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Bio

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CEO SPOTLIGHT:

Gaston Salinas

The chief executive of Botanical Solution Inc. (BSI) speaks about the development of QS-21 adjuvant for vaccines from *Quillaja saponaria* trees grown in BSI labs.

Quillaja saponaria, or the soap bark tree, is the source of a highly purified product derived from the tree's bark. It's called QS-21 and is used as an adjuvant in subunit vaccines to help boost immunity. Adjuvants help the effectiveness of the active in a vaccine.

QS-21 is currently used in GSK's Shingrix vaccine, RSV vaccine and COVID-19 vaccines. It is also being studied among other vaccine candidates with broader target diseases in different stages of development.

However, because of its limited supply due to the deforestation laws in its native Chile, as well as high manufacturing costs, QS-21 is very expensive—current costs per gram are between $400,000 to $500,000.

To solve this problem, Botanical Solution Inc. (BSI), a Davis, CA-based provider of advanced botanical materials, has developed a novel platform to produce *Quillaja saponaria in vitro* using scalable tissue culture techniques that create ingredients at high purity and consistency, and at a low cost.

Although BSI was founded back in 2013 and is a recognized leader in the agrochemical industry, it wasn't until 2020 when the company's founder and CEO, Gaston Salinas, steered the company into the life sciences sector when he realized that BSI's in-lab techniques could also provide value for vaccine manufacturers.

Since beginning operations in the pharma industry just a few years ago, BSI has achieved significant milestones including the opening of new, dedicated labs in Davis, CA for growing *Quillaja saponaria* trees and extracting the advanced botanical materials for QS-21; securing nearly $20 million in venture capital funding; partnering with Croda Pharma; and winning industry awards within the past year for "Best Process Innovation," "Best Start-up of the Year," and "Best Biological Product of the Year."

In this Q&A, Gaston talks with *Contract Pharma* about BSI's sustainable in-lab growth of *Quillaja saponaria* trees and extraction of the active ingredients for the "Gold Standard" vaccine adjuvant, QS-21.

Contract Pharma: *Tell me about BSI's journey over the past several years and the challenges it has faced in innovating and scaling production of QS-21?*

Gaston Salinas: Even though the company started operations back in 2013, we entered the pharmaceutical space, or the vaccine adjuvant space, in early 2020, just pre-COVID. The reason why we decided to enter the space, was because as a company we had been working with this plant material called *Quillaja saponaria* for about seven or eight years by that time. But we were using it for a different purpose. We were using it to make a crude extract for agriculture with the vision to develop the most advanced botanical materials for production of active ingredients without relying on external sources of raw materials.

And by that, I mean without needing to go into the field, or to rely on plantations, or even get materials from the wild. BSI's core technology platform, which is based on plant tissue culture technologies, allows us to deliver on that value proposition.

It has taken two to three years to get to the point where we can back completely a value proposition focused on getting, or supplying, virtually unlimited amounts of QS-21 for the vaccine industry. Not only for vaccines that are intended to protect populations in high-income countries, but also, to somehow make this compound available for developing new vaccines for different diseases that are prevalent in low-income countries.

To get to where we are, we have had to put a lot of effort into raising capital, which has led us through several financing rounds. We've been fortunate that we found a group of resilient investors that believe in what we're doing.

However, the main base of investors in BSI come from the agriculture world. So, when we brought the idea of moving into the pharmaceutical space into the equation, we did not have easy discussions at the board-level to try and convince investors to keep on supporting BSI's journey throughout this new business opportunity. But I was convinced that I couldn't let go of this opportunity to make a clear and positive impact on society.

So far, we have raised about $17 million in venture capital, and we believe that we have the most compelling value proposition for making QS-21 at scale and under GMP.

CP: *What is unique about QS-21 and the advantages it offers?*

Gaston: First, it's worth mentioning that not all types of vaccines require an adjuvant. Typically, recombinant protein-based vaccines are the ones that need an adjuvant to work. You cannot have an antigen without a vaccine adjuvant.

As for QS-21, it has been available as an adjuvant for over thirty years now. What is interesting to understand is that when you work with different vaccine adjuvants, it's not like you're trying to replace one adjuvant for another. Different vaccine adjuvants provide different modes of actions. The type of immune response that you get from QS-21 is unique. Most of the work done by GSK in the early 1990s when they were able to combine QS-21 with other components and other vaccine adjuvants somehow made this shift from working with the standalone compounds towards a science behind developing adjuvant systems.

QS-21 is a toxic molecule that needs to be stabilized in a formulation, and when this is done, has proven to be one of the gold standard vaccine adjuvants to date. During the post-COVID period, we're used to seeing vaccines that can provide up to 97-98% of protection. That wasn't the case in the past, but QS-21 can offer that level of protection.

Another key benefit provided by QS-21 is durability—this type of vaccine adjuvant clearly provides durable protection for a longer period. For example, with modern mRNA vaccines, where patients must get the shot every six to 12 months, the latest study covering the shingles vaccine Shingrix, which is the first blockbuster vaccine that contains QS-21, offers 10 years of protection.

So, QS-21 has found a position as part of a value proposition, where we will need, effectively, vaccines that are going to be intended for rapid response in case of another pandemic. In addition, there are other diseases that will benefit from long-lasting vaccines that are going to provide durable protection, just like in the case of Shingrix, or the most recent RSV vaccines launched by GSK.

CP: *How important have partnerships been to BSI's growth and success?*

Gaston: Over the past few years we have formed two different types of strategic collaborations. First, by partnering directly with Big Pharma firms that have a strong interest in QS-21, know exactly what they need to do with QS-21 and all the formulation work has been brought in-house at the company.

However, most vaccine manufacturers don't have the internal capabilities to design or develop proprietary adjuvant systems and there are a limited number of companies that know how to work with QS-21 specifically. So, they need other companies, called Enabling Technology Companies, to somehow fill that gap. To this end, we entered an agreement with Croda Pharma that enables the use of QS-21 in broader applications for vaccine manufacturers.

The value added by Croda is that they know how to make adjuvant systems so they can provide a turnkey solution to vaccine manufacturers, who then have to just couple their proprietary antigens with these adjuvant systems in order to develop a new vaccine.

This agreement was formed in May of 2023 and just a few weeks ago Croda announced a major milestone at the World Vaccine Congress in Washington, DC (April 2024) that BSI's

Quillaja saponaria trees growing in BSI's lab from which QS-21 adjuvant is extracted for shingles, RSV, malaria, Covid-19 and other vaccines.

QS-21, made in partnership with them, is going to be available later this year.

There is such a healthy appetite for access to QS-21 among the major pharmaceutical companies we talk to. They see an opportunity in investing in new therapeutics based on a robust and resilient supply of QS-21 now that we're close to the marketplace.

CP: *What are the challenges of using QS-21 in vaccine manufacturing?*

Gaston: I would say there are two main challenges with QS-21 these days. First, is making it at scale. GSK, which produces QS-21 in-house, is the only company today making QS-21 at kilogram scale—no other company is delivering on that promise.

The second challenge with QS-21 is associated with cost—the retail price these days is about $400,000 per gram. The reason for this high cost is due to an issue with the last step of purification under GMP that makes this product very costly to be manufactured.

BSI started its journey into pharma with a strong value proposition on the side of making the raw materials necessary for purification of QS-21. In addition, we have also made an important breakthrough in developing a novel purification system that is going to allow the industry to access a more cost-effective compound.

This breakthrough is why I'm so optimistic that QS-21, in the mid-term, is going to be available not only to high-income countries that are in a position to get expensive vaccines like Shingrix but will be available to low-income countries for use in different indications like malaria, for example, or tuberculosis. These are opportunities that BSI's approach allows to happen in the mid- and long-term.

CP: *How is BSI's platform having a positive impact on the environment?*

Gaston: It's very simple. We're removing the *Quillaja saponaria* forest out of the equation to make QS-21 available at a level of billions of doses in the future. In addition, we're able to make QS-21 without any geopolitical restriction. We can make it in the U.S., in Europe, or anywhere. That's something that we're bringing to the industry that wasn't available before.

Moving forward, I'm confident that coupling our proprietary raw materials and our proprietary purification system will allow us to solve the cost and scale issues and tell a true green story around QS-21. **CP**