By Kim Ribbink

SOUTH KOREA from Strength to Strength

Proven R&D capabilities, a strong regulatory system, government support, and a wealth of talent are among the factors that draw pharma companies to South Korea.

South Korea, or the Republic of Korea, is an industrialized nation with a strong standing on the world stage. It was the first Asian country to host the G20 summit in 2010. The country's population is around 50.2 million, and it has one of the highest population densities in the world.

The government is committed to strengthening the economy for long-term growth and regards the pharmaceutical sector as integral to the country's prospects. Already, the country's pharmaceutical industry is one of the largest in Asia at around $17 billion with growth expected to reach $24.3 billion by 2020.

"Prescription drugs are projected to account for 80% of the total pharmaceutical market due to the growing elderly population and the prevalence of chronic diseases," says Ash Kuchel, global group president, Publicis Healthcare.

According to Korea Trade-Investment Promotion Agency, Korea's production of pharmaceuticals in 2012 was to 15.71 trillion won ($14.12 billion). The same year, it invested 2.58 trillion won ($2.32 billion) or 19% of its total R&D budget, in the biotech sector.

An Attractive Market

South Korea's demographics and healthcare system present attractive opportunities for biopharmaceutical companies, says Deborah Chee, M.D., Ph.D., president of the Korea National Enterprise for Clinical Trials (KoNECT).

"In 2011, 96.8% of the population had healthcare coverage, Dr. Chee notes.

There is much to recommend the country as a pharmaceutical destination, including an ethical work environment, a strong and stable regulatory system, and good geographical positioning to tap into this growing market.

For example, the government issued a US-Korea Free Trade Agreement (KORUS FTA), which strengthens intellectual property protections in Korea and promotes increased transparency in the pricing and reimbursement process, Mr. Kuchel notes.

Government support of the industry is another draw card. The Korean government created the 2012 Pharmaceutical Industry Competitiveness Enhancement Plan, offering varied support and changing the categorization of pharma companies into three groups: specialist pharma firms, global generic companies, and major global firms, Mr. Kuchel says.

The government has fostered development of its biopharmaceutical industry at many levels and in many ways, says MiSook Hyun, general manager of Quintiles, South Korea.

"This began in the mid-1980s and has included such steps as creating the first Framework Plan for Biotechnology Promotion (Biotech 2000) in 1994; the Korean Health Industry Development Institute (KHIDI) in 1999 to expand healthcare R&D investment and competitiveness; KoNECT in 2007 to underscore South Korea as a global clinical trial hub; and the Pharma Korea 2020 Roadmap announced in 2012 to stimulate innovative

South Korea's supportive clinical trial infrastructure makes it a robust setting to conduct studies and pursue market entry.

DR. DEBORAH CHEE
KoNECT

South Korea boasts of a large pool of R&D experts to support its biotech industry.

MISOOK HYUN
Quintiles Korea

The generics industry is the most active in Korea in terms of country-based innovation.

LEE JUNGHWA
Kantar Health Korea

The South Korean pharma market is expected to reach $24.3 billion by 2020, with prescription drugs projected to account for 80% of the total market.

ASH KUCHEL
Publicis Healthcare

drug development and overseas expansion of Korean pharma companies," Ms. Hyun says.

Mr. Kuchel says that within the 2020 roadmap the government has announced a goal to develop 10 new global drugs and create 12 global companies.

"To reach these goals, the government is trying to boost the pharma market with a fund for R&D, tax deductions for R&D costs, promoting mergers and acquisitions, training workers in the industry, and creating and sustaining a national pharma company to compete on the international stage," he says. "Many local pharma companies will find it hard to compete if they do not engage in R&D as they will not get government support."

"Tax breaks and loans are available for innovative companies," Mr. Kuchel continues. "Public sector investment in new drug development has been expanded, including training pharma graduates and specialists in licensing and regulatory affairs."

Top global companies in Korea include Pfizer, Sanofi, GlaxoSmithKline, and Novartis. To foster research activities, global MNCs are forging strong partnerships with local organizations.

There are already a number of examples of such alliances, including Sanofi's collaboration with SK Chemicals, Bristol-Myers Squibb and OliPass, and Otsuka and the Ministry of Health and Welfare.

"Although these pharma companies' prescription drugs have dominated the marketplace, occupying the top rankings in prescription drug sales, South Korea has about 250 pharmaceutical manufacturers, mostly focused on generic and over-the-counter (OTC) drugs," Mr. Kuchel notes.

FAST FACT

SOUTH KOREA WAS THE FIRST COUNTRY TO APPROVE ADULT STEM CELL THERAPY IN 2011.

Source: Decision Resources

Home-Grown Innovation

The country also boasts a strong talent pool with a growing number of graduates in bioengineering. This is leading to strong outcomes in terms of innovative product development. In fact, according to KHIDI, 19 new drugs were developed in the country between 1999 and 2012.

"An example is Cartisem, which was developed by Seoul-based Medipost and approved in 2012 as the world's first approved genetic stem cell drug to treat patients with degenerative arthritis," Ms. Hyun says.

The development of incrementally modified drugs has also been active and 64 IMDs have been approved in Korea, Dr. Chee says.

The area of greatest in country-based innovation is the development of biologics including biosimilars, Dr. Chee notes. Korea is one of the leading markets globally for biosimilars and started developing biosimilars in the early 1990s, including growth hormone, EPO, and G-CSF.

"The Korean government published the biosimilar guideline as early as 2009 following EU and Japan and the world's first monoclonal antibody infliximab biosimilar, Remsima was developed by Celltrion and approved by the KFDA — the Korean regulatory authority — and the European Medicines Agency in July 2012 and June 2013 respectively," Dr. Chee says. "The Ministry of Food and Drug Safety approved Hanwha Chemicals' Davictrel, the biosimilar of Enbrel, on Nov. 11, 2014."

Remsima has also received approval from the FDA, Japan's PDMA, and Health Canada.

In addition, Dong A, a leading Korean drug maker, has received U.S. FDA approval for its super-bacteria antibiotic Sivextro.

As of 2012, 467 drug candidates, including 250 NMEs, 200 IMDs, and 25 biosimilars, were under development by Korean pharmaceutical companies and bioventures. As of Jan-

Korea's Clinical Advantages

- **Patent Extension granted** by participation in clinical trials.
- **Fully introduced ICH-GCP** and well-aligned local regulation for clinical trial
- **Protocol based review system**; No requirement of Asian PK for conducting P2/P3 studies.
- **Comparatively short study initiation time** (2-3 months); the MFDS can approve a clinical trial application within 30 working days when no further information is requested and IRB process is in parallel.
- **Less translation burden;** only protocol, ICF and some info of IB.
- **Least issues with different registered doses** and medical practice from those of major Western markets.
- **Centralized patients and centers with experienced investigators** in accredited clinical trial sites by MFDS. There are around 160 accredited clinical trial sites.
- **The possible role as an Asian reference country** with Asian data with minimum delay from the approval of US/EU in NDA.
- **Future chance for mutual recognition among East-Asian countries**; on-going Korea-China-Japan tripartite discussions.

Source: Dr. Deborah Chee, KoNECT

uary 2014, 14 biosimilars had been approved. The Ministry of Knowledge & Economy has announced significant capital and regulatory support to boost the biosimilars industry in Korea and has set an ambitious target for the domestic industry to capture 22% of global biosimilar market share by 2020.

In addition, the Korea government has identified and designated 10 "research-driven hospitals" in 2013 by the act to foster health technology (HT) R&D in university hospitals.

When it comes to therapeutic-specific research, the leading focus is on oncology (18.9%) followed by diabetes (9.7%), according to a survey from the Korea Drug Research Association.

Ms. Hyun says oncology and hematology also lead the number of studies done by Quintiles Korea, followed by studies in the anti-infective, immunology and allergy, and cardiovascular therapeutic areas.

Medical Access

Healthcare in South Korea is provided through contributions to a compulsory National Health Insurance plan, with 97.1% of the population covered by NHI in 2012 and the remainder by Medical Aid. Koreans over a certain income level must pay into the NHI plan, while Medical Aid provides access to healthcare services for the under-privileged, Ms. Hyun says.

"Korea's high-quality healthcare system is based on choice; consumers can select between a universal plan that covers employees and relatives, long-term care medical insurance program, or Medical Aid Program, which is co-funded by central government and the National Health Insurance Corporation," Mr. Kuchel says.

The NHI plan also pays for new or alternative treatments without the high-cost burden usually associated with less common treatments in other countries, says Junghwa Lee, general manager, Kantar Health Korea.

"For instance, a surgery that is uncommon in another country but is popular in Korea will get on the reimbursement list and provide patients coverage," Ms. Lee says. "Patients' out-of-pocket medical expenses are lower compared with other developed countries. Reimbursement coverage is expanding to more diseases; as a result the cost burden to patients has continued to go down. Making sure their drugs are included on the reimbursement list is a key criterion for many pharmaceutical companies operating in Korea."

The national expenditure on healthcare in 2011 was US$91 billion and is expected to rise because of expanding NHI coverage and an aging population. Although the NHI budget is currently in a healthy state, reforms will be needed to ensure the long-term financial viability of the system, Ms. Hyun says.

The South Korean healthcare system is tightly controlled and the government regulates the cost of treatments and drugs.

"The government has enacted regulations to ensure fair trade and commercial practices," Ms. Lee says. "For example, a measure was introduced in July 2014 to curb the commercial practice of offering rebates to drive drug sales. Under the 'two strikes and your out' framework of the measure, if a pharma company is found to offer rebates to physicians a second time, that drug will be removed from the national insurance reimbursement list. As a result, we expect that pharma companies will take a less aggressive approach to drug marketing."

According to Mr. Kuchel, about 90% of specialist doctors and healthcare institutions are private. Data show that Koreans visit physicians 11.3 times per year on average, which is 6.8 times more than the Organization for Economic Co-operation and Development (OECD) average.

Additionally, consumers rely heavily on physicians and pharmacists for OTC advice, Mr. Kuchel adds.

"There are 21,000 pharmacies in Korea, and OTC drugs represent a majority of their revenue," he says.

With regard to product promotion, the Korean Pharmaceutical Affairs Law (KPAL) strictly regulates advertising of OTC drugs and prohibits provision of information to the public about prescription drugs, Mr. Kuchel says. KPAL does not, however, restrict industry-funded disease awareness campaigns, so pharma companies can advertise preventive prescription drugs for infectious or chronic diseases and sponsor awareness campaigns.

"Strides are being made toward more laid back DTC advertising restrictions," he notes. "There are debates that DTC advertising should remain banned as the information in the advertisements could be unbalanced or inaccurate, rather than educational for the consumer. The issues in this debate are reviewed from both a clinical and an economic perspective, including the perspectives from healthcare professionals, consumers, and the pharmaceutical industry."

Ms. Lee notes that market research to track brand equity and salesforce effectiveness will continue to be important in 2015.

"Companies will continue to invest their marketing dollars on such basic research as they still need market intelligence to plan and evaluate their activities," she says.

FAST FACT

SOUTH KOREA BOASTS AROUND 250 PHARMACEUTICAL MANUFACTURERS, INCLUDING 47 MULTINATIONALS.

Source: Decision Resources

A Clinical Outlook

The number of clinical trials conducted in South Korea has grown significantly since 2002 when the country's clinical trial regulations were changed and it adopted ICH GCP and ICH E5 guidelines.

According to IMS market data the Korean regulatory authority — the Ministry of Food and Drug Safety (MFDS) — approved 503 trials in 2011, up from 45 in 2001, and more than 300 in the first half of 2012. In fact, according to a news report, Seoul is the leading city in terms of having investigators involved in global clinical trials for potential new therapies.

"This is evidence of the scale and sophistication of South Korea's research infrastructure, which has medical institutions and researchers comparable with those in North America and Western Europe," Ms. Hyun says.

Dr. Chee says the country's supportive trial infrastructure makes it a robust setting to conduct studies and pursue market entry.

"With many well-trained investigators and world-class clinical trial sites, South Korea maintains a healthy environment for conducting clinical trials," Dr. Chee says.

"More than 160 sites have been accredited by the MFDS to join clinical trials, enabling rapid patient recruitment," she says. "In addition, changes in the regulatory climate have allowed smoother and earlier market access for innovative drugs. The MFDS can approve a clinical trial application within 30 working days when no further information is requested."

Accordingly, clinical trials undertaken by global pharma companies have grown substantially. Various sources report that global companies sponsored 248 clinical trials in 2013.

"Ten years ago, the focus was mostly on Phase III trials, whereas now there are more trials in earlier phases, another indication that South Korea's healthcare infrastructure has matured and has the capabilities to support a broader array of trials," Ms. Hyun notes, adding that Quintiles Korea has conducted more than 280 studies involving close to 12,000 patients since its establishment in 2000.

In 2012, the Korean government started a new initiative called Global Centers of Excellence for Clinical Trials. Five consortia of clinical trial centers were designated and received financial support for further development of clinical trial technologies and infrastructure that can lead global clinical development, especially in early phase trials and in specialized areas of clinical trials, including special population studies and new biomarker studies, Dr. Chee says.

"Local studies started to outpace multinational studies in Korea starting in 2011 due to increasing local R&D activities for new drug development, including IMDs and biosimilars," Dr. Chee says. "In 2013, among studies approved by MFDS, 58.6% of the 607 studies were local studies. Biopharma companies are responding to advantages of the increasing clinical trial infrastructure."

Based on the MFDS data on clinical trial authorization, endocrine and metabolism studies accounted for the highest proportion of approved protocols — 14% of 356 domestic trials — followed by oncology at 13%. Cardiovascular and gastrointestinal compound studies accounted for 12.6% and 9% of the studies, respectively.

Meanwhile, at a regulatory level, the country has been focused on improving oversight and increasing safeguards. In 2013, the Korean Food and Drug Administration was renamed the MFDS.

"In addition to abolishing import duties for investigational new drugs and placebos, the MFDS has also streamlined regulatory procedures surrounding INDs and brought them in line with International Conference on Harmonization requirements," Ms. Hyun says.

Mr. Kuchel says the Korean government is trying to restructure the pharma industry by containing cost and ending illegal practices, and eliminating long litigation negotiations that delay the launch of new drugs.

But the country's move to adopting health technology assessments — the first country in the Asia-Pacific to do so — has led to delayed market access for new drugs. It could take anywhere from 17 months, in case of locally produced drugs, to 40 months — especially in case of oncology drugs — for final drug listing once marketing approval is received. Moreover, out of a total of 209 drugs submitted for assessment from 2007, when HTA was introduced, to July 2014, only 69% of the drugs were finally listed, highlighting the market access hurdle that drug makers face.

Some recent proposals and regulatory changes aim to improve the time to market for new pharmaceutical products in Korea. The MFDS has said it will implement the "Patent — National Health Insurance price evaluation linkage system" in 2015.

Currently, pharmaceutical companies apply for drug price evaluation after receiving approval from the MFDS. Under the new system, the MFDS will notify the Health Insurance Review and Assessment Service of the marketing approval application before the approval is granted, hence speeding up the process.

FAST FACT

THE MINISTRY OF KNOWLEDGE & ECONOMY HAS SET A TARGET FOR THE DOMESTIC INDUSTRY TO CAPTURE 22% OF GLOBAL BIOSIMILAR MARKET SHARE BY 2020.

Source: Decision Resources

The History of KoNECT

In 2007, the **Korea National Enterprise for Clinical Trials (KoNECT)** was established as a nonprofit organization by the Korean government to foster clinical trial capabilities and build clinical trial infrastructure through the establishment of clinical trial centers, training and development of clinical trial professionals, and supporting R&D of new clinical trial technologies.

"**KoNECT** was so successful, and despite the challenges in new drug clinical development, between 2008 and 2014 the CAGR of clinical trials was 14% in Korea," says Deborah Chee, M.D., Ph.D., president of KoNECT. "Korea was ranked in the top 10 for industry-sponsored trials and Seoul was ranked as the No. 1 city based on the number of sites in 2013."

In April 2014, KoNECT was transformed into a foundation funded mainly by the Korean government.

KoNECT is committed to further developing the Korean clinical trial infrastructure and the country's capabilities to achieve global excellence level. Furthermore, the vision is for the country to become a clinical trial hub for global partners and a preferred partner for global drug development, especially for Asian development. Ultimately, the goal is to provide patients with earlier access to innovative treatments to be developed either in Korea or outside Korea.

KoNECT is regarded as one of the most successful national initiative in clinical trial infrastructure development by many experts.

Source: Dr. Deborah Chee, KoNECT