# Jiang Lei â?? Co-Founder and CEO; Shou Jianyong â?? Co-Founder and CSO, EnnovaBio, China

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*Dr Jiang Lei and Dr Shou Jianyong, EnnovaBioâ??s co-founders, introduce their strategy and outline the progress being made in the Chinese biopharma industry at large.*

**Could you please introduce EnnovaBio to our international audience?**

Dr Jiang Lei (JL): The name EnnovaBio reflects our ambitions. We want to focus on innovation, hence â??novaâ??; the â??enâ?? at the beginning means constant innovation, not just once-off; and also in Chinese, the name of the company is â??è½¶è¯ºâ?? , which evokes the very serious promise that our company has made to Chinese patients as well as patients globally.

Dr Shou Jianyong (SJ): We aim to develop innovative medicines for Chinese people and patients globally. Both Dr Jiang and I have worked for MNCs for many years and we have witnessed both their successes and setbacks in China. When we designed our research strategy, we wanted to differentiate ourselves from MNCs, who after all have rich resources that we do not have. We also wanted to differentiate ourselves from local companies that also have many talented people with rich expertise. While we do not want to be different for the sake of being different, it is important that EnnovaBio has some key differentiators to set ourselves up for success.

Firstly, on the big-picture level, we are a Chinese company so we really want to benefit Chinese patients and meet unmet medical needs in China. Otherwise, why would we start a company in China? Secondly, working on China-prevalent diseases will also support our companyâ??s business development. The attrition rate for biotech projects is so high and the human proof-of-concept (POC) stage is really fundamental. Strategically, we want our projects to achieve human POC rapidly in China. Since we focus on the most significant unmet medical needs domestically, that would motivate local stakeholders â?? government, physicians and patients â?? to move quickly and work with us.

Next, we considered which diseases and targets to focus on. Developing innovative drugs is difficult so we wanted to have a balanced portfolio. As EnnovaBio is still small, we are not equipped to do de novo target discovery but we still want to do something new. In that regard, we have focused on the use of bioinformatics as a key technical differentiator. Looking at major biotech success stories like Amgenâ??s PCSK9 inhibitor drug Repatha, BMSâ?? PD-1 drug Opdivo and MSDâ??s (Merck & Co. in the U.S. and Canada) PD-1 drug Keytruda, they did not discover these targets from scratch themselves. As a small biotech, we are not equipped to discover new targets ourselves but if we manage to develop strong data-mining capabilities to extract useful information from publicly available data, that would give us the competitive edge we need to develop first-in-class (FIC) compounds eventually.

Finally, we also prioritize external collaborations with academics, institutions and other companies.

**Given your companyâ??s strategic focus, particularly the emphasis on bioinformatics, how easy was it to assemble the right team with the right capabilities?**

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JL: Throughout Dr Shouâ??s career, he has seen significant success across major disease areas like neuroscience, oncology and metabolic diseases. A major part of that success has been his ability to tap into informatics to guide his research. For instance, when I worked with him at Novartis, he was working on an early-stage epigenetic project. He used informatics to figure out how one of the epigenetic targets might be associated with a key tumour-suppressor gene, quickly discovered an innovative approach to address that gene, and subsequently published a very nice paper.

SJ: The use of bioinformatics is one of our core technical strategies and we have invested heavily in this area with our own bioinformatics team, in addition to my own long history and track record in this field. A few years ago, AstraZeneca published a paper in Nature Review about how they planned to improve their R&D productivity by focusing on the 5R framework: we have invested in our informatics capabilities in all five Rs: from target, tissue, safety, patient to commercial potential.

We do not see drug discovery linearly but rather, we view complex diseases as a network. We perform sophisticated network analysis to identify key nodes in disease pathology, which may not only produce higher success rates when it comes to target selection but also means that these targets have increased opportunities to extend into multiple indications, which would de-risk our overall pipeline.

On that note, I must highlight Dr Jiangâ??s specialty area as well. We had first met in Novartis in 2009 and I firmly believe he is one of the medicinal chemists that understands biology very well. This has been a factor driving our focus on small molecule projects, which form the majority of our portfolio. With him being a seasoned drug hunter and medicinal chemist with a track record of success, I think we have a competitive edge here. The other reason for our focus on small molecules is that the chemical space is enormous. Even existing drugs on the market are not perfect, so we have many opportunities to develop novel medicines, as long as we choose interesting disease areas and good targets with good molecular profiles. This also further differentiates us from the wave of Chinese biotechs focusing on biologics, particularly antibodies.

**EnnovaBioâ??s current research is focused on two areas: immunotherapies for oncology, inflammatory and autoimmune diseases, as well as targeted therapies for cancer cell resistance. Could you share the progress that has been made in both areas?**

SJ: I am very excited to share two of our flagship projects, which have both seen significant progress in recent months. The first is an oral medication for diabetic retinopathy (DR). Diabetes is highly prevalent in China, and glycemic control and overall disease management are not as good as in the U.S., which also means that diabetes-related conditions like DR also appear to be more severe in China. There is currently no treatment for DR in China besides laser surgery for late-stage DR, which also requires three follow-up eye injections. You can imagine that patient compliance with this surgical procedure is low. An oral medication would be much better received by physicians and patients, and it could also benefit both early-stage and late-stage patients.

Our DR project has advanced to the preclinical development stage. The non-GLP toxicology data suggests that our compound is safe. We are currently working on CMC and GLP studies for IND-enabling and we think this is promising. In addition, since we chose to work on key pathway nodes, this target is also a key regulator of inflammation so we believe it not only has potential in DR but also in other chronic inflammatory diseases, which can also help de-risk our efforts on this target.

What is very encouraging is that last year, two major pharma companies, Novartis and Eli Lilly, individually announced AI-driven initiatives to identify early-stage DR patients. This demonstrates that this is an area of significant unmet medical needs in China and also that there may be

opportunities to facilitate our compoundâ??s clinical development in the future.

Our second project is a small-molecule project within the immuno-oncology (IO) space. Many companies are focusing on the antibody approach for PD-1/PDL1 interaction, which is a well-validated target. While this space is rather crowded, we are focusing on the small-molecule approach. The technical challenge to target protein-protein interaction (PPI) is to balance the potency and physicochemical properties of the inhibitors. We are very excited that we have recently identified our proprietary molecules that possess both excellent in vitro activities and in vivo drug-like properties. We believe our compounds can complement the antibody therapies and facilitate future combination treatments.

**It is interesting that your second project may help immuno-oncology combination therapies, which is a very popular area at the moment. Some of the other biotechs we have met in this space have commented that a robust pipeline with many assets is essential to success in combination trials. What is your view on this?**

SJ: Having attended the American Society for Clinical Oncology (ASCO) conference earlier this month, a key message at the conference was that combination therapy is the future of cancer treatment but so far the industry met limited success. There is a need for rational combination design.

For EnnovaBio, we take an informatics-driven approach using our proprietary bioinformatics platform. Of course, informatics is not a replacement for human POC but could generate a testable hypothesis that may help rational IO combination study design. For instance, we recently met with another company to discuss the potential for collaboration with their assets. We presented our in silico analysis results on combination, which were in nice agreement with their bench work data. We are very encouraged and would like to apply this approach to the IO combination strategy design as well.

JL: Drug discovery is fundamentally risky and uncertain so to mitigate that, we focus on rational design as much as possible, and the same applies to combination studies. While there are many combination studies ongoing, many lack strong theoretical support. Since there are almost an infinite number of ways to combine different compounds, without a rational basis, it is challenging to have clinical success with limited resource. Having a broad portfolio with many assets is definitely an advantage when it comes to combination studies but we would like to explore the possibility to win in this crowded space if we focus on rational design and identify a good partner that can bring complementary assets as well as clinical resources.

**With that in mind, how have you defined EnnovaBioâ??s partnership strategy?**

SJ: From a big-picture perspective, we focus on â??value-created collaborationâ?? to build win-win strategic partnerships. We must provide something very unique so that our partners view us as a valued collaborator. We want to ensure that we make our mark on partnerships we are part of. We are certainly interested in acquiring or out-licensing assets but we are more concerned about value creation and sharing. We want to bring our scientific insights and expertise to potential partners so that both sides can maximize the value of their assets.

In the same vein, we do not prioritize attending pure business conferences at this moment too much. Firstly, we want to wait until we have very solid data so that any potential discussions can be more

substantial. However, during this early stage, we do try to speak to multiple companies to keep them updated on our projects so that future discussions will be smoother. Secondly, as responsible collaborators, we also want to de-risk our projects to some extent before seeking partners. We do not view partnerships simply as a matter of risk-sharing. Furthermore, we have a â??play-to-winâ?? mindset â?? the later-stage a project is, the more valuable it is, so we want to maximize the value of any asset before we enter negotiations.

We are also very committed to ensuring that the quality of our projects matches the highest international standards. Having been in the opposite position of working in Big Pharma and reviewing external projects, I have seen many sub-par dossiers with quality issues, and it does not inspire confidence or interest from potential partners.

JL: Since we have both worked for Big Pharma for many years, we have set the bar quite high. Ultimately, we do not just want to take an asset into the clinic, we also hope that it will exit the clinic successfully. For instance, we even use statistical analysis to ensure that our assays are robust. This is not even something that all Big Pharma MNCs would necessarily do. Ultimately, we want to ensure that our data is reproducible and meaningful before we submit dossiers to potential partners.

**It is undeniable that the Chinese biopharma industry is booming at the moment with a lot of talent and capital flowing into the sector. How has that affected the playing field for companies like EnnovaBio?**

JL: On one hand, we are fortunate because the hype has created a great opportunity for companies like EnnovaBio. This has ignited the biopharma industry in China, certainly. We should find a way to seize this opportunity. How can we build our strengths and capabilities to capitalize on this boom? We do not want to jump on the bandwagon and follow what others are doing. We need to analyze what we are good at, what we can do, and how we can contribute to this entire process.

However, amidst all these opportunities, we have to remain calm. Regardless of the hype, the fundamental business has not changed. Drug discovery remains very challenging and risky. We have to be realistic that the success rate is low and there are many roadblocks ahead of us. The hype will go down eventually. Ultimately, you win through your product(s).

SJ: Just recently, a local magazine interviewed me, with one of the questions being, â??what is the key element of a drug hunter?â?? My answer was passion â?? the passion for science. While ultimately rewarding, drug discovery is a tedious and time-consuming process with many failures and setbacks. To be a truly good discovery scientist and drug hunter, money cannot be the most important factor. This is why we look at commitment and passion when we hire people for EnnovaBio.

Nevertheless, talent turnover is a fact of the industry. The important thing is to behave professionally and always to the highest standards of integrity. This is how EnnovaBio operates.

**To begin wrapping up, what have you learnt about biotech entrepreneurship in the course of establishing EnnovaBio?**

SJ: As a scientist, I believe that we are always driven by curiosity to try different approaches. A key learning point for me in moving from an MNC to a biotech start-up was how to be successful within a research setting with limited resources? In an MNC, you are able to work with internal experts in a

variety of fields and hire CROs to solve problems. For a biotech, sometimes these options are not available but you still have to find solutions to problems. It is about how to do things smarter and differently.

Secondly, people development is even more important. We cannot offer the financial compensation that MNCs can so we need to offer other compelling reasons for talented people to join us. For instance, we often organize training and lectures for our staff. We also empower them with opportunities to lead their own projects. If you are a junior scientist in an MNC, you may not have the opportunity to drive a project or build your own portfolio. Here, we encourage everyone to be involved in decision-making.

I like to say to our employees, doing science is stressful so we do not want to give you more stress. If we can help, we will even take some of the stress from you!

JL: EnnovaBio is actually my second company as CEO. I have benefitted greatly through my first entrepreneurship stint. My greatest takeaway was the importance of company culture. As a biotech startup, it is of paramount importance to share everyone in the company on our mission and vision. This is what binds the company together at the start-up stage. Today, we are very pleased that the company is bonding very well together. We are all progressing in one direction together: to deliver innovative therapies to patients in China and globally.

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