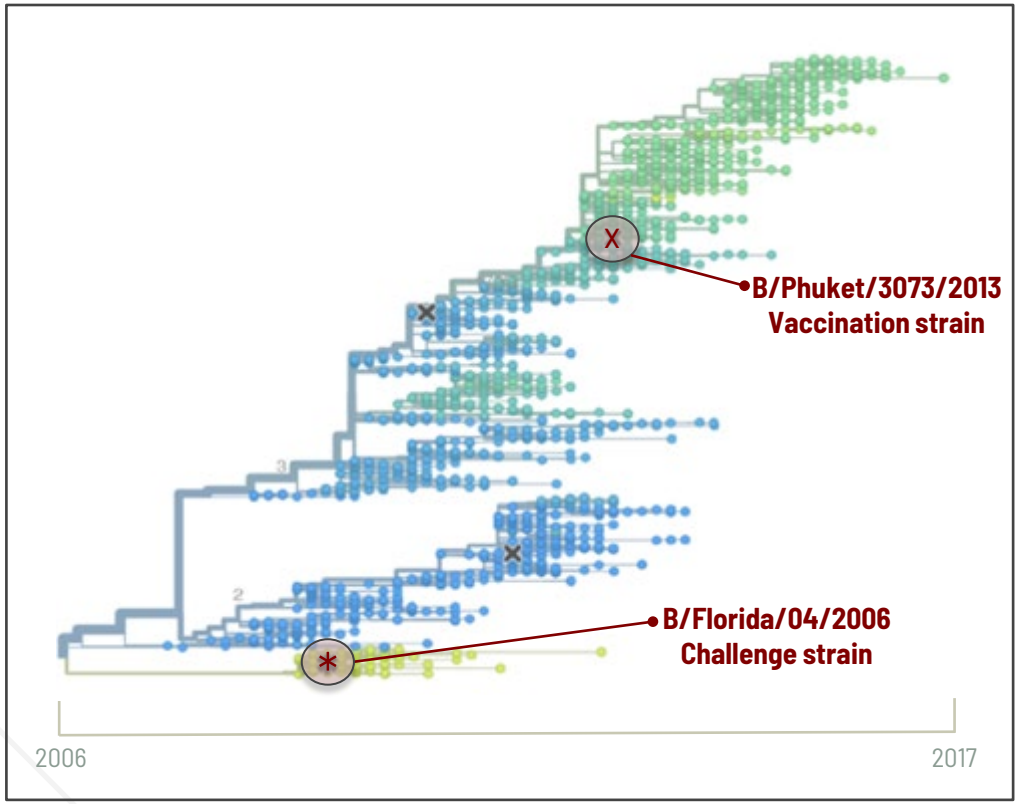
- Administration Routes
  - Intravenous
  - Subcutaneous and Intramuscular administration in development

Efficacy Against Mutational Drift

Adaptive & Cross Reactive to Mutating Strains

Highly-Mutational Influenza Virus

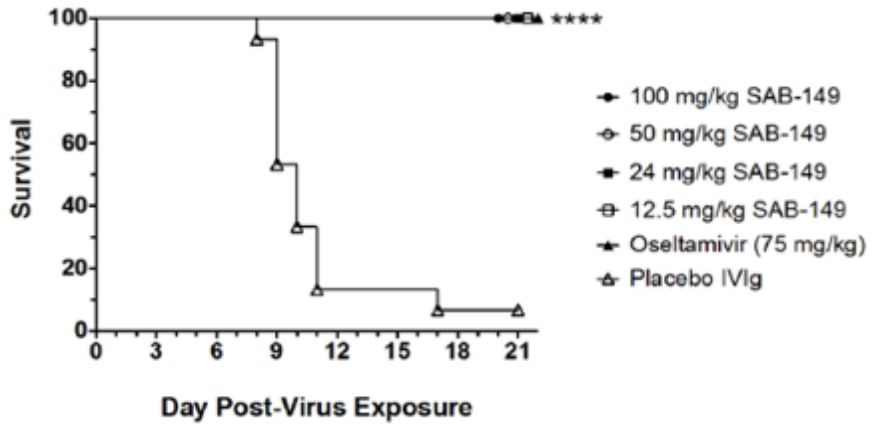
BYAM PHYLOGENIC TREE



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 –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

		H1N1				H3N2			B-Vic			B Yam	
	Sample Started at 5mg/ml	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

Trial Design and Methods

- **Trial design: Randomized, Double-Blind, Placebo-Controlled Influenza Challenge Study**
- **Study sample size**: 60 Healthy volunteers, 18-45 years of age
- **Study flow**:
  - Participants were admitted into the hVIVO facility 2 days prior inoculation and were quarantined for up to 11 days (Day -2 to 8) with Influenza challenge occurring on day 0 and SAB-176/placebo infusion on day 1. Participants were discharged on day 8. Participants returned for 1 outpatient visit on day 28.
  - Subjects were randomized 1:1 prior to receive SAB-176 or matching placebo 20-24 hours after influenza challenge.
- **Challenge virus:** A previously utilized Influenza **pandemic H1N1** A/California/2009-like challenge virus was produced by Meridian Life Sciences under Good Manufacturing Practices (Watson et al., 2015; Leibowitz et al., 2020)
- I**nvestigational treatment**: Participants received 25 mg/kg of SAB-176 diluted in normal saline at a concentration of 20 mg/ml or an equivalent volume of normal saline (placebo) in a single IV infusion.

EudraCT # 2021-001254-56
ClinicalTrials.gov number NCT04850898

Primary and Selected Secondary Outcome Measures

Primary Outcome Measure:

- Area under the viral load-time curve (VL-AUC) of Influenza A/California/2009 H1N1 virus as determined by qRT-PCR on nasal samples of SAB-176 when compared to placebo. [Time Frame: 8 Days]

- **Selected Secondary Outcome Measures:**

- Area under the curve over time of total clinical symptoms score (TSS-AUC) as measured by graded symptom scoring system (categorical and visual analogue scales) to evaluate the effect of SAB-176 in reducing symptoms due to Influenza A/California/2009 H1N1 virus compared to placebo. [Time Frame: 8 Days]

- Duration of influenza quantifiable by cell culture measurement to evaluate the effect of SAB-176 in reducing viral loads in cell culture due to Influenza A/California/2009 H1N1 virus, compared to placebo.

- Safety

Emerging Safety Profile

- Overall, the challenge virus inoculation and subsequent single IV infusion of SAB-176 were safe and well tolerated. There were no SAEs in this study, no AEs leading to early withdrawal from the study, and none of the AEs were of grade 3 or higher in severity.

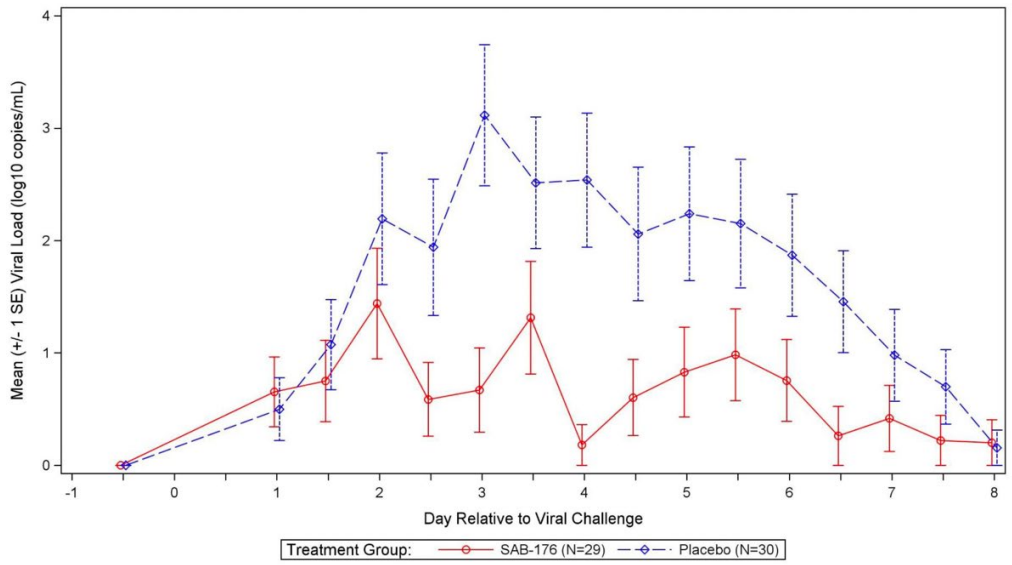
- **The incidence of AEs was similar between the treatment groups**: 18 (60.0%) participants in the SAB-176 group reported 27 AEs and 16 (53.3%) participants in the placebo group reported 23 AEs from viral challenge (Day 0) onwards.

    - Most TEAEs were reported in the SOC general disorders and administration site conditions (8 TEAEs in 5 [16.7%] participants in the SAB-176 group, and 1 TEAE in 1 [3.3%] participant in the placebo group). **Almost all TEAEs were mild in intensity.** One TEAE of neutrophil count decreased in the SAB-176 group and 4 TEAEs (ALT increased [n=1], lymphocyte count decreased [n=2], and rash [n=1]) in the placebo group were moderate in intensity.

    - **TEAEs that were at least possibly related to the study treatment** were reported by **2 (6.7%) participants in the SAB-176 group** (1 TEAE of blood pressure systolic decreased and 1 TEAE of paraesthesia) and **by 4 (13.3%) participants in the placebo group** (1 TEAE of rhinorrhoea, 1 TEAE of ALT increased, 1 TEAE of pain in extremity, and 1 TEAE of procedural hypotension).

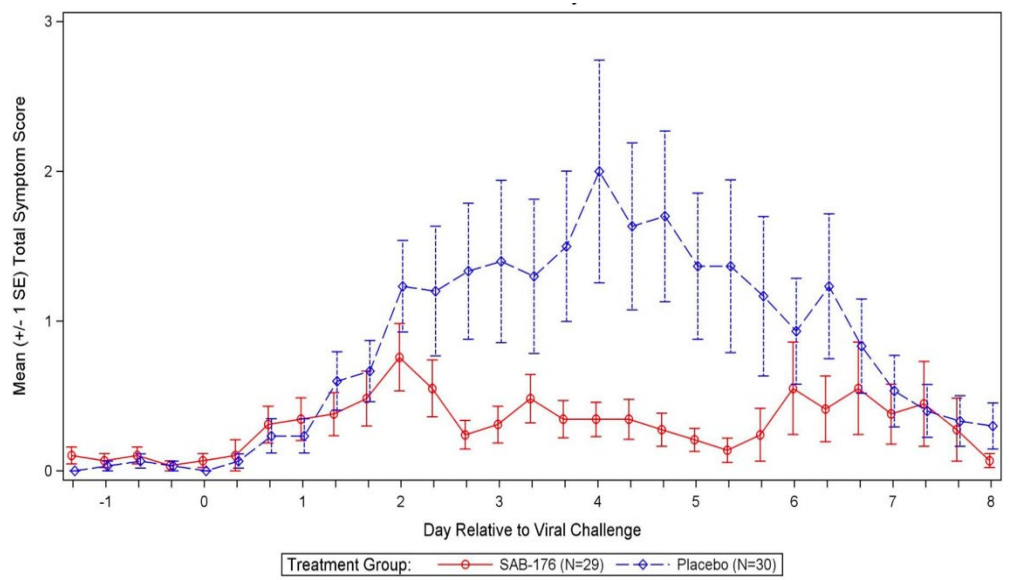
SAB-176 Met the Primary Endpoint of Viral Load and Secondary Endpoint of Symptom Reduction

Achieved Statistically Significant (p = 0.026) Reduction in Viral Load



Mean Viral Load by Nasal Samples qRT-qPCR by Day Relative to Viral Challenge

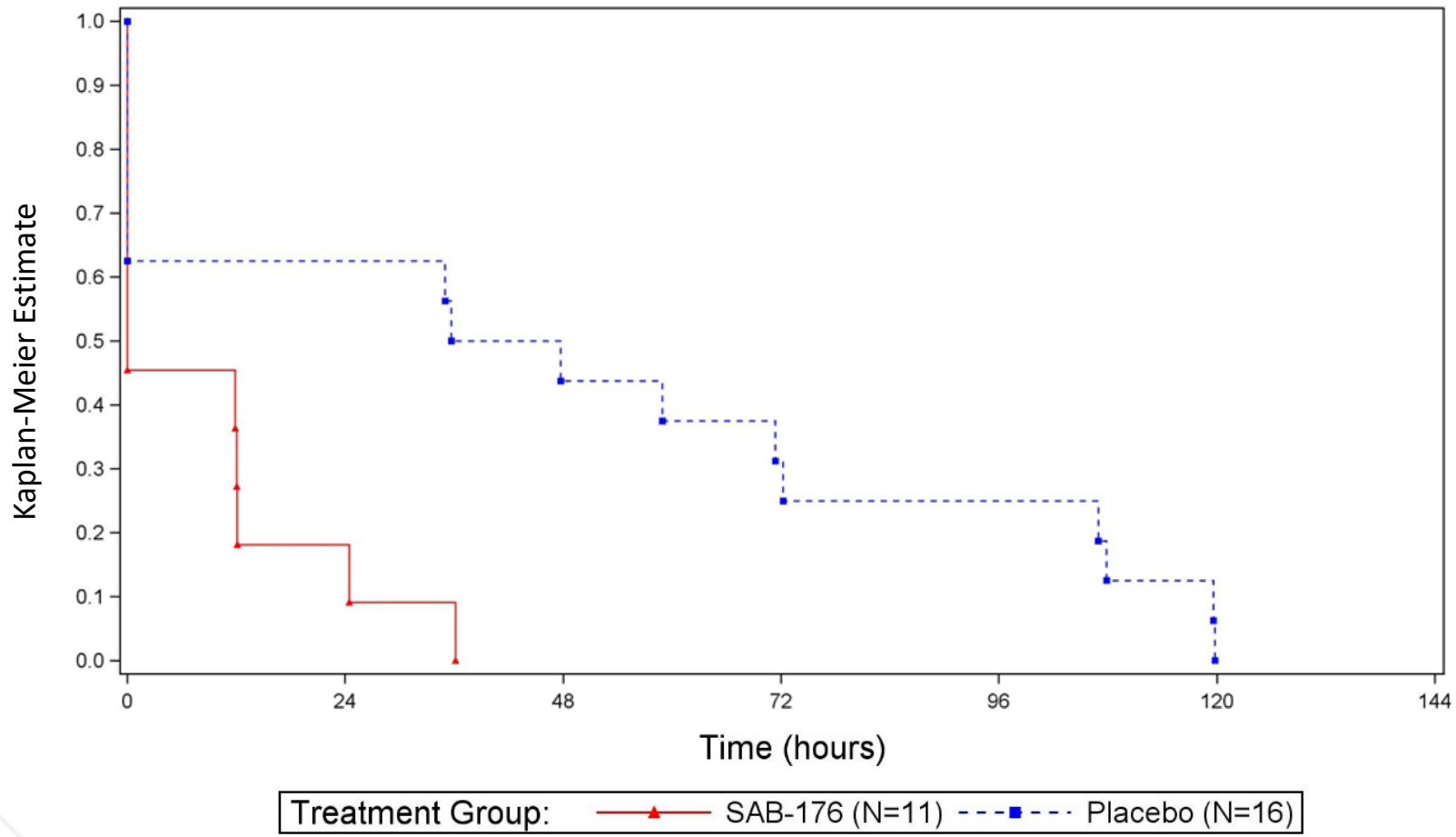
SAB-176 Achieved Statistically Significant (p = 0.013) Improvement in Symptomology at Day 4



Mean Total Symptom Score by Day Relative to Viral Challenge

Kaplan-Meier Time to Resolution of Positive Viral Cultures Following First Positive Culture Starting 2 Days After Intranasal Viral Challenge

Shortened time of viral shedding, as measured by lack of culturable virus



Conclusions

SAB-176: A novel pan influenza polyclonal immunotherapeutic

- Demonstrates significant HAI titers to multiple Type A and B and pandemic influenza strains
- In response to pandemic H1N1 viral challenge met primary endpoint of reducing nasopharyngeal viral load as determined by qRT-PCR
- Met secondary endpoint of reducing symptoms
- Shortened the time of infectious viral shedding, as measured by inability to culture virus in vitro
- IV infusion of SAB-176 appeared to be safe and well tolerated. The incidence of AEs was similar between SAB-176 and placebo.
- Next step is conducting a Phase 2b dose-range finding study in influenza patients at high risk of developing severe influenza complications