Interview: Ko-Chung Lin PhD – Founder & CEO, PharmaEssentia, Taiwan

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Ko-Chung Lin, founder and CEO of PharmaEssentia, documents the main specificities of the company's groundbreaking ropeginterferon alfa-2b, a once-every-two-week interferon displaying a unique toxicity profile. In this regard, Mr. Lin also provides insights into PharmaEssentia's approach to the upcoming launch of this product into the US market as well as his vision for the international development of the company, which already stands as one of the most advanced and ambitious biopharmaceutical companies headquartered in Taiwan.

On December 5th 2016, PharmaEssentia announced eye-catching phase III results for its Ropeginterferon Alfa-2b in Polycythemia Vera (PV) at the American Society of Hematology (ASH)'s Annual Meeting 2016. Why do these results stand as great news for patients?

PharmaEssentia is on the verge of bringing what we believe is a significant, safe, and efficacious new therapy to patients with Polycythemia Vera (PV).

Patients with Polycythemia Vera (PV), a myeloproliferative neoplasm (MPN) characterized by an increase in red blood cells, have heightened risks of hemorrhage and thrombosis as well as of long-term development of mylefibrosis (MF), acute myeloid leukemia (AML), and chronic myeloid leukemia (CML). PV has unfortunately been a devastating disease for more than 25 years, while prevalence in the US (57 per 100,000) is higher than for any other MPNs and appears to be

increasing. When the disease leads to the development of AML, patients' life expectancy unfortunately does not exceed five years. Nevertheless, by treating patients early, we could prevent the disease from evolving into such dramatic conditions, while improving patients' quality of life overall.

In the absence of any FDA-approved first-line therapy, treatments like hydroxyurea (HU) have been used around the world for almost 30 years in PV. This unsatisfactory therapeutic option primarily focuses on avoiding cardiovascular complications and reducing disease symptoms (headaches, sweating, blurred vision, dizziness itching, and fatigue) – but does not prevent the development of cancer.

In this regard, the clinical results you mentioned indisputably mark a significant milestone in medical history. Our licensing partner, Austria-based AOP Pharma, conducted the randomized, open-label, multicenter, controlled, parallel arm study involving 254 PV patients from 48 centers across Europe – treated either once every two weeks with our ropeginterferon alfa-2b or daily with HU.

Our ropeginterferon alfa-2b showed non-inferiority to HU in Complete Hematologic Response (CHR) and demonstrated a significantly better safety and tolerability profile than HU. Most importantly, throughout the phase III program, five related secondary malignancies were observed, all in the HU cohort (two acute leukemias, two basal carcinomas and one melanoma). None of the patients treated with our ropeginterferon alfa-2b has contracted any malignancies, while some of our first patients have been under treatment for more than five years now.

Some of your competitors' interferons alfa have already been approved for the treatment of chronic hepatitis C, chronic hepatitis B, CML, MM, among many others… What sets PharmaEssentia's ropeginterferon alfa-2b apart from the products already available in the market?

Tolerability, safety, and a significant improvement in dosing schedule, which we believe will have a hugely positive impact on patients' lives. This is truly a new and best-in-class interferon.

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As you know, interferons are signaling proteins made and released by host cells in response to the presence of viruses, bacteria, parasites and tumor cells and that cause cells to heighten their anti-viral defenses. Currently, there are three main interferons alpha on the market. The first type encompasses what is called "conventional interferons", which are very similar to natural

interferons present in the human body. Although conventional interferons require injections once every two days and display terrible side effects (flu symptoms and depression have been scientifically reported), they are particularly cheap and remain largely used in some developing countries, such as China. The two other interferons alpha on the market are Merck's PEG-Intron® and Roche's Pegasys®, which both are once-a–week injectable products. Since their entry into the market, these two products have indeed been widely used – notably for hepatitis C, although they still present the side effects commonly associated with interferons alpha, such as flue symptoms and depressions, prompting Gilead Sciences to describe interferons as treatments that " make patients feel sick" when they released their competing hepatitis C treatment Sovaldi®.

In 2009, we started developing our own interferon, deeply convinced that we could bring onto the market a better product than these already available. In 2012, Novartis also stopped the hepatitis C race as U.S. regulators put a hold on their clinical trial for their compound developed in combination with a pegylated interferon, after cases of pancreatitis were reported in the trial and one patient died. At this time, most pharmaceutical companies seemed to consider it was impossible to further improve interferons. We however conducted our phase I clinical study in Montreal, Canada and its results quickly confirmed that our product could display outcomes that the industry as a whole has considered unreachable for an interferon.

Eight years after we initiated the development of our ropeginterferon alfa-2b, we are now confident we hold a product that surpasses all other treatments in the market. First, we have managed to develop a once-every-two-week injectable product, which makes our treatment indisputably more convenient than its aforementioned competitors that all require once-a-week injections. Second, as a result of our product's pure composition, we now have proven evidence of its greatly improved side effect profile – and this stands as great news for patients around the world and their relatives. Looking specifically at psychiatric issues, slightly over one percent of the patients involved in our treatment's clinical arm have displayed psychiatric side effects, while this percentage goes up to over 20 percent when treated with HU and around 30 percent for patients treated with Roche's Pegasys®, for example. We are pleased to announce that our clinical trials displayed similar positive results for all side affects commonly associated with interferons, while our product's efficacy is at least equal to Roche's and Merck's products.

Overall, our ropeginterferon alfa-2b proudly stands as an exceptionally active and manageable drug, which eliminates resistance issues while displaying a unique and improved toxicity profile.

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As part of PharmaEssentia's licensing agreement with AOP Pharma, you notably retained the rights of your interferon in PV for the US, Japanese, Korean, Chinese, and South American markets. Although you definitely hold a game-changing product, you also stand as one of the very first Taiwan-based, R&D-driven companies to develop its own marketing and sales capacity in the US. How are you positioning the company to make a success of this critical next step?

Although we are indeed headquartered in Taiwan, our company's philosophy, whether in terms of drug development or marketing approach, is similar to the philosophies of the most innovative biotech companies in Boston or San Francisco. As a matter of fact, our recently appointed CMO, Albert Xiao Qin, PharmaEssentia's General Manager, Jack Hwang, and I have decades of experience in these two innovative hotspots for biotech, and we have worked for some of the most prestigious biopharmaceutical companies for most of our careers. Moreover, our senior management team was educated in the United States at some of the most prestigious universities, including Harvard University, University of Michigan, and University of Pennsylvania.

I decided to set up the company in Taiwan and not in the US because Taiwan probably stands as the best country in the world to raise funding for biotech companies, which – according to our very successful and recent IPO – has proven being particularly true for us too. With a market capitalization of over one billion US dollars, PharmaEssentia belongs to the top half of biotech companies globally.

Bringing our products onto international markets has been integrated into the core of our overall strategy from day 1. This is notably why we conducted our phase I clinical trial in PV in Canada and established US FDA approval as the primary objective of our product's development. Furthermore, the results of the phase III study conducted in Europe by AOP Pharma, a company that holds a deep expertise in the MPN area, can now be used for our FDA's submission without having to repeat any clinical trial in the US. As part of our licensing agreement, we in turn agreed to take care of the trials for hepatitis C in Asia, a continent that makes up 75 percent of hepatitis C patients.

We are currently expanding our footprint in Boston, MA, where our American office already gathers ten of PharmaEssentia's 160 employees. This US branch will be in charge of coordinating the pre-launch activities of our ropeginterferon alfa 2-b, and, more importantly, of submitting our FDA NDA within the next three months, while, in February 2017, AOP Pharma already submitted a EMA's MAA which would take around three weeks to be completed. Given that our product was granted an orphan drug designation, we can expect to receive FDA market approval within less than 12

months and potentially launch our product in the US during the first quarter of 2018.

Considering the substantial size of the PV patient population in the US [about 150.000 PV patients according the literature], your product undeniably holds a great market potential. In the meantime, does that mean that your company will have to implement a strong commercial footprint to make a success of this product's launch?

Nowadays, being able to reach out to KOLs stands as the most important aspect of the launch of any innovative products. In this regard, we have been nurturing a particularly interesting relationship with first-tier medical doctors in the US, as proven by our successful attendance of ASH's annual meeting a few months ago.

Furthermore, Roche recently announced it would conclude two PV studies (MPD-RC 112 and MPD-RC 111) by June 2017, leaving a number of patients enrolled in these studies without the guarantee of getting the Pegasys® that they were graciously receiving. Given the urgency of the situation, we announced at ASH that PharmaEssentia was ready to take over these two trials, which were then renamed the RESCUE trial, enrolling 47 sites overall, one-third in Europe and the rest in the US, and encompassing some of the country's most prestigious hospitals, such as Cornell University Hospital, the John Hopkins Hospital, University of Michigan's Hospital, and Stanford medical Center, among many others. This trial demonstrates our continued commitment to the MPN patient community, while the eagerness of the medical doctors attending ASH to provide their patients with our ropeginterferon alfa-2b clearly stands as a great evidence of the quality and attractiveness of its main specificities.

We are operating in a very focused therapeutic area, where the number of medical specialists is particularly limited. In this regard, we do not have to build a Big Pharma-like commercial capacity to ensure our product gets the recognition it deserves. More importantly, there is absolutely no other treatment on the market or about to reach the market that displays similar outcome – and this competitive advantage has undoubtedly drawn the attention of the medical community.

In the meantime, we are setting up our Japanese operations: as from March, 1st 2017, PharmaEssentia's Japanese subsidiary will handle the development of the clinical trials to be conducted in this country as well as implement our marketing strategy in that country.

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We understand the main asset of PharmaEssentia is its technology platform, Pegylation, which is designed to increase the protein drug's efficacy by prolonging its circulation in the bloodstream. Considering your recent success with ropeginterferon alfa-2b, what are the new products that will soon enrich your R&D pipeline?

Our newly appointed CMO Albert Xiao Qin, holds a PhD degree from Harvard and has worked for a long time at Biogen, where he was bringing to the American company his unrivalled expertise in the interferon field. His eagerness to join our company undeniably stands as a great achievement, for two main reasons: first, it proves to our shareholders that we are continuously strengthening our company's talent pool in the interferon field. Second, his appointment demonstrates PharmaEssentia has now reached a development stage where it can attract some of the best scientists globally in our field of focus. As a matter of fact, we expect our company to grow from 150 to over 200 employees before the end of 2017. Interestingly, it will bring PharmaEssentia to the size of Biogen when I joined this company at the end of the 1980s. When considering Biogen has now established itself as one of the largest and most reputed pharmaceutical companies in the world, it strengthens my belief that we can also follow this successful path– if we do everything right.

In this endeavor, our first objective will be to maximize the value of our lead compound. Our IPO allowed us to raise over USD135 million and we plan to use half of this money to move forward our three on-going phase III trials in Hepatitis C, while the phase II data we got were absolutely mind-blowing.

In the meantime, we want to expand our presence in other important MPN areas. We will for example become the main sponsor of a global phase III clinical trial in Essential Thrombocythemia (ET) conducted in the US, Japan, Taiwan, and Europe and set to start by the second half of 2017.

The second aspect of our R&D approach relates to cancer treatments. Interferons mainly stopped being used as cancer treatments because of their dramatic side effects, which did not fit within the global ambition of the research community to turn cancer into a chronic, manageable disease. Furthermore, limited dosage forms of current interferons also prevented these treatments from becoming first-choice options in oncology.

Once again, Albert Xiao Qin, our CMO, is one of the world's experts in the interferon field, and we now deeply believe that we can leverage both his expertise and the quality of our product and technology platforms to open a new era of cancer treatment for interferon products. In this regard, we want to develop longer-actin protein drugs, with the objective to decrease to the minimum the

number of injections needed over the course of a year.

Finally, we are also working on immuno-oncology products, such as our lead compound PD-1. In this field, we indisputably lag far behind the most advanced Big Pharm companies; nevertheless, our main objective is to develop products that could be used in combination with our interferon, in light with our great ambitions in the oncology field.

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What is the vision for the future development of PharmaEssentia?

Within the next decade, our objective is to generate revenues of between USD 5 and USD 10 billion and establish PharmaEssentia as one of top 50 biopharmaceutical companies in the world. With the great support of Taiwan’s government, the scientific capacity of our team as well as our robust and ambitious strategy, we definitely hold the means to reach this objective and become one of the very first, R&D driven, Taiwan-based success stories internationally. PharmaEssentia truly stands as a company which cares about patients’ quality of life, and we will continue to gather the best scientists in the world to develop ground-breaking, highly needed products, with the objective to maximize drugs’ efficacy while eliminating side effects for the benefit of patients and their families.

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