Interview: Yita Lee Ph.D â?? Deputy Chairman, Sinphar Group; Muh-Hwan Su Ph.D. â?? Chief Technology Officer, Sinphar Group & General Manager, SynCore Bio, Taiwan

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15.02.2017

Tags:

Taiwan, Sinphar Group, SynCore Bio, Pharma, Biotech, Generics, R&D, Innovation, Manufacturing

Yita Lee & Muh-Hwan Su of Sinphar Group & SynCore Bio describe the exciting R&D projects of SynCore Bio, the oncology & dry AMD focused innovation-driven company of the group, and the advantages of SynCore Bioâ??s integration within Sinphar Group.

As an introduction to our international readers, could you provide us with an overview of Sinphar Group and explain its positioning within the Taiwanese pharmaceutical landscape?

Yita Lee (YL): Sinphar Pharmaceutical was founded in 1977 by my father, Tim Lee, the current Chairman of the Sinphar Group. As a result, Sinphar proudly stands as a historical contributor to the improvement of Taiwanâ??s health ecosystem. Over the past decades, Sinphar Pharmaceutical has moreover been successfully expanding its presence in Taiwan to become a top 10 domestic pharmaceutical company thanks to the development of a comprehensive portfolio of high-quality, affordable medicines. In the meantime, the Sinphar Group has truly established itself as the partner of choice of international companies for a range of crucial services spanning from contract manufacturing to product development, while the opening of our groupâ??s subsidiaries in China and North America further accelerated Sinpharâ??s international expansion.

Although Sinphar has been historically focused on generics, our Chairman has been steadily steering the direction of our group toward a more R&D-driven approach for already two decades. Actually, Sinpharâ??s first step into the R&D field was related to the development of innovative botanical drugs, which are extremely popular in China and also increasingly considered for the treatment of diseases in Western countries. In the objective to bring our R&D team closer to our botanical drugsâ?? raw materials (i.e. Chinese herbs), we set up in 2001 a new subsidiary in Hangzhou, China, called Sinphar Tian-Li. This R&D-driven subsidiary is mainly focused on the development of products based on extracts of *Cistanche tubulosa*, a holoparasitic desert plant that obtains nutrients and water from host plants that its roots parasitize, while it has been traditionally used for medicines in China. A few years after having set up our R&D footprint in China, we opened a cGMP manufacturing plant in Western China to produce our botanical new drugs, transforming Sinphar Tian-Li into a fully vertically integrated company. Leveraging this R&D experience honed with the development of new botanical drugs, we then moved to the NCE field and set up SynCore Bio in 2008, which now stands as the R&D-driven entity of the Sinphar Group.

Sinpharâ??s overarching objective is to find cure and prevent diseases affecting Asian countriesâ?? aging population, such as cancer, vascular dementia (a disease which can notably be treated with products based on extracts from *Cistanche tubulosa*), and immune disorders â?? among many others.

Considering you have been building such a strong reputation in the generics (generics drugs) field, what prompted the Sinphar Group to move into the new drug development area?

YL: Our Chairman, Mr. Tim Lee, deeply believes our country can bring a new, innovative drug onto the global market. In Taiwan, most of our scientists have studied and/or worked abroad, usually among the most prominent North American universities and pharmaceutical companies. After all, if these scientists were perfectly able to develop new drugs in the US, they should be able to do it in Taiwan too â?? as long as we provide them with the means to reach this crucial objective. Leveraging the expertise acquired by these industry leaders and scientists over the course of their international careers, Taiwan now definitely can join other advanced pharmaceutical hubs in the global competition for the development of game-changing treatments.

Initially, Sinpharâ??s strategy was to remain focused on the development of innovative botanical products, in which we have already been quite successful. As a matter of fact, we are currently pursuing two new clinical trials in chronic stable angina for a new green tea extract which should soon further enrich our innovative botanical product portfolio. Nevertheless, when Taiwanâ??s National Healthcare Research Institution (NHRI) contacted us in 2007 and offered to jointly set up an innovative company that would then become SynCore Bio, it truly stood as an opportunity we could not refuse. From a legal perspective, the NHRI cannot fund a spin-off company by itself. As a result, they were looking for a private partner that would handle the clinical and commercial development of their early-phase projects, while on the other hand this partnership provides us with access to innovative compounds developed by one of the most prestigious research institutions in Taiwan.

Muh-Hwan Su (M-H.S): This partnership undoubtedly stands as a great asset for the future development of our company. While the NHRI takes care of the pre-clinical development of our products, we nonetheless keep the opportunity to jointly design their Chemistry, manufacturing, and control (CMC) and pre-clinical guidelines, which are absolutely critical when it comes to receive IND (from US FDA) and CTA (from EMA) for their clinical development.

How does the licensing of VeregenÂ®, an innovative topical ointment for the treatment of external genital and perianal warts developed by Medigene, a Munich-based biopharmaceutical company, fit within SynCore Bioâ??s R&D strategy?

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YL: Medigene heard about our expertise in botanical drug development and considered there would be a natural fit with this productâ??s positioning, as VeregenÂ® contains a concentrate of catechins with a complex defined composition extracted from green tea leaves. At this time, we had already brought a first botanical product to the Chinese market and were looking at entering the US and European markets with our *Cistanche tubulosa* product. In this regard, we identified that partnering with Medigene to bring VeregenÂ® (which was not yet marketed in Taiwan) to our domestic market would stand as a great opportunity to further develop our regulatory, marketing, and sales expertise, while learning from Medigeneâ??s expertise in the meantime.

Initially, we decided to exclusively acquire the commercial rights of this product for the Taiwanese market, the country where we naturally hold the largest understanding of the regulatory ecosystem. After having successfully brought this product to Taiwan in 2013, we decided to fully leverage the experience we gained with this first achievement and negotiated the acquisition of the Asian rights of VeregenÂ® â?? to the exception of China and South Korea. We now plan to enter new Asian markets over the upcoming years, while VeregenÂ®â??s sales in Taiwan have been significantly growing over the last three years.

Nevertheless, one of the challenges we have been facing in our regional strategy relates to the reimbursement price of this product. VeregenÂ® is a revolutionary product developed by one of the leading European biotech companies, and it is highly priced in both the US and the EU. Getting a similar reimbursement price in many Asian countries will however be particularly challenging.

M-H.S: The green tea for VeregenÂ® is grown in China, where are the only two farms approved by the US FDA. Extract purification is then conducted in Japan, while the ointment manufacturing is outsourced to a third-party, and also manufactured by Sinphar in Taiwan.

VeregenÂ® was the first and is one of a very small number of innovative botanical drugs approved by the US FDA. Medigene conducted the preclinical and clinical development of VeregenÂ® globally and successfully obtained market approval in the US, in Europe and in more than 20 countries overall.

In 2016, SynCore Bioâ??s SB05, a triple negative breast cancer (TNBC) combination received approval to start phase III clinical trials in Taiwan and Australia. How do you plan to move forward on the clinical development and commercialization of this interesting product?

M-H.S: In 2011, we closed a first partnership with Medigene regarding the clinical development of this product in Taiwan, before renegotiating it in 2013 to ultimately become the main sponsor of this TNBC trial in Europe and Asia. Yita Lee also successfully negotiated the acquisition of the global rights for this product from Medigene, covering all potential indications in all countries.

SB05, an innovative composition of the established cytostatic drug paclitaxel combined with neutral and positive lipids, is expected to prevent the formation of new tumor blood vessels and to inhibit tumor growth. The phase III trial started in December 2016 in Taiwan and we had our pre-IND meeting with the US FDA on December 6th 2016. We now look to submit our IND application during the first quarter of 2017.

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YL: We however expect patient recruitment for this phase III trial for TNBC to be rather slow. This is why we are currently evaluating the opportunity to start SB05â??s clinical development in other indications, where we could bring it onto the market more swiftly.

For example, we plan to start clinical trials for pancreatic cancer in the US in parallel to our TNBC trials, which explains why we were so keen on getting this productâ??s comprehensive rights for all indications. In the meantime, pancreatic cancer stands as a very interesting niche for SB05, as the market is less competitive than breast cancer treatments.

M-H.S: Furthermore, the overall survival rate remains particularly low for pancreatic cancer patient. Given the huge need for new treatments in this area, we expect that we could complete the required clinical trials within three years.

YL: Finally, we are already looking for robust partners which would contribute to ramp up the development of this unique product. It is particularly tricky for a company of our size to sustain by itself the clinical development of a product that aims to simultaneously receive market approvals by some of the most stringent regulatory agencies in world.

We are now in discussion with well established partners in Europe and the US, while we may retain the development and commercial rights in some Asian countries, where we already have gained the experience to market it by ourself.

How do you see SynCore Bioâ??s R&D pipeline evolving in the upcoming years?

YL: We are ready to inlicense new products and further enrich our R&D pipeline. New drug development stands as a risky business, and we do not want to let any difficulties we could meet in our ongoing trials hinder the growth prospects of our company. As a result, expanding our pipeline will allow us to reduce SynCore Bioâ??s risk exposure, increase our chances of success, and further gain in experience.

M-H.S: In December 2015, SynCore Bio acquired Medigeneâ??s drug technology platform EndoTAGÂ®, which is based on a novel, cationic liposomal technology that targets vascular endothelial cells in regenerated blood vessels carrying negative electric charges within the tumor. EndoTAGÂ® was for example used in the development of SB05, SynCore Bioâ??s most advanced clinical project, but it is not our companyâ??s only technology platform.

SynCore Bio now holds several of these assets in the oncology and dry AMD (a retinal disease) fields, which are SynCore Bios main areas of focus. For dry AMD, we for example hold two different technology platforms: one for the development of new drugs and the other one for diagnostic instruments.

On the other hand, we have been able to assemble a team of very experienced scientists, which is particularly strong in project evaluation. Our business model remains essentially based on the in-licensing of early stage compounds, meaning our enduring ability to identify the best compounds that we could integrate in our R&D pipeline â?? with regards to our technology capacity â?? will be critical to nurture the long term growth of SynCore Bio.

Among Taiwanâ??s R&D driven companies, SynCore Bio probably stands as one of the few innovative companies integrated within an historical, well-established pharmaceutical group holding international operations. How does it stand as a competitive advantage for the company?

M-H.S: In 2001, Tim Lee, the chairman of the Sinphar Group, decided to set up a R&D center comprising a cutting-edge technology in formulation development, a nano-technique development laboratory, as well as microbiology and molecular biochemistry laboratories mainly focused on the development of botanical new drugs and dietary supplements. This centerâ??s R&D teams have already reached some particularly interesting achievements, as we received market approval from

China FDA for our *Cistanche tubulosa* in 2005.

As a result, Sinpharâ??s core R&D capacity was already up and running even before we set up Syncore Bio in 2008, and we then only had to strengthen and adapt the focus of our R&D teams rather than building from scratch SynCore Bioâ??s innovation-centered capacity.

In terms of manufacturing, Sinphar Group also holds an automated manufacturing facility dedicated to the production of oncological parenteral drug products, which we will be able to leverage for the production of SynCore Bioâ??s liposomal products.

YL: When it comes to dosage development, CMC, or product manufacturing, SynCore Bio can now fully leverage the expertise that the Sinphar Group has been honing for forty years.

> â??Sinphar generates through generics sales and CMO activities the profits we need to nurture the R&D maturation of SynCore Bio.â?•

As you said, it is rather unique in Taiwan to see an R&D driven company emerging from an historical, well-established generics company. This undoubtedly stands as a great asset for SynCore Bio and its future development, as Sinphar generates through generics sales and CMO activities the profits we need to nurture the R&D maturation of SynCore Bio. Talking about Sinpharâ??s profitability, we now look at further developing Sinpharâ??s footprint throughout Southeast Asia and China, where we truly want become a leader in the generics and dietary supplements fields.

We see a great variety of innovation-driven companies within Taiwanâ??s biopharmaceutical landscape, all of them leveraging different business models and implementing diverse strategic approaches. What is the development path that SynCore Bio will follow over the upcoming years?

YL: SynCore Bioâ??s first priority will be to move its current R&D projects forward in our two main therapeutic areas: oncology and dry AMD. Overall, we already hold four drugs currently under clinical development (three in oncology, one in dry AMD) and we want to continue to integrate new projects into our pipeline, whether they would be developed internally, through our partnership with the NHRI, or any other licensing agreements.

As our R&D pipeline is maturing, we are already gaining momentum in terms of commercial negotiations to find partners and further co-develop our products and bring them onto the international stage. In this respect, we expect to soon close agreements with strategic partners in many key regions to jointly advance some of our most advanced projects, such as SB05, for TNBC and pancreatic cancer.

In the meantime, SynCore Bio can rely on its unique positioning within the Sinphar Group and access the resources needed to rapidly establish itself as an international frontrunner in new drug development and become the first Taiwan-based companies to bring a NCE to international markets.

Overall, our plan is to remain loyal to the two-fold vision of my father, the founder of Sinphar. First, ensuring that Sinphar Pharmaceutical remains committed to our historical mission of providing Taiwanese and international patients with high-quality, affordable treatments, while also becoming the partner of choice of international companies to bring their products to the Taiwanese and Chinese markets. In the meantime, we are building an innovative company â?? SynCore Bio â?? that holds the scientific and financial means to deliver groundbreaking treatments to patients around the world.

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