SAB Biotherapeutics
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Novel biologic modality proven to maintain its efficacy against rapidly-mutating pathogens

SAB Biotherapeutics' DiversitAb novel drug development platform creates targeted fully human multi-epitope binding immunoglobulins (polyclonal antibodies) without the need for human donors. Its proprietary immunotherapies show promise for treating and preventing infectious diseases and autoimmune and oncological disorders.

Over the past two decades, SAB Biotherapeutics, a clinical-stage biopharmaceutical company, has optimized and advanced genetic engineering and antibody science to develop transchromosomic cattle (Tc Bovine) that can produce twice as much human targeted antibody as a human or smaller animal.

"We believe we are the only company in the world that can produce truly polyclonal human antibodies at scale without the need for human donors," said Eddie J. Sullivan, co-founder, president and CEO of SAB. "DiversitAb has the unique ability to generate large quantities of high-potency, target-specific multi-epitope binding antibodies made up of human immunoglobulin G1 (hIgG1).

"While complex diseases are driven by multiple dysregulated pathways, treatments such as monoclonal antibodies may have limited efficacy because they bind to a single site with a single mode of action and mediate only one dysfunctional pathway. We are exploring immunotherapies that can bind to multiple targets, and target multiple modes of action in infectious and autoimmune diseases that have significant mortality and morbidity."

Lead candidate for the treatment of *Clostridioides difficile*

SAB Biotherapeutics' lead candidate for the treatment of *Clostridioides difficile* (*C. difficile*) is SAB-195. *C. difficile* is the most prevalent healthcare-associated bacterial infection in the United States (US) and the developed world (Fig. 1). There are some 500,000 people infected with *C. difficile* and 30,000 deaths in the US annually, responsible for up to $4.8 billion in excess healthcare costs for acute care facilities.

"This is one of the very complex infectious diseases being treated by multiple drugs that address only one challenge at a time," said Alexandra Kropotova, executive vice president and CMO of SAB Biotherapeutics. "There is a significant unmet need here, as multiple drugs can result in antimicrobial resistance (AMR), medication errors, high cost and suboptimal management of the disease resulting in repeat episodes of infection, in particular in the most vulnerable high-risk patients. Our platform is unique in that it can address an entire lifecycle of this difficult-to-treat pathogen and its numerous toxins with one treatment, tackling each stage of the complex bacterial lifecycle with multi-epitope binding and preventing AMR, something that existing antibiotic treatment can't do."

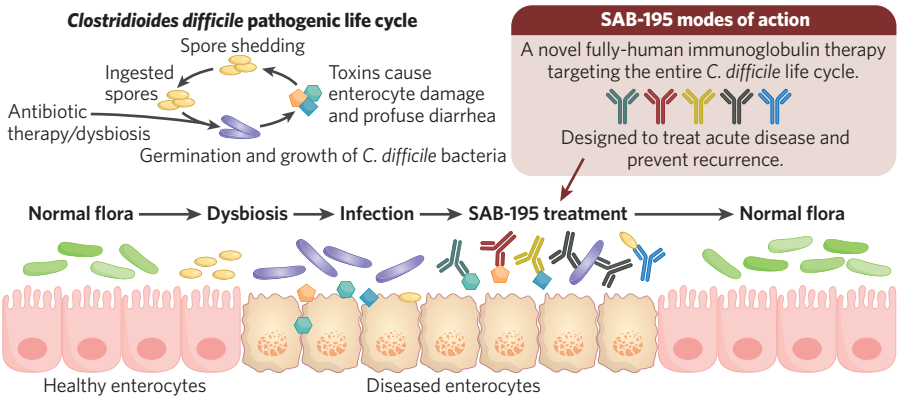

Fig. 1 | SAB Biotherapeutics' lead candidate to treat *Clostridioides difficile* (*C. difficile*) is SAB-195. The schematic shows the SAB-195 mode of action against *C. difficile*, a traditionally difficult-to-treat infection that can cause a range of disease severity in humans.

Administration of antibiotics for *C. difficile* has unintended consequences and can create a vicious cycle of infection treatment, disruption of the healthy biome and a 25% increase in the risk of recurring infection. Subsequent antibiotics carry a 45% risk of a third infection. Recurrent *C. difficile* infections also increase the risk of death by 33%.

"Our product will be targeting the spores and live cells, neutralizing their activity and simultaneously targeting multiple toxins produced by multiple strains of the live bacterial cells, including epidemic strains," Kropotova said.

A single dose of SAB-195 would allow patients to be treated for the acute symptoms of *C. difficile* and reduce the risk of recurrent infection. It will fully preserve a good microbiome.

SARS-CoV-2, epidemics and pandemics

Monoclonal antibody treatments for SARS-CoV-2 have already been withdrawn from many countries due to the loss of efficacy. Targeting a single site on a highly mutating virus will eventually lead to loss of neutralizing activity when a virus mutates, which resulted in all emergency-use authorized monoclonal antibodies losing efficacy against new SARS-CoV-2 variants.

"Pathogens mutate very rapidly, and targeting a pathogen with only one binding epitope is doomed to fail over time," Kropotova said. "The monoclonal antibody will lose its efficacy eventually, but it may also potentially create the hazard of escape mutants that will perpetuate the pandemic or endemic infection."

SAB Biotherapeutics has tested its hIgG therapeutic, SAB-185, which was shown to be effective against tested strains, from Delta to Omicron, including some Omicron sub-variants tested in a phase 3 clinical trial. "Our technology has a second advantage, which is the ability to strain change," Sullivan said. "Should those mutations continue to develop and decrease the efficacy of the polyclonal antibodies, we can hyper-immunize the cattle with a new strain variant."

For example, for SAB's influenza therapeutic candidate, SAB-176, cattle are immunized annually with the same influenza vaccines used in humans. The proprietary formulation and immunization process produces large quantities of high-potency, high-avidity hIgGs that keep up with the mutation over time.

SAB Biotherapeutics will file investigational new drug (IND) applications for delaying onset and progression of type 1 diabetes and *C. difficile* treatment in early 2024, and hopes to establish proof of biological activity and safety results in the clinic by the end of that year. The company is interested in attracting strategic partners and capital.

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