HUTCHISON CHINA MEDITECH LTD

MEDIA CENTRE

Press Cutting

Publication: The Deal.com, Corporate Dealmaker
Date: 16th November 2007

Climbing the life-sciences curve

by K.C. Swanson

As Chinese businesses improve their capabilities in multiple fields, they're entering into deals with multinational companies that would have been unthinkable just a few years ago. A prime example is the tie-up announced in August between Eli Lilly and Co. and drug R&D firm Hutchison MediPharma Ltd.

The deal marks a big advance in the place of Chinese companies in global drug discovery and development. Shanghai-based Hutchison will be responsible for identifying and selecting chemical compounds focused on targets in cancer and inflammation, while Lilly will give technical advice and take care of clinical development.

That may not sound like a milestone, since big Western pharmas — including Lilly — have been rapidly boosting their R&D presence in China over the past few years. But most of those collaborations have involved fairly straightforward, albeit sophisticated, chemistry work. What's striking about Lilly's deal with Hutchison is that, for the first time, a foreign drugmaker is handing off a key part of its research process to a mainland company — a collaboration that requires drug discovery expertise, not just chemistry skills. More such deals are probably ahead.

It's not surprising that Lilly is behind the first one. Over the past few years, Lilly has made partnerships like this a key ingredient of its R&D strategy (see Corporate Dealmaker, Spring 2004). As one of the smaller of the big pharmas, with 2006 revenue of $15.7 billion, it has sought to cut overhead while tapping into new, external research pipelines — especially at biotechs that have supplied many of the drugs that have lately made it into clinical trials.

Now China's coming into the picture. "We see Asia as an opportunity to try to experiment with different ways to do drug discovery," says Guoxin Zhu, Lilly's director of discovery chemistry research. "We can leverage small biotechs to make quick decisions, be more flexible, maybe specialize in a particular area. It's more a networking approach rather than capital investment."

China is figuring ever more prominently in the strategies of global drugmakers, both as a locale for R&D projects and as a major source of customers. From the ninth-biggest pharma market worldwide in 2005, the nation is expected to become the seventh largest by 2010, according to IMS Health Inc.

For now, the local industry is dominated by generic drugmakers, but foreign firms would like to win approval to sell more of their own medicines into China (see sidebar about how some are working to improve the drug regulatory process). Besides being a venue for early-stage research on new drugs, China could one day become an important hub for the later-stage work of clinical

development. Drug multinationals are pushing to cut down on red tape so they can conduct clinical trials more easily.

In the meantime, China's own research talent pool has been rapidly developing. More and more of its top-flight scientists are returning home from overseas, helping build up an R&D ecosystem.

Five year-old biotech firm Hutchison, backed by the deep-pocketed Hutchison Whampoa Ltd. conglomerate, is one of the rising stars in this market. It has developed two of its own drug candidates, now in clinical development in the U.S. — one focused on head and neck cancer, the other on inflammatory bowel diseases — and has filed 66 patents in the U.S. and China. Last year it struck two separate collaboration deals, one with Merck KGaA to research anti-cancer drugs and another with Procter & Gamble Co. to develop ingredients from traditional Chinese medicine for use in cosmetics.

Hutchison's top managers are mostly Chinese nationals who studied abroad and claim heavyweight experience at multinational pharmas. Run by Samantha Du, who earned a Ph.D. in the U.S. and worked for Pfizer Inc.'s R&D arm, Hutchison employs a staff of 140 in Shanghai's Zhangjiang Hi-Tech Park, where it has a 54,000-square-foot research site.

Hutchison's deal with Lilly follows the general outlines of those struck between biotechs and pharmas elsewhere in the world, with Hutchison pocketing an up-front payment and annual R&D support fees. It's also in line to receive milestone payments of up to $29 million per drug candidate and royalties on the sale of any drugs that go to market. Lilly, viewed as a leader in oncology research, can offer useful insights during the R&D process, says Du. "And because Lilly also has global development capabilities, they can then commercialize" the fruits of research.

For Lilly, the collaboration reflects the latest evolution in its increasingly ambitious plans for China. As long ago as 1928, Lilly opened a sales office in Shanghai. In 1995, after a long hiatus following the Communist takeover, it formed a joint venture to open a $28 million pharmaceuticals manufacturing plant.

On the research side, Lilly started working with local academics on a handful of projects around 2000, then decided to scale up its R&D work. A logical next step was to outsource to a contract research organization. These firms typically take on discrete, specific R&D assignments for a fee, freeing up pharmas to focus on the more innovative work. China didn't have any contract research organizations, or CROs, though — so Lilly decided to help create one. It recruited a retired government official and former director of the Shanghai Institute of Organic Chemistry to found Shanghai ChemExplorer Co. Ltd., a dedicated CRO. ChemExplorer, which now claims some 200 employees, has conducted research exclusively for Lilly since its opening in June 2002.

The partnership with ChemExplorer is essentially a pay-for-service arrangement, says Zhu. The Hutchison deal, by contrast, calls for risk sharing and intellectual input from the Chinese partner. "With Hutchison we're looking for new capabilities, some that Lilly may not have," Zhu explains.

Lilly's Hutchison relationship also reflects a new willingness to allow mainland-based scientists to delve into research where the company has significant intellectual property to safeguard. Historically, Lilly — like every other foreign pharma in China — has been anxious to protect its intellectual property there. Last year, in an interview sponsored by the Kaiser Family Foundation in Washington, Lilly CEO and chairman Sidney Taurel talked about the need for precautions in China, where the company employs 20% of its global chemists.

"So what we have done so far is to sort of separate our R&D activities between what we would call judgment-based activities and rules-based activities," he said at the time. In China, Taurel explained, Lilly's researchers "work more on the latter, on the rules-based activities."

The deal with Hutchison this year marks a shift from that approach. Unlike the CROs typically involved in research partnerships on the mainland, Hutchison views innovation as central to its own mission. In fact, Du says Hutchison may subcontract out some of the more basic work involved in the Lilly project to local CROs. That way, Hutchison's own scientists can focus on more complex problems. "In terms of the design, the thinking, the model building, that's all what we'll be doing internally. We're doing very novel, innovative research."

Industry watchers say they expect more deals like the Lilly-Hutchison one to follow as China's R&D capabilities evolve — especially as more of its top scientists return home and take up leading research roles for global pharmas on the mainland.

"I think it's a reasonable prediction to say that as more companies like Hutchison MediPharma are created and mature, many Western pharmas will want to do deals with them," says Eric Meyers, vice president of global initiatives at Cambridge Healthtech Associates in Waltham, Mass. Through such deals, mainland research firms can nab partners with global sales and distribution arms, while Western pharmas, by bringing on partners with lower labor costs, can "put many more molecules through the pipeline" for the same amount of money, Meyers says.

Another force driving the China-based research trend is the convergence of disease patterns in the West and the East. As Asians have become richer, they've also gotten fatter and more sedentary. As a result, Lilly's therapeutic focus in China has shifted over the past decade from antibiotics to treatments for developed-world maladies such as diabetes and heart conditions.

There are a few exceptions: for example, hepatitis B is more prevalent in Asia and hepatitis C more common in the U.S.

In the past, we had a project for hepatitis B that was only for Asia, specifically China," recalls Rajiv Gulati, director, China-–India strategy for Eli Lilly. But now, he adds, "we're basically doing global research for global purposes, since the disease pattern in China has begun to resemble the U.S. and other Western countries."

High-end research deals have the added benefit of helping sweeten government relations. Beijing wants China's own hidebound pharma sector, dominated by generic drugmakers, to become more competitive. R&D collaborations feed into that push.

"It would be very hard for Chinese pharma by itself to become more innovative. But with the emergence of MNC [multinational-corporation] R&D in China, I do think it's going to foster a talent pool for innovative research," says James Shen, publisher of Pharma China, an English-language report. "And this talent is likely eventually to be transferred, so it will help foster the innovativeness of the local pharma industry."

Lately, a number of the leading pharmas have started bulking up their research presence in China. In the past 18 months AstraZeneca plc, Novartis AG and Glaxo–SmithKline plc have all pledged to spend hundreds of millions of dollars on setting up and outfitting their own R&D centers. Some say they want their China facilities to eventually become key hubs in their global research. Many more drugmakers are outsourcing work to China's fast-emerging crop of CROs.

But so far, no one besides Lilly has a strategy that relies so much on a local firm, and for such high-level research. And that's not all Lilly is doing. In part to gain a better understanding of the emerging local biotech scene, this June Lilly Asian Ventures — a new spinoff of the company's main venture capital arm — invested $10 million in BioVeda China, a Shanghai-based VC fund focused on life sciences in China.

Certainly, Lilly takes care to cast its China strategy — involving investments both in know-how and dollars — as one that will ultimately benefit the local pharmaceuticals industry. As Zhu puts it,

"We're committed to drug discovery capabilities in the chain, but our approach is working with local companies and helping them reach the highest level of drug discovery."

Lilly's move to offshore more R&D has already met with some resistance at home. At Lilly's 2007 annual shareholder meeting in April, shareholders acting on behalf of People for the Ethical Treatment of Animals submitted proposals asking the board of directors to report both on its international outsourcing of animal research and on whether the company's animal care guidelines could be extended to cover contract laboratories.

"Many of the countries to which the company [Lilly] is re-locating its animal research and testing are known for having no or poor animal welfare standards and negligible oversight," said one of the Peta statements, highlighting China as one of them.

In its statement opposing the proposal, Lilly didn't mention China but said it requires all its contractors to "treat animals in a humane manner." It also said it has increased oversight of such firms to make sure they adhere to its requirements. Both of the Peta proposals failed to pass.

As pharmas extend their collaborations in China beyond straightforward chemistry, preclinical safety studies — typically involving tests on animals — are likely to be one of the next growth areas.

One study in early 2007 by Cambridge Healthtech Associates in Waltham, Mass., on behalf of seven Western pharmaceuticals companies found that several Chinese CROs were close to being able to carry out preclinical safety studies in China according to Western standards of animal care and the prevailing protocol known as Good Laboratory Practices. They would require extra mentoring, to be sure. But even accounting for the expense of extra oversight, shifting such a project to China would likely cut costs by some 40% to 60%, estimates Meyers.

Not only is demand growing for more R&D-related services in China, but the supply side is rising to meet it. Several hundred CROs have sprung up in China in just the past five years or so. While some manufacture active pharmaceutical ingredients and conduct outsourced clinical studies, a select group is starting to branch into more complex offerings. WuXi Pharmatech Co. Ltd., a CRO that listed on the New York Stock Exchange in August, focuses on discovery chemistry work for foreign pharmas, but this year it also started doing research in drug metabolism and pharmacokinetics, or DMPK, and general toxicology. Its two biggest customers are Pfizer and Merck.

The CROs don't begin to rival Hutchison, but their growth highlights how China's research industry is gaining momentum — a process that's bound to accelerate as more foreign-funded R&D centers get up and running. Du says she looks forward to having more mainland competitors, the better to spur local innovation in drug R&D. If that happens, expect to see a lot more deals like the Lilly-Hutchison one. CD

###

SIDEBAR
Helping to build a regulatory framework

China's State Food and Drug Administration is underfunded, understaffed and smeared by scandal. This July the head of the agency, who was found to have taken hundreds of thousands of dollars in bribes, was executed.

Foreign pharmas know their plans in China require a better regulatory system. So they are teaching local regulators how drug regulation works in the U.S. and Europe and helping set up academic programs in pharmaceutical studies.

Last year Merck & Co. created a novel position in its Beijing office, tapping a Chinese national, Zili Li, who'd notched up years of experience at the U.S. Food and Drug Administration. Li's job title is director of clinical research operations in Asia-Pacific, but one of his main responsibilities is working with the SFDA on international best practices in drug regulation.

That's not easy, given the SFDA works under severe constraints. In 2005, its Center for Drug Evaluation had only 120 employees and approved 1,113 new drugs for sale. Its counterpart at the U.S. FDA, with a far bigger staff of 1,800, approved a mere 20 new drugs. Yet Li gives the agency credit for "trying to be more scientific in its decision making. Without that, we wouldn’t have a role."

This August the agency pledged to spend $1.2 billion to upgrade drug and food oversight. It's also working to cut review time to approve the sale of priority drugs in China.

"China has an interest in being an international player," Li says. "But they need improvement in late phase drug development capacity—not only on how to conduct clinical trials, but on how to design clinical trial protocols, and how to interact with U.S. regulatory agencies. If they don’t have this knowledge, how will they move products overseas?"

Merck is also now preparing 2,000 Chinese-language copies of the U.S.-published "Textbook of Pharmacoepidemiology" (list price: $80). Early next year, it plans to distribute the textbook free of charge to regulatory agencies and universities.

Merck — along with a host of other companies, including Eli Lilly and Co., Pfizer Inc., Amgen Inc. and Novartis AG — also helped advise on the creation of a new master's program at Beijing University. The first class of students for the program in international pharmaceuticals engineering management were enrolled in March 2007.

###