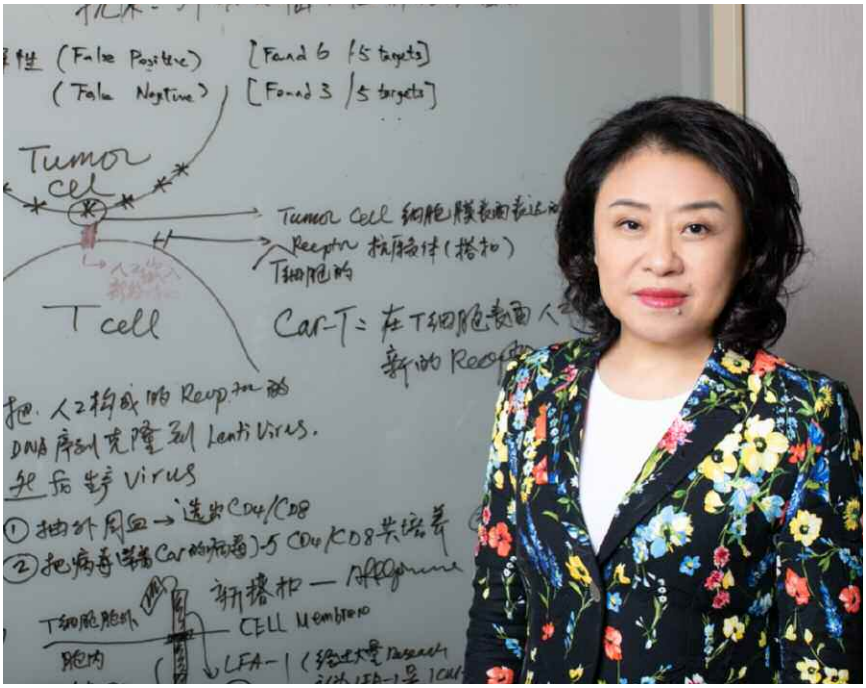
A cure for cancer?

Simone Song discusses her fund and its focus on biotech breakthroughs

Last year was a bumper one for biotech IPOs: 81 companies raised $13.5 billion, says SVB Leerink, a US bank with a focus on healthcare and life sciences. The bulk of the funding went to developers of new cancer drugs, which made up 52% of the deal flow and 64% of the capital raised. To learn more about the economics behind next-generation therapeutic investments, WiC sat down with Simone Song, founder of Hong Kong-based healthcare venture capital firm ORI Capital. Since launching her first healthcare investment vehicle in 2015, Song has had two blockbuster exits through trade sales and is backing another firm that listed on Nasdaq. Her second fund, doubling the size of its predecessor to $400 million, reached its first close early last month.



Simone Song: founder of the healthcare venture capital fund ORI Capital

What inspired you to start ORI Capital?

There was both a long-term inspiration and short-term trigger. The long-term inspiration came from my parents. My father is a member of the Chinese Academy of Sciences and he has spent his entire life on biotech research to combat cancer. He's 94 years-old now and he's still doing it, working every day at the biotech company he owns. In fact, he is China's first scientist-turned-biotech entrepreneur, being very accomplished in both endeavours.

The same can be said of my mother, who invented China's first novel biotech treatment for blood clots. She took her scientific discovery – which won global intellectual property rights – from the lab and started a biotech company.

So, you see, biotech and entrepreneurship are in my genes – even when I was working in investment banking, I focused on the healthcare sector.

The short-term trigger happened in 2015 when I was diagnosed with a colon tumour. While I was waiting for the biopsy report, I told myself that if the result was benign – meaning that I didn't have cancer and still had the second half of my life ahead of me – I would devote my life to supporting biotech companies to develop treatments against the deadliest diseases. The surgery made me realise that it was time to leave banking and take my parents' torch: that is, to innovate, to change people's lives, and to save lives.

What's your investment thesis?

Sharing the same vision as my family, the fund focuses on diseases with very high mortality rates such as cancers, acute diseases caused by metabolic disorders, neurodegenerative diseases (like Alzheimer's and Parkinson's) and rare conditions caused by a single genetic disorder (which mostly kill children).

Across this group, we look for disruptive technologies and companies in the areas of diagnostics, drug delivery and therapeutics. We're completely stage-agnostic and geography-agnostic.

How do you find your targets, which are mostly private companies?

We are very methodical and we take a data-driven approach. To help our-

selves identify the right technology to invest in and look for potential targets that don't normally have much public information, we've built an artificial intelligence information platform called Orizon. It tracks more than 15,000 young healthcare companies, 1,000 fund managers and 600 key opinion leaders (KOLs), as well as top-tier journals through crawling information from public databases.

The platform has enabled us to narrow down our universe to 4,000 companies, to follow what our peers and their portfolio companies are doing, and to keep abreast of developments in each scientific approach. The reviews it generates inform our investment decisions on a daily, weekly, monthly and even annual basis. They guide us through the full cycle of the investment process: from deal origination and portfolio management all the way to exit strategy.

How do you pick early-stage companies?

It's a process combining human and artificial intelligence. Based on a list of criteria and algorithms, a much smaller pool of companies is selected and put on our watchlists. They have to pass 10 tests before more in-depth due diligence comes in to qualify them as potential investees.

What are the 10 tests?

Five are related to science, and the rest to business. We start with scientific bloodline – for the technology to be really disruptive, it takes years of basic research, so we need to understand where the research was done, for how long and by whom. Second, the company has to have patents, and their research needs to be published in peer-reviewed journals, which means the work is validated by other leading scientists.

Third, the company needs to have the freedom to operate, meaning that if there's an intellectual property dispute, the company will likely win. And fourth, data. Even if the data is derived at the animal model stage, it should give a full-cycle picture, from safety to efficacy. It's even better if the company has excellent clinical data, which is the fifth test.

On the business side of things we want to see who the CEO is. A scientist-founder might not be the best choice, given that running a business requires a different skillset. Second, the CEO has to be supported by a well-rounded team: a chief medical officer, a VP of manufacturing, a VP of regulatory affairs, a VP of finance, etc. Third, the company needs to have a high calibre scientific advisory board. That will give us comfort to invest on a long-term basis because the advisory team will be there to steer the company, which is still young, in the right scientific direction.

The fourth test is the quality of the board of directors, who, ideally, should be resourceful with excellent connections in the financial and pharmaceutical worlds so that they can help in hiring the right people and meeting the right potential partners. Young companies just can't afford to pay to get all the same resources.

Last is having the right shareholders – people who don't force the company to go public tomorrow, who understand that it takes time to come up with data and create value.

Of course, no company passes all the 10 tests! This is where we need to make decisions. We fight the battles worth fighting and then make the necessary compromises. Afterwards, we deploy lawyers, accountants and our internal science advisory board for a formal due diligence process. Here, our platform Orizon comes into play too. Its relationship mapping function can guide us on finding the right experts for external opinions or co-investors before we write a cheque to our investee.

How often do you co-invest?

For very early-stage companies that we incubate, we don't mind going solo, from seed to Series B financing, because of the potentially lucrative returns.

For later-stage companies, which typically need more funding, we tend to invite other investors. We co-led a $120 million Series B financing round for Orchard Therapeutics with Baillie Gifford before it went public, for instance.

How is your Fund 2 going to be different from Fund 1, apart from the size?

Fund 1 lasts seven years, extendable for two years maximum. Fund 2 lasts 10 years, also extendable for two years. Our investing principles will stay the same. The only difference is that we will make more follow-on investments. Some companies that we invested in with Fund 1 will also become a holding in Fund 2. As they get bigger, we need a bigger fund to support them.

Your portfolio is quite heavily skewed toward Western companies. Will Chinese firms have a

bigger presence in Fund 2?
We do not discriminate against companies based on their geographical origins. But my guesstimate is that there will be companies from China in Fund 2 because there are just so many innovative and science-driven firms being incubated in China over the past five years. I see good business leaders, excellent scientific breakthroughs and sector infrastructure that is maturing fast.

I have a dear friend who in my view has established the world's best and largest incubation hub in Shanghai's Zhangjiang [Hi-Tech Park in Pudong]. It has everything. A company being incubated there will see its development accelerated because of the centre's excellent infrastructure.

China is maturing. It has the right market size, the right people, the right infrastructure – similar to what we see in places like Cambridge in Boston, or Cambridge in the UK.

Of course, there will be newly successful biotech companies coming from China. And of course, they will be ones that pass our stringent qualifying tests!

What is the biggest factor driving the boom of China's biotech industry?
The biggest factor that drives the biotech boom is universal, it is innovation. What drives innovation is breakthroughs in basic science which requires continuous funding support by the government. Government needs to take the lead in providing grants to understand biology of different disease states, to develop different modalities to treat such disease states, to come up with better tools to support basic researches, i.e., genomic sequencing, gene editing, AI-enhanced data analyses. I am very glad to witness the enormous efforts made by the Chinese central government, provincial governments and municipal governments to support scientific research and discovery in the past 10 years. These efforts are paying off by providing industry with ample technologies readily to be transformed.

What would potentially derail the growth of China's biotech sector?
Government is there to support basic science research. The investing community needs to take the torch to fund the innovative companies to grow from discovery to development to commercialisation. Such growth process could be long and volatile. The industry needs long term investors who have the ability to select future stars and have the skill sets to raise them in terms of corporate governance, growth roadmap, financing strategies and so forth. Biotech is no place for asset flippers who would only create tragedies for themselves and the industry because investing in biotech comes with binary risks.

You listed Orchard Therapeutics on Nasdaq in 2018. Can you give us some colour behind the deal and that firm's prospects?
Soon after we led the Series B round of financing in the London-based company, the board made a decision to bid for other gene therapy assets from GlaxoSmithKline. It was successful and the company got a lot bigger to the point that we could take it public immediately. From acquiring the asset to going public – everything happened in 10 months.

Orchard is still in our portfolio as we have high hopes for it. It has a pipeline of mature clinical assets. Its first drug has already been approved in Europe and the company has started its commercialisation effort [Libmeldy is a vector-based gene therapy].

We really want to see the company mature further, with more products gaining approval and commercial success.

What about the $1.1 billion trade sale of Kymab to Sanofi?
It's a common practice for smaller biotech companies to be sold to multinationals. The latter have become willing buyers because they are suffering from "patent cliffs", meaning that a lot of their blockbusters are going off-patent so there's an absolute need for them to replenish their pipelines.

However, the inhouse return on research and development is often very low, so the natural strategy for the bigger firms is to acquire innovative companies with approved products or products in clinical trials with a high chance of completing the regulatory process.

In fact, multinationals are buying assets at earlier stages because it is getting harder to acquire biotech companies that have reached phase 2 clinical trials as they are ready to go public for funding and carry on on their own instead of selling to multinationals.

In the case of Kymab, it had excellent, almost stunning, data for its clinical programmes. Its pipeline was also very synergistic with that of Sanofi, which explains why the deal happened [Kymab develops antibody-based drugs against cancers, inflammation and infectious diseases].

Does the same story apply to Semma Therapeutics, which you sold to Vertex in 2019?
Exactly. It points to what I mentioned about multinationals buying into earlier-stage companies.

Semma was founded by the legendary Douglas Melton (a member of the US Science Academy, an absolute leader in the stem cell field). It aims to provide stem-cell solutions to Type-1 diabetes. It is an extremely disruptive innovation but it has yet to enter clinical trials. However, Ver-

tex simply couldn't wait, paying $950 million for the preclinical asset. If a multinational company is willing to pay this kind of money, it implies that it is determined to take the innovation through the regulatory approval process.

Which company is going to be your next exit?

We're an authentic VC fund, meaning that our returns will most likely be realised in year six (or later). We made our first investment on April 19, 2016. You can expect a good part of our portfolio to mature into liquidity events within the next few years.

Which treatment modalities do you view as most promising? Gene therapies? CAR-T treatments? Checkpoint inhibitors?

All the modalities you mentioned are basically being developed to deal with cancers. We saw breakthroughs in all approaches, broadly classified into small molecule drugs, large molecule drugs and cell therapies (e.g. CAR-T, oncolytic virus).

For small molecule drugs, there are now better, more targeted drugs. For example, we are looking a differentiated third-generation, small-molecule drugs that target non-small cell lung cancer driven by EGFR (epidermal growth factor receptor) mutation, [a genetic mutation in this protein is a cause of cancer].

Bear in mind that there are about 500 key cancer-related driving mutations. More and more therapies are being developed to treat patients with those mutations, and therefore we will see a great leap forward in target therapies.

For large molecule drugs, we are looking at PD-1 checkpoint, which is an antibody drug, and we're also talking about biospecific antibodies, meaning antibodies that can target dual targets.

We see maturing of the ADC space as well; ADCs are conjugate drugs that target cancer cells but avoid damage to healthy cells. And in cell therapy of course you have CAR-T therapy in trying to treat solid tumours too. Previously that has only been successful in treating liquid cancers.

The bottom line is that cancer treatment cannot be managed by a single approach. Cancer is an individualised disease. Therefore, the more tools that physicians or oncologists have, the higher the possibility to turn cancer into a chronic disease [i.e. with lower fatality rates]

What about precision medicine?

If you look at the term narrowly it is focusing on getting the patient the best-targeted therapies. In the broader sense it means treating patients with an individualised, multi-pronged approach. There will be a lot more investment going into this field because we need to lower the costs of using next-generation sequencing (NGS) methodologies for testing cancer bloods and tissues on an ongoing basis. The industry needs an FDA-approved testing product so that hospitals can assess samples from patients in-house rather than sending them to specialised labs. For precision medicine to be a first-line treatment, you need to have precision diagnostics. Our fund is exposed to this area as well.

How long will the current biotech IPO boom last?

In my opinion the boom will stay because it is supported by fundamental breakthroughs in technology that have created a flow of good companies. The number and size of biotech deals might fluctuate with market sentiment but biotech IPOs, by and large, will be a constant.

Honestly, I pay no attention to whether there is a boom or not. Good companies will always get support from the market. You just have to have good data. And if a company is lousy, it will not get financed.

What kind of returns are your investors looking at?

We exited Semma with 5.3 times return and Kymab with 2.88 times. Our DPI, or distribution to paid-in capital product, has reached 80%. It's a pretty good number. Once it reaches 100%, then I can sleep at night.

Will Sino-US trade and tech tensions affect the growth of the biotech industry?

I personally have not experienced any difficulty in investing globally. We sometimes get enquiries from CFIUS [the Committee of Foreign Investment in the United States] but that's part of the investment process. You just have to answer the questions honestly.

I do hope that sentiment can improve. There has been a feeling of hostility towards Chinese investors over the past four years. I'm not sure whether changes will come about with the Biden administration. But we cannot reach the point at which politicians – of whatever background – block flows of capital into biotech.

That would hurt the interests of patients suffering from deadly diseases, which would be a disgrace to the human race. ■