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Good investors should look into the specific unmet medical needs companies are trying to address and how they are addressing them rather than simply focusing on certain therapeutic areas

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Zhenkun Ma, founder and CEO of TenNor Therapeutics, shares his cross-sectorial experiences in Big Pharma, biotech and non-profit organization that led to the establishment of TenNor Therapeutics; their mission to develop highly differentiated therapies for infectious diseases with clear unmet medical needs, such as biofilm-associated medical device infections, H. pylori infections, hepatic encephalopathy and gastrointestinal tract infections; as well as the importance of collaboration and partnership in this area.

Zhenkun, you have a rather interesting background compared to many other Chinese biotech CEOs having worked at Big Pharma, a U.S. biotech and also a global non-profit organization, the Global Alliance for TB Drug Development (the TB Alliance). How did this motivate you to establish TenNor Therapeutics in 2013?

My previous experiences in different sectors of the industry have helped immensely in the establishment of TenNor Therapeutics. I spent eight years with Abbott (in the part of the business now spun off into Abbvie) where I led a medicinal chemistry team for the discovery of new antibiotics to address drug resistance problems, before joining Cumbre, a U.S. biotech that has now become part of TenNor, as Director of Research and Development, and finally, immediately prior to forming TenNor, I spent nine years at the Global Alliance for TB Drug Development (the TB Alliance) first as Head of Research and then as Chief Scientific Officer (CSO). This has given me a very holistic understanding of how the drug discovery and development ecosystem works.

At Abbott, I was purely focused on drug discovery research. At Cumbre, I led a team working not only involved in research but also in development. At the TB Alliance, my role expanded further and I actually spent a lot of time in building partnerships with external organizations. The TB Alliance is a unique organization really focuses on leveraging collaboration, partnership and outsourcing to develop new drugs. One of my major responsibilities was to direct and supervise both internal and external programs in collaboration with external entities including pharma companies, biotechs, and academic and research institutions. This gave me the opportunity to see how different organizations manage projects.

All these experiences have inspired me to establish TenNor as an efficient drug development organization with a sharp focus on meeting patient needs. We are developing new therapies for infectious diseases and we are committed to serving our purpose.

Infectious diseases, particularly antibacterial diseases, are a very challenging area that many Big Pharma players have exited in recent years. How can TenNor succeed where these companies have failed?

Anti-infectives â?? particularly antibiotics â?? is a very mature field. The issue of antimicrobial resistance (AMR) is becoming increasingly serious and many countries and international organizations are realizing that this need has to be addressed. At the same time, there are two key challenges present in this space.

Firstly, from a scientific and technical standpoint, all the low-hanging fruit have already been taken so it is more difficult to find a breakthrough. However, I believe that the technical challenges are manageable. We see that Big Pharma companies are exiting this area not because of technical challenges, but for commercial reasons. The market situation for antibiotics can be challenging for

companies. There are many generic drugs available in this space and the current insurance reimbursement system â?? in both mature and emerging markets â?? is not set up well to promote innovation. Doctors and patients tend to use older and cheaper generic drugs that may be less effective and face drug resistance issues.

To become a successful company, we have to overcome both the scientific and commercial challenges. We thought very hard about the right business model to ensure the success of TenNor and we made a conscious decision to focus on a strategy of developing differentiated candidates for clear unmet medical needs that can be used as first-line treatment instead of being reserved as second- or third-line therapies. This can ensure that our business model is sustainable. This approach is perhaps different from other companies working in the same space, which tend to focus on developing next-generation products to have an incremental improvement over existing drugs on the market in terms of efficacy and/or safety. However, we strive to develop new drugs that will truly change the standard of care for patients and ensure that these drugs will be widely accepted in the market.

As Big Pharma have exited this space, we actually see opportunities to take advantage of the situation by recruiting ex-Big Pharma talents to join us. So far, we have already found many people with solid industry experience to join TenNor as both staff and consultants, which enable us in building one of the best anti-infectives R&D team in the world!

Antimicrobial resistance (AMR) is a major issue globally. How is this being handled in China?

The antibiotic resistance problem is historic in China. There used to be a lot of overuse and improper use of antibiotics but in August 2012, China adopted much more stringent standards on the use of antibiotics. This resulted in the antibiotics market shrinking for a few years after that. However, in the past few years, we have seen the Chinese antibiotics market growing again, and this time, the growth is mainly driven by genuine patient needs instead of improper use.

Infectious diseases pose serious challenges to public health, particularly in resource limited countries. While China has developed rapidly in a short span of time, the diseases burdens generally lag behind. Therefore, China need more resources to develop new technologies and new therapies to treat these diseases, which cause a significant health and economic burden on society.

What are the main projects you are working on right now at TenNor Therapeutics?

We currently have three exciting programs in clinical development focusing on true unmet needs. Through our efforts, I hope we can change how these diseases are treated and improve the current standards of care.

The first is on biofilm infections associated with medical implants or devices. This is one area where the current standard of care is inadequate. These types of infections are very hard to treat and often requires surgery to remove the implant or device, which is not only expensive but results in significant patient suffering. We believe that this is a significant unmet medical need. We are developing an innovative new therapy, TNP-2092, which is in Phase II clinical trials at the moment. Through the successful development of TNP-2092, we hope to improve the way patients are treated.

The second program is focused on developing locally acting antibacterial agents for diseases associated with gastrointestinal (GI) tract infections or dysbiosis. This includes cirrhosis hepatic

encephalopathy (HE). HE is associated with liver dysfunction and the accumulation of ammonia in the blood (hyperammonemia). The current therapies are all through reduction of ammonia in the blood but at the moment, only three drugs have been approved by the US FDA for this indication, and one of them is effectively not in use because of kidney toxicity. We hope our treatment can improve the treatment of HE and other diseases associated with GI tract infections and dysbiosis (the condition of having imbalances in the microbial communities either in or on the body).

We have a third program currently in Phase I clinical trials that is focusing on treating anaerobic bacterial infections, which are associated with many diseases. The current standard of care, such as metronidazole, is an extremely old antibiotic developed over 60 years ago. As a result, drug resistance to this drug is very high. We are looking to target a few indications, the first being *H. pylori* infection. In China, an estimated 50 percent of the population carries this infection, which is associated with gastric ulcer, as well as gastric cancer. In other East Asian countries like Japan and South Korea, the eradication of *H. pylori* has become a national strategy and we expect China to adopt a similar strategy. However, the current treatment is very complicated and difficult to implement, involving four different drugs that also have to be personalized for the individual patient. Therefore, this is clearly not a viable large-scale treatment option. We hope we can develop a shorter, simpler and much more effective *H. pylori* treatment that could become the cornerstone of a national eradication strategy.

A second indication we are working on is bacterial vaginosis, a very common infection in women and a major reason for hospital visits and drug prescriptions for them. Again, the first-line treatment is metronidazole but the resistance rate for the main pathogen for this disease is extremely high, estimated between 70 to 90 percent in China and 30 to 40 percent in the US. We really need new drugs to replace the current first-line treatment.

Given the broad scale of infectious diseases, how do you expect to build your commercial strategy in the future?

This would be new territory for us. Currently, TenNor is focused on innovation and drug development. Commercialization is not our strength â?? yet. We do believe that having the right commercial strategy will be crucial for success, both to allow the company to be sustainable and also to ensure that patients in need are able to access our products.

In terms of our market strategies and pricing models, they will depend on the diseases and indications we choose, patient populations and so on. For certain focused indications that small companies could handle, such as prosthetic joint infections, we might commercialize them ourselves. But for diseases like *H. pylori* infections or bacterial vaginosis, partnership or co-commercialization would be a sound strategy.

We will also have different strategies for the U.S., China and other international markets. Certainly, outside of China, we will focus more on collaboration, and I believe the right timing should be after Phase II trials.

It is clear that the Chinese biotech industry is booming but much of the investment seem to be channelled into â??hotâ?? areas like immuno-oncology and CAR-T. Despite that, TenNor has managed to secure reputable investors like 6 Dimensions Capital. How did you communicate the purpose of the company to them?

This has been a challenge when we spoke to investors. IO has indeed been a very hot area, especially in China over the past few years, and we have seen that the majority of investment went into it. It is an exciting area with potential for breakthroughs. At the same time, it seems that many investors are more focused on the upsides rather than the risks in this area.

My view â?? which I did share with many of our potential investors â?? is that unmet medical needs exist in all therapeutic areas. It is not the case that only a certain therapeutic area has opportunities that others do not. Good investors should look into the specific unmet medical needs companies are trying to address and how they are addressing them rather than simply focusing on certain therapeutic areas.

Infectious disease is an area with many challenges but also ample opportunities â?? and I think TenNor is definitely taking advantage of these opportunities to build a more successful business model.

One thing that I have learnt throughout my career was how to strike a balance between protecting intellectual property (IP) while remaining as open and collaborative as possible. In a healthy ecosystem with the right balance, companies can collaborate openly and share knowledge, which avoid a lot of repeated investments and mistakes. If everyone works behind closed doors, the result is that people all end on working on the same things, which is a waste of resources. At the same time, we must protect our core assets and products so that we can deliver returns to our shareholders. TenNorâ??s model is a very open and collaborative one, and we have many partnerships with academic and research institutions, as well as service providers.

A final message on behalf of TenNor Therapeutics to our international audience?

Innovation has no borders. Whether it is done in the US, China or somewhere else, innovation eventually benefits the entire world. With the current environment in China, I believe China will become an innovation centre for the global pharma and biotech industry in the years to come.

At TenNor, we want to bring products useful to patients to the market, and we have the right strategy and business model to achieve our mission.

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