Johnsee Lee – Chairman & CEO & Eric Yang – VP, Quark Biosciences

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17.06.2020

Tags: Taiwan, Quark Bio, Precision Medicine, Diagnostics

Johnsee Lee and Eric Yang of Taiwanese precision medicine diagnostics firm Quark Biosciences outline their technology's unique characteristics, how it differs from sequencing technologies in terms of cost and speed, and their strategy for the Asia-Pacific region and beyond.

Can you introduce Quark Bio's products and systems and how they work together?

Eric Yang (EY): Quark's NextAmp™ Analysis Technology enables real-time precision medicine through diagnostics. The technology has a fast turnaround time in analysing medium to high complexity assays, providing results within two hours. Because of this speed, aligned with its simple operation and cost-effectiveness, we are able to decentralize real-time precision oncology diagnostic, allowing doctors and patients to access high-quality diagnostics on the spot when they immediately need them.

Real-time precision medicine is increasingly playing an important role, especially in terminal stage cancer patients. According to the I-Predict Study, published last year in Nature Medicine, more than 30 percent of the terminally ill cancer patients either deteriorated clinically or died before they got their genomics testing results. Therefore, if we can provide genomic test results with a short turnaround time, we can potentially save people's lives.

Dr Lee, can you outline the initial business idea behind Quark Bio and the problem you set out to solve?

Johnsee Lee (JL): Our initial concept was based on the idea that in precision medicine, a researcher is not looking for a single biomarker or gene, but for many. Because of this, they use next generation sequencing (NGS), which provides a broader spectrum of genes so that they can get the result in one test. That is the basic direction in which precision medicine and precision oncology have been moving.

However, sequencing today is still not very clinically friendly. One of the reasons for this is that it takes at least a few days – on average two weeks – to get results. Secondly, it is very complicated and requires very sophisticated bioinformatic analysis. In clinical diagnostics, there need to be clear cut results and a high level of precision and specificity. That is more difficult in sequencing which gives a lot of information but is not focused on diagnostic of particular clinical target and does not provide highly accurate reproducible results.

An alternative to NGS is amplification. The theory behind this technology is to amplify from one to tens of thousands within a short period of time so that even very low concentrations of signals can be detected with high specificity and sensitivity. That is the advantage of amplification. Nevertheless, traditionally, if a researcher or doctor wanted to run many different markers using conventional amplification, they would have to do a lot of manual manipulation which takes a long time and is also more susceptible to human error.

NextAmp™ Analysis System is our platform for simultaneous amplification of many biomarkers in a chip within two hours and is an excellent alternative to sequencing. With NextAmp™, all the markers are pre-loaded onto a chip, giving all the advantages of amplification without these traditional stumbling blocks. The chip contains many different markers, about 100 of which can be amplified simultaneously in short time, which fulfils the needs of real-time precision medicine. NextAmp™ allows users to be precise and fast while also testing many markers at once. Additionally, we have also pre-loaded the probes and primers for each marker on the chip with our high-speed arraying technology so that the user does not have to do any pipetting.

What some of the key milestones in the development of this technology from concept to market?

JL: We started to develop the predecessor platform to NextAmp™, PanelChip®, back in 2012. The technology has moved from version 0.1 to 0.5, and more recently 1.0 and 1.1. We have redesigned the whole instrument as well as the chip. The other important component is the content – depending on the application we need to develop which biomarkers to use, how to design them, and put them on the chip in many tiny wells.

Now moving into mass production, we have also developed many different applications. What we are commercialising is not only the platform itself but also the application products, which covers precision oncology and reproductive genetics.

Can you run us through your product portfolio and outline the importance of 'real-time oncology'?

JL: One of our key products is a Tumour Micro-Environment (TME) test for cancer immunotherapy. This test uses around 100 markers so that, based on the gene expression, physicians are able to evaluate the micro-environment around a tumour and its immunopheno score.

With this technology, doctors are able to decide whether a particular patient is suitable for immunotherapy or not. Currently, the only approved marker for testing whether someone is suitable for immunotherapy is PDL-1. However, PDL-1 markers have, so far, been very inadequate. Therefore, we think it is extremely important to develop TME to, perhaps in combination with other markers, increase the accuracy of selecting appropriate patients.

Immunotherapy is very expensive, so there is a pressing need not to waste money. For example, most insurance companies require that patients have the test first before they are given immunotherapy. Our test is first-in-class and via our platform will be capable of testing up to 100 markers simultaneously, providing a high level of precision using amplification, and, most importantly, do so within only two hours instead of many days. This 'real-time oncology' provides faster analysis that is crucial, given that cancer is changing every day and after waiting two weeks for a test result, patient's cancer may be in a very different status.

Another of our key products is MoDEL, a liquid biopsy for non-small-cell lung cancer. Blood plasma is used in detecting the variation of certain genes to judge whether they are recurrent after the treatment and also detecting if there is drug resistance – if there is, the therapeutics have to be changed.

As well as oncology, Quark is also present in reproductive health. What is your footprint in this area?

EY: Quark has dedicated resources to developing testing in reproductive healthcare. The WHO has stated that infertility will be the third most significant disease of this century. Therefore, we focus our application development on a test that can help increase the success rate in in vitro fertilisation (IVF). Globally, IVF has a success rate hovering around 25-30 percent.

The low success rate is influenced by many major and minor factors. One major factor is the window of implantation (WOI), a period of time within each menstrual cycle that's ideal for embryo implantation. We have developed a best-in-class assay that can predict the window, providing the exact time that's best for personalized embryo transfer to increase implantation success. The capability of the NextAmp™ Analysis System to provide quantitative clinical precision is the driving force behind the development of the assay, MIRA, for WOI prediction.

We have already launched MIRA in China and Taiwan. We will launch MIRA in the US in late 2020 and in Europe in 2021.

How does your platform compare to other solutions in the market?

JL: Our platform is unique in many ways. The testing labs need not only a good product but also one that is very efficient. The fact that our chips are pre-loaded with markers gives labs convenience and allows them to operate with lower costs and higher efficiency.

To use an analogy from another industry, our solution is akin to capsule coffee. One machine can provide a wide variety of coffee as the coffee capsules themselves have already been pre-mixed and formulated. We have pre-loaded, formulated, and designed in advance so at the user end it is a very simple operation of letting the machine run for a few minutes.

What are your KPIs that have put Quark Bio on this road to success?

EY: There are three major KPIs we need to consistently evaluate for us to be successful. 1. We want and need to continue to develop first-in-class and best-in-class diagnostic assays utilizing NextAmp™. 2. We will and need to continue to build relationships with pharmaceutical companies. That is how we build value because in precision medicine, drugs and diagnostics are in a symbiotic relationship. 3. We need to have impressive revenue growth. Our goal is to achieve a 3-5x growth

in revenue in the next three years.

How would you characterise your value proposition to pharma companies?

EY: Pharmaceutical companies want their drugs to be accessible to patients who will benefit the most from the treatment. Some cancer drugs, such as target therapy, cost USD 15,000 to 20,000 per month. We want to position ourselves as a partner that can help pharma companies pinpoint the right patient population cost-effectively during post-market launch. Many of the target therapies currently being developed with good response rates are targeting low percentage mutations. As a result, there is a need for affordable companion diagnostics to identify a very small group of people within a large population.

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Similarly, we have a significant value proposition to pharma companies conducting clinical trials for drugs targeting low percentage mutations. A good example would be drugs targeting NTRK gene rearrangements, which has been found to be ubiquitous, though accounting for only up to one percent of solid tumours, in various types of cancers. Imagine only one percent of participants in a clinical trial had the specific mutation, 5,000 patients would have to be screened in order to get 50 patients for the trials. NGS, now the often-used method, is too costly for the task, whereas we provide a cost-effective and fast solution for the large-scale screening of patients.

How easy is it to bring this cutting-edge technology to market?

EY: It is very challenging! There are many stakeholders that have to be convinced. In the world of precision medicine, patients' treatment involves doctors, pharma, service and insurance companies, all of whom have to be convinced of our performances. It is even more challenging for us because we have both the hardware technology and the assays, meaning that we have to convince the stakeholders on both fronts.

For the NextAmp™ Analysis System, we have to illustrate that the technology has robust and consistent performance through peer-reviewed publications. Because it is a new technology,

stakeholders would want to know the instrument's reliability and quality, adaptability in the clinical laboratory, geographical footprint and closest competitors, not to mention the company's financial stability.

On the assay/test front, the most important thing is whether the assay has clinical utility – does it actually help the patient? This usually takes sizable patient data to prove. In addition, stakeholders want to evaluate our clinical and analytical data as well as our ability to develop the assay.

In terms of infrastructure in Taiwan, what are the benefits of being located where you are?

EY: It is much easier to be located in Taiwan than in Europe or the US because of the comparatively lower costs. There are very good hardware and software engineers for hardware technology development. Clinical studies are also much more economical to conduct here in Taiwan. Additionally, Taiwan has great data scientists and bioinformaticians, which is essential given the huge amount of data that is needed for precision medicine diagnostics.

What are the opportunities and challenges in consolidation and partnerships for Quark Bio and for the diagnostics industry more broadly?

JL: There is definitely a significant opportunity out there, but it is not easy to execute. Everyone wants to be their own boss so there tend to be many small companies. However, sometimes a crisis can force greater levels of collaboration or even mergers. For example, during the COVID-19 pandemic, there has been great demand for diagnostic kits and companies are trying to work together to meet that demand. Any individual firm would not be able to handle that level of volume.

For a single test, there needs to be sample preparation, testing, analysis, platforms, and reagents. Therefore, companies in this sector must work together. Some companies have better sales channels so if they work together, they may be able to better meet demand.

We are engaged in a lot of discussions about how we can work together, which requires trust. Leaders who can convey a high degree of trust to everyone are needed and, if that kind of leader is in place, we see the potential for a consolidation trend.

How are you pricing your application product and ensuring that it is accessible?

JL: Immunotherapy treatments are expensive, but the test itself is relatively affordable and is only a small fraction of the total treatment costs. It is, however, still relatively expensive in comparison to infectious disease tests.

To ensure that our costs are kept relatively low while quality remains high, we use technology that is readily available here on Taiwan, such as semiconductors and electronic. Moreover, the price of a product is different from the cost; price is usually the value of a product. We are typically compared with sequencing, which is generally very expensive even though their cost is now lower. We offer something priced much lower than that although some variations in product and market affect the pricing.

Who do you see as your key strategic allies?

JL: Hospitals and laboratories are our customers. We select some of them as product development allies to collaborate with as our reference or standard labs. For example, we have a hospital in Taiwan with whom we jointly set up a precision oncology lab so that we could carry out various projects to transfer into a clinical setting.

Additionally, we have many allies in pharmaceutical companies who are interested in TME and MoDEL. We are talking to a few international companies on how to use our tools to help the drug development process. In the discovery stage, they would prefer to use sequencing but in the later clinical and promotional stages, they can use our tools to more efficiently, precisely pin down their applications and extend their indications.

What are your key priorities for the future?

EY: First, it is important to ensure that we develop a variety of tests on the system. We want NextAmp™ to become a common platform for performing multiple diagnostic assays in the field of oncology and reproductive genetics.

Second, we want to become the leading platform for gene expression biomarkers. That is what NextAmp™ is really good at – being able to measure precisely the expression level of the genes.

Third, in the immediate future, we need to establish business operations in neighbouring regions such as China, Japan, and South-East Asia.

What is your market entry strategy in Asia?

EY: Though we have a global vision, it is important to remember that we are just a small company. We have a business to business operation; therefore, we partnered with regional service and pharma companies to market our products. Our strategy is to leverage the sale and marketing channels of our partner to create a win-win situation. For example, we have found a number of very capable partners in China to distribute our products. We continue to seek world-class partners in Japan and South-East Asia.

Do you have a final message for our international audience?

EY: I have been with Quark for a little bit over five years, from its very beginning to now the commercialisation stage. I see great opportunities ahead! We are now in a position where demand is outstripping supply – a good sign but a key challenge for our team.

We have a golden chance in the era of precision medicine to take the NextAmp™ Analysis System to the global stage. We have a technology and multiple assays that resolve unmet needs on the clinical end. As long as we implement and execute our strategies well, we should be very successful.

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