BIOWORLD™ ASIA

CONCISE, ACTIONABLE INSIGHT

MAY 14, 2014 | BIOTECH'S MOST RESPECTED NEWS SOURCE FOR MORE THAN 20 YEARS | VOLUME 2, NO. 20

Go early, go big, go global: Aslan licenses preclinical MAb for asthma

By Shannon Ellis, Staff Writer

SHANGHAI – Aslan Pharmaceuticals Pte Ltd. signed an agreement for global rights with CSL Ltd. to develop an anti-IL13 receptor monoclonal antibody, CSL334, for severe to moderate asthma.

Aslan, of Taipei and Singapore, will fund and develop the drug to become known as Aslan004 through to clinical proof of concept in a development program to be conducted in Asia.

Deal terms were undisclosed, but CSL, of Melbourne, will be entitled to a share of returns generated by Aslan from partnering the project at a later stage.

"The licensing deal, allows us to develop and ultimately sublicense the global

See Aslan, page 6

Daiichi Sankyo reveals 4 patient deaths in halted nimotuzumab trial

By Dan Poppy, Contributing Writer

Tokyo-based Daiichi Sankyo Co. Ltd. discontinued a phase III trial for nimotuzumab on the recommendation of an independent data monitoring committee after four treatment-related deaths were observed, all in the nimotuzumab arm.

An ongoing phase III nimotuzumab trial

See Daiichi, page 7

THE BIOWORLD BIOME

Further doubts cast on purported STAP stem cell technique

By John Fox, Staff Writer

HONG KONG – Chinese University of Hong Kong (CUHK) researchers report being unable to replicate controversial research purporting to create stimulus-triggered acquisition of pluripotent

See Stem cells, page 8

IN THE CLINIC

Yakult Honsha, 4SC to tackle liver cancer in Japanese patients

By Dan Poppy, Contributing Writer

Japanese firm Yakult Honsha Co. Ltd. completed phase I trials for resminostat – licensed from German firm 4SC AG – in solid tumors, as the partners hope to move forward with the target indication

See Liver cancer, page 9

INDIA

Prequalification status issued for Shantha's pentavalent vaccine

By Cornelia Zou, Staff Writer

HONG KONG – Four years after it was sidelined, a pentavalent vaccine produced by the Indian arm of Sanofi Pasteur (the vaccine division of Sanofi SA) – Shantha Biotechnics

See Shantha, page 10

IN THIS ISSUE

JAPAN

Riken will not review misconduct verdict on stem cell biologist

By Cornelia Zou, Staff Writer

HONG KONG – A Japanese research institute has closed a controversial chapter in its history by refusing to reinvestigate misconduct by a high-profile scientist and has set up a

See Riken, page 11

REGULATORY

FDA approves first ever China-made biologic for use in U.S. trials

By Cornelia Zou, Staff Writer

HONG KONG – The U.S. FDA has, for the first time ever, approved the use of a biologic product made by a Chinese company in U.S. investigational new drug trials.

See Biologic, page 12

To subscribe, call (770) 810-3144 or (800) 477-6307 if calling from the U.S. and Canada or email bioworld.sales-support@thomsonreuters.com. For customer service inquiries call (215) 386-0100 or (800) 336-4474 if calling from the U.S. and Canada or email bioworld.support@thomsonreuters.com.

THOMSON REUTERS™

Local VCs boost prospects of China's life sciences sector

By Marie Powers, Staff Writer

SUZHOU, China – Venture investing in China's life sciences industry continued a three-year upswing in 2013, according to speakers at the Chinabio Partnering Forum, with more than $1 billion in publicly disclosed deals last year. Cynics might correctly argue the amount represents just a fraction of the annual R&D budget of a single large pharma. Still, the steady rise in venture capital (VC) – much of it homegrown – represents another key indicator that China is building a sustainable life sciences ecosystem.

Capital is flowing to China's life sciences industry from a variety of sources, including government funds and outside partners, Greg Scott, president and founder of Shanghai-based Chinabio LLC, said during a panel on investment activity. But domestic VCs play an increasingly important role. For example, Qiming Venture Partners LLC, which raised its first fund in 2006, now manages four funds exclusively focused on China that collectively account for more than $1.6 billion in assets, according to Nisa Leung, managing partner for health care. Investments in life sciences companies – drug development, medical devices, health care information technology and health care services – account for roughly one-third of the firm's 90 portfolio companies. For example, the Shanghai-based VC co-led last year's $20 million series C for Shenogen Pharma Group, of Beijing. (See *BioWorld Asia*, Nov. 6, 2013.)

Cenova Ventures, a boutique life sciences investment firm founded in 2010, has two funds under management, with Merck & Co. Inc. as lead investor in its Innovation Fund, established in 2012. The Shanghai-based VC invests "very selectively" across China's health care sector, said Jun Wu, chairman and managing partner. For example, the company holds stakes in immunotherapy developers Birdie Biotech and Oriengene Biotechnology.

Both Cenova funds also are based on China's yuan renminbi (RMB) currency, mirroring a larger movement in China to conduct business in RMB. Banking experts predict that, by next year, about 30 percent of China's trade, or about $2 trillion, will be settled in RMB rather than dollars or other currencies.

For small deals looking for an exit in China, RMB can be deployed more quickly than U.S. dollars, VC panelists agreed, characterizing RMB transactions as "more mainstream" than in years past. The downside is that most life sciences limited partners, including big pharmas, are located outside China and don't want to deal with the currency hassle, Wu said.

SEEKING 'REALLY SUCCESSFUL STORY IN DRUG DEVELOPMENT'

Some of China's life sciences VC investments also are flowing from domestic success stories. For example, Wuxi Venture Fund, the corporate VC fund of global contract research organization Wuxi App Tec, has made a $50 million commitment to the sector, including therapeutics, diagnostics, research tools and technology, said Sofie Qiao, managing director. Before joining the Wuxi fund late last year, Qiao was helping to guide U.S./China hybrid company Lead Therapeutics Inc. to a potential $100 million acquisition by Biomarin Pharmaceuticals Inc. less than three years after the company's $17 million series A. (See *BioWorld Today*, Nov. 6, 2007, and Feb. 8, 2010.)

The Wuxi fund invests in companies both in China and the States, "and the U.S.-China hybrid model is favored," Qiao said, describing life science innovation developed in the U.S. for deployment in China.

The fund is not afraid to invest in promising preclinical assets, last year participating with Arch Venture Partners and Flagship Ventures in a $30 million series A for Watertown, Mass.-based Syros Pharmaceuticals Inc. The discovery-stage biotech is exploring the use of gene control to develop cancer therapeutics. Syros was co-founded by professors Richard Young, of the Whitehead Institute at the Massachusetts Institute of Technology, and Jay Bradner and Nathanael Gray,

See VCs, page 13

BIOWORLD ASIA

BioWorld™ Asia (ISSN# 1541-0587) is published every Wednesday by Thomson Reuters, 115 Perimeter Center Place, Suite 1100, Atlanta, GA 30346 U.S.A.

OUR NEWSROOM

Atlanta - Lynn Yoffee (Executive Editor), Jennifer Boggs & Amanda Lanier (Managing Editors), Peter Winter (*BioWorld Insight* Editor), Karen Pihl-Carey (Database Editor), Ann Duncan (Senior Production Editor), Marie Powers & Randy Osborne (Staff Writers) // **Asia -** Shannon Ellis, John Fox, Dave Silver & Cornelia Zou (Staff Writers) // **East Coast -** Anette Breindl (Science Editor), Mari Serebrov (Regulatory Editor) // **West Coast -** Michael Fitzhugh // **Europe -** Sharon Kingman, Nuala Moran & Cormac Sheridan (Staff Writers)

PRACTICAL INFORMATION

To subscribe, please contact our Sales Team at (800) 477-6307; outside the U.S. and Canada, call (770) 810-3144.

For ad rates and information, please contact an Account Manager at (770) 810-3121.

For photocopy rights or reprints, call our reprints department at (770) 810-3121.

Send all **press releases and related information** to newsdesk@bioworld.com.

BUSINESS OFFICE

Donald R. Johnston (Senior Director, Editorial), Sarah Cross (Marketing Director), Matt Hartzog, Paul Marino & Greg Rouse (Account Representatives)

CONTACT US

Jennifer Boggs, (770) 810-3120 // Anette Breindl, (770) 810-3134 // Michael Fitzhugh (770) 810-3064 // Donald R. Johnston, (770) 810-3118 // Sharon Kingman, 44 20-8995-3336 // Nuala Moran, 44 127-0812775 // Randy Osborne, (770) 810-3139 // Marie Powers, (770) 810-3136 // Mari Serebrov, (770) 810-3141 // Cormac Sheridan, 353-87-6864323 // Peter Winter, (770) 810-3142 // Lynn Yoffee, (770) 810-3123

Panel advises working the system to get a CFDA greenlight

By Shannon Ellis, Staff Writer

SUZHOU, China – Navigating the obstacle course of China's regulatory system requires strategic thinking, long-term planning, creative problem solving and it doesn't hurt to have deep pockets, according to the experts discussing cross-border approvals at the Chinabio Partnering conference.

When trying to get a novel drug approved, it is important to understand that Chinese regulations are based on a legacy of manufacturing and generics, said Ling Su, life sciences regulatory expert at Sidley Austin LLP in Beijing.

That explains the importance of determining whether to seek approval for a domestic drug, which means setting up costly biologic manufacturing in China, or to shoot for an imported drug license (IDL), which has its own pros and cons, namely fewer risks but longer time frames.

An obvious hurdle is the bottleneck at the understaffed CFDA's Center for Drug Evaluation (CDE), ill equipped to handle the challenge of approving complex innovative drugs. "A lot of resources and expertise within the agency is quite limited," Ling said.

That's not to say the CFDA is not evolving rapidly.

"We are seeing a good trend of improvement with small-molecule drugs. We were able to get an approval very fast, within eight months," said Jimmy Wei, venture partner at KCPB China. "The big challenge is for biologics, vaccines, antibodies – these can take more than two years to get approved."

Consider that reviewers have personal responsibility for their professional decisions leading to possibly heavy consequences, and it becomes easier to understand the conservative regulatory regime. "Our society needs to understand that those that work in a public agency work on behalf of the government; they should not be punished individually," Ling said.

In China at every step of the way there is a need to get permission and approvals. "No other agency in the world is doing this," said Hua Mu, senior vice president of operations at Wuxi Apptec Co. Ltd., of Shanghai. In China, the responsibility for the efficacy and safety of the drug weighs heavily on the regulators' shoulders.

While it might seem that merely adding more reviewers would solve a lot of problems, Ling said, "if we get 600 more reviewers, then you create 600 times more problems. Where do you find the qualified people with the training and experience?"

Later this year, it is expected that the CFDA will come out with a draft Drug Administration law, that if passed by the State Council and the National People's Congress could go into effect by 2016.

Ling pointed out that the chance to reform has come around only twice before in the last 30 years. "We may not be around for the next revision so this is our opportunity to facilitate reform," Ling added.

NOT WAITING FOR GOVERNMENT

The panel concurred the issue of meeting China's substantial unmet medical needs is a shared responsibility requiring the combined effort of regulators, society and industry. But industry can't afford to wait for government to change.

As CEO of a small biotech, Dajun Yang, of Ascentage Pharma Group Co. Ltd., of Shanghai, said he finds it is important to define a strategy from the outset. "Every year we file two INDs [investigational new drug applications] with the CDE; the CDE might be 12 or 15 months, but you put yourself in a position to de-risk with multiple shots at a target."

During the long wait to get IND approval in China, some look outside to Australia and increasingly to Taiwan to initiate phase I trials, getting a start on in-human data. With a recent cross-strait agreement, Taiwan has become an increasingly attractive option.

With phase I data in hand, time lost has the possibility of being made up during the new drug application phase. "Look at the whole process and whole value chain on your portfolio, not just the CDE IND process," Yang advised.

Taking that idea a substantial step further, KCPB's Wei announced that his firm is in the process of building two state-of-the-art identical biologic manufacturing facilities in Germany, with one shipping to Taiwan and the other to China, with "the same process, same supplier and same equipment to reduce the risk of a bridging study."

That innovative approach garnered appreciative murmurs from the audience with Mu also alluding to a similar plan in the works at his company.

The longer-term bet is that government eventually will allow biotechs to take advantage of high-quality contract manufacturing organization (CMO) facilities to safely manufacture for clinical trials. Using a reliable CMO "will save a lot of money and reduce the price for biologics product, which right now are very expensive in China," Wei said.

NOTHING REASSURES LIKE QUALITY

A sentiment echoed by many but perhaps said best by Peng Wang, president of R&D at Yaobao Pharmaceutical Group Co. Ltd., of Beijing, is that "it comes down to the quality; if the science is really good, it is my impression the [approval] time will be shorter."

China can deliver international standard data, assured Mu, citing his past experience with Hutchinson Medipharma, where during licensing deals with big pharma the firm's data were heavily vetted and returned with high marks.

"I don't believe there is a so-called China standard," Yang said. "Maybe there are some different practices in terms of quality of product [and] standard operating procedures to run the trials, but everything we do has to follow a international standard."

But he admits quality programs are still elusive for many traditional pharma companies, though they know they need

See CFDA, page 6

India looking at noncommercial use for BMS' dasatinib

By Alfred Romann, Staff Writer

India is considering waiving a global patent for cancer drug dasatanib under provisions of the country's Patent Act that allow it to make the move for public noncommercial use.

Other countries, most notably Brazil, have been frequent users of similar types of provisions, but the move would be a first in India, which has used compulsory licensing (CL) schemes in the past to facilitate the production of generic drugs.

Drugmaker Bristol-Myers Squibb Co. (BMS) makes dasatanib and distributes it in India under the brand name Sprycel. The drug is used to treat chronic myelogenous leukemia and Philadelphia chromosome-positive acute lymphoblastic leukemia. BMS has a patent on the drug until 2020. In 2012, sales of dasatinib topped $1 billion.

But the drug is expensive, selling for around Rs165,000 (US$2,750) for a month's supply.

"It is exactly what Brazil and others do, [but] we have not been doing it in India," said Shamnad Basheer, an high-profile intellectual property lawyer, former professor and founder of the well-known blog Spicy IP.

Basheer said he believes the government is committed to issuing a license but, in the most likely scenario, a final decision will wait until the next government is formed in mid-June. Elections are being held across the country and should be done next week.

A license under the public noncommercial use would pose little threat to the originator company, Basheer said.

"The government [would be] distributing to a certain underprivileged population. They are not going to distribute in the mansions in Delhi," he said. The people who would get the generic drug would not have the money to buy the much more expensive original.

A couple of domestic generics makers have sought CLs to manufacture dasatanib in the past. By some estimates, a CL could help bring the price of dasatanib to about Rs8,000.

Last February, BDR Pharma applied to the India Patent Office for a CL to make the drug, but regulators said the company had not made a case that a license was warranted and had not worked hard enough to attain a voluntary license from BMS. BDR applied for the CL on the basis of Section 84 of the Indian Patents Act, claiming the price of the drug is too high. In 2011, BMS took to the courts and effectively blocked Natco Pharma, another generics maker, from getting a CL for dasatanib.

Neither BMS nor Mumbai-based BDR Pharma responded to requests for comments by press time, and the Mumbai law firm representing the company, Gopakumar Nair Associates, declined to comment.

India has been among the most aggressive countries in the world in facilitating the production of generics, but regulators there have come under the crosshairs of other governments, most notably the U.S.

In 2012, the Patent Office granted Natco a CL to manufacture generic versions of Bayer Corp.'s Nexavar (sorafenib), a renal cancer drug. Natco's drug sells for about Rs8,880 compared to the Rs284,000 Bayer charged. The CL also requires Natco to pay Bayer a 6 percent royalty and expires in 2021.

That was the first time India granted a CL based on Section 84 of the Indian Patents Act

In April, an Indian court banned Natco from exporting the drug, saying the license applied only to the Indian market. (See *Bioworld Asia*, April 9, 2014.)

The approach regulators are now considering with dasatanib is different. Under the public noncommercial clause, it would be the government that would hold the license and it would only be able to distribute it at no profit. Natco or BDR Pharma could manufacture the drug under contract to the government. Cipla, another generics maker, could also be in a position to manufacture dasatanib.

The World Trade Organization's Agreement on Trade-Related Aspects of Intellectual Property Rights (Trips) allows governments to issues CLs for the manufacture and distribution of drugs it might need to deal with emergencies or to facilitate access if the price is too high.

Section 92 of India's Patents Act, 1970, gives the Ministry of Health the right to consider whether there is a national emergency or a need for public noncommercial use of a drug. Section 84 opens the door for a license on issues of affordability.

Two years ago, the Ministry of Health started the process of issuing compulsory licenses for three cancer drugs: Herceptin (trastuzumab, Roche AG) a monoclonal antibody used for breast cancer, Ixabepilone used in chemotherapy and dasatanib.

Believed to be toxic, Ixabepilone was later removed from the list. BMS also makes Ixabepilone.

Roche, which makes the biologic trastuzumab, relied on issues of regulatory compliance rather than IP concerns to try to block Bengaluru-based Biocon Ltd. and U.S.-based Mylan Inc. from marketing Canmab as a biosimilar. Roche claimed that since the protocol and trial design for the drug were approved before the Drug Controller General of India had approved a biosimilar path in 2012, the drug was not developed as a biosimilar.

The Delhi High Court granted an injunction in February prohibiting Biocon and Mylan from referring to their drug as a biosimilar or comparing it with Roche's Herceptin. (See *BioWorld Asia*, Feb. 12, 2014.)

Roche had allowed its patent on trastuzumab to lapse last year in India. Sales of the drug hit $6.75 billion in 2013, of which just $21 million were in India. Biocon and Mylan launched Canmab in January. //

Chinese biopharmas eager to translate 'innovation' into drug approvals

By Marie Powers, Staff Writer

SUZHOU, China – "Innovation" is a prominent theme in China's life sciences community, but for all the talk about the need to move from generics to novel drugs, focusing on the science without generating results is a wasted effort. That, in short, is a key message emerging from Chinese life science executives and research leaders at the Chinabio Partnering Forum.

Without question, the country's changing market – an aging population but also a wealthier one seeking higher-quality therapies – is driving the development of innovative drugs. Central, provincial and local governments have created programs to fund new drug development, providing up to $10 million per grant. And China's universities and institutes are generating significant intellectual property, resulting in a growing number of patents for new molecular entities.

But the payoff – approval and commercialization of new molecular entities using new mechanisms of action to treat diseases affecting Chinese citizens – remains elusive.

That shortcoming has not gone unnoticed. China has rocketed to the top in a host of industries, from computer technology to heavy equipment, with at least one Chinese company among the top 10 global leaders in virtually every major business segment.

"But pharma is a very different industry," observed Lewis Ho, partner and head of life sciences in Asia for Dechert LLP. Not a single Chinese company has broken into the top 100 in drug development, let alone the top 10, he said. Thus, when he's asked whether innovative drug development is occurring in China, Ho said his response, for now, is "not yet."

The Chinese government is spending plenty of money in the life sciences sector with the goal of moving beyond the rhetoric of innovation to the goal of novel drug approvals. In some ways, Chinese biotechs have almost too much access to capital, Ho maintained, which has prevented them from making disciplined decisions and establishing reasonable priorities.

Some would argue the funding is simply following the market. The average life span in China is now 84 years for women and 81 for men, said Yang Ye, deputy director general of the Shanghai Institute of Materia Medica (SIMM), during a panel presentation on the evolution of R&D in Chinese pharma. Developing therapies for the country's population – which also faces health burdens ranging from cancer to diabetes to stroke – is a huge unmet medical need.

Seasoned business management is another resource in short supply among Chinese biotechs. Although Chinese nationals educated in the West are returning home in droves, many lack experience running a sizable operation, Ho pointed out, and their years away from China have created a gap in their understanding of the country's complex regulatory system.

"To actually navigate the Chinese market, you need to spend more time in China," Ho told *BioWorld Asia*.

Multinational companies can help to bridge these gaps by collaborating with Chinese biotechs to migrate their candidates through early and midstage clinical development in return for handling eventual market launch, distribution and product positioning, according to Ho.

"Some Chinese biotechs want to grow into a one-stop shop, which is ambitious," he said. "But in terms of the success rate, it's better to focus on the science."

'INNOVATION IS GOOD, BUT WE'RE LOOKING TO DEVELOP DRUGS'

That's precisely what Shenogen Pharma Group is seeking to do. After eight painstaking years of effort, the Beijing-based company has advanced its lead compound, SNG-162 (lcaritin), into a phase II study in China. The first-in-class small molecule is a naturally derived traditional Chinese medicine targeting ER-alpha 36 to treat liver, breast and potentially other forms of cancer.

"Innovation is good, but we're looking to develop drugs," Jun Bao, Shenogen's senior vice president and chief business officer, told Chinabio attendees. The company's business acumen and scientific prowess last year helped Shenogen attract a $20 million series C from a syndicate that included Qiming Venture Partners LLC, of Shanghai, and Legend Capital, of Beijing, an affiliate of tech company Lenovo, along with China Investment Wealth Venture Fund and Shenzhen Venture, a venture arm of the municipal government. Lead investors from Shenogen's series B, including IDG Venture and Lapham Group Inc., also joined. (See *BioWorld Asia*, Nov. 6, 2013.)

Although the science emerging from Chinese universities is compelling, no Chinese biopharma can go it alone in drug development so partnerships with pharmas are welcomed, Bao said. He cautioned, however, that many Chinese biopharmas are still working with early stage assets. Thus, pharmas looking for "ready-made drugs to license" are likely to be disappointed.

In general, the infrastructure to conduct drug development in China is improving, according to Bao, who credited Wuxi Pharmatech Inc. as a trailblazer in growing from a small biotech into an integrated R&D services giant. This week, the FDA granted the first approval for the use of a biologic manufactured by a Chinese company in a U.S. investigational new drug trial. Wuxi is manufacturing the HIV therapy, known as ibalizumab (TMB-355), for Taiwan Taimed Biologics Inc., of Taipei. (See the article in this issue.)

But regulatory uncertainties in China loom large, Chinabio panelists agreed. Despite the vast government investment in scientific innovation, the pipeline of novel drugs developed in China faces a bottleneck at the CFDA, where reviewers

See Innovation, page 7

Aslan

Continued from page 1

commercial rights downstream," Carl Firth, Asla's CEO, told *BioWorld Asia*.

The project shows Aslan's appetite to go ever earlier in its hunt for the right opportunity with the right partner. The project may be preclinical but according to Firth it is ready to go into "GLP tox" and fits well into their strategy.

Aslan has a unique business model, licensing global rights for innovative assets to be developed by leveraging Asian clinical resources. (See *BioWorld Asia*, Feb. 19, 2014, and Oct. 18, 2013).

It expects to partner at phase III, after conducting phase I and phase II trials in countries like Korea, Taiwan, Singapore and Australia where approval can be timely and the investigators are experienced. Not forgetting the elephant in the room, China comes in at a later stage.

"When we are phase IIb or even beyond, I think that is a perfect time to make sure we start to involve China," said Firth. "To make sure we have the right data, the right experience, to ensure China can ultimately offer an approval there."

Asthma is a worldwide issue but is particularly acute in Asia where air pollution is rife. Globally, asthma is a $13 billion a year market, Firth said, and many patients are using a combination of inhaled products such as Advair (fluticasone/salmeterol) from Glaxosmithkline plc or Symbicort (formoterol and budesonide) from Astrazeneca plc. There is one biologic product, Xolair (omalizumab), a $1.4 billion product.

The challenge is to provide solutions for sufferers of moderate to severe asthma, said Firth where the condition can be fatal and very costly to treat.

"The ones that are not controlled live in fear of their next exacerbation," said Firth, "whether it is a chest infection or something else, it may mean being taken to hospital and in some cases this can be a life threatening event. And though it is a small number of asthmatics that are not controlled, it is this small number that represents 50 percent of the total cost of treating asthma."

While asthma affects 3 percent to 9 percent of the world's population, in China there is a particular unmet need with some 15,000 fatalities a year related to asthma.

Aslan is aware many large companies are going after a better solution to asthma, but is counting on their nimble, innovative approach to get them ahead faster. This is in part how they convinced CSL to work with them, said Firth.

Compared to Aslan, CSL is a much larger player with offices in Australia, Germany, Switzerland and the U.S., employing some 11,000 people.

"Aslan's focus on efficiently designing and executing innovative clinical strategies, combined with its teams experience in asthma drug development, make it the ideal partner for moving this therapy forward," said Andrew Nash, CSL's senior vice president, research.

It was important for Aslan to seek out a drug that would provide more than a marginal benefit to existing therapies but rather "have a significant impact on how patients are treated" and that his how the company regards Aslan004.

The drug is a fully human monoclonal antibody (MAb) against interleukin-13 receptor α1 that has been shown to block binding and signal transduction of both IL4 and IL13.

"The antibody itself is in a very exciting area of inflammatory biology," said Firth, "in particular the antibody blocks a path to the IL-13 receptor, this is a receptor involved in the information cascade responsible for a number of different diseases including asthma."

Taking on the challenge of its first preclinical drug and a MAb seem to be alleviated by Aslan's confidence in its partner. "They [CSL] worked in this area for a long time and put together an incredibly fantastic package of data," said Firth. "It certainly helps to know you are working with one of the world's strongest companies in a particular space. That gave us a lot of reassurance."

Aslan has three other assets in its pipeline, a pan-HER inhibitor licensed from Array Biopharma Inc., of Boulder, Colo., in phase IIb; a cMET inhibitor from Bristol-Myers Squibb Co., of Princeton, N.J., in phase I; and a DHODH inhibitor licensed from Almirall S.A., of Barcelona, in phase I for rheumatoid arthritis. //

CFDA

Continued from page 3

such programs to survive, opening the doors ever wider to cross-border opportunities. "Historically speaking, there is a great window of opportunity for co-development," Yang said.

In the last seven years, Wei observed he has seen a jump in co-development deals – within the KPCB portfolio alone, he said, there have been at least a dozen – leveraging innovation that was generated in the U.S. or Europe to bring to China.

In his experience with the right science and the right indication he found "from the day we signed the license to the day we launched the product it took two years. Actually, that never happened before to my understanding, but I foresee there will be more and more deals like this."

While hopes were expressed that the Chinese government will change the regulatory process, Yang observed, "Overall, I do not have too much hope that the regulatory process will become more predictable or transparent. We can only do our best from the scientific aspect and provide quality product." //

Daiichi

Continued from page 1

for stomach cancer and a phase Ib trial for esophageal cancer will continue.

The phase III trial for patients with unresectable and locally advanced squamous cell lung cancer includes an arm for nimotuzumab in combination with chemoradiotherapy and an arm with a placebo in combination with chemoradiotherapy. The independent data monitoring committee advised that continuing the trial with the investigational drug should not be allowed, a spokesman for Daiichi Sankyo told *BioWorld Asia*, but the company added that it will continue the remaining nimotuzumab studies as planned.

Daiichi Sankyo anticipated nimotuzumab to be a best-in-class epidermal growth factor receptor (EGFR) monoclonal antibody, and the company had touted the drug's safety profile against skin toxicity and efficacy to other EGFR antibodies in its 2013 annual report. The phase III trial for non-small-cell lung cancer (NSCLC) was launched in March 2013, followed by the gastric cancer phase III trial in April 2013.

The compound originally was discovered in Havana, Cuba, at the Center of Molecular Immunology. CIMYM Biosciences – a joint ventures between YM Biosciences Inc. and CIMAB S.A. – licensed Japan rights for nimotuzumab to Daiichi Sankyo in 2006 for an up-front payment of $14.5 million and undisclosed milestone payments. CIMAB is the exclusive commercialization representative for Cuba's Center of Molecular Immunology.

Nimotuzumab was approved in India in July 2006 for head and neck cancers. YM Biosciences licensed the compound in India to Biocon Ltd., of Bangalor, and in Europe to Oncoscience AG, of Wedel, Germany.

Daiichi Sankyo still has an EGFR antibody in development for NSCLC in Japan. Patritumab is in phase I development in Japan for lung cancer as well as in a U.S./EU phase II trial. The compound came to Daiichi Sankyo in the $235 million acquisition of Martinsried, Germany-based biotech U3 Pharma AG in 2008 and was considered the lead compound in the deal.

Daiichi Sankyo has designated oncology, along with cardiovascular and "frontier fields," as priorities for its R&D plans, and the company said last year it will continue to pursue "the active use of outside resources."

Daiichi Sankyo recently extracted itself from a tumultuous relationship with its India acquisition Ranbaxy Laboratories Ltd. Ranbaxy has been plagued by manufacturing issues that led to import bans by the U.S. FDA, and Daiichi Sankyo recently announced it would sell its stake in the company to Indian firm Sun Pharmaceutical Industries Ltd. Daiichi Sankyo paid $4.6 billion for a controlling share of Ranbaxy in 2008, and Sun agreed to buy Ranbaxy for $3.2 billion. Daiichi Sankyo will hold a 9 percent share in the merged Indian companies. Some analysts have viewed the sale as a positive for both Daiichi Sankyo and Ranbaxy in that it will allow Daiichi Sankyo to realign its focus on R&D development instead of distractions from Ranbaxy's manufacturing issues, while at the same time giving Sun Pharma a chance to try to right the Ranbaxy ship.

JAPAN'S LUNG CANCER MARKET

The unmet need for lung cancer therapies in Japan represents a dynamic market. Roche's Tarceva (erlotinib), an EGFR antibody for lung cancer, is on a fast growth trajectory in Japan. The company reported CHF25 million in Tarceva sales in the first quarter of 2014 in Japan, a 42 percent increase from the same quarter in 2013.

In the U.S., Tarceva sales growth dropped 6 percent, and in Europe sales growth dropped 12 percent. While Japan growth was strong, the CHF25 million in sales represented only a small portion of the first quarter Tarceva global sales of CHF304 million. Roche has attributed the global sales growth decline to the competitive market.

Boehringer Ingelheim's Gilotrif (afatinib) was approved in Japan in early 2014, and is looking to make an impact a first-line therapy for NSCLC with common EGFR mutations.

Astrazeneca plc's Iressa (gefitinib) was the first inhibitor of EGFR tyrosine kinase approved in Japan for advanced NSCLC. But between 2004 and 2008, seven claims were filed against Astrazeneca alleging Iressa caused deaths from interstitial lung disease in Japanese patients. District courts in Tokyo and Osaka initially ruled in favor of the patients, but after years of appeals, the Japan Supreme Court ultimately ruled in April 2013 to reject all appeals against Astrazeneca and Japan's Ministry of Health, Labor and Welfare that the company or the ministry had any liability for the claims.

Iressa loses patent protection in Japan in 2018. Doctors are slower to switch to generic versions of drugs in Japan than they are in the U.S., although the Japanese government has introduced economic incentives to encourage changes in prescription behavior to increase generic utilization. //

Innovation

Continued from page 5

are accustomed to seeing generics but have little experience handling innovative drugs. Plus, the work force is limited – by most counts, just one-tenth the reviewers as the U.S. FDA.

Acknowledgment of those challenges prompted Anand Gautam, director of biopharma innovation sourcing at Novo Nordisk A/S, to observe that China may be ahead of the curve in drug discovery, "but we do not see that converted into biotech companies or investments." If China can grow its pool of pharmaceutical business talent, leverage the use of venture and government funding and manage the regulatory work flow, opportunities to in-license promising drug candidates could grow exponentially over the next three to four years, Gautam suggested, "but we don't see those opportunities yet."

The Chinabio conference concludes Thursday. //

Stem cells

Continued from page 1

(STAP) stem cells, which behave like induced pluripotent stem (iPS) cells, by simple acid-based treatment of somatic cells, suggesting that the method is not as simple or straightforward as initially claimed.

Led by Kenneth Lee Ka Ho, a professor and chief of the Key Laboratory for Regenerative Medicine in the School of Biomedical Sciences at CUHK, the researchers reported their findings in the May 8, 2014, issue of *F1000Research*.

Because they can propagate indefinitely and eventually develop into almost every other cell type in the human body, iPS cells are considered the holy grail of regenerative medicine, representing a single source of cells that could be used to replace those lost to damage or disease, without the problems surrounding use of embryonic stem cells.

"Embryonic stem cells are pluripotent stem cells that can be induced to become any cell type in our body, making them extremely useful for repairing damaged organs and tissues," said Lee.

"These cells would be rejected by the immune system, if they did not originate from the same person, whereas iPS cells can be tailor-made from the cells of any individual, which means they would not be rejected," he said, noting that use of iPS cells also "bypasses the ethical issues of using human embryos to produce pluripotent stem cells."

However, the production of iPS cells is difficult and, while there are currently various genetic- and chemical-based methods available for producing pluripotent stem cells from somatic cells, all of these are extremely inefficient.

"The [currently available] iPS production techniques are extremely inefficient and only have a yield rate of 0.01 percent, although it has been claimed that this yield could be increased to 10 percent with supplements," Lee told *BioWorld Asia*.

Moreover, "some of these iPS techniques involve genetic manipulation, which may potentially disrupt the genome and affect the cell's function," he said, noting it is now possible to produce iPS cells using small molecules alone, without the addition of extra genes that might increase the risk of potentially dangerous mutations or cancer.

Although iPS cells can also be produced using a combination of genetic and chemical approaches, such as the use of microRNA or recombinant proteins, "a lot of these procedures have still not been independently validated," cautioned Lee.

Given the difficulties and inefficiency of the different iPS cell production methods, the scientific community was surprised when Haruko Obokata at the Riken Center for Developmental Biology in Japan published two papers in the Jan. 30, 2014, issue of *Nature* claiming that simply treating cells in mild acid at a pH of 5.7 could produce STAP cells that were simpler than even the latest methods for the generation of iPS cells, as well as faster to produce.

"This was an astounding announcement, especially in Japan, where [Kyoto University's] Shinya Yamanaka had been awarded the 2012 Nobel Prize for his iPS cell work and it was thought that the work by Obokata et al also had the potential [to win] another Nobel Prize," said Lee.

However, "because this technique was so simple, most stem cell biologists around the world tried to replicate it, but without success," casting considerable doubt on the findings reported by Obokata et al., Lee told *BioWorld Asia*.

Unfortunately, however, those stem cell scientists had to report their findings on online social media platforms, including blogs such as the Knoeffler Lab Stem Cell Blog and networking sites like Researchgate, "because journals do not generally accept failed experiments for publication," he pointed out.

Lee and his group at CUHK also failed to produce STAP stem cells from neonatal somatic cells using the acid-based method reported by Obokata et al., despite using their latest protocol, as reported in the March 5, 2014, online edition of *Protocol Exchange*. "We used her exact methods to try and produce STAP cells," but without success.

And just like the other stem cell scientists, their negative findings were not accepted for publication in conventional journals.

"We tried publishing it in *Nature* as a short communication and it was rejected [but] *F1000Research* wanted it because of the impact it would have," Lee said.

This reluctance by conventional scientific journals to accept negative results has important research implications, as studies that subsequently become contentious after publication can linger in the literature for too long, before being eventually retracted or confirmed by other researchers, resulting in wasted time, resources and possibly even lives.

Lee's pre-paper, which already had been accessed 3,773 times on the fourth day of publication, will be openly peer reviewed after publication and the identity of the reviewers, their reports, comments and the full data set associated with the work will be freely available for download, ensuring that the scientific community has sufficient information to properly evaluate the work.

He explained that in the open journal context, a 'pre-paper' refers to a manuscript that it has not yet been accepted as a form paper by the referees and, as such, "could still be rejected for publication if the referees had problems with it."

Although the original *Nature* papers by Obokata et al. were also peer reviewed, as is standard practice for scientific journals, the reviewers were anonymous and the reviewers' criticisms and requests for revision were not available to readers, which is how most journals approach data presentation and the review of manuscripts.

In contrast, *F1000Research* offers rapid open access publication, transparent post-publication peer review by invited referees, and full data deposition and sharing. The journal accepts all scientifically sound articles, including single findings, case reports,

See Stem cells, page 9

Liver cancer

Continued from page 1

of hepatocellular carcinoma (HCC) in Japan, where liver cancer is one of the largest causes of cancer-related death.

A 4SC spokesman said the companies aim to initiate a phase IIb trial of the histone deacetylase inhibitor in Japan in late 2014 or early 2015.

According to 4SC, resminostat demonstrated a clean safety profile in Japanese cancer patients, clearing the way for the drug's future clinical study. 4SC licensed the drug to Yakult Honsha for the Japanese market in 2011 in exchange for an up-front payment of €6 million (US$8.3 million) and up to €127 million in clinical and regulatory milestone payments, as well as double-digit royalties on any Japanese sales linked to resminostat. (See *BioWorld Asia*, April 20, 2011.)

In May 2013, Yakult Honsha commenced a 164-patient phase I/II trial for resminostat in combination with Nexavar (sorafenib, Amgen Inc. and Bayer AG) as a first-line therapy for HCC. 4SC said the findings of the study could be "significant for 4SC's planned market registration program."

Japan holds a higher rate of liver cancer than markets in the U.S. and EU, and Nexavar is the only approved HCC therapy. Bayer and Onyx (now part of Amgen) split global profits for Nexavar except in Japan, where Bayer paid a one-time payment of $160 million in 2011 to update its agreement.

Bayer announced Nexavar sales of €183 million in the first quarter of 2014, a 5.8 percent increase from the same period in 2013, and the company said the drug made gains in all regions. However, in March 2014, a phase II study of Nexavar did not meet its primary endpoint of improving recurrence-free survival when used as an adjuvant treatment for patients in whom all detectable tumors had been removed.

Yakult Honsha is conducting two phase I/II studies for resminostat in Japan: a comparison study of resminostat in combination with sorafenib vs. sorafenib monotherapy for HCC and a comparison of resminostat in combination with docetaxel vs. docetaxel monotherapy for non-small-cell lung cancer (NSCLC).

Resminostat lags behind Arqule's tivantinib, which is making its way through phase III trials in Japan. However, resminostat has the benefit of being developed as a first-line therapy in combination with sorafenib, whereas tivantinib is being developed as a second-line therapy. Kyowa Hakko Kirin initiated a phase III study of tivantinib in Japanese patients with c-Met diagnostic-high inoperable HCC patients treated previously with sorafenib.

Under its deal with Arqule, Kyowa Hakko Kirin holds rights to the compound in Japan, China, South Korea and Taiwan, while fellow Japanese firm Daiichi Sankyo Co. Ltd. holds all ex-U.S. rights for the drug. Kyowa Hakko Kirin paid $30 million up front, with the potential for $93 million in milestone payments and midteen/low 20s royalties. Daiichi Sankyo paid $60 million up front, with $560 million in potential milestone payments in addition to double-digit royalties. (See *BioWorld Today*, Nov. 11, 2008.)

Tivantinib, however, has encountered some snags. The drug missed its endpoint in a NSCLC phase III trial, though subset analysis showed the drug had activity in patients with high c-MET expression. The data monitoring committee for the phase III HCC trial of tivantinib in Japan recommended the trial continue with a lower dose of tivantinib – 120 mg instead of 240 mg – to reduce the incidence of neutropenia. (See *BioWorld Today*, Oct. 1, 2013.)

4SC SUCCESS TIED TO RESMINOSTAT

4SC, which has struggled in the past year, has staked its future to the success of resminostat. The company cut its staff by 15 percent and reduced R&D costs by 21 percent in 2013 to realign its focus on the development of resminostat in liver cancer. The company's share price dropped 23 percent in 2013, which the company attributed to "the lack of another pharmaceutical partner for resminostat [that] also likely dampened the impulse to buy."

The German company announced May 8 in its first quarter results that it is pursuing a blinded, randomized phase II trial in advanced liver cancer in combination with sorafenib as a first-line therapy. "In contrast to a previously considered combined phase IIb/III trial with no interim unblinding and an adaptive study design, this study design, which has been fine-tuned over the last few months, can deliver a significant, clearly defined addition to enterprise value while also significantly reducing study costs," 4SC said ahead of its earnings call with analysts.

The company identified in September 2013 that the elevated expression of ZFP64 biomarker correlated with a doubling of patient survival, and the company plans to incorporate ZFP64 into future studies to examine the potential of the compound as a personalized medicine.

4SC said it is still talking with potential partners and investors to finance the study, and if it's able to secure adequate funding, it could submit a U.S. investigational new drug application by the end of 2014. The company has said it has "broadened the financing options under consideration" to find partners and investors.

The 4SC management board will receive a bonus equal to four times the base salary if a license agreement is reached for resminostat. //

Stem cells

Continued from page 8

protocols, replications, and null/negative results.

The rapid publication of results and ensuring that all of the important information associated with the paper is openly available should help counteract the shortfalls of the traditional journal paradigm.

Concluding, Lee called for conventional journals to "only accept ground-breaking findings that have been reviewed by more than four reviewers" and urged that journals "also consider publishing results that are negative, or adopt some form of open peer review process." //

Shantha

Continued from page 1

Ltd. – received prequalification status from the World Health Organization. The prequalification means that United Nations agencies like UNICEF can now purchase the vaccine for use across its programs, mostly in emerging countries.

In 2009, Sanofi Pasteur acquired India's Shantha to develop vaccines for emerging countries. The Shan5 vaccine was developed and manufactured in Shantha's facility in Hyderabad. It received marketing approval in India in March.

Shan5 is the first vaccine jointly developed by Shantha and Sanofi Pasteur.

"We hope the vaccine will generate $83 million sales in five years," Shantha's communications manager Tashif Ayaz told *BioWorld Asia*. "It will be available on the market by the end of this year."

Shan5 is a combined, fully liquid pentavalent vaccine that contains diphtheria and tetanus toxoids, whole cell pertussis recombinant DNA-derived hepatitis B surface antigen and components of haemophilus influenza type b (Hib).

It protects children older than 6 weeks from diphtheria, tetanus, pertussis, Hib and hepatitis B. The vaccine will be exported to more than 50 emerging and low-income countries.

"We're only focusing on vaccines now," Ayaz said. "We have worked with the WHO and UNICEF before to bring vaccines to countries like South Sudan and Pakistan."

Access to vaccination remains a significant concern for national and global health agencies.

"A significant number of babies born every year do not have access to modern vaccination programs," said Olivier Charmeil, president and CEO at Sanofi Pasteur. "By delivering large supplies of high-quality and affordable vaccines to emerging and low-income countries, Shantha will be contributing to filling this gap for the benefit of babies and their parents."

The acquisition of the Indian company five years ago provided Sanofi Pasteur with a platform to produce more targeted products.

"Shantha's manufacturing platform in India will serve Indian needs and provide Sanofi Pasteur access to additional vaccine markets globally," said Harish Iyer, CEO of Shantha, at a recent media briefing.

Shan5 had already been granted pre-qualification status by the WHO before concerns with the original product surfaced and forced the company to go through the process all over again.

On July 28, 2010, the WHO removed Shan5 from its list of prequalified vaccines after white sediment was found sticking to the vaccine vials. The sediment proved to be difficult to resuspend.

Several months before the delisting, the WHO received complaints from countries like Colombia, Comoros and Nepal about the sediment in Shan5 vaccines.

A WHO committee reviewed the reports of an investigation by Shantha and then recommended a recall and the destruction of all lots of the Shan5 vaccine in stock. The WHO also recommended countries use alternative manufacturers for the pentavalent vaccine.

Shantha conducted investigations and submitted a report on the root cause of the problem with a robust plan for corrective action. The cause of the sediment was identified but the corrective plan required revisions to the product.

In turn, the WHO found it implausible to link the quality, safety and immunogenicity tests of the original and the revised product. The organization asked Shantha to submit a new application for prequalification and took the vaccine off the prequalified list during the process.

"[The] waiting period of four years has ended, and we are very jubilant," said Varaprasad Reddy, founder and non-executive chairman of Shantha.

Shantha has another vaccine under development that would upgrade Shan5. The new vaccine, Shan6, will add polio prevention to the five diseases Shan5 already covers.

"We just started developing Shan6," Tashif noted. "It's still early. We don't know when it will be launched."

Sanofi Pasteur is the biggest provider of injectable and oral polio vaccines. When it acquired Shantha, it brought that expertise in polio vaccine development to India.

Polio eradication campaigns have been gathering momentum around the world. The WHO certified India as polio-free in March after the country went three years without an endemic case of the crippling disease. //

OTHER NEWS TO NOTE

Acura Pharmaceuticals Inc., of Palatine, Ill., entered a settlement agreement with **Ranbaxy Laboratories Inc.**, of Gurgaon, India, to dismiss, without prejudice, its patent infringement action pending against Ranbaxy in the U.S. District Court for the District of Delaware. In the suit, Acura alleges that a generic of Acura's Aversion oxycodone product, previously marketed by **Pfizer Inc.**, of New York, under its brand name Oxecta – for which Ranbaxy is seeking approval to market in the U.S. pursuant to an abbreviated new drug application filing (ANDA) – infringes patents owned by Acura. The settlement agreement provides that Ranbaxy's current product that is the subject of its ANDA does not infringe Acura's Orange Book-listed patents with the FDA.

Riken

Continued from page 1

committee of outside experts to suggest future steps to prevent fraud.

The government-funded Institute of Physical and Chemical Research, Rikagaku Kenkyusho (Riken), decided not to reinvestigate its findings that a disputed paper on stimulus-triggered acquisition of pluripotency (STAP) cells published in January contained data that was falsified and manipulated.

The institute also has advised the author, Haruko Obokata, a stem-cell biologist at Riken's Center for Developmental Biology, to retract the paper.

The institute has set up a separate committee to consider disciplinary measures against Obokata.

Those decisions will be reached within a month, the institute announced last week.

STAP cells could theoretically be used to make embryonic-like stem cells that could then be turned into any type of cell in the body. What's more, they could be matched to individual patients and eliminate the risk of immune rejection.

In a research paper and a letter published in *Nature* at the end of January, Obokata claimed to have found a relatively easy way to produce STAP cells. Soon thereafter, however, stem cell researchers began to question the authenticity of the papers, alleging image manipulation and duplication. The issue became more controversial when no other researchers managed to duplicate the results Obokata claimed to have achieved.

Faced with a whirlwind of allegations against its researcher, Riken set up an investigative committee of five scientists headed by lawyer Jun Watanabe. Other members were Atsushi Iwama, professor at Chiba University; Haruhiko Koseki, deputy director of the Riken Center for Integrated Medical Sciences; Yoichi Shinkai, chief scientist at Riken Cellular Memory Laboratory; and Tetsuya Taga, vice president of the Tokyo Medical and Dental University.

On March 31 the committee said it had found fabrication had indeed taken place.

A little more than a week later Obokata apologized for making mistakes but claimed that she had in fact produced STAP cells more than 200 times. She called for the issue to be reinvestigated with a focus on findings of misconduct, saying any mistakes made did not affect the final results.

The committee considered whether another investigation was warranted but announced on May 7 that, after examining Obokata's appeal and arguments, "there is no need to re-investigate the results of the committee's investigation issued on March 31, 2014." Obokata was told to retract the paper associated with research misconduct.

The decision effectively endorses the earlier findings of misconduct.

"Hereafter, Riken will proceed with the necessary measures stipulated in its relevant regulations," said President Ryoji Noyori in a letter made public on May 8 following the release of a 21-page report by the investigating committee.

But Noyori also was obliged to address separate allegations of research misconduct associated with earlier papers made against members of the investigative committee.

Shunsuke Ishii, a senior scientist of Riken Molecular Genetics Laboratory, had originally headed the committee. Ishii resigned after images from his own early works that appeared to be manipulated were posted on the Internet.

A whistle-blower alleged that two members of the committee, Koseki and Shinkai, also had indulged in data manipulation. There were also reports of manipulations in papers co-authored by Taga but the university denied the allegations.

"As regards the allegations of research misconduct in past papers published by members of the investigative committee, we believe the committee has nevertheless carried out its investigation appropriately and have concluded that the allegations do not affect the committee's findings concerning the STAP cell papers," Noyori said.

Noyori said Riken's committee members whose own papers have been called into question would be investigated separately as per the institute's regulations. Members not affiliated with Riken will face investigation in line with their own institutions' regulations.

Riken's also has created a new office for internal reform made up of outside experts to suggest ways to prevent research misconduct in future. The committee is currently in deliberations and will submit recommendations to help Riken regain public trust.

"I would like to reiterate that Riken takes this issue very seriously and will make every effort to prevent further instances of research misconduct and to regain public trust in our research activities," Noyori said.

A group led by the special advisor of Riken, Shinichi Aizawa, has begun verifying the results of the STAP experiments.

By press time, Riken did not respond to requests for further information. //

APPOINTMENTS AND ADVANCEMENTS

Lupin Ltd., of Mumbai, India, appointed Theresa Stevens chief corporate development officer for its global operations.

Qrxpharma Ltd., of Sydney, Australia, named Edward Rudnic CEO; he has been the company's chief operating officer since 2012.

Rich Pharmaceuticals Inc., of Beverly Hills, Calif., appointed Chieanchuang Kalayanamitr to its medical advisory board. Kalayanamitr received his PhD in systems management sciences from Greenwich University and serves as an advisor to the government of Thailand and its prime minister's office on various matters. //

Biologic

Continued from page 1

R&D services giant Wuxi Pharmatech Inc. (NYSE:WX) got the green light for HIV therapy drug ibalizumab (TMB-355), which it is manufacturing for Taiwan Taimed Biologics Inc., of Taipei, Taiwan.

"Taimed is pleased with the speed and excellent execution of this project to ensure the success of this important drug," said Taimed CEO James Chang. "We look forward to the next phase of collaboration with Wuxi to successfully bring the drug to marketing approval."

Ibalizumab is a humanized monoclonal antibody (MAb) that belongs to an emerging class of HIV therapies called viral-entry inhibitors. It binds to the CD4 molecule, the primary receptor for HIV infection, to interfere with the penetration of the virus into the cells. It is the first entry-blocking humanized MAb used to treat HIV infection.

Wuxi and Taimed reached an agreement on the manufacturing of ibalizumab in support of phase II and phase III trials globally in August 2012. Although Taimed is developing the drug, Wuxi is providing a range of services, including manufacturing at its facilities in Wuxi.

Taiwanese biopharmaceutical company Taimed was founded in 2007 by former Vice Premier Tsai Ing-wen and David Ho, a prominent HIV/AIDS researcher. The company is based out of the Hsinchu Biomedical Park in Northern Taiwan.

Shortly after it was founded, Taimed signed a licensing agreement with San Francisco-based Genentech Inc. for ibalizumab shortly after the company was founded. Genentech is now part of the Roche Group.

Other drug candidates Taimed is developing include TMB-607, an HIV-1 protease inhibitor, and TMB-571, a small-molecule inhibitor of influenza virus neuraminidase against H1N1 and H5N1 influenza viruses.

Two months after the agreement was inked, Wuxi announced the establishment of a biologics manufacturing facility to produce drugs like ibalizumab. It was the first biologics producing facility in China that met current Good Manufacturing Practice (cGMP) standards from the U.S., the European Union and China.

The automated filling line of Wuxi Pharmatech's manufacturing facility can accommodate two to 50 ml liquid and lyophilized vial products for global clinical trials and product launches.

"Besides manufacturing, we offer fully integrated development services from target to product approval and regulatory support, but no marketing services for now," Aaron Shi, associate director of corporate communications at Wuxi, told *BioWorld Asia*. "For ibalizumab specifically, we also help in late phase development and regulatory support."

The cooperation between the Taiwanese and Chinese companies has made it possible to speed up the development of the promising drug.

Wuxi last month kicked off construction of its new cell therapy facility in Philadelphia and got FDA approval for its analytical and stability testing facilities in Shanghai.

The new facility in the Philadelphia Navy Yard consists of 45,000 square feet of clinical and commercial manufacturing space and will support Wuxi Pharmatech's existing cGMP facility for the manufacture of cell therapies.

Wuxi Pharmatech's expansion in the U.S. will help support growing customer demand for its products with single-source contract development and increased manufacturing capacity for allogeneic and autologous cell-based therapeutics. The new U.S. facility is expected to start operating in the second quarter of 2015.

At the end of April, Wuxi Pharmatech passed U.S. FDA inspection for general GMP approval of its drug analytical and stability testing facilities in the Shanghai Waigaoqiao Free Trade Zone.

The approval translates into regulatory advantages and potential faster approval for Wuxi's clients. //

To subscribe, call (770) 810-3144 or (800) 477-6307 if calling from the U.S. and Canada or email bioworld.salessupport@thomsonreuters.com.
For customer service inquiries call (215) 386-0100 or (800) 336-4474 if calling from the U.S. and Canada or email bioworld.support@thomsonreuters.com.

VCs

Continued from page 2

of the Dana Farber Cancer Institute and Harvard Medical School.

For now, Wuxi is content to follow the lead of U.S. VCs such as Arch and Third Rock, Qiao said.

"As a young venture fund, one way to learn is to work with the best in the field," she observed. "We're a balance sheet fund, so we're definitely looking at leading deals in specific areas in China, but outside China we'll continue to follow U.S. venture firms."

The list goes on. Last month, Shanghai-based BVCF (formerly Bioveda China) closed its third fund, raising $190 million for early and growth-stage companies in pharmaceuticals, biotechnology, traditional Chinese medicine, medical devices and health care consumer products, according to Rachel Zhao, principal. Of the 20 portfolio companies based in China, half are in drug development, Zhao said.

Chinabio also is launching an ¥300 million (US$48.2 million) VC fund, Chinabio Life Sciences Ventures, with partners Da'an Gene and the Foshan city government in Guangdong province. The fund is designed to help Western companies with late-stage or commercial medical devices, diagnostics, services and therapeutics that represent a strong fit for China's market, said Scott, who was a San Francisco-based life sciences angel investor before moving to Shanghai in 2008 to start Chinabio.

The fund, which expects to back 15 to 20 companies over the next three to four years, plans to be lead investor and first money in China for life sciences firms seeking to develop technologies for the Chinese market.

In general, the Chinabio panelists agreed that VC funds invest on the basis of well-defined criteria, with compelling science at the top of the list, followed by management prowess. Although Wu conceded that it's "almost impossible" to find experienced management teams at Chinese life science start-ups, Qiming Venture's Leung observed that the skill sets needed in China are different than those in the U.S. For example, the ability to navigate multiple layers of government is much more important in China than in the U.S., Leung maintained.

Like other countries, VCs in China sometimes are willing to overlook their stated investment philosophies to back a serial entrepreneur who will "make things happen," as Qiao observed. In China, serial entrepreneurs in the life sciences are in short supply, but investors are hopeful about the future.

"China still hasn't had a really successful story in drug development," Wu said, defining such an accomplishment as approval and commercialization of a novel drug, developed from original research, that achieves $1 billion or more in annual sales.

"But we hope we can be part of this," he added. Considering the rapid pulse of China's life sciences industry, "we don't want to miss it." //

OTHER NEWS TO NOTE

Advance Pharmaceutical Co., of Hong Kong, and **Boston Therapeutics Inc.**, of Manchester, N.H., signed an agreement with pharmaceutical manufacturer Patheon Inc. to manufacture pharmaceutical-grade tablets of the firm's lead candidate, BTI-320, a compound designed to reduce post-meal elevation of blood glucose. The agreement was secured in anticipation of Boston Therapeutics filing an investigational new drug application in late 2014 and initiating an international phase III study of BTI-320 in 2015.

Alexion Pharmaceuticals Inc., of Cheshire, Conn., said researchers presented data from a large, retrospective, natural history study of patients with severe perinatal and infantile hypophosphatasia, an inherited, rare metabolic disorder that can lead to progressive damage to multiple vital organs, destruction and deformity of bones and death. Early and sustained improvements were observed in infants, children and juveniles receiving asfotase alfa, according to phase II data presented at the Pediatric Academic Societies and the Asian Society for Pediatric Research meeting in Vancouver, British Columbia. Last year, the FDA granted breakthrough therapy designation to asfotase alfa for perinatal-, infantile- and juvenile-onset hypophosphatasia.

Astellas Pharma Inc., of Tokyo, and **Medivation Inc.**, of San Francisco, reported that the FDA has accepted their supplemental new drug application (sNDA) to extend the indication for Xtandi (enzalutamide) capsules for the treatment of men with metastatic castration-resistant prostate cancer (mCRPC) who have not received chemotherapy. The application was granted a priority review designation with a PDUFA date of Sept. 18. Xtandi is currently approved for the treatment of patients with mCRPC who have previously received docetaxel chemotherapy. The FDA's acceptance of the sNDA triggers a milestone payment to Medivation under its collaboration agreement with Astellas. The companies submitted an application to extend Xtandi's European marketing authorization application for mCRPC on April 2.

Chase Pharmaceuticals Corp., of Washington, said it raised $21 million in a series B financing from a syndicate led by New Rhein Healthcare Investors LLC. Other new investors in the round included Edmond de Rothschild Investment Partners and Cipla Ventures, the new venture capital arm of **Cipla Pharmaceuticals**, of Mumbai, India. Cipla said it will also collaborate with the company to develop the drug. If successful, Cipla may provide low cost access to Chase's lead drug in India and South Africa. The original venture investor, Brain Trust Accelerator Fund, also participated in the financing. The company plans to use the proceeds to fund phase IIa and IIb trials of the company's lead product CPC-201 targeting Alzheimer's disease.

OTHER NEWS TO NOTE

Circadian Technologies Ltd., of Melbourne, Australia, reported data at the Association for Research in Vision and Ophthalmology meeting in Orlando, Fla., showing that OPT-302 (formerly VGX-300), an inhibitor of VEGF-C, can prevent the formation of wet age-related macular degeneration (AMD) lesions and regress established lesions in the laser-induced mouse model of wet AMD. The drug reduced wet AMD lesion size and vessel leakage to a comparable extent as marketed agent Eylea (aflibercept, Regeneron Pharmaceuticals Inc.). Data also showed that VEGF-C levels are elevated in wet AMD and that OPT-302 can also reduce the expression of genes involved in blood vessel growth and inflammation in the mouse model. In other news, Circadian said wholly owned subsidiary Opthea Pty Ltd. completed a type B pre-investigational new drug application (IND) meeting with the FDA for OPT-302, a soluble receptor designed to block VEGF-C and VEGF-D, for the treatment of wet age-related macular degeneration. The company said it aims to submit an IND and initiate a phase I/IIa study in the first half of 2015.

Gloria Pharmaceuticals Co., of Beijing, and **Cumberland Pharmaceuticals Inc.**, of Nashville, Tenn., formed a joint R&D initiative. Each company has made a $1 million investment in Cumberland Emerging Technologies (CET), which is majority-owned by Cumberland and partnered with academic research centers to develop promising biopharmaceutical technologies. The new funds will be used to accelerate development of CET's pipeline of new product candidates emerging from Vanderbilt University and other regional research centers.

Medivation Inc., of San Francisco, reported U.S. net sales of prostate cancer drug Xtandi (enzalutamide) of $124.5 million, as posted by partner **Astellas Pharma Inc.**, of Tokyo. Ex-U.S. sales were $47.8 million. Medivatin's collaboration revenue, which consists of revenue attributable to U.S. sales, to ex-U.S. sales and to up-front and milestone payments, totaled $87.2 million for the quarter. The companies are looking to expand the use of Xtandi into pre-chemotherapy patients, with a priority review PDUFA date of Sept. 18. The company's net loss for the first three months of 2014 was $13.7 million, or 18 cents per share, a wider loss than the 9 cents per share analysts predicted. As of March 31, the firm had $241.5 million on its balance sheet. Shares of Medivation (NASDAQ:MDVN) closed Friday at $65.11, a gain of $5.11.

Scinopharm Taiwan Ltd., an active pharmaceutical ingredient manufacturer, has inked two new collaboration agreements with Hong Kong-based **Lee's Pharmaceutical Holdings Ltd.** The companies will jointly develop and produce Fondaparinux, an anti-thrombotic agent, and Travoprost and Bimatoprost, two prostaglandin derivative drugs for treating glaucoma. Scinopharm and Lee's expect the products – both posing high technical entry barriers in process development and manufacturing – will offer competitive advantages in the Chinese high-end generic drug market.

If c-kit cells are a bust as far as heart muscle repair is concerned, such repair might be achieved through treatment with thyroid hormone. That is the upshot of work reported by scientists from the Australian **Victor Chang Cardiac Research University** and **Emory University**. Currently, the theory is that heart muscle cells stop dividing after birth. The heart rapidly enlarges right before adolescence, to prepare for the demands of pumping blood through a bigger body, but that enlargement has been thought to be due to the growth of individual cells. However, the authors discovered that, in mice, a burst of thyroid hormone at the onset of adolescence led to cell division of heart muscle cells. The authors pointed out that "if replicated in humans, this may allow novel regenerative therapies for heart diseases." They published their findings in the May 8, 2014, issue of *Cell*.

During an infection with respiratory viruses, such as influenza or MERS-CoV, the immune system's response to the virus can cause as much damage as the virus itself. Now, researchers from the Australian **Walter and Eliza Hall Research Institute** have reported that the protein SOCS4 plays a key role in keeping the immune response to such respiratory viruses in check. As a group, the suppressor of cytokine signaling (SOCS) proteins are important for immune regulation, but the function of SOCS4 in particular had not been determined. The authors showed that mice lacking SOCS4 rapidly died after infection with the pandemic flu strain H1N1, and they were more susceptible to infection with the less virulent H3N2 strain. The animals had a much stronger proinflammatory cytokine response, along with a weaker killer T-cell response. The findings appeared in the May 8, 2014, issue of *PLoS Pathogens*.

Wuxi Pharmatech Inc., of Shanghai, said its manufacturing subsidiary, Syn-The-All Pharmaceuticals Co. Ltd., started construction on a fully integrated R&D and cGMP manufacturing site in Changzhou, about 110 miles west of Shanghai. //