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PharmaEngine wants to be highly competitive within the industry. Building a strong and diversified portfolio is a key competency

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Grace Yeh, president and founder of PharmaEngine, gives an update on the company's recent growth and development of their second nanomedicine cancer treatment. Yeh goes on to explain the unique positioning of nanomedicine within oncology and Taiwan's role as an active participant in the global fight against cancer.

What have been PharmaEngine's major developments over the past three years since our last interview?

PharmaEngine's biggest news has been that our French partner Nanobiotix SA received European market approval for our second product, Hensify® just this April. Obtaining a CE mark will enable the commercialization of the nanoparticle radio-enhancer in the 27 EU countries for the treatment of locally advanced soft tissue sarcoma.

Speaking about our lead product ONYVIDE®, the product received EMA approval in 2016. Furthermore, in 2017 ONYVIDE® received market authorization in Singapore and South Korea. Most recently, in August 2018, ONIVYDE® was granted reimbursement by the National Health Insurance program in Taiwan which drove sales of the product substantially.

Meanwhile, we have built ONIVYDE®'s sales and marketing activity in Taiwan from the ground up. Although we could have chosen to partner with MNCs for international licensing, as a Taiwanese company, we connected with many domestic hospitals and KOLs during the development of the product, so we decided to take on this task internally.

Last year, our former licensing partner Shire made the decision to sell its oncology business to Servier Laboratories Ltd for USD 2.4 billion. We hope that this new partnership will bring greater access to ONYVIDE® to the Chinese market. Servier is France's second-largest pharmaceutical company, and with its resources and ~5,000 employees in China, we expect to speed up the regulatory approval process in the country.

What is the outlook for ONYVIDE® in the Asian Pacific market?

As a product developed in Taiwan, we have a lot of pride in being able to deliver ONIVYDE® back to the patients here. Before reimbursement, PharmaEngine was committed to treating Taiwanese patients and we took initiatives to cover the cost after three months of treatment for those who were unable to afford the drug. We even sold ONIVYDE® as "buy one get one free" in Taiwan. After all, what good is a drug if we make the effort to develop it but patients cannot afford the treatment? This is part of PharmaEngine's social responsibility.

ONYVIDE® has a bright future in Taiwan. Currently, we have expanded our sales force to cover a large area of Taiwan and all medical centers carry our product. In fact, ONIVYDE® was given the highest price within its drug class by the government, however, it is still 40 percent less expensive than in the US market. Today, we are working to develop new indications for the drug. We have approval for second-line pancreatic cancer, but now ONIVYDE® is being used in trials with Ipsen for first-line pancreatic cancer and second-line small cell lung cancer and we are collaborating with Taiho in Japan for GI tumors. Additionally, ONIVYDE® is being tested in over 20 investigator sponsored trials. The life cycle management of ONIVYDE® is a key priority. Furthermore, in 2017 ONIVYDE® received market authorization for Singapore and South Korea, and our partner Servier is currently applying for reimbursement. Servier is also in the process of gaining market authorization for Japan.

PharmaEngine has also made significant progress with its second product, Hensify®. Tell us more about these advances.

Hensify® is an aqueous suspension of crystalline hafnium oxide nanoparticles designed for injection directly into a tumor prior to a patient's first standard radiotherapy treatment. When exposed to ionizing radiation, Hensify® amplifies the localized, intra-tumor killing effect of that radiation. The dose of X-ray delivered to the tumor is magnified, whilst the dose passing through healthy tissues remains unchanged. Hensify® requires a single administration and will fit into current worldwide standards of radiation care – because it is injected directly into the tumor it will not harm normal tissue.

Hensify® is actively being evaluated in head and neck cancer with locally advanced squamous cell carcinoma of the oral cavity or oropharynx in elderly and frail patients unable to receive chemotherapy or cetuximab with very limited therapeutic options. Positive results which have been observed in Phase I/II trials of head and neck cancer in elderly patients, the dose-escalation (phase I) are complete, and promising results will be presented in the American Society of Clinical Oncology (ASCO) this year. The abstract has been released on their website https://meetinglibrary.asco.org/record/176753/abstract.

Soft tissue sarcomas (STS) are rare cancers that develop in different types of soft tissues including fat, muscles, joint structures, and blood vessels. Hensify® is the only product of its kind on the market. There are other radiation enhancement treatments that exist but Hensify® is the only product that remains inert when not activated by radiation, resulting in a more precise and safer treatment.

What strategy does PharmaEngine have for the commercialization of Hensify® in the Asia Pacific?

Here in Asia Pacific where we hold the rights, most countries view Hensify® as a drug rather than a device like in Europe. For that reason, we are aiming to receive approvals from countries in Asia Pacific where they deem Hensify® to be a drug. Additionally, we focus on head and neck cancer with the use of radiation and chemotherapy rather than radiation alone, as in Europe. The European market is more focusing on elderly patients who cannot withstand the side effect of chemotherapy while in Asia we are positioned within the standard of care. Although the applications may be different, we are able to share data from trials with each other.

One of the most promising applications of nanotechnology is in the field of medicine. How can the emerging nanomedicine discipline reshape the paradigm of disease prevention and treatment?

Nanomedicine is an important step in treatment accuracy and drug delivery. Nanomedicine is a solution to the issue of drugs which are unable to reach the specific site of action. Taking the example of ONIVYDE®, the new blood vessels grown around tumors are often abnormal with larger pores. The problem results in extravasation or leakage of plasma components including nanoparticles and lipid particles such as ONIVYDE® into the tumor tissues. ONIVYDE® is a liposome formulation of irinotecan which uses site specific activation. Irinotecan will be converted into the 100- to 1000-fold active metabolite, SN-38, by enzymes around tumors.

CAR-T has been a recent major development in the treatment of cancer. How does ONIVYDE® compare to this technology and how active is Taiwan in the adoption of next-generation oncology?

Although CAR-T is a breakthrough treatment, it still faces several barriers. I believe that any of these new immunotherapies cannot be stand-alone treatments. For some cancers like head & neck cancer and non-small cell lung cancer, immunotherapies are only effective in 15 to 20 percent of patient populations, so chemotherapy and targeted therapies are still needed to cover the other 80 percent of patients.

Such personalized medicines while innovative are very complex with tremendous production costs. There are a few startups in Taiwan working on cell and gene therapies, each with their own strengths and focus. Overall in Taiwan, we are creating an arsenal of weapons in the fight against cancer, all with different focuses ranging from early-stage tumor control to curative treatments. Taiwan has a strong innovative potential and the country will continue to develop a wide range of solutions, which is also why PharmaEngine is constantly searching for new, diverse development projects to undertake.

How does PharmaEngine build its development network and what is the company’s competitive advantage in the field?

PharmaEngine has a strong network within the global industry and the key to our success is in discovering goldmines which others have yet to identify. We are able to find out about potential

projects from bioindustry meetings and also referrals from our own network.

Looking at our advisors, the talent pool we have in the company is very experienced and professional. The advisors that are part of PharmaEngine are pioneers in their field, having had successful careers in both industry and academic sectors. They are able to look at our projects from many different perspectives, bringing a high level of expertise which is unique to PharmaEngine.

In your last interview, you identified a goal of becoming one of Asia's leading biopharmaceutical companies, providing patients and healthcare professionals with game-changing oncology therapies. What are your priorities moving forward to continue the pursuit of this ambition?

PharmaEngine wants to be highly competitive within the industry. Building a strong and diversified portfolio is a key competency. Over the past three years, we have been involved in several negotiation discussions for new development projects, and we are excited to see the outcomes.

Of course, we will manage the commercialization of products within Taiwan, but in other markets, this is still to be decided. Fundamentally, PharmaEngine is an R&D company and our marketing strategy is typically decided on a case by case basis. In our globalization strategy, we will build several business units to maximize our presence. Today, PharmaEngine has its French subsidiary and we continually consider opportunities to expand our network of subsidiaries.

Furthermore, we will continue to have a strategic focus on funding, Currently, PharmaEngine is a cash-rich organization with over USD 120 million in the bank in addition to receiving revenues from ONIVYDE®. Our aim is to continue this trend of building a sound financial structure, invest smartly, and drive new revenues from projects.

Any advice to others in the space about merging science with a business mindset?

I started my career as a scientist and always enjoyed challenges. While working in the US, my CEO at the time offered me a role in project management – something I had never done before. I then learned to manage development projects and negotiate licensing-out agreements. The ability to learn is an asset and in the industry, you cannot become boxed into one knowledge area. The science is very important but being able to negotiate within the industry and communicate with partners and investors is crucial as well. For people coming from a science background within the

biotechnology sector, my advice is to open their mind and learn on the job. I believe that a bit of luck and a sense of instinct is also a key!

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