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*Phillipe Archinard CEO of Transgene shares insights on the latest technologies being developed by the gene therapy specialist, explains how France's innovation landscape is improving, and highlights the current opportunities in the market.*

**Could you give us a brief introduction to Transgene?**

Historically and from the very beginning, Transgene has been entirely focused around gene engineering. The Mérieux family acquired the company in the mid-90s and remains its controlling shareholder following its IPO. The 2000s were challenging for the tech industry and especially for the gene therapy area. At that time, a controversy on an unrelated clinical trial had a negative impact on the industry overall, resulting in a lack of financing from biotech investors.

The company thus moved from gene replacement towards gene immunization and reshuffled its portfolio. Transgene kept working on gene editing of its viral vectors for different purposes, focusing on active immunotherapy right before it became more popular. Our approach lies in the stimulation and education of the patient's immune system to fight against the disease. This can be applied to oncology and a selection of infectious diseases. We first faced notable scepticism that the stimulation of the immune system could help cure cancer and, while it is now admitted that the immune system plays a role in the control of tumour growth, Transgene had to deal with this scepticism, being one of the pioneers in the field. Today, Transgene runs on two legs – therapeutic

vaccines and oncolytic viruses. At Transgene, both technologies are being assessed through clinical trials and are also being pushed forward with next generations deemed to enter the clinic in the next 12-18 months.

**What makes Transgene’s products revolutionary?**

Transgene is setting a new standard of care with our therapeutic vaccines TG4010 and TG4001 and with our new generation of oncolytic virus. These molecules have shown promising preclinical data and have been quite successful in trials so far and are the ideal complement to the immune checkpoint inhibitors which are today the backbone of solid tumours treatment.

Nowadays, all our clinical trials are combination trials with other immunotherapies to further increase the potential of efficacy and better position our drugs in the oncology market. Even though there have been years of research and work behind immunotherapeutic approaches, we are still at the beginning for this class. We have two very ambitious programs, both being in clinical development, and with the next generation of therapeutic vaccines and oncolytic coming soon to clinics.

**How would you describe Transgene’s current product pipeline?**

Overall Transgene has five clinical-stage products. Most of the development aims at treating solid tumours. We also have one product in for the treatment of hepatitis B. Nevertheless, our major focus will be in oncology moving forward.

Recently, Transgene attended the AASLD conference in the United States where we presented the results of the large Phase I-B trial which had positive outcomes exhibiting safety and immunogenicity. Transgene also published data on preclinical combinations with the aim of finding a partner to move forward and combine different treatment modalities.

There have been treatments for diseases such as Hepatitis B and AIDS which help patients control the disease, but a cure has not been found. The goal is to find a cure for the patients in different chronic infectious diseases by helping them boost their immune system and allow it to fight the disease.

Regarding oncology, two vaccines and two oncolytic therapies are in clinical development. We currently run trials from Phase I and II to Phase III. Transgene is targeting large medical needs such

as lung, liver and HPV-positive head and neck cancers. We have made significant progress for which results will start showing in 2019.

**How does Transgene create partnerships within the industry?**

Transgene partners with pharmaceutical players for clinical collaboration like the one with Bristol-Myers Squibb (BMS) for TG4010 in advanced non-small cell lung cancer and the one with Merck and Pfizer for TG4001 in HPV-positive cancers. But we are also licensing rights to our products like the recent agreement with Tasly Biopharmaceutical in Greater China.

**Last September, Transgene launched the Invir.IO™ technology platform. What does this innovation mean for the field of immunotherapy?**

Invir.IO™, is a new technology platform dedicated to the design of a new generation of oncolytic viruses. The platform is based on our proprietary technology and will allow us to generate a variety of multifunctional immunotherapies aimed at modulating the tumour microenvironment.

Through the Invir.IO™ platform, Transgene is aiming to attack tumours on several fronts. Firstly, by improving the oncolytic (cancer cell destruction) factor to create a more potent therapeutic effect. When looking at the clinical data from the first generation of oncolytic products, this so-called “debulking” effect could be further improved. To accomplish this, we selected a more potent strain within the Vaccinia family of viruses and modified it in such a way that the oncolytic impact can be more substantial than in the first generation.

Next, we are focused on creating a safe and effective IV (intravenous) administration platform. For example, the first candidate of this new generation is in development and we have recently begun a clinical trial with IV administration for colorectal cancer patients.

Oncolytic viruses are optimized to selectively replicate in tumour cells and not in normal cells. They can infect virtually all cells but we deleted several genes that prevent their replication in normal cells while making it possible only in tumour cells. With this peculiarity, we can use viral replication in the tumour cells to locally express therapeutic payloads that can significantly amplify the anti-cancer effects of viral oncolysis. This method allows a better modulation of the tumour microenvironment and an increase in the immunocompetency of the tumour while at the same time reducing the systemic exposure to these molecules. We believe it is possible to dramatically

improve the therapeutic index of these molecules which are known to be extremely efficacious and extremely toxic when administered systemically.

The tumour microenvironment is a complex ecosystem. With oncolytic viruses, our objective is to bring a multifunctional approach to treatment. There are many different mechanisms and moving parts that if one target is hit, it is unlikely to alter the whole disease ecosystem. Thanks to their versatility, oncolytic viruses can, therefore, be very potent. Our Invir.IO™ platform will be revolutionary for tumours that resist currently available treatments.

**To what extent having this platform makes you a go-to partner of choice for pharma companies that want to enter this field?**

Compared to other companies, Transgene has a long experience in molecular biology and has been genetically modifying viruses for many years now. The majority of players in the oncolytic field come from academia and are typically only working on one specific virus. We, however, continuously test all viruses in our labs and have selected and engineered them based on research and cross-strain comparison. We are experts in this field with more than 15 years of experience, giving us a unique offering.

**What does the recently launched Myvac™ mean for the future of immunotherapy?**

Myvac™ is an individualized immunotherapy against solid tumours – the next generation of vaccine. With Myvac™, we aim to be pioneers in the field. It is also important to recognize that although there is an aim towards treating large populations, each patient’s cancer is unique. If Transgene is able to identify specific gene mutations of a given patient and predict properly the immunogenicity of these neoantigens, one could hope to build better vaccines by inducing an even stronger immune response against the tumour. With this novel approach, Transgene is using individualized data to formulate customized vaccines which are unique to patients. And we do so through a strong partnership with NEC.

**What are your thoughts on the impact of personalized medicine?**

Personalized medicine is one of the key priorities of the French government, and as such, the Myvac$^{TM}$ consortium is supported by Bpifrance. This support is revolutionizing the whole sector and

the manufacturing infrastructure as companies must adapt to smaller batch production. Timing is also a key consideration. The cycle time of constructing, producing, and quality control of the therapeutic vaccine needs to be reduced dramatically to provide patients with their treatment in less than four months. This requires innovation across the board. This is a very different way of thinking and it is important that regulatory agencies acknowledge it.

Personalized medicine is something that Transgene has acknowledged very early, which is why we have entered into a collaboration with NEC to clinically assess the predictive capabilities of artificial intelligence. Together we are taking advantage of the recent progress in AI and advances in genome sequencing to create an individualized immunotherapy treatment, which will target the unique characteristics of each patient's mutational landscape as well as their predicted immune responses. We aim to start two clinical trials by the end of 2019 both in Europe and in the USA. We are very proud to have the right network of partners and the right technology. The partnership has been very innovative and if the results of the project are successful, we look forward to the challenge of industrializing.

**How is Transgene managing its finances and how is the business environment in France helping businesses like Transgene raise financial support?**

Today, Transgene has about a year cash runway. The company just sold the Chinese right of two of our products so we have the equivalent of 48 million USD in Tasly Biopharmaceutical shares which will further extend Transgene's cash flow. The company is also looking at non-dilutive financing such as licensing deals.

It is clear that France is quite good at seeding startups compared to other parts of the world. There is a lot of money to be invested but as companies move forward into the growth stage, the funding gap becomes greater as more capital is needed for development. The more money startups need, the more difficult it becomes to get it – a problematic loop. There are very few significant VCs in France which work together, which limits the opportunities available. I believe there is a duty to foster a wider variety of approaches. All in all, there is substantial financing for seeding in France but for too few for scale up.

**A few words that you would like to send to our audience?**

I would like to invite stakeholders to pay more attention to the events taking place in Europe. There is a momentous innovation movement everywhere, here in France but also in China for instance. You do not have to go to the USA always to find ingenuity as some people mistakenly think. There are different ways in the world nowadays and we have to learn to look for them!

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