Stephen Farr â?? President & CEO, Zogenix

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Zogenixâ??s Dr Stephen Farr shares his remarkable career journey from academia to industry, the companyâ??s transition from pain therapeutics into rare diseases, product launch strategies, access and affordability issues, and talent attraction challenges.

Steve, could you start by sharing some career highlights? What brought you from being a professor in Wales to the CEO of a biopharmaceutical company based in the US?

I am a pharmacist by training with a PhD in pharmaceutical chemistry. After getting my PhD, I intended to re-enter industry but received the rare opportunity to extend my academic career through a professorship at the university where I was in Cardiff. I really enjoyed my years in academia. I taught undergraduates and was engaged in a lot in research. During that time, I also consulted for the pharma industry so always kept an interest in the industry.

During a sabbatical year from my academic position, I joined a very small start-up in the San Francisco Bay Area that was looking to develop an inhaled insulin for the treatment of diabetes. Inhalation drug delivery was one of my areas of expertise, so it was a great opportunity for me to contribute to the early stages of a company and learn about setting up a biopharma company.

During this time, the companyâ??s CEO made me an offer to stay. It was one of the toughest decisions Iâ??ve made in my career: leaving a tenured position in academia to move to the US to join a start-up with three monthsâ?? worth of money in the bank, with my young family in tow.

In retrospect I am thrilled I made that decision. While it is true you can make great contributions in academia, I think you can make an even bigger contribution in industry because you are closer to the end user, the patient. There is also more opportunity to seek investment to fund your ideas. Private as well as public markets are always open to good ideas.

I have now spent more than 25 years in the US with various companies, most recently at Zogenix, which I co-founded in 2006 with then-CEO Roger Hawley.

You assumed the CEO position in 2015. What have the milestones been for Zogenix in the past five years?

Prior to 2015, we were a commercial company in pain therapeutics. In 2015, Roger and I decided that, as a small company, we could contribute more meaningfully in the rare disease space After Roger decided to step down, I transitioned from president and COO to become CEO, and have been leading our rare disease strategy ever since.

We were very fortunate because the first rare disease asset we acquired generated truly remarkable Phase 3 data for the treatment seizures associated with Dravet syndrome, and in June 2020, our first product, FINTEPLAÂ®, was approved by the US FDA. This allowed us to build and grow Zogenix into a rare disease company with a commercial asset and a healthy pipeline.

Dravet syndrome is an infant- and childhood-onset paediatric epilepsy that is highly refractory and very difficult to treat. Patients suffer from numerous convulsive seizures every month, and, due to the frequency and length of these seizures, the condition is associated with quite devastating long-term outcomes that include cognition deficits and impaired motor ability. It is not uncommon to see children with Dravet syndrome lose the ability to walk unassisted as they enter adolescence. Dravet syndrome is also associated with a high mortality rate of 15-20 percent through childhood.

Many Dravet syndrome patients, despite taking multiple antiepileptic drugs daily, continue to suffer from convulsive seizures. We brought patients into our FINTEPLAÂ® trial who were experiencing an average of 40 convulsive seizures per month even on their existing treatments and saw a dramatic reduction in the number of convulsive seizures relative to placebo added to their existing standard of care. This seizure reduction continued in our open label, long-term studies, so many patients are experiencing long-term improvements in seizure reduction, which research increasingly links to long-term improvement in cognition and motor ability.

In Europe, we recently received a positive opinion for FINTEPLAÂ® in Dravet syndrome from the European Medicine Agencyâ??s Committee for Medical Products for Human Use (CHMP). If that positive opinion is accepted by the European Medicines Agency (EMA), they could issue final approval there by the end of 2020 or early 2021.

With the transition from pain therapeutics to rare diseases, how did you restructure the company?

From an R&D perspective, I donâ??t see a huge number of differences between developing drugs for large patient communities versus small patient communities. It is all hard work. Of course, we had to bring in experts in CNS drug development, which was critical.

But the commercial preparation was completely different. The size of the CNS team needed was different, and there continues to be a lot more collaboration with rare disease patient communities. This involved building relationships with patient advocacy groups to understand their unmet needs and to clarify how we might best help and support them and be a true partner to them.

How were the commercial preparations for the launch of FINTEPLAÂ® considering the external COVID-19 climate?

With COVID-19, we could see FINTEPLAÂ® would launch into a completely different environment. A priority during our initial launch in the US was creating new digital tools to effectively educate physicians about the disease and product in a virtual environment. Weâ??ve had good success but of course miss the person-to-person connections when explaining the merits of a new drug to healthcare professionals. Similarly, with medical conferences currently all being held virtually, we miss the interactions that happen outside the formal agenda during in-person conferences.

Because FINTEPLAÂ® was launched in the US through a restricted distribution program called the FINTEPLAÂ® Risk Evaluation and Mitigation Strategy (REMS) program, we built a comprehensive program called Zogenix Centralâ?¢ to help certify doctors to prescribe FINTEPLAÂ® and provide support services to patients and their families from start of therapy through long-term treatment. Our digital tools have been essential to this and to our work to achieve reimbursement coverage here.

US biopharmaceutical companies often struggle with the decision to launch their products abroad themselves or through partners. What is Zogenixâ??s global commercial strategy?

Although we received FDA approval first, we were never going to be just US-centric in our approach. We want FINTEPLAÂ® to reach as many patients with Dravet syndrome globally as possible.

Because the prescribing physician community is relatively small and typically concentrated in key academic institutions and medical centres in both the EU and the US, we feel we are best suited to bring FINTEPLAÂ® to these markets.

The potential for FINTEPLAÂ® as a treatment for severe, rare epilepsies was discovered by two paediatric epileptologists in Belgium, so I have always felt a deep conviction to make it available in Europe as quickly after approval there as possible.

Early on, we established Zogenix European headquarters in Maidenhead, UK, and now have around 20 employees there. We have also opened country offices in Germany, Italy and Ireland, the last of which is helping us with our Brexit strategy. If approved in Europe, we expect to launch FINTEPLAÂ® in Germany as early as Q1 2021 and are excited to have already hired a country manager, medical director, and our first salesperson there. Our launches of FINTEPLAÂ® in other European markets will follow later.

In Japan, where we recently concluded a Phase 3 trial and expect to file an NDA in in Q3 2021, our commercial strategy is to partner with Nippon Shinyaku, with whom we signed an exclusive distribution deal in 2019.

In the rest of the world, we expect to work through distribution partners and are exploring options in other countries now.

Access and affordability are key topics in the US market as well as globally. Rare disease therapies, in particular, tend to be rather pricey, though they of course deliver great value to patients. How do you see this balance?

FINTEPLAÂ® offers remarkable efficacy to patients *and* the potential for significant healthcare savings to the system.

FINTEPLA is dosed on weight and effective dose and has a maximum dose limit regardless of the patientâ??s weight. In the US, based on the trends of dosing and weight of potential patients in our clinical studies, we estimate the average annual price to be around USD 96,000. Through numerous discussions with commercial, federal and state payers, we have seen an acknowledgment of the value that FINTEPLA brings to the Dravet patient community, and the recognition that we are talking about a rare disease with an extremely small patient community. The overall cost to any individual plan is relatively small but the drug delivers immense benefit to patients.

In Europe, while awaiting approval, we are conducting outcomes research now to put forth the appropriate value proposition to the authorities in each country there.

In addition to the medical value, I think the price also needs to reflect the value of all the work undertaken to bring this drug to market and the drugâ??s value to patient communities. Based on efficacy and safety profiles for FINTEPLAÂ®, we anticipate it could become a new standard of care for Dravet syndrome. It is not a conventional anti-epileptic drug and especially serves patients who do not respond to multiple antiepileptic drugs and lack other treatment options.

With one commercial asset on the market, what can we expect from Zogenixâ??s R&D pipeline?

Our vision has always been to become a leading rare disease company. With the success of FINTEPLAÂ® in Dravet syndrome, we will continue to explore its potential in other childhood-onset epilepsies. We have already established safety and efficacy in a pivotal Phase 3 trial in Lennox-Gastaut Syndrome (LGS), and hope to move ahead with a supplemental NDA in the US and a Type II variation marketing authorization application (MAA) in Europe to expand the label to include LGS.

COVID-19 delayed start of a new Phase 2 signal-seeking study for FINTEPLAÂ® in several other rare epilepsies earlier this year, but we hope to get that up and running in 2021.

Separately, we are developing a novel investigational deoxynucleoside substrate enhancement therapy for the treatment of a devastating genetic disease called Thymidine Kinase 2 deficiency (TK2d), an ultrarare mitochondrial DNA depletion disorder that causes rapidly progressive muscle weakening. This is an asset Zogenix acquired in 2019 through the acquisition of Modis Therapeutics.

The prognosis for TK2 deficiency â?? for which no approved treatment options currently exist â?? is extremely poor. Many patients die before they are formally diagnosed, due to a lack of awareness of this disease. Our goal is to increase disease awareness, help improve diagnosis, and hopefully launch MT1621, which has shown a transformative impact for study patients in terms of improving survival and, in some cases, regaining lost motor functions. We hope to conclude our development program by end of 2021 and file new drug applications in the US and Eurpe in 2022.

Zogenix is not a discovery company, so we also have a strong business development team looking for other assets to continue building our pipeline.

Being based in one of the most competitive biopharma ecosystems in California, how do you ensure you attract the best talents to Zogenix?

Many employees join Zogenix from highly successful and far larger companies, even though we are a much smaller company with a higher risk profile. Often they are attracted by the opportunity to do a lot more in their roles at Zogenix than they could in these larger organizations, where employees are hired for a specific position and are typically expected to only do that on a day-to-day basis.

Our employees also have the opportunity to know and present ideas to Zogenixâ??s executive team. In their previous companies, they often didnâ??t have the ability to interact so closely with the C-level executives.

What is most important, however, is our shared compassion for and desire to connect with the rare disease patients, families, and network, a culture we strongly foster at Zogenix. For instance, nearly half of our employees attended the American Epilepsy Conference at the end of 2019. We think it is very important that our employees understand as much as possible about the rare diseases we are working to treat, know the needs and concerns of the people treating and living with these diseases, and appreciate the patientâ??s journey within this space. We feel strongly that our passion to work together to take on the complex challenges of developing and commercializing new rare disease therapies lies at the heart of our ability to attract the best talent to Zogenix.

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