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WKMJ

World Korean Medical Journal

Cover Story

Inspirational Korean Healthcare Leader

Dr. Kyung Sun, Chairman of Osong Medical Innovation Foundation

Special Report

Korea Rise: New Strategies Transforming Korean Biopharma Landscape

Dialogue on the Global Health Disparities

Biopharmaceutical Report

South Korea Trials Drive Further Opportunities for Global Pharma and CROs

PCSK9 Inhibitor Competition: Amgen, Sanofi, and Regeneron Show Equally Decent CVOT Outlooks

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FROM THE PUBLISHER

Dear Colleagues,

In this issue of WKMJ, we interview Dr. Kyung Sun, a renowned cardiovascular surgeon and the current chairman of the Osong Medical Innovation Foundation. Medical research is a very expensive and time consuming process, which can hinder progress and easily exceed the expected costs. K-Bio is an ambitious program to foster biotech hubs to be more efficient with modern infrastructure. While pharmaceutical industries and medical devices are essential for improving healthcare, the introduction of new therapies remains quite challenging. With its vision to become a leading global bio cluster, the Osong Medical Innovation Foundation is at the forefront of Korea's drive for biomedical infrastructure innovation.

WKMO has had a busy year with the regional forum in Seoul in February and the Annual meeting in Washington DC in June. In Seoul, the meeting was held at the Seoul National University Medical Center where we had the Chairman of the National Assembly, Dr. Ui-Hwa Chung, who was featured in a prior issue of WKMJ, participate. The DC meeting was held at the Halls of US Congress with special guest speakers: Congressman Charles Rangel, Mike Honda and Bill Pascrell. The topics discussed during the forum are extremely relevant and important today; in Seoul, we discussed healthcare in North Korea and in DC we focused on the various health disparities throughout the world. We had amazing speakers at both meetings and appreciate the sharing of their expertise. Hopefully it will make some headway in these disparities in brief future.

This is already the 10th issue of WKMJ and I must commend the staff of the WKMJ in producing a high-quality publication. Please share the magazine with your friends and colleagues and join us at our next WKMO meeting. As the summer Olympics are approaching, we wish the Korean athletes their best performance at the spectacular world gathering and that in the future the Koreas can march as one country.

Yours,

David Y. Ko, MD
Publisher
President of WKMO
Keck School of Medicine of USC

FROM THE EDITOR-IN-CHIEF

Bioclusters, the geographic co-location of life science entities—including industries, academia, medical and research facilities, service providers, and financial investors—have emerged as a global trend. This is the result of the collaborative action led by increased competition and the productivity crisis the bio industry is facing to battle through the scientific innovation. Bioclusters have several key strengths which can be addressed as geographic, social and intelligent proximity. Entities work closely together to effectively communicate and share their expertise and knowledge, creating an atmosphere for better collaboration and networking.

For this edition's cover story, we had the opportunity to feature the Osong Medical Innovation Foundation and interview its chairman, Dr. Kyung Sun. Dr. Sun is a well-known cardiovascular surgeon and a professor at Korea University's School of Medicine. He shared his personal story and provided insight and perspective on the Osong Medical Innovation Foundation and increasing growth of Korea's biohealth industry.

New trends and current issues of the bio-health industry were featured in the special reports and biopharmaceutical articles. In the article from BioCentury titled "Korea Rise: New Strategies Transforming Korean Biopharma Landscape," the writer examines the current status and recently established strength of the Korean pharma industry, which has garnered increased attention.

In this edition's "Brief View of the Latest Healthcare Industry," we included major deals, developments and governmental policies occurring within the life sciences industry. Our findings identified an increase of M&As and a growing interest in the stock market. We have also gathered a list of upcoming conferences, symposiums, and forums that may intrigue our readers including the 6th New York Health Forum, which is to be held in September at The Yale Club of New York.

WKMJ has made major progress over the past few years and is celebrating the completion and publishing of our 10th edition. Thank you for your continued support. We will remain committed to our goal of always providing a quality journal for our readers. I hope that you enjoy our selection of articles and find them to be inspiring.

Thank you.

DoHyun Cho, PhD
Editor in Chief
President & CEO of W Medical Strategy Group
Chairman of New York Health Forum

WKMJ RECAP OF THE LAST ISSUE

Cover Story

A New Direction: Physicians Beyond Clinical Medicine
Charles Cho, MD | Han Choi, MD, LLM | Doug Yoon, MD, PhD, MPH, MBA

The past edition's cover story focused on the career paths of three physicians Dr. Charles Cho, Dr. Han Choi, and Dr. Doug Yoon and their thoughts on the evolving relationship between and beyond their clinical roles. Dr. Charles Cho is the Managing Director at Palo Alto Investors, specializing in the healthcare sector, and is also a practicing board certified faculty member at the Stanford Medical Center. Dr. Han Choi is currently a Principal at Oracle Investment Management, a healthcare hedge fund based in Greenwich, Connecticut. Lastly, Dr. Doug Yoon is the Chief Scientist of Washington Scientific, a health science consulting firm based in the Washington metropolitan area. Please refer to the 9th edition of the WKMJ to learn more about what led them to pursue medicine, the experiences they've gathered working in their respective professions, and their thoughts and opinions on the healthcare industry.

Special Report I

Joseph P. McMenamin, MD, JD, FCLM

Joseph P. McMenamin currently serves as the General Counsel and Executive Vice President at W Medical Strategy Group, and is the Principal at McMenamin Law Offices. Before starting his own firm, he was a litigation partner at McGuireWoods LLP. He received his MD from the University of Pennsylvania School of Medicine and his JD from the University of Pennsylvania School of Law. Dr. McMenamin shares his experiences and thoughts on working in the non-clinical setting. To find out more about how Dr. McMenamin handles medicolegal issues and what it's like to work as a physician trained lawyer in the healthcare industry, please refer to the 9th edition of the WKMJ.

Special Report II

Key Trends in U.S. Biopharma/Medtech Investing

The 5th New York Health Forum was held at The Yale Club of New York City on March 31st, 2016.The theme for this forum was "Key Trends in U.S. Biopharma/Medtech Investing". It provided a setting for stimulating informative discussions on topics such as investment trends, landscapes, and risks in the current healthcare industry. To continue reading more on the NYHF, please refer to the 9th edition of the WKMJ.

Biopharmaceutical Report I

Samsung RA Biosimilar EU Uptake Tied to Perceived Cost Despite Physician Concerns

Samsung Bioepis' three rheumatoid arthritis (RA) biosimilar candidates will lead to pricing wars in the cost-conscious EU once approved. The EU is aggressive about trying to save costs so biosimilars with their anticipated lower sticker prices to originator drugs are keenly eyed. However, as biosimilars enter the market, reference product companies are lowering the prices of their drugs, diluting the financial advantage of biosimilars. To continue reading about the "drug pricing wars," please check out the 9th edition of the WKMJ.

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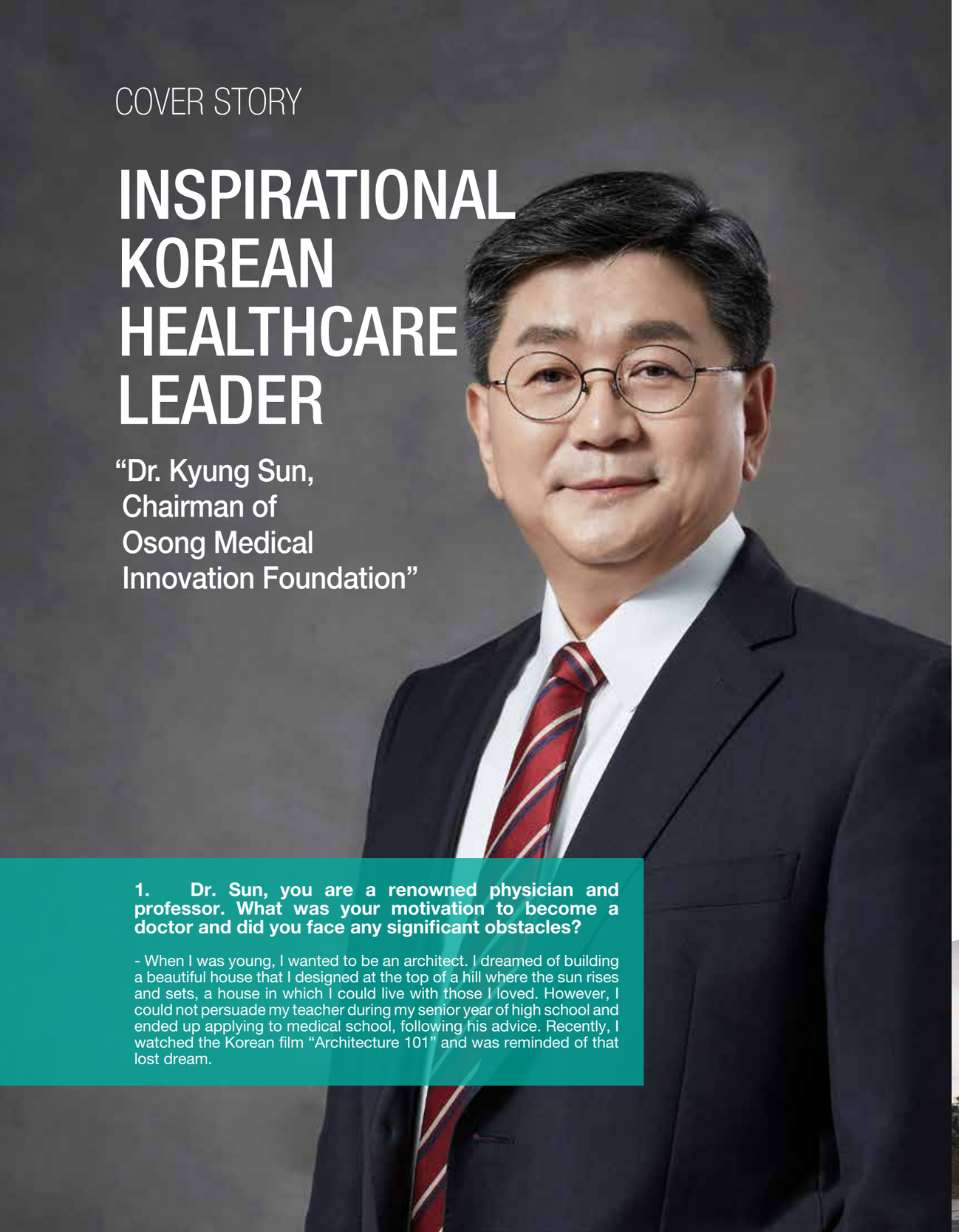
INSPIRATIONAL KOREAN HEALTHCARE LEADER

“Dr. Kyung Sun, Chairman of Osong Medical Innovation Foundation”



1. Dr. Sun, you are a renowned physician and professor. What was your motivation to become a doctor and did you face any significant obstacles?

- When I was young, I wanted to be an architect. I dreamed of building a beautiful house that I designed at the top of a hill where the sun rises and sets, a house in which I could live with those I loved. However, I could not persuade my teacher during my senior year of high school and ended up applying to medical school, following his advice. Recently, I watched the Korean film “Architecture 101” and was reminded of that lost dream.

COVER STORY

- In the beginning, studying medical-related courses was quite boring for me. However, during my second year of medical school, I began taking clinical courses and studying suddenly became very interesting. Looking back, I think that the reason I decided to become a surgeon is because like architecture, medicine involves many geometric elements. I became particularly attracted to the field of cardiovascular surgery, where one could come into contact with complex human organs and work with state-of-the-art medical equipment. I began following my cardiovascular surgery professors around to learn more about this new field. After meeting the renowned Professor Kim Hyung Mook and observing talented senior classmates, I was so inspired by their passion that I practically lived at the cardiovascular surgery department during my school vacations and was determined to apply to the department to follow their path. If anyone asks me what the luckiest thing that has ever happened to me is, I would be able to answer without hesitation. It would be meeting a great mentor, my professor.

- I began a residency after I graduated medical school in 1981. Although I was often exhausted physically, I truly enjoyed my time as a resident because I learned more about cardiothoracic surgery and began to envision my future as a surgeon. The most difficult experience I had during my residency was conducting animal experimentation in order to domestically develop medical devices. The laboratory environment at the time was not as developed as today, and I remember spending my weekends performing experiments in that environment. I spent so much time at the hospital that I only visited my house 27 times during my first year of residency. Nevertheless, that experience remains a treasured memory.

> **“The future establishment of clinical drug testing and production facilities will be very important for biohealth industrialization. Our goal is to cultivate and eventually promote a company that can successfully compete in the global market. We will work to help the domestic biohealth industry advance, expand, and ultimately contribute to national growth.”**

- The most rewarding thing as a cardiovascular surgeon is being able to make a difference in the lives of patients. Although I have come to believe that there is something greater that dictates life and death as time has passed, I still believe the abilities of a doctor can be a powerful tool. If mankind is at the center of the macrocosmos, the heart is at the center of every man. The heart is the most important organ for a human to live and surprisingly, its functions are much simpler than other organs. As a doctor, this is why I am so interested in the development of artificial heart research and heart surgery.

2. We understand that you served as a professor at a prominent medical school and are currently serving as the chairman of Osong Medical Innovation Foundation (K-Bio Health), a government organization. How did you make the transition from being a physician to a successful government organization leader?

- After I completed my studies and began my work as a clinical professional, I encountered limits in various aspects of South Korea's medical technology. For years, South Korea's clinical medicine had been simply utilizing the techniques of developed countries. As a result, I searched for more creative and advanced medical technology and began to develop appropriate medical devices for my country.

- As I held various positions within academia, I realized that treating patients was not the only aspect of medicine. So I applied to graduate school to study business and received my Master of Business Administration degree. After that, I became interested in the Humanities and Social Sciences and continued to look for opportunities to learn, taking a variety of courses at different universities, including Seoul National University and Korea University. I still take online classes despite the limited time I have apart from work and other responsibilities.

- I believe that South Korea's biohealth industry can advance its medical technology and healthcare sector. In order for the biohealth industry to grow, it is important for medical technology and the healthcare sector to simultaneously work together to develop innovative technology. My research on artificial organs and my work as a board member of South Korea's National Science & Technology Council, Co-CEO of the HT Forum, and head of KHIDI's R&D department embody my vision for South Korea's medical industrialization.

- After I joined the Osong Medical Innovation Foundation (K-Bio Health) as chairman, I have been able to operate a larger role in driving medical industrialization. As a public institution, K-Bio Health supports the development of biomedicine and medical devices and provides necessary infrastructure to private organizations. It is difficult for the private sector to pursue R&D alone, but with state-of-the-art equipment from the public sector, medical industrialization can be sped up and the possibilities for failure can be significantly reduced. I believe that K-Bio Health is an essential institution that will play an important role in the industrialization of South Korea's biohealth industry, which will drive growth in the future. Thus, with a strong sense of responsibility, K-Bio Health will continue to work hard to contribute to Korea's economic growth.

Dr. Kyung Sun is a professor at Korea University's School of Medicine.

3. Please introduce the Osong Medical Innovation Foundation (K-Bio Health). What are the philosophies or strategies of the institution? How do you distinguish the Osong Foundation from other potential competitors throughout the globe?

- As it became clear that the biotechnology industry would become an engine for future economic growth, the Korean government decided to provide direct support for the R&D of domestic companies. This is how K-Bio Health was established in 2011. Currently, K-Bio Health is actively supported by Korea's national government, as well as the Chungbuk provincial government.

- K-Bio Health expedites the development period for new drugs and medical equipment, which typically takes around 10-15 years. Equipped with four comprehensive research centers and a fast licensing support system, we have built an unprecedented and impressive framework for the medical industry.

- The new drug development center promotes the development of biomedical candidates and the medical device development center supports all other aspects of equipment research and development, including design, manufacturing and testing. Additionally, the animal experiment center provides a specialized preclinical environment with the largest veterinary diagnostic imaging system in the country. The clinical drug manufacturing center recently acquired a Good Manufacturing Practice (GMP) certificate, verifying the high quality pharmaceutical production that occurs in the center.

Dr. Kyung Sun (pictured, center) at the Groundbreaking Ceremony of the Osong Medical Clinical Research Center

Dr. Kyung Sun with WKMJ's Editor-in-Chief Dr. Dohyun Cho after the interview

- Once the clinical drug testing and production facilities are completely established, K-Bio Health will become an important one-stop system that plays an important role in everything from basic research to industrialization. We will become the only bio cluster in the world.

4. As the Chairman of Osong Medical Innovation Foundation, what are some of the major performances and outcomes you have accomplished under your leadership? What are the long-term goals and visions you hope to see the foundation achieve?

- Despite the fact that only a few years have passed since the K-Bio Health sites were established, both the operating capacity of each center and the number of research cases have increased dramatically. The research and development business has begun to show substantial results. Although it usually takes around 10-15 years for a biodrug to be developed, with our support for R&D and efficient license support business, we expect this period of time to be shortened and the probability of success to be increased. The future establishment of clinical drug testing and production facilities will be very important for biohealth industrialization. Our goal is to cultivate and eventually promote a company that can successfully compete in the global market. We will work to help the domestic biohealth industry advance, expand, and ultimately contribute to national growth.

5. As a key opinion leader in the Korean healthcare industry, what are some significant changes you have noticed in South Korea's medical and healthcare industry? And what do you forecast the industry will be like in the next five years?

- In recent years, the South Korean government has provided increased support for the biohealth industry after realizing its importance and potential for growth. In 2014, the biohealth market was valued at about $1.4 trillion, almost as much as the semiconductor, chemical products and automobile markets combined ($1.5 trillion). Over the next 10 years, the biohealth market is expected to grow even larger. Last year, one Korean pharmaceutical company acquired an $8 billion license agreement and others entered European and American markets. Korean domestic companies are being encouraged to look outside the domestic market. They have now began to change their business strategies and are shifting from developing and producing generic medicine to developing and producing bio medicine. I strongly believe that biohealth will become a defining industry for South Korea in the near future.

6. What advice do you have for young students interested in pursuing a career in medicine?

- It is vital to ask and consider why you want to study medicine. Amongst yourselves, there may be those who aspire to research or practice medicine, as well as some who may have interest in the biotechnology industry. There are infinite opportunities in the healthcare industry. Taking various opportunities such as going on observations will be of great help. With the biohealth industry growing rapidly, the role of physicians in both the research and business realm is receiving increasing attention. It is important and necessary to take this fact into consideration.

7. WKMJ has readers over 10 countries. Please share your final words or thoughts with our readers.

- It is my pleasure to have this interview with WKMJ. Please support K-Bio Health as the Korean biohealth industry continues to expand beyond East Asia and develop worldwide. I will do my best to achieve our goals. Thank you very much.

Kyung Sun, MD, MS, PhD, MBA

Chairman, Osong Medical Innovation Foundation

Dr. Sun graduated from Korea University's School of Medicine in 1981 with a medical degree. He received a masters in Medical Science in 1984. He also received a PhD in Medical Science in 1990, and an MBA in Business & Administration in 2007. Dr. Sun is currently chairman of the Osong Medical Innovation Foundation since 2015. In the past, he served as a director of the Korea Artificial Organ Center, a president of the Korean Society of Medical and Biologic Engineering, and a chair of the Board in Korean Society for Thoracic and Cardiovascular Surgery. Dr. Sun received an award for his contributions to Health Industry Technology from Ministry of Health and Welfare in 2008 and a National Medal for Presentation Order from the Korean Government in 2013. He is also a cardiovascular surgeon who serves as a professor at Korea University. The main scientific publications he has written or participated in include: Transparent and Flexible Force Sensor Array Based on Optical Waveguide (2012, Optic Express), A Durability Study of a Paracorporeal Pulsatile Electro-Mechanical Pneumatic Biventricular Assist Device (2011, Artificial Organs), Hemodynamic Energy Changes After Ischemia-Reperfusion Injury in an Aortic Cross-Clamped Rabbit Model (2010, ASAIOJ), and Korean Artificial Heart (Any Heart)—An Experimental Study and the First Human Application—(2003, Artificial Organs).

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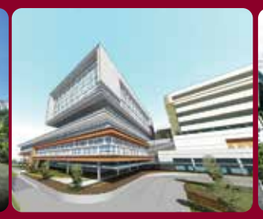

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Special Report

SPECIAL REPORT I

KOREA RISE : NEW STRATEGIES TRANSFORMING KOREAN BIOPHARMA LANDSCAPE

SPECIAL REPORT II

DIALOGUE ON THE GLOBAL HEALTH DISPARITIES : WKMO ANNUAL FORUM 2016

Korea Rise: New Strategies Transforming Korean Biopharma Landscape

PRODUCT DEVELOPMENT

KOREA RISING

BY ERIN MCCALLISTER, SENIOR EDITOR

The Korean biopharma industry is mainly known for biosimilars and me-too products. But a cohort of innovator biotechs in Korea is coming of age, bolstered by an infusion of cash from the government and by the clinical and business success of bellwether Hanmi Pharmaceutical Co. Ltd.

As government investment and partnering money have begun to flow into the sector, a virtuous circle has been set in motion in which Korean biotechs are deploying a larger proportion of their revenues to R&D. That in turn is expected to lead to innovative products that could attract more multinationals to the partnering table.

VCs are also coming on board. In 2015 alone, venture investors poured $270-$360 million into Korean life sciences, compared to $197 million in 2014 and $166 million in 2013, according to an analysis by Citi Asia Healthcare.

B. Christopher Kim, managing partner of the Korea-Seoul Life Sciences Fund, started the fund four years ago because he said he could find science that was just as innovative as that in Boston, but was considerably cheaper (see “Korea Comps”).

Additionally, Korea has the largest concentration of clinical trial facilities in the world, making it more efficient and cost-effective for companies to conduct clinical studies. And a few of the nation’s large pharmas are starting to adopt some of the open innovation models used by U.S. and European companies to tap early stage discoveries (see “Korea Opens Up”).

Seven Korean biotechs that spoke to BioCentury are working on programs with the potential to be first- or best-in-class in diseases including cancer, ophthalmology and infectious disease.

Three U.S. companies that have partnered with Korean biotechs told BioCentury it’s not only the programs that are impressive, but also the Korean companies’ expertise and efficiency in executing clinical trials.

However, the Korean market is small, and the domestic biotechs recognize that to become players on the global stage they will have to get drugs approved and on the market in the U.S. and Europe. Achieving this milestone would demonstrate to international biotechs and pharmas that science discovered and developed in the region can pass muster with Western regulatory agencies.

The Korean companies are taking a variety of routes. Some are out-licensing rights in China and using the revenue stream to support early clinical trials in Korea or elsewhere in the Asia-Pacific region. Others are going directly to trials in the U.S. with the hope that early Phase I data, coupled with the relationships they build with U.S. KOLs, will facilitate a partnership.

In the meantime, the government is opening up parts of the global market through recently enacted regulatory reciprocity, which will allow drugs approved in Korea to be marketed in countries such as Brazil and regions including the Middle East without additional clinical work or regulatory review.

One hope has not yet been realized: that the focus on innovative drug development will grow the pool of drug discovery and development experts who know how to prioritize preclinical and clinical programs that could be differentiating on a global scale (see “Baby Steps”).

STIMULATING INNOVATION

For decades, Korea’s economic mainstays have been automobile manufacturing, shipbuilding and IT. But in 2012, with growth in those sectors declining, the Korean government set its sights on a new growth driver — biopharmaceuticals. The Ministry of Health and Welfare outlined a strategy to make the nation home to one of the largest global biopharma industries by 2020.

The plan includes three funds that will invest a total of $1 billion in Korean companies to develop innovative drugs and

promote expansion of the Korean biotech industry globally. Recipients are expected to raise matching funds.

A fourth fund called the Korea Drug Development Fund (KDDF) is awarding $1 billion in translational and clinical research grants (see "Korea Funds").

Kiyean Nam, CEO of Qurient Co. Ltd., said the structure of the three investment funds reflects the government's understanding that drug development takes time. Qurient has received two grants from KDDF.

"They understand that this is the kind of area that you need to invest in and wait, and you need to have good science behind it," he told BioCentury.

R&D investment in Korea is growing and outpacing that of other developed nations. The compound annual growth rate (CAGR) for the Korean pharmaceutical industry is 10% over 2009-13, higher than four of the five largest countries by GDP (see "R&D Growth").

Nam noted that Hanmi has helped demonstrate that patience and R&D investment can pay off.

Hanmi, founded in 1973, began to invest in discovery platforms for biologics and novel small molecules about 15 years ago.

Hanmi's LAPSCOVERY technology, short for long-acting protein/peptide discovery, achieves weekly or monthly dosing by conjugating a biologic drug to an aglycosylated monomeric Fc region via a flexible linker. The most advanced program is eflapegrastim (SPI-2012), a long-acting G-CSF analog that is in Phase III testing to treat chemotherapy-induced neutropenia. Hanmi is co-developing eflapegrastim with Spectrum Pharmaceuticals Inc.

The small molecule platform produces targeted NCEs for cancer and autoimmune disease. HM61713 is the most advanced program. The EGFR mutation-specific tyrosine kinase inhibitor is in a global Phase II trial to treat non-small cell lung cancer (NSCLC).

In 2011, Hanmi invested W84 billion ($72.5 million) in R&D, or 14% of its sales. Its R&D investment reached 20% of sales in 2014 at W153 billion ($140.3 million). The proportion dropped back down to 14% in 2015 with W187 billion ($159.9 million), but the dip was driven by record-high revenues of W1.318 trillion ($1.1 billion) and the transfer of some of its clinical programs to its new partners.

Hanmi's R&D investment culminated in six deals announced last year worth $656 million in upfront payments. The deals were with multinational companies including Johnson & Johnson, Sanofi and Eli Lilly and Co.

"Hanmi is one of the cases demonstrating that investment in R&D pans out — if you invest, you will get something out of it," said Nam.

Qurient's KDDF grants were for preclinical and clinical studies of its Q203. The first-in-class inhibitor of *Mycobacterium tuberculosis* cytochrome bc1, a bacterial enzyme complex needed for respiration, is in Phase I testing to treat multi-drug resistant and extensively drug-resistant TB.

Qurient was founded in 2008 to develop compounds discovered by and licensed from the Institut Pasteur Korea and other research facilities. Q203 was discovered at the institute and licensed to Qurient.

Qurient's most advanced program is Q301, a topical leukotriene inhibitor that has completed Phase IIa testing to treat atopic dermatitis. Other novel programs in development include Q-4, an AXL inhibitor in preclinical testing for cancer. Qurient licensed the compound from the Max Planck Institute in 2013.

POOL OF POTENTIAL

Other companies that have received government funding include PharmAbcine Inc., Genexine Co. Ltd. and CrystalGenomics Inc.

PharmAbcine has received more than $3 million from the Ministry of Health and was founded in 2008 based on research at the Korean Research Institute of Bioscience and Biotechnology (KRIBB).

The company's lead program is tanibirumab, a human mAb against VEGF receptor 2 (KDR/Flk-1; VEGFR-2) in Phase II testing for triple-negative breast cancer.

Tanibirumab is cross-reactive with other species, which allows the biotech to test it in different animal models prior to putting it in the clinic, making design and execution of clinical trials more efficient. Cyramza ramucirumab, a marketed human IgG1 mAb VEGFR-2 antagonist from Lilly, does not have the same cross-reactivity.

"We learn every tumor it might be sensitive to based on the tumor angiogenesis. And we can use that to design better and more sophisticated clinical trials," said CEO Jin-San Yoo.

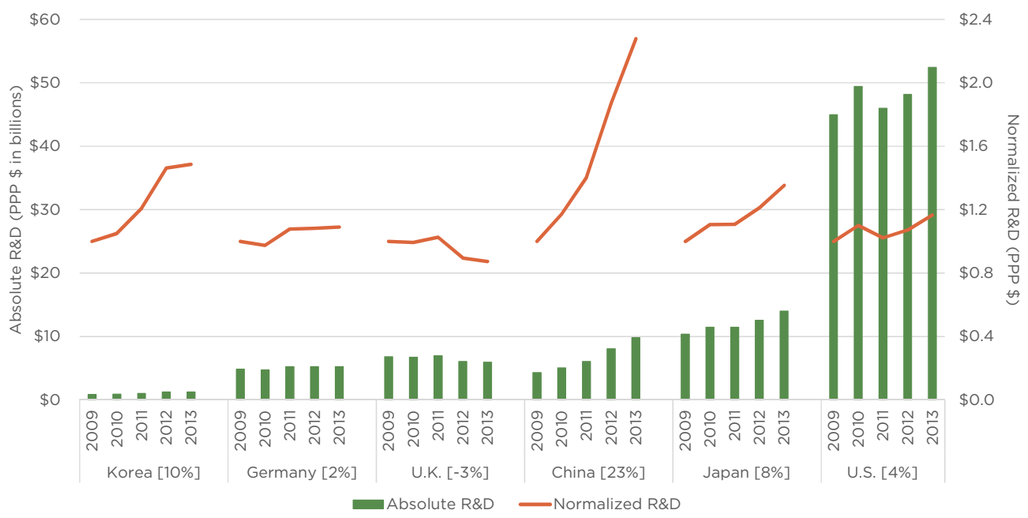
Lilly markets Cyramza for gastric cancer in the U.S. and Europe. The drug is also approved in the U.S. to treat metastatic colorectal cancer (mCRC) and NSCLC. It is in a Phase III trial in HER2-negative breast cancer, and multiple Phase II and Phase III studies in other solid tumors.

PharmAbcine suggested that tanibirumab may have a larger therapeutic window based on Phase I data. According to Yoo, there was no dose-limiting toxicity for the mAb at 24 mg/kg. In Phase I studies, dose-limiting toxicity of Cyramza was reached at a16 mg/kg dose. Additionally, Yoo said that PharmAbcine hasn't yet seen the hypertension and hemorrhage side

R&D GROWTH

From 2009 to 2013, R&D spending by the Korean pharmaceutical industry has increased. While absolute spending still pales in comparison to larger countries, Korea's R&D outlays have grown at about 10% per year to $1.2 billion. This is a higher compound annual growth rate (CAGR) than that seen by four of the five largest countries by GDP. The only country with a higher CAGR over this period was China, where R&D investment grew 23% to $9.8 billion.

Data below are adjusted for purchasing power parity (PPP). The bars below show absolute R&D expenditures in USD. The red lines depict the R&D spending for each country normalized to $1 at 2009. The U.S. figures exclude most or all capital expenditures. Each country's 2009-13 CAGR is in brackets. *Source: OECD*



KOREA COMPS

B. Christopher Kim, managing partner at Korea-Seoul Life Sciences Fund, told BioCentury the firm did not start out with a Korea focus.

The fund closed at W75 billion ($67.5 million) in January 2012 and has now invested in 20 companies, almost all in Korea.

"If you look at our portfolio companies, they are predominately Korean, but it didn't start that way. We envisioned a global fund," he said. "The reason is that when we started out, there was a lot of deal flow in Boston, where deals are very competitive and very expensive. Korea wasn't like that. The science was just as good, but it wasn't as expensive."

One example is PharmAbcine Inc., which has a bispecific antibody platform. "Today a lot of companies do bispecifics and variations on biologics, but when PharmAbcine first came out with its bispecific platform, it was one of the earliest," Kim said.

Another example is CrystalGenomics Inc., which markets Acelex polmacoxib, a dual-acting cyclooxygenase-2 (COX-2) and carbonic anhydrase inhibitor. The dual mechanism of action prevents COX-2 inhibition in tissues where it causes adverse events. "A tissue-selective COX-2 inhibitor, that is also novel stuff," Kim said.

The fund has seen some of its companies go public, including two clinical-stage stem cell plays last year — Kangstem Biotech Co. Ltd. and Corestem Inc.

Kim wouldn't disclose the specific return the fund got on the IPOs or since its inception, but he said that in comparison to the returns reported by U.S.-focused funds, Korea-Seoul Life Sciences "is among the top quartile."

Money from local VCs in Korea continues to flow into companies, Kim said, but he thinks the funding window for VCs is narrowing based on increased government investment in biotech and the high valuations companies are able to attract on KOSDAQ.

"We're seeing very early stage companies start to go public, and so we're holding steady right now with the portfolio companies we have," Kim said. He also expects at least one of his portfolio companies to go public this year.

OrbiMed and Novartis Venture Fund have also invested in Korean companies, including PharmAbcine. The VCs declined to be interviewed.

— ERIN MCCALLISTER

effects that are common with other VEGF inhibitors and have also been reported for Cyramza.

PharmAbcine also has a bispecific antibody technology and has out-licensed lead candidate DIG-KT, which targets VEGFR-2 and tyrosine kinase receptor 2 (Tie2). DIG-KT is in preclinical testing for solid tumors.

China's 3SBio Inc. has exclusive rights to develop, manufacture and market the antibody in Taiwan, Korea and China, including Macau and Hong Kong. Triphase Accelerator Corp. has rights elsewhere, and Celgene Corp. has an option to acquire the program from Triphase.

CrystalGenomics received W13 billion ($10.4 million) from the Ministry of Health in 2014 to support commercialization of Acelex polmacoxib and global clinical trials of the biotech's clinical programs. The company uses structure-based biology to develop small molecules, with a focus on cancer, inflammation and infectious disease.

Acelex, a dual-acting cyclooxygenase-2 (COX-2) and carbonic anhydrase (CA) inhibitor, was approved in Korea in February 2015 to treat osteoarthritis and is marketed there by Dong-A Socio Holdings Co. Ltd.

CrystalGenomics designed-in the molecule's CA inhibition, because competitive binding to CA reduces COX-2 inhibition in tissues where that mechanism causes side effects, such as the GI tract, blood and kidneys.

The company's next-most advanced program is CG400549, a potential first-in-class compound in Phase II testing to treat complicated acute bacterial skin and skin structure infections and to treat vancomycin-resistant *Staphylococcus aureus* infections. CG400549 is an antibiotic targeting fabI enoyl-(acyl carrier protein) reductase.

Genexine received W7 billion ($5.6 million) from the government to develop its DNA vaccine platform. Its GX-188E is an HPV DNA therapeutic vaccine in Phase II testing to treat cervical cancer. The vaccine expresses the E6 and E7 proteins of HPV16 and HPV18.

CLINICAL PROS

Domestic innovators and multinational companies developing medical products in Korea have access to one of the largest clinical trial hubs in the world. According to an analysis by the Ministry of Health, in 2012, Seoul was home to 545 industry-sponsored clinical trials — more than any other city in the world.

In 2014, 652 clinical trials were approved across all of Korea, a 7.4% increase compared to 607 in 2013, according to Korea National Enterprise for Clinical Trials (KoNECT).

"The quality of physicians and their clinical trial experience makes it easier to do clinical trials here, particularly certain therapeutic areas like oncology," said H. Michael Keyoung, president and CEO of Genexine. He noted that multinationals run clinical trials in Korea from Phase I through Phase III because of the efficiency with which local physicians are able to execute the trials.

Dong Wu, head of J&J's Asia Pacific Innovation Center, likened Korean clinical research facilities to those of University of Texas MD Anderson Cancer Center and Johns Hopkins University.

"Korea could be another serious drug discovery and development player. Not only in the Asia-Pacific region, but also globally," Wu told BioCentury.

He added that Korean facilities have generations' worth of medical records for families, which is of particular interest for the U.S. pharma company's disease interception research.

"If you can go back all these generations and build a family tree on that and see certain patterns like Type I or Type II diabetes and how to prevent that, it could be valuable," Wu said.

He said the Asia Pacific center is evaluating potential collaborations with the 10 top research hospitals in Korea.

J&J has also been impressed with the level of academic and research talent and last November announced a partnership with the KDDF to put out a call for grant proposals for Type II diabetes programs. The goal of the program is to identify and co-invest in first- or best-in-class assets, he told BioCentury.

EFFICIENTLY SURPRISED

The efficiency of development and the quality of the data are beginning to attract U.S. companies to partner their own programs with Korean biotechs.

For instance, in 2015 RegeneRx Biopharmaceuticals Inc. formed a JV with G-treeBNT Co. Ltd. to develop and commercialize RegeneRx's RGN-259 to treat dry eye and neurotropic keratitis in the U.S.

G-treeBNT has a majority stake in the JV and is responsible for development.

KOREA OPENS UP

Much like in the U.S. and Europe, established Korean biopharma companies have started to work with local universities and small biotechs to identify and invest in innovative technologies.

"What Korean pharma is doing now is that they will start funding start-up companies and universities directly in exchange for something like right of first refusal or license rights," said B. Christopher Kim, managing partner at Korea-Seoul Life Sciences Fund.

In 2011, Hanmi Pharmaceutical Co. Ltd. launched eR&D, an external R&D group, to access novel pipelines and technologies through collaborations.

"Through this team, along with several others from global BD and R&D, we are catalyzing the opportunities of collaboration and research as well as in-licensing and JV opportunities," SVP & CMO Jeewoong Son told BioCentury. "It's about the development of stakeholders as well."

In November, Yuhan Corp. announced a W20 billion ($16 million) investment in Genexine Co. Ltd., which has a DNA vaccine platform and a hybrid Fc technology to make long-acting biologics. In a statement, Yuhan said the hybrid Fc technology was strategically important for the pharma's pipeline.

President B.G. Rhee said Green Cross Corp. is hoping to grow the next generation of companies via co-development deals and equity investments in start-ups. The pharma invested in a $6 million series A round for cancer antibody company PharmAbcine Inc.

— ERIN MCCALLISTER

"One of the key components of their development process was to do CMC work because we had done very little. They took that on as part of their obligations and really got it done within a year, which was certainly sooner than we expected," said J.J. Finkelstein, president and CEO of RegeneRx.

RGN-259 is a topical eye drop formulation of thymosin beta 4 (TB4), a naturally occurring 43-amino acid peptide. The compound is in Phase IIb testing for dry eye in the U.S., with data expected by early April.

Sorrento Therapeutics Inc. has had similar experiences. On March 2, Sorrento announced a JV with Yuhan Corp. to develop immuno-oncology therapeutics.

Yuhan will contribute $10 million to the JV and will receive rights outside the U.S., EU and Japan to one immune checkpoint antibody against an undisclosed target, plus global rights to two additional Sorrento antibodies selected by the JV.

Yuhan will have a 51% stake in the JV.

Yuhan declined to be interviewed. According to Sorrento CEO Henry Ji, Yuhan has a "strong R&D team that is clinically experienced and have developed quite a few programs now in-house."

The company markets Pruvel prulifloxacin for bacterial infection and Revanex revaprazan, an acid pump antagonist, for gastric ulcers. Pruvel is a fluoroquinolone antibacterial agent.

Yuhan has 23 programs in its pipeline, many of which are undisclosed. Novel programs that are disclosed include a preclinical G protein-coupled receptor 119 (GPR119) agonist for diabetes.

Yuhan also has YH14618, a transforming growth factor (TGF) beta 1 (TGFB1) antagonist in Phase I/II to treat degenerative disc disease.

Sorrento also has in-licensed programs developed in Korea. In 2013, the company gained rights to Nant-paclitaxel (Cynviloq), an injectable nanoparticle formulation of paclitaxel from Samyang Corp.

Samyang was already marketing the drug in Korea to treat NSCLC and metastatic breast cancer. According to clinicaltrials.gov, the compound is in the pivotal TRIBECA trial to determine bioequivalence to Abraxane nab-paclitaxel in patients with metastatic or locally recurrent breast cancer. Nant-paclitaxel was acquired by NantWorks LLC last May for $90 million up front and $1.2 billion in regulatory and sales milestones.

"They had already done exhaustive clinical studies and we were impressed by the very high quality of the data," Ji said.

Korean biotechs in general "have very high standards in terms of data quality and management, sometimes even higher than in the U.S.," Ji said.

He predicted that "we'll start to see more activity in Korea in terms of U.S. companies looking for assets and collaborations because they do have innovative stuff."

GOING GLOBAL

All of the Korean biotechs contacted by BioCentury have global ambitions.

"To succeed in this business, we have to focus from A to Z on the global market," said PharmAbcine's Yoo.

Some, such as PharmAbcine and LegoChem Biosciences Inc., are conducting early development in the Asia-Pacific region to produce data that will attract global partners.

PharmAbcine is using revenues from its licensing deals for DIG-KT to conduct further development of tanibirumab in the hopes of attracting a global partner.

Despite the quality of Korea's clinical trial infrastructure, the biotech is conducting its Phase II study of the mAb in Australia because it believes the POC data generated there will carry more weight with potential partners.

"When I told potential partners that we were going to do our trial in Korea, they said, 'Okay, we'll see,'" said Yoo. "And then when we decided to do the triple-negative trial in Australia, and get proof-of-concept data from Caucasians, they said, 'Wow, we're interested. Keep us updated.'"

LegoChem is counting on POC data from its China partner to attract a more global licensing deal. Last year, the company announced a deal with Fosun International Ltd. to develop and commercialize LCB14 in China.

LCB14 is LegoChem's lead next-generation antibody-drug conjugate. The preclinical candidate targets HER2.

KOREA FUNDS

The South Korean government has launched four funding initiatives totalling $2 billion to help spur R&D for innovative drugs and promote global expansion of the nation's biotech industry. Three of the funds, totalling $1 billion, invest in companies with the expectation of generating returns. The Korea Drug Development Fund (KDDF) also has $1 billion to distribute via grants to support translational and clinical research. Funds are listed below in ascending order by total fund size. *Source: Ministry of Health and Welfare, KDDF website*

Fund	Administrator	Purpose	Type	Fund size	Investment horizon	Funding per project
Global Pharmaceutical Industry Development Fund	Ministry of Health and Welfare	Support global expansion of domestic programs	Investment	$100M	8 yrs (4-yr investment; 4-yr return)	$5-$15M
Pharma Corporate Partnership Fund	National Pension Service	Business development with foreign pharmas	Investment	$400M	10 yrs (4-yr investment; 6-yr return)	$100M
Pharmaceutical Industry Project Fund	Korea Financial Corporation	New drug development and pharma M&A	Investment	$500M	10 yrs (5-yr investment; 5-yr return)	$50M
Korean Drug Development Fund (KDDF)	KDDF	Support translational research and clinical trials of domestic biotechs	Grant	$1B	NA	NA

Spokesperson Wooshik Kim said Fosun will conduct development in China, and the preclinical and clinical data will be available to LegoChem to support future worldwide out-licensing opportunities.

Kim said LegoChem has more than 10 ongoing collaborations with global and local partner companies for its ADC technology, including a 2015 partnership with Theranyx to co-develop ADCs based on targets selected by the French company. Upon candidate selection, the partners plan to jointly out-license the ADCs to a third party.

CrystalGenomics aims to keep Korean rights to get its feet wet in commercialization.

"The first stage is to do an alliance with an MNC outside of Korea to penetrate other countries and do Korea by ourself. Then eventually we will take on commercialization in other countries to become an integrated global biopharma company in Korea," President and CEO Joong Myung Cho told BioCentury.

Qurient is starting in the U.S.

"We are working with new chemical entities and KOLs in the U.S., as well as regulators in the U.S., who have a good amount of experience in working with NCEs," Nam told BioCentury.

"It's much easier having a KOL on board and in our Phase II trial in the U.S. because we are able to get direct comments from the KOL field much more easily than showing them data we generated in Korea and trying to convince them," Nam said.

G-treeBNT is hoping its JV with RegeneRx will give it some early experience in the U.S. commercial market that will help it launch its other programs.

"This is our initial approach to developing a pipeline in the U.S. and then commercialize. We hope to build on that," said CEO Won Yang.

In addition to its ophthalmic program, G-treeBNT also has OKN-007, a disulfonyl derivative that targets sulfatase 2 (SULF2) that is overexpressed on cancer cells. The program has completed Phase Ib testing in glioblastoma.

Green Cross Corp., which markets its IVIG-SN IgG in more than 30 countries in Asia, South America and the Middle East, will use distributors for the product in the U.S.

Green Cross will seek partners in the U.S. and Europe for some of its other pipeline programs, including GC1102 and GC1101C. G1102 is a recombinant HBV immune globulin that is in Phase II testing to prevent the recurrence of HBV infection following liver transplant. The product has Orphan Drug designation for the indication from FDA and EMA.

GC1101C is a recombinant Factor VIII that is in Phase III testing to achieve homeostasis in patients with hemophilia A.

Additionally, the company's allogeneic NK cell program is moving into a Phase II trial for hepatocellular carcinoma in Korea. "Definitely for global market entry we will need and are looking for global partnerships," President B.G. Rhee told BioCentury.

Green Cross wants to in-license technologies developed by U.S. companies for unmet medical needs that are predominant in Asian countries, such as hepatitis.

BABY STEPS

Several Korean biotechs told BioCentury that despite an increase in development of innovator products, the country is lacking in the expertise needed to execute global clinical development programs that can demonstrate product differentiation.

"Education is the number one priority for families in Korea, but experience in novel drug development is one of our handicaps," said Joong Myung Cho, president and CEO of structural biology company CrystalGenomics Inc.

He noted many of the current leadership positions overseeing clinical development in Korean biotechs are held by people with experience outside of Korea.

Cho himself was previously research director for a JV between Chiron Corp. (now part of Novartis AG) and LG Life Sciences Ltd. He then spent 16 years heading up the life science research group at LG before he started CrystalGenomics in 2000.

H. Michael Keyoung, president and CEO at DNA vaccine company Genexine Co. Ltd., was previously president of hematology and inflammation company Catalyst Biosciences Inc.

Sejin Park, CFO of ADC company LegoChem Biosciences Inc., added that experience with global Phase II and III development programs is lacking.

"There are really few experts for that in Korea," he told BioCentury.

The government is working with MNCs to help the country develop that expertise.

Under an MOU signed with the Ministry of Health and Welfare in 2014, Johnson & Johnson would invest $25 million in programs aimed at enhancing Korea's clinical capabilities for medical devices.

One goal is to expand the scope and scale of local experts' participation in global clinical research programs.

J&J's Asia Pacific Innovation Center is already providing Korean companies advice on discovering and developing novel products.

"We have dedicated a specific resource person in Korea. Her job is to help those companies who fall into our strategic area to define targets and design clinical pathways with the greatest chance of success at this early stage rather than spending money to find out it didn't work," said innovation center head Dong Wu.

The position is held by Hong Xin, new ventures director for Korea.

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"We want to also bring their technology from the U.S. to the Asian market," said Rhee.

Companies seeking to globalize could get a leg up from an MOU signed last year by Korea's Ministry of Health and Welfare, along with South American and Middle East countries. The agreement would allow drugs approved in Korea to be approved and marketed in these other countries without having to do additional testing.

"That's a good sign for my company because now we can export any new drugs approved by Korea Ministry of Health to some of these other countries, which can help grow our global presence," CrystalGenomics' Cho said.

At the end of the day, the mark of success for the Korean industry will be U.S. or European approval and commercial launch.

"For the excitement we've seen from investors to last, things have to translate into a successful product. Not only for the domestic market but for the global market," said investor Kim.

"We need to give our potential partners out there a credential that we can actually make data in a relevant way and that we have integrity in our R&D system," said Qurient's Nam.

COMPANIES AND INSTITUTIONS MENTIONED

Catalyst Biosciences Inc. (NASDAQ:CBIO), South San Francisco, Calif.
Celgene Corp. (NASDAQ:CELG), Summit, N.J.
Corestem Inc. (KOSDAQ:166480), Seoul, South Korea
CrystalGenomics Inc. (KOSDAQ:083790), Seongnam, South Korea
Dong-A Socio Holdings Co. Ltd. (KOSDAQ:000640), Seoul, South Korea
Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.
Fosun International Ltd. (HKSE:0656), Shanghai, China
Genexine Co. Ltd. (KOSDAQ:095700), Seoul, South Korea
Green Cross Corp. (KSE:006280), Yongin-si, South Korea
G-treeBNT Co. Ltd. (KOSDAQ:115450), Seongnam, South Korea
Hanmi Pharmaceutical Co. Ltd. (KOSDAQ:128940), Seoul, South Korea
Institut Pasteur Korea, Seongnam, South Korea
The Johns Hopkins University, Baltimore, Md.
Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.
Kangstem Biotech Co. Ltd. (KOSDAQ:217730), Seoul, South Korea
Korea National Enterprise for Clinical Trials (KoNECT), Seoul, South Korea
Korean Research Institute of Bioscience and Biotechnology (KRIBB), Daejon, South Korea
LegoChem Biosciences Inc. (KOSDAQ:141080), Daejon, South Korea
LG Life Sciences Ltd. (KSE:068870), Seoul, South Korea
Max Planck Institute, Berlin, Germany
Ministry of Health and Welfare, Seoul, South Korea
NantWorks LLC, Los Angeles, Calif.
Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland
PharmAbcine Inc., Daejon, South Korea
Qurient Co. Ltd. (KOSDAQ:115180), Seongnam, South Korea
RegeneRx Biopharmaceuticals Inc. (OTCBB:RGRX), Rockville, Md.
Samyang Corp. (KSE:000070), Seoul, South Korea
Sanofi (Euronext:SAN; NYSE:SNY), Paris, France
Sorrento Therapeutics Inc. (NASDAQ:SRNE), San Diego, Calif.
Spectrum Pharmaceuticals Inc. (NASDAQ:SPPI), Henderson, Nev.
Theranyx, Marseille, France
3SBio Inc. (HKSE:1530), Shenyang, China
Triphase Accelerator Corp., San Diego, Calif.
University of Texas MD Anderson Cancer Center, Houston, Texas
Yuhan Corp. (KSE:000100), Seoul, South Korea

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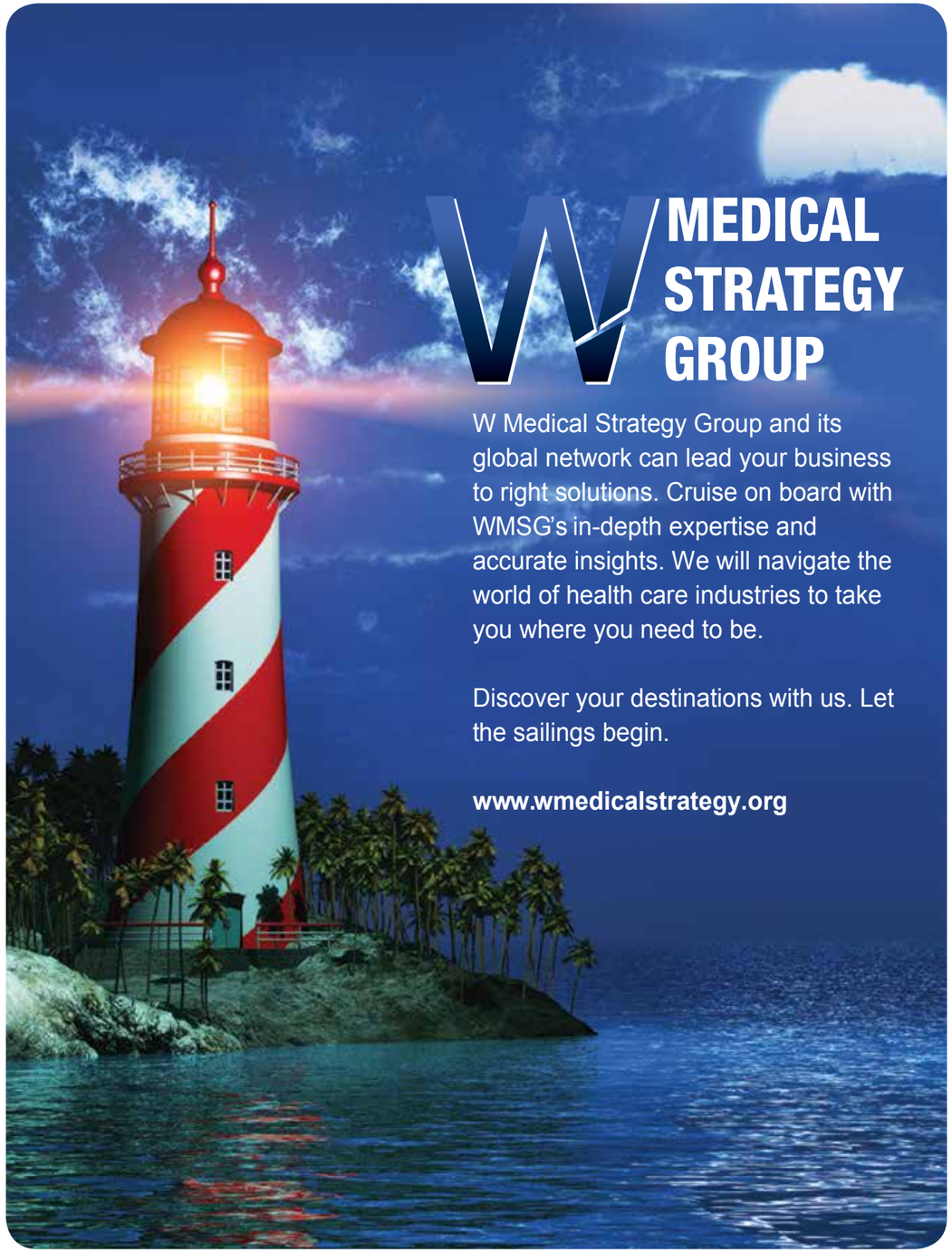

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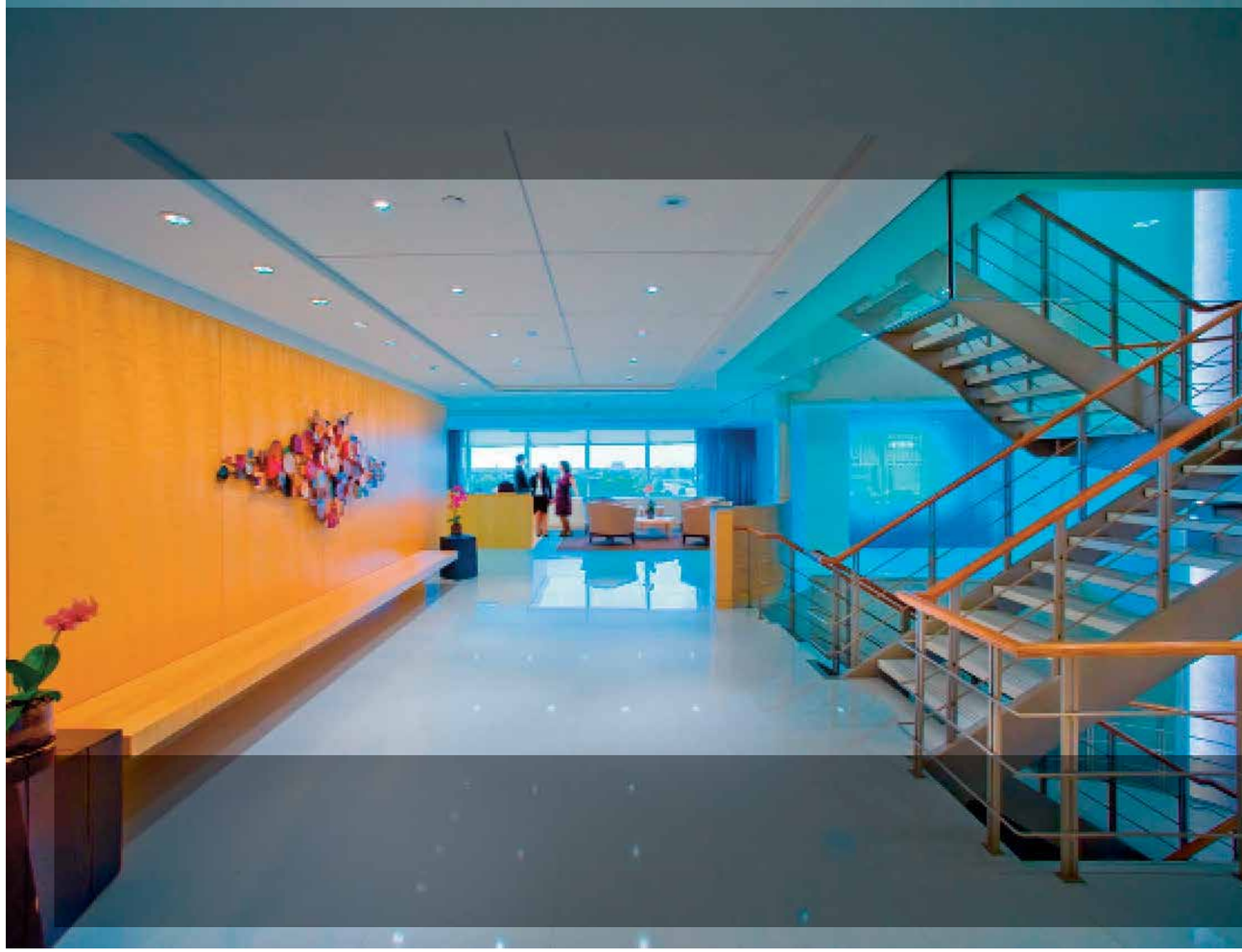

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Dialogue on the Global Health Disparities :

World Korean Medical Organization Annual Forum 2016

The 2016 Annual WKMO Forum was held in Washington, D.C. on June 9-10th at the Rayburn House Office Building. The venue chosen for this year's forum was significant for two reasons. First, the Rayburn House Office Building is one of the three congressional office buildings for the U.S. House of Representatives. Second, and more importantly, it was where the Asian-Pacific American Heritage week was established to celebrate the achievements and contributions of Asian and Pacific Islander Americans to U.S. history and culture. Later, in 1992, Congress extended the time frame of the week and officially designated the month of May as Asian American and Pacific Islander Heritage Month.

WKMO visited this historical site for Asian and Pacific Islander Americans with Asian American Representatives Mike Honda (from California) and Charles Rangel (from New York). Representative Honda and Representative Rangel shared their views and ideas about the global health industry and were also honored for their achievements.

The title of the 2016 Annual WKMO Forum was the "Symposium on Global Health Disparities." The goal of the forum was to spread greater awareness about the various healthcare inequities that the world sees today and to identify the various ways through which physicians can collaborate to improve these inequities and therefore global health.

Rayburn House Office Building

Drs. Yoonkyo An (Australia), Winston Wong (Chairman of Board - NCAPIP- National Coalition of Asian pacific Islander Physicians), Chul Hyun, Congressman Charles Rangle, David Ko, Joe Mcmenamin, James Lewis (Georgetown Univ Hospital), David Roh (PUST Medical school dean), Taekyoung Kim (Canada), Hee young Shin (SNU), Jinha Park (US chapter president).

One example of a source of numerous health disparities that was addressed was the North Korean healthcare system. Forum participants discussed policies and initiatives intended to provide humanitarian assistance, combat health inequity, and improve the quality of healthcare in North Korea. Although North Korea has continued to be a hostile nation, the healthcare industry has been able to establish several channels that facilitate cooperative communication and interaction. Dr. Hee Young Shin of Seoul National University College of Medicine delivered a presentation titled "R&D for Health Care Initiatives for North Korea". Dr. Shin, who currently presides over the Institute for Medical Cooperation between North and South Korea, spoke of her institution's plans for the integration of healthcare. Dr. David Roh, dean of the only international medical school in North Korea (PUST DMS), shared his perspectives on "Engaging North Korea through Medical Education." The school offers medical education in English and provides unprecedented and continuous long-term healthcare access to its students in North Korea.

Another issue that was discussed was the prevalence of Hepatitis in the Asian community. This discussion was led by Dr. Chul Hyun, Dr. James Lewis, and Dr. Winston Wong. Health disparities in Australia and Canada were also addressed by Dr. Yoon Kyo An from Brisbane and Dr. Tae Kyoung Kim from Toronto. Furthermore, the potential role of telemedicine in combating global health disparities was examined by Dr. Joseph McMenamin.

The 2016 Annual WKMO Forum was successful in stimulating the discussion of global health disparities, a topic that is extremely pertinent and important to the diverse community of healthcare professionals and leaders who attended the forum. WKMO hopes there will be as much progress next year, when it holds its 2017 Annual WKMO Forum. W

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Biopharmaceutical Report I

South Korea Trials Drive Further Opportunities for Global Pharma and CROs

- Goals to improve regulation and site standards
- Korean data used in Japanese approvals
- Big pharma interest in earlier Korea-based trials

South Korea's foreign sponsor and CRO attraction over the last decade has scope to increase if it can improve capabilities in early-phase and complex trials, experts said.

The region may also continue to attract multinationals aiming to exploit a potentially more streamlined drug approval process across Asia, they added.

Clinical trial registration in South Korea shot up from 17 multinational-sponsored trials in 2002 to 296 in 2015, according to figures from Korea's Ministry of Food and Drug Safety (MFDS). The US National Institutes of Health clinical trials database indicates 293 trials registered in Korea so far in 2016, and ranks South Korea first in Asia by number of protocols.

Korea National Enterprise for Clinical Trials (KoNECT), an organisation funded by the government since 2007 to improve the quality of research sites - drove the increase in trials, agreed Greg Koski, CEO of US-based Alliance for Clinical Research Excellence and Safety (ACRES) and Fred Pritchard, VP, global drug development, at US CRO Celerion. Koski and Pritchard said KoNECT's funding of an accreditation programme for sites and training for clinical monitors over the last decade improved start-up times, completion rates, accuracy of data, and enrolment. According to KoNECT, while the

number of global clinical trial sites decreased 14% over 2010-2014, South Korea grew 6.8%, ranking it 11th in 2014 globally for industry-sponsored clinical sites. But the site standards are not very robust, said Koski, adding ACRES and KoNECT are working together to improve site efficiency by creating global site accreditation.

Site standards and Phase I regulation has room for improvement

Koski and Pritchard added although Korea has strongly attracted late-phase research, it lags in capabilities for early-phase trials - still limited by red tape - and complex studies, such as those for precision medicine. Pritchard said CROs Parexel (NASDAQ:PRXL), Covance, owned by LabCorp (NYSE:LH), INC Research (NASDAQ:INCR), Quintiles (NYSE:Q) and PPD have placed later-stage clinical trials in South Korea, but now they and large pharma, among them J&J (NYSE:JNJ), Merck (NYSE:MRK) and Sanofi (EPA:SAN), are interested in moving earlier- phase trials into the country.

KoNECT President Deborah Chee said KoNECT and umbrella initiative Korea Clinical Trials Global Initiative (KCGI) have been working to improve early-phase and complex clinical trial capabilities by establishing clinical pharmacology units - supporting Phase I research -- at 15 university hospitals by 2014. A separate investment was made in early phase-focused personnel, equipment and training at five trial site clusters across the country, and in translational research, said Chee and Min Soo Park, KCGI Chair.

Additional hurdles to overcome in order for Korea to retain foreign sponsor engagement include the need for greater global visibility and a more transparent review process from MFDS, said Park. Chee added KoNECT may work to allow a single institutional review board (IRB) review for multi-site trials, instead of currently required separate submissions. Pritchard noted medium-sized CROs like Celerion moving into South Korea should be aware of different business requirements from the US - like needing to establish a physical office in Korea before obtaining a formal business licence and hiring staff.

Chee added KoNECT is also consulting with the industry to reduce trial review bottlenecks, launching a campaign to improve patient awareness of trials, and developing KoNECT Integrated Clinical Trial Information System (KIIS), a database available to sponsors with epidemiology and investigator data. KoNECT last year opened a support centre for foreign sponsors, with a match-making service with local partners, said Chee.

Gateway to earlier Asia approvals and launches

For multinationals wishing to secure earlier market approvals in Asia and decrease the launch lag after EMA and FDA approvals, conducting

research in South Korea is the best gateway, said Pritchard.

The common lag is partly due to Korean, Japanese and Chinese regulators' requirement that some research, often pharmacokinetic, be performed in the countries' own ethnic populations, said experts. Typically pharma companies leave Asian regulatory strategy until Phase II or III when they realise they have neglected to include enough Asian subjects, said Kenneth Kim, CEO of US CRO WCCT. "These companies are leaving money on the table by neglecting a market for five years, and it can amount to USD 100m or more per year in lost sales," said Kim, whose company, like Celerion, Parexel and a handful of other CROs, performs bridging trials in the US with patients of Japanese ethnic origin in order to show safety and efficacy in Asian populations. There has been a gradual and significant decrease in the global need for bridging studies, Park confirmed, which he attributed to multinationals moving more trials to South Korea, and so including Asian subjects throughout the clinical programme. Kim noted starting clinical programmes in Asian patients from the beginning is cheaper than performing a bridging study, which costs around USD 1m.

As pharma moves away from viewing Asian markets as an afterthought, many will decide Korea is the easiest Asian country for US and European companies to run trials, said Pritchard, especially as regulators in Japan, China and South Korea agreed to begin accepting Asian PK data from each others' populations. Since 2006, the Japanese regulator, PMDA, has approved

more than 20 compounds supported by Asian sub-group analysis data obtained abroad, including in Korea, Chee confirmed.

Chee agreed Korea will prove the most attractive region for sponsors seeking Asian trials, citing the shortest study start-up time of all Asian countries. Trial review for study initiation takes 30 days in South Korea if there are no supplementary requirements, she said, and on average takes four to eight weeks, with the IRB process running in parallel. Pritchard claimed the Japanese regulator is perceived to lag in trial approval time. The Chinese regulator, CFDA, can take up to 18 months for study approval, as amendments to trial applications require restarting the review process, according to research by PPD. W

Fiona Barry

Journalist, France

Fiona previously worked in France as a journalist at William Reed Business Media, covering global manufacturing, regulatory and outsourcing news for the biopharmaceutical industry. She has also reported on global food and beverage companies. Fiona holds an M.A. in English and a B.A. in English and Philosophy from Bristol University. She speaks English and French.

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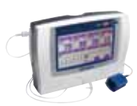
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Biopharmaceutical Report II

PCSK9 Inhibitor Competition: Amgen, Sanofi, and Regeneron Show Equally Decent CVOT Outlooks

- Comparable CV effect expected across PCSK9 inhibitor class
- Post-hoc MACE results in previous trials viewed with some restraint
- 50% MACE reduction unlikely, 35% realistic and meaningful for both

Amgen's (NASDAQ:AMGN) Repatha (evolocumab) and Sanofi (EPA: SAN)/Regeneron Pharmaceuticals' (NASDAQ:REGN) Praluent (alirocumab) are expected to produce positive cardiovascular (CV) event outcomes in their respective CV outcomes trials (CVOTs), experts agreed. Previous post-hoc major cardiovascular event (MACE) analysis data and low-density lipoprotein-cholesterol (LDL-C) lowering outcomes inspires continued positive signal optimism for the PCSK9 inhibitors. However, experts stressed previous small study sizes and trial design disparities makes signal translation to larger trials difficult to predict and any small differentiator could determine a market winner.

These CVOT results on MACE reduction extent will determine each PCSK9 inhibitor's cost-benefit profile and subsequent competitive value. Repatha and Praluent are approved as an adjunct to maximally tolerated statin therapy in heterozygous familial hypercholesterolemia (HeFH) and atherosclerotic CV disease, with Repatha also being approved for homozygous FH (HoFH). CVOT results aim to expand drug labels into primary prevention of CV events in statin intolerant patients.

Assuming label expansion, analysts predict

Repatha and Praluent could achieve respective peak sales of USD 7bn and USD 6.1bn peak sales.

Repatha's Phase III FOURIER 27,564-patient dyslipidemia CVOT (NCT01764633) has primary completion expected in October 2017. Amgen expects topline results in 1Q17.

Praluent's Phase III ODYSSEY Outcomes 18,600-patient acute coronary syndrome (ACS) CVOT (NCT01663402) is due to complete in December 2017. Analysts expect interim efficacy analyses around 2H16-1Q17.

Both trials have similar primary endpoints of time to MACE, with Repatha being 60 months long and Praluent 64 months.

Amgen declined to comment. Regeneron did not respond to a comment request.

Three CVOT results on MACE reduction extent will determine each PCSK9 inhibitor's costbenefit profile and subsequent competitive value

Previous MACE reduction signals creates CVOT hope

Praluent's previous MACE reduction data in its 78 week ODYSSEY trial (NCT01507831) -- in 2,341 high risk CV patients receiving Praluent or placebo every fortnight -- somewhat encourages CVOT read out optimism, said Dr Robert Rosenson, professor, cardiology, Mount Sinai Hospital, New York. Although the primary endpoint was LDL-C change from baseline to week 24, a post-hoc analysis demonstrated a lower MACE rate with Praluent over placebo at 1.7% versus 3.3% respectively (p=0.02), (Robinson et al. NEJM 2015; 372(16):1489-99).

Further to Praluent's positive MACE signal, Rosenson and Dr Steven Nissen, chairman, department of cardiovascular medicine, Cleveland Clinic Foundation, Ohio added there is no foreseeable reason why CV outcomes should substantially differ between Praluent and Repatha. Dr Christie Mitchell Ballantyne, director, Atherosclerosis Clinical Research Laboratory, Baylor College of Medicine, Houston, Texas agreed similar PCSK9 inhibitor class effects are expected, however, disparities between the CVOT's duration, inclusion criteria and dosing regimens may drive some drug class differentiation, which is currently unpredictable.

Neither Praluent nor Repatha will likely demonstrate a 50% MACE reduction rate as their CVOTs include heart disease patients with background therapy and therefore PCSK9 inhibitor treatment will unlikely induce such a large incremental benefit, said Rosenson. A 35% MACE reduction is realistic and potentially clinically meaningful, he added.

Rosenson also noted patient inclusion disparity between ODYSSEY and ODYSSEY Outcomes creates some uncertainty over MACE results being replicated across trials.

ODYSSEY enrolled patients with either HeFH, with or without coronary heart disease (CHD) or CHD risk; or hypercholesterolemia patients with established CHD or CHD risk. Contrastingly, ODYSSEY Outcomes is simply recruiting hospitalized ACS patients in the past year.

Overall, post-hoc MACE results encourage a positive CV signal in ODYSSEY Outcomes, however, post-hoc studies are insufficiently powered to definitively demonstrate a therapy's CV effect, added Ballantyne and Nissen. Although Rosenson maintained CVOT optimism from prior signals, he acknowledged the post-hoc analysis' limitations, namely its shorter duration (by around 178 weeks), doesn't guarantee result comparability in a longer, larger study.

Further to past MACE data, PCSK9 inhibitor's LDL-C lowering mechanism also supports favourable CVOT outcomes for both drugs, experts agreed on the sidelines of the British Cardiovascular Society congress in Manchester this week.

A two stage 511-patient trial (NCT01984424) in uncontrolled LDL-C individuals with a history of statin intolerance evaluated Repatha's lipid lowering effects in patients receiving subcutaneous evolocumab (Repatha) versus oral ezetimibe (Nissen et al. JAMA 2016;315(15):1580-90). Mean week 22 and 24 results demonstrated a between group LDL-C difference of -37.8%, favouring evolocumab.

Despite being a surrogate endpoint, a -37.8% LDL-C lowering outcome over commonly prescribed ezetimibe indicates a potentially protective CV effect, however, this is unclear ahead of long-term CVOT read outs, said Ballantyne, Nissen and Rosenson.

CVOT results critical to uptake prospects

Although positive CVOT results are expected, the extent of the potential benefit will drive physician prescription habits, said Ballantyne, Nissen and Rosenson. CVOT results will resolve PCSK9 inhibitors' currently unknown cost/benefit profile, said Dr Saul Myerson, associate professor, cardiovascular medicine, John Radcliffe Hospital, Oxford, UK. Praluent and Repatha cost around USD 14,000 annually. This news service previously reported PCSK9 inhibitors' high price makes them reserved for severe patients.

Furthermore, positive CVOT data may sway payer willingness towards permitting the expensive treatments, added Nissen. Payer reluctance is PCSK9 inhibitors' main uptake barrier as prescriptions require extensive cost justification, whilst patients reluctantly initiate treatment due to potentially large out-of-pocket payments and anticipated prescription hassle, said Ballantyne. Positive CVOT read outs could overcome these issues for both drugs, said Ballantyne.

The realistic expectation of a 35% MACE reduction may boost uptake, however, if a lower rate is demonstrated, treatment benefit may not outweigh its cost, said Rosenson.

Contrastingly, efficacious statins are affordable and have been used clinically for around 50 years in millions of patients, said Dr Pasquale Maffia, honorary senior lecturer, institute of cardiovascular and medical sciences, University of Glasgow, UK. This could dampen PCSK9 inhibitor uptake at its current price -- despite an improved cost-benefit profile -- until longer term data speaks to improved quality of life, said Maffia.

Aside from determining the agents' CV effects, Amgen and Regeneron's CVOTs may uncover potential long-term toxicities, potentially influencing uptake, added Ballantyne. Allergic reactions are the most common Praluent/Repatha-associated adverse events. Praluent and Repatha's past studies included around 500-2,000 patients for around six months, whereas CVOTs include many thousands of patients on several years of therapy, he explained. CVOTs therefore include a much longer treatment exposure period and should therefore better determine the therapy's risk/benefit profile, said Ballantyne.

Amgen has a market cap of USD 117.7bn.

Regeneron has a market cap of USD 39.9bn. W

Alexandra Thompson

Journalist, London

Alexandra is an award-winning healthcare professional journalist. Prior to joining BioPharm Insight, Alex was Editorial Assistant at CIG Healthcare, covering pharmaceutical news for pharmacists and pharmaceutical support staff. She was awarded the annual Johnson & Johnson 'Best Healthcare Professional Trade Journalist of the Year' award in 2014 for an article on eczema. Alex graduated from the University of Leeds with a 2.1 Hons in Biology in 2012.

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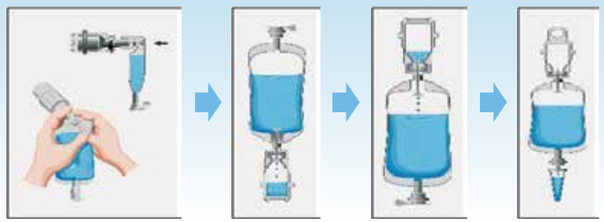

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FOLLOW THE JOURNEY OF VIREAD

COMPLETE RESPONSE RESULTS AT YEAR 1...

AT YEAR 1
The primary endpoint—complete response*—was evaluated in Studies 102 and 103[2]

THROUGH YEAR 8
Resistance was evaluated as a secondary endpoint[2,3]

In Study 102 (HBeAg–, n=375) and Study 103 (HBeAg+, n=266), a combined total of 641 adult patients with chronic hepatitis B (CHB) and compensated liver disease who were primarily nucleoside treatment naïve entered a 48-week, randomized, double-blind, active-controlled treatment period comparing VIREAD 300 mg to adefovir dipivoxil 10 mg. Subjects who completed double-blind treatment at Week 48 were eligible to roll over with no interruption in treatment to open-label VIREAD. Of 641 patients enrolled in the initial trials, 412 (64%) completed 384 weeks of treatment.[2]

***The primary endpoint in Studies 102 and 103 was complete response to treatment at 48 weeks as defined by HBV DNA <400 copies/mL (69 IU/mL) + histological response (Knodell necroinflammatory score improvement of ≥2 points without worsening in Knodell fibrosis score). Annual evaluation of resistance was a prespecified secondary endpoint. Cumulative VIREAD genotypic resistance was evaluated annually for up to 384 weeks in Studies 102, 103, 106, 108, and 121.[2,3]**

71% of HBeAg– VIREAD patients vs **49%** of adefovir dipivoxil patients.[2-4]
67% of HBeAg+ VIREAD patients vs **12%** of adefovir dipivoxil patients.[2,3,5]

INDICATION AND USAGE

VIREAD® (tenofovir disoproxil fumarate) is indicated for the treatment of chronic hepatitis B in adults and pediatric patients 12 years of age and older.

The following points should be considered when initiating therapy with VIREAD for the treatment of HBV infection:

- The indication in adults is based on data from treatment of subjects who were nucleoside–treatment-naïve and treatment-experienced with documented resistance to lamivudine. Subjects were adults with HBeAg-positive and HBeAg-negative chronic hepatitis B with compensated liver disease
- VIREAD was evaluated in a limited number of subjects with chronic hepatitis B and decompensated liver disease
- The numbers of subjects in clinical trials who had adefovir resistance-associated substitutions at baseline were too small to reach conclusions of efficacy

IMPORTANT SAFETY INFORMATION

BOXED WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT EXACERBATION OF HEPATITIS

- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, in combination with other antiretrovirals**
- **Severe acute exacerbations of hepatitis have been reported in HBV-infected patients who have discontinued anti-hepatitis B therapy, including VIREAD. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including VIREAD. If appropriate, resumption of anti-hepatitis B therapy may be warranted**

[a]Healthcare Analytics Monthly data, August 2014-June 2015.

Please see Brief Summary of full Prescribing Information including **BOXED WARNING** on the following pages.

GILEAD IS COMMITTED TO THE EDUCATION AND TREATMENT OF CHRONIC HEPATITIS B.

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Viread®
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Not an actual patient, but is representative of a real patient type. Models are used for illustrative purposes only.

...AT 8 YEARS: NO RESISTANCE WAS DETECTED AT YEAR 1 THROUGH YEAR 8

Annual evaluation of resistance was a prespecified secondary endpoint for Studies 102 and 103 in HBeAg- and HBeAg+ chronic hepatitis B patients[3]; no evidence of resistance was found. Cumulative VIREAD genotypic resistance was evaluated annually for up to 384 weeks in Studies 102, 103, 106, 108, and 121.[2,4,5]

- In the nucleotide-naïve population from Studies 102 and 103, HBeAg+ subjects had a higher baseline viral load than HBeAg– subjects and a significantly higher proportion of the subjects remained viremic at their last time point on VIREAD monotherapy (15% vs 5%, respectively)[2]
- HBV isolates from these subjects who remained viremic showed treatment-emergent substitutions; however, no specific substitutions occurred at a sufficient frequency to be associated with resistance to VIREAD (genotypic and phenotypic analyses)[2]

0%

NO HBV RESISTANCE DEVELOPED
YEAR 1 through YEAR 8
in clinical trials (Studies 102 and 103)[2,3]*

*Data for Years 2 through 8 are from the open-label phase.[6]

- There was a 64% (412/641) retention rate at Year 8: 266/426 patients given VIREAD→VIREAD; 146/215 patients given adefovir dipivoxil→VIREAD[2,6]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS

- **New onset or worsening renal impairment:** Cases of acute renal failure and Fanconi syndrome have been reported with the use of VIREAD. In all patients, assess estimated creatinine clearance (CrCl) prior to initiating and during therapy. In patients at risk for renal dysfunction, including those who previously experienced renal events while receiving adefovir dipivoxil, additionally monitor serum phosphorus, urine glucose, and urine protein. In patients with CrCl <50 mL/min, adjust dosing interval and closely monitor renal function. Avoid concurrent or recent use with a nephrotoxic agent. Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after initiation of high dose or multiple NSAIDs in HIV-infected patients with risk factors for renal dysfunction; consider alternatives to NSAIDs in these patients. Persistent or worsening bone pain, pain in extremities, fractures and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function
- **Coadministration with other products:**
  - Do not use in combination with other products containing tenofovir disoproxil fumarate
  - Do not administer in combination with adefovir dipivoxil
- **Patients coinfected with HIV-1 and HBV:** Due to the risk of development of HIV-1 resistance, VIREAD should only be used in HIV-1 and HBV coinfected patients as part of an appropriate antiretroviral combination regimen. HIV-1 antibody testing should be offered to all HBV-infected patients before initiating therapy with VIREAD
- **Bone effects:** Decreases in bone mineral density (BMD) and mineralization defects, including osteomalacia, have been seen in patients treated with VIREAD. Consider assessment of BMD in adult and pediatric patients who have a history of pathologic bone fracture or other risk factors for bone loss. In a clinical trial conducted in pediatric subjects 12 to <18 years of age with chronic hepatitis B, total body BMD gain was less in VIREAD-treated subjects as compared to the control group. In patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms, hypophosphatemia and osteomalacia secondary to proximal renal tubulopathy should be considered

ADVERSE REACTIONS

- **In HBV-infected subjects with compensated liver disease:** Most common adverse reaction (all grades) was nausea (9%). Other treatment-emergent adverse reactions reported in >5% of patients treated with VIREAD included: abdominal pain, diarrhea, headache, dizziness, fatigue, nasopharyngitis, back pain, and skin rash
- **In HBV-infected subjects with decompensated liver disease:** Most common adverse reactions (all grades) reported in ≥10% of patients treated with VIREAD were abdominal pain (22%), nausea (20%), insomnia (18%), pruritus (16%), vomiting (13%), dizziness (13%), and pyrexia (11%)

DRUG INTERACTIONS

- **Didanosine:** Coadministration increases didanosine concentrations. Use with caution and monitor for evidence of didanosine toxicity (e.g., pancreatitis, neuropathy). Didanosine should be discontinued in patients who develop didanosine-associated adverse reactions. In patients weighing >60 kg, the didanosine dose should be reduced to 250 mg once daily when it is coadministered with VIREAD and in patients weighing <60kg, the didanosine dose should be reduced to 200 mg once daily when coadministered with VIREAD

IMPORTANT SAFETY INFORMATION (cont'd)

DRUG INTERACTIONS (cont'd)

- **HIV-1 protease inhibitors:** Coadministration decreases atazanavir concentrations and increases tenofovir concentrations; use atazanavir given with ritonavir. Coadministration of VIREAD with atazanavir and ritonavir, darunavir and ritonavir, or lopinavir/ritonavir increases tenofovir concentrations. Monitor for evidence of tenofovir toxicity
- **Drugs affecting renal function:** Coadministration of VIREAD with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of tenofovir

DOSAGE AND ADMINISTRATION

- Recommended dose, in adults and pediatric patients ≥12 years of age (≥35 kg), for the treatment of chronic hepatitis B: one 300 mg tablet, once daily, taken orally, without regard to food
- In the treatment of chronic hepatitis B, the optimal duration of treatment is unknown
- Safety and efficacy in pediatric patients <12 years of age or weighing <35kg with chronic hepatitis B have not been established
- The dosing interval of VIREAD should be adjusted (using recommendations in the table below) and renal function closely monitored in patients with baseline creatinine clearance <50 mL/min

DOSAGE ADJUSTMENT FOR PATIENTS WITH ALTERED CREATININE CLEARANCE

	Creatinine clearance (mL/min)[a]			Hemodialysis patients
	≥50	30-49	10-29	
Recommended 300 mg dosing interval	Every 24 hours	Every 48 hours	Every 72 to 96 hours	Every 7 days or after a total of approximately 12 hours of dialysis[b]

[a]Calculated using ideal (lean) body weight.

[b]Generally once weekly assuming three hemodialysis sessions a week of approximately 4 hours duration. VIREAD should be administered following completion of dialysis.

- The pharmacokinetics of tenofovir have not been evaluated in non-hemodialysis patients with creatinine clearance <10 mL/min; therefore, no dosing recommendation is available for these patients
- No dose adjustment is necessary for patients with mild renal impairment (creatinine clearance 50-80 mL/min). Routine monitoring of estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein should be performed in these patients
- No data are available to make dose recommendations in pediatric patients with renal impairment

Please see Brief Summary of full Prescribing Information including **BOXED WARNING** on the following pages.

References: 1. Data on file, Gilead Sciences, Inc. Healthcare Analytics. **2.** VIREAD [package insert]. Foster City, CA: Gilead Sciences, Inc.; May 2015. **3.** Marcellin P, Heathcote EJ, Buti M, et al. Tenofovir disoproxil fumarate versus adefovir dipivoxil for chronic hepatitis B. *N Engl J Med.* 2008;359(23):2442-2455. **4.** Data on file, Gilead Sciences, Inc. Study 102 CSR. **5.** Data on file, Gilead Sciences, Inc. Study 103 CSR. **6.** Marcellin P, Gane EJ, Flisiak R, et al. Long term treatment with tenofovir disoproxil fumarate for chronic hepatitis B infection is safe and well tolerated and associated with durable virologic response with no detectable resistance: 8 year results from two phase 3 trials [AASLD abstract 229]. *Hepatology.* 2014;60(4)(suppl):313A-314A.

VIREAD® (tenofovir disoproxil fumarate) tablets

Brief summary of full Prescribing Information. Please see full Prescribing Information including Boxed WARNING. Rx only

WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT EXACERBATION OF HEPATITIS

- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, in combination with other antiretrovirals *(See Warnings and Precautions)***
- **Severe acute exacerbations of hepatitis have been reported in HBV-infected patients who have discontinued anti-hepatitis therapy, including VIREAD. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including VIREAD. If appropriate, resumption of anti-hepatitis B therapy may be warranted *(See Warnings and Precautions)***

INDICATIONS AND USAGE: VIREAD is indicated for the treatment of chronic hepatitis B in adults and pediatric patients 12 years of age and older.

The following points should be considered when initiating therapy with VIREAD for the treatment of HBV infection:

- The indication in adults is based on safety and efficacy data from treatment of subjects who were nucleoside-treatment-naïve and subjects who were treatment-experienced with documented resistance to lamivudine. Subjects were adults with HBeAg-positive and HBeAg-negative chronic hepatitis B with compensated liver disease *(See Adverse Reactions)*
- VIREAD was evaluated in a limited number of subjects with chronic hepatitis B and decompensated liver disease *(See Adverse Reactions)*
- The numbers of subjects in clinical trials who had adefovir resistance-associated substitutions at baseline were too small to reach conclusions of efficacy

DOSAGE AND ADMINISTRATION: For the treatment of chronic hepatitis B the recommended dose, in adults and pediatric patients ≥12 years of age (≥35 kg), is one 300 mg tablet, once daily, taken orally, without regard to food. In the treatment of chronic hepatitis B, the optimal duration of treatment is unknown. Safety and efficacy in pediatric patients <12 years of age with chronic hepatitis B weighing <35 kg have not been established. **Dose Adjustment for Renal Impairment in Adults:** Significantly increased drug exposures occurred when VIREAD was administered to subjects with moderate to severe renal impairment. Therefore, the dosing interval of VIREAD tablets 300 mg should be adjusted in patients with baseline creatinine clearance <50 mL/min using the recommendations in Table 1. These dosing interval recommendations are based on modeling of single-dose pharmacokinetic data in non-HIV and non-HBV infected subjects with varying degrees of renal impairment, including end-stage renal disease (ESRD) requiring hemodialysis. The safety and effectiveness of these dosing interval adjustment recommendations have not been clinically evaluated in patients with moderate or severe renal impairment, therefore clinical response to treatment and renal function should be closely monitored in these patients *(See Warnings and Precautions)*. No dose adjustment of VIREAD tablets 300 mg is necessary for patients with mild renal impairment (creatinine clearance 50–80 mL/min). Routine monitoring of calculated creatinine clearance, serum phosphorus, urine glucose and urine protein should be performed in patients with mild renal impairment *(See Warnings and Precautions)*.

Dosage Adjustment for Adult Patients with Altered Creatinine Clearance

	Creatinine clearance (mL/min)[a]			Hemodialysis patients
	≥50	30-49	10-29	
Recommended 300 mg dosing interval	Every 24 hours	Every 48 hours	Every 72 to 96 hours	Every 7 days or after a total of approximately 12 hours of dialysis[b]

a. Calculated using ideal (lean) body weight.
b. Generally once weekly assuming three hemodialysis sessions a week of approximately 4 hours duration. VIREAD should be administered following completion of dialysis.

The pharmacokinetics of tenofovir have not been evaluated in non-hemodialysis patients with creatinine clearance <10 mL/min; therefore, no dosing recommendation is available for these patients. No data are available to make dose recommendations in pediatric patients with renal impairment.

CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS: Lactic Acidosis/Severe Hepatomegaly with Steatosis: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, in combination with other antiretrovirals. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Particular caution should be exercised when administering nucleoside analogs to any patient with known risk factors for liver disease; however, cases have also been reported in patients with no known risk factors. Treatment with VIREAD should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations). **Exacerbation of Hepatitis after Discontinuation of Treatment:** Discontinuation of anti-HBV therapy, including VIREAD, may be associated with severe acute exacerbations of hepatitis. Patients infected with HBV who discontinue VIREAD should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment. If appropriate, resumption of anti-hepatitis B therapy may be warranted. **New Onset or Worsening Renal Impairment:** Tenofovir is principally eliminated by the kidney. Renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported with the use of VIREAD *(See Adverse Reactions)*. It is recommended that estimated creatinine clearance be assessed in all patients prior to initiating therapy and as clinically appropriate during therapy with VIREAD. In patients at risk of renal dysfunction, including patients who have previously experienced renal events while receiving adefovir dipivoxil, it is recommended that estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein be assessed prior to initiation of VIREAD, and periodically during VIREAD therapy. Dosing interval adjustment of VIREAD and close monitoring of renal function are recommended in all patients with creatinine clearance <50 mL/min *(See Dosage and Administration)*. No safety or efficacy data are available in patients with renal impairment who received VIREAD using these dosing guidelines, so the potential benefit of VIREAD therapy should be assessed against the potential risk of renal toxicity. VIREAD should be avoided with concurrent or recent use of a nephrotoxic agent (e.g., high-dose or multiple non-steroidal anti-inflammatory drugs (NSAIDs)) *(See Drug Interactions)*. Cases of acute renal failure after initiation of high dose or multiple NSAIDs have been reported in HIV-infected patients with risk factors for renal dysfunction who appeared stable on tenofovir DF. Some patients required hospitalization and renal replacement therapy. Alternatives to NSAIDs should be considered, if needed, in patients at risk for renal dysfunction. Persistent or worsening bone pain, pain in extremities, fractures and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function in at-risk patients. **Coadministration with Other Products:** VIREAD should not be used in combination with the fixed-dose combination products ATRIPLA®, COMPLERA®, STRIBILD® or TRUVADA® since tenofovir disoproxil fumarate is a component of these products. VIREAD should not be administered in combination with adefovir dipivoxil *(See Drug Interactions)*. **Patients Coinfected with HIV-1 and HBV:** Due to the risk of development of HIV-1 resistance, VIREAD should only be used in HIV-1 and HBV coinfected patients as part of an appropriate antiretroviral combination regimen. HIV-1 antibody testing should be offered to all HBV-infected patients before initiating therapy with VIREAD. It is also recommended that all patients with HIV-1 be tested for the presence of chronic hepatitis B before initiating treatment with VIREAD.

Bone Effects

Bone Mineral Density: In clinical trials in HIV-1 infected adults, VIREAD was associated with slightly greater decreases in bone mineral density (BMD) and increases in biochemical markers of bone metabolism, suggesting increased bone turnover relative to comparators. Serum parathyroid hormone levels and 1,25 Vitamin D levels were also higher in subjects receiving VIREAD *(See Adverse Reactions)*.

Clinical trials evaluating VIREAD in pediatric and adolescent subjects were conducted. Under normal circumstances, BMD increases rapidly in pediatric patients. In HIV-1 infected subjects aged 2 years to less than 18 years, bone effects were similar to those observed in adult subjects and suggest increased bone turnover. Total body BMD gain was less in the VIREAD-treated HIV-1 infected pediatric subjects as compared to the control groups. Similar trends were observed in chronic hepatitis B infected adolescent subjects aged 12 years to less than 18 years. In all pediatric trials, skeletal growth (height) appeared to be unaffected *(See Adverse Reactions)*.

The effects of VIREAD-associated changes in BMD and biochemical markers on long-term bone health and future fracture risk are unknown. Assessment of BMD should be considered for adults and pediatric patients who have a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss. Although the effect of supplementation with calcium and vitamin D was not studied, such supplementation may be beneficial for all patients. If bone abnormalities are suspected then appropriate consultation should be obtained.

Mineralization Defects: Cases of osteomalacia associated with proximal renal tubulopathy, manifested as bone pain or pain in extremities and which may contribute to fractures, have been reported in association with the use of VIREAD *(See Adverse Reactions)*. Arthralgias and muscle pain or weakness have also been reported in cases of proximal renal tubulopathy. Hypophosphatemia and osteomalacia secondary to proximal renal tubulopathy should be considered in patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms while receiving products containing tenofovir DF *(See Warnings and Precautions)*.

Brief Summary (Cont'd)

ADVERSE REACTIONS: Clinical Trials in Adult Subjects with Chronic Hepatitis B and Compensated Liver Disease: *Treatment-Emergent Adverse Reactions:* In controlled clinical trials in subjects with chronic hepatitis B (0102 and 0103), more subjects treated with VIREAD during the 48-week double-blind period experienced nausea: 9% with VIREAD versus 2% with adefovir dipivoxil. Other treatment-emergent adverse reactions reported in >5% of subjects treated with VIREAD included: abdominal pain, diarrhea, headache, dizziness, fatigue, nasopharyngitis, back pain, and skin rash. No significant change in the tolerability profile was observed with continued treatment with VIREAD for up to 384 weeks.

Laboratory Abnormalities: in Studies 0102 and 0103 (0–48 Weeks) laboratory abnormalities (Grades 3–4) reported in ≥1% of subjects treated with Viread (n=426) and adefovir dipivoxil (n=215), respectively, were: any ≥Grade 3 laboratory abnormality (19%, 13%); creatine kinase (M: >990 U/L; F: >845 U/L) (2%, 3%); serum amylase (>175 U/L) (4%, 1%); glycosuria (≥3+) (3%, <1%); AST (M: >180 U/L; F: >170 U/L) (4%, 4%); and ALT (M: >215 U/L; F: >170 U/L) (10%, 6%). Laboratory abnormalities (Grades 3–4) were similar in subjects continuing VIREAD treatment for up to 384 weeks in these trials.

The overall incidence of on-treatment ALT flares (defined as serum ALT >2 × baseline and >10 × ULN, with or without associated symptoms) was similar between VIREAD (2.6%) and adefovir dipivoxil (2%). ALT flares generally occurred within the first 4-8 weeks of treatment and were accompanied by decreases in HBV DNA levels. No subject had evidence of decompensation. ALT flares typically resolved within 4-8 weeks without changes in study medication. The adverse reactions observed in subjects with chronic hepatitis B and lamivudine resistance who received treatment with VIREAD were consistent with those observed in other hepatitis B clinical trials in adults. *Clinical Trial in Adult Subjects with Chronic Hepatitis B and Decompensated Liver Disease:* In a small randomized, double-blind, active-controlled trial (0108), subjects with CHB and decompensated liver disease received treatment with VIREAD or other antiviral drugs for up to 48 weeks. Among the 45 subjects receiving VIREAD, the most frequently reported treatment-emergent adverse reactions of any severity were abdominal pain (22%), nausea (20%), insomnia (18%), pruritus (16%), vomiting (13%), dizziness (13%), and pyrexia (11%). Two of 45 (4%) subjects died through Week 48 of the trial due to progression of liver disease. Three of 45 (7%) subjects discontinued treatment due to an adverse event. Four of 45 (9%) subjects experienced a confirmed increase in serum creatinine of 0.5 mg/dL (1 subject also had a confirmed serum phosphorus <2 mg/dL through Week 48). Three of these subjects (each of whom had a Child-Pugh score ≥10 and MELD score ≥14 at entry) developed renal failure. Because both VIREAD and decompensated liver disease may have an impact on renal function, the contribution of VIREAD to renal impairment in this population is difficult to ascertain. One of 45 subjects experienced an on-treatment hepatic flare during the 48 week trial.

Clinical Trials in Pediatric Subjects 12 Years of Age and Older with Chronic Hepatitis B: Assessment of adverse reactions is based on one randomized study (0115) in 106 pediatric subjects (12 to less than 18 years of age) infected with chronic hepatitis B receiving treatment with VIREAD (N = 52) or placebo (N = 54) for 72 weeks. The adverse reactions observed in pediatric subjects who received treatment with VIREAD were consistent with those observed in clinical trials of VIREAD in adults. In this study, both the VIREAD and placebo treatment arms experienced an overall increase in mean lumbar spine BMD over 72 weeks, as expected for an adolescent population. The BMD gains from baseline to Week 72 in lumbar spine and total body BMD in VIREAD-treated subjects (+5% and +3%, respectively) were less than the BMD gains observed in placebo-treated subjects (+8% and +5%, respectively). Three subjects in the VIREAD group and two subjects in the placebo group had significant (greater than 4%) lumbar spine BMD loss at Week 72. At baseline, mean BMD Z-scores in subjects randomized to VIREAD were −0.43 for lumbar spine and −0.20 for total body, and mean BMD Z-scores in subjects randomized to placebo were −0.28 for lumbar spine and −0.26 for total body. In subjects receiving VIREAD for 72 weeks, the mean change in BMD Z-score was −0.05 for lumbar spine and −0.15 for total body compared to +0.07 and +0.06, respectively, in subjects receiving placebo. As observed in pediatric studies of HIV-infected patients, skeletal growth (height) appeared to be unaffected *(See Warnings and Precautions)*.

Postmarketing Experience: The following adverse reactions have been identified during postapproval use of VIREAD. Because postmarketing reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: allergic reaction, including angioedema, lactic acidosis, hypokalemia, hypophosphatemia, dyspnea, pancreatitis, increased amylase, abdominal pain, hepatic steatosis, hepatitis, increased liver enzymes (most commonly AST, ALT gamma GT), rash, rhabdomyolysis, osteomalacia (manifested as bone pain and which may contribute to fractures), muscular weakness, myopathy, acute renal failure, renal failure, acute tubular necrosis, Fanconi syndrome, proximal renal tubulopathy, interstitial nephritis (including acute cases), nephrogenic diabetes insipidus, renal insufficiency, increased creatinine, proteinuria, polyuria, asthenia. The following adverse reactions listed above, may occur as a consequence of proximal renal tubulopathy: rhabdomyolysis, osteomalacia, hypokalemia, muscular weakness, myopathy, hypophosphatemia.

DRUG INTERACTIONS: Didanosine: Coadministration of VIREAD and didanosine should be undertaken with caution and patients receiving this combination should be monitored closely for didanosine-associated adverse reactions. Didanosine should be discontinued in patients who develop didanosine-associated adverse reactions. When administered with VIREAD, C_{max} and AUC of didanosine increased significantly. The mechanism of this interaction is unknown. Higher didanosine concentrations could potentiate didanosine-associated adverse reactions, including pancreatitis and neuropathy. Suppression of $CD4^+$ cell counts has been observed in patients receiving VIREAD with didanosine 400 mg daily. In patients weighing >60 kg, the didanosine dose should be reduced to 250 mg once daily when it is coadministered with VIREAD. In patients weighing <60 kg, the didanosine dose should be reduced to 200 mg once daily when it is coadministered with VIREAD. When coadministered, VIREAD and didanosine EC may be taken under fasted conditions or with a light meal (<400 kcal, 20% fat). For additional information on coadministration of VIREAD and didanosine, please refer to the full Prescribing Information for didanosine. **HIV-1 Protease Inhibitors:** VIREAD decreases the AUC and C_{min} of atazanavir. Viread should not be coadministered with atazanavir without ritonavir. Lopinavir/ritonavir, atazanavir coadministered with ritonavir, and darunavir coadministered with ritonavir have been shown to increase tenofovir concentrations. Tenofovir disoproxil fumarate is a substrate of P-glycoprotein (Pgp) and breast cancer resistance protein (BCRP) transporters. When tenofovir disoproxil fumarate is coadministered with an inhibitor of these transporters, an increase in absorption may be observed. Patients receiving VIREAD concomitantly with lopinavir/ritonavir, ritonavir-boosted atazanavir, or ritonavir-boosted darunavir should be monitored for VIREAD-associated adverse reactions. VIREAD should be discontinued in patients who develop VIREAD-associated adverse reactions. **Drugs Affecting Renal Function:** Since tenofovir is primarily eliminated by the kidneys, coadministration of VIREAD with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of tenofovir and/or increase the concentrations of other renally eliminated drugs. Some examples include, but are not limited to cidofovir, acyclovir, valacyclovir, ganciclovir, valganciclovir, aminoglycosides (e.g., gentamicin), and high-dose or multiple NSAIDs *(See Warnings and Precautions)*. In the treatment of chronic hepatitis B, VIREAD should not be administered in combination with adefovir dipivoxil.

USE IN SPECIFIC POPULATIONS: Pregnancy: *Pregnancy Category B:* There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, VIREAD should be used during pregnancy only if clearly needed. *Antiretroviral Pregnancy Registry:* To monitor fetal outcomes of pregnant women exposed to VIREAD, an Antiretroviral Pregnancy Registry has been established. Healthcare providers are encouraged to register patients by calling 1-800-258-4263. *Animal Data:* Reproduction studies have been performed in rats and rabbits at doses up to 14 and 19 times the human dose based on body surface area comparisons and revealed no evidence of impaired fertility or harm to the fetus due to tenofovir. **Nursing Mothers: The Centers for Disease Control and Prevention recommend that HIV-1-infected mothers not breastfeed their infants to avoid risking postnatal transmission of HIV-1.** Samples of breast milk obtained from five HIV-1 infected mothers in the first post-partum week show that tenofovir is secreted in human milk. The impact of this exposure in breastfed infants is unknown. Because of both the potential for HIV-1 transmission and the potential for serious adverse reactions in nursing infants, **mothers should be instructed not to breastfeed if they are receiving VIREAD. Geriatric Use:** Clinical studies of VIREAD did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for the elderly patient should be cautious, keeping in mind the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. **Patients with Impaired Renal Function:** It is recommended that the dosing interval for VIREAD be modified in patients with estimated creatinine clearance <50 mL/min or in patients with ESRD who require dialysis *(See Dosage and Administration)*.

For detailed information, please see full Prescribing Information. To learn more call 1-800-GILEAD-5 (1-800-445-3235) or visit www.VIREAD.com.

Conference Alerts

North America

2016 Annual Meeting: Best of ASCO Washington, DC

July 15-16, 2016 | Washington, D.C. USA

Website: https://east-boa.asco.org/
Contact: customerservice@asco.org

The Best of ASCO Meetings condense the most cutting-edge science and education from the world's premier oncology event, the ASCO Annual Meeting, into a two-day program. The abstracts chosen for presentation and discussion reflect the foremost research and strategies in oncology that will directly impact patient care. The program features in-depth discussion and analysis on the latest scientific findings in primary disease sites and practice-changing advances in cancer treatment. Expert faculty will place abstract findings into clinical context and discuss how the results may change the current standard of care.

The 43rd International Society of Oncology and Biomarkers (ISOBM) Annual Congress

September 1-6, 2016 | Chicago, Illinois USA

Website: https://isobm2016congress.com
Contact: info@isobm2016congress.com

With the theme "Towards Precision Medicine: From Biomarker Discovery to Novel Therapies," the Congress links all fields of cancer research and oncology. The 2016 theme of the ISOBM Congress is to translate new findings into clinical practice, and to invite interdisciplinary and innovative approaches. The latest findings in cancer research, diagnosis and clinical oncology will be presented in oral and poster format, along with panel discussions and special topic seminars. The conference seeks to engage professionals in the field of cancer research, oncology, and biomarkers in collaboration and exchange ideas and expertise on a global platform.

11th Biennial Ovarian Cancer Research Symposium

September 12-13, 2016 | Seattle, Washington USA

Website: http://www.rivkin.org/events/symposium/
Contact: info@marsharivkin.org

The 11th Biennial Ovarian Cancer Research Symposium is presented by the Rivkin Center for Ovarian Cancer and the American Association for Cancer Research. The goal of the Symposium is to bring together clinicians and researchers from across many disciplines and institutions worldwide in order to encourage collaborations toward advancing the field of ovarian cancer research. The conference seeks to enhance the understanding and knowledge of ovarian cancer, especially among junior investigators, discuss the most recent innovations in the field of ovarian cancer research, and address pressing concerns of the leaders in the clinical and research community. This year's Symposium will focus on the following topics: "detection & prevention of ovarian cancer," "mechanisms of initiation & progression of ovarian cancer," "tumor microenvironment & models of ovarian cancer," and "novel therapeutics for ovarian cancer".

2016 ASH Meeting on Hematologic Malignancies

September 16-17, 2016 | Chicago, Illinois USA

Website: http://www.hematology.org/Malignancies/
Contact: (202) 776-0544

World-class experts in hematologic malignancies will discuss their personal evidence-based treatment approaches and the latest developments in clinical care at the 2016 ASH Meeting on Hematologic Malignancies. The majority of the program content will be structured as "How I Treat" sessions on core malignancies, including leukemia, lymphoma, myelodysplastic syndromes, myeloma, and myeloproliferative neoplasms. Each presentation will showcase the speaker's evidence-based treatment approaches, ranging from standard of care, specialized disease complications, and novel agent discussions. The meeting will also feature topic-based panel discussions which will allow participants to get answers to their most challenging patient care questions.

The 6th New York Health Forum

September 27, 2016 | New York, New York USA

Website: http://newyorkhealthforum.net/
Contact: info@wmedicalstrategy.org

The New York Health Forum's mission is to present the significant agendas for the healthcare industry, contribute to public health by bringing out the public concerns to be discussed and solved, and gather the sound of health policy, science innovation and industry development. A major goal of the NYHF is to create the foundation of communication among all areas of the healthcare industry resulting in solution, which combines the ideas of science, industry, and policy for a healthier society.

National Comprehensive Cancer Network (NCCN) 11th Annual Congress: Hematologic Malignancies

September 30, October 1, 2016 | New York, New York USA

Website: https://www.nccn.org/professionals/meetings/hematological/default.aspx
Contact: conferences@nccn.org

Treatment of hematologic malignancies is increasingly complex. Issues relating to pathology, transplantation, and various new therapies require oncologists and hematologists to stay abreast of breakthrough advances. In addition, targeted therapies and oral treatments bring the latest benefits to patients. This congress focuses on the new approaches that have been incorporated into patient management, including the use of drugs, biologics, and diagnostics.

7th Annual World Antibody-Drug Conjugates (ADC)

October 10-13, 2016 | San Diego, California USA

Website: http://worldadc-usa.com/
Contact: adc@hansonwade.com

World ADC San Diego is the definitive forum for sharing new antibody drug conjugate insights and data. Specifically focussed on ADCs and crafted with the field's thought-leaders, World ADC is the industry's definitive forum for learning and networking. Across 4 streams and 96 sessions, World ADC will cover every element of drug development from discovery to preclinical, clinical and manufacturing offering you an unparalleled breadth and depth of cutting-edge knowledge. You will learn from 90 ADC experts at the likes of Stemcentrx, Seattle Genetics and Genentech as they share their latest intelligence on how to: design ADCs which have superior efficacy and safety profiles, improve the preclinical predictability of your ADC to effectively translate into the clinic, expand the clinical therapeutic window of your ADC, and advance your ADC drug manufacturing to robustly scale up from phase 1 to phase 3.

The 34th Annual Chemotherapy Foundation Symposium: Innovative Cancer Therapy for Tomorrow

November 9-11, 2016 | New York, New York USA

Website: http://www.gotoper.com/conferences/chemo/meetings/34th-annual-chemotherapy-foundation-symposium-innovative-cancer-therapy-for-tomorrow
Contact: info@gotoper.com

The annual Chemotherapy Foundation Symposium: Innovative Cancer Therapy for Tomorrow® (CFS) has brought together over 2,000 oncologists, hematologists, radiation oncologists, immunologists, oncology nurses, nurse practitioners, physician assistants, and case managers each year for 33 years, with the aim of educating these disciplines on state-of-the-art treatments across solid and hematologic malignancies and diverse clinical scenarios. At the 34th Annual Chemotherapy Foundation Symposium: Innovative Cancer Therapy for Tomorrow® (CFS), leading clinical innovators in virtually every tumor subspecialty will provide expert insights on new developments in cancer therapeutics, and provide oncology professionals with the opportunity to learn about new compounds, novel approaches to diagnosis and treatment with currently available agents, ongoing clinical trials, and emerging developments that define current progress aimed at the goal of control and cure of cancer.

The 58th American Society of Hematology (ASH) Annual Meeting & Exposition

December 3-6, 2016 | San Diego, California USA

Website: http://www.hematology.org/Annual-Meeting/

Contact: (202)776-0544

The ASH Annual Meeting provides an invaluable educational experience and an opportunity to review thousands of scientific abstracts highlighting updates in the hottest topics in hematology. Participants will be able to network with top minds in the field, as well as a global community of more than 20,000 hematology professionals from every subspecialty.

Europe

The 16th International Conference on Progress in Vaccination Against Cancer (PIVAC-16)

September 12-14, 2016 | Winchester, United Kingdom

Website: http://www.eacr.org/pivac16/index.php?utm_source=PIVAC16&utm_medium=Website&utm_campaign=PIVAC16

Contact: kathryn.wass@nottingham.ac.uk

Progress in Vaccination Against Cancer (PIVAC) aims to bring together translational and clinical oncologists and immunologists dealing with active vaccination against cancer for three days of presentations on the most recent advances in the field. The meeting provides an up-to-date overview of many aspects of tumour immunology. Thanks to its friendly atmosphere and the limited number (max 100) of participants, PIVAC cultivates lively and fruitful discussions, promotes interactions between participants, speakers and companies attending the conference and encourages the emergence of new partnerships.

Translational Vaccinology for Global Health

October 26-30, 2016 | London, United Kingdom

Website: http://www.keystonesymposia.org/16S1

Contact: info@keystonesymposia.org

This conference aims to bring together those pioneering novel, creative solutions to problems of global vaccine discovery and development across the academic/biotech/product development partner/pharma spectrum.

EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium

November 29-December 2, 2016 | Munich, Germany

Website: https://www.ecco-org.eu/ENA

Contact: ena2016@ecco-org.eu

Hosted by the European Organisation for Research and Treatment of Cancer (EORTC), the National Cancer Institute (NCI) and the American Association for Cancer Research (AACR), the 2016 Symposium will bring together around 2000 academics, scientists and pharmaceutical industry representatives from across the globe to discuss innovations in drug development, target selection and the impact of new discoveries in molecular biology. As a one-of-a-kind Symposium at the forefront of drug development, it will enable participants to apply the latest findings and knowledge in their work and practice.

International Association for the Study of Lung Cancer (IASLC) 17th World Conference on Lung Cancer

December 4-7, 2016 | Vienna, Austria

Website: http://wclc2016.iaslc.org/

Contact: Pia.Hirsch@iaslc.org

The IASLC World Conference on Lung Cancer (WCLC) is the world's largest meeting dedicated to lung cancer and other thoracic malignancies. More than 7,000 delegates come from more than 100 countries to discuss the latest developments in thoracic malignancy research. Attendees include surgeons, medical oncologists, radiation oncologists, pulmonologists, radiologists, pathologists, epidemiologists, basic research scientists, nurses and allied health professionals and patients.

Asia

The 33rd World Congress of Internal Medicine

August 22-25, 2016 | Bali, Indonesia

Website: http://www.wcimbali2016.org/index.php

Contact: wcim2016ser@pharma-pro.com

The International Society of Internal Medicine (ISIM) was founded in 1948 in Basel, Switzerland. Its purpose is to promote scientific knowledge and unity in Internal Medicine, to further the education of young internists and to encourage friendship between physicians in all over the world. The 33rd World Congress of Internal Medicine will discuss important subjects such as medical, internal medicine, chemical biology and health care. The ISIM holds the congress biennially.

ISPOR 7th Asia-Pacific Conference

September 3-6, 2016 | Suntec City, Singapore

Website: http://www.ispor.org/event/index/2016singapore

Contact: info@ispor.org

The ISPOR Asia-Pacific Congress features 3 thought-provoking plenary sessions and more than 600 presentations in the form of workshops, issue panels and podium presentations plus posters on innovative research methods, health policy development using outcomes research, patient preferences, real world data, clinical, economic, and patient-reported outcomes.

International Continence Society 46th Annual Meeting (ICS 2016)

September 13-16, 2016 | Tokyo, Japan

Website: http://www.ics.org/2016

Contact: reg_ics16@kenes.com

The meeting is an international event on continence medicine and care. It is unique in bringing together multidisciplinary professionals including urologists, gynaecologists, neurologists, physiotherapists, nurses, physiologists and scientists. The topics discussed will be issues on pathophysiology, diagnosis and management of incontinence. The scope of the meeting will widely range from basic laboratory/animal experiments to surgical; physical and medical treatments to psychosocial aspects of elimination problems.

The 9th Asia Pacific Heart Rhythm Society Scientific Session

October 12-15, 2016 | Seoul, Republic of Korea

Website: http://www.aphrs2016.com/start.asp

Contact: aphrs2016-info@intercom.co.kr

APHRS 2016 will bring together over 3,000 attendees including professionals and experts from the Asia Pacific region to keep up-to-date on the latest clinical trials and studies in the sphere of arrhythmia, share their experience, ideas and strategies, and to discuss the current issues facing those involved in this field.

May - June

1. Visium's Valvani Charged With Insider Trading on FDA Leaks

U.S. Attorney Preet Bharara in Manhattan charged Sanjay Valvani of Visium Asset Management LP of fraudulently making $25 million by gaining advance word about U.S. Food and Drug Administration approvals of generic drug applications from 2005 to 2011. The case is one of the biggest insider trading cases since a 2014 court ruling made it more difficult for U.S. prosecutors to pursue traders and prove them guilty. Prosecutors assert that Valvani obtained inside information from consultant Gordon Johnston, who had contacted a former colleague and friend at the FDA. Valvani subsequently passed a portion of this information to Christopher Plaford, then a Visium portfolio manager, who made his own illegal trades. Johnston and Plaford have pleaded guilty to related charges and are cooperating with prosecutors. Stefan Lumiere, another former Visium portfolio manager, was charged with securities fraud, wire fraud and conspiracy, and freed on $1 million bond, but did not enter a plea. Valvani pleaded not guilty to five counts including securities fraud, wire fraud and conspiracy and was freed on $5 million bond.

http://www.reuters.com/article/us-usa-fraud-insidertrading-idUSKCN0Z11TB

2. Brexit spells upheaval for EU and UK drug regulation

Britain's vote to withdraw from the European Union, known as "Brexit," spells uncertainty for drug companies as the London-based European Medicines Agency (EMA) is expected to have to relocate. Industry executives are concerned that the upheaval of the EMA, which has overseen pan-European drug approvals since 1995 from its home in London, could complicate the EU's drug approval process. There is also a concern over how Britain will domestically regulate drugs going forward. While the Brexit is not expected to negatively impact profits for global drug manufacturers, many scientists are concerned that funding and collaboration for academic research, which has been well supported by the EU in recent decades, will now be jeopardized.

http://www.reuters.com/article/us-britain-eu-corporates-pharmaceuticals-idUSKCN0ZA26J

3. Hunting growth, Samsung races to get up to speed on biosimilar drugs

With four-year-old Bioepis, South Korea's Samsung Group hopes to offset a slowing smartphone market and capture the potentially lucrative biosimilars market, which is estimated to generate $26.6 billion global revenue by 2020 from $2.6 billion in 2014. Fixated on speed, Bioepis took only four years of development, roughly two times faster than most biosimilars that come to market, to launch a biosimilar version of Enbrel, Amgen's blockbuster rheumatoid arthritis drug, earlier this year. Bioepis has not shied away from taking risks, including mass production ahead of clinical trials, and plans to make a U.S. initial public offering over the next few years. With large pharmaceutical companies like Pfizer dipping into the biosimilar market, Samsung must continue its large-scale investment in Bioepis to succeed.

http://www.reuters.com/article/us-samsung-group-biosimilars-idUSKCN0YS2JL

4. U.S. to invest $200 million to shorten organ transplant wait lists

The U.S. government plans to invest $200 million to help shorten the waiting list for patients waiting for organ transplants. The investment will be led by the Department of Defense, and is designed to support technologies aimed at repairing and replacing cells and tissues. More than $160 million will go to a new Advanced Tissue Biofabrication Manufacturing Innovation Institute to help develop next-generation manufacturing techniques for cell therapies and $7 million will be earmarked for awards to small businesses working to advance the science of tissue preservation. The funding comes at an important time; more than 120,000 people in the United States are currently on a donor waiting list and just last year, the U.S. saw a record of more than 30,000 transplants.

http://www.reuters.com/article/us-usa-transplants-idUSKCN0YZ1RY

5. House Republicans unveil healthcare alternative to Obamacare

Republicans in the U.S. House of Representatives recently introduced a proposal challenging President Barack Obama's signature 2010 Affordable Care Act. The proposal, part of a broader effort by House Speaker Paul Ryan to maintain control of both the House and the Senate before the upcoming November 8 presidential elections, criticizes Obamacare for limiting patients' choices, increasing consumer costs, and burying employers and health care providers under new regulations. Although it includes long-held Republican proposals such as allowing consumers to buy health insurance across state lines, expanding health savings accounts, and giving block grants to states to run Medicaid programs for the poor, the alternative plan keeps some of Obamacare's popular provisions, including not allowing people with pre-existing conditions to be denied coverage and permitting children to stay on their parents' coverage until age 26. While Democrats have dismissed Ryan's proposals as merely trite ideas, industry groups remain ready to work with both parties to improve access and affordability for consumers, as the elections have yet to happen.

http://www.reuters.com/article/us-usa-election-healthcare-ryan-idUSKCN0Z80AQ

6. Pfizer completes $5.2bn acquisition of Anacor

Pfizer has completed its acquisition of all outstanding common stock shares of the Silicon Valley biotech group Anacor for $99.25 per share, equating to a total deal value of about $5.2 billion. Through this acquisition, Pfizer has secured access to the non-steroidal topical PDE4 inhibitor crisaborole, a treatment for mild-to-moderate atopic dermatitis that is currently being reviewed by U.S. regulators. A decision is expected in by January 7 of 2017 and Pfizer believes the drug could achieve at least $2 billion a year if it makes it to market; it is estimated that up to 25 million people in the U.S. suffer from atopic dermatitis.

http://www.pharmatimes.com/news/pfizer_completes_$5.2bn_acquisition_of_anacor_1049226

7. Shire, Baxalta Complete $32B Merger

Shire has completed its $32 billion merger with Baxalta, a biopharmaceutical business focusing on treatments for orphan diseases and underserved conditions in hematology, immunology, and oncology. Baxalta, which was spun off by Baxter International in 2015, will now be an indirect wholly-owned subsidiary of Shire. Shire, which currently has products in gastrointestinal/endocrine diseases, hereditary angioedema, neuroscience, and lysosomal storage diseases, maintains that this merger has made it the global market leader in rare diseases, with the number one rare diseases platform based on both revenue and pipeline programs. It projects that the combined company will generate approximately 65% of its total annual revenues, which is forecasted to rise to more than $20 billion by 2020. Within the next three years, Shire also plans to cut more than $500 million in costs by increasing efficiency, scaling up of the combined business, aligning Baxalta programs to Shire's lean operating model, and optimizing the combined R&D portfolio.

http://www.genengnews.com/gen-news-highlights/shire-baxalta-complete-32b-merger/81252788/

8. Shire picks up two breakthrough badges for rare disease drugs

U.S. regulators have awarded Breakthrough Therapy badges to two of Shire's investigational products. The first is a novel formulation of budesonide for eosinophilic esophagitis (EoE), a chronic rare disease resulting from an elevated number of eosinophils that causes inflammation in the esophagus and affects about 15-55 per 100,000 persons. Twelve weeks of the budesonide oral suspension treatment in a Phase II trial has significantly reduced both dysphagia symptoms and achieved higher proportion of subjects with histologic response compared to placebo. The second drug is maralixibat (LUM001) for type 2 progressive familial intrahepatic cholestasis (PFIC), the most common type of a group of child autosomal-recessive liver disorders that disrupt bile formation and cause cholestasis. The conditions affect around 1 in 50,000 to 1 in 100,000 births, and PFIC2 is the most common type, accounting for around half of cases. A Phase II study of LUM001-501 (INDIGO) in pediatric patients with PFIC has shown decreases in a subpopulation of patients, reductions in pruritus, and normalization of liver parameters in patients with liver enzymes.

http://www.pharmatimes.com/news/shire_picks_up_two_breakthrough_badges_for_rare_disease_drugs_1040537

9. India's Dr Reddy's in $350 million deal to buy eight U.S. drugs from Teva, Allergan

With an 86 percent slump in profit for its March quarter, India's second-largest drugmaker Dr Reddy's Laboratories Ltd has agreed to purchase eight generic drugs from Teva Pharmaceutical Industries and Allergan Plc for $350 million in cash to bolster its slowing U.S. business. The products being divested consist of generic drugs that have not yet been U.S. approved, as well as drugs that are already on the market. Teva hopes to win the U.S. Federal Trade Commission's antitrust clearance for its $40.5 billion acquisition of Allergan's generic drugs portfolio through this deal with Dr Reddy's.

http://www.reuters.com/article/us-dr-reddys-m-a-teva-pharm-ind-idUSKCN0YX060

10. Sanofi, Boehringer to swap animal, consumer health assets

Sanofi and Boehringer Ingelheim have signed contracts to exchange their respective animal health and consumer healthcare businesses. Sanofi's Merial business, which is valued at approximately 11.4 billion Euros, will be transferred to Boehringer in return for 4.7 billion Euros and Boehringer's CHC business, which is worth around 6.7 billion Euros. Sanofi expects the transaction to be accretive after 2017, and forecasts joint CHC sales to be around 4.9 billion Euros. Boehringer believes that by combining its portfolios and technology platforms in anti-parasitics, vaccines and pharmaceutical specialties with Merial's, it will be able to boost its competitiveness and increase its health sales by more than two times, to bring in revenue of around 3.8 billion Euros.

http://www.pharmatimes.com/news/sanofi,_boehringer_to_swap_animal,_consumer_health_assets_1049222

11. Takeda to Invest $65M in Ultragenyx under Rare Disease Drug Collaboration

Takeda Pharmaceutical has agreed to purchase $25 million of stock from Ultragenyx Pharmaceutical along with a $15 million cash premium at closing and with a 12 month period in between, purchase another $25 million with no additional premium. As part of the strategic partnership between the two companies, Ultragenyx will license and co-develop at least one and up to six Takeda product candidates for rare diseases over a 5 year research collaboration period. Takeda will receive an exclusive option to commercialize any licensed products developed through the collaboration in Asia and an option to license one Ultragenyx pipeline treatment in Japan. This collaboration provides Ultragenyx with a continued source of product candidates and Takeda access to strong patient-centric development and regulatory capabilities in the field of rare disease; Takeda's therapeutic areas consist of "general medicine," including oncology, cardiovascular and metabolic, central nervous system, gastrointestinal, respiratory, immunology, and vaccines. Recently, the company has been actively pursuing development for rare disease drugs, with its partnership with BioXcel and collaboration with Kyoto University's Center for iPS Cell Research Application last year.

http://www.genengnews.com/gen-news-highlights/takeda-to-invest-65m-in-ultragenyx-under-rare-disease-drug-collaboration/81252798/

12. Korean biopharma firms rush into IPO market this year

The largest number of stock market debuts by Korean pharmaceutical companies is expected this year. The Korean pharmaceutical industry is expected to continue steady growth as companies search for funds for global market expansion. Amid growing market expectations, Green Cross LabCell and ST Pharm got the green light for new listings on the tech-heavy KOSDAQ bourse Thursday. The two firms are part of a long list of bio companies jumping into the initial public offerings market; in the first half of 2016, five companies went public, raising a combined $216 million through IPOs. In the second half of the year, heavy lifters like Samsung BioLogics, Celltrion Healthcare, and CJ Healthcare have indicated that they will be listing as well. Samsung BioLogics, in particular, is expected to be one of the biggest IPOs this year, with industry analysts estimating about 3 trillion won worth of shares in the IPO. The rush to raise funds for R&D and production capacity increases by biopharmaceutical companies in Korea represents the hopeful mood in the industry.

http://www.koreaherald.com/view.php?ud=20160622001020

13. Global cancer drug spending to exceed $150 billion by 2020: IMS report

In a global oncology report released by IMS Health Holdings Worldwide, worldwide spending on cancer medicines is expected to exceed $150 billion by 2020. This forecast represents an annual global growth rate for oncology drug spending of 7.5 percent to 10.5 percent through 2020, up from last year's prediction of 6 percent to 8 percent growth through 2018. Taking into account prescription medicine list prices and supportive care drugs to address side effects, IMS found that global oncology drug spending reached $107 billion in 2015, an 11.5 percent increase over the prior year and up from $90 billion in 2011. As cancer is being redefined as a large number of narrowly defined diseases, many expensive new therapies designed to improve patient immune systems have emerged in the past five years, which is believed to be the cause of the dramatic spending increases.

http://www.reuters.com/article/us-health-cancer-spending-idUSKCN0YO0BQ

14. Medtronic to buy HeartWare for $1.1 billion

Medtronic PLC has agreed to acquire HeartWare International Inc. at a premium for $1.1 billion. The acquisition gives Medtronic more diagnostic tools and treatments for heart failure. Over the past year, HeartWare's stock has fallen 60% amid declining sales, problems with product studies and a terminated acquisition. The company creates ventricular assist devices (VAD) and serves a global VAD market of about $800 million, which is expected to grow by a percentage in the mid-to-high single digits this year and accelerate to a percentage in the high-single, low-double digits in future years. The deal is expected to close by late October and add to Medtronic's earnings in its third year.

http://www.wsj.com/articles/medtronic-to-buy-heartware-for-1-1-billion-1467029614

15. EU wants more transparency on AbbVie's Humira, world's top drug

The European Union's ombudsman Emily O'Reilly recently announced that four specific data redactions regarding clinical trial details of AbbVie's rheumatoid arthritis drug Humira, the world's top-selling prescription medicine, are unjustified. These data redactions were part of a 2014 deal between AbbVie and the European Medicines Agency (EMA), when AbbVie dropped a lawsuit against the EMA after the agency agreed to certain data redactions on the grounds of commercial interest. Since 2010, the EMA has pushed for increased transparency, an initiative that has remained ineffective after the 2014 case. In response to O'Reilly's statements, the EMA said it was pleased O'Reilly had found no maladministration in its handling of the matter, adding there was no agreed definition of commercially confidential data and that specific commercial interests change over time. AbbVie, while mentioning its commitment to responsible transparency, defended its previous actions, stating that there is a need to protect commercially confidential information. In recent years, drug companies around the world have come under increasing pressure to provide full disclosure of clinical trial results, following complaints by doctors and campaigners who believe access to such data is essential for consumers and medical experts.

http://www.reuters.com/article/us-pharmaceuticals-europe-abbvie-idUSKCN0YW1D6

IT WAS HARD TO TELL THE McCARTHY TWINS APART. THEY EVEN HAD THE SAME CANCER.

Fortunately, they also had the same hospital: the University of Chicago Medicine. Kelly McCarthy was eight months pregnant when she was diagnosed with stage IIB breast cancer. After her son was born, she underwent chemotherapy, radiation, and surgery to remove her right breast. Just four months later, her identical twin Kristen was diagnosed with stage 0 breast cancer, requiring a double mastectomy followed by reconstructive surgery. Later, when Kelly underwent a second mastectomy and also required reconstruction, **Dr. David Song** transplanted some of Kristen's skin and tissue to create one of Kelly's new breasts. Which is why these twins will tell you the same thing: There's no other medical center like the University of Chicago Medicine. For more information, contact James Bae, Regional Manager of International Programs at youngjoo.bae@uchospitals.edu or call +1-224-315-3948.

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