Kim Ribbink

CHINA'S Pharma Star Shines Bright

With a large patient population, government commitment to healthcare reform, a huge depth of scientific talent, and a powerful economy, China has been identified by many as the world's most important emerging biopharma market.

With a population of 1.3 billion people, China is both the world's most populous nation and the fastest-growing major economy.

China has long had a reputation for low-cost labor and cheap exports. But according to a report from KPMG, China's Pharmaceutical Industry Poised for the Giant Leap, China is turning away from this model and is focusing on socioeconomic development and resource sustainability.

The Chinese government laid out development goals in 2010 called the "125" plan, the country's 12 Five-Year Plan (2011-2015), which places emphasis on greater welfare measures, public service, and more equitable distribution of wealth. Top priorities for the government are healthcare reform to ensure all citizens have basic medical coverage, modernizing the health infrastructure, improving healthcare delivery, and overhauling the pharma industry, the KPMG report notes.

According to Business Monitor, China's pharmaceutical market, valued at $66.9 billion, is the third largest behind the United States and Japan.

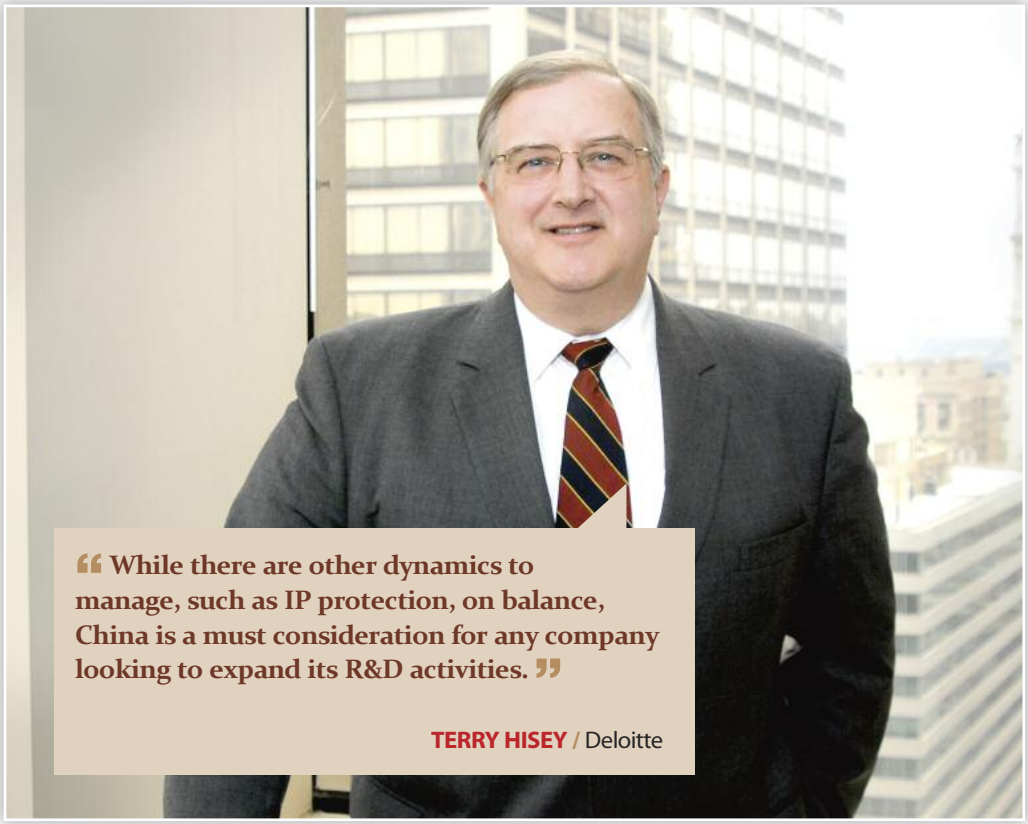
China has the potential to be the world's second-largest biopharma market, behind only the United States, as soon as 2016, and high-level initiatives are being driven by the Chinese government to support clinical research, says Ling Zhen, general manager of Quintiles, China.

"One example is the multibillion (RMB) drug discovery megaproject that China's health ministry kicked off in September 2010 to fund research that ranges from discovery to hospital-based clinical trial infrastructure," Mr. Zhen says. "In 2010, the Chinese government established 20 provincial high-tech venture funds valued at RMB 9 billion to be based in Shanghai, Beijing, Shenzhen, and four other locales."

FAST FACT

IN CHINA'S 12TH FIVE-YEAR PLAN, THE GOVERNMENT IS ENCOURAGING KEY PHARMACEUTICAL COMPANIES TO INVEST MORE THAN 5% OF ANNUAL REVENUE IN R&D.

Source: Business Monitor



> "While there are other dynamics to manage, such as IP protection, on balance, China is a must consideration for any company looking to expand its R&D activities."
>
> **TERRY HISEY** / Deloitte

The State of the Research Industry

Pharmaceutical research in China has come a long way over a comparatively short period of time, says Simon Li, general manager, Kantar Health China.

He says few multinational companies considered China as an option despite endeavors

by the Chinese government to attract foreign pharma companies. But in recent years there has been a rapid expansion of CRO and outsourcing services as well as commitment from pharma companies to invest in Chinese R&D facilities.

"By the end of last year, there were more than 20 R&D centers in China with more than 3,300 employees," Mr. Li says.

There are a number of considerations that contribute to making China an attractive location for life-sciences companies looking to expand their R&D activities, says Terry Hisey, vice chairman and U.S. life sciences leader, Deloitte.

"Factors that drive this include access to significant numbers of clinical research organizations; a talent market fueled by tens of thousands of graduates each year who specialize in relevant scientific areas; a large patient population available for clinical trials; government support from both an economic and policy standpoint to drive innovation in life sciences; plus a commitment to provide healthcare for China's billion-plus citizens," he says. "These and other factors in combination, can lead to lower costs and shorter times to market. While there are other dynamics to manage, such as IP protection, on balance, China is a must consideration for any company looking to expand its R&D activities."

China also is attractive to global companies because of the relatively low cost of conducting research in the country.

In addition, strong productivity standards, and access to low-cost APIs and raw materials made locally contribute to an attractive market, says Marc Finn, senior director, business development for Suzhou Pharma Services.

The country's strong economy is also attractive to companies looking to bring products to market in China, and this has been a major driver behind the country's own growing pharmaceutical industry.

Clancey Houston, managing director of Chandler Chicco Companies' China operations, says scale is the big differentiator in China.

"Whether we're talking about general population metrics or specific ones — such as urbanization and aging, the macroeconomic environment and its impact on annual growth rates and income levels, or lifestyle changes that are impacting the incidence and prevalence of disease — the scale of these elements in China is massive," Ms. Houston says. "Add to this the government's current healthcare reform efforts and the potential they hold to effect a significant transformation of health outcomes across the population, and China truly stands apart."

Another advantage, Mr. Finn says, is the creation of specialized industrial/economic zones, such as Suzhou Industrial Park, with access to shipping, labor, tax incentives, housing, transportation, and so on.

Pharma Trends

Francis Cao, senior director of government affairs and public relations at the Chinese biotech company Beigene, says the R&D scenario has evolved rapidly in recent years. In the early days, led by Wuxi, PharmaTech, and others, many CRO companies were burgeoning in China. As the market became more established and multinational pharma began to outsource more and more to China, increasing numbers of multinational pharma players established their R&D facilities or centers in China themselves and leveraged talent from within the country and from Chinese scientists, who had returned from working in Europe and the United States.

Now China is into its next wave, Mr. Cao

China: The Top 20 Conditions

1. Headache
2. Insomnia
3. Abdominal Pain
4. Abdominal Bloating
5. Gingivitis
6. Sleep Difficulties
7. Migraine
8. Arthritis
9. Pain
10. High Blood Pressure
11. Nasal Allergies
12. Dermatitis
13. Anxiety
14. Anemia
15. Arrhythmia
16. Chronic Constipation
17. Eczema
18. Ulcer Disease
19. Fungal Infections
20. Osteoporosis

Editor's note: The National Health and Wellness Survey (NHWS) is a nationally representative, self-administered survey conducted annually via the Internet. The survey is the largest self-reported database in the healthcare industry. Nine of the top 20 conditions in China are not in the top 20 in the U.S. or EU.

Source: The National Health and Wellness Survey Database, Kantar Health 2010.

says, which is innovative home-grown biotech and pharma companies, such as Beigene.

The development of China-based R&D facilities to create innovative products that are tailored to address the unique disease mechanisms that exist in China has led to the establishment of centers by a large number of the world's top pharma companies, Ms. Houston says.

Mr. Hisey says there are a number of continuing trends that are adding to China's challenges and attractiveness as a pharmaceutical hub, such as the Chinese focus on generics and the healthcare needs of a billion-plus Chinese citizens.

Business Monitor notes generic drugs — valued at $42.9 billion — comprise the majority of China's pharmaceutical market, with sales of OTC medicines valued at about $16.4 billion, supported by a cultural acceptance of self-medication and fairly liberal sales channels. Patented drugs — $7.6 billion — account for just 10.4% of the pharmaceutical market.

There are also significant government support and investments through tax incentives and direct investment in drug R&D for companies that develop drugs in China and an unprecedented level of collaboration across the healthcare ecosystem, including hospitals, academic institutions, government agencies, and pharmaceuticals companies, Mr. Hisey says.

"Beyond this, we expect to see a continuing trend of alliances, joint ventures, and M&A activity both between Chinese companies as well as Chinese companies with non-Chinese multinational corporations," he adds.

Some examples of China-global alliances include an agreement between Pfizer and the Chinese company Zhejiang Hisun Pharmaceutical to set up a joint venture to develop, produce, and commercialize off-patent products in China and other markets.

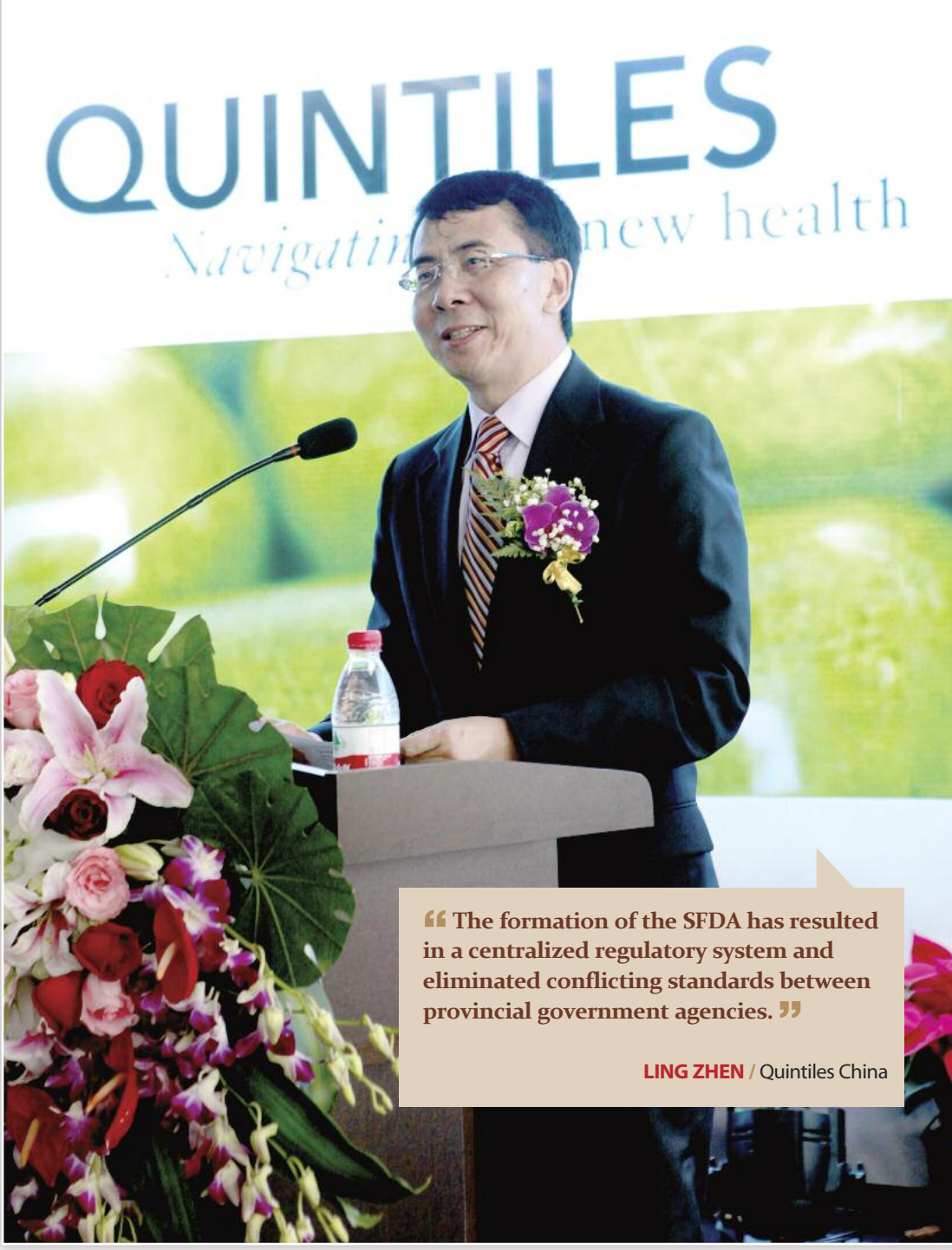
Another emerging trend, Mr. Hisey says, is increased interest beyond generics toward the development of a branded pharmaceutical business in support of both the Chinese market as well as potential export to the rest of the world.

Mr. Li says another trend, and the main way for multinational companies to achieve profitability in China, is the promotion of value-added services.

"The '125,' or the 12th five-year national development plan, opened up opportunities for foreign companies to share their expertise in logistics, IT systems, supply chains, and strategic integration," he says.

Mr. Finn points out the importance of local expertise in product manufacturing.

"It is important to establish a quality system that also includes guidance from local Chinese regulatory experts, such as the Chinese State Food and Drug Administration," he says, adding, however, that global companies that use Western-style quality standards and models and implement them in China can have a major operating and business advantage compared with domestic Chinese companies.



> **"The formation of the SFDA has resulted in a centralized regulatory system and eliminated conflicting standards between provincial government agencies."**
>
> **LING ZHEN** / Quintiles China

Clinical Appeal

China's large population often has limited access to newer drugs, making clinical study participation attractive, and the fact that the doctor-patient relationship remains traditional enables easier enrollment and improved retention once a trial begins, Ms. Houston notes.

A population of 1.3 billion people offers opportunities for productive clinical research in terms of disease profiles, including increased rates of diseases associated with Western populations, and large, concentrated patient pools, Mr. Zhen says.

FAST FACT

THE TOP THREE CAUSES OF DEATH IN CHINA ARE CEREBROVASCULAR DISEASE (18%), CHRONIC OBSTRUCTIVE PULMONARY DISEASE (14%) AND ISCHEMIC HEART DISEASE (8%).

Source: Cutting Edge Information

Ms. Houston adds, however, that patient recruitment and retention remains a real challenge, despite the large population, as the number of government-approved trial sites remains

limited, an issue that will only grow as the volume of trials coming to China increases.

According to Mr. Zhen, long regulatory approval timelines and the requirement to obtain import and export licenses may delay trials, especially where blood or tissue samples export is necessary.

"The limited number of accredited sites and investigators for clinical studies also pose additional challenges, which can be attributed to the SFDA's requirement for clinical studies to be conducted in authorized sites in China," he says. "It doesn't help that qualified logistic support, such as central storage and IVRS, in China can also be rather limited."

Clinical research in China spans a wide spectrum of therapeutic areas, including respiratory and cardiovascular diseases, as well as diabetes and oncology. And the incidence of cancer is growing as a result of an aging population and popularity of lifestyles associated with cancer, such as smoking, sedentariness, and Westernized' diets, Mr. Zhen says.

Mr. Cao says three of the main areas of clinical need in China are oncology, infectious diseases — such as HIV and HPV, and cardiovascular, with health problems increasing alongside improving living standards.

He notes that the prevalent cancer types in China are gastric, liver, as well as lung.

"At Beigene, we are developing drugs to address the unmet medical needs in China and have the aspiration to bring these innovative drugs to the world market," he says.

The company has obtained several clinical-stage oncology assets through partnership and is undertaking several preclinical programs. Among products in its pipeline are a product set to enter Phase III trials for melanoma, one set to enter Phase II for lung cancer, and several products in early stage trials for other cancers.

Traditional Chinese medicine (TCM) is also increasingly a drug development focus for pharmaceutical companies in China because of public interest and government promotion, Mr. Zhen says.

Vaccines are another area where an increasing number of studies are being sponsored by both local and global pharmaceutical companies in China, Mr. Zhen continues.

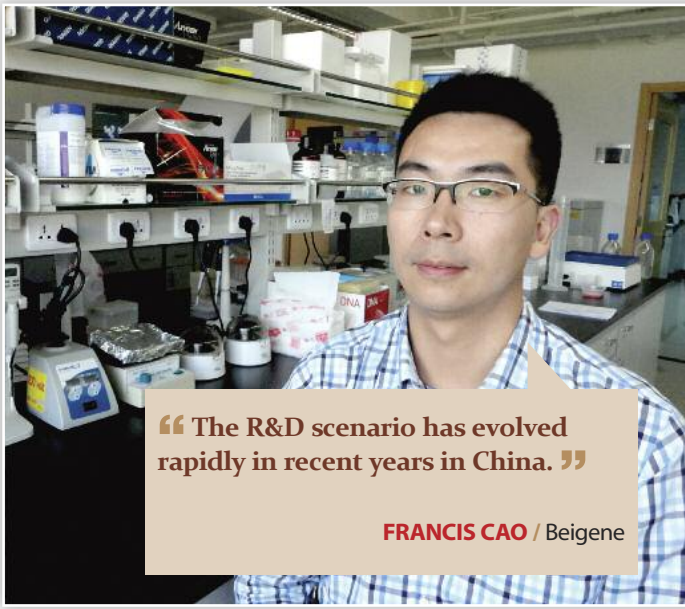
Regulatory and Marketing

China's main regulatory authority is the State Food and Drug Administration (SFDA), which was created in 2003 to replace the State Drug Administration (SDA).

The formation of the SFDA has resulted in a centralized regulatory system and eliminated conflicting standards between provincial government agencies, Mr. Zhen says.

Mr. Cao says until recently, regulatory policies in China still lagged behind needs from an innovative standpoint for R&D companies.

"For example, entry into clinical-stage development in countries like the United States is fairly rapid, but in China companies have to receive permission and that can take a year or sometimes longer, which apparently does not provide a competitive advantage to China pharma R&D," Mr. Cao says. "China's regulators have heard these needs and voices in recent years, and are planning to take steps to change the situation. We're hoping that change can come as quickly as possible to help create a more encouraging environment for drug innovation in China, which is also part of China's national strategy in building an innovative nation."



> "The R&D scenario has evolved rapidly in recent years in China."
>
> **FRANCIS CAO** / Beigene

Regulatory Opportunities and Challenges

China: A Market Overview

China's pharmaceutical industry generated an estimated $81 billion in 2009 and some analysts believe China could possibly double its drug sales by 2013.

Despite the country's population size, the pharmaceutical market in China represents only 1.5% of global drug sales. Part of the reason for this disparity is that until recently, healthcare coverage for much of the population has been nonexistent. As many as 800 million people lack healthcare coverage of any kind.

In April 2009, the Chinese government initiated a new policy to reform healthcare coverage and as these policies roll out the pharmaceutical market will open up to a greater extent.

Part of the healthcare reform package established a new National List of Essential Medicine (NLEM). The list includes more than 300 drugs, almost two-thirds of which are Western medicines. The Chinese government reimburses for a significant percentage of these drugs' costs and allows for greater access to these medicines in all public healthcare facilities by 2020.

The largest group of medications on the NLEM is anti-infectives. But the NLEM also covers cardiovascular medications and pain management drugs. Every three years, the Chinese government will update the essential medicines list, and prices will be reset three times per year. Despite the level of government control over prices, the system is an improvement over the existing market access infrastructure. Hospitals, which have been able to prescribe and administer medications outside the NLEM, will continue to do so, but they must negotiate prices directly with drug manufacturers.

The pharmaceutical industry within China is a complex collection of several thousand domestic companies — many of which are generic manufacturers — and about 14,000 distributors.

The introduction of the essential medicine list, however, threatens the domestic generics industry because many brand-name drugs will be available to the public at little to no out-of-pocket expense. Major pharmaceutical manufacturers will look at the potential decrease in the number of Chinese generics manufacturers as an opportunity as historically, the country has had a reputation for poor intellectual property protection.

The Chinese government has established incentive programs to build the domestic pharma and biotech industries, mining tax benefits, direct funding and the development of biotechnology parks. Biotech parks around China, including the Shanghai Zhangjiang Hi-Tech Park, houses pharmaceutical companies such as Roche, Novartis, GlaxoSmithKline, Lilly, Johnson & Johnson, and Pfizer, as well as local and international CROs.

Source: Emerging Markets Clinical Development Series, Cutting Edge Information. For more information, visit cuttingedgeinfo.com.

> **"China's large population often has limited access to newer drugs, making trial participation attractive."**
>
> **CLANCEY HOUSTON** / Chandler Chicco Companies / China

According to Mr. Zhen, there has been a greater focus to reduce the number of days for approvals as the government seeks to develop the capacity and capability for conducting clinical trials in the region.

He says an example would be the "Green Channel," which was started in 2009 by the SFDA to provide an accelerated application process for new chemical entities, new combination treatments, or in case of severe medical needs. Concurrently, the SFDA also established a pre-investigational new drug consultation office to complement the Green Channel.

Mr. Zhen says since its formation, the SFDA has issued a number of regulatory guidelines to address important clinical research issues. More recently, the agency has indicated its resolve to streamline processes and review its requirements for information to promote greater transparency and shorten the regulatory approval process.

The SFDA has been consistently working to reach international standards in terms of its regulation. In October 2011, it released a report that said it approved 1,000 drugs in 2010, highlighting the different categories of drugs approved, a Business Monitor report notes.

In November 2011, the SFDA announced that it will visit five to 10 overseas manufacturing facilities in five countries. The majority of these companies have agreed to be examined to help the SFDA refine its inspection standards, Business Monitor reports. This decision was followed by the revision of good manufacturing practices (GMP) in March 2011, which all pharmaceutical firms in China must adhere to by 2015.

While there have been new or adjusted regulations for clinical trials and new drug applications around imported drugs and in the areas of tendering and pricing, arguably one of the most significant legislative issues for the industry in China remains regulations governing the protection of intellectual property (IP) and enforcement, Ms. Houston says.

"Since China's accession to the WTO the IP environment has improved, but still more needs to be done," she says.

In particular, she notes, there is a gap between legislation and enforcement, and disparity in the latter from one province or city to another, driven in part because of ongoing amendments to the IP law as the environment and China's regulatory framework change with the times.

"The government realizes the importance of protecting IP, for both foreign and local players, but interpreting the laws and enforcing them remains a challenge," Ms. Houston says.

> **"Large pharma companies will continue to expand through M&A, acquisition, and diversification in China."**
>
> **SIMON LI** / Kantar Health China

On a promotional level, while OTC medicines can be advertised through mass media in China, the promotion of prescription medicine is restricted, with a majority of communications still focused on information in professional medical journals, direct physician engagement, and recommendations from doctors to patients, Ms. Houston says.

"This leads to considerable emphasis by the industry on physician engagement, through detailing and invitations to medical congresses and symposia, for example, but increasingly also through tailored continuing medical education efforts" she says. PV

EXPERTS

FRANCIS CAO. Senior Director of Government Affairs and Public Relations, Beigene, a Chinese biotechnology company based in Beijing that is focused on discovering and developing innovative oncology drugs to address unmet medical needs in cancers that are prevalent in China and the Asia-Pacific region. For more information, visit beigene.com.

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CLANCEY HOUSTON. Managing Director, Chandler Chicco Companies' China operations, which operates as inVentiv Health Communications company, is a multi-disciplinary integrated communications group. For more information, visit chandlerchiccocompanies.com or inventivhealth.com.

SIMON LI. General Manager, Kantar Health China, a global, evidence-based decision support partner to pharmaceutical, biotech, device, and diagnostic companies. For more information, visit kantarhealth.com.

LING ZHEN. General Manager, Quintiles, China, a fully integrated biopharma services company offering clinical, commercial, consulting, and capital solutions worldwide. For more information, visit quintiles.com.

9.15pm
San Antonio, U.S.

ICON Development Solutions
Pharmacodynamic specialists conduct complex models to identify early efficacy signals for candidate compounds.

10.14am
Tokyo, Japan.

ICON Clinical Research
EDC data is reviewed within our integrated reporting system to provide comprehensive information for a global clinical trial.

ICON Central Laboratories
Chemistry samples for a cardiovascular study are being tested in our Central Laboratory.

4.45pm
Tianjin, China.

ICON Medical Imaging
Patient information including Medical images, lab summaries and the eCRF are electronically hosted for remote review by a Clinical Endpoint Committee.

3.28pm
Zurich, Switzerland.

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