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): June 21, 2023

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.

SAB Biotherapeutics, Inc., a Delaware corporation (the "Company" or "SAB") will present a poster presentation over new data showing SAB-142 is a first in class, fully human polyclonal antithymocyte globulin ("ATG") that demonstrates safety and dose-dependent anticipated pharmacologic effects in nonhuman primates ("NHPs") in a Good Laboratory Practice ("GLP") Toxicology Study, (the "Presentation"), at the Federation of Clinical Immunology Societies (the "FOCIS") 2023 Annual Meeting held in Boston on June 22, 2023. A copy of the Presentation is furnished herewith as Exhibit 99.1 and is incorporated herein by reference. A copy of the press release which discusses this matter is furnished hereto as Exhibit 99.2, and incorporated herein by reference.

The information furnished under this Item 7.01, including Exhibits 99.1 and 99.2, will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section, and will not be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, except as expressly set forth by specific reference in such a filing.

Cautionary Note Regarding 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, the development and efficacy of our influenza program, C. diff. program, type 1 diabetes program, and other discovery programs, the results, including timing, of the development of SAB-176, SAB-185, SAB-142 and SAB-195, including SAB-176 Fast Track designation and the outcome of and potential future government and other third-party collaborations or funded programs.

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.

Item 9.01 Financial Statements and Exhibits.

Exhibit Number	Description
99.1	Presentation, dated June 21, 2023
99.2	Press release of the Company, dated June 21, 2023
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: June 21, 2023

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

Safety and Pharmacodynamic Effects of Novel Fully Human Anti-Thymocyte Polyclonal IgG Antibodies in an IND Enabling GLP Toxicology Study

First in Class, Human ATG (SAB-142) Therapeutic Developed to Delay Onset and Progression of Type 1 Diabetes

Eric Sandhurst[1], Thomas Luke[1], Hua Wu[1], Diane Maher[1], Eddie Sullivan[1], Christoph Bausch[1], Alexandra Kropotova[1], Mohamed Ezzelarab[2], Kurt Griffin[3], Jared Wollman[3], Alexei Savinov[3]

[1]SAB Biotherapeutics, Sioux Falls, SD 57104; [2]Thomas E. Starzl Transplantation Institute, Pittsburgh, PA 15261; [3]Sanford Research, Sioux Falls, SD 5701

Abstract

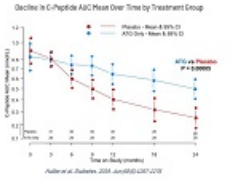
- SAB-142 is a first-in-class fully human polyclonal immune modulating anti-thymocyte immunoglobulin (hATG) produced in SAB Biotherapeutics' proprietary Transchromosomic (Tc) Bovine platform.
- SAB-142 is expected to be efficacious, non-immunogenic, and well tolerated when used in humans, as previously demonstrated by several clinical phase investigational products produced in the in the Tc Bovine™ platform. In contrast, other anti-thymocyte immune modulating agents currently on the market, such as rabbit ATG (rATG, Thymoglobulin) or equine ATG (ATGAM), are known to cause serum sickness and severe hypersensitivity reactions in humans.
- Tc bovines that produce fully human polyclonal antibodies underwent a series of immunizations with human thymocytes. Post immunization plasma was processed into (SAB-142). *In vitro* characterization of SAB-142 demonstrated minimal red blood cell binding, higher complement-dependent cytotoxicity (CDC) and similar binding to human PBMCs as compared to rabbit ATG (rATG).
- In an IND-enabling GLP NHP study, a single infusion of SAB-142 was administered at 1, 5, and 10 mg/kg (6 animals per dose) and rATG was administered at 5 mg/kg (6 animals). All 24 animals were assessed for safety and pharmacological activity with clinical assessments, clinical labs and PBMCs collected at various timepoints. Analysis of peripheral blood lymphocyte populations post-treatment showed dose-dependent impact on total lymphocytes and memory CD4⁺ and CD⁸ T lymphocytes through day 28.
- Our data suggest that SAB-142 (hATG) demonstrates safety and dose-dependent pharmacological activity in NHPs. These results support an Investigational New Drug (IND) application for clinical investigation of SAB-142 in clinical trials as a potential disease-modifying treatment for Type 1 Diabetes (T1D) and other autoimmune diseases.

Background

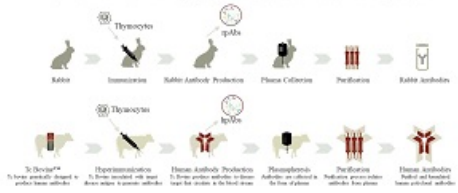
Type 1 Diabetes and Clinical Intervention with Anti-Thymocyte Immunoglobulin (ATG)

- Type 1 Diabetes (T1D) affects 1 in 300 Children and accounts for 1 in 7 health care dollars.
- Since 2000, the prevalence of T1D has increased at four times the rate of the global population.
- As of 2021, an estimated 8.4 million people are living with T1D globally with a predicted increase to 13.5-17.4 million by 2040.
- T1D is currently not preventable nor curable and is only managed via life-long administration of insulin.

- Rabbit ATG, FDA-approved for kidney transplantation, was used experimentally in clinical trials and showed a delay progression of T1D but is associated with significant adverse reactions such as serum sickness related to animal origin of antibody.



- **SAB-142 is a first in class fully human ATG therapeutic produced in SAB's Tc Bovine platform.**
- **SAB-142 was produced using a process similar to rATG but is expected to be non-immunogenic and well-tolerated when used in humans,** as previously demonstrated in several Phase 1-3 clinical trials with investigational products produced in SAB's Tc Bovine platform.



IND-Enabling GLP NHP Toxicology Study Design

A single infusion of SAB-142 (hATG) or rATG was administered to cynomolgus monkeys, and all 24 animals were assessed for safety and pharmacological activity with clinical assessments, clinical labs and PBMCs collected at various timepoints.

Group No.	Test Material	Dose Level (mg/kg)	No. of Males	No of Females
1	rATG	5	3	3
2	SAB-142	1	3	3
3	SAB-142	5	3	3
4	SAB-142	10	3	3

Results

SAB-142 (hATG) has Potential for a Best-in-Class Safety Profile with Higher Potency Compared to rATG

A) Better Safety Profile

Red Blood Cell Binding

Sample	Activity (µg/mL)
rATG	20
SAB-142	280

B) Higher Potency

Complement-dependent cytotoxicity (CDC)

Sample	Mean EC_{50} ±SD (µg/mL)
rATG	162 ± 8
SAB-142	22 ± 2

Figure 1. Red Blood Cell Hemagglutination and Complement-Dependent Cytotoxicity (CDC)

A) The Hemagglutinin (HA) Titer was determined by the following formula: (Protein conc/endpoint titer/dilution)*1000 = relative active concentration of antibody to cause complete agglutination of the red blood cells. (Higher number = decreased RBC binding (desired). **B)** CDC activity was measured in human PBMCs using human complement. N=4 replicates (Lower number = higher activity/potency)

SAB-142 (hATG) Demonstrates Proportional Binding to Human T Cell Subsets as rATG

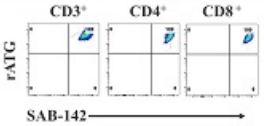


Figure 2. Binding affinity of SAB-142 and rATG to CD3⁺, CD4⁺, CD8⁺ T lymphocytes

PBMCs were co-incubated with the respective fluorescently labeled CD marker and fluorescently labeled preparations of SAB-142 and rATG. Cell populations were gated for the respective CD marker and assessed for labeling by SAB-142 and rATG

SAB-142 (hATG) Demonstrates Similar Immunomodulatory Effect on Human T Cell Subsets *in vitro* as rATG

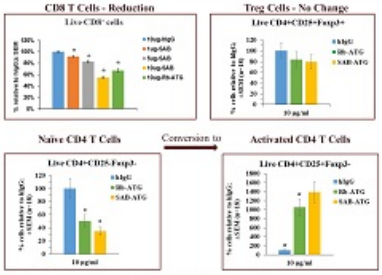


Figure 3. *In vitro* effect of SAB-142 and rATG

Total PBMCs or PBMCs enriched for Tregs ($CD4^+$, $CD127^{low}$, $CD49d^0$) were cultured with SAB-142 or rATG overnight. Cells were then stained as indicated and analyzed by flow cytometry. * Indicates $p<0.05$ compared to negative control hIgG.

Acknowledgements

SANFORD RESEARCH

Sanford Research Flow Cytometry Core funded by NIH Centers of Biomedical Research Excellence grant 2P20GM103548

SAB-142 (hATG) modulates CD4⁺ and CD8⁺ Memory T cell subsets *in vivo* similarly to rATG in an NHP GLP Study

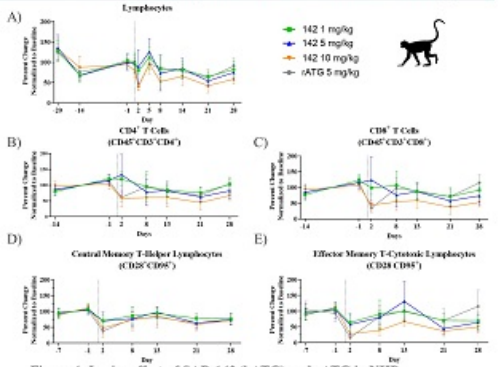


Figure 4. *In vivo* effect of SAB-142 (hATG) and rATG in NHPs

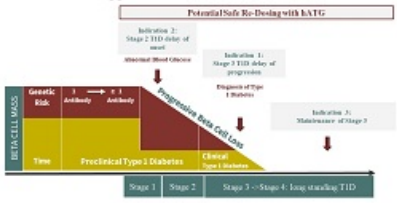
A) Lymphocyte counts, obtained by hematological analysis, were normalized to the average pre-dose counts (collected on days -20, -14, -1 and 1). **B-E)** Absolute counts of the indicated subsets were normalized to the average pre-dose counts (collected on days -14 and -1 or days -7 and -1 as indicated). Vertical dotted line indicates time of dosing with either SAB-142 or rATG. Error bars show standard deviation.

Conclusions

- SAB-142 is a first in class, fully human polyclonal ATG that demonstrates safety and dose-dependent anticipated pharmacologic effects in NHPs in a GLP Toxicology Study.
- SAB-142 demonstrates the following:
  - Minimal Red Blood Cell binding and higher CDC activity compared to rATG, suggesting less potential adverse effects with higher potency.
  - Proportional binding to human T Cell subsets ($CD3^+$, $CD4^+$, and $CD8^+$) as rATG.
  - Similar *in vitro* immunomodulatory activity in T lymphocyte subsets as rATG.
  - Modulation of central memory $CD4^+$ and effector memory $CD8^+$ T lymphocyte populations *in vivo* in cynomolgus monkeys, similarly to rATG.
- The successful completion of a GLP Tox study is a significant IND enabling milestone in the development of SAB-142.

Future Clinical Impact

These data support clinical trials to determine if SAB-142 can prevent and/or delay the progression of Type 1 Diabetes with an enhanced safety profile over current approaches.



SAB Biotherapeutics Presents Positive IND-Enabling GLP Toxicology Study for SAB-142, a Novel Immunotherapeutic for Type 1 Diabetes at FOCIS 2023

SAB highlights results from GLP toxicology study confirming SAB-142's mechanism of action at the 23rd Federation of Clinical Immunology Societies (FOCIS)

Study shows SAB's fully-human multi-target immune modulating therapeutic for treatment of Type 1 Diabetes is well tolerated

SIOUX FALLS, S.D., June 21, 2023 (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 multi-target immunoglobulin (hIgG) antibodies (fully-human polyclonal antibodies) without the need for human donors, today announced the presentation of positive safety and pharmacologic data from a GLP toxicology study for SAB-142, a first in class fully human immunotherapeutic being developed for delaying onset and progression of Type 1 Diabetes (T1D), at the Federation of Clinical Immunology Societies (FOCIS) in Boston. Results from the IND-enabling GLP tox study confirmed that SAB-142 affects the same subsets of immune cells associated with T1D as commercially available rabbit-derived anti-thymocite globulin (rATG) *in vivo*.

SAB-142 is a first-in-class fully-human, multi-target anti-thymocyte immunoglobulin treatment aimed to provide a superior profile for delaying onset or progression of T1D. SAB-142's unique multi-target strategy can be directed at the multiple immunological cell subsets associated with T1D and other autoimmune diseases. Another anti-thymocyte product produced in rabbits and FDA-approved for kidney transplantation, rATG, was investigated in patients with Type 1 Diabetes and showed significant efficacy in delaying progression of the disease by preserving C-peptide levels, a surrogate measure for endogenous insulin production by pancreatic beta cells. Commercially available products for T-cell mediated autoimmune diseases, such as fully-animal antibodies often induce immune-mediated reactions such as serum sickness. By contrast, SAB-142, which is a fully-human polyclonal antibody therapeutic, may be administered multiple times without causing these immune-related adverse reactions, which is particularly desirable for patients with lifelong diseases such as T1D.

Taking place June 20-23, 2023, in Boston, the FOCIS 2023 Annual Meeting is a leading translational immunology conference that explores research developments across immune-mediated diseases with a focus on molecular pathways and their implications in human disease. SAB will present a poster titled, "*Safety and Pharmacodynamic Effects of Novel Fully Human Anti-Thymocyte Polyclonal IgG Antibodies in an IND Enabling GLP Toxicology Study. First in Class, Human ATG (SAB-142) Therapeutic Developed to Delay Onset and Progression of Type 1 Diabetes*," on June 22 at 6:30pm ET.

"We are excited to present results from our recently completed GLP tox study, which confirms our lead candidate's mechanism of action *in vivo* and paves the way for an IND submission," said Alexandra Kropotova, MD, Chief Medical Officer of SAB. "With over 8.4 million people affected by Type 1 Diabetes worldwide and only a single disease-modifying treatment available for patients, there is a pressing need for new and effective disease-modifying treatments. We are proud to share this milestone study and remain committed to evaluating SAB-142's promising potential as a disease-modifying therapy as we are planning to enter Phase 1 stage of clinical development in the next few months. "

In the in vivo study conducted under GLP conditions, SAB-142 was administered at three dose levels of 1, 5, and 10 mg/kg. Its active control, FDA-approved anti-thymocyte rabbit globulin (ATG) was administered at 5 mg/kg. The study results showed that both SAB-142 and the rabbit ATG modulate key T-cell subsets relevant for T1D in a similar fashion thus confirming that SAB-142's mechanism of action is similar to rabbit ATG. Based on the absence of SAB-142-related findings in any safety parameter evaluated in the study, the No Observed-Adverse-Effect-Level (NOAEL) was determined to be 10 mg/kg SAB-142, the highest dose level evaluated, thus meeting its main objective to generate preclinical safety data in support of upcoming IND and CTA filings.

SAB plans to submit an Investigational New Drug (IND) application for SAB-142 to the U.S. Food and Drug Administration and initiate a Phase 1 trial in the next few months.

For more details on the FOCIS program, please visit the conference website here.

More information on SAB's T1D candidate, SAB-142, can be found on the pipeline page of SAB's website: SAB-142: Type 1 Diabetes.

About SAB Biotherapeutics, Inc.

SAB Biotherapeutics, Inc. (SAB) is 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

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