UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 27, 2022

SAB BIOTHERAPEUTICS, INC.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-39871**	**85-3899721**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
2100 East 54th Street North Sioux Falls, South Dakota		**57104**
(Address of Principal Executive Offices)		**(Zip Code)**

Registrant's Telephone Number, Including Area Code: 605 679-6980

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock, $0.0001 par value per share	SABS	The NASDAQ Stock Market LLC
Warrants, each exercisable for one share of Common Stock at an exercise price of $11.50 per share	SABSW	The NASDAQ Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On September 27, 2022, SAB Biotherapeutics, Inc. (the “Company” or “SAB”) conducted a poster presentation at the Options for Control of Influenza ("OPTIONS XI") conference highlighting data that its SAB-185 COVID-19 polyclonal antibody therapeutic candidate was effective in animal models. A copy of the poster presentation is furnished herewith as Exhibit 99.1 and is incorporated herein by reference. On September 29, 2022 the Company will deliver a PowerPoint presentation of its Phase 2a challenge trial that shows SAB-176 reduced the viral load in subjects exposed to H1N1 influenza virus, improved symptoms by day four and shortened the timeframe for viral shedding. A copy of the PowerPoint presentation is furnished herewith as Exhibit 99.2 and is incorporated herein by reference.

The foregoing (including Exhibit 99.1 and 99.2) is being furnished pursuant to Item 7.01 and will not be deemed to be filed for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise be subject to the liabilities of that section, nor will it be deemed to be incorporated by reference in any filing under the Securities Act of 1933, as amended (the “Securities Act”), or the Exchange Act. The information contained in each presentation is summary information that should be considered in the context of the Company’s filings with the Securities and Exchange Commission (the "Commission") and other public announcements the Company may make by press release or otherwise from time to time.

Cautionary Note Regarding Forward-Looking Statements

Certain statements made in this current report and the presentations that are not historical facts are forward-looking statements for purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Forward-looking statements generally are accompanied by words such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect,” “should,” “would,” “plan,” “predict,” “potential,” “seem,” “seek,” “future,” “outlook” and similar expressions that predict or indicate future events or trends or that are not statements of historical matters. These forward-looking statements include, but are not limited to, statements regarding future events, including the development and efficacy of the Company's influenza program, C. diff. program, Type 1 Diabetes program, and other discovery programs, the likelihood that a patent will issue from any patent application, the results, including timing, of the development of SAB-195 (including any IND filing or proposed clinical trials), financial projections and future financial and operating results (including estimated cost savings and cash runway), the outcome of and potential future government and other third-party collaborations or funded programs (including negotiations with the DoD). These statements are based on the current expectations of the Company and are not predictions of actual performance, and are not intended to serve as, and must not be relied on, by any investor as a guarantee, prediction, definitive statement, or an assurance, of fact or probability. These statements are only current predictions or expectations, and are subject to known and unknown risks, uncertainties and other factors which may be beyond the Company's control. Actual events and circumstances are difficult or impossible to predict, and these risks and uncertainties may cause the Company's or the industry’s results, performance, or achievements to be materially different from those anticipated by these forward-looking statements. A further description of risks and uncertainties can be found in the sections captioned “Risk Factors” in the Company's most recent annual report on Form 10-K, subsequent quarterly reports on Form 10-Q, and other filings with or submissions to, the U.S. Securities and Exchange Commission, which are available at https://www.sec.gov/ Except as otherwise required by law, the Company's disclaims any intention or obligation to update or revise any forward-looking statements, which speak only as of the date they were made, whether as a result of new information, future events or circumstances or otherwise.

Item 8.01 Other Events.

On September 28, 2022, the Company released today new data presented at the OPTIONS XI conference, showing its fully-human polyclonal antibody platform maintains its efficacy against multiple variants of several highly mutating viruses.

A copy of the press release is attached as Exhibit 99.3 to this Current Report on Form 8-K and is hereby incorporated by reference herein.

Item 9.01 Financial Statements and Exhibits.

Exhibit Number	Description
99.1	Poster Presentation dated September 28, 2022
99.2	PowerPoint Presentation dated September 29, 2022
99.3	Press Release of the Company, dated September 28, 2022
104	Cover Page Interactive Data File-the cover page XBRL tags are embedded within the Inline XBRL document.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

SAB Biotherapeutics, Inc.

Date: September 28, 2022

By: */s/ Eddie J. Sullivan*
Eddie J. Sullivan
Chief Executive Officer

EXHIBIT 99.1

Transchromosomic bovine-derived human anti-SARS-CoV-2 polyclonal antibodies protect hACE2 transgenic Syrian hamsters against multiple SARS CoV-2 variants

Theron Gilliland[1,#], Yanan Li[3,#], Rong Li[3,#], Matthew Dunn[1, #], Maria Alcorn[1], Yutaka Terada[1], Shauna Vasilatos[1], Jeneveve Lundy[1], Shamkumar Nambulli[2], Deanna Larson[3], Paul Duprex[2], Hua Wu[4], Thomas Luke[4], Christoph Bausch[4], Kristi Egland[4], Eddie Sullivan[4], Zhongde Wang[3,*] and William B. Klimstra[1,*]

1 Center for Vaccine Research and Department of Immunology, University of Pittsburgh, Pittsburgh, PA 15261. 2 Center for Vaccine Research and Department of Microbiology and Molecular Genetics, University of Pittsburgh, Pittsburgh, PA 15261. 3 Department of Animal Dairy, and Veterinary Sciences, Utah State University, Logan UT 84341, United States. 4 SAb Biotherapeutics, Inc. Sioux Falls, SD 57104. * Corresponding authors, # These authors contributed equally

Abstract

Pandemic SARS CoV-2 has undergone rapid evolution resulting in the successive emergence of many variants with novel mutations in the Spike protein, some of which appear to evade antibody neutralization, transmit more efficiently and/or exhibit altered virulence. This raises significant concerns regarding the efficacy of protection elicited after primary infection or from vaccines derived from single virus Spike (S) genotypes, as well as the efficacy of anti-S monoclonal antibody based therapeutics. To address this concern, SAB-185, a human anti-SARS-CoV-2 polyclonal antibody (pAb) was generated in the DiversitAb™ platform. This platform uses human artificial chromosome-transgenic bovines to produce human IgG preparations after hyper-immunization. The *in vitro* neutralizing capacity of SAB-185 was tested against ten variant SARS-CoV-2 strains including several Omicron variants. SAB-185 exhibited equivalent neutralization of the Munich, alpha, beta, gamma and D144-146 variants and retained neutralization of the delta variant AY.1 and omicron variants BA.1.1.529, BA.2.12.1, BA.4 and BA.5, with only modest losses of neutralization efficacy. For *in vivo* protection studies, we used a new human ACE2 (hACE2) transgenic Syrian hamster model that exhibits rapid lethality after intratracheal SARS-CoV-2 challenge with the Munich, Alpha, Beta, Delta, and D144-146 variants; the Omicron B.1.1529 variant resulted in a delayed, less severe and non-lethal disease. Prophylactic SAB-185 treatment protected the hamsters from death and minimized clinical signs of infection when challenged with the variant viruses tested. This suggests that SAB-185 may be an effective immunotherapy even in the presence of ongoing viral mutation.

Results

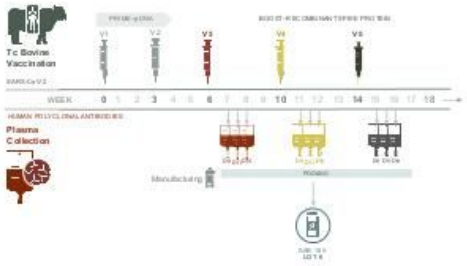


Figure 1. Tc bovine immunization schedule and SAB-185 production strategy using the DiversitAb™ platform (as described in Liu et al., Hum. Vaccin. Immunother. 18:1940652, 2022 PMID34228597). Tc bovines were immunized twice with plasmid DNA expressing the Wuhan WA-1 strain spike protein at three-week intervals. Starting week six, animals were boosted three times with recombinant WA-1 spike ectodomain protein derived from insect cells. Plasma from weeks 7-8, 11-12 and 15-16 were pooled and human IgG was purified for the SAB-185 final preparation. Tc bovine plasma was thawed, pooled, fractionated by caprylic acid (CA), and clarified by depth filtration in the presence of Celpure P1000 filter aid. The clarified sample containing Tc bovine-derived human IgG is further purified by affinity chromatography, first using an anti-human IgG kappa light chain-specific column, KappaSelect (GE Healthcare Life Sciences) to capture hIgG followed by a low pH treatment, and second, by passing through an anti-bovine IgG heavy chain-specific affinity column, Capto HC15 (GE Healthcare Life Sciences). To further remove residual IgG that contains bovine heavy chain, the human IgG fraction was then subjected to a Q Sepharose chromatography polishing step to further reduce impurities, nanofiltration, final buffer exchange, concentration, and sterile filtration. Finally, the SAB-185 product was terminally filtered and filled into vials.

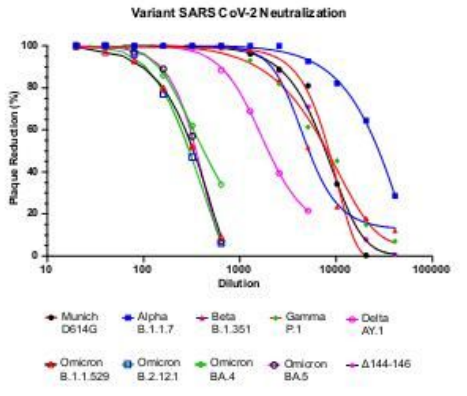


Figure 2. SAB-185 neutralization potential *versus* the Munich variant (Spike D614G) and other variants. Neutralization capacity of SAB-185 was assayed by Vero E6 or Vero hAce2/TMPRSS2 cell plaque neutralization assay. SAB-185 was diluted to 1mg/ml in PBS and then diluted serially two-fold before reaction with viruses. All Ab samples were heat inactivated by incubation at 56°C for 30 minutes. Viruses were diluted in OPTI-MEM (Gibco) with 2% FBS to approximately 200 PFU in 250 ml and reacted with an equal volume of serial two-fold dilutions of each antibody (in PBS) for 1 hour at 37°C followed by infection of Vero E6 monolayers for 1 hour at 37°C. A solution of 0.1% immunodiffusion agarose (MP Bio) in 2X Vero E6 growth medium was then added and plaques were developed at 37°C for 72-96 hours followed by removal of agarose, staining of cells with crystal violet (Fisher Scientific) and counting of plaques. Data points are averages of results from 3 replicates with 2 duplicate wells at each dilution. Error bars are omitted for clarity.

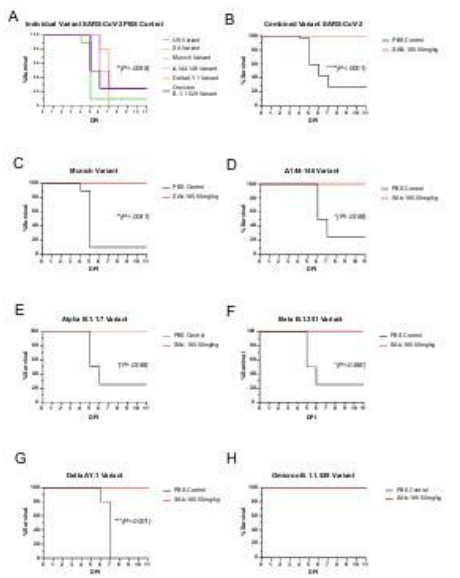


Figure 3. SAB-185 protection from mortality in hamsters challenged with six variant SARS CoV-2 isolates. Hamsters were administered SAB-185 or PBS intramuscularly and then challenged intratracheally 24 hours later with 1000 plaque forming units of variant viruses. Mortality for individual variant PBS controls (A) and for combined (all SARS-CoV-2 variants tested) PBS control *versus* SAB-185 treated groups (B). Individual mortality data for Munich (C), D144-146 (D) Alpha (E), Beta (F), Delta (G), and Omicron (H) viruses. Mantel-Cox log-rank significance is indicated within each panel. * p<0.05, **p<0.01, ***p<0.005. .

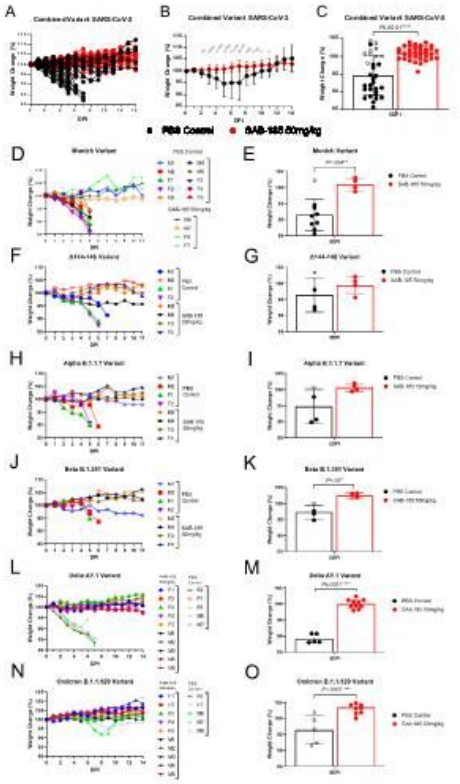


Figure 4. SAB-185 protection from weight loss in hamsters challenged with six variant SARS CoV-2 isolates. (A) Weight loss for individual hamsters in all groups. (B) Combined (all SARS-CoV-2 variants tested) average weight loss data for SAB-185-treated and PBS control hamsters. (C) Combined average weight loss data for SAB-185-treated and PBS control hamsters on D5 (last day all animals were alive). Omicron infected animals are omitted due to delayed disease development. Individual weight loss data for Munich (D), D144-146 (F), Alpha (H), Beta (J), Delta (L) and Omicron (N) viruses. Combined average weight loss data for Munich (E), D144-146 (G), Alpha (I), Beta (K) and Delta (M) variants on D5 (last day all animals were alive) post challenge or D8 post challenge for Omicron-infected animals (O) (peak weight loss). * p<0.05, **p<0.01, ***p<0.005. Open circles are surviving animals (controls and Omicron) and the SAB-185 treated animal that exhibited delayed replication (data not shown).

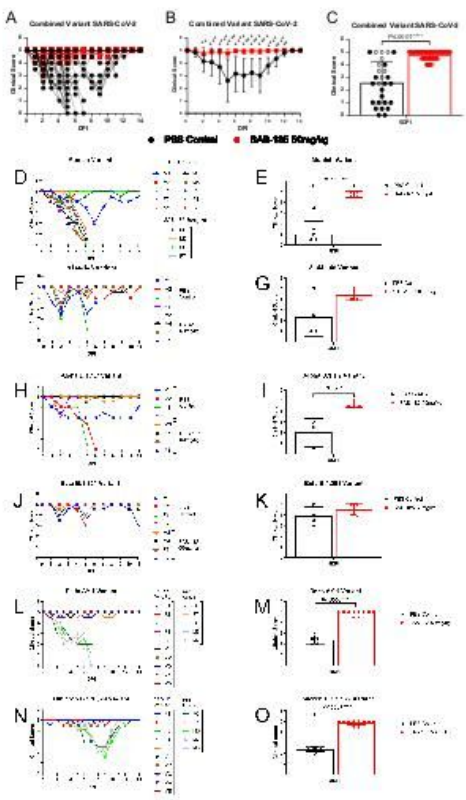


Figure 5. SAB-185 protection from clinical signs in hamsters challenged with six variant SARS CoV-2 isolates. Data is presented as the inverse of the clinical score sum values, as described in Materials and Methods, to be comparable to weight loss data. Each datum point represents an average of morning and afternoon observations. A) Clinical sign scoring for individual hamsters in all groups. B) Combined clinical sign scoring data for SAB-185-treated and control hamsters. (C) Combined clinical sign scoring data for SAB-185-treated and control hamsters on D5 (last day all animals were alive) post challenge or D8 post challenge for Omicron-infected animals (peak clinical signs). Individual clinical sign scoring data for Munich (D), D144-146 (F) Alpha (H), Beta (J), Delta (L) and Omicron (N) viruses. Individual clinical sign scoring data for Munich (E), D144-146 (G) UK (I), SA (K), Delta (M) and Omicron (O) variants on D5 (last day all animals were alive) post challenge or D8 post challenge for Omicron (peak clinical signs). * p<0.05, **p<0.01, ***p<0.005. Open circles are surviving (controls and Omicron) and the SAB-185 treated animal that exhibited delayed replication (data not shown).

Conclusions

The occurrence of successive waves of SARS CoV-2 variants with novel spike protein mutations throughout the COVID-19 pandemic has reduced the prophylactic efficacy of vaccines and abrogated the efficacy of many antibody-based therapeutics. SAB-185 is a human polyclonal IgG generated from the DiversitAb™ platform produced using spike protein from the WA-1 SARS CoV-2. The current studies demonstrated that a single IM injection of SAB-185 protected recombinant hACE2 hamsters from mortality and/or severe morbidity when intratracheally infected with successive SARS CoV-2 variants including omicron. Although reduced *in vitro* SAb-185 $PRNT_{80}$ and $PRNT_{90}$ neutralization titers were observed with delta and omicron variants, SAB-185 was still highly protective at human-relevant doses *in vivo*. Therefore, reduced in *vitro* neutralization titers of SAB-185 against SARS CoV-2 variants were not associated with any reduction of in *vivo* efficacy.

Reasons underlying the protective efficacy of SAB-185 *versus* multiple strains, may include the hyper-immunization of Tc bovines with full length spike pDNA for priming and recombinant spike ectodomain protein for boosting, which may increase stimulation of polyclonal antibodies reactive with subdominant epitopes that are less likely/able to mutate during widespread human infection. Loss of reactivity of monoclonal antibodies that bind various epitopes in the S protein has been demonstrated clearly and the broad reactivity provided by polyclonal Ab products may have an advantage in neutralization and protection against variants. In addition, other factors such as non-neutralizing anti-spike antibodies and/or innate immune mechanisms such as effector cell function(s) could be important in *vivo*.

In summary, the DiversitAb™ platform represents a highly scalable system that produces high neutralizing titer, fully human polyclonal antibodies. The data in this study suggest that human anti-SARS-CoV-2 polyclonal antibody, SAB-185, may have broad efficacy in preventing or treating SARS CoV-2 variant infections in humans.

Acknowledgments

SAB Biotherapeutics, Inc., has received support from the Department of Defense (DoD) Joint Program Executive Office for Chemical, Biological, Radiological, and Nuclear Defense (JPEO - CBRND) Joint Project Lead for Enabling Biotechnologies (JPL-EB), and from the Biomedical Advanced Research Development Authority (BARDA), part of the Assistant Secretary for Preparedness and Response (ASPR) at the U.S. Department of Health and Human Services, to develop SAB-185, a countermeasure to SARS-CoV-2 (Effort sponsored by the U.S. Government under Other Transaction number W15QKN-16-9-1002 between the Medical CBRN Defense Consortium (MCDC), and the Government). The views and conclusions contained herein are those of the authors and should not be interpreted as necessarily representing the official policies or endorsements, either expressed or implied, of the U.S. Government. HW, TL, CB, KE, and ES are employees of SAB Biotherapeutics and have financial interests. This work was supported by a contract from SAB Biotherapeutics, Inc., to the University of Pittsburgh (WK). MDHA was supported by an NIH/NIAID T32 grant (T32 AI049820).

EXHIBIT 99.2

SAb BIOTHERAPEUTICS

Efficacy and Safety of SAB-176, a Novel Anti-Type A and B Influenza Immunotherapeutic: A Phase 2a, Randomized, Double-Blind Trial in H1N1 Challenged Adults

Thomas C. Luke, MD.
Senior Vice President, Research and Development
SAB Biotherapeutics, Inc.
*As an employee, Dr. Luke has a potential financial conflict of interest.

Forward-Looking Statements

The material in this presentation has been prepared by SAB Biotherapeutics, Inc. ("SAB") and is general background information about SAB's activities current as of the date of this presentation. This information is given in summary form and is not intended to be complete. Information in this presentation, including financial forecasts, should not be considered advice or a recommendation to investors or potential investors in relation to holding, purchasing, or selling securities or other financial products or instruments and does not take into account any particular investment objectives, financial situation or needs.

This presentation may contain forward-looking statements including statements regarding our intent, belief, or current expectations with respect to SAB's businesses and operations, market conditions, results of operations and financial condition, capital adequacy, specific provisions, and risk management practices. Readers are cautioned not to place undue reliance on these forward-looking statements. SAB does not undertake any obligation to update any information herein for any reason or to publicly release the result of any revisions to these forward-looking statements to reflect events or circumstances after the date hereof to reflect the occurrence of unanticipated events unless required by law. While due care has been used in the preparation of forecast information, actual results may vary in a materially positive or negative manner and the presentation may contain errors or omissions. Forecasts and hypothetical examples are subject to uncertainty and contingencies outside SAB's control. Past performance is not a reliable indication of future performance. The forward-looking statements contained or implied in this presentation are subject to other risks and uncertainties, including those discussed under the heading "Risk Factors" in SAB's most recent Annual Report on Form 10-K with the Securities and Exchange Commission (the "SEC") and in other filings that SAB makes with the SEC.

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

Targeted Product Profile and Administration Routes

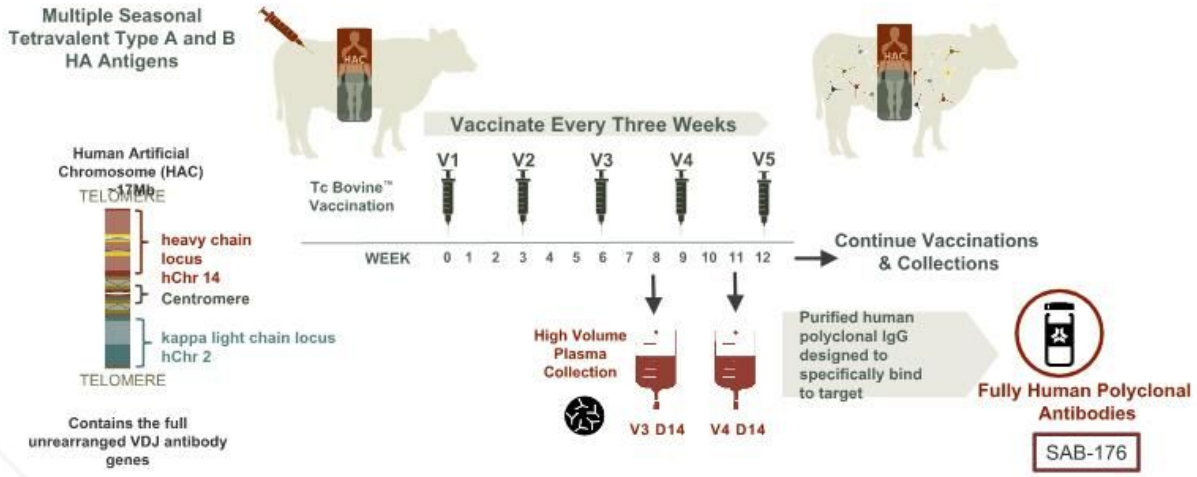
Treat high-risk influenza adult patients prior to the development of severe disease:

- 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

DiversitAb™ Development Process for SAB-176



SAB-176 had Higher HAI Titers than Anti-Flu hIVIGs Against Multiple Influenza Vaccine Strains and Non-Vaccine Strains

	H1N1							H3N2				B-Vic			B-Yam		
Sample Started at 5mg/ml	A/California/4/2009 (hVIVO)	A/California/4/2009 (Huber stock)	A/Michigan/45/2015	A/Brisbane/02/2018	A/Guangdong-maonan/2019 (Egg)	A/Guangdong-maonan/2019 (Cell)	A/Victoria/2570/2019 (2021-22)	A/Singapore/INIFMH-16-0019/2016	A/Kansas/14/2017	A/Hong Kong/2671/2019 (Egg)	A/Cambodia/e0826360/2020 (2021-22)	B/Maryland/15/2016	B/Colorado/06/2017	B/Washington/02/2019	B/Phuket/3073/2013	B/California/12/2015	G4HA
SAB-176 Lot 4 V3-V12	1:512 (8X)	1:512 (8-16X)	1:512 (16X)	1:512 (16-32X)	1:512 (16-32X)	1:512 (16X)	1:256 (16-32X)	1:512 (8-32X)	1:256 (8-64X)	1:256 (16-32X)	1:256 (8-16X)	1:256 (16-32X)	1:256 (16-32X)	1:128 (16-32X)	1:128 (16X)	1:128 (16-32X)	1:512 (16X)
SAB-176 Lot 3 V3-V12	1:512 (8X)	1:512 (8-16X)	1:512 (16X)	1:512 (16-32X)	1:512 (16-32X)	1:512 (16X)	1:256 (16-32X)	1:512 (8-32X)	1:512 (16-128X)	1:256 (16-32X)	1:256 (8-16X)	1:128 (8-16X)	1:256 (16-32X)	1:64 (8-16X)	1:128 (16X)	1:128 (16-32X)	1:512 (16X)
SAB-176 Lot 2 V3-V5	1:1024 (16X)	1:512 (8-16X)	1:512 (16X)	1:512 (16-32X)	1:512 (16-32X)	1:512 (16X)	1:256 (16-32X)	1:512 (8-32X)	1:64 (2-16X)	1:128 (8-16X)	1:256 (8-16X)	1:256 (16-32X)	1:256 (16-32X)	1:128 (16-32X)	1:256 (32X)	1:128 (16-32X)	1:512 (16X)
SAB-176 Lot 1 V3	1:512 (8X)	1:512 (8-16X)	1:512 (16X)	1:512 (16-32X)	1:512 (16-32X)	1:512 (16X)	1:256 (16-32X)	1:512 (8-32X)	1:64 (2-16X)	1:64 (4-8X)	1:128 (4-8X)	1:256 (16-32X)	1:256 (16-32X)	1:64 (8-16X)	1:128 (16X)	1:128 (16-32X)	1:512 (16X)
Anti-Flu hIVIG 2013	1:64	1:32	1:32	1:32	1:16	1:32	1:8	1:16	1:4	1:8	1:16	1:8	1:8	1:4	1:8	1:4	1:32
Anti-Flu hIVIG 2017	1:64	1:32	1:32	1:16	1:16	1:32	1:16	1:64	1:32	1:16	1:32	1:16	1:16	1:8	1:8	1:8	1:32
Anti-Flu hIVIG 2018	1:64	1:64	1:32	1:32	1:32	1:32	1:16	1:64	1:32	1:16	1:32	1:16	1:16	1:8	1:8	1:8	1:32
NC Ab	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1

Non-Vaccine strains Vaccine strains

Dr. Victor Huber, University of South Dakota

Trial Design and Methods

- The trial was sponsored by SAB Biotherapeutics and designed with hVIVO Services Limited. The study was conducted at hVIVO Services Limited screening and quarantine facilities in London, England. (EudraCT reference number 2021-001254-56 and registered with ClinicalTrials.gov number NCT04850898).
- Healthy volunteers aged between 18 and 45 years were enrolled between 23 June and 20 Sept 2020. They were screened per protocol to be nonsmokers, healthy, with a body mass index ≥18 and ≤35, no vaccine received within 30 days of infusion, and a A/California/2009/H1N1 serum hemagglutination inhibition (HAI) antibody titer of ≤1:10 within 90 days prior to enrollment.
- 60 Participants were randomized prior to challenge 1:1, double-blinded, to receive SAB-176 or placebo 20-24 hours after influenza challenge. 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.
- 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.
- A previously utilized Influenza 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)

Primary and Selected Secondary Outcome Measures

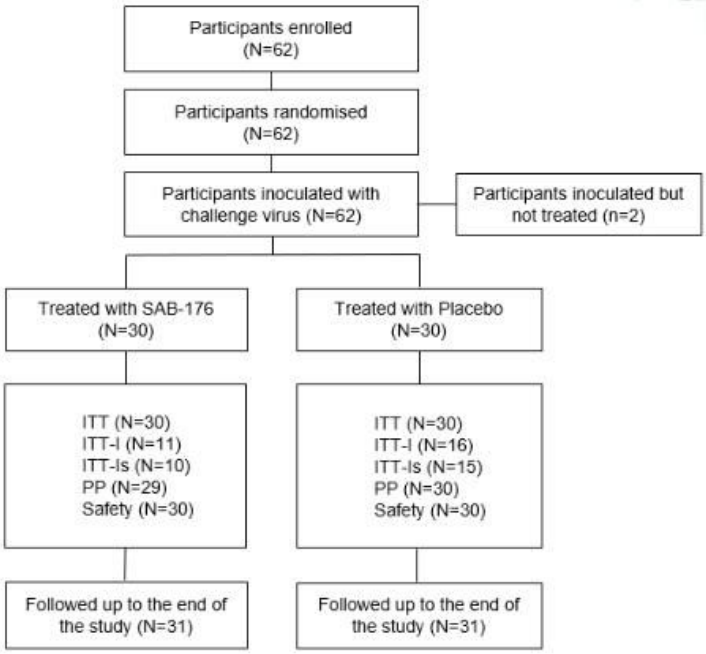
Primary Outcome Measure:

- 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:

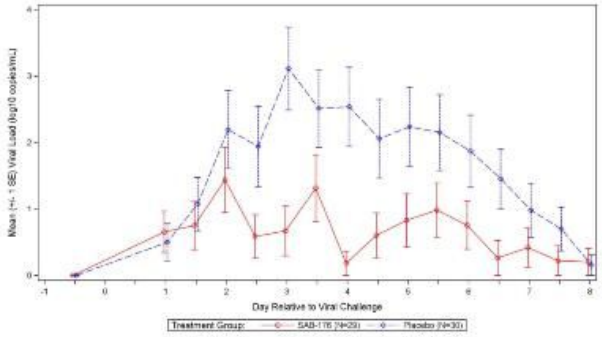
- Area under the curve over time of total clinical symptoms score (TSS-AUC) as measured by graded symptom scoring system (categorical and visual analogue scales) to evaluate the effect of SAB-176 in reducing symptoms due to Influenza A/California/2009 H1N1 virus compared to placebo. [Time Frame: 8 Days]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

Disposition of Participants



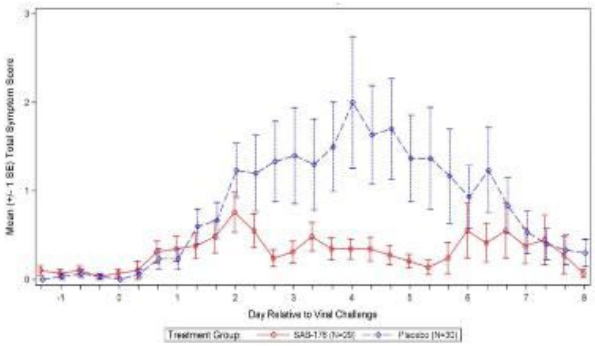
SAB-176 Met the Primary Endpoint of Viral Load and Secondary Endpoint of Symptom Reduction

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



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

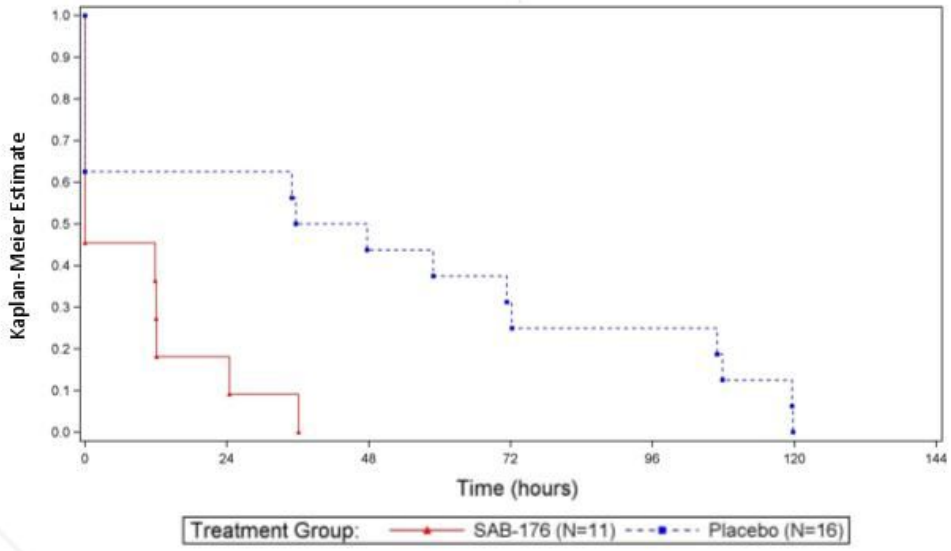
SAB-176 Achieved Statistically Significant (p = 0.013) Improvement in Symptomology at Day 4



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 anti-Type A and B influenza polyclonal immunotherapeutic

- Demonstrates significant HAI titers to multiple Type A and B influenza strains
- 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
- Demonstrated safety and tolerability
- Future studies in high-risk patients should be conducted

Acknowledgements

SAB Biotherapeutics, Inc., would like to acknowledge the support of Dr. Victor Huber, University of South Dakota, for HAI assessment of influenza strains.

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SAB Biotherapeutics Unveils New Data at ISIRV OPTIONS XI Conference Validating SAB-176 Proof of Concept in Reducing Viral Load and Improving Symptoms of Influenza and Showing SAB-185 Effective Against Multiple COVID-19 Variants Including Omicron

SAB's fully-human polyclonal antibody platform maintains its efficacy against multiple variants of several highly mutating viruses

SIOUX FALLS, S.D., Sept. 28, 2022 (GLOBE NEWSWIRE) – SAB Biotherapeutics (Nasdaq: SABS), ("SAB"), a clinical-stage biopharmaceutical company with a novel immunotherapy platform that produces specifically targeted, high-potency, fully-human polyclonal antibodies without the need for human donors, released today new data presented at the Options for Control of Influenza (OPTIONS XI) conference, which is hosted by the International Society for Influenza and other Respiratory Virus Diseases (ISIRV) in Belfast, Northern Ireland, from Sept. 26-29, showing its fully-human polyclonal antibody platform maintains its efficacy against multiple variants of several highly mutating viruses.

On Thursday, Sept. 29, at 11:24 am BST, SAB will deliver an oral presentation of its Phase 2a challenge trial that shows SAB-176 reduced the viral load in subjects exposed to H1N1 influenza virus, improved symptoms by day four and shortened the timeframe for viral shedding. On Tuesday, Sept. 27, SAB conducted a poster presentation highlighting data that its SAB-185 COVID-19 polyclonal antibody therapeutic candidate was effective in animal models against the majority of known SARS-CoV2 variants, including the recently evolving Omicron variants.

"Both of these programs show the power of polyclonal antibodies to neutralize highly mutating viruses and the differentiation of SAB's novel therapeutic products," said Eddie Sullivan, co-founder, President, and Chief Executive Officer of SAB. "These data highlight that our technology produces neutralizing antibodies that create an envisioned evergreen therapeutic aimed to maintain efficacy against rapidly mutating pathogens."

SAB's oral presentation, titled "Efficacy and Safety of SAB-176, a Novel Anti-Type A and B Influenza Immunotherapeutic: A Phase 2a, Randomized, Double-Blind Trial in H1N1 Challenged Adults," presents clinical data that SAB-176 met its primary endpoint of reducing the nasopharyngeal viral load in subjects challenged with H1N1 A/California/2009-like virus. SAB-176 also met secondary endpoints of reducing symptoms by day four and shortened the timeframe of the ability to culture virus *in vitro*, suggesting reduced viral shedding, and was safe and well tolerated.

For this randomized and double-blinded trial, 60 participants were randomized in 1:1 fashion – 30 participants received SAB-176 and 30 received placebo 20-24 hours after influenza H1N1 virus challenge on day 0. Participants received 25 mg/kg of SAB-176 diluted in normal saline or an equivalent volume of normal saline (placebo) in a single IV infusion. Participants were quarantined for up to 11 days (day 2 to 8) and were discharged on day 8. Participants returned for one outpatient visit on day 28.

The trial achieved a statistically significant reduction in nasopharyngeal viral load and symptom reduction at day 4, shortened the time of viable virus shedding and demonstrated safety. Further, SAB-176 developed against recent seasonal influenza A and B strains, demonstrated efficacy against the 2009 pandemic H1N1 strain in this clinical trial. These clinical results were anticipated as SAB-176 showed

significant preclinical HAI titers to multiple current and previous seasonal Type A and Type B influenza strains.

“SAB’s challenge trial for SAB-176 established proof of concept for this important clinical program,” said Alexandra Kropotova, M.D., Chief Medical Officer at SAB. “The trial not only proved that viral load and symptoms could be reduced, but it also reinforced SAB-176’s ability to generate broadly neutralizing antibodies to H1N1 pandemic strain as well as all tested viral variants of influenza A and B. Overall, these results demonstrate the potential for broad efficacy against current and unknown future influenza strains that will undergo mutational changes. This trial is an important leap forward in SAB’s clinical progress.”

SAB’s poster presentation, titled “Transchromosomic Bovine-Derived Human Anti-SARS-CoV-2 Polyclonal Antibodies Protect hACE2 Transgenic Syrian Hamsters Against Multiple SARS CoV-2 Variants,” presented on Tuesday, Sept. 27, detailed SAB’s approach using a human anti-SARS-CoV-2 polyclonal antibody (pAb) generated through SAB’s DiversitAb™ platform, which uses human artificial chromosome-transgenic bovines to produce human IgG preparations after hyperimmunization.

The *in vitro* neutralizing capacity of SAB-185 was tested against 10 variant SARS-CoV-2 strains, including several Omicron variants. SAB-185 exhibited equivalent neutralization of the Munich, Alpha, Beta, Gamma and D144-146 variants, and retained neutralization of the delta variant AY.1 and Omicron variants BA.1.1.529, BA.2.12.1, BA.4 and BA.5, with only modest losses of neutralization activity. For *in vivo* protection studies, SAB used a human ACE2 (hACE2) transgenic Syrian hamster model that exhibits rapid lethality after intratracheal SARS-CoV-2 challenge with the Munich, Alpha, Beta, Delta, and D144-146 variants; the Omicron B.1.1529 variant resulted in a delayed, less severe, and non-lethal disease. Prophylactic SAB-185 treatment protected the hamsters from death and minimized clinical signs of infection when challenged with the variant viruses tested.

“This data suggests that SAB-185 may be an effective immunotherapy even in the presence of ongoing viral mutation,” Dr. Kropotova said. “SAB’s data showing efficacy for all tested prominent COVID variants points to the benefits of our approach to use fully-human polyclonal antibodies in effectively targeting pathogens that mutate over time. The loss of efficacy of some current COVID-19 therapies against prevalent COVID strain highlights the potential of high potency, broadly neutralizing fully-human polyclonal therapies such as SAB-185 against SARS-CoV2 and other rapidly mutating viruses.”

About SAB Biotherapeutics, Inc.
SAB Biotherapeutics, Inc. (SAB) We are a clinical-stage biopharmaceutical company focused on the development of powerful and proprietary immunotherapeutic polyclonal human antibodies to treat and prevent infectious diseases and immune and autoimmune disorders. Our development programs include infectious diseases resulting from outbreaks and pandemics, as well as immunological, gastroenterological, and respiratory diseases that have significant mortality and health impacts on immune compromised patients. SAB has applied advanced genetic engineering and antibody science to develop transchromosomic (Tc) Bovine™. Our versatile DiversitAb™ platform is applicable to a wide range of serious unmet needs in human diseases. It produces natural, specifically targeted, high-potency, fully-human polyclonal immunotherapies without the need for human donors. SAB currently has multiple drug development programs underway and collaborations with the US government and

global pharmaceutical companies. For more information on SAB, visit: https://www.SAb.bio/ and follow SAB on Twitter and LinkedIn.

Forward-Looking Statements
Certain statements made herein that are not historical facts are forward-looking statements for purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Forward-looking statements generally are accompanied by words such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect,” “should,” “would,” “plan,” “predict,” “potential,” “seem,” “seek,” “future,” “outlook” and similar expressions that predict or indicate future events or trends or that are not statements of historical matters. These forward-looking statements include, but are not limited to, statements regarding future events, including the development and efficacy of our influenza program, C. diff. program, Type 1 Diabetes program, and other discovery programs, the likelihood that a patent will issue from any patent application, the results, including timing, of the development of SAB-195 (including any IND filing or proposed clinical trials), financial projections and future financial and operating results (including estimated cost savings and cash runway), the outcome of and potential future government and other third-party collaborations or funded programs (including negotiations with the DoD). These statements are based on the current expectations of SAB and are not predictions of actual performance, and are not intended to serve as, and must not be relied on, by any investor as a guarantee, prediction, definitive statement, or an assurance, of fact or probability. These statements are only current predictions or expectations, and are subject to known and unknown risks, uncertainties and other factors which may be beyond our control. Actual events and circumstances are difficult or impossible to predict, and these risks and uncertainties may cause our or our industry’s results, performance, or achievements to be materially different from those anticipated by these forward-looking statements. A further description of risks and uncertainties can be found in the sections captioned “Risk Factors” in our most recent annual report on Form 10-K, subsequent quarterly reports on Form 10-Q, and other filings with or submissions to, the U.S. Securities and Exchange Commission, which are available at https://www.sec.gov/ Except as otherwise required by law, SAB disclaims any intention or obligation to update or revise any forward-looking statements, which speak only as of the date they were made, whether as a result of new information, future events or circumstances or otherwise.

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