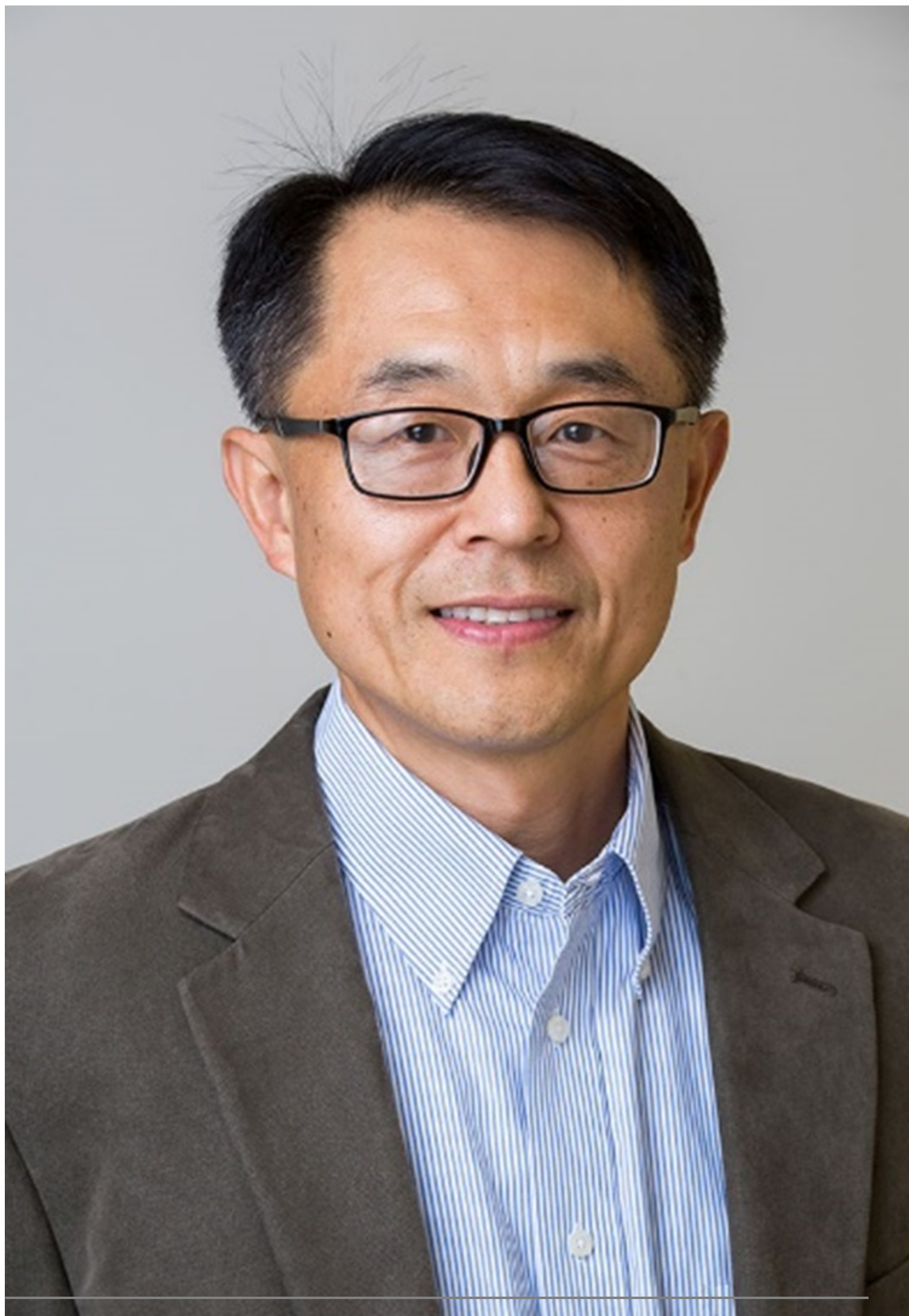


Weidong Zhong    Founder & CEO, Terns Pharmaceuticals, China



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Terns Pharmaceuticals is developing innovative drugs for the treatment of NASH and liver disease. It has established a diverse product pipeline with drug candidates targeting different stages of the disease and with complementary mechanisms of action, through partnerships with global pharma companies as well as in-house discovery efforts. With offices in Shanghai and the San Francisco Bay Area, and a highly experienced research and management team, the company has global ambitions and a passion for innovation. Its CEO Dr Weidong Zhong goes back on the reasons why he started Terns Pharmaceuticals, explains the difference the company can make for NASH and cancer patients, and breaks down the challenges of bringing innovative drugs to China.

Weidong, after a career focused on R&D at big pharmaceutical firms, why did you decide to start your own company?

After over two decades of working in big biopharmaceutical companies like Novartis, Gilead and Schering-Plough, mainly overseeing discovery and early-stage development of drugs for virology and liver disease, I started thinking about setting up my own biotech start-up. I felt I could do more and have more impact by building and running a small, nimble and highly efficient organization to discover and develop innovative medicines, especially to help patients in the underserved markets such as China. In large corporations, it can be such an uphill battle sometimes to get things done because of the bureaucratic processes and risk-averse mindset. Moreover, inside such big machines, individuals' talents may not necessarily be utilized to the maximum.

Fortunately, I met investors that put their trust in me, supported my vision and helped me and my co-founders kick off the company in early 2017, with operations first in the Bay Area, and shortly after in Shanghai. Our goal was, and still is, to bridge global drug discovery innovation with accelerated clinical development in China, to bring high-quality, innovative drugs to patients with NASH and liver disease in China as quickly as possible.

How did you adapt to the realities of entrepreneurship?

When I think about the last couple of years, I had to make quite a few adjustments. The most important thing to keep in mind when starting a business, especially a biotech company, is that you have a limited amount of resources and a limited amount of time to leverage these resources in order to get to a meaningful data point. For these reasons, you cannot make projections too far into the future. You need to think strategically and pragmatically at the same time and determine what

your priorities are for the near-term. I must admit that this way of thinking was not natural to me, and I had to adapt.

Moreover, one of the critical steps to get the business off the ground is to raise capital by convincing investors of the value of your programs and the quality of your team. Most scientists are not good salespeople – and they should not be! They deal with facts and focus on what is rather than what could be. As an entrepreneur, you need to sell a vision of what the company will become in the future. You need to inspire trust in you, your team, the great potential of your company and the soundness of your plan to reach success. Obviously, this is something I had little experience before. I had to shed my scientist skin a bit and put on the entrepreneur hat. You also need to build and maintain strong credibility within the biotech and pharma community in order to recruit the best possible talent in the industry and build a strong company.

As you said, your expertise is in anti-viral drugs. Why did you decide to focus on developing treatments against NASH?

My background is mainly in anti-viral drug discovery and development. Many viruses, such as hepatitis B and C, live in the liver. As a result, I have accumulated throughout the years an extensive knowledge of the liver. When I was at Gilead Sciences over a decade ago, I led discovery and early stage research efforts to combat not only viral pathogens but also liver diseases. At the time, liver disease was starting to emerge as the next battle ground for the pharma industry. NASH, together with liver fibrosis, was one of the areas where my team and I started research on at Gilead, trying to identify promising targets for drug discovery. To date, this field is still largely underexplored. There are so many unanswered questions, both scientifically and clinically. Our long-term aim is to combine the latest scientific research with state-of-the-art drug discovery technology to identify and bring innovative treatments to patients in a timely fashion.

You can read in the news all the hype about the NASH market and predictions about growth and market size. For us, the patients are the focus. The number of people afflicted by fatty liver diseases is staggering and is growing year-on-year, especially in China. The main culprits are well-known: Western diet, overfeeding and lack of physical activity. The accumulation of excessive fat in the liver will cause damage down the road, leading in many people to end-stage liver disease or cancer. Moreover, unlike some infections, there is no easy fix. Fatty liver diseases are multifactorial chronic lifestyle conditions for which a one-size-fits-all treatment approach is unlikely to work. Lifestyle change is of course going to be crucial. What we are trying to do is to come up with therapies that will prevent the disease from advancing to more severe states, help people make the necessary lifestyle transition, and provide a better quality of life for the patients. Realistically, I do not think this problem will be completely addressed during my lifetime. It is going to take generations of innovative research to reach that goal.

A lot of companies, both MNCs and biotechs, are jumping on the NASH bandwagon. What makes Terns Pharmaceuticals different?

What Terns Pharmaceuticals is inspired to do is to start this process and make a dent in this growing public health issue.

Coming back to the development landscape, there is a lot of talking about what the industry can offer to tackle NASH. As far as I can tell, we do not have anything resembling a cure. Treatments currently under development seem to work a little bit here, a little bit there. But we do not have an

obvious breakthrough and highly effective treatment that can tackle such a complex condition. NASH is a complex disease that experts no longer view it as one disease, but as an evolving multi-stage condition with each stage likely requiring different therapies. This situation is both a challenge for the scientific and healthcare industry, but also represents a tremendous opportunity for us to make a difference. As of today, large companies with abundant resources have been working on several assets simultaneously, hoping some of them will eventually turn out to be good. For smaller companies, on the other hand due to limited resources, tend to focus on a single asset, with a more or less "make it or break it" mentality. At Terns, we would like to position our efforts for the long-haul, to be patient and focus on the science first and foremost.

Just like what we have witnessed in antiviral and anti-cancer treatment, we believe that combination therapy is going to be key to increasing the effectiveness and breadth of future NASH therapies. More importantly, because it is a chronic disease, ensuring the safety of drugs, both individually and in combination, is paramount. In addition to enhancing treatment effectiveness, we believe that combination therapy can also have the potential to improve safety of treatment. It is conceivable that when a given host target got hit too hard by a single drug, the human body would likely react to it leading to tolerability or safety issues. Conceptually, combination of drugs that target different host pathways may offer opportunities to fine-tune doses not only based on efficacy, but as importantly if not more so, on safety and tolerability.

In the US, it is still unclear how physicians are going to react to a NASH drug because a diagnosis requires an invasive liver biopsy. Is the situation similar in China?

Yes, it is quite similar. In Chinese culture, the liver is viewed as a critical and fragile organ, so actually Chinese physicians and patients are even more reluctant to perforate the liver with a needle. Moreover, even though many Chinese people have a fatty liver, because it has not yet caused problems, physicians would be reluctant to take invasive measures to look closely at the state of their patient's liver. This is regrettable because early diagnosis could prevent more serious issues down the line. If nothing is done, it is just a matter of time before the liver enters more serious diseased states such as advanced fibrosis, cirrhosis or even liver cancer. When that happens, there is currently little treatment option for the patients.

However, I am confident that when physicians and patients start to see the positive impacts of good drugs, mindsets will change. This would be similar to what happened for many other disease areas after effective drugs are approved and administered to patients broadly, people started to observe the superior long-term benefits of the therapies. For these reasons, I am optimistic that public health systems will adapt once we show that new NASH drugs are safe and effective.

Running clinical trials in China can be challenging especially regarding infrastructure limitations with clinical trial centers and a lack of incentives for overworked healthcare practitioners to engage in clinical research. How do you plan to execute?

We are collaborating with both global and Chinese KOLs with the goal to be the first company to launch NASH drugs in China. The sets of challenges in running NASH clinical trials in the U.S. and China are slightly different.

In China, the main challenge is to recruit enough patients for late stage NASH trials. Currently, in order to run a registration trial for NASH, you need to recruit approximately a thousand or more patients. I think in the future this will be possible in China. Furthermore, in recent years, the

regulatory policies in China have changed significantly and global clinical trial data conducted outside of China have become more and more acceptable. It is possible that, for NASH drug approval in China, global trials with adequate participation of Chinese patients would be sufficient in the future, something that we as well as other companies in this space should monitor closely and communicate early with the Chinese health authorities before we get to that point.

The second challenge is infrastructure. China is on its way to build more high-quality clinical trial centers on par with international standards. We are assessing what we can do with the current capability at each stage of clinical development for our programs. I am very confident that in the not-so-distant future more and more of our clinical development activities will be carried out in China.

Apart from NASH, Terns is also conducting discovery activities in oncology. It seems most innovative biotech companies in China are developing oncology drugs, especially in the field of immuno-oncology with CAR-T and anti-PD-1/PD-L1 therapies. Where is your focus here?

While two of our advanced stage molecules for NASH are licensed from Eli Lilly, we also allocate a significant amount of resources to conducting in-house discovery research in the field of liver disease and oncology. We are very excited that several of our in-house programs have advanced quickly and expect to deliver molecules to the clinic in the next couple of year. Our overall strategy is to constantly enrich and diversify our product portfolio through a combination of partnerships with global and local pharma and biotech companies and internal discovery efforts by utilizing our team's in-depth expertise in disease biology and chemical innovation.

In oncology, we are focusing our energy on cancers that are highly relevant to China's areas where we know we can bring value. We are not doing immuno-oncology. As you said, there are enough companies working in this space already. Instead, we are applying a unique approach to chemotherapy that may lead to more effective and safe treatments. So far, existing treatments for solid tumors have not worked too well in many cases including liver cancer. Chemotherapy remains the default treatment option for solid tumors, especially for hard-to-treat cancers, but it presents a lot of issues. First, chemotherapeutic agents can spread to other parts of the body and have a deleterious effect that limits dose escalation and consequently treatment effect. In the case of liver cancer, they do not work well because the liver breaks them down quickly before they can accumulate to reach therapeutic concentrations.

We are developing novel treatments that can circumvent liver tumor resistance to chemotherapy by leveraging the expertise we have accumulated through developing anti-viral treatments targeting the liver. We are using a unique prodrug technology, administering pharmacologically inactive chemotherapeutic agents that are quickly metabolized into an active form within the body. This technique also has the advantage of targeting specific organs, thus limiting distribution to other parts of the body. We are hoping that combining this type of next-generation chemotherapy with molecularly targeted or immuno-oncology treatments will lead to improved treatment outcome for cancer patients for whom current therapies do not provide adequate benefit.

Many biotech companies in China have told us about the challenge of recruiting top talent suited for innovative drug development and commercial success. Terns does not seem to have this issue. How did the company manage to assemble such an experienced team of people in such a short time?

In the US, we quickly built a highly experienced team as people I have worked with and known for a long time decided to come together, attracted by the shared inspiration to build Terns into a company that can truly help patients. In order to maintain a robust and sustainable drug discovery engine, we decided from day one to set up our discovery organization in the San Francisco Bay Area where we could tap into the talent pool and innovative ideas of the academic and biotech ecosystem.

However, if we were hoping to reach any kind of success in China, we also needed to assemble a highly competent clinical development team on the ground in China and develop strong relationships with local KOLs and scientific communities. In China, finding the right talent has been more of a challenge for many reasons. It is only recently that MNCs and local companies have started conducting early-stage clinical trials. As a result, identifying people who have experience in early clinical development has been challenging. Every company faces the same issue and are competing for the same talent pool, which drives up the cost evidently.

What Terns has put extra effort on is to cultivate and grow our own people and talent by forging a close collaborative relationship between our teams. It takes patience, dedication, as well as timely and constant communication for all parties. Our US and China teams have been working together as one team essentially on all projects, producing a strong bonding and cohesiveness among the teams regardless of physical locations. Through close interactions, on-the-job coaching and learning, I am very satisfied to see that the knowledge and expertise of our China team have grown so quickly, who are now in position to not only support clinical trials in China but global studies as well.

What we also learned through the process is that attracting top talent is not just about paying the right amount of money, but also about offering the opportunity to work with colleagues with a shared inspiration, that is to make positive impacts on people's lives by bringing innovative, life-saving treatments to patients in China and across the globe.

This is what Terns Pharmaceuticals is about. We search for people who share this long-term vision and look at the big picture. We also look for individuals suited to a start-up environment where you need to keep going despite difficulties and challenges. We cheer for each other with Terns motto "Let's build something special together".

What is your favorite part of the job?

What gets me excited is brainstorming with my colleagues about the science: How do we design a novel molecule? What is the quickest way to get this tested? How do we find a novel target to treat the disease? Or a new disease that this molecule might help with?

In big organizations, people have the tendency to settle into a complaining mode, always something to complain about or pointing fingers at. But at Terns, complaining is not part of our vocabulary. Since we are small and nimble, we make decisions on-the-go and execute as one team with everyone's participation. There is no place for conflict as we together own up to our decisions and must align our thinking to move forward. I love to engage and interact with all my colleagues. To me, they are not just people I work with on daily basis, it feels more like a second family.

When I try to raise funds for the company, I put my CEO cap on. But in here I am just trying to solve problems by thinking critically with everyone else. It is also a great opportunity for me to pass on the knowledge I have accumulated during my 20-plus years in the industry to young scientists, which has always been a rewarding part of my career.

Looking forward, what do you plan to accomplish in the next five years?

For our oncology programs, we could conceivably bring a drug to market in the next 5 years. However, for NASH, clinical trials take much longer. The new FDA guidelines for NASH drug development published at the end of last year mandate the treatment duration of Phase IIb and Phase III trials to be at least 12-18 months. Also, finding enough patients willing to go through liver biopsy will continue to be challenging for large NASH trials no matter where you go. As a result, we project it is going to take five to ten years in order to have a drug approved for NASH. We will do our best to explore all enabling strategies to speed up the process including partnering with global companies which have more resources and capabilities than us. It is too soon to predict how things will shape up in the future.

Our first priority right now is to deliver good molecules. It is a prerequisite for any success we can achieve down the road.

Even though we are still a long way from getting a NASH or cancer drug to patients in China, I am confident that we will eventually get there. As you may know, terns are migratory birds that hold the record for longest distance traveled. Although we are small, Terns Pharmaceuticals is built to aim far and go the distance.

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