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BIOBUSINESS

Year of the Compound

Will a novel codevelopment model open up China's drug discovery platform?

Mireille Gingras

Five years ago, Mireille Gingras was struggling to find early-stage drug compounds for a San Diego–based licensing consultancy company she founded called Sitara. She turned to the "usual pool" of companies and research institutions in Europe and Japan, but they'd all been picked dry, she says.

Then Gingras visited China, where she was "so impressed," she says, by the talent and scientific know-how of the so-called "returnees"—Chinese nationals who had trained and worked in Western countries but returned home to run academic labs and local biotech companies—that she rushed home and folded Sitara. She immediately set to work fundraising and amassing a team for a new company focused exclusively on the untapped treasure trove of Chinese compounds.

In January 2005, Gingras, a self-described "serial entrepreneur" who also started the software company MIR3 in 1999 after finishing two postdocs in neurobiology, founded HUYA Bioscience International, named after the Chinese abbreviations for Shanghai (Hù) and Asia (Yà). She set up offices in San Diego and Shanghai, and spent the bulk of the year traveling throughout China, meeting with the heads of research institutions, government biotechnology parks, and start-up companies, always keeping an eye out for the most promising new drug candidates.

China is a mammoth country that makes up around 20% of the world's population, yet its pharmaceutical industry accounts for only 3% of the global market. Innovative new drugs are rarely seen in China because the government sets drug prices based on manufacturing costs, not the costs of research and development. Thus, some Chinese drug developers are starting to look beyond their borders, and the United States, which accounts for nearly half of the world's $700 billion–plus pharmaceutical market, offers a potentially lucrative bazaar.

HUYA is pioneering a unique codevelopment model in which the company licenses early-stage compounds for development in Western countries, yet the local partners always retain the rights to the Chinese market. "There's no other company on the ground that's doing what we're doing," says Jan Tuttleman, HUYA's vice president of marketing. At last count, the company is now tracking close to 1,000 compounds that aren't in the public record, but which HUYA discovered through its "relationships with our partners that have taken the last four years to develop," says Tuttleman.

HUYA already licensed its first compound, a histone deacytelase (HDAC) inhibitor with antitumor activity, from Shenzhen-based Chipscreen Biosciences in March 2007. Seven months later, they also snapped up their second, an antiarrhythmic compound based on a traditional Chinese herbal medicine, which they licensed from the Shanghai Institute of Materia Medica. With that, HUYA became the first Western company ever to in-license two early-stage compounds in China, Gingras says. The first compound is now in two ongoing Phase II trials in China and similar trials are expected to start for the second compound shortly. The company also plans to start parallel Phase I trials in the United States for both compounds early next year. But despite the company's early success, the process has not been an easy one. One of the first hurdles: convincing the US Food and Drug Administration (FDA) to accept data coming out of another, largely unknown, country.

HUYA gonna call?

Last May, Gingras and her colleagues met with FDA officials to chat about moving forward with an Investigational New Drug ▶

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(IND) application for their HDAC inhibitor. "We really didn't know what to expect," says Michael Newman, executive vice president of HUYA's oncology unit. How would the FDA view data coming out of a developing nation? "We went out on a limb" by presenting all of the clinical and preclinical Chinese data to the FDA, he says. It paid off. The FDA agreed to accept all the Chinese data as supportive for opening an IND, which HUYA plans to file later this year. "It was the best possible outcome and it really validated our approach," Newman says.

> **"There's no other company on the ground that's doing what we're doing." *—Jan Tuttleman***

David LePay, the FDA's senior advisor for clinical science, declined to comment on any specific IND application, but says that HUYA is "probably taking the best approach" by coming to the FDA early in the development process. "Ultimately, there are certain flexibilities that exist, specifically in the regulations that apply to preclinical data" coming from outside the United States, he says.

HUYA is certainly not the only Western player in China. Most large pharmaceutical companies have marketing and manufacturing operations in China, and some, such as Roche and Bayer Schering Pharma, are even building research centers in the country. But HUYA is taking a different approach.

Once an early-stage compound is identified and licensed, HUYA uses the Chinese data to decide which experiments to repeat under different clinical and laboratory standards and which further efficacy and toxicity studies are still needed to move the compound into the Western development process, including the IND. Ultimately, HUYA plans to sell off its compounds to big Pharma so it can turn a profit. "Our model is up to and through to Phase II; we don't go further on," says Gingras. In the meantime, HUYA has angel investments keeping it afloat, Gingras says, though she declined to go into specifics.

HUYA's expertise is critical in a country where innovative drug discovery has been lacking, says Xiaoping Ye, CEO and founder of Tigermed, one of China's largest contract research organizations, which is working with HUYA to develop its two licensed compounds. "Until now, there have been less than 100 such filings" for innovative drug compounds with the Chinese FDA, he says. Furthermore, "because HUYA has an expert committee, they can provide more advice for how to develop a compound according to international standards."

"I think it's a great model," says Paul DeRidder, a venture partner at Crystal Cove Capital in Irvine, Calif., and a partner at Ample Luck International Capital Group in Beijing. "There's a lot of hidden IP and technology out of the academic centers in China that is yet to be mined."

Licensing early-stage compounds in China "certainly is unique," says Ding Ding, a China healthcare analyst with Susquehanna Financial Group in New York City. However, "the flipside is that it seems to be a reverse way of doing things." In terms of innovation, drug development, and cutting edge research, "the US is still by far the most advanced country in a rich field," she says, and she's not convinced that all that many promising compounds are being developed in China.

For all the compounds in China

HUYA now has around a dozen staff spread around four offices located in the major Chinese biotech hubs of Shanghai, Beijing, Shengzhen, and Hangzhou, as well as the same number of employees back at its US headquarters. HUYA's on-the-ground Chinese team continues to scout potential drug candidates in 17 therapeutic areas.

Around 30% of the compounds in HUYA's ever-growing database are IND-ready or IND-approved in China—what Gingras calls the "sweet spot"—and around 15% are in clinical development. HUYA has first-right-of-refusal for some of these, they've signed confidential disclosure agreements for others, and they're just keeping their eye on many more. (The company declined to provide a detailed breakdown of the portfolio.) To find more compounds, HUYA also has proprietary first-look agreements with six government bioparks, one research institution, and one university. "It's disproportionate how much intellectual property they have considering they're a pretty small outfit," says Eric Topol, chief academic officer for Scripps Health in La Jolla, Calif., who advises HUYA on cardiovascular medicine.

In December, HUYA announced an agreement with New Jersey–based Schering-Plough (SP) that granted the pharmaceutical giant exclusive leads on compounds relating to one specific therapeutic area (HUYA and SP declined to say which one). "This is a good way for us to rapidly establish contact with a large number of [Chinese] biotech companies and research parks," says David Nicholson, SP's senior vice president of global project management. In April, HUYA announced another "strategic alliance" with Illinois-based Abbott Laboratories.

These agreements with big Pharma illustrate HUYA's expanding business model, says Tuttleman. "Whereas before it was individual compounds we were just looking at, now we can monetize the whole portfolio and we can monetize our relationships with our Chinese partners." But Sarah Frew, a global health researcher at the University Health Network and the University of Toronto, warns that HUYA might have trouble finding willing partners for further licensing agreements. "Most Chinese companies are very internal looking" and wary of outside partners, she says.

Gingras remains optimistic. She credits her success partly on a "first mover advantage," but, moreover, she says, HUYA has excelled because it has developed the trust of its local Chinese partners.

"The world is clearly shrinking," says Peter Kowey, one of HUYA's clinical advisors at Thomas Jefferson University College of Medicine in Wynnewood, Penn. "There are a lot of places like China where they've caught up significantly in terms of their ability to do important medical and scientific trials. Partnering with these countries can only make things better." ■