

BRIDGE TO INNOVATION

BY STEPHEN HANSEN, ASSOCIATE EDITOR

While **Zai Lab Ltd.** has joined the ranks of Chinese biotechs making a splash on NASDAQ, less noticed may be the first wave of China-based players moving into Boston to jump-start their push into novel drug development.

This year has seen Chinese pharmas like **Qilu Pharmaceutical Co. Ltd.** and **Luye Pharma Group Ltd.** open R&D operations in the East Coast life sciences hub, viewing the city as a gateway to top-tier translational science and scientific talent as well as potential partners.

According to eight Chinese executives and investors contacted by BioCentury, scientific talent is the primary draw to Boston.

And while investors are pouring huge amounts of capital into China-based companies, domestically discovered innovative assets remain rare, and, therefore expensive. Setting up R&D in a region that is richly supported by both VCs and NIH funding means the innovative translational opportunities are plentiful, even if they don't come at a discount.

"In terms of innovative drug discovery and research, there is still a gap between China and the Western world," Lijun Wu, an entrepreneur-in-residence at Atlas Ventures, told BioCentury. "That is probably one of the major reasons a lot of Chinese companies are setting up shop in the Boston area."

The companies say they aren't looking to Boston as a short-cut to snatch up technologies and transfer them back home. Instead, they are viewing their new subsidiaries as the heart of their innovation strategies. Assuming initial success, each of the five companies that spoke to BioCentury has plans to expand.

Moreover the Chinese executives and investors expect to see more domestic Chinese companies follow this group of first movers into Boston.

BOSTON ADVANTAGE

June's entrance of **China FDA** into the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) is widely viewed as a watershed in the government's wave of regulatory, reimbursement and data exclusivity reforms to create a globally competitive life science ecosystem in China.

The reforms, coupled with an influx of capital, have triggered a growth in biotech start-ups pursuing innovative science, while many domestic pharmas that historically focused on generics or me-toos now want to transform their businesses with novel drug development.

"In recent years there's been a lot of money that's wanted to invest in biotech or drug development," Wu said. "I think it is still in its infancy in a lot of places because it just happened so fast, but there are definitely capital resources and recognition that biotech and drug discovery is really the key. The government is supporting it like crazy."

The challenge, however, is that innovative translational programs and the pool of scientists to develop them is not growing fast enough to meet domestic demand.

"In China, in terms of the quality of the innovation and the number of novel programs, it still has a gap behind the U.S., for sure," said Jonathan Zhao of Lilly Asia Ventures.

"If you try to find true innovation in China, the price is often fairly high. The bang for the buck isn't there. You have more capital, but fewer innovations, so it is supply and demand," he added. "From an investment point of view, the value is higher in the U.S. You get more bang for your buck in the U.S. for early innovation."

VcanBio Cell & Gene Engineering Corp. Ltd. decided it needed to establish a beachhead in the U.S. to expand its cell banking business into cell and gene therapy.

The company, which is listed in Shanghai with a market cap of RMB11 billion (\$1.7 billion) and has subsidiaries in 25 Chinese provinces, chose Boston to improve its access to the most advanced cell and gene therapy technologies, and to people who have experience developing them.

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“For biologics and biopharmaceuticals, you need access to more advanced technologies,” said John Lu, president and CEO of VcanBio Center for Translational Biotechnology, one of VcanBio’s U.S. subsidiaries. “Boston is No. 1 in the world for biological sciences, like its own Silicon Valley.”

While none of the Chinese would discount the importance of the San Francisco Bay Area and other life science centers in the U.S., the sheer density of new and existing companies is a compelling reason to build a presence in Boston.

For example, **WuXi AppTec Co. Ltd.**, a subsidiary of **New WuXi Life Science Ltd.**, established a presence in Boston in early 2015 to expand its clinical development and manufacturing services business.

Shortly thereafter New WuXi Life Science acquired Boston genomic analysis and bioinformatics play NextCode Health, which is now known as **W u Xi NextCode Gen omi cs In c.**

The parent company’s VC arm, WuXi Healthcare Ventures, also has an office in Cambridge, Mass.

The funding provided to local academic institutions for translational science, along with a healthy VC environment for start-ups that could be future partners are further draws.

Qilu’s Larry Cai, who is head of business development, New England, cited the NIH funding to Boston-area institutions.

In 2016, five of the top six independent hospitals to receive NIH funding were in Boston: **Massach u setts Gen er al Hospital , Brigham and Women’s Hospital , Boston Children’s Hospital , Beth Israel Deaconess Medical Center** and **Dan a-Farber Cancer Institute.**

Total NIH funding for academic institutions, hospitals and non-profits in the Boston area was over \$2.2 billion in 2016.

On the industry side, New England companies raised over \$2.8 billion in venture capital in 2016, the largest of any U.S. region, according to BioCentury’s BCIQ database. The Bay Area and Texas came in at \$2.5 billion, although the Texas figure included \$2.3 billion raised by wound care company **Acel i ty H ol di n gs In c.** in three rounds of venture debt. The Bay Area and New England figures do not include any venture debt.

New England companies also raised the most in series A rounds at \$850.6 million, with the Bay Area second at \$688 million.

Cai said Qilu and other Chinese companies also have been drawn by local government support for the sector. He cited state legislation from 2008 that provided over \$1 billion to the life sciences industry and established the Massachusetts Life Sciences Center, plus recent proposals in the Massachusetts Legislature for an additional \$500 million for the next five years.

PEOPLE FIRST

“The best and the brightest scientists are still in the U.S., including Chinese-Americans,” Lilly Asia Ventures’ Zhao told BioCentury.

And for many of Chinese newcomers, this is the main reason for picking Boston.

“The most important thing we are focused on is the people, the talent,” Lu said. “If you don’t have the talent, you can’t do anything.”

VcanBio set up its two U.S. subsidiaries in Boston. In 2015, the company established VcanBio USA, its R&D center and strategic investment arm, and the following year it created the VcanBio Center for Translational Biotechnology (VCTB), a cell therapy and biologics services business.

VcanBio USA has six employees so far, while VCTB has five employees with plans to hire another 10 by year end across both subsidiaries.

Lu noted that institutions such as **Harvard University** and **Massachusetts Institute of Technology** churn out life science Ph.D.’s. Indeed, according to the Massachusetts Biotechnology Council (MassBio), Massachusetts universities produced 1,563 Ph.D. graduates with a life sciences-related degree in 2016, an increase of 31% vs. 2011.

“In China, if you find an MIT or Harvard Ph.D., it is very rare,” Lu said. “Now that we are here, we have a building with four or five of the team that are MIT or Harvard graduates. It is so concentrated, it makes it unique for recruiting people and that is one of the most important points.”

VcanBio’s R&D programs include a preclinical **CD19**-targeted chimeric antigen receptor (CAR) T therapy to treat acute leukemias, as well as preclinical hematopoietic stem cell programs for a variety of indications, including liver diseases and graft-versus-host disease (GvHD).

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Linjun Wu, Atlas Ventures

VcanBio also has a joint venture with **Eureka Therapeutics Inc.** to develop ET1402L1-CAR, a CAR T therapy against **alpha fetoprotein (AFP)** that is expected to enter the clinic this year to treat liver cancer.

The Chinese government has been aggressively recruiting scientific talent back to the country via programs such as The Thousand Talents Plan. And many of China’s biotech start-ups, such as Zai Lab and **Canbridge Life Sciences Ltd.**, were founded by Chinese nationals who returned after accumulating experience working for Western pharma companies.

Many of the ex-pats and their families have settled into the U.S., however, which has created a pool of Chinese expertise that can help the newcomer companies get established in the Boston ecosystem.

“They recognize there’s a lot of talent here that for whatever reasons cannot relocate back to China,” said Wu.

Wu was SVP of preclinical and early clinical development at Boston autoimmune play **Delinia Inc.**, which this year was acquired by **Celgene Corp.** She also had held R&D positions at Boston area companies **Concert Pharmaceuticals Inc.** and **Resolvix Pharmaceuticals Inc.**

Lu is another example. VcanBio recruited the former senior director of research at Boston cell therapy company **Ocata Therapeutics Inc.** in 2016, after **Astellas Pharma Inc.** acquired Ocata for \$379 million.

“So how could a Chinese company tap into their talent? They can set up a shop or early stage lab,” said Lilly Asia’s Zhao. “The talent, because it is so concentrated in Boston, makes it a lot easier for these Chinese companies to find these talents locally, but that have a global impact.”

Zhao was previously executive director of global commercial operations at **Amgen Inc.**, and prior to that was based in Boston as Asia strategy lead, strategy and portfolio solutions at **Pfizer Inc.**

Most of the Chinese executives said they were agnostic to nationality of prospective employees, but until their companies become better known in the Boston community, working through established Chinese networks often proved the easier route to attracting talent.

Sean Fu, president of Luye Boston R&D LLC, said attracting talent was a struggle at first. “Luye is not well known,” he said. “It takes a lot of introductions, a lot of work to get our name out there.”

Fu has had to initially rely on established Chinese networks to hire employees to the subsidiary of Shanghai specialty pharma Luye Pharma Group. “We want to tap into the broader talent base, but I think it takes time,” he said.

Still, Fu has seen a change in attitude. Luye has been able to hire non-Chinese in business development and research positions. “That’s a good sign, moving in the right direction,” he said.

VcanBio’s initial U.S. hires similarly were mostly through its Chinese network. But Lu also noted, “Our official working language in our organization is English, so anyone who is fluent in English and has the proper education will be fine working in our company.”

Hiring non-Chinese nationals wasn’t an issue for Sean Cao, who now is managing director of C-Bridge Capital, when he set up **Simcere Pharmaceuticals Group’s** U.S. subsidiary, Simcere of America Inc.

Cao, who was president of the unit, relied on his own pharma and alumni networks. He was based in the Boston area as senior director of alternative partnerships at **Sanofi** and has an MBA from The Wharton School at the **University of Pennsylvania** and a Ph.D. from the **University of Virginia**.

“Most of the people we brought in are not Chinese,” said Cao.

Simcere is a large domestic pharma that is building a more innovative pipeline through in-house discovery and licensing. The company raised \$181.3 million in a 2007 IPO on NASDAQ, but was taken private in 2013 through a management-led buyout. It doesn’t disclose its annual sales.

Cao moved on to found the Boston office of C-Bridge Capital, which in May closed its second fund at \$400 million.

INNOVATION CONCENTRATION

Beyond the people, Chinese companies cited access to the innovation ecosystem -- translational science and prospective partners in small biotechs and big pharma -- as a driving factor for establishing a presence in Boston.

Cai said this was a key driver for Qilu as the company seeks to expand beyond generics into immuno-oncology.

The Chinese pharma posted sales of \$2.1 billion in 2016.

“We all know that to have sustainable growth, you cannot simply rely on generics or biosimilars, you have to get into innovation,” he said. “To implement this strategy, Qilu really looked at where is the hotbed for innovation? And they found Boston is certainly the epicenter of life sciences innovation.”

Qilu first entered the U.S. in 2015 by opening a site in Seattle, Sound Biologics, which is registered as **Q i l u P u g e t S o u n d B i o t h e r a p e u t i c s C o r p.** But the company made its largest U.S. commitment in Boston when it founded QLB Biotherapeutics Inc. with a \$40 million investment last year. The unit comprises Qilu’s global early stage R&D center for the discovery and preclinical development of immuno-oncology biologics.

“Boston has distanced itself from the rest of the pack for being the hotbed for life sciences innovation,” he said. “Boston is very focused on life sciences, from the government, academia, biotech and pharma, it is all focused on this area heavily.”

Details of Qilu’s internal immuno-oncology pipeline are not disclosed. But once QLB’s projects are ready to enter the clinic, they’ll be further developed and commercialized in China, where the company has expertise in conducting clinical trials.

Cai said Qilu may seek partnerships for ex-China rights, with a long-term goal of global commercialization.

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John Lu, VcanBio

Qilu is also hoping to access innovation via its Qilu Boston Innovation Center (QBIC), which launched in tandem with QLB. Cai said QBIC is an “open innovation platform” that plans to incubate start-ups that are pursuing therapies that fit into Qilu’s strategy.

He said these could be for cancer or one of the other therapy areas where Qilu has expertise, such as cardiovascular, infectious diseases, neurology, psychiatry and ophthalmology. Cai said several start-ups are in talks to join the incubator.

Qilu views QLB as a long-term investment, said Cai.

“This is not just setting up a BD office to try and in-license some projects back to China,” he said. “Qilu realized you need a lot more than that to be able to establish credibility and relationships; you need a physical presence here. You need to have a lab, a team that utilizes the talents in the area, and the easy access to the most innovative ideas.”

Cai added: “As long as it is advantageous to do innovative research in the U.S., which should last for the foreseeable future, Qilu is committed to being here. The experience and talent need the right environment to thrive and we see the innovative research in the U.S. still leads the world.”

PARTNER POTENTIAL

Luye established its Boston R&D center in July to build capabilities toward more innovative drug discovery and development. The HK\$15.1 billion (\$1.9 billion) Hong Kong-listed company develops small molecules for cancer, neurology and endocrine/metabolic indications, traditional Chinese medicines and biosimilars.

Fu said most of Luye’s innovation has been focused on drug delivery, where the company takes a known molecule and seeks to improve administration, compliance or the therapeutic window of the drug.

Fu said Luye aims to use its new R&D Center to add new biology and drug discovery capabilities.

“This is the jump-off point for building Luye’s innovative R&D capability,” he said. “We want to move up to new entities, and we want to eventually move up to covering the entire spectrum of innovation, including new targets.”

Fu said he realizes that Luye can’t immediately dive into new target discovery. To start, the Boston unit will focus on partnering with other biotechs to co-develop biologics. He said Boston was Luye’s first choice so the R&D center could be located close to so many potential partners.

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Larry Cai, Qilu Pharma

He said Luye is looking to partner with companies developing therapies in cancer, in particular assets that can be combined in the immuno-oncology setting, as well as neurology, cardiovascular and diabetes.

Luye Boston R&D has 13,000 square feet of lab space with options to expand. Fu said the unit aims to have 10 employees by year end. But the long-term goal is to grow to 30-50 people.

“Think about a start-up company that can deliver meaningful assets; that’s probably the sweet spot in terms of size,” he said.

Cambridge Life Sciences also established its first U.S. presence in Boston to be close to innovative potential partners. The company in-licenses Chinese or Asian rights to therapies developed by Western biotechs and conducts the Chinese clinical development.

Setting up a BD office in Boston last year was a natural step for founder and CEO James Xue, who has a network of former **Genzyme Corp.** colleagues who have gone on to populate numerous Boston-based biotechs.

Xue said Cambridge’s goal is to expand beyond China-focused development.

“Just like how Western companies have built R&D centers in China to help their global reach and eventually their global launch, we have the same desires and aspirations,” he told BioCentury. “One day we’d like to launch truly first-in-class products not just in the China market, but beyond in Western markets. We therefore have started to build our organization and capabilities that eventually would allow that to happen.”

Xue said Cambridge hopes to use its Boston office as the base for conducting clinical operations in the U.S. for future pipeline candidates.

“It is quite straightforward for us to build not just business development facilities in the Boston area, but it would also give us a base to further recruit talent and build a team to help us implement the global development plan, using Boston as a hub,” he said.

Cambridge’s lead program is asunercept (**CAN-008**, APG101), a fusion protein consisting of the extracellular domain of **Fas receptor (CD95)** fused to the Fc region of human IgG that inhibits CD95-**CD95 ligand** interactions. The molecule is in a Phase I/II trial in Taiwan to treat newly diagnosed glioblastoma multiforme (GBM), and is expected to start a Phase II/III for GBM in China early next year.

Cambridge has Chinese rights to asunercept from **Apogenix AG** under a 2015 deal.

COMPANIES AND INSTITUTIONS MENTIONED

Acelity Holdings Inc., San Antonio, Texas
Amgen Inc. (NASDAQ:AMGN), Thousand Oaks, Calif.
Apogenix AG, Heidelberg, Germany
Astellas Pharma Inc. (Tokyo:4503), Tokyo, Japan
Beth Israel Deaconess Medical Center, Boston, Mass.
Boston Children’s Hospital, Boston, Mass.
Brigham and Women’s Hospital, Boston, Mass.
Cambridge Life Sciences Ltd., Beijing, China
Celgene Corp. (NASDAQ:CELG), Summit, N.J.
China Food and Drug Administration (CFDA), Beijing, China
Concert Pharmaceuticals Inc. (NASDAQ:CNCE), Lexington, Mass.
Dana-Farber Cancer Institute, Boston, Mass.
Eureka Therapeutics Inc., Emeryville, Calif.
Harvard University, Cambridge, Mass.
Genzyme Corp., Cambridge, Mass.
Luye Pharma Group Ltd. (HKSE:2186), Shanghai, China
Massachusetts Biotechnology Council (MassBio), Boston, Mass.
Massachusetts General Hospital, Boston, Mass.
Massachusetts Institute of Technology, Cambridge, Mass.
National Institutes of Health, Bethesda, Md.
New WuXi Life Science Ltd., Shanghai, China
Pfizer Inc. (NYSE:PFE), New York, N.Y.
Qilu Pharmaceutical Co. Ltd., Jinan, China
Resolvix Pharmaceuticals Inc., Cambridge, Mass.
Sanofi (Euronext:SAN; NYSE:SNY), Paris, France
Sincere Pharmaceutical Group, Nanjing, China
University of Virginia, Charlottesville, Va.
VcanBio Cell & Gene Engineering Corp. Ltd. (Shanghai:600645), Tianjin, China
The Wharton School at the University of Pennsylvania, Philadelphia, Pa.
Zai Lab Ltd. (NASDAQ:ZLAB), Shanghai, China

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