How Genetically Engineered Cows Could Help People With Type 1 Diabetes

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Ross Wollen December 11, 2023



Could one small herd of cows slow or prevent the development of type 1 diabetes in many thousands of people worldwide? A biotech startup named SAb Biotherapeutics is betting that it can. Scientists from the firm have genetically engineered cows to produce human antibodies that have been demonstrated to protect against the autoimmune attack that defines type 1 diabetes. These antibodies can be extracted — with little or no harm to the cow — and administered to people with newly diagnosed type 1.

The first human trials of the therapy, which is currently named SAB-142, are beginning right now. SAb's leaders expect that the antibody infusion will provide safe and durable protection to participants' capacity to secrete insulin. They believe that SAB-142 could deliver lifelong benefits to people with newly diagnosed type 1 diabetes — and possibly even prevent its development in the first place.

The therapy, if it ever sees the light of day, is years away. But investors are betting big on its potential: SAb recently secured $67 million in financing from a constellation of venture capital firms, including the JDRF T1D Fund.

It Starts With Rabbits

The story of this futuristic bovine medicine actually starts with rabbits. For decades, doctors have used rabbit antithymocyte globulin (ATG) as an antirejection medication for organ transplants. Rabbit ATG powerfully blocks the immune system attacks that lead to acute organ rejection. Naturally, researchers have explored its potential to inhibit autoimmune attacks, too.

“That very same action can also be used to stop an autoimmune reaction, which is exactly what type 1 diabetes is,” says Eddie Sullivan, the president and CEO of SAb Biotherapeutics. And it works: “ATG has been used in multiple clinical trials and has shown some of the best efficacy data in preventing the progression of type 1 diabetes.”

A 2019 experiment, for example, showed that a low quantity of ATG, delivered in two doses over two days, helped preserve beta cell function and reduced A1C levels for at least two years in people with newly diagnosed type 1 diabetes. In essence, the drug infusion strengthened and extended the honeymoon phase.

Despite the extremely promising results, ATG has never been developed as a commercial therapy for type 1 diabetes. Sullivan speculates that it must be because of ATG’s side effects, which can be considerable.

“The problem is, if you give humans an animal antibody, like a rabbit antibody, there is an immune reaction called serum sickness that can be quite severe,” says Sullivan. “The patient will also create antibodies to attack the drug itself, which is a foreign protein.”

Rabbit ATG’s side effects are well worth the risk in the case of a life-saving organ transplant. But for a person with new-onset type 1 diabetes, who can treat their condition without the need for drastic measures, the risk may not be worthwhile.

But what if doctors had a source of human ATG, which ought to be much less likely to provoke bad auto-immune reactions?

Enter the Genetically Engineered Cows

It sounds like science fiction. In South Dakota, there is a herd of cloned cows that have been genetically engineered to grow medicine for humans. SAb’s cows are transgenic: Their cells contain human DNA which is designed to “turn off the cow antibody genes and produce fully human antibodies.”

“We can immunize these animals to specific targets, such as autoimmune diseases,” says Sullivan. And their first target is type 1 diabetes. They create human ATG.

The cows, SAb Executive Chairman Sam Reich insists, are treated “like royalty.”

“They’re on a beautiful farm that would resemble a dairy farm. They can go inside and outside, and their pens are both heated and air-conditioned.” These cows are valuable — each one can produce enough medicine to treat several thousand people.

About three times per month, each cow “donates” blood. “These cows donate plasma instead of milk, but they’re handled the same way,” says Reich. “We’re not doing anything to these cows that humans don’t voluntarily do to themselves.”

Because each cow is so productive, Reich said, SAb will never require a large herd. At launch, as few as 15 cows would provide more than enough human ATG for the company’s demand projections. Even if every human on earth with new-onset type 1 diabetes received SAB-142 — about half a million people are diagnosed with type 1 diabetes worldwide in a year — SAb would still require only a small dairy’s worth of cows.

SAB-142

Nobody has ever tried redosing rabbit ATG in people with type 1 diabetes, perhaps because the risk of side effects is believed to increase after exposure. Serum sickness is considerably more common even in people who have previously kept rabbits as pets, according to an academic survey.

Human ATG, however, could potentially be redosed regularly, according to Alexandra Kropotova, SAb’s chief medical officer:

“Once a year redosing could keep the beta cells protected from the autoimmune response.”

While SAB-142 will not cure diabetes or confer insulin independence, it could help patients preserve some endogenous insulin production for years. And if it can be redosed regularly, there’s no telling how long the effect might last.

We know that a robust honeymoon phase “is associated with reduced prevalence of long-term complications.” Even a small amount of natural insulin production is strongly associated with better health outcomes; in a study of Joslin gold medalists, some were found to have measurable natural insulin production even *50* years after diagnosis with type 1, suggesting that residual insulin production may be a key to longevity. And lucky patients with higher levels of beta cell activity also enjoy improved blood sugar control and reduced risk of hypoglycemia, presumably leading to both better health and higher quality of life.

Many drugs have been evaluated to extend the honeymoon period; the latest news is that the buzzy blockbuster semaglutide (Ozempic) may be able to reduce insulin requirements, according to Everyday Health. But to date, no drug has been approved by the U.S. Food and Drug Administration (FDA) to slow the progression of type 1 diabetes after diagnosis.

“Only 30 percent of people with type 1 diabetes maintain an A1C below 7.0 percent,” says Kropotova. “We are failing 70 percent of patients, despite the availability of very advanced technologies.”

SAB-142 has many hurdles to pass before it is ready for FDA approval. The phase 1 study beginning now will mostly evaluate the drug’s safety in a fairly small number of people. Results may be complete by the end of 2024. If all goes well, phase 2 would enroll volunteers soon after; those results would not be ready until the end of 2026. If SBA-142 has proved to be safe and effective after those two major tests, SAb will embark on one or more phase 3 trials, the longest and largest experiments required by the FDA. In the best-case scenario, assuming that the therapy has the terrific results that its backers believe it will, SBA-142 may be ready for FDA approval in six or seven years.

Though the majority of medical therapies do not survive the entire multiphase clinical trial process, Reich is confident that SAB-142 is “uniquely positioned, because we already know that it works. Rabbit ATG has already proved itself, and our therapy is mechanistically identical.”

Could SAB-142 Prevent T1D in the First Place?

While SAb is currently focused on extending the honeymoon period for people with newly diagnosed type 1 diabetes, the firm also plans to see if its experimental therapy can delay or prevent the development of full-blown T1D in people with a very high risk of developing the condition.

There is exactly one medication currently approved to do this: the recently approved teplizumab (Tzield). When given to patients known to carry the antibodies that cause type 1 diabetes, Tzield delays the onset of symptoms by an average of nearly three years.

Kropotova calls Tzield “a trailblazer and a significant, life-changing drug.” But she believes that SAB-142 could be even more effective than Tzield, because it is a polyclonal as opposed to monoclonal treatment.

“Monoclonal antibodies [like Tzield] by definition only affect one specific cell lineage. But other broken pathways are not being corrected. And the pathogenic cells are still alive, still active, and still attacking and destroying the beta cells.”

“Using a polyclonal approach, we achieve two goals. Number one, we bind to several cell subsets that participate in autoimmune destruction. Number two, this platform allows a much higher probability of a higher proportion of patients who will respond to the drug.”

We may know more soon about ATG’s potential in this patient population. Type 1 Diabetes TrialNet — a leader in diabetes antibody testing — is spearheading the STOP-T1D trial, which will test rabbit ATG in volunteers with stage 2 type 1 diabetes.

Antithymocyte Globulin (rabbits) Injection. Cleveland Clinic.

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Read more about A1c, beta cells, honeymoon phase, insulin, Intensive management, JDRF, joslin, low blood sugar (hypoglycemia), SAB Biotherapeutics, SAB-142, type 1 diabetes, type 1 diabetes study, tzield, U.S. Food & Drug Administration (FDA).