Interview: Jesús Martin-Garcia – Chairman & CEO, GeNeuro, Switzerland



"Our ambition is to create an Actelion-like company in our region."

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Jesús Martin-Garcia, Chairman and CEO of GeNeuro, discusses their positive partnership with Servier to develop an antibody against a possible cause of MS, as well as the reasons for choosing Geneva when working with multiple sclerosis.

Following 15 years of research performed by French-based Institut Mérieux and INSERM, GeNeuro was officially launched in 2006 in Geneva, Switzerland. Could you please maybe start by introducing the company's history and background?

The early 90s were marked by the discovery of new retroviruses such as AIDS and HTLVs. One of the areas of interest of this research at the time was autoimmune diseases, as many thought retroviruses could play a key role in these pathologies. But while there have been several epidemiological links between retroviruses and autoimmune diseases, none actually seem to drive the development of these pathologies.

Yet back in 1991, Hervé Perron, our CSO, discovered and published in the Lancet the discovery of virus-like proteins isolated from the cells of multiple sclerosis patients. These were virus-like proteins but not viruses, and the technology at the time did not allow to clearly classify them into any known category. This discovery could have been left aside if it had not been for the Mérieux family who funded, in partnership with INSERM, the 15 years of fundamental research that resulted

in a very comprehensive understanding of where these virus-like proteins were coming from and what their role in an autoimmune disease such as MS could be.

In short, the proteins that were first identified by Hervé Perron are encoded by viral genes in our own DNA. We know today that 8% of our DNA is made of such viral genes, which are remnants of viruses that contaminated our ancestors and made it to the human germ line. These viral genes are repressed in our DNA, but under certain circumstances they can encode for proteins, most notably when external viruses can replicate into a cell and bring with them viral gene promoters. The production of functional proteins from our viral genes remains a rare phenomenon, but it could start explaining the etiology of some poorly understood diseases, such as multiple sclerosis. We started GeNeuro in 2006 with the mission to develop safe and effective treatments against neurological disorders and autoimmune diseases, such as multiple sclerosis, by neutralizing causal factors encoded by viral genes in human DNA. Today, 10 years later, we are months away from reading the first results of our lead compound GNbAC1 in a double-blind Phase 2b study on 260 patients with remitting MS.

And how did you personally come about joining this exciting adventure?

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I am a Harvard MBA, McKinsey trained professional who decided to take the entrepreneurship path in the early 90s. Having had a few successes in the internet space, I was approached in the early 2000s by the academic and political authorities in our region to try to understand why we had so few biotech start-ups, despite the quality of the science in our institutes. I was attracted to the huge potential of this area to change people’s lives, and ended up creating both an incubator in Geneva—called Fondation Eclosion—in partnership with the State of Geneva and key academic institutions, to help scientists take discoveries from the bench to proof-of-principle, and a fund—called Eclosion2—with a group of investors, to be able to launch and support promising companies. This incubator-fund is a fantastic combination which has allowed the creation of over 20 companies.

I was looking for projects for Eclosion when I met Christophe Mérieux and Hervé Perron in 2004. I was impressed by the early scientific evidence they had developed. We decided to work together as we shared a passion for true scientific innovation and the same long-term view. From 2004 to 2006, the project was in the incubator, we decided to create the company in 2006, and I have led it to this day.

Could you please introduce this product to our international readership and tell us why it is pioneering in its segment?

GeNeuro is targeting a potential cause of MS, the protein MSRV-ENV, which is found on all the active lesions of MS patients. It has been shown to have both a pro-inflammatory action via interaction with the TLR4 receptor of innate immunity, as well as to stop the differentiation of oligodendrocyte precursor cells, which are responsible for remyelinating brain lesions. By neutralizing MSRV-ENV, GeNeuro's antibody GNbAC1 could block a key factor promoting the inflammation on the plaques, as well as allowing the remyelination repair process to restart.

This approach is radically new as today's main MS treatments act through modulating the response of the immune system of the patient to the disease. GeNeuro's lead antibody targets a potential cause of the disease, acting on both inflammation and remyelination, with the potential to slow down or stop the progression of all forms of MS. Because MSRV-ENV has no known physiological function, GNbAC1 is expected to have a good safety profile, without affecting the patient's immune system.

What are the ambitions and expectations for GNbAC1 in the short, middle and long term for MS?

Full enrollment of the 260-patient CHANGE-MS Phase 2b study of GNbAC1 in remitting relapsing multiple sclerosis (RRMS) was completed at the end of 2016, several months ahead of schedule, and is indicative of strong interest from physicians in this pioneering new treatment for MS. Based on this accelerated timeline, GeNeuro now expects the availability of top-line results from the first 6 months of the study early in the fourth quarter of 2017, versus the previous estimate by year-end 2017. This double-blind, placebo-controlled study is evaluating the efficacy of GNbAC1 in reducing the number of new inflammatory lesions as well as measures of neurodegeneration on brain MRI in patients with RRMS. The CHANGE-MS Phase 2b study is fully funded through GeNeuro's €362.5 million partnership with Servier, which was signed in 2014. The full one-year results for CHANGE-MS will be available in 2Q2018, and will open the way for Phase 3 trials, possibly in different MS indications in parallel as the target MSRV-ENV is present in the brains of patients affected by all types of MS.

Recently, we have also announced that our partner, Servier, has agreed to fund a new trial, called ANGEL-MS, that will propose two more years of treatment to all patients that will complete the ongoing Phase 2b. This trial will give patients an opportunity to continue their treatment, and provide long-term data on GNbAC1, particularly on its tolerance, the durability of its effect and the

patients' quality of life. This study is expected to last two years and will start in April 2017, once the first patient included in the CHANGE-MS trial will have completed the 12-month study.

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The partnership with Servier has demonstrated to be a great strategic asset for GeNeuro.

Servier is a long-term focused organization, offering true scientific excellence, and providing real hands-on support when it is needed. Yet Servier is able to trust a much smaller organization in key decisions, and the governance systems we have in place are very effective. At the end of Phase 2b in mid-2018, our agreement provides Servier an option to license GNbAC1 for MS worldwide, except for the US and Japan, where GeNeuro retains full commercial rights. We look forward to developing GNbAC1 in MS together with Servier.

Which other indications is GeNeuro focusing on and what progress has been made?

Beyond MS, GeNeuro has established relationships with third-party research groups studying the MSRV-ENV protein and other HERV proteins in different diseases. GeNeuro and third-party research groups have substantiated the presence of the toxic MSRV-Env protein in other organs affected by poorly understood diseases, such as in the pancreas of Type 1 diabetes (T1D) patients and in the peripheral nerves in chronic inflammatory demyelinating polyneuropathy (CIDP), an orphan neurological disease also called "peripheral MS". GeNeuro is preparing a Phase 2a proof-of-concept trial focusing on T1D patients that will start in the first half of 2017.

The understanding of the biology of the viral genes in our genome and of the proteins they encode for is only at the beginning. The potential of this area to shed light on some poorly understood diseases is enormous, and GeNeuro is the clear pioneer to transform this new knowledge into effective treatments in areas of huge medical need.

Beyond the programs described above, GeNeuro has preclinical initiatives against amyotrophic lateral sclerosis and against inflammatory psychosis. GeNeuro remains focused on exploiting the full potential of this biology for all its stakeholders.

How would you assess the operating environment for biotech companies in Switzerland and what would you say are the strengths and weaknesses of this environment?

Switzerland has a long standing tradition of excellence in scientific research. Its top Academic Institutes are largely recognized in international rankings. They produce top level science and educate top-level students coming from Switzerland and from all over the world, which helps us

recruit people or have access to experts of very high caliber.

Geneva is actually a key city for the treatment of multiple sclerosis, having been the birthplace of two of the early pioneers in MS treatment, Biogen and Serono. While these companies are no longer in Geneva for different reasons, the expertise and many of the people that allowed the development of these companies are still here, and it is a fantastic pool of talent to recruit managers with a great experience in multiple sclerosis. Geneva is also very well located. There is an international airport that can take you anywhere and daily travel is easy.

The downside of being in Switzerland is the relatively high cost of doing business, especially due to the strength of the Swiss Franc. But it is in my view compensated by the excellent quality of life to attract and retain talent, the outstanding work ethics and the reasonable corporate tax rates, that should become even more attractive if the upcoming fiscal reform is accepted by the Swiss voters this year.

Also, in Switzerland as in the rest of Europe, there is still a very timid approach to innovation and risk in general. Our venture capital and public stock markets lack the critical mass achieved by the USA, where the ecosystem funding innovation is particularly efficient. This explains why, in my view, only American start-ups grow into the list of the top companies in the world.

In April 2016, GeNeuro decided to launch an IPO. Could you please share with us the result and assess whether or not the IPO was successful?

The IPO was successful as we were able to raise €33 million in April 2016, which was the amount we were seeking, in an extremely complicated market context. As the Phase 2b in MS was already funded through our partnership with Servier, these funds have been dedicated to prepare for the start of our clinical operations in the US, and to develop new clinical and preclinical programs beyond MS. We want to make sure that by the time we bring the proof of the relevance of this new biology in MS, we will have developed other programs to capture the full value of this technology for patients and all our stakeholders.

Obviously, the IPO was not made at a very supportive timing in terms of the general environment for biotech, and it has had some repercussions on the share price fluctuation, which we cannot control. The only way we can deliver long term value to our shareholders is by succeeding in executing the plan we have set and, thus far, we have hit all the major milestones.

> “Success for a small company is about developing the right partnerships, such as the one we have with Servier, creating different development options, and executing

them.”

What is your overall “grand plan” for GeNeuro, and what can we expect for the future?

As a first step, by 2018, we will have completed Phase 2b in RRMS, a Phase 2a in Type 1 Diabetes, and will have new assets ready to drive to the clinic in other indications. GeNeuro will have all options open, for example for partnering US rights in MS, or new products in other indications. Success for a small company is about developing the right partnerships, such as the one we have with Servier, creating different development options, and executing them.

I have a lot of respect for Jean-Paul Clozel (CEO of Actelion) and what he and his team have accomplished in developing one of the few highly successful independent European biotechs. Our ambition is to create an Actelion-like company in our region.

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