Interview: Jose Escribano – Founder, ALGENEX, Spain



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Jose Escribano, founder of Spanish biotech success story ALGENEX, discusses the company's focus on using insects in its research, difficulties in accessing capital, and its future growth strategy.

Can you please start by describing the opportunities that presented themselves, allowing you to create ALGENEX?

The initial idea for ALGENEX was developed at a conference in Canada in the 1990s. Conversing with an American colleague in a Poxvirus meeting, we realised the huge potential for the use of living organisms in the production of recombinant proteins, and from that conversation, we began collaborating. Firstly, we started to develop vaccines in transgenic green plants, publishing several papers and generating a large amount of interest. Years later, a scientist, based out of the US, who was exploring the possibility of harnessing the baculovirus vectors to infect insects, subsequently contacted me. In the end, I agreed to exchange a proprietary baculovirus for some infected insects he obtained, with a view to gaining a better understanding of the potential that insects held. The results were overwhelming

Once I realised just how great this potential was, I made a clear decision to move away from plants and towards insects. However, I had no prior knowledge in this field, so I began collaborating with entomologists in my institution. During this period, I began to form agreements with various companies in a move towards working with this technology at a larger scale. Beforehand, we were using very primitive technology at laboratory scale, essentially breeding insects in plastic cages.

While we received a very positive response from key stakeholders in the industry who were fascinated by the concept, they all emphasised the need for industrialisation of the technology to progress any further. This was the point at which, jointly with my wife Covadonga Alonso, a scientist in the field of virology, we decided that we had to create our own company. This was breaking new ground for me since I had very little knowledge relating to business. However, we were able to secure appropriate funding and, from that point on, we underwent significant growth.

What challenges did you face in accessing capital during this initial phase?

In Spain, the first round of investment is in general relatively easy to access. That first round took place back in 2007. We received several competitive grants, government and bank loans, which allowed us to develop the business from scratch. However, the real bottleneck in Spain for biotech industries occur at the secondary rounds of investment that are often necessary to further mature a company. It is at this point that a certain risk-adversity often kicks in. That is precisely the reason why we have resorted to seeking investment outside of Spain. We have pursued opportunities in European countries like England, Belgium and in Italy to access capital through a variety of financial backers including family businesses, angel investors, institutional lenders and certain affluent individuals such as former-executives of pharmaceutical companies.

Why is attracting second-round funding so problematic in Spain?

I believe that there is a combination of factors that contribute to the complicated fund-raising environment in Spain. Primarily, there needs to be more success stories because currently there are only a few and the investment community tends to be overly cautious because of this. The point at which they prove to be willing to bet big on a venture is generally when the innovation has already demonstrated its worth and is firmly on the pathway to success.

Uncertainty in the life sciences domain tends to be amplified by the length of time associated with growing biotech companies. It takes a long period of time to deliver the first product to the market and there are also significant costs related to developing products associated with animal health and much more with human health.

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What is ALGENEX’s process to creating this innovative and speciality product?

Mother nature provides for the most sophisticated cellular systems. When we learn how to manipulate them, they can be used to our benefit to produce complex biological molecules. This is all about finding creative, cost-effective ways to produce these molecules, the proteins, which are

the basic biological bricks from which we obtain the medicines or vaccines that serve to treat diseases or prevent them. What we have done is to reconceptualize the recombinant protein manufacturing process by taking inspiration from nature and striving to harness organisms that evolved from millions of years of evolution. We firmly believe that this can be far more effective than resorting to costly and complex bioreactors needed to keep production cells alive to deliver the same products. In a nutshell, we sequester the organisms, insects, and put them at our service.

The process is very simple and logical. We develop special genetically modified viruses, the baculovirus vectors widely use for the industry to produce in insect cells growing in bioreactors. These vectors pose zero risks to humans and are used to introduce the genetic material that we want to reproduce into the caterpillar of the cabbage looper moth (*Trichoplusia ni*) and to infect it. The virus then hijacks the body of the host, essentially turning it into a protein factory. Instead of the organism replicating and transcribing its own DNA, the virus vector manipulates the biosynthetic machinery of the cells and producing the desired molecule.

The specific moment in the lifecycle of the insect that we choose to perform this action is the pupae stage of metamorphosis when it is transitioning from a worm into a butterfly. This means that we exploit that very special moment in the biology of transformation when the organism’s capacity to generate biological material is at its most intense and productive. The time of infection lasts between four and six days and in that time the caterpillar can produce up to 5 milligrams of the active principle, which is ordinarily enough for between 20 and 160 doses of a vaccine. To obtain it, with what remains of the chrysalises after the infection process, an extract is made and then purified to extract the active principle with the desired degree of purity.

What are the main characteristics of your patented technology CrisBio™?

We believe that we can break the technological barriers that restrict many companies in producing biologics and making viable products that must be commercialized at low prices, like many animal vaccines or human vaccines for developing countries. Today, protein subunits derived from pathogens represent the innovation focus of vaccines and diagnostic methods, yet in-vitro cultured productive cells normally require complex bioreactors that are out of reach for many businesses. Not only are these bioreactors technically complex to build, validate, maintain and operate, but they are also exorbitantly expensive to run, limited in scalability and ultimately inefficient. What we have come up with is a bioreactor-free production technology that has the potential to render recombinant proteins globally accessible.

Our technology avoids the use of bioreactors entirely and may produce any biotech recombinant product encoded by a genetically modified baculovirus vector (vaccines, therapeutic and diagnostic molecules). No biosafety measures are required. Our CrisBio® technology combines robotics, biomimicry, and patented biotechnologies to offer a completely new turnkey, modular and scalable platform that enables us to produce complex proteins in weeks. Moreover, compared to using bioreactors, CrisBio® delivers a 95% reduction in CAPEX and 20 times more productivity, along with unprecedented simplicity, safety, robustness, and efficiency. Our technology may produce almost any biotech protein-derived product.

If we can deliver on this ambition, we could soon see complex proteins not only being produced in mature, advanced, industrialised, affluent economic countries but also across the developing world. This would have a massive impact in treating infectious disease.

We hope to streamline the process through which vaccines are developed, with the aim to increase cost-effectiveness and simplification of the process. We have 200 different proteins successfully created from our platform so far and have experienced zero side effects in vaccinating animals with our vaccines.

What distinguishes ALGENEX from its competitors?

ALGENEX’s primary distinguishing factor is that we own a large amount of intellectual property. Secondly, we are using insect pupae instead of insect larvae. We have the robotization of the technology which has allowed us to increase the scale of our production. However, most significantly the utilisation of Top-Bac® technological platform, which consists in improved baculovirus vectors, has allowed us to become four times more productive than any competitor. We have licensed Top-Bac® to several companies as it is easy to integrate for companies still using bioreactors and insect cells.

Overall, I believe that we are years in advance of our competitors. We have put a lot of effort into scientific development. Top-Bac® took more than six years to develop. For more than 30 years both big and small companies were unable to increase the productivity of baculovirus vectors by more than 30-50 percent, where as at ALGENEX, we have increased productivity by 400 percent! We have constantly been refining the efficiency of our processes and are now close to reaching the market with our products. We have 12 patent families that cover various aspects of the business and have published more than 30 scientific papers related to our technologies. These are the best marketing tools that we have.

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What are the advantages and disadvantages of developing a biotech company in Madrid as opposed to Barcelona?

Competition in scientific and technology development among cities in the same country is a healthy exercise, unless other factors, such as political views, contaminate the game. Madrid's scientific environment is similar if not equal to Barcelona's and both contribute to around 60-70% of the total scientific knowledge generated in Spain. In addition, there are also a lot of research groups and facilities in Madrid which are essential to the development of these businesses, and investors are aware of this.

What milestones do you see ALGENEX achieving in coming years?

We hope to be able to gain the support of international and government organisations, particularly in assisting us in achieving our goals related to vaccines in humans. I would like the company to increase the standard of living in countries where people suffer terribly from preventable diseases, so we are currently in the process of submitting grant applications and exploring different opportunities. We aim to enter the first developments relating to the production of a human vaccine.

My intention for the future is to establish an ALGENEX office in the US precisely to be able to tap into this superior fund-raising ecosystem and extend our business there, due to the country being much more hospitable to life sciences start-ups

As a final statement to our international audience, what do you consider to be your greatest achievement so far?

From a personal point of view, having been an academic for 35 years, it was particularly interesting for me to interact with the industry. Overall, I am proud of the progress we have made in developing ALGENEX and the company's ability to survive the European financial crisis and continue to thrive. It is a great feeling to be on the cusp of a scientific breakthrough that is simultaneously simple and revolutionary, and which will have far-reaching effects on the world.

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