Jun Bao â?? President & CEO, Impact Therapeutics, China

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Dr Jun Bao, appointed president and CEO of Impact Therapeutics in October 2018, shares his aspirations for Impact to be a leader in synthetic lethality in oncology; the importance of â??operating locally but selling globallyâ??; his learnings from his distinguished career across biotech and pharma companies in the US and China; and Impactâ??s portfolio of exciting cancer therapeutics.

Dr Bao, you have had a very varied and interesting career having worked for both biotech and pharma companies in the US and China, mainly in business development and commercial

operations. Why did you decide to join Impact Therapeutics as CEO in October 2018?

After many years of working in many different executive management roles, to assume the role of CEO and make decisions for the whole company is personally quite exciting. I decided to join Impact Therapeutics as the CEO because the company is in a very pivotal stage of its development.

Impact has been very successful in its in-house R&D efforts, having discovered some very innovative and interesting molecules, but now the company is entering the drug development phase with products in the POC testing stage. I like to say that Impact is starting to grow up! The companyâ??s operations are no longer focused on a team of scientists doing science and research in the labs.

This is where I believe my previous experience in commercial operations can bring value. BD and licensing are in my blood. This means that I am not only able to contribute to the clinical development of Impactâ??s own pipeline programs but I can also help Impact generate and explore potential opportunities to collaborate with other companies, whether through combination therapies or in-licensing other companiesâ?? programs into Impact.

The role of a CEO within a biotech company is slightly different from the same role within a pharma company, and even more so, companies in other industries. We interact very closely with the scientists within the company, including Impactâ??s cofounders. I do not dictate what the scientific or R&D teams do. My role is to bring the complementary commercial and business skills and experience to support the companyâ??s science and R&D development. In this way, I connect the science and business sides of the company!

Having worked in such different innovation ecosystems, what can you share about the ways in which different profiles of companies function?

It has been very insightful to see the way different companies work and each model has its pros and cons. Having worked in three US biotechs including Onyx, which was acquired by Amgen, I would say that their decision-making is very efficient and focused. Execution is critical, so everyone is rather driven and very proactive. In the US, as a biotech, typically you are in one of the biotech hubs like Boston or San Francisco so you would have ready access to innovation. You could attend a conference every week if you wanted to, which is great for forming partnerships.

For pharma companies in the US, they are more passive when it comes to collaboration. After all, biotech companies would approach them with new ideas and projects, since everyone wants to out-license a product to Big Pharma! Within these companies, decision-making is also consensus-driven so the process is longer but once the company makes the decision to move forward, they have huge amounts of resources and capital to invest in the project.

In China, perhaps it has to do with the youth of the biopharma industry but I find that both Chinese pharma and biotech companies behave more like US biotechs. The leadership team â?? usually the C-suite â?? is absolutely critical to the companyâ??s operations. They set the vision, the strategy and also the direction and execution of the company. They usually are the ones driving the company forward rather than the company working through different departments and functions, with set processes in place. This means that decisions are made faster but the decision-making process is down to a few individuals and may not always be rational. I think this is also because there is a shortage of skilled and experienced people to fill the different management roles within a company.

Recently I had the opportunity to attend BIO-Europe Spring in Vienna, Austria, where I spoke to a number of different European biotech companies. I was impressed by how innovative some of them were but my impression was that they tend to be rather underfunded compared to biotechs in the US and China, for a number of reasons. What I was pleased to see was that these European biotech companies were starting to understand the Chinese industry a little better. Previously, there were a lot of concerns over IP and regulatory systems, but now that these areas have improved significantly, European biotechs are now starting to understand how much potential there is within the Chinese market.

Impactâ??s flagship candidate IMP4297 is a PARP inhibitor that has recently finished Phase I clinical trials in China and Australia. What is the potential you see for this asset?

Impact is a clinical-stage company with a unique small-molecule drug discovery and development platform targeting DDR.

Impact was founded on the basis of the mechanism of DNA damage response (DDR), which can be exploited by the synthetic lethality approach.

We are very excited about IMP4297 because we already have very positive results from our Phase I trial. We were able to see an encouraging patient response as measured by tumour shrinkages in a number of different tumour types and also at different doses. For sure, further clinical development and more results are needed but at the moment, we are very impressed with the safety profile of IMP4297, and I believe this will be the main differentiator. We have not seen maximum tolerated dose (MTD) in this Phase I trial yet, which suggests that IMP4297 could have the widest therapeutic window amongst all existing PARP inhibitors. This would bring significant benefits for patients that have to use the drug for longer periods, for instance, for maintenance therapy that could last over two years. In that case, having a safer and more efficacious drug would help patients.

We are looking to start Phase II and Phase III trials for IMP4297 in China for ovarian cancer. We could benefit from the rapid patient enrollment in China, which certainly helps to speed up clinical development. From Phase I data, we also see efficacy signals for IMP4297 not just in ovarian cancer but also other cancers like bladder and brain cancers, which suggests that there could be a much wider use for our drug.

We also have two other pre-clinical products: one is a novel Hedgehog inhibitor and the other is another novel DDR, both of which have entered IND-enabling studies. We expect to move them both into the clinic by the second-half of 2020.

What is the rationale behind Impactâ??s focus on â??best-in-classâ?? therapeutics instead of â??first-in-classâ???

> As long as you can demonstrate that your drug has some differentiated benefit, there is always a place in the market for it, even if it is a so-called â??me betterâ?? or â??me tooâ?? drug

The former US FDA Commissioner Scott Gottlieb delivered a speech once where he emphasized the need to provide a variety of options to physicians and patients so that physicians can choose the best drug for their patient and patients to have options to rely on. Particularly for cancer, which is a

very heterogenetic disease, different patients might respond to different drugs differently in terms of toxicity and tolerability. Different drugs have different profiles even if their efficacies seem on par during clinical trials. Some physicians have shared with me that for them personally, it can be very difficult to tell a patient that they have no more drugs to prescribe them. As long as there is another drug available for that condition, it offers an alternative treatment that may help the patient.

For this reason, I believe that as long as you can demonstrate that your drug has some differentiated benefit, there is always a place in the market for it, even if it is a so-called â??me betterâ?? or â??me tooâ?? drug.

When new companies start to discover and develop innovative drugs, it is also natural for them to gravitate towards validated targets. The risks are lower and you can learn from your predecessorsâ?? mistakes to improve on the existing products. Thereafter, you can focus on finding differentiated products that could become a â??best-in-classâ?? drug!

For Impact, we think that IMP4297 is a very differentiated drug in terms of its safety profile and as a result, it has a lot of potential to be developed as a â??best-in-classâ?? PARP inhibitor for the treatment of cancers with defects in DNA repair mechanisms, such as with BRCA1 and BRCA2 mutations, including breast, ovarian and prostate cancers.

You mention that Impact is also open to collaboration and partnerships with other biotech and pharma companies. What is your focus here?

We are looking for assets that fit our focus on the platform of synthetic lethality, either on their own or in combination with our current assets. For instance, we currently have a collaboration with another Chinese biotech company, CStone Pharmaceuticals, and their flagship candidate CS1001, which is a PD-L1 antibody.

Existing preclinical and clinical data indicate the possible synergistic effect of combining PARP inhibitors and PD-L1 antibodies. Some of the Big Pharma companies are already exploring this area with some early but promising results. From my perspective, PARP inhibitors tend to generate more mutations in cancer cells because of DNA damage that cannot be repaired. In theory, this means that cells should be more responsive to immunotherapies. We look forward to seeing how this collaboration develops.

We are also scouring the world for more companies to work on these exciting projects. For biotechs like us, we have to be very proactive and cast a very wide net so that we can snap up the good projects. We want to be the first to spot the next big thing!

In the meantime, we work with many CROs and CMOs so that our core team can remain nimble and fast. A lot of our work within Impact is actually virtual and we focus on being as efficient as possible. This is what will drive our competitive edge.

While it maybe a little early to consider the commercial side, for the Chinese market, have you considered how Impactâ??s IMP4297 will compete with the current category leader for ovarian cancer, AstraZenecaâ??s LYNPARZAÂ®?

In general, biotech companies either have to set up their own commercial infrastructure or they can work with a partner that already has an existing sales and marketing network. For now, we are

leaning more towards the latter since we want to be capital-efficient. We will probably work with a local company that already has its own commercial network set up, and we will focus only on the medical marketing since we know our product best. Subsequently, when we have a few more products on the market, we can consider establishing our own sales team. This would also allow Impact to grow sustainably.

At the moment, we have not yet engaged with physicians in terms of switching products. But we see that physicians are very willing to enroll their patients in our clinical trials, which suggests that they see something attractive about IMP4297â??s profile.

Finally, the market is always sensitive to price. That said, we want to be competitive on price but we do not want to compete on price alone. As mentioned, our drug seems like it has a very promising safety profile, especially for maintenance therapy.

Looking forward, what is your vision for Impactâ??s growth in the next few years?

In terms of building the corporate culture and organization here at Impact as CEO, I have a couple of priorities. The first is that we must operate locally but sell globally. This means adapting operations to the local market: for instance, you can have a global clinical study protocol but when you bring that into different hospitals in different countries, physicians will operate differently. It is not that some do things wrongly, but simply that processes and systems in different hospitals in different cities and countries differ. This is why operating locally is important, you have to adapt and make global protocols more practical for the local HCPs.

However, at the same time, you must sell globally, which means developing the drugs for the global market and maintaining your operations and processes to global standards.

Secondly, we must find and train more talents, particularly in China. This will contribute to the sustainable growth and development of Impact in the future.

My vision for Impact is to be a leader in synthetic lethality â?? first in China, next in the world â?? and operating locally while selling globally our novel and â??best-in-classâ?? therapeutics for cancer and other life-threatening diseases!

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