CONTENTS

A Jump on COVID-19

A tiny Chinese vaccine company headquartered on the outskirts of Beijing held the fate of hundreds of millions of people on three continents in its vials. Sinovac Biotech Ltd. came out of nowhere in 2020 and onto the world stage to proclaim it would become a major ally in the fight against COVID-19.

Sinovac started in 2001 as a biotech company focused on vaccines. Its founding partner was Sinobioway, which was affiliated with Peking University. The driving forces behind the new venture were university biologist Dr. Aihua Pan and his protege, a former government scientist named Weidong Yin.

Yin graduated in the 1980s from the Tangshan Health School. According to Sinovac, he then worked as a medical doctor at the government's Center for Disease Control near his alma mater. From 1993, Yin had cut his teeth developing a hepatitis A vaccine, later known as Healive.

In the early 1990s, Yin and a partner from Singapore formed a joint venture in China called the TangShan YiAn Biological Engineering Co.

A profile of Yin published in 2009, titled "The Flu Terminator," stated that from 1993 to 2000, "His biggest headache was how to make the company live an extra day."

Yin's company grew bean sprouts on the side that he sold to restaurants to stay afloat.

"As an entrepreneur you were born for difficulties, not for enjoying the aura," Yin told the Chinese magazine, Entrepreneur.

Yin drew inspiration from the fabled story of Lenovo, the giant PC company that started in the 1980s in a bungalow in China, experienced its share of ups and downs, then grew large enough by 2005 to acquire IBM's personal computer business for $1.25 billion.

In 2000, he enrolled at Singapore's National University and soon returned to China with an executive MBA.

"The most important thing about the joint venture is to open up my horizons," Yin said. "I had never been abroad at the time. I didn't know what it looked like outside, or how a normal company should operate."

Yin settled in the southern city of Shenzhen, where he met Pan. They agreed to become partners in a new vaccine venture in a large factory in Beijing with investment capital from Peking University, one of China's top schools and research universities.

Yin had a vaccine, Healive, but needed money to commercialize it; Pan was a powerful scientist with the backing of the university. He brought Yin into his exclusive community and attracted funding. They started a new company, Beijing Sinovac, and set up a 43,000-square-foot factory in the Peking University Biological Park.

In the 2009 profile, Yin indicated he was impressed by Pan, his new partner and respected scientist. He identified Pan as one of the two people who most influenced him.

"I am not a graduate from a prestigious university. I am not a master or doctorate," Yin told the magazine. His alma mater merged with four schools in 2001 to become Tangshan Vocational and Technical College.

Pan has an impressive resume. A PhD in biochemistry from Peking University, Pan parlayed his expertise into commercial success. He started a company in 1992 with his boss in the biology department, $61,000 from Peking University and six part-time employees. They

named it for the scenic lake on campus, Weiming Bioengineering Company, and found success with an interferon drug, Seruojin, that won market share. Today Pan is the chairman of Shandong Sinobioway Biomedicine, a $1.4 billion company that trades on the Shenzhen Stock Exchange, and the author of several books.

In China there are masters of many crafts. Some pursue traditional ones, calligraphy or the tea ceremony. Yin's talent was creating vaccines. In 1985 he had isolated the hepatitis A virus and by 1987 developed an antibody. Yin said of his early 20s, "I was (locked in) on the hepatitis A virus. Why? Because I like to do this. I have a natural complex to study infectious diseases. I have no other ability, only to do this."

Sinovac produced vaccines for hepatitis, beginning with Yin's Healive, for China and Southeast Asia. Its revenue, $649,319 in 2002, progressed slowly and steadily. Sinovac quietly did its research, manufactured its vaccines, and worked on new projects to fill its pipeline and grow its portfolio. Sinovac had raised $6 million to launch its small operation. It was more like an extension of an academic department that commercialized its research.

Compared with the omnipresent and massive state-owned enterprises that run China's economy and produce its vaccines, Sinovac is small, nimble, and aggressive. It didn't need state direction to move forward on research and development of a new vaccine. Sinovac needed to keep up in a competitive hothouse of university research. Pan and Yin would pursue science for its own sake, for prestige, bragging rights and for profit. And deliver new vaccines. Beijing noticed.

Then SARS hit. Severe Acute Respiratory Syndrome was caused by a virus that presumably originated in civets, a cat-like mongoose. It first appeared in 2003 in southern China's Guangdong Province. The outbreak sent China, Hong Kong, Taiwan and Singapore into panicked lockdowns and enforced quarantines as the mysterious and frightening disease spread there and to 33 other countries, killing 774 people due to

the impairment of the lungs. In China alone, between March and June 2003, 5,327 were infected, mostly health care workers, and 349 were dead.

Yin first encountered SARS in 2003, when an American expert fainted while giving a lecture at a seminar Sinovac held at a Beijing hotel. He was diagnosed with SARS.

Sinovac sought to capitalize on the outbreak. With its expertise, affiliation with the Peking University, and base in Beijing, Sinovac garnered a little more than $1 million in government grants for research and development of a vaccine. By late 2003, Sinovac had successfully tested the vaccine on monkeys.

Yin and a colleague presented Sinovac's research at a 2004 WHO workshop in Beijing. He was no longer under the wing of Pan, now an international expert on a vaccine to fight a deadly outbreak.

At a later SARS conference in Germany, leading epidemiologists from 15 countries sounded the alarm: "No country is adequately prepared to face the grave health threats posed to their urban populations by such viruses."

Then came this prescient and bold prediction from 17 years ago: "a recurrence of SARS could develop into a full-blown global pandemic."

The effort took a major step forward in May with the world's first clinical trials of its SARS vaccine on 36 volunteers. In late 2004, Sinovac announced good news: none of the volunteers experienced negative side effects and all had developed immunity to SARS. Both outcomes had satisfied the key requirements for a vaccine – safety and effectiveness.

Sinovac, growing with $6.5 million in sales in 2004, appeared to be en route to a major scientific and commercial breakthrough of global

magnitude. The successful creation of a SARS vaccine would place this tiny company at the forefront of a future battle against another SARS epidemic. Or worse, a global pandemic, as predicted by scientists in their downbeat assessment of a likely recurrence and unpreparedness for a new, or novel, coronavirus.

Then, in the middle of 2004, almost as suddenly as SARS arrived, new cases inexplicably stopped. And without new cases, interest in a vaccine vanished.

Despite the successful Phase I clinical trials, Sinovac did not move forward into a Phase II trial to test 300 volunteers for safe dosage and to calibrate the scheduling of the double-dose SARS vaccination. It remains unclear how this decision was made, only that the company insisted in July 2006, "(S)hould another outbreak happen in the future, we believe that we could initiate the Phase II and Phase III trials."

This is how vaccine economics works in the private sector. Pharmaceutical companies invest heavily in drug and research development. Clinical trials of humans also can take longer than other pharmaceuticals due to the risks of infection from a vaccine when it includes the virus, as the SARS vaccine did. Measuring efficacy and safety of vaccines is painstaking and expensive.

If an epidemic has subsided, as the SARS outbreak did, does continuing the pursuit of a vaccine make economic sense? For a tiny, unprofitable company like Sinovac, which had just listed its stock on a U.S. stock exchange and had to answer to shareholders seeking profit, growth and return on their investment, the answer was no.

For research and development of vaccines, the Chinese government had granted Sinovac $3.5 million between 2003 and 2005, with $1.5 million spent on the research and development of its SARS vaccine. However, it wasn't enough to boost Sinovac into profitability. Sinovac had lost $4.7 million in 2004, and headed to a wider loss of $5.1 million in 2005, the

year the SARS vaccine trials were halted. Chinese government grants helped slow Sinovac's growing financial losses during the period, but still management forecasted losses to continue for years.

With the pressure off to find a SARS vaccine, China's government also may have been eager to fund defenses for more immediate dangers. A new disease, H5N1, known as avian or bird flu, emerged, threatening another epidemic. At the time the money might have been better spent against this new, real enemy instead of preparing a defense against a potential re-emergence of a SARS coronavirus – despite the alarming potential for a global coronavirus pandemic and the world's lack of preparedness to fight it.

A major bird flu outbreak followed in 2004 that in weeks reached 10 countries in Asia, including China. Human deaths totaled 23 in Vietnam and Thailand, and there were mass slaughters on poultry farms. Now the pressure was on governments and scientists to stop this new killer flu, fast.

In retrospect, it is easy to criticize Sinovac and China for not pursuing the completion of a SARS vaccine that may have established a foundation to research vaccines with cross-protection potential to fight future diseases, such as the Middle East Respiratory Syndrome (MERS), which appeared in 2012.

But they were not alone. Vaccine economics world-wide is brutal and unforgiving, rewarding short-term, reactive approaches that punish imagination and foresight. After years of sinking millions into research and development, more years of expensive evaluation in clinical trials for safety and effectiveness would follow. At the time vaccines could easily take a decade or more to launch commercially, and success was uncertain. An investment could easily be for naught. Stockpiling was unattractive; many pandemic vaccines cannot be manufactured in advance because all the attributes of the virus in the next pandemic cannot be predicted.

Such an outcome was a tough sell for investors and shareholders. Sinovac had just joined this capitalist club by going public. Already bleeding losses, it wasn't eager to serve Wall Street a cold dish of failure. (Sinovac is now listed on Nasdaq under the ticker symbol "SVA," but trading has been suspended since February 2019 because of a fight for control between Yin and Pan.)

With 2020 hindsight, the decision not to push through with a SARS vaccine was a mistake. The DNA structure of the first SARS virus, known to scientists as SARS-CoV-1, is similar to COVID-19, the successor known technically as SARS-CoV-2.

If a SARS vaccine had been developed that had cross-over protection for COVID-19, that ounce of prevention − several million dollars − might have generated a cure much more quickly to contain the current massive economic losses – estimated at $9 trillion to $16 trillion, roughly equal at the top of the range to a year of economic output in China, the world's second-largest economy.

The fault for not pursuing the SARS vaccine cannot be laid on China. Where were the other 14 governments that attended the 2004 International Conference on SARS that made its alarming forecasts about the likelihood of a future coronavirus global pandemic? Couldn't these governments have pooled several million dollars to finance Phase II and III trials of Sinovac's SARS vaccine? These are questions that should haunt a world now trapped in fighting a war from a huge disadvantage, due to unpreparedness and a failure to heed the warnings.

Scientists in 2004 were not alone in this missed opportunity. In 2016, the United States also had a potential coronavirus vaccine in its grasp. As in the case of Sinovac, the opportunity slipped away due to a lack of funding.

Dr. Peter Hotez, dean of the National School of Tropical Medicine at the Baylor College of Medicine in Houston, Texas, told a Congressional committee in March that his group developed a SARS vaccine in 2016 that could have been used now to vaccinate against COVID-19. Clinical trials were never pursued.

“The bottom line is had we had these investments early on to carry this all the way through clinical trials years ago, we could have had a (COVID-19) vaccine ready to go,” Hotez told the U.S. House of Representatives Science, Space, and Technology Committee on March 5, 2020.

While SARS and Sinovac’s first big break faded, Yin and Pan knew they had something valuable. A powerful research and development machine for innovative and new vaccines in an outbreak-prone world. China wanted to be counted as a global leader in scientific and medical research, not merely a massive factory producing goods designed and commissioned by the West. Sinovac would get another chance at the spotlight.