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JUNE 10, 2015 | BIOTECH'S MOST RESPECTED NEWS SOURCE FOR MORE THAN 20 YEARS | VOLUME 3, NO. 23

China accelerating genetics efforts through public, private initiatives

By Cornelia Zou, Staff Writer

HONG KONG – A series of initiatives by both government and the private sector could give a powerful boost to genetic research in China.

In what may be the beginning of the largest publicly funded project in the space to date, the Chinese Academy of Sciences (CAS) broke ground on its first genetic resources center. Located in Jiangsu Province, the center will be the academy's first large project involving technology transfers and the application of both regenerative medicine and modern agriculture.

"This is very exciting because the new center is the academy's first genetics R&D center with proprietary research to industrialize research findings," said Guo

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Beigene's PD-1 MAb goes to Australia for first-in-human trials

By Shannon Ellis, Staff Writer

SHANGHAI – The Beijing-based oncology company Beigene Co. Ltd. continuing its string of upbeat news, announcing the first human dosing of its programmed death-1 (PD-1) antibody, BGB-A317, in Australia.

That marks the company's fourth oncology candidate to enter the clinic in

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TAIWAN

FOLLOWS U.S., EU SUBMISSIONS

Pharmaengine files pancreatic cancer drug NDA in Taiwan

By Dave Silver, Staff Writer

TAIPEI, Taiwan – Pharmaengine Inc. said it submitted a new drug application (NDA) to the TFDA, Taiwan's drug regulatory body, for the liposome version

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Government commits $14M to biocluster plan for research, innovation

By T.V. Padma, Staff Writer

LUCKNOW, India – An Indian government-funded drug research institute plans to set up a biopharma industry incubation center to attract entrepreneurs in northern and central

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'BOOSTER' SHOT

Pharmas join Japan initiative to tackle neglected diseases

By Catherine Makino, Staff Writer

TOKYO – A new initiative in Japan aims to bring together the research resources of multiple stakeholders, including a handful of multinational

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NEWCO NEWS

China's Neupharma launches phase I trials for sodium pump drug

By Shannon Ellis, Staff Writer

SHANGHAI – New out of the gate, Suzhou Neupharma Co. Ltd., has put its first candidate, RX-108, into clinical trials. Like many companies in China with global ambitions, Neupharma is collecting its first-in-human data in Australia while it waits for its trials to get a green light in China. (See Beigene story this issue.)

RX-108 is a novel small-molecule inhibitor of sodium-potassium adenosine triphosphatase (Na+/K+-ATPase), also referred as a sodium-potassium pump, or sodium pump.

When Neupharma was first established in 2009 the company's founders knew from the outset they wanted to discover compounds with worldwide potential. Using a structure-based drug design platform, RX-108 was discovered

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China

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Chunshan, manager of the cooperation department of CAS's Institute of Genetics and Development Biology (IGDB).

The CAS, along with the government of Changzhou City, is building the ¥2 billion (US$322 million) Genetic Resources R&D Center (South) in the high-tech zone of the city in Southern China. The center will focus on two areas of genetic studies: regenerative medicine and modern agriculture. The regenerative medicine unit will include a stem cell bank, a clinical studies center and an animal experiment center.

"We plan to build a corresponding North R&D center in Beijing, but it's just a plan at the moment," said Guo. "We will also consider bringing in international genetic research companies."

The 60-acre facility is being built with support from the CAS, Chang Zhou City and the Changzhou National Hi-tech Zone. The plan is for the center to be completed and operating at the end of 2016.

"We want to become an advocate for the industry," said Guo. "We'll cultivate some new biotech companies to commercialize research results as well as work with existing ones."

"Although the construction of the center is expected to be completed at the end of next year, we plan to bring in projects pretty soon," Guo added. "But it will still be a while before we see any marketing results."

The CAS's goal is to combine the projects with key local industries to boost economic growth in the region.

"This is a collaboration of the academy and society. We're looking for collaboration opportunities," said Guo. "Recently, we have been talking to Changzhou's No. 4 People's Hospital near the center and expect to make it a partner for our technology transfer."

The IGDB was founded in 2001 through a merger of three CAS institutes: the Institute of Genetics, the Institute of Developmental Biology and the Shijiazhuang Institute of Agricultural Modernization. It aims to develop key technologies in areas such as the genetic control of growth and development, gene expression, signal transduction, structural and functional genomics, biotechnology, molecular breeding, bioinformatics and systems biology.

To accelerate genetic studies in China, the industry is also providing support to research institutes.

WUXI APPTEC OFFERING NEXTCODE

Wuxi Apptec, a leading clinical research organization, announced a partnership with Fudan University to bring Wuxi's population human genomics database system and integrated research and clinical solutions to the Fudan-led Collaborative Innovation Center of Genetics and Development (CICGD).

The CICGD brings together world-renowned Chinese research institutions such as Shanghai Jiaotong University, Nanjing University, Zhongshan University, Central South University, the Shanghai Institutes for Biological Sciences, the Institute of Genetics and Developmental Biology and the Beijing Institute of Genomics.

Wuxi's Nextcode technology will allow CICGD scientists to perform gene sequencing and bioinformatics analysis with higher speed and precision to accelerate the whole process of research, clinical diagnosis and treatment of rare inherited diseases as well as malignant tumors. It can be used to analyze and manage whole-genome data on 350,000 people.

"This is the world's largest collection of sequence data, and the only covering an entire population . . . our platform was developed there over the course of 18 years, and in 2013 we

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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.

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Beigene

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18 months, and the company's first foray into large molecules. "Beigene, as new as it is, now has experience in both small molecule and biologics. We have experience in solid and hematological cancers, as well as experience in targeted and immuno-oncology therapies," Jason Yang, senior vice president and head of clinical development at Beigene, told *BioWorld Asia*. "We are learning, but we have built a solid foundation."

Beigene will seek to establish proof of concept in indications in which other PD-1 antibodies have shown to be efficacious, such as non-small-cell lung cancer (NSCLC) and melanoma, as a first step, and then look to expand to other indications.

The trial for BGB-A317, a humanized anti-PD-1 monoclonal antibody, will be a dose-escalation and expansion cohort in 30 to 40 patients with advanced malignancies to evaluate the safety, pharmacokinetics and preliminary antitumor activities, with plans to expand quickly if all goes well.

"This is a big accomplishment for a company like us – developing an antibody drug is much more complex, both preclinically and clinically, than a small molecule," said Yang. "We are happy to see the first two patients that have been dosed are doing well."

PD-1 plays an important role in immune modulation of tumor progression by regulating the key inhibitory signaling in the T cells when engaged by its ligands.

In the U.S., the PD-1 star is on the rise with the FDA approvals of Opdivo (nivolumab) from Bristol-Meyers Squibb Co. (BMS) for squamous NSCLC and melanoma and Merck & Co Inc.'s Keytruda (pembrolizumab), which is approved for melanoma and now is going after NSCLC. It was naturally the hot topic at the recent American Society of Clinical Oncology and American Association for Cancer Research meetings, and there is potential for PD-1 to be effective in numerous cancers. (See *BioWorld Today*, April 21, 2015.)

But China is just getting started in that area of immunotherapy and is still a long way off from commercialization.

"The development of PD-1 in China is in its early stage right now. We expect some competition, but we also believe that we have the scientific expertise and operational capacity to compete in China," said Yang.

One possible competitor is China Oncology Focus Ltd., an affiliate of Lee's Pharmaceutical Holdings Ltd., of Hong Kong.

In October 2014, Lee's in-licensed an anti-PD-1 candidate from Sorrento Therapeutics Inc. in a deal valued at $46 million plus stock purchase, to develop and commercialize STI-A1014 in Greater China. But the company has not announced clinical trials. (See *BioWorld Today*, Oct. 8, 2014.)

AUSTRALIA FIRST

Beigene is well known for making use of Australia to conduct early stage clinical trials.

There are several advantages for a China-based oncology company in doing so but speed is the biggest one.

Currently, the CFDA has an enormous backlog to clear, in particular for clinical trial applications, and many companies have to wait longer than 24 months to get a response, even if addressing a significant unmet medical need like NSCLC. Obtaining approval for a phase I study in Australia can occur months faster than in the U.S.

And with its fourth oncology trial in Australia, Yang said Beigene has built a solid reputation with cancer hospitals and investigators.

"The drugs we have already put into clinical trials in Australia have shown very good activity. They know they are dealing with a credible company that has good drugs that benefit their patients. That is an advantage," Yang said.

While patient enrollment from the outset is expected to be quick, the downside to trials in Australia is the overall patient population is still relatively small, and that naturally impacts the number of patients a company can enroll.

Beigene is also not the first to trial a PD-1 candidate in Australia; Yang said Merck and BMS have also tested their PD-1 candidates there.

"We don't expect major difficulty in recruiting patients right now," said Yang. "In one year or so, it may be a different story. The competition is always very fierce."

It is also difficult to find Asian or Chinese patients for trials.

"It is not difficult to find a common cancer at a late stage, perhaps after multiple lines of treatment. It is more difficult to find rare cancers, or to find cancers that are prevalent in China with genetic or epidemiological factors," said Yang, explaining the pros and cons for Chinese companies doing phase I trials in Australia.

One concern the company does not have is with respect to financing.

In the last six months, Beigene raised $75 million followed by $97 million in venture financing. With $172 million on hand, there is enough to finance its four candidates well into the next stage of trials. (See *BioWorld Today*, Nov. 19, 2014, and May 20, 2015.)

In addition to BGB-A317, Beigene has three small-molecule inhibitors in phase I trials: BGB-3111 (BTKi), BGB-283 (BRAFi dimer-i) and BGB-290 (PARPi). The company's overall pipeline consists of seven small-molecule candidates, two of them selected as national priority projects in the 12th five-year plan, and three large molecules. (See *BioWorld Today*, May 5, 2015.)

Coming next to the clinic, the company has a programmed death ligand 1, or PD-L1, candidate. **//**

Pharmaengine

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of irinotecan, PEP02, as a second-line treatment for pancreatic cancer patients who have failed gemcitabine therapy.

That follows announcements in April by its partner, Merrimack Pharmaceuticals Inc., of Cambridge, Mass., of an NDA submission to the FDA for the same drug (named MM-398 by Merrimack), and by Merrimack's MM-398 licensee, Baxter International Inc., for the submission of a marketing authorization application (MAA) to Europe's EMA in May.

Those regulatory submissions are based on positive results of a multinational phase III trial (NANDO-1) for MM-398 run by Merrimack and Pharmaengine, in which the injectable drug was taken in combination with 5-flourouacil (5-FU) and leucovorin (LV) against two control arms of MM-398 alone, and 5-FU/LV alone. Patients on the combination dose showed an impressive 1.9-month improved survival over the 4.2 months average survival for patients at that stage of the disease receiving 5-FU/LV alone.

That U.S., EU and Taiwan regulatory trifecta is a major milestone for Pharmaengine, an oncology-focused 20-person firm that epitomizes the "in-license, develop, out-license" model of drug development that many biotechs in Taiwan are following.

"We call it the 'no research, development only' model, or 'NRDO,'" explained Pharmaengine CEO Grace Yeh, a veteran of the industry in the U.S., including a stint at Millennium Pharmaceuticals Inc., where she was involved in project management and corporate management. Yeh returned to Taiwan at the urging of Lin Rong-jin, founder of Taipei, Taiwan-based TTY Biopharm, to co-found Pharmaengine with TTY in 2003. Although now a public company, TTY still owns a 19.7 percent stake in Pharmaengine, with the Taiwan government's National Development Fund holding a 15.5 percent stake, and the rest in the hands of institutional investors and individuals.

MILESTONES ACCRUING

With its NRDO model, the company has no need for its own labs or manufacturing facilities. Its current pipeline of three drugs consists of in-licensed assets from partners Hermes Biosciences Inc., of San Francisco, (acquired by Merrimack in 2009); Nanobiotix SA, of Paris; and Guangzhou Bebetter Medicine, of Guangzhou, China. The company performs preclinical and clinical trials working with CROs, CMOs and hospitals, with the aim of eventually licensing those assets out again.

Even without labs or factories, Pharmaengine still employs scientists who are experts in all aspects of pharmaceutical development.

"These people select the CROs or CMOs, design the studies, monitor how they work and make the reports for regulatory agencies," Yeh said. "For example, for the CMC part we don't have a plant to scale up, but our people will go to the plant and work with the operators to come up with the scale-up process."

And with the successful out-licensing of PEP02 to Merrimack in 2011 for Europe and Asian (excluding Taiwan) territories in a deal worth $220 million, Pharmaengine has been one of only a few local companies to strike out-licensing gold. The gains have been impressive, considering the company acquired Asian and European rights for PEP02 from Hermes back in 2003 for only $3 million.

And the drug keeps growing in value: Merrimack found a sublicensee partner for Asian and European rights in September 2014 in Deerfield, Ill.-based Baxter, in a deal worth up to $970 million, with Pharmaengine eligible for up to $46.5 million in sublicense revenue. The company had already received $27 million in up-front payments as of Sunday, and said it expects to receive an additional $11 million from Merrimack for reaching milestones related to the recent NDA and MAA submissions. And with China beckoning for sublicensee and Asian territory holder Baxter, the molecule has a bright future.

Results like those and the prospect of more to come have driven Pharmaengine's stock price from its 2012 IPO price of NT$89 (US$2.85) per share to its current NT$230 value, although off its peak of NT$344 from about a year ago. Its market capitalization currently stands at around $760 million, impressive considering the still-small operational scale of the company.

NEW SALES, MARKETING DIVISION

Yeh said she expects the U.S., EU and Taiwan regulators to approve the NDA and MAA applications at the latest by 2016, with the FDA expected to announce first. Once PEP02 is approved for sale in Taiwan, Pharmaengine intends to take on sales and marketing responsibilities itself, an all-new role for the company and something Yeh is excited about.

"At that stage, we will need more than [the current staff number of] 20 people. We will be a very focused sales team, because sales will be hospital-based, or to medical centers. It will be a limited sales force, which we can handle," said Yeh. And with the company having just moved into brand-new 10,000-square-foot office space, there's plenty of room for that new division.

With Taiwan's pancreatic cancer population at about 1,500, the company expects the drug to appeal to at least half of that number. But the real potential is for indications still in clinical trials. For conventional irinotecan, sales in Taiwan alone are around $15 million a year, according to Pharmaengine. As a liposomal version, PEP02 has potential in numerous oncology applications. The drug also is under development in gastric cancer, currently in a phase II trial; colorectal cancer, also in phase II; brain cancer, in phase I; and Ewing's sarcoma, a pediatric bone cancer, also in phase I.

Aside from PEP02, the company is developing PEP503, a nanoparticle formulation of hafnium oxide with oncology applications, in-licensed from Nanobiotix, currently in a pivotal

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India

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India, areas that are home to a number of high-quality research laboratories but are in dire need of bioclusters.

The Indian government has allocated $14 million (Rs900 million) to the Department of Biotechnology to set up bioclusters to promote its biotech industry.

Ram Vishwakarma, director of Central Drug research Institute (CDRI), Lucknow, one of the 38 institutes under India's Council of Scientific and Industrial Research (CSIR), told *BioWorld Asia* that CDRI would provide business incubation centers to cater to the needs of four states – Uttar Pradesh, Bihar, Madhya Pradesh and Odisha – which remain "untouched by a knowledge-driven industrial base."

Lucknow is home to several top research institutes engaged in biology research, and nearby Kanpur is home to a prestigious Indian Institute of Technology that has "high-level expertise" in biodesign and biocomputing, Vishwakarma said. However, the region has generally missed out on the success of India's biopharma industry because early government investments were made in southern cities such as Bangalore and Hyderabad, and later investments went to western India. Both the south and west of the country are now home to global biotech hubs.

By spreading out funding and tapping into researchers elsewhere in the vast and densely populated country, India may be able to leverage both more resources and more innovation to power the industry forward.

Vishwakarma said the proposed CDRI hub would be a new delivery platform for high-end areas in biotechnology, and its focus would include monoclonal antibodies, enzyme-based therapeutics, stem cells technology, fermentation technologies and peptide therapeutics.

"Creating these kinds of advanced facilities would require heavy investments which small companies would not be able to afford. The CDRI facility hopes to attract knowledge-driven companies," he said.

CSIR-CDRI scientist Anand Kulkarni said the proposed incubator is an example of public private partnership (PPP) in which CDRI would provide the technical expertise and small- and medium-scale enterprises would be drawn to work on their areas of interest.

India's minister for science and technology Harsh Vardhan recently announced, during a visit to CSIR-CDRI, the government's intent to set up a business industry incubator at CDRI and noted that the government "would strive to build a new generation of enterprises in the health care sector."

The minister also said that the ministry of science and technology is also considering setting up good laboratory practices (GLP)-certified labs in CSIR-CDRI for the complete range of investigational new drug (IND) studies, a step that would foster new drug development and "shore up the financial bottom line of the laboratory."

He said several CSIR-CDRI are carrying out IND studies on lead molecules for fracture-healing, cancers, thrombosis, malaria and hyperglycemia.

Vardhan also announced plans to set up a National Centre for Laboratory Animals in the institute, which would serve as a referral center for lab animal breeding and experimentation for new drug development.

He told scientists during his visit that India's Prime Minister Narendra Modi was committed to making India one of the leading global destinations for end-to-end drug discovery and innovation by 2020; and that strengthening the R&D ecosystem for drug development was a priority for the government.

CDRI is India's only public-funded research institute wholly focused on drug discovery and development, while a few other CSIR institutes, notably Indian Institute of Chemical Technology in Hyderabad; Indian Institute of Chemical Biology (IICB) in Kolkata, Indian Institute of Integrative Medicine (IIIM) in Jammu, Institute of Microbial Technology (IMTECH) in Chandigarh and National Chemical Laboratory in Pune also are engaged in relatively advanced drug development research.

For example, In February 2014, India's drug controller gave the nod to conduct phase II trials on a new clot-specific streptokinase (CSSK) developed at IMTECH, Chandigarh, in heart attack patients. CSSK could be an alternative to more expensive thrombolytic agents like tPA.

Streptokinases are enzyme-based, which dissolve blood clots, and are on the World Health Organization's essential list of medicines; and according to IMTECH, CSSK's novelty lies in its ability to reduce bleeding in patients, which is a common problem encountered with clot-dissolving drugs.

The CSSK technology was licensed to U.S.-based Nostrum Pharmaceuticals LLC for drug development and testing, through the latter's Indian subsidiary Symmetrix Biotech Private Ltd., Chandigarh.

Similarly, studies by IIIM, Jammu, in rats have confirmed the anti-inflammatory properties of an extract from an endangered Himalayan plant *Gentiana kuroo*, and its ability to reduce symptoms of rheumatoid arthritis. And IICB, Kolkata, has developed a herbal extract for the treatment of benign prostate hyperplasia – a precancerous condition that involves excess production of cells. **//**

Neupharma

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with computational modeling they developed for virtual screening.

"Basically, we took existing knowledge and then made modifications using our computational structure-based design to improve the physical, chemical and drug-like properties," Shawn Qian, president and CEO of Neupharma, told *BioWorld Asia*.

The company now has four small-molecule compounds in its pipeline, with plans for all four to be in clinical trials by next year. While the firm has a candidate for neurodegenerative diseases, oncology is Neupharma's main focus. And it is betting that targeting Na+/K+-ATPase will be an effective approach for the development of novel cancer therapies.

First discovered in 1957 by Jens Christian Skou in Denmark – he went on to receive one half of the Nobel Prize in Chemistry "for the first discovery of an ion-transporting enzyme, Na+/K+-ATPase."

Cardiac glycosides, which inhibit the plasma membrane Na+/K+-ATPase, were developed for the treatment of heart failure but later antitumor properties were observed in heart patients who were also suffering from cancer.

It is now understood that expression of Na+/K+-ATPase is elevated in various tumors. When Na+/K+-ATPase is inhibited in cancer cells, it triggers a series of downstream signaling activities that lead to cell-cycle arrest, apoptosis and autophagic cell death.

Believing in its potential in a range of cancers, "targeting Na+/K+-ATPase is a unique approach to develop anticancer therapies," said Paul de Souza, professor and chair of medical oncology, school of medicine, University of Western Sydney, who will be conducting the RX-108 study.

The phase I study will evaluate the safety, tolerability, pharmacokinetic and pharmacodynamic profile of RX-108 administered to patients with locally advanced or metastatic solid tumors. The study has two stages: one is a dose-escalation cohort and the other is a dose-expansion cohort to reach maximum tolerated dose.

In the next phase, for the efficacy and proof-of-concept study, Qian said the Neupharma would like to focus on liver and colon cancers. "This is based on our existing in vitro in vivo model which showed our compound performs well in these two cancer models," said Qian.

Last year, the company filed its clinical trial application with the local CFDA and national CDE. They have received expedited "green channel" status given to innovators and hope to commence the phase I trial in China soon. Qian said executives will discuss with the authorities the possibility of including the human data collected from Australia in the application.

There are also plans for a phase II trial in the U.S.

A RETURNEE STORY

Neupharma's beginnings are similar to many biotechs founded by Chinese returnees. Co-founder Qian is a medicinal chemist who spent more than 20 years in the U.S. He worked for Cytokinetics Inc. on projects with Amgen Inc. and Glaxosmithkline plc before deciding to go down the path of biotech entrepreneur.

As a native son of Suzhou, he was returning to a city that has developed one of the top three life science parks in the country, Suzhou BioBay, and boasts a vibrant ecosystem of clinical research organizations, financiers, big pharma and start-up biotech companies.

Qian said the government policy incentivizing experts to come back, and the support for innovation overall, has helped to set up the right environment, but his return was motivated even more by doing something for China: "I want to do pharmaceutical innovation, especially in China, given the huge patient needs; there is a lot to be improved, a lot of room for activities."

In March, Neupharma scored a financial uplift when it out-licensed rights, excluding some Asian countries, for a third-generation EGFR inhibitor in preclinical development to Coronado Biosciences Inc., now known as Fortress Biotech Inc., of New York. The deal provided Neupharma with an unspecified up-front payment and potential development and sales-based milestones going forward.

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biotech companies, to bear on the fight against some insidious neglected diseases.

The Drugs for Neglected Diseases Initiative (DNDi) recently announced a plan to work with pharmaceutical companies to accelerate the discovery of new drugs and lower the cost of developing new treatments for leishmaniasis and Chagas. The companies involved in the initiative are Japan's Eisai Co., Shionogi & Co. and Takeda Pharmaceutical Ltd., along with London-headquartered Astrazeneca plc.

"Given Japan's proven pharmaceutical strengths, it makes sense for DNDi to partner with a number of leaders in the field, and to make full use of the expertise and experience of these world-class enterprises," said Hugh Ashton, a Japan-based industry watcher.

The companies will give DNDi access to millions of unique compounds in their research libraries to search out new treatment leads using the Drug Discovery Booster program. The approach of using libraries from several companies and state of the art technology to pinpoint compounds with potential for further testing is relatively new, according to the DNDi.

"This could be a game-changing milestone in the fight against diseases that destroy the health and livelihoods of the world's poorest," said BT Singsby, CEO of the Global Health Innovative Technology Fund (GHIT Fund).

A key hurdle in identifying new approaches to treat neglected diseases is the high cost of the initial stages of drug discovery. The process can be both expensive and time consuming.

"It is an experimental approach to radically modernize drug development for neglected diseases, which is the result of a decade of growing partnerships with pharmaceutical companies," said DNDi Executive Director Bernard Pecoul. "This experiment could significantly reduce the time and money it takes to find new promising treatment leads."

In the past DNDi had worked bilaterally with a number of pharma partners, looking for and then testing compounds.

This multicollaboration with a number of partners has the potential to cut two years from the early drug discovery process that normally takes five years or more. It could also significantly lower the cost of research.

"Based on our strong partnership with DNDi, Shionogi is leveraging its experience and strengths in the infectious disease field to deliver new drugs to patients struggling against leishmaniasis and Chagas disease as soon as possible," said Isao Teshirogi, president and CEO of Shionogi.

Diseases in the leishmaniasis family are caused by protozoan parasites from more than 20 species of *Leishmania* parasite, transmitted to humans through the bites of infected female phlebotomine sandflies, according to the World Health Organization (WHO). Visceral leishmaniasis (VL) is known as one of the oldest diseases of humanity; however, it is not one that is easily identified because it is often confused with other diseases like malaria, although its etiologic agent was identified in 1903.

Chagas disease, also known as American trypanosomiasis, is a potentially life-threatening illness caused by the protozoan parasite *Trypanosoma cruzi*. Chagas can manifest itself as a sudden and brief acute illness or as a long-lasting chronic condition with symptoms ranging from mild to severe. The Brazilian physician Carlos Chagas discovered the disease in 1909. Even after a century, there are just two compounds typically used to treat the disease. If left untreated, the infection persists and, in some cases, advances to the chronic phase.

About 6 million to 7 million people are infected worldwide, mostly in Latin America, though it is spreading to other areas. It is mostly vector-borne, transmitted to humans by contact with feces of triatomine bugs, known as "kissing bugs," among other names. Antiparastic treatment can prevent or stop the disease from progressing.

Controlling the diseases and blood screening are important to prevent infection through transfusions and organ transplantation.

DNDi was founded in 2003 and brings together academic, medical, public health and pharmaceutical stakeholders to find ways to tackle neglected diseases.

DNDi has introduced four new treatments, including two for drug-resistant malaria that have reached 80 million people, the first new treatment in 25 years for the advanced stage of sleeping sickness and a new combination therapy for visceral leishmaniasis in Africa. //

China

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were spun out as a separate company to bring this platform to rest of the world," said Hannes Smarason, co-founder and chief operating officer of Wuxi Nextcode Genomics. "Now as part of Wuxi Apptec, we are very excited to be bringing it to China."

Nextcode's system is fully integrated. Its Shanghai facility has a full range of sequencing technologies and talents that make it the most comprehensive platform for using the genome in medicine.

"Our key advantage is our database model. Unlike every other system today, it was developed to enable the efficient use of massive genomic datasets," said Smarason. "That means that people using our system can diagnose more cases faster, identifying the causes of rare disease and the mutations behind cancers."

Wuxi Nextcode, a wholly owned subsidiary of Wuxi Apptec, offers fully integrated turnkey solutions for genomic medicine, from CLIA sequencing to bioinformatics, clinical interpretation and diagnostic test development and delivery. //

OTHER NEWS TO NOTE

Anokion SA, of Ecublens, Switzerland, is spinning out a new start-up, **Kanyos Bio Inc.**, to serve as the vehicle for a development alliance in autoimmune disease with Tokyo-based **Astellas Pharma Inc.**, which could be worth up to $760 million in R&D funding, option exercise payments and milestones. Kanyos is straight out of Versant Ventures' build-to-sell stable – and in keeping with the Versant model, Astellas has an option to buy the company outright on pre-agreed terms. The acquisition price is included in the headline deal value. Kanyos Bio, of Cambridge, Mass., has closed a $16 million funding round as part of the agreement, with participation from Astellas, as well as Versant and two corporate venture capital arms, Novo Ventures and Novartis Venture Fund. The new firm will focus on developing candidate therapies in two indications initially, celiac disease and type 1 diabetes, while Astellas also has an option to add a program in a third indication. Anokion, a spinout from the École Polytechnique Fédérale de Lausanne (EPFL), is commercializing a method for tolerizing the immune system to specific antigens. It was developed by Jeffrey Hubbell, its academic founder and chief scientific officer, who holds dual appointments at EPFL and at the University of Chicago. Hubbell's lab has found a way to exploit the natural immune tolerance mechanisms that kick in when erythrocytes undergo apoptosis.

Astellas Pharma Inc., of Tokyo, said preliminary data from a phase I/II trial demonstrated that ASP2215, a selective inhibitor of FLT3/AXL, in patients with relapsed or refractory acute myeloid leukemia (AML) had inhibitory activity against FLT3 internal tandem duplication as well as tyrosine kinase domain, two common types of FLT3 mutations that are seen in up to one-third of patients with AML. Data showed a 57.5 percent overall response rate and a 47.2 percent composite complete response in 106 patients with FLT3 mutations who received 80 mg and higher doses. Furthermore, median duration of response was 18 weeks across all doses and median overall survival was approximately 27 weeks at 80 mg and above in FLT3 mutation-positive patients. The data were released at the American Society of Clinical Oncology annual meeting.

Cellular Biomedicine Group, of Shanghai, said preclinical data published in the *Journal of Molecular Sciences* showed that xenogeneic human adipose-derived mesenchymal progenitor cells (haMPCs) engrafted into rabbit articular cartilage promoted cartilage repair. Researchers also observed positive staining of human mitochondrial marker and HLA-I but not HLA-II DR on rabbit cartilage in the treated animals. The company is testing its autologous haMPC therapy, Rejoin, in a phase IIb trial in knee osteoarthritis.

Circadian Technologies Ltd., of Melbourne, Australia, announced that its partner **Eli Lilly and Co.**, of Indianapolis, presented data from the phase I trial of VEGFR-3 antibody IMC-3C5 (LY3022856). In a dose-escalation study and an expansion cohort to evaluate IMC-3C5 monotherapy at 30 mg/kg in 21 patients with colorectal cancer, weekly intravenous administration was shown to be well tolerated up to the highest planned dose of 30 mg/kg and a maximum tolerated dose was not reached. The median progression-free survival at the 30-mg/kg dose was 6.3 weeks. The data were released at the American Society of Clinical Oncology annual meeting.

Scenesse (afamelanotide), a product owned by **Clinuvel Pharmaceuticals Ltd.**, of Melbourne, Australia, was approved almost six months ago for patients with erythropoietic protoporphyria (EPP), an extreme sensitivity to sunlight, but the post-authorization requirements laid down by the EMA mean the first prescription is yet to be written. Now, though, there is progress, as the first convention of EPP specialists took place in Paris on Friday, as part of a commitment to the EMA to train expert physicians and their staff. At the convention, 33 physicians from 23 centers in 15 countries were instructed in the administration of Scenesse. The extent of the interest in prescribing the drug has exceeded expectations, and Clinuvel said it will hold a number of other expert meetings. EPP is so severe that a placebo-controlled phase III would have been unethical and the recommendation to approve Scenesse was notable for being the first time the EMA had heard testimony from patients during its deliberations on a marketing application. In the absence of statistically significant proof of efficacy, Clinuvel is required to establish a centralized European EPP registry and carry out a post-authorization study of all patients. The company will have to provide biannual safety reports to the EMA for the first two years and a data and safety monitoring board will oversee the registry. (See *BioWorld Today*, Oct. 28, 2014.)

Pharmaengine

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trial for soft-tissue sarcoma. And the company's third drug, PEP06, in-licensed from Guangzhou Bebetter, is targeted to an as-yet unnamed indication but one that Yeh promised will be exciting.

PEP06 differs from Pharmaengine's other assets in that it's at a very early drug discovery stage, and it could still develop into several candidates. "We hope to select one drug candidate for preclinical development, and finish the study in one year. For this drug, we have the rights for all territories outside of China, with Bebetter retaining China rights," said Yeh.

Pharmaengine sees the role of Bebetter as being its laboratory arm, albeit one based in China, potentially providing a steady supply of novel oncology drugs to Pharmaengine's pipeline.

"We expect this relationship to generate at least one drug candidate every two or three years," Yeh said. //

OTHER NEWS TO NOTE

Eli Lilly and Co., of Indianapolis, reported results from a new study of Japanese patients with type 2 diabetes, showing that once-weekly Trulicity (dulaglutide) 0.75 mg provided greater HbA1c reduction compared to once-daily Victoza (liraglutide, Novo Nordisk A/S) 0.9 mg after 52 weeks of treatment. Trulicity also significantly lowered average postmeal blood glucose levels from baseline compared to Victoza. Another study showed that Trulicity reduced HbA1c levels better than Lantus (insulin glargine, Sanofi SA) after 26 weeks of treatment. The data were presented at the American Diabetes Association's Scientific Sessions in Boston.

Hanmi Pharmaceutical Co. Ltd., of Seoul, Korea, presented interim results of the phase I/II domestic trial of HM61713, an orally active epidermal growth factor receptor (EGFR) mutant selective inhibitor, in T790M mutation-positive non-small-cell lung cancer patients. Daily single administration of HM61713 800 mg showed 95.2 percent disease control rate (DCR) in 59 of 62 patients with T790M-positive mutation who developed resistance to previous EGFR tyrosine kinase inhibition. Objective response rate of 54.8 percent was observed in 34 of 59 patients. The data were released at the American Society of Clinical Oncology annual meeting. In other news, at the American Diabetes Association's Scientific Sessions in Boston, Hanmi reported nonclinical results showing that the once-weekly combo of Lapsinsulin 115 and GLP-1 drug efpeglenatide exhibited therapeutic benefits while reducing adverse effects such as weight gain. Results showed that when mono-treatment was switched to the Lapsinsulin combo, HbA1C level quickly and strongly dropped without hypoglycemia risk. In addition, the combo effectively protected from the apoptotic death of pancreatic beta-cell.

Hutchison China Meditech Ltd., of Shanghai, said partner **Astrazeneca plc**, of London, presented preliminary data from the ongoing phase Ib trial of the c-Met inhibitor savolitinib (AZD6094) combined with Astrazeneca's drug candidate, AZD9291, in non-small-cell lung cancer. Twelve patients were dosed with either 600 mg or 800 mg daily of savolitinib in combination with 80 mg once daily AZD9291. The 600-mg combination dose was well tolerated, with toxicity profiles allowing for combination therapy at doses previously shown to be biologically active. Of the 11 evaluable patients in the study, six partial responses (confirmed and unconfirmed) were observed to date. Responses to date include four of seven patients with confirmed T790M-negative status. The data were released at the American Society of Clinical Oncology annual meeting.

Medivation Inc., South San Francisco, and **Astellas Pharma Inc.**, of Tokyo, reported hopeful phase II results in androgen-receptor (AR)-positive triple-negative breast cancer (TNBC) in the approved prostate-cancer (PC) drug Xtandi (enzalutamide). The data were released at the American Society of Clinical Oncology annual meeting, where attendees heard about a 118-patient, single-arm, multicenter experiment in TNBC that took place in two stages. The primary endpoint of the trial was clinical benefit rate at 16 weeks (CBR16), defined as the proportion of women with a complete response (CR), partial response (PR) or stable disease for at least 16 weeks. Two patient populations were evaluated. The evaluable patient population had at least 10 percent of the cells in their primary tumor sample test positive for the AR and had at least one follow-up tumor assessment, and the intent-to-treat population (ITT) received at least one dose of Xtandi and had breast cancers with any amount of AR immunohistochemistry (IHC) staining present. Seventy-five patients met the evaluable criteria, and 118 were included in the ITT category. No limit was placed on the number of prior treatments. In the 75 evaluable subjects, CBR16 was achieved in 35 percent (95 percent confidence interval [CI]: 24-46) including six CR/PR (8 percent). Clinical benefit rate at 24 weeks (CBR24) was achieved in 29 percent (95 percent CI: 20-41). The median progression-free survival (PFS) was 14.7 weeks (95 percent CI: 8.1-19.3). In the ITT population, CBR16 was achieved in 25 percent (95 percent CI: 17-33) including seven CR/PR (6 percent). CBR24 was achieved in 20 percent (95 percent CI: 14-29). Median PFS was 12.6 weeks (95 percent CI: 8.1-15.7).

OTHER NEWS TO NOTE

Mesoblast Ltd., of Melbourne, Australia, said it received $5.8 million from the Australian government for R&D activities conducted during the 2014 financial year. The funds were provided under the government's R&D Tax Incentive Program. Mesoblast said it expects to receive funds from the program for R&D activities during the 2015 financial year, including the development of cell-based product candidates.

Neostem Inc., of New York, filed a prospectus supplement to its shelf registration with the SEC enabling it to sell up to $30 million in shares of common stock to Aspire Capital Fund LLC subject to certain conditions over a two-year period. As of the March 31, Neostem had about $41 million in cash to fund operations. Last month, the company signed an exclusive license agreement with **Cellular Biomedicine Group**, of Shanghai, for its patient-specific immunotherapy to treat late-stage hepatocellular carcinoma in China. (See *BioWorld Today*, May 21, 2014.)

Orexigen Therapeutics Inc., of San Diego, and its North American partner, Takeda Pharmaceuticals USA Inc., part of Osaka, Japan-based **Takeda Pharmaceutical Col Ltd.**, are suing subsidiaries of Dublin-based **Actavis plc** to block them from marketing a generic version of obesity drug Contrave (naltrexone HCl/bupropion HCl extended release). Actavis has filed an abbreviated new drug application seeking to market and sell generic versions of Contrave prior to the expiration of U.S. patents on the drug. The suit was filed in the U.S. District Court for the District of Delaware.

Pluristem Therapeutics Inc., of Haifa, Israel, said it has been awarded a Smart Money grant from Israel's Ministry of Economy. The program's aim is to assist companies to extend their activities in international markets. The Israeli government will grant Pluristem budget and resources for the marketing of its advanced cell therapy products in Japan and for regulatory activities there. Pluristem will also receive assistance from Israel's trade attachés stationed in Japan, and from experts appointed especially by the program.

Prana Biotechnology Ltd., of Melbourne, Australia, said the European Commission approved orphan designation for PBT2 for the treatment of Huntington's disease. The drug, which also has orphan status in the U.S., yielded positive phase II data last year, and Prana said further work in the U.S. will continue after the removal of a partial clinical hold.

Prima Biomed Ltd., of Sydney, said it received a notice from Nasdaq indicating that the firm has regained compliance with the minimum $1 bid price requirement for continued listing.

Prolynx LLC, of San Francisco, said the FDA cleared its investigational new drug application for ultra-long-acting PEG~SN-38 (PLX-0264; DFP-13318), which comprises a pegylated version of the active metabolite of widely used cancer drug irinotecan. The product is designed to provide greater efficacy than irinotecan or other SN-38 prodrugs, while avoiding their serious intestinal toxicity. The planned phase I trial in solid tumor patients is expected to begin later this year. Prolynx is developing PEG-SN-38 in collaboration **Delta-Fly Pharma Inc.**, of Tokushima, Japan.

The Lead Discovery Center GmbH (LDC), of Dortmund, Germany, entered a license agreement giving **Qurient Co. Ltd.**, of Gyeonggi-do, South Korea, exclusive worldwide rights to a series of highly selective CDK7 inhibitors for the treatment of cancer, inflammation and viral infections. The partners plan to collaborate to advance the technology from validated lead stage into clinical development. Following completion of a successful proof-of-concept study in humans, they will seek to license the technology to a partner. LDC is set to receive undisclosed up-front and milestone payments upon the achievement of predetermined development events, and Qurient will fund future development activities within the collaboration. Other terms were not disclosed. The partners have an ongoing collaboration, inked in 2013, to advance Axl kinase inhibitors.

OTHER NEWS TO NOTE

R-Tech Ueno Ltd., of Tokyo, disclosed plans to conduct collaborative research with Autonomous University of Barcelona and Vall d'Hebron Institute of Research, in Catalonia, Spain, to develop a VAP-1 inhibitor for the treatment of cerebral infarction. The drug, RTU-009, is believed to have an anti-inflammatory and neuroprotective effect. Terms were not disclosed.

Takeda Pharmaceutical Co. Ltd., of Osaka, Japan, presented additional posthoc analyses from the EXAMINE (EXamination of CArdiovascular OutcoMes: AlogliptIN vs. Standard of CarE in Patients with Type 2 Diabetes Mellitus and Acute Coronary Syndrome) cardiovascular outcomes trial, showing that composite rates of major adverse cardiac events were similar for DPP-4 inhibitor alogliptin compared with placebo in patients taking angiotensin-converting enzyme inhibitors (11.4 percent vs. 11.8 percent, p = 0.76). Additional posthoc analyses from the EXAMINE data showed that alogliptin compared with placebo did not significantly increase the incidence of cardiac ischemic events (24.6 vs. 25.1, p = 0.72) and cardiovascular hospitalizations (16.4 vs. 16, p = 0.73). The data were presented at the American Diabetes Association's Scientific Sessions in Boston.

Scientists from the Australian **University of Queensland** have shown that there are two distinct types of neuronal precursor cells in the hippocampus, a brain region that plays a role in both memory and mood. Furthermore, the birth of new neurons is important for memory formation but may also be part of the mechanism of antidepressants' action. In their experiments, the authors purified neuronal stem cells and activated them via several different mechanisms. They were able to identify two distinct populations that were activated and modulated by distinct stimuli. "These results demonstrate that the adult hippocampus contains phenotypically similar but stimulus-specific populations of quiescent precursors, which may give rise to neural progeny with different functional capacity," the authors concluded. Such distinct cell populations might be targeted specifically for the treatment of memory and mood disorders. Their work appeared in the May 27, 2105, issue of the *Journal of Neuroscience*. In other news, researchers from the University of Queensland reported phase I data from a trial to induce tolerance to autoantigens in rheumatoid arthritis (RA). The majority of RA patients have antigens to specific peptides with a surface modification called citrullination, and patients with specific HLA alleles are at high risk. In their work, the authors showed that Rheumavax, which consisted of dendritic cells exposed to a mix of citrullinated autoantigens, was well tolerated and led to a decrease in number of T cells and inflammatory cytokines in 18 patients. "This exploratory study demonstrates safety and biological activity of a single intradermal injection [of Rheumavax] . . ., and provides rationale for further studies to assess clinical efficacy and antigen-specific effects of autoantigen immunomodulatory therapy," the authors concluded. They published their trial in the June 3, 2015, issue of *Science Translational Medicine*.

Viralytics Ltd., of Sydney, provided positive final data from a phase II CALM trial of lead drug candidate Cavatak, an investigational cancer immunotherapy based on a proprietary bioselected common cold virus that has been shown to preferentially infect and attack cancer cells. Final results showed that 22 of the 57 patients achieved the immune-related progression-free survival (irPFS) endpoint, more than doubling the target of 10 of 54 evaluable patients reporting irPFS at six months after the first dose of Cavatak. Investigators also reported an overall response rate in 16 of 57 (28 percent) patients. Of those, eight patients achieved a complete response and disappearance of their total tumor burden and the other eight achieved a partial response being at least a 30 percent reduction in the tumor burden. Durable responses, persisting for six months or more, were seen in 21 percent of patients. The data were released at the American Society of Clinical Oncology annual meeting. //

Neupharma

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The company is now in the process of raising its series B financing.

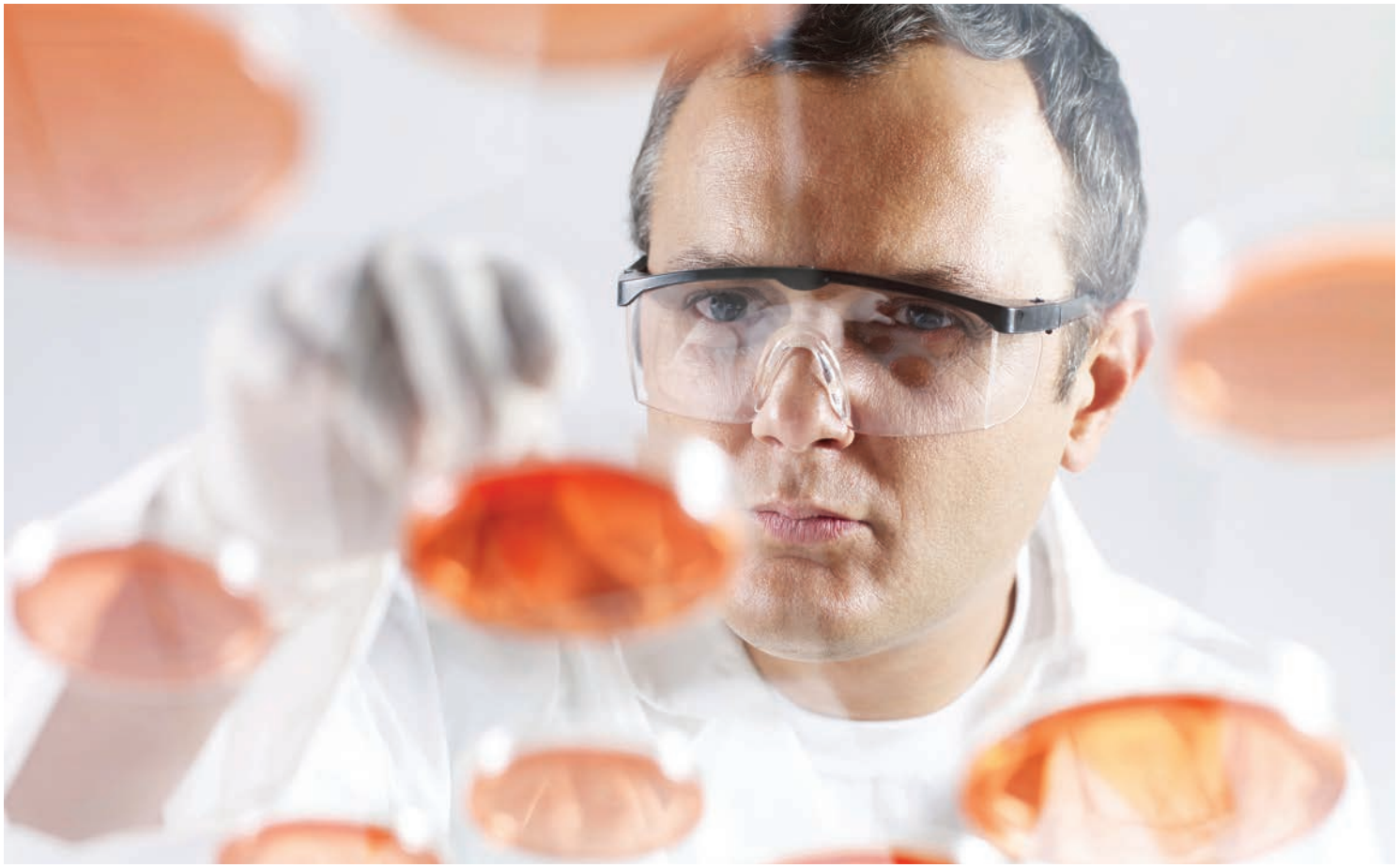
Qian said Neupharma has come this far by being capital efficient; having built the technology platform to discover drugs, the firm has sped up the process, reducing time and costs.

"In terms of our strategy, we combine first in class and best in class and, in time, we want to balance out novel target vs. validated target," Qian said.

With a global vision, the company has invested in its global patents as well. "We want to develop a drug not just for China. We want to be in China, for the globe," Qian said.

"We want to use common practices like U.S. biotech companies," he added. "We push as much as we can with very limited funding. We stay lean to get the program pushed forward. At the same time we look to collaborate with biopharma companies to minimize our risk and obtain cash flow to co-develop our assets.

"That is our strategy, to survive and push forward." //



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