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WKMJ

Cover Story

INSPIRATIONAL KOREAN HEALTHCARE LEADER

"Congressman Chung Ui-Hwa's Journey from Medicine to the National Assembly"

Entrepreneur Interview

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WKMO Report

The 3rd WKMO Annual Conference in NYC

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WKMJ
WORLD KOREAN MEDICAL JOURNAL

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FROM THE PUBLISHER

Welcome to the third issue of our magazine.

In this issue, we feature the World Korean Medical Organization (WKMO) convention held on July 3-5 at Le Parker Meridien Hotel in New York City, where there was a true atmosphere for wholesome networking in which we were able to connect face-to-face. Dr. Kwang Tae Kim, President of International Hospital Federation, gave an inspiring keynote speech. WKMO also recognized Drs. Han Kwang Yang, Kyoung Ryul Lee, Kee Park, Hyung Kwon Kim and Yoon Kyo An for their achievements and contributions.

The students of World Korean Medical Student Organization participated by presenting their first research abstract poster and essay book publication 'An Open Discourse in Global Patient Care'. This book explores the role of cultural and ethnic diversity, and how these elements affect patient care. I welcome all the readers to this wonderful opportunity to listen to our new generation of global minded doctors.

This issue also features interviews with two prominent leaders in the field of healthcare: Physician- politician Dr. Ui Hwa Chung and physician–entrepreneur Dr. Kyoung Ryul Lee. The interviews give insights into these two respected doctors and the career choices they made after becoming successful academic physicians. Dr. Chung states "doctors not only cure patients but also have obligation to know the pathology and treat human and social society" and seek support from WKMO for all the efforts towards the unification of South and North Korea. Dr. Lee, a renowned international expert in the field of preventive medicine, who heads the Seoul based Hanaro Medical Foundation and SCL Health Care, Inc. leads an innovative life to improve global health.

This issue has few more excellent articles. One of them, found under the section of Special Reports, is an informative article by Dr. Joe McMenamin on anti-kickback statute entitled "Laboratory Payments to Referring Physicians".

WKMJ continues to promote a dialogue to bring positive impact for the advancement of medicine and healthcare. Kudos to all of us for building an inquisitive, compassionate, and global medical community!

Chul S. Hyun, MD, PhD
Publisher
President of WKMO

FROM THE EDITOR IN CHIEF

Dear Colleagues,

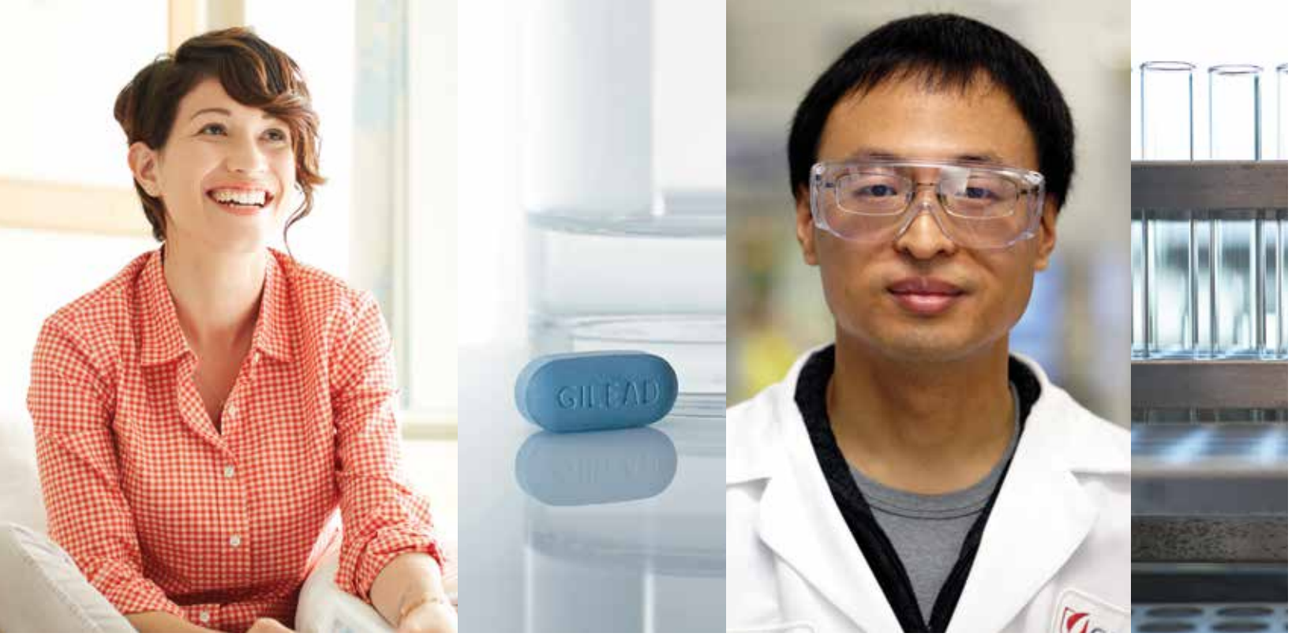
It was good to see many of you at the 3rd WKMO Convention in New York. The forums were excellent with top speakers addressing many ethnic, regional, global issues. The medical student posters and essays demonstrated the talent of the next generation of Korean heritage physicians. There were many guests and dignitaries including UN representative from N. Korea as well as S. Korea, which is symbolic of possible improved relations.

In this issue we feature Dr. Ui-Hwa Chung who was a Keynote speaker at the WKMO/KAMA Annual meeting in Las Vegas along with US Congressmen Mike Honda. The Honorable Mike Honda prophetically said Dr. Chung would be Speaker and this became reality. Dr. Chung is an accomplished Neurosurgeon but entered politics and has been successful there as well serving 5 terms in National Assembly where he was Vice Speaker and now is Speaker. Healthcare in every country is a complex issue undergoing tremendous change and to have a physician leader in government is an exceptional opportunity. Dr Chung is not only addressing issues in S. Korea but has an agenda to improve healthcare in N. Korea which he presented in the WKMO/KAMA meeting of 30 hospitals with 30 beds.

The entrepreneur physician featured is Kyoung-Ryu Lee, MD PhD who has had multiple successful medical roles. He is an academic physician as Adjunct Professor of Laboratoy Medicine at Yonsei University and Deputy of Clinical Laboratory Management of Korea. Dr. Lee is Chairman of Hanaro Medical Foundation emphasizing preventive medicine and has developed comprehensive medical clinics which are cost and time efficient incorporating the latest technologies. He has a global vision and opened a clinic in Mongolia and China. Dr. Lee has been a founding leader of WKMO and has been very active Board Member and Executive Vice President ensuring the success of WKMO.

The WKMO meeting was exciting, expanding horizons with incredible networking opportunities. Next years regional WKMO meeting in March will be in London and the 4th WKMO Convention will be in Korea in July so hope to see you there. I was privileged to serve as KAMA President in its 40th Anniversary year which is a time of reflection and look forward to what KAMA and WKMO will do in 40 years.

David Y. Ko, MD
Editor in Chief
Board Director of WKMO
President of KAMA



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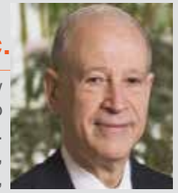
WKMJ RECAP OF MAY ISSUE

Cover Story
A Public Health Advocate for the Poor: Dr. Jong-wok Lee (1945-2006), WHO Director-General

Believing that the nation's poverty level was responsible for high disease risks, Dr. Jong-wook Lee, former WHO Director-general, dedicated his life to helping the poorest, most marginalized countries. He spent his life traveling around the world leading multiple efforts to cure diseases. His programs, such as the "3 by 5" program to treat AIDS, are testaments to his commitment and vision. Taking on challenges bravely and willing to take responsibility for failure, Dr. Lee became a role model to many. Dr. JimYong Kim, the current president of World Bank Group, said that Dr. Lee's leadership "fundamentally changed people's attitude to the possibility of treatment for a chronic disease." Even after his death, Dr. Lee's vision survives through his wife and son, as they continue to carry out his mission.

Entrepreneur Interview
Dr. Phillip Frost, CEO and Chairman, OPKO Health Inc.



Dr. Philip Frost discusses some strategies OPKO uses to efficiently expand and grow with the changes of healthcare. Frost emphasizes the importance of the relationship between physicians and patients, as this is crucial in an era of economic pressure. OPKO makes efforts every day to find new ways to engage with patients. Additionally, Frost highlights the importance of being entrepreneurial and willing to embrace change, especially in the healthcare arena.

Special Report I
"The Biotechnology Industry in Korea: Ripe for Investment"

Korean pharmaceutical and biotechnology sectors have seen some promising developments that are becoming increasingly investable. Specifically, immuno-oncology and stem cell therapies have been developing with many of them nearing approval. Developments like these are examples of significant opportunities for investors to capitalize on the enormous potential within Korea's pharmaceutical and biotechnology sectors.

Special Report II
"Tracking the Affordable Care"

In order to track the Affordable Care Act, it is necessary to address the cost issues, impact on both physicians and patients, and the challenges ahead. One of the challenges the ACA faces is the greater financial responsibility on the consumer. This report covers the issues related to the ACA's impact on both health care infrastructure and physician shortage. Currently, the ACA's effectiveness remains a question as evidence of its progress is yet to be determined

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WKMO 3rd Annual Convention

On July 3-5, World Korean Medical Organization (WKMO) hosted its 3rd Annual Convention at Le Parker Meridien hotel in New York City. This convention provided an opportunity for all healthcare professionals to interact and create global leadership. The convention focused on the theme of "Cultural Competence in Healthcare" and featured various programs focusing on issues of ethnic disparity and medical and surgical symposia. All of the programs during the convention allowed for greater discussion and exchange of ideas. Ultimately, this convention aimed to enforce the solidarity among Korean health care professionals in order to globalize and advance connections in healthcare.

There were over 250 participants including students, physicians, non-physicians, industry experts and community leaders. Participants came from over 12 different countries including Brazil, China, Paraguay, Korea, New Zealand, and the UK.

Registration on July 3rd

Korean Drum (Buk) Performance

The registration session on July 3rd marked the start of the 3rd WKMO Annual Convention. During registration, all participants came to check in and receive their name-tags, programs, and other items in preparation for the convention.

Later that night, the opening reception took place at the Penthouse of Le Parker Meridien. The opening reception was a great time of networking and socializing for all participants. Opening statements were made by Chul S. Hyun, President of WKMO, and Hyung Kwon Kim, WKMO Convention Chair, after the Korean Drum Performance. Next, congratulatory remarks were made by Woo-Kyung Kim, President of Korea University Medical Center, Richard Rhee, Professor at Rutgers University, and Augustine Choi, Sanford I. Weill Chairman and Professor of Medicine. Overall, the opening reception was a fruitful event and generated a positive synergy that lasted throughout the convention.

There was a total of 10 forum sessions including all lunch sessions and other student forums, with a total of 41 speakers. The forum sessions began on the morning of Friday, July 4 with Session A focusing on Stomach Cancer: Epidemiology and Treatments. Speakers were Han-Kwang Yang, MD, Ph.D., FACS, Professor and Chief of Gastrointestinal Surgery in the Department of Surgery & Cancer Research Institute at Seoul National University College of Medicine, Andre Lee, MD, Ph.D., Assistant Professor and attending physician in the Department of Liver Transplantation and Surgery at Hospital Das Clinicas University of Dao Paulo Medical School, Yoonmi Lee, MD, Ph.D., Instructor at Columbia University Medical Center, Woo Jin Hyung, MD, Ph.D., Professor in Department of Surgery at Yonsei University and Yanghee Woo, MD, Assistant Professor of Surgery at Columbia University Medical Center.

Left to right: Drs. Hyunick Kim, Hyeyeon Kang, Sanghoo Kim, Hyunmi Park, Joonsoo Ha

The following lunch session was titled 'W Medical Strategy Dialogs.' In this session, a number of industry and academic leaders were present. Introduction of current status of bio-medical R&D in Korea and Health Science Programs of University of Tennessee were the major topics of presentations. Further discussions of various potential collaboration opportunities with both Korea and US were followed. Speakers were Kyung Sun, Director of Korea Artificial Organ

Dr. Han-Kwang Yang giving his talk on "The International Disparities of Gastric Cancer Patient Outcomes Compared to Korea."

WKMO Report

Group picture after Session A

Dr. Kennard D. Brown speaking at the W Medical Strategy Dialogs Session about "Health Science Strength in University of Tennessee."

Center, President of Korean Society of Medical and Biologic Engineering, and a chair of Board for the Korean Society for Thoracic and Cardiovascular Surgery, and Kennard D. Brown, Executive Vice Chancellor and Chief Operations Officer at the University of Tennessee Health Science Center.

The day continued with Session B, focusing on Mental Health Issues of Korean Americans. Speakers were Su Yeon Lee, Ph.D., Associate at Department of Mental Health at Johns Hopkins Bloomberg School of Public Health, Hochang Benjamin Lee, MD, Associate Professor and Director of Psychological Medicine Service at Yale University, Wunjung Kim, MD, MPH, Professor and Director of Child and Adolescent Psychiatry in the Department of Psychiatry at Rutgers University, David Ko, MD, President of Korean American Medical Association (KAMA) and Associate Professor of Neurology at USC, and Tai P. Yoo, MD, MBA, DLFAPA, Professor, Chairman, and Director of Psychiatry at the UCLA Kern Medical Center. Many of the speakers spoke about how mental illness is looked down upon in Korea and how Korean American patients are therefore unwilling to see a doctor about their problems.

Dr. Tai P. Yoo speaking on the "History, Culture and Mental Health Issues of Korean Americans."

"Father of Telemedicine" Dr. Jay Sanders, speaking about "The Potential of Telemedicine: Increased access to care."

The last session of the day, Session C, focused on Telemedicine: Opportunities, Challenges, and Practical Application in Europe and US. Telemedicine is the use of telecommunication and technology to provide clinical healthcare at a distance. Speakers were Jay H. Sanders, MD, FACP, FACAAI, CEO of The Global Telemedicine Group and Professor of Medicine (Adjunct) at Johns Hopkins School of Medicine, Joe McMenamin, MD, JD, Chief Legal Officer of W Medical Strategy Group, Laura Ryan, MD, Associate Medical Director with NHS24, Scotland's National Telehealth and Telecare Organization, and Mark Paxton, JD, an Executive Vice President of W Medical Strategy Group.

Dr. Augustine Choi giving his Keynote speech at the WKMSO Gala.

The day ended with the WKMSO (World Korean Medical Student Organization) Gala, held at the Penthouse of Le Parker Meridien. Keynote speeches were given by Augustine Choi, Sanford I. Weill Chairman and Professor of Medicine, and Kyung Sun, Professor at Korea University Medical School.
The morning of July 5th started with productive activity, Run for One Korea. 40 participants took part in this 2- mile run through Central Park designed to invite medial representatives from South Korea to promote unification in medicine.

Run for One Korea taking place at Central Park on Saturday morning, July 5th

Run for One Korea

The forums sessions for the day began with Session D which focused on Models to Improve Cultural Competence in Healthcare. Speakers were Samuel Noh, Ph.D., Professor of Psychiatry at the University of Toronto, Kyung Hee Choi, Vice President of the Korean Medical Program of Holy Name Medical Center, Paul Mustacchia, MD, FACP, MBA, Chief Physician and Gastroenterology Fellowship Program Director at Nassau University Medical Center, Helaine B. Ledany, MPA, CNHA, FACHCA, Administrator of Buckingham at Norwood, and Dongsoo Kim, Ph.D., Clinical Director of the Clinical Psychology Externship Program at Korean Medical Program of Holy Name Medical Center.

Following Session D was the WKMSO Research Poster Presentation. This was the 1st Annual WKMSO Medical Student Research Symposium. Through this opportunity, students could showcase their research to other students and physicians. The research posters covered a variety of topics, many including patient-related clinical data and experiences. There were 12 students who presented, and their research posters were displayed throughout the forum rooms.

Kyunghee Choi, Vice President of the Korean Medical Program of Holy Name Medical Center speaking on "Health Care Access Model: Delivering Culturally Competent and economically viable medical services to Korean American population."

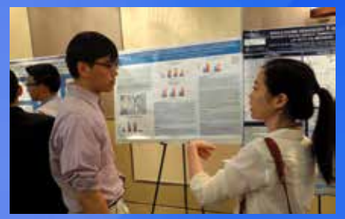
Dongsoo Kim giving his talk on "Cultural Competence and Psychological Implications: A Theoretical Framework"

After the Research Poster Presentation was Lunch Session 2. The speaker for this session was Robert S. Brown, Jr., MD, MPH, who is affiliated with New York-Presbyterian/Weill Cornell and New York-Presbyterian/Columbia. The topic of his talk was Hepatitis C: Transforming The Treatment Paradigm.

The next session, Session E, focused on the Future of Medical Imaging. This session was sponsored by Samsung. Speakers were Jinha Park, MD, Ph.D., Director of MRI and Radiology Research at the City of Hope Medical Center and Beckman Research Institute, John Park, MD, Ph.D., Chief of the Division of Interventional Radiology at the City of Hope Medical Center, Dong Jun Lim, MD, Ph.D., Assistant and Associate Professor in Department of Internal Medicine, Division of Endocrinology & Metabolism at Seoul St. Mary's Hospital, Tae Kyoung Kim, MD, Ph.D., FRCPC, Radiologist and Professor at University of Toronto, Sang Choon Cha, MD, Ph.D., President of Brazilian Society of Fetal Medicine, and Kyongtae Ty Bae, MD, Ph.D., Chairman and Professor of the Department of Radiology at the University of Pittsburgh.

The last session, Session F, focused on Hepatitis B: Epidemiology and Treatments in Asian Population. Speakers were Chul S. Hyun, MD, Ph.D., attending gastroenterologist at New York Presbyterian Hospital and current President of World Korean Medical Organization, W. Ray Kim, MD, current treasurer of American Association for the Study of Liver Diseases, Chair of the Development Committee, and Chief of the Division of Gastroenterology and Hepatology at Stanford University and Joseph Ahn, MD, MS, FACG, AGAF, attending physician, director of Clinical Hepatology, and Associate Professor of Medicine in

Left to right: Dr. Tai P. Yoo, Dr. Kwang Tae Kim, Hon. Se-joo Son and his spouse.



WKMSO Medical Student Research Symposium

Dr. Robert S. Brown giving his talk on Hepatitis C

Dr. Dong Jun Lim speaking on "Ultrasound Elastrography In Predicting Malignant Thyroid Nodule."

Dr. Ray Kim giving his talk on "Screening and management of Advanced Liver Disease."

the Division of Gastroenterology and Hepatology at Oregon Health & Science University. The entire convention concluded with the WKMO Gala, held at the Penthouse of Le Parker Meridien. The gala opened with a wonderful performance by Soprano Haeran Hong. After opening statements by Hyung Kwon Kim, 2014 WKMO Convention Chair, congratulatory remarks were made by David Ko, current KAMA President, Hon. Se-joo Son, Korean Consulate, Young ho Lee, Embassy of the Republic of Korea, Hon. Grace Meng, Member of US Congress, and Woo Kyung Kim, President of Korea University Hospital. Congratulatory remarks were followed by dinner. A welcoming address by Chul S. Hyun, MD, Ph.D., President of WKMO was also made.

Next, Kwang Tae Kim, MD, Ph.D., President of International Hospital Federation, gave his keynote speech. Then, WKMO recognized five individuals during the Award Ceremony. The first award, Achievement Award, went to Han-Kwang Yang, MD, Ph.D., FACS, for his outstanding contribution to the development of academic and clinical medicine. The second award, Global Health & Medical Diplomacy Award, went to Kee Park, MD, to recognize his achievement, performance, and contribution to the advancement of human and diplomatic value of healthcare throughout the world.

1. WKMO Gala on the Penthouse of Le Parker Meridien, July 5th
2. Hon. Grace Meng giving congratulatory remarks.
3. Dr. Chul Hyun, President of WKMO, at the Gala on July 5th.
4. Dr. Kwang Tae Kim giving his keynote speech.

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The second award, Young Leader Award, went to Yoon-Kyo An for her constant encouragement and fostering of the young generation of medical students and physicians around the world. The fourth and fifth awards, Awards of Appreciation, went to Kyoung-Ryul Lee, MD, Ph.D., and Hyung-Kwon Kim, MD, for their generous and unique contributions to the promotion and advancement of World Korean Medical Organization and its vision.

Left to right: Drs. Chul S. Hyun, Han Kwang Yang, Hyung Kwon Kim, Kyoung Ryul Lee

Overall, the 3rd Annual WKMO Convention was a huge accomplishment. The convention truly succeeded in bringing together an international congregation of healthcare professionals, ensuring a promising future for WKMO.

All forums and galas were highly attended and provided opportunities for participants from different arenas of healthcare to interact, as the forums covered a wide range of topics from Hepatitis C to Telemedicine. The speakers gave intellectually stimulating talks, and the participants were fully engaged. The other programs included in the convention were successful as well. Specifically, the Mentor-Mentee Program gave the students a chance to meet physicians in their respective fields, explore career opportunities, and gain mentors as they look ahead to their futures.

Dr. Chul S. Hyun speaking at the Gala on July 5th.

Dr. Kyoung Ryul Lee accepting his award.

In conclusion, the convention served as an excellent platform for all healthcare professionals. Participants from all sectors of global health were convened to innovate and develop strategies for the rapidly changing healthcare delivery system. The convention gave ample opportunity for all participants to network and build long lasting relationships, all of which are essential to the future of WKMO and global healthcare.

Dr. Woo Kyung Kim, President of Korea University Hospital, making congratulatory remarks during the Gala on July 5th.

Sangji Lee
Associate Director
World Korean Medical Organization

Sarah Hyun
Assistant Editor
World Korean Medical Organization

INSPIRATIONAL KOREAN HEALTHCARE LEADER

"Congressman Chung Ui-Hwa's Journey from Medicine to the National Assembly"

COVER STORY

1. What was your major reason for attending medical school? Why did you want to become a physician? While practicing as a physician, what have been some of the difficulties and memorable moments?

- As a child, I always dreamed of becoming a diplomat or judge. I initially wanted to study political science and law in college. However, because my brother was attending a medical school, my father wanted me to follow his footsteps and pursue a degree in a medical field as well. I accepted his advice and decided to pursue a medical career.

- Although I entered the medical profession and became a physician as my father had wished for, I actually believe that I am a politician now because of my decision to follow his advice. In that way, my father has shaped my life in a profound way and continues to inspire me. I am grateful for his influence and guidance.

- After entering a medical school, I thought I'd like to pursue my dream as Albert Schweitzer had done by helping those in need and making a difference in the lives of others. I strived to learn as much as I could and concentrated on my studies in order to become a respected physician. I was also actively involved in many school activities, including writing as a reporter for my university's medical science newspaper. Applying the Hippocratic Oath to medicine, I try to remind of myself the original intention to heal with a conscience and keep the dignity of patient's life and health first.

- I specialize in neurosurgery, especially cerebrovascular surgery. I used a surgical knife many times a day when I was practicing, and there were many days when I had to be on my feet for nearly 24 hours to operate on patients. Since my residency, I have performed brain and spinal cord surgeries for more than 5,000 patients over 30 years. At that moment, the workload was sometimes difficult and challenging. However, I have learned that what I could provide through my work to save lives was well worth all the long hours and hard times making life and death decisions. From my experiences as a physician, I have learned much and gained strong willpower, wisdom and calm judgment. These features have helped me overcome crises in my political life later on.
Some of the most diffic ult moments I had encountered were operating hospital under-budget due to low cost medical treatments and dealing with possible medical accidents.

- During my 30 years of practice, I looked after needy patients as my first priority. In my heart, the needy were like Jesus; the hospital represented the church, and I was the priest wearing the white gown with a power to heal and stop suffering. I always believed with all my heart that it would be honorable to spend my whole life at a hospital providing medical care to patient. That is how much I valued and was satisfied with my life, and being a physician made each day worthwhile.

2. You are a physician-turned-politician. What were your motivations to get involved in politics as a member of the National Assembly? Also, in politics, are there pros and cons to being a physician?

- Simply, I think I was destined to become a politician. Before the 15th general election in 1996, Former President Kim Young Sam started the nomination revolution in the New Korea Party, and I was engaged as a health care expert. That was how I first started my political career.

- At that time, I was a neurosurgeon, well known as a leading microvascular specialist. I succeeded in expanding the Bong Sang Neurosurgery to a larger-scale general hospital. Then I became a successful physician and CEO who created thousands of jobs based on my management principle, "profits made from patients will be used for patients." I was involved in welfare reform and various cultural businesses, which made me realize that being a politician might be truly my destiny.

- Seeing political corruptions everywhere for too long in a way pushed me toward politics. My determination to heal and make the society healthier led me to serve as a physician. I wanted to become the best physician in Busan by raising the quality of medical and healthcare services in the region. I have always believed that medicine must be a benevolent art. I also believe that the ethics of humanism should resonate strongly for both physicians and politicians.

-One of the most significant advantages of being a physician-politician is my understanding of human lives as I have learned from experiences as a medical doctor. Furthermore, the knowledge I have of human lives at core has helped facilitating my genuine respect for diversity and attention towards social minorities. I was ready and eager to serve the society.
- I strictly follow meticulous professionalism that does not allow mistakes when it comes to handling the lives of people. The way I examine every aspect of each diagnosis and medical situation in order to perform a successful surgery has certainly helped me deal with legislation and policy decisions through a more comprehensive and macroscopic approach.

- Unfortunately though, there's often prejudice against politicians with non-political backgrounds, such as physicians. To overcome this prejudice, I expanded my area of specialization by actively participating in a lot of committee, including Finance and Economic Committee, Foreign Affairs, Trade and Unification Committee. I constantly keep active and try to achieve balance and harmony in the way I engage issues, domestic or international. I am much concerned with the fair and just dealings between the eastern and western countries, and the reunification of the North and South Koreas.

3. Since 1996, you have been actively involved in politics as an influential Congresswoman. Especially, you were recently appointed as the Chairwoman of the National Assembly. As one of Korea's most powerful leaders, what political philosophy do you have?

- If I were to sum up my political philosophy into four different parts: 1) balanced development of the domestic regions, 2) harmony of the East and West, 3) development of the healthy society for society of trust, 4) the unification of the North and South Koreas

- Currently, Korea is divided into the North and South. Within the South Korea, there is an invisible yet pronounced regional boundary that has been drawn between the Eastern and Western regions due to intense political polarization and regional rivalry.

- I don't see our nation's future possible with the divided Korean Peninsula nor a huge socioeconomic gap between the capital and noncapital regions. The conflicts of the Eastern and Western areas have risen to surface while the enormous gap between the capital and noncapital regions has been ignored among us.

- To correct this imbalance, harmony between these regions must be made. I guarantee that the Republic of Korea will grow exponentially with balanced and strategic development of the national land.

- Korea should seek unification for its long term growth, while pursuing the harmonious and balanced relationship building between the Eastern and Western areas. One of my career goals is to help the nation overcome this challenge.

- My ultimate task as a politician is to create a 'healthy society for Korea' where law and justice are respected and alive, and everyone is given fair and just consideration and has trust for one another. Honesty to me is always transparent.

- It has been 18 years since I began my political career to cure our societal ills similarly to how a physician cures a patient's disease. I have also been actively pursuing and supporting our nation's aim for Korea's eventual unification and overall health of our society.

- Haeng-baek-ri-ja-ban-gu-sib (行百里者半九十), 'it's still half way even though one has made 90 miles out of a 100-mile journey." Meaning, one may still fail the journey if one doesn't persist to the last.
As this proverb reminds the last part of an endeavor being the hardest to finish, I will meditate my original motivation of becoming a politician and dedicate my best efforts to make 'healthy society for Korea' for every Korean.

4. Currently, many Korean doctors are demonstrating their knowledge and skills around the world in medical industry. Do you have anything to say to those who dream of becoming a doctor one day and also to those who are currently medical students?

- Even though it is a tough life living away from home country, I would like to thank all Korean doctors for their dedication and contribution to humanity. Your practice has improved the status of our country and I give my heart of respect and gratitude to you all over the world.

- From a medical book that is known to be a bible to surgeons, it says that a good doctor is not who succeeds every surgery. Good doctor means a warm-hearted individual who really cares about the patient. Being a doctor is not always about good techniques and astonishing skills, it is always patient-first mind.

- As it is said in the book to become a patient-first minded doctor, here I include a 'preparation' step to make a perfect doctor. With the preparation step, the doctor can prepare for any outbreak incidents that occur during operation which will lead to success of surgery and patients can fully regain their health.

- I would like to tell all of you prospective doctors to set clear goals and a topic for your life to go beyond the scope and limits of medical career. Keep in mind to challenge and experience constantly to make this happen.

- You will find yourself growing up step by step when you put the patient-first mind in the bottom and stack with knowledge, skills, preparation, and constant effort to go beyond the limit.

5. WKMO is an organization of global Korean doctors who have the Korean pride, knowledge and skills to enhance the health-care sector for South Korea. What would be your expectations to our organization if any? As we prepare the 'World Korean Doctors' Week,' an international medical convention in Seoul in July 2015, what do you hope to see as an outcome of this event?

- Korea has come a long way since the colonial era and is still divided into the South and North Koreas. Our nation has overcome wars and poverty to stand now just outside the top 10 in as one of the most prosperous and powerful economies around the world. Korea is the one and only nation in history that has become a donor to help other underdeveloped nations from once being a beneficiary of the international aid.

- This has been possible in part because of our fellow Korean physicians and medical researchers around the world who have helped raise the status of Korea through their dedication and effort beyond the Korean community. These efforts have had a tremendous impact on increasing the Korean medical industry's competitiveness leading Korea to prominence in the global medical environment.

- I am convinced that Korea's medical innovation and leadership today is due to every hard-working medical personnel's commitment to the Hippocratic oath and Korean's unique national characteristics of enthusiasm and dedicated workmanship.

- Physicians have the obligations to not only cure patients' diseases but also to know the pathology and treat humans to function well in a larger society. Korea is currently suffering from a chronic illness of so called a 'divided nation' syndrome. It is time for WKMO to step up and help us treat and cure this disease.

- This should be our people's mission. I ask for all of the WKMO members to support this cause to unite Korea. We need to pay more attention to the potentials which can facilitate Korea's unification. For instance, we can improve the relationship with North by developing collaborative healthcare activities within the private sector.

- As I am looking forward to meeting everyone at the 2015 World Korean Doctors' Week, my hope is to find an opportunity there to discuss and mobilize global Korean physicians on providing medical assistance to North Koreans and figure out realistic cooperation and support plans for North Korea's underdeveloped health care facilities. With this in mind, this convention will become the cornerstone for the growth of inter-Korean reconciliation and cooperation.

- Also, I see the convention as an outlet to promote thought leadership on Korea's unification worldwide and convey our effort to avoid conflict and enhance mutual understanding for our nation's better future.

6. Could you share your future vision for the Republic of Korea with our readers from more than 10 countries around the world?

- I am the 19th Chairman of the National Assembly in Republic of Korea, serving now close to 100 days for the second half in that capacity since being appointed. During this time period, I have worked hard to restore our people's trust through progressive parliamentary reform and to improve the relationship between the South and North Koreas and the regional security and unity.

- Although my appointment is relatively recent, I am committed to keep the promises I have made to my people and the nation. I would be thrilled to get to know all of your readers and earn their support and trust through their encouragement and advice.
Without a doubt, my future vision for Korea is to see it becoming a united nation at peace with its neighbors and in strong partnerships with its allies for making the world a better place. Overcoming the regional conflict in Northeast Asia and taking bold yet careful steps toward unifying the South and North Koreas remain the top priority, which I consider as one of the most important and urgent task we have .

- I firmly believe that the unified Korea will become an open and peace-loving, non-nuclear nation, contributing to the peace and harmony of the mankind.

- I would like to ask all of your readers to keep an eye on the Republic of Korea and its hopes and dreams, and the future transformation.

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Entrepreneur Interview

Dr. Kyoung-Ryul Lee, Hanaro Medical Foundation

1. What was your motivation for attending a medical school? Why did you decide to become a physician? What are particularly difficult or memorable incidents you recall in your career as a physician?

When I encountered people with leprosy or disabilities as a child, I felt more sadness than fear. I had this vague thought that I would someday like to help heal those suffering from illnesses and isolation from society. During my teen years in high school, I was stronger in math and sciences fields, which led me to medical school.

Looking back, every single moment of my academic career has helped me to become a better health management professional through meaningful challenges, including studying laboratory medicine, preventive medicine and biotechnology in medical school. These experiences built a strong foundation for me as a consummate physician seeking new medical technologies and ways to treat patients effectively.

The difficulties I had encountered as a physician included a low level of accessibility to preventive medical technology and the underdeveloped environment only consist of evidence-based medical treatment system. What I realized then was the importance of early detection and diagnosis before people became seriously ill. Ensuring the health of an individual through medical prophylaxis before one becomes a patient is as critical, if not more than saving one's life. Indeed, a noble mission of medical professionals lies in ceaseless research and exploration dedicated not only for curing sickness, but also maintaining and promoting health of a population.

2. You've had a significant role in developing and expanding one of the Korea's most renowned medical examination centers and establishing a developer for diagnostic reagents and testing laboratories. As a visionary in the global medical field, you have successfully built and managed a Korean-style comprehensive medical examination center in Hangzhou, China and a medical center in Mongolia. What are your business philosophies and strategies?

Korea is already a medically advanced nation of which medical technology and services are internationally recognized and revered. However, the reality for a patient in Korea is such that finding a trustworthy hospital for him or her to rely on among many seemingly capable physicians and hospitals is rather difficult. As a result, patients tend to engage in "medical shopping" and seek only large and well-branched hospitals. This has at times caused societal problems with increased medical cost and undermining balanced development of regions.

Due to this current medical reality in Korea, it is hard for physicians to realize their vocational mission and contribute to making a healthier and happier society. The basis of my business philosophy comes foremost from the love I have for my family and the society. As a health care professional, I work hard to seek new technological progress and to advance evidence-based preventive medicine.

Additionally, all of my education from middle school to university completed at mission schools naturally instilled in me a strong sense of faith and spirituality, sharing and responsibility for taking actions. This is much relevant to my business philosophy of serving and having consideration for others.

Seoul Clinical Laboratories Health Care, Inc. celebrated its 30th anniversary last year, which meant a lot to me. Our new motto is 'health keeper of humanity through evidence-based medicine.' In the last 30 years, we have been recognized and trusted in the field of preventive medicine through evidence-based medicine. With that knowledge and trust, we will continue our effort in sharing our medical technology not only in Korea but also globally with countries, such as China, Mongolia, and CIS region.

3. You have made an impressive transition from an influential physician to a successful CEO. As a physician and a CEO, what are your future aspirations and plans?

The dual position I have is neither complicated nor simple when I consider my future plans and aspirations. It all begins at a common place of dealing with people; furthermore, managing life and death situations requires me as a CEO to seriously contemplate the sanctity of life and human diseases before profit and materialism. Hence, my employees and I are trying our best in order to serve and care for the human health and welfare.

Although it had taken 30 years to properly accept evidence-based medical assessment and preventive medicine in Korea's domestic diagnostic testing, its value in relevant medical fields was not fully recognized at the time. However, our hard work along with advancement in medical technology has enabled SCL Health Care Group to succeed. As we continue to contribute to the betterment of global health, it is my wish to see SCL thrive as one of the world's premier bio-medical institutions.

4. You were selected as one of the world's most influential 500 leaders by the renowned American Biographical Institute (ABI) in the United States because your achievements as a physician and a CEO were well recognized. What would be your advice to medical students and aspiring physicians?

I was much grateful and humbled to receive the award news from ABI in 2008, which was very meaningful to me as an individual and also physician. It was an assurance for the transition I made from a physician to a CEO in order to develop a medical system for diagnostic testing based on continuous diagnostic research on hepatocarcinogen I had worked on as a professor at Yonsei University.

There are important corporate responsibilities for our management charter. A corporation must be mindful of the needs of patients and their families, and also those of the medical and research team who will use our diagnostic test results. The goal of the corporation we lead should be to help process accurate and rapid testing for correct diagnosis that allows patients to receive effective treatment for fast recovery and health promotion.

Medicine is a profession that deals with human body, more critically of life and death. This requires a careful observation of patents' pain and respect for the sanctity of life. Physicians and medical professionals should never forget these principles.

5. You have contributed to WKMO, which you currently serve as Executive Vice President. What do you envision for WKMO and its roles?

I recently read a medical column which was about how Stanford Medical School teaches students from around the world to become outstanding medial leaders. The column discussed how Stanford provides high-quality early education systems for pre-med students and medical training programs that allow self-growth opportunities. I especially was envious of their simulation center, funded by donations, where students can actually experience clinical trials, patient surgery and emergency response based on scientific scenarios. It's not hard to imagine that Stanford Medical School's innovative programs reinforce early development of academic capabilities in students to become potentially prominent physicians.

Since its foundation, WKMO has become a central organization to help bring together Korean physicians from all around the world. One of WKMO's core functions has been to promote a mentoring program for Korean medical students so that they can become dedicated physicians who will contribute to their society. It has helped establish a solid basis among Korean health care professionals around the world to strengthen their Korean heritage and identity. I truly believe that through continuous progress, WKMO's systematic programs and projects will create brilliant global Korean physicians leading the way in eradicating diseases and maintaining health of people everywhere.

I hope to see WKMO bring more and more participants and generous support of the global medical communities through consistent development of WKMO's brand value.

6. Readers of the World Korean Medical Journal are leaders of health and medical care service industry in more than 10 different countries. As an entrepreneur and senior executive of WKMO, what would you like to share with us?

We first entered Mongolia in 2002, and 10 years later, Hanaro Medical Foundation has established and run successfully a Korean-style medical examination center in Hangzhou, Zhejjang Provice in Eastern China. The big plan now is to work with our local partners in China to set up similar health examination facilities in every province in China within 20 years.

30 years ago when the "Seoul Medical Science Institute" was founded, there was no substantive revenue-generating model for the institute given national income in Korea remained very low. The general public was not ready to spend expenses related to preventive medicine practice and examination services. Nonetheless, I am convinced that it was the right choice to make at the time. I feel a great sense of pride as a health service executive to see the medical world advancing toward more preventive medicine and care and being recognized for its benefits.

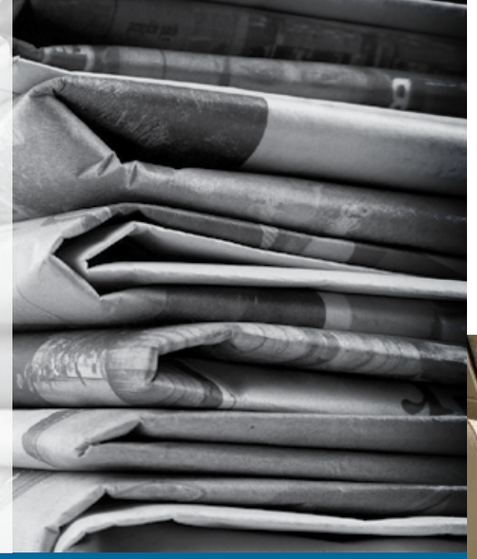
Korea's health medical examination model is very unique and superior system, which developed nations have not yet produced themselves. It is a future-oriented business that provides health care services to healthy people, not patients; it also encourages innovation and development of new subsidiaries in a wide range of areas, including pharmaceutical industry, nurturing medical and health care education, and other related products and systems. Therefore, I hope to further collaborate with WKMO to strengthen cooperation and penetrate the global market to share Korea's excellent health examination business and medical systems.

I would like to close by wishing all of WKMO members, Korean medical professionals around the world and their families much happiness and blessings. Thank you.

Dr. Kyoung-Ryul Lee, Chairman of Hanaro Medical Foundation

의료법인 하나로 의료재단
Hanaro Medical Foundation

In 1991, Dr. Lee graduated with his MA degree from Yonsei University Graduate School of Medicine. 6 years later in 1997, he successfully achieved his PhD from Yonsei University Graduate School of Medicine. Then, he worked as a Research Associate in the Scripps Research Institute, Department of Molecular & Experimental Medicine for two years. Dr. Lee became the Chairman of BioCore in 2002, adjunctive associate professor in Department of Laboratory Medicine, Yonsei University in 2003, branch president of Korea Federation of AIDS Prevention Seoul in 2005 and Committee Member of Drug Resource Center in 2006. Also, in 2008, he took several important steps in his career which include being inaugurated as the 2nd Chairman, becoming adjunct professor in Department of Laboratory Medicine, Yonsei University, and executive Director of Health and Welfare Division Yonsei University Alumni Association. Further, Dr. Lee worked as a Senior Vice-President of the Korean World Society and was awarded for "Underprivileged Welfare Achievement Award" from Mayor of Seoul, Korea. Currently, Dr. Lee is the Chairman of Hanaro Medical Foundation, the Vice President of Yonsei University of Medicine Alumni Association and the Deputy of Clinical Laboratory management Association of Korea since 2013, the year when he also received Appreciation Plaque from Global Health and Welfare.



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Special Report I

Laboratory Payments to Referring Physicians

According to its Web site, the mission of the HHS Office of Inspector General ("OIG") "is to protect the integrity…of HHS programs as well as the health and welfare of program beneficiaries." Among other functions, OIG periodically issues Special Fraud Alerts to address what it perceives as industry-wide practices of concern to it, including what it deems to be trends in health care fraud, and to provide guidance to health care professionals and institutions on violations of Federal law, including the anti-kickback statute ("AKS"). HHS, Publication of OIG Special Fraud Alerts, 59 FR 65372 (Dec. 19, 1994).

The AKS, 42 U.S.C. § 1320a-7b, is a criminal statute that prohibits the exchange of anything of value, or even an offer to do so, to induce (or reward) the referral of federal health care program business. AKS is an intent-based statute: it prohibits knowing and willful payments if even one of their purposes is to induce or reward referrals of Federal health care program business, even if the sum paid reflects fair market value for the service(s) rendered. Remuneration need not be in cash to qualify as unlawful remuneration under the AKS. An unlawful arrangement might include provision of free or below-market supplies, for example. OIG may infer intent from a number of factors, such as the legal structure of the arrangement, its operational safeguards, and the conduct of the parties. OIG has been aggressive in alleging AKS violations regarding agreements that in businesses other than healthcare would be commonplace and perfectly lawful.

It is important to understand that AKS ascribes criminal liability to parties on both sides of an impermissible "kickback" arrangement. One must also understand that a violation of AKS, a felony, can have serious consequences. Convictions are punishable by a maximum fine of $25,000, imprisonment up to 5 years, or both. In particularly serious cases, conviction can lead to exclusion from Federal health care programs, including Medicare and Medicaid. OIG can also impose civil money penalties. Hence, health care professionals and institutions need to be mindful of this law and of its teeth.

About two months ago, OIG issued a Special Fraud Alert concerned with laboratory payments to referring physicians, specifically payments "for blood specimen collection, processing, and packaging ("Specimen Processing Arrangements"), and for submitting patient data to a registry or database ("Registry Arrangements") which typically involve payments by a laboratory to a physician to compensate him for data collection and reporting services. OIG, "Special Fraud Alert: Laboratory Payments to Referring Physicians" (June 25, 2014), (hereinafter "SFA."). Neither of these practices is per se unlawful. According to the SFA, however, each is vulnerable to abuse, and the SFA lays out criteria the Agency will rely on to identify those arrangements that it deems to be suspect. Hence, engaging in the practices delineated in the SFA is apt to invite attention and inquiry, even if it does not necessarily result in conviction. In general, OIG may view as suspect laboratory payments to physicians for services that in its judgment are compensated at rates above fair market value, or that the laboratory does not actually need, or for which the physician is otherwise compensated.

In the SFA, OIG pointed out that it had previously admonished that "providing free or below-market goods or services to a physician who is a source of referrals, or paying such a physician more than fair market value for his or her services,

could constitute illegal remuneration under the anti-kickback statute.".

Emphasizing the relatively minimal role the patient plays in laboratory testing, OIG identified in its SFA

> four major concerns typically associated with kickbacks—corruption of medical judgment, overutilization, increased costs to the Federal health care programs and beneficiaries, and unfair competition. This is because such transfers of value may induce physicians to order tests from a laboratory that provides them with remuneration, rather than the laboratory that provides the best, most clinically appropriate service. Such transfers of value also may induce physicians to order more laboratory tests than are medically necessary, particularly when the transfers of value are tied to, or take into account, the volume or value of business generated by the physician.

SFA, at 2. Physicians of a certain age may find the implications offensive, but the language quoted is nevertheless the prevailing view at OIG today.

Let us examine more closely the two classes of agreement that OIG singled out as problematic:

1.Blood-Specimen Collection, Processing, and Packaging Arrangements.

Specimen Processing Arrangements characteristically provide for laboratory payments to physicians for collecting blood specimens, centrifuging specimens, storing them at an appropriate temperature, and packaging them for transport. According to the SFA, many Specimen Processing Arrangements provide for payments

"made on a per-specimen or per-patient-encounter basis and often are associated with expensive or specialized tests." SFA at 3.

In limited circumstances, under CPT Code 36415, Medicare will reimburse (a little) for venipuncture. Similarly, subject to some restrictions, "Medicare reimburses physicians for processing and packaging specimens for transport to a clinical laboratory through a bundled payment." CPT Code 90000. Where laboratories are separately paying the same physician for specimen collection, however, OIG may see the double billing as evidence of an intent to induce referrals.

OIG specifically identified as suspect the following payments made by a lab to a physician:

A. Payment exceeds fair market value for services actually rendered by the party receiving the payment.
B. Payment is for services for which payment is also made by a third party, such as Medicare.
C. Payment is made directly to the ordering physician rather than to the ordering physician's group practice, which may bear the cost of collecting and processing the specimen.
D. Payment is made on a per-specimen basis for more than one specimen collected during a single patient encounter or on a per-test, per-patient, or other basis that takes into account the volume or value of referrals.
E. Payment is offered on the condition that the physician order either a specified volume or type of tests or test panel, especially if the panel includes duplicative tests (e.g., two or more tests performed using different methodologies that are intended to provide the same clinical information), or tests that otherwise are not reasonable and necessary or reimbursable.
F. Payment is made to the physician or the physician's group practice, despite the fact that the specimen processing is actually being performed by a phlebotomist placed in the physician's office by the laboratory or a third party.

SFA at 4, 5. Note that from OIG's perspective, limiting such payments to services rendered to non-Medicare, non-Medicaid patients is not a solution:

Because physicians typically wish to minimize the number of laboratories to which they refer for reasons of convenience and administrative efficiency, Specimen Processing Arrangements that carve out Federal health care program business may nevertheless be intended to influence physicians' referrals of Federal health care program business to the offering laboratories.

SFA at 5.

2.Registry Payments.

OIG says it is aware that "clinical laboratories are establishing, coordinating, or maintaining databases, either directly or through an agent, purportedly to collect data on the demographics, presentation, diagnosis, treatment, outcomes, or other attributes of patients who have undergone, or who may undergo, certain tests performed by the offering laboratories." SFA at 5. It asserts that the labs involved deceitfully claim that these data bases "are intended to advance clinical research to promote treatment, to provide physicians with valuable clinical knowledge for patients with similar disease profiles, and to provide other benefits to physicians or the health care industry generally" SFA, 5, 6. It expressed concern that in reality such agreements, despite the stated purposes, "may induce physicians to order medically unnecessary or duplicative tests, including duplicative tests performed for the purpose of obtaining comparative data, and to order those tests from laboratories that offer Registry Arrangements in lieu of other, potentially clinically superior, laboratories." SFA, 6. OIG identifies the following characteristics as suspect:

A. The laboratory requires, encourages, or recommends that physicians who enter into Registry Arrangements perform the tests with a stated frequency (e.g., four times per year) to be eligible to receive, or to not receive a reduction in, compensation.
B. The laboratory collects comparative data for the Registry from, and bills for, multiple tests that may be duplicative (e.g., two or more tests performed using different methodologies that are intended to provide the same clinical information) or that otherwise are not reasonable and necessary.
C. Compensation paid to physicians pursuant to Registry Arrangements is on a per-patient or other basis that takes into account the value or volume of referrals.
D. Compensation paid to physicians pursuant to Registry Arrangements is not fair market value for the physicians' efforts in collecting and reporting patient data.
E. Compensation paid to physicians pursuant to Registry Arrangements is not supported by documentation, submitted by the physicians in a timely manner, memorializing the physicians' efforts.
F. The laboratory offers Registry Arrangements only for tests (or disease states associated with tests) for which it has obtained patents or that it exclusively performs.
G. When a test is performed by multiple laboratories, the laboratory collects data only from the tests it performs.
H. The tests associated with the Registry Arrangement are presented on the offering laboratory's requisition in a manner that makes it more difficult for the ordering physician

to make an independent medical necessity decision with regard to each test for which the laboratory will bill (e.g., disease-related panels).

SFA, at 6. Also characterized as suspect: "if a laboratory were to pay, and collect data for its Registry from, only a subset of physicians who were selected on the basis of their prior or anticipated referral volume, rather than their specialty, sub-specialty, or other relevant attribute." SFA at 7.

Analysis

The logical inference from the SFA is that laboratories and the physicians they work with need to be cautious in how they structure their agreements. They can still enter into Specimen Processing Arrangements and Registry Arrangements, but should recognize that the authorities may well scrutinize the details. This may be an opportune time, then, for clinical laboratories and physicians that are party to such arrangements to examine their practices and consider whether they should be restructured, or perhaps even abandoned altogether. The question to be asked always is whether OIG might be able to assert that one of the reasons for the arrangement is to induce referrals of patients for lab services.

To reduce the risk of regulatory scrutiny, payment should be offered to physicians through some formula independent of past or anticipated referrals. For example, Specimen Processing Arrangements can be set up to provide for a fair market value, set-in-advance fixed fee that does not take into account individual patients, encounters or specimens. It may be useful to expressly disclaim in the agreement any intent to induce or reward referrals. It would certainly be prudent to studiously avoid arrangements with any of the features that OIG has now in its SFA expressly identified as suspect. Note, however, that an agreement with none of the characteristics OIG has expressly questioned could still violate, or could allegedly violate, AKS. The list above should be seen as illustrative, not exhaustive.

This area of the law can be confusing. Allegations of violations have serious consequences, even for those who are exonerated, as investigation and defense are often costly in time, money, and emotional capital. As discussed above, conviction can have dire consequences. Parties to these arrangements, therefore, should proceed with caution, and should seek advice of counsel.

An option that in certain circumstances might be attractive is to seek an OIG Advisory Opinion. OIG has discretion to opine on whether a proposed arrangement is likely to be seen as violative. Deciding to entrain this process, however, is no small matter. The government may require highly detailed information, it may take many months to furnish an answer, or decline to answer at all, and the answer, if given, may not be what the inquiring parties want to see. They are then faced with the dilemma of how to proceed in the face of a critical opinion. On the other hand, a favorable opinion, though not a guarantee that all will be well, is nevertheless highly reassuring. Again, it would be prudent to confer with counsel before deciding whether to seek an advisory opinion from OIG.

If it appears that the benefits of proceeding outweigh the risks, and seeking the opinion is reasonable, those involved should understand the rules. The inquiring party must certify that all of the information it provides in its request is true and correct and constitutes a complete description of the relevant facts and agreements among the parties. If OIG elects to provide the information sought, it will expressly say that it relied solely on the facts and information presented to it. OIG will not undertake an independent investigation of the information presented. It will limit its opinion to the facts presented. OIG will expressly state that "if material facts have not been disclosed or have been misrepresented, this opinion is without force and effect." OIG will also standardly issue two other caveats:

1) Any definitive conclusion regarding the existence of an anti-kickback violation requires a determination of the parties' intent, which determination is beyond the scope of the advisory opinion process; and

2) OIG's opinion may not be relied on by any persons other than the requestor. This language notwithstanding, these opinions, identifiers redacted, are matters of public record, and are often studied to attempt to ascertain how by analogy OIG is likely to evaluate a given agreement.

Additional information about the advisory opinion process may be found at: http://oig.hhs.gov/faqs/advisory-opinions-faq.asp.

Finally, readers are reminded that, in addition to the Federal AKS discussed above, many states have enacted similar legislation that also governs agreements between laboratories and physicians as well as other common agreements in health care. Discussion of that topic is beyond the scope of this paper, but complying with the federal rules does not necessarily mean that state law has also been complied with, and vice-versa. In structuring arrangements, both sets of law must be taken into account.

Joseph P. McMenamin
MD, LLM.
Chief Legal Officer,
W Medical Strategy Group

Joe is the Chief Legal Officer of W Medical Strategy Group. Joe also practices law at McMenamin Law Offices, PLLC. He has more than 25 years of experience in defending biotech, pharmaceutical and other healthcare organizations against a variety of allegations in state and federal court. He also has advised them on a variety of legal issues. Joe has counseled hospitals, nursing homes, physicians, and other health care providers with respect to a wide array of legal issues as well, including their interactions with regulated industry.

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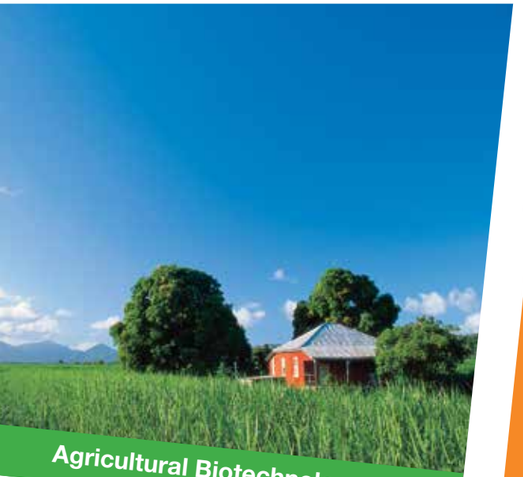

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Bio Pharmaceutical Report I

Celgene's Revlimid has experts optimistic about potential in Phase III non-del (5q) MDS trial in transfusion-dependent patients

- Historical responses meaningful, but approvability based on transfusion changes unclear
- Gene expression based screening could better direct use of drug considering its expense

Celgene's (NASDAQ:CELG) Phase III trial of Revlimid (lenalidomide) in non-5q deletion lower-risk myelodysplastic syndrome (non-del (5q) MDS) has experts generally optimistic about the chances of achieving the primary endpoint. The study is being done in patients with MDS-related anemia who are transfusion dependent and aims to reduce the number of red blood cell transfusions.

Still, experts said, while the drug could demonstrate clinical meaningfulness by making at least 25% of patients transfusion-independent, they were not unified on whether such a rate would be sufficient for regulatory approval.

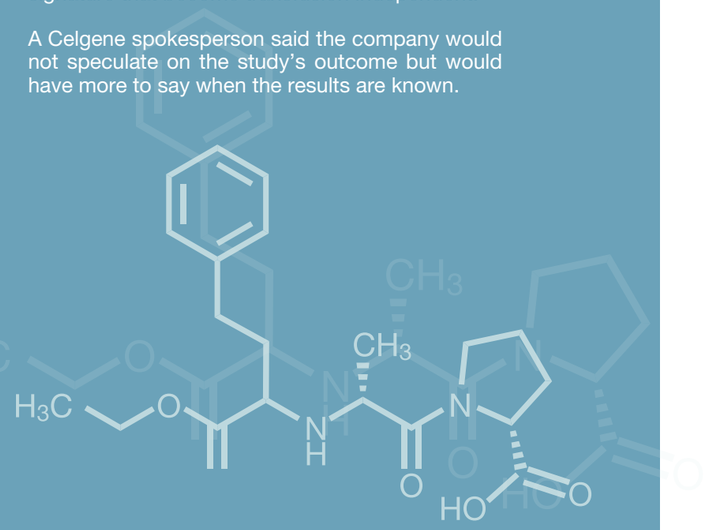
Identifying a gene signature would allow for more directed use of the drug in non-del(5q) MDS, which could be helpful because of the drug's high cost and increasing scrutiny of off-label prescribing in some countries, several experts noted. Revlimid is approved for patients with transfusion-dependent anemia due to low- or intermediate-1 risk MDS associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities.

The randomized, placebo-controlled, double-blind Phase III trial (NCT01029262) is expected to have data in 2H14, according to Celgene. The trial has an estimated primary completion date of April 2016, according to ClinicalTrials.gov.

Approximately 228 patients with low or intermediate-1 risk MDS will be enrolled and randomized to receive either 10 mg of Revlimid if their creatinine clearance is at least 60 milliliters per minute or 5 mg if their creatinine clearance is between 40-60 milliliters per minute. Dose adjustments for creatinine clearance rates are recommended in the prescribing information for Revlimid.

The primary endpoint is proportion of subjects that become transfusion independent and proportion with an erythroid differentiation gene expression signature that become transfusion independent.

A Celgene spokesperson said the company would not speculate on the study's outcome but would have more to say when the results are known.



Interim data from the Phase II MDS-002 trail showed that 25% of patients became transfusion-independent

Enthusiasm about primary endpoint success

The trial has a very good chance of meeting the primary endpoint, said Dr. Steve Allen, professor, medicine, Hofstra North Shore-LIJ School of Medicine, Lake Success, New York, pointing to previously published studies.

Interim data from the Phase II MDS-002 trial showed that 25% of patients became transfusion-independent (Ther Clin Risk Manag. Aug 2007; 3(4): 553- 562.), though later analysis showed the rate to be 26% (Seminars in Oncology, Vol. 38, No 5, October 2011, pp 648-657).

The drug has a medium probability of reaching its primary endpoint, said Dr. Emmanuel Gyan, hematologist, School of Medicine, François Rabelais University, Tours, France. Previous data indicates Revlimid is an active drug in non-del (5q) MDS, he noted.

If the trial indicates there is a significant reduction in blood transfusions and is associated with lower transformation rates to acute myeloid leukemia or lower rates of death, then Revlimid could be very interesting, noted Dr. Amit Verma, associate professor, Albert Einstein College of Medicine, New York.

Investigator Dr. Maria Diez Campelo, hematologist, University Hospital of Salamanca, Spain, said she was uncertain the primary measure would show success, though it was a reachable endpoint. She also pointed to previous study data and estimated that among her five trial patients, there appeared to be a 25% response rate.

It is hard to say whether the trial will reach the primary endpoint, said Dr Johnson Liu, associate professor, Hofstra North Shore-LIJ School of Medicine, Lake Success, New York, but the drug will add to the armamentarium even if it is not a game changer. Liu said he did not expect response rates in non-del(5q) to be as high as in del(5q). Studies have indicated Revlimid makes about 70% of del(5q) patients transfusion independent.

Historical response rates meaningful but unclear if sufficient for approval

At least 30% of patients achieving transfusion independence would not be bad, Verma said, though in the absence of good therapies in this setting, 25% is also worthwhile. It is unclear whether 25% would be enough for FDA approval, and the bar for approval is higher than in the past, he noted.

"They want survival; sometimes they are not happy with transfusion independence," he added. Still, it might be good enough if there is a large enough difference between the study arm and the placebo arm, he said.

EU approval would be more difficult than in the US, Gyan noted. He was not aware if the FDA or EMA had any defined threshold.

But 25% could be enough for FDA approval, Allen said. Low and intermediate-1 risk patients can have severe, life-threatening anemia, risks associated with transfusions including viral infections, fluid overload, iron overload and congestive heart failure. After 20 transfusions, patients are at risk for significant iron overload that can cause organ damage, Allen noted, adding that iron chelation therapy is controversial, because it is expensive and not well tolerated.

Secondary end points in the trial include safety as well as impact on health-related quality of life and use of healthcare resources.

Besides the 25% benchmark, the FDA would have to look at other issues like quality of life and survival, a Florida expert noted. Still, he said, the FDA has approved drugs before based on factors like reductions in transfusions, and definitely if there is a survival benefit.

Secondary endpoints in the trial include safety as well as impact on health-related quality of life and use of healthcare resources.

The toxicity profile is unlikely to be different in non-del(5q) MDS from del(5q), Liu said. Nonmyeloid toxicity should not be different, but the drug may be more myelosuppressive in non-del (5q) than in del(5q), because the drug drives down blood counts, and MDS patients already have low counts, Allen added. If the patients respond to treatment, he explained, the counts rise, but if not, then they can drop to levels lower than without Revlimid.

Screening could better direct use of drug

While the ability of patients with non-del (5q) MDS to respond to Revlimid has been known for some time, it is unknown whether the response is because patients have the same kind of target as those with del(5q) disease, so there is a lot of interest in trying to understand why that is, Liu said. Revlimid can be clinically significant in non-del (5q) despite being not as effective as in del(5q), he added.

Part of the problem with Revlimid is its pricing, two experts noted. Gyan pointed out that it costs EUR 6,000-8,000 per month, while Allen said in the US it is USD 7,500-10,000. Hence, said Gyan, a biomarker is needed to avoid “throwing away” too much of the drug. Even though 25% would indicate the drug’s activity, he noted, “I don’t want to treat 10 patients and only see three responses.”

Gyan and Allen pointed to a February 2008 study (PLoS Med 5(2): e35. doi:10.1371/journal.pmed.0050035) that identified a molecular signature in a set of 16 pretreatment bone marrow aspirates from non-del(5q) MDS patients. It is on the basis of this study that patients are being screened for the gene expression signature before starting treatment, the Celgene spokesperson said.

Proving that the gene signature is predictive, Allen said, would help direct Revlimid usage in the non-del (5q) population. Even if a test for such a signature is expensive, Gyan added, it could mitigate giving a costly drug to nonresponsive patients.

Gyan and Liu said they would like to see anything that could indicate whether a response is seen in 70% or more patients.

The trial is analyzing how many subjects with the gene expression profile achieve transfusion independence, the Celgene spokesperson noted but could not say yet whether the information would translate into a biomarker.

Celgene’s market cap is USD 64.8bn.

Alaric DeArment
Reporter
BioPharm Insight

Alaric DeArment covers cancer drugs and vaccines for BioPharm Insight. Previously, he was associate editor at Drug Store News, covering retail and specialty pharmacy, pharmaceuticals, biologics and regulatory affairs. A native of Seattle, he graduated with honors with a bachelor degree in journalism from Ball State University and also lived in China from 2001-2004

Bio Pharmaceutical Report II

Novartis' LCZ696 for CHF draws approval optimism after meeting difficult Phase III endpoints – experts

- Superiority to standard therapy bodes well for approvals
- Regulators may require dropout explanation
- Good potential for first line and combination use

Novartis' (VTX:NOVN) LCZ696 will likely secure EMA and FDA approval after showing Phase III superior efficacy over generic comparator enalapril in chronic heart failure (CHF), experts said. Reducing cardiovascular (CV) deaths and hospitalisations will likely be looked at favourably by regulators, they added.

The PARADIGM-HF study enrolled 8,436 HF with reduced ejection fraction (HF-REF) patients to evaluate the efficacy and safety of LCZ696 versus standard of care angiotensin-converting-enzyme (ACE) inhibitor enalapril.

At the third interim analysis of PARADIGM-HF, the Data Monitoring Committee (DMC) confirmed the primary composite endpoint had been met, showing LCZ696 delayed CV death and reduced HF hospitalizations versus enalapril, according to a 31 March press release. The analysis also confirmed significance on reduction of CV death against enalapril independently, according to a Novartis spokesperson.

The PARADIGM-HF data is likely to show at least 15% reduction in the composite primary endpoint with LCZ696 use over enalapril and the full data set will be presented at the European Society of Cardiology meeting in August and submitted to the New England Journal of Medicine, this news service recently reported.

LCZ696 twice-daily pill, is an Angiotensin Receptor Neprilysin Inhibitor (ARNI) thought to reduce the strain on the failing heart, promoting the ability of the heart muscle to recover, according to Novartis' website.

A 20% or above reduction in the risk of mortality would be extremely useful and show a clear additional benefit for LCZ696 over standard of care

Added mortality benefit sufficient for approval

Phase II data and an early trial closure after an interim analysis, shows the clear clinical treatment benefit of LCZ696 and a potential mortality benefit which will be looked at favourably by regulators, said Dr. Miguel Camafort-Babkowski, cardiologist, IDIBAPS Hospital Clinic, Barcelona, Spain. A 20% or above reduction in the risk of mortality would be extremely useful and show a clear additional benefit for LCZ696 over standard of care, agreed Shelby Reed, Assistant Professor, Duke Clinical Research Institute, Durham, North Carolina.

The early trial closure provides unequivocal evidence for superiority of LCZ696 over enalapril which should be sufficient for approval in HF-REF, an investigator agreed. The combined endpoint of CV death and hospitalizations is difficult to meet in such a large HF trial, a second investigator said, adding if it met statistical significance as expected, this should be sufficient for FDA and EMA approval.

LCZ696 is likely to exceed the bar for approval if there is a clear mortality benefit, agreed Reed, adding even if the mortality benefit is not statistically significant, approval chances are high because CV death and hospitalizations are both important and rigorous endpoints. All-cause mortality is a secondary endpoint, according to ClinicalTrials.gov.

Given the number of approved treatments for HF-REF, the regulatory agencies are likely to scrutinize LCZ696 data to ensure superior safety and efficacy over standard of care, Camafort-Babkowski said.

This head-to-head trial design with gold standard 10mg enalapril twice daily is important to clearly show superiority and avoid skepticism, a third investigator said. Clear efficacy on top of optimal background care will be looked at favorably in the eyes of regulators, Reed said.

Safety an unlikely hurdle though dropouts need clarification

Although efficacy is clear, LCZ696 has a number of hoops to go through before approval, including quantitative evidence that it is well tolerated and safe, a fourth investigator said, though agreed that based on safety data he had seen, approval is achievable.

It is unlikely that there will be significant safety signals based on Phase II data, Reed and Camafort-Babkowski agreed. However, because of its dual mechanism of action and targeting beta amyloid metabolism, there is a theoretical possibility that this could contribute to development of Alzheimer's disease or other cognitive impairments with long term use, Camafort-Babkowski added, though this may not be evident in PARADIGM-HF.

The dropout rate in PARADIGM-HF is as expected in a CHF trial of this size and investigators estimated 15%-20% dropout, this news service recently reported. This rate may be too high for regulators and could hold up an approval as the company will need to explain the reasons for such a high dropout rate, Camafort-Babkowski said. Feedback from the FDA and

All experts agreed that LCZ696 has good potential for use in combination to standard of care and drug interactions should be tested in future studies.

EMA during Novo Nordisk's (NYSE:NVO) Victoza (liraglutide) for diabetes said a threshold of up to 15% dropout was tolerable, and CV indications are assessed similarly, he added.

Many factors contribute to a high dropout rate and a 15%-20% dropout will not necessarily hinder approval, Reed said. Dropout rates can be a result of trial location, conduct or individual patient differences rather than a negative reflection of the drug's safety profile, she said, but agreed regulators will require explanations for these high rates.

No apparent safety concerns have been noted by the DMC after three interim analyses and multiple safety reviews of the data, according to the spokesperson.

First-line treatment as it trumps best ACE inhibitor

Despite numerous options for HF-REF, there is a persistently high mortality rate in these patients, the third investigator said. All experts agreed there has been a plateau in CHF treatments and regulators are well aware of the clinical need for options with added benefits over the standard of care. Enalapril and other ACE inhibitors have dominated the CHF market since the first approval 27 years ago and very few drugs have changed the treatment paradigm, the third investigator said. LCZ696 has potential to be a first-line treatment in HF-REF because of its superiority to enalapril, the first and fourth investigators said.

LCZ696 has peak sales forecast of USD 3bn, according to an analyst report.

Regulators may ask for further studies to assess LCZ696's safety in combination with standard therapies including ACE inhibitors, angiotensin II receptor blockers (ARBs) and beta blockers because in clinical practice it is likely to be used in combination regimens, Camafort-Babkowski said, though noted this would not be a requirement for approval.

All experts agreed that LCZ696 has good potential for use in combination to standard of care and drug interactions should be tested in future studies.

Subsequent trials will need to assess LCZ696's efficacy in other CHF patients subgroups for a broader label, the fourth investigator and Camafort-Babkowski said. CHF with preserved ejection fraction is where the biggest clinical need is, the first investigator agreed, adding this is the next step for Novartis as the Phase III PARAGON-HF trial (NCT01920711) will start recruitment soon.

Novartis has a market cap of CHF 196.8bn (EUR 161.2bn).

Jinan Harb
Reporter
BioPharm Insight

Jinan was a freelance journalist before joining BioPharm Insight, writing for numerous magazines and websites covering health and science stories. She has a BSc in Physiology from King's College London and an MA in Science Journalism from City University London.

Bio Pharmaceutical Report III

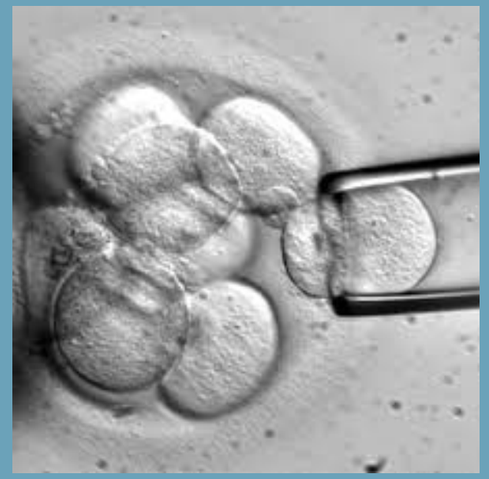
The Unrealized Potential of Stem Cell Therapy

Over the last decade or so, I have observed a tempering of what was once a large and growing interest in stem cell therapies by patients, physicians and investors. I believe this dampening of enthusiasm has occurred as the public has awakened to some of the realities surrounding the logistics of the mass production, regulatory approval and eventual administration of living cells into people. In this article are my opinions as to why the stem cell industry may be deserving of this love-hate relationship and why the "stem cell" products currently closest to approval aren't "stem cells" at all.

In February 2004, Dr. Woo Suk Hwang of South Korea announced he had successfully derived stem cells from a cloned human embryo, an achievement that earned him the reputation as a 'national treasure' in South Korea and the "king of cloning" throughout the rest of the world. Despite Dr. Hwang's subsequent disgrace and conviction for falsifying data, the damage had been done. The public believed the ability to regenerate organs from "stem cells" was right around the corner. These events signaled the controversial popularity surrounding embryonic stem cells (ESCs), the harvesting of which involves the destruction of embryos. President Bush's restrictions on research involving ESCs combined with the opinions of organizations such as the Catholic Church had a chilling effect but could not contain the public's interest and misconceptions that ESCs could regenerate entire organs such as hearts and livers.

In 2009, Geron Corporation, a US public company dealing with embryonic stem cell therapy aimed at spinal cord injuries, enjoyed a market value in excess of $1B. However, in one of the most significant blows to ESCs in particular, the stem cell industry in general and a wake-up call for Joe Q occurred three years later when Geron announced that they were exiting the stem cell market. Geron stated this decision was made after a "strategic review of the costs, value inflection timelines and clinical, manufacturing and regulatory complexities" associated with pursuing the continued research and development of ESCs versus other assets they owned. I would emphasize the regulatory complexities part of this statement. Geron's Investigational New Drug (IND) application totaled 21,000 pages, of lot which was devoted to addressing the regulators concerns that, at the end of the day, how can you approve a product containing ESCs when ESCs, by definition, forms tumors (teratomas).

However, obscured in the shadow of the ESCs popularity, preclinical and clinical work was being conducted on its stepchild, the adult stem cell. For the purpose of this article, we define ASCs as any cell therapeutic that is not an ESC or hematopoietic stem cell (HSC), the cell that differentiates into our blood lineages. Adult stem cells harbor no ethical



allogeneic MSCs have emerged as the regenerative medicine industry's best chance of developing commercial products over the near term. geron

controversies, as the procurement of these cells does not entail destroying the embryo. The vast majority of adult stem cells being used in preclinical and clinical trials for a variety of indications exist under the general category of mesenchymal stem cells (MSCs), although these cells come under different names, such as mesenchymal stromal cells, mesenchymal precursor cells and mesenchymal-like stromal cells. MSCs can be obtained from several different sources such as bone marrow, adipose tissue, the placenta and menstrual fluid. Additionally, MSCs can be obtained from the patient (autologous) or from a source other than the patient (allogeneic). Several entities are attempting to commercialize their particular MSC and are represented by companies such as Mesoblast Limited, Athersys Inc., Aastrom Biosciences, Inc., and Osiris Therapeutics, Inc. which use bone marrow as a source of their MSCs and Pluristem, which uses the placenta (PLacental eXpanded cells), Medistem Inc., which uses menstrual fluid and Cytori Therapeutics, Inc. and TiGenix NV which use adipose tissue. All of the companies mentioned are allogeneic-based other than Aastrom and Cytori, which are autologous-based companies. Autologous-based therapies exploit a business model that is not intended to supply cells for the general population, as allogeneic therapy is potentially able to provide. Although still believed to fulfill a niche, the popularity of the autologous "personalized-medicine" approach has softened since the discovery that allogeneic MSCs are immune competent and can be administered to patients without histocompatibility matching.

Interestingly, the mechanism of action of MSCs is not one of differentiation into tissue and organs. Instead, these cells act as drug delivery devices. They respond to signals from injured tissue by secreting a cocktail of anti-inflammatory, angiogenic, and cytoprotective therapeutic proteins that exert their pharmacologic effects on the injured tissue. Therefore, if you define a stem cell as Webster's dictionary does (i.e. a stem cell is an unspecialized cell that gives rise to differentiated cells), then the MSCs currently in clinical trials should not rightfully be called "stem" cells.

Regardless of whether they are categorized as "stem" cells or not, allogeneic MSCs have emerged as the regenerative medicine industry's best chance of developing commercial products over the near term. This is the unrecognized potential of cell therapy. ASCs were the king. Allogeneic MSCs are now the king. Allogeneic cell therapy products are already being marketed for Graft versus Host Disease (GvHD), a complication of bone marrow transplantation, and Diabetic Ulcers. More importantly, however, are the allogeneic MSCs in advanced clinical trials for important indications. Companies are currently involved in Phase II or III clinical trials for degenerative indications that include Rheumatoid Arthritis, Inflammatory Bowel Disease, Diabetes, Emphysema, Ischemic Heart Disease, Congestive Heart Failure, Osteoarthritis, Ischemic Stroke, Peripheral Artery Disease, Bone Marrow Transplantation and Muscle Injury. Examining these indications reveal why allogeneic MSC-related products will be the reason the "stem cell" regenerative medicine industry should be highly successful in the future.

Cell Therapy in South Korea

Just recently, Pluristem announced the initiation of South Korean sites in the Phase II study assessing (PLX) cells in the treatment of intermittent claudication (IC). Patient screening is now underway at three clinical centers, making South Korea the fourth country to participate in this randomized, double-blind, placebo-controlled Phase II trial. The trial has been ongoing at clinical sites in the U.S., Israel and Germany with an enrollment target of 150 patients. The study is being conducted by CHA BioTech

Just recently, Pluristem announced the initiation of South Korean sites in the Phase II study assessing (PLX) cells in the treatment of intermittent claudication (IC)

Zami Aberman
Chief Executive Officer
Pluristem Therapeutics, Inc.

(Kosdaq: CHA) under an exclusive licensing agreement for the use of PLX cells for peripheral artery disease (PAD) in South Korea. Under the terms of Pluristem's licensing agreement with CHA, if there is regulatory approval for a PLX product in South Korea Pluristem and CHA will establish a joint venture (JV) co-owned by the parties; they will share the revenues and income generated through sales of PLX cell therapies in the South Korean market. It is estimated that one million people in South Korea suffer from PAD and this number is expected to grow. These products have the potential to significantly modify degenerative diseases where the current relief enjoyed in the past by patients has only been symptomatic.

Zami Aberman Chairman & CEO joined Pluristem in September 2005 and changed the Company's strategy towards cellular therapeutics. Mr. Aberman's vision to use the maternal section of the Placenta (Decidua) as a source for cell therapy, combined with Pluristem's 3D culturing technology, led to the development of the Company's unique products. Mr. Aberman has 20 years of experience in marketing and management in the high technology industry. He has held positions of Chief Executive Officer and Chairman in Israel, the USA, Europe, Japan and Korea. He has operated within high-tech global companies in the fields of automatic optical inspection, network security, video over IP, software, chip design and robotics. Mr. Aberman serves as the Chairman of Rose Hitech Ltd., a private investment company. In the past he has served as the Chairman of VLScom Ltd., a private company specializing in video compression for HDTV and video over IP and as a Director of Ori Software Ltd., a company involved in data management.

Prior to that, he served as the President and CEO of Elbit Vision Systems (EVSNF.OB), which supplies inspection systems for the microelectronics industry. Mr. Aberman has served as President and CEO of Netect Ltd., specializing in the field of internet security software and was the Co-Founder, President and CEO of Associative Computing Ltd., which developed an associative parallel processor for real-time video processing. He has also served as Chairman of Display Inspection Systems Inc., specializing in laser based inspection machines and as President and CEO of Robomatix Technologies Ltd. (RBMXF.OB). In 1992, Mr. Aberman was awarded the Rothschild Prize for excellence in his field from the President of the State of Israel. Mr. Aberman holds a B.Sc. in Mechanical Engineering from Ben Gurion University in Israel.

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

IN THE TREATMENT OF CHRONIC HEPATITIS B (CHB) IN ADULTS WITH COMPENSATED LIVER DISEASE

TAKE A CLOSER LOOK AT LAMIVUDINE (LAM) RESISTANCE

MORE THAN 50% of Americans living with CHB are Asian and Pacific Islanders[1]

NEARLY 70% of Asian Americans were born or have parents born in countries where CHB is common[1]

70% of patients receiving lamivudine develop resistance at 5 years[2]

2% of patients in the United States use lamivudine; **up to 88%** in Asia[3]

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**

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

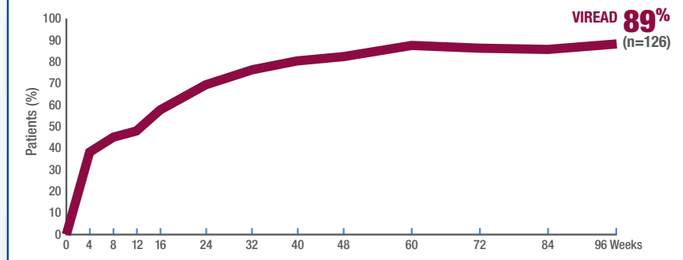
Adverse Reactions

- **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

TAKE A CLOSER LOOK AT VIREAD

LAM-resistant VIREAD patients (Study 121)

achieving viral suppression (HBV DNA <400 copies/mL) at 96 weeks of treatment[4,5]



Study 121 was a randomized, double-blind, active-controlled 96-week trial evaluating the safety and efficacy of VIREAD (n=141) compared to an unapproved antiviral regimen (n=139) in subjects with CHB, persistent viremia (HBV DNA ≥1000 IU/mL), and genotypic evidence of LAM resistance. The primary endpoint in Study 121 was HBV DNA <400 copies/mL (69 IU/mL) at Week 96.[4,5]

- As a secondary endpoint, **no HBV resistance (0%)** was detected at **96 weeks** in CHB patients with LAM resistance[4]

Important Safety Information (cont'd)

- **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
- **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 adjacent pages.

References: 1. CDC Web site. CDC Features-August 2011: Chronic hepatitis B and Asian & Pacific Islanders. Centers for Disease Control and Prevention. http://www.cdc.gov/Features/ChronicHepatitisB/. Accessed June 26, 2013. **2.** European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of chronic hepatitis B virus infection. *J Hepatol.* 2012;57:167-185. **3.** Data on file, Gilead Sciences, Inc. Gilead HBV LAM assessment, IMS MIDAS data. May 2013. **4.** Data on file, Gilead Sciences, Inc. 0121 CSR. **5.** VIREAD Prescribing Information, Foster City, CA: Gilead Sciences, Inc.; October 2013.

300mg tablets®
Viread®
tenofovir disoproxil fumarate

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 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 *(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 estimated 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)*.

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 240 weeks.

Laboratory Abnormalities: in Studies 0102 and 0103 (0–48 Weeks) laboratory

Brief Summary (cont'd)

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 240 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 co-administered 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 breast-feed 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 breast-feed 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.

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Conference Alerts

North America

40TH ANNIVERSARY CONFERENCE OF INTERNATIONAL SOCIETY FOR PEDIATRIC & ADOLESCENT DIABETES (ISPAD)

SEPTEMBER 3RD TO 6TH ONTARIO / TORONTO ENDOCRINOLOGY

Attend and participate in the 40th Annual Conference of ISPAD to be held from September 3rd to 6th 2014 in Toronto: The City Where Insulin was Discovered! The theme of ISPAD 2014 is: DIVERSITY IN DIABETES, appropriate on many levels. First, Toronto is one of the world's most ethnically diverse cities. Second, diabetes research, education and care have exploded in many diverse directions, new diagnostic categories, new understandings of etiology and pathogenesis of all types of diabetes, many and varied approaches to therapy, molecular science, human and animal physiology, epidemiology, clinical trials, models of care…the list is endless! ISPAD and its annual conference are about improving the lives of children and youth with diabetes, and our meeting provides the ideal opportunity for those who have dedicated their careers to this goal to meet, discuss and share their wisdom in an atmosphere of collegiality and a spirit of optimism.
Contact: ISPAD Executive Office , Secretariat , K.I.T. Group GmbH
Phone: 011-49-30-2460-3210 Fax: 011-49-30-2460-3200
Email: secretariat@ispad.org
http://www.ispad.org/2014/home

North America

2014 AMERICAN COLLEGE OF PHYSICIANS (ACP) MISSISSIPPI/LOUISIANA CHAPTERS EDUCATIONAL/SCIENTIFIC MEETING

SEPTEMBER 4TH TO 6TH ALABAMA / POINT CLEAR FAMILY MEDICINE, GENERAL MEDICINE, INTERNAL MEDICINE

We invite you to join us and your colleagues in internal medicine at the next educational/scientific meeting of the Mississippi/Louisiana Chapters of the American College of Physicians, being held September 4–6, at the Grand Hotel Marriott Resort, Golf Club and Spa in Point Clear, Alabama. This meeting is not just for ACP members. We particularly want to invite nonmembers to join us for this important clinical update and to learn about the benefits of membership at the same time. In addition to earning 9.5 CME credits, by attending this meeting you will gain insight into recent medical advances, discuss local and national issues affecting the practice and teaching of internal medicine, greet old friends, meet new friends, and develop a network of colleagues in your area and take some time for yourself or with your family to relax and enjoy the sights around Point Clear.
Contact: Member & Customer Service, ACP
Phone: 800-523-1546 ext. 2600 or 215-351-2600 Fax: 215-351-2799
Email: custserv@acponline.org
Website: http://www.acponline.org/meetings/chapter/

North America

2014 BREAST CANCER SYMPOSIUM

SEPTEMBER 4TH TO 6TH CALIFORNIA / SAN FRANCISCO ONCOLOGY

Case-based learning discussions are the focus of the 2014 Breast Cancer Symposium (September 4-6 in San Francisco, California). This unique learning method is an opportunity for research and academic experts to provide real-world context to the latest scientific advances. Each day, a Framing Case Presentation will provide a narrative encompassing the educational content presented in the general sessions that day.
Sessions will include panel discussions and debates on the following topics: Breast-Conserving Surgery Guidelines, Risk Management including Risk-Adjusted Screening and Genetic Testing, Early Disease and Metastatic Tumor Boards, Neoadjuvant Therapy Controversies, Evidence-Based Lifestyle Choices and Surveillance Options, Multidisciplinary Considerations for Breast Reconstruction, and Genomics and Reversing Hormone Resistance
Contact: American Society of Clinical Oncology
Phone: 571-483-1300
Email: meetings@asco.org
http://breastcasym.org/

North America

15TH INTERNATIONAL CONFERENCE ON ALZHEIMER'S DRUG DISCOVERY

SEPTEMBER 8TH TO 9TH NEW JERSEY / JERSEY CITY NEUROLOGY

This annual Alzheimer's Drug Discovery Foundation (ADDF) conference brings together academic and industry scientists intent on accelerating the development of innovative treatments for Alzheimer's disease and related dementias. The ADDF's funded investigators and top level scientists in the field will present on their current research progress and stimulate discussion. The conference offers ample opportunities for collaboration and partnering.
Contact: Sara Classen , Alzheimer's Drug Discovery Foundation
Phone: 212-901-8009
Email: sclassen@alzdiscovery.org
http://www.worldeventsforum.com/addf/addrugdiscovery/index.html

North America

MINIMALLY INVASIVE SURGERY WEEK: ANNUAL MEETING & ENDO EXPO 2014 PRESENTED BY SLS & AFFILIATED SOCIETIES

SEPTEMBER 10TH TO 13TH NEVADA / LAS VEGAS OBSTETRICS/GYNECOLOGY, SURGERY, UROLOGY

An Event in Late August-Early September, this multispecialty conference of a number of MIS Societies, helps increase knowledge of laparoscopic, endoscopic, and minimally invasive surgical techniques. The Meeting consists of Postgraduate Master's Classes; Plenary Sessions; Lap Updates of multiple topics; Expert review and discussion of surgical videos showing accidents, mishaps, and surprises; Deconstruction of video-taped surgeries performed by master surgeons; Exhibitions; Competitions for Best Papers, Videos, and Posters from Professors to Fellows and Residents; Future Technology Sessions; and over 200 General Surgery, Gynecology, Urology, and Multispecialty Scientific Presentations.
Contact: , Society of Laparoendoscopic Surgeons
Phone: 305-665-9959 Fax: 305-667-4123
Email: info@sls.org
http://www.sls.org/

North America

2014 ULTRASOUND GUIDED REGIONAL ANESTHESIA & VASCULAR ACCESS WORKSHOP

OCTOBER 1ST TENNESSEE / GATLINBURG ANESTHESIOLOGY

This workshop is intended for the practitioner already possessing skill and experience with regional anesthetic administration and/or peripheral and central vascular cannulation who wish instruction and the opportunity to handle the equipment for these procedures and instructor - assisted practice identifying anatomy and procuring the ergonomic skill of managing the equipment while performing the techniques.
Contact: Northwest Anesthesia Seminars
Phone: 800-222-6927 Fax: 509-547-1265
http://www.nwas.com/full-schedule.html

North America

42ND ANNUAL SICKLE CELL DISEASE ASSOCIATION OF AMERICA (SCDAA) CONVENTION

OCTOBER 1ST TO 4TH MARYLAND / BALTIMORE GENETICS, HEMATOLOGY

The SCDAA Annual Convention is a four-day conference designed to address the multi-factorial aspects of Sickle Cell Disease. This year the event will be held in Baltimore, Maryland, home of the SCDAA National Office. In an effort to advocate for improved quality of life for individuals and families affected with sickle cell disease and its associated morbidity and mortality, the conference fosters the exchange of the latest scientific and clinical information related to the disease. This is done through the offering of innovative symposium, training seminars, and interactive panel discussions. In addition this year's convention offers an array of exciting activities designed to educate and motivate the entire community to get involved in the fight against Sickle Cell Disease.
Contact: SCDAA
Phone: 410-528-1555 Fax: 410-528-1495
Email: scdaa@sicklecelldisease.org
http://www.sicklecelldisease.org/index.cfm?page=annual-convention

North America

HEALTHTECH CONFERENCE

October 14-15, 2014, San Mateo, CA.

The HealthTech Conference has emerged after the last two years as the leading conference on how to build successful HealthTech companies. We focus on practical and in depth discussions on how emerging and established companies can grow their innovative products that enable existing healthcare players to adapt to a fast changing healthcare system. The conference provides a unique blend of all the key players in the same room:
Providers
Investors
Payers
Emerging companies
Established companies
http://www.healthtechconference.com/

North America

70TH ANNUAL AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE (ASRM) MEETING

OCTOBER 18TH TO 22ND HAWAII / HONOLULU ENDOCRINOLOGY, OBSTETRICS/GYNECOLOGY, OTHER SPECIALTIES, UROLOGY

The mission of WIPO is to promote the prevention and treatment of immune-associated disorders through education and research activities and to establish communication between specialists in various fields of medical science and practice. We welcome doctors and researchers involved in various areas of modern medical biological research and clinical practice who deal in their everyday practice with any kind of immunopathology. WIPO sections will feature: Allergy, Asthma, Basic Immunology, Clinical Immunology, Autoimmunity, AIDS, Pediatrics, ENT, Dermatology, and Junior Section.
Contact: , ASRM
Phone: 205-978-5000 Fax: 205-978-5018
Email: asrm@asrm.org
http://www.asrm.org/Upcoming_Meetings/

North America

15TH ANNUAL FALL CONFERENCE ON EMERGENCY MEDICINE

NOVEMBER 19TH TO 22ND MEXICO / PLAYA DEL CARMEN EMERGENCY MEDICINE

Our 15th Annual Fall Conference on Emergency Medicine is designed to provide emergency physicians, nurses, nurse practitioners, physician assistants, as well as out-of-hospital providers, with
state-of-the-art information on a wide variety of topics in emergency medicine. The goal of this conference is to increase knowledge and enhance the competence of attendees. Emphasis will be placed on practical application of the evidence-based topics presented.
Contact: Symposia Medicus
Phone: 800-327-3161 or 925-969-1789 Fax: 925-969-1795
http://symposiamedicus.org/Conferences.aspx

South America

15TH INTERNATIONAL ASSOCIATION FOR THE STUDY OF PAIN (IASP) WORLD CONGRESS ON PAIN

OCTOBER 6TH TO 11TH ARGENTINA / BUENOS AIRES PAIN MANAGEMENT

The World Congress on Pain is the premier congress devoted to the research and treatment of pain. Every two years the Congress boasts a hearty program composed of refresher courses, plenary lectures, topical workshops and symposia, and poster presentations. The Scientific Program Committee determines the content and an esteemed faculty of experts from around the world conducts the sessions. A Local Arrangements Committee works with the Congress Secretariat and IASP to present receptions, dinners, and other social events in keeping with the host city's culture.
The World Congress on Pain is designed to:
- Provide a state-of-the-art overview of a wide range of topics in the area of pain
- Offer practical reviews of current research and therapies
- Provide continuing education credits for clinicians
- Allow delegates to participate in formal and informal discussions with international experts on pain management and pain research

Contact: , IASP Secretariat
Phone: 202-524-5300 Fax: 202-524-5301
Email: IASPdesk@iasp-pain.org
http://www.iasp-pain.org/Content/NavigationMenu/WorldCongressonPain2/15thWorldCongressonPain/default.htm

Europe

15TH WORLD CONGRESS ON CANCER OF THE SKIN

SEPTEMBER 3RD TO 6TH SCOTLAND / EDINBURGH DERMATOLOGY, ONCOLOGY

The 15th WCCS will appropriately consider all aspects of this subject, from the clinical, histological and genetic nature of these cancers, to how best to prevent and treat them. Addressing this major issue will be a superior faculty of speakers drawn from all of the UK, continental Europe, the USA, Canada, Africa, South America, Asia, Australia and New Zealand, clearly demonstrating the thoroughly global importance of the topic. The venue for this signal event will be the superbly suitable Edinburgh International Congress Centre (EICC) situated in the city center.
Contact: Danielle , Conference and Event Services , British Association of Dermatologists
Phone: 011-44-20-7391-6343
Email: danielle@bad.org.uk
http://www.wccs2014.org/

Europe

3RD ANNUAL CANCER VACCINES CONFERENCE

SEPTEMBER 15TH TO 16TH UNITED KINGDOM / LONDON IMMUNOLOGY/ALLERGY, ONCOLOGY, OTHER SPECIALTIES, RADIOLOGY/IMAGING

SEPTEMBER 15TH TO 16TH UNITED KINGDOM / LONDON IMMUNOLOGY/ALLERGY, ONCOLOGY, OTHER SPECIALTIES, RADIOLOGY/IMAGING
SMi presents the 3rd Annual Cancer Vaccines Conference taking place in Central London on Monday 15th and Tuesday 16th September 2014. This year's event will focus on the pre-clinical entities that are crucial when moving forward in clinical trials. This will include, assessing antigen discovery and genome sequencing in addition to evaluation biomarkers and chimeric antigen receptors. There is a growing demand for combination therapies and ssessing clinical trial design, especially with failures in the clinic increasing, the question to be asked is how can we learn from this and move forward to ensure phase III developments and regulatory approval? The agenda will focus on in vivo targeting of antigens to dendritic cells for therapeutic anti-cancer vaccines, reviewing preventive vaccine novel adjuvants programs as well as evaluating patient stratification. Furthermore, it will enable a broad range of academics, small biotechs, and large pharmaceutical companies to review analytical methods to enable reliability upon standardization of assays.
Contact: Teri Arri , Marketing Exec , SMi Group
Phone: 011-44-20-7827-6000
Email: tarri@smi-online.co.uk
http://www.smi-online.co.uk/goto/2014cancervaccinesevent44.asp

Europe

18TH INTERNATIONAL FORUM OF PSYCHOANALYSIS

SEPTEMBER 17TH TO 19TH LITHUANIA / KAUNAS PSYCHIATRY

The conference will focus on psychoanalysis and severe psychopathology. Psychosis, traumas, severe personality disorders, severe eating disorders, forensic psychiatry/psychology, self-harms and serious psychosomatic reactions are among the issues which we hope will be discussed. The aim of the Forum is to promote both clinical and theoretical discussions concerning the themes covered by the title, although communications from a research angle are welcomed as well.
Contact: Karolina Vilkeviciute , Conference Secretariat , EVENT MANAGEMENT LT
Phone: 011-370-6-440-0344
Email: secretariat@ifps-forum2014.com
http://www.ifps-forum2014.com/

Europe

2014 CANCER PHARMACOGENOMICS & TARGETED THERAPIES

SEPTEMBER 17TH TO 19TH UNITED KINGDOM / CAMBRIDGE BIOCHEMISTRY, CLINICAL PHARMACOLOGY, ONCOLOGY

We are pleased to announce the 2nd Trust Conference on Cancer Pharmacogenomics and Targeted Therapies. The conference will once again bring together leading scientists and clinician-scientists from academia and industry to focus on the key challenges in the design, development and clinical implementation of targeted cancer therapies.
The meeting will focus on the key concepts and challenges in this field, including:

- Insights from the mutational landscape of cancers
- Tumour heterogeneity and the impact on therapies
- New and emerging therapeutic targets
- Pre-clinical biomarker discovery and evaluation
- Effects of tumour environment on therapeutic response
- Immunotherapy
- Deployment of targeted therapies in the clinic

Contact: Jemma Beard , Conference Organizer , Wellcome Trust
Phone: 011-44-12-2349-5120 Fax: 011-44-12-2349-5023
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https://registration.hinxton.wellcome.ac.uk/display_info.asp?id=431

Europe

3RD INTERNATIONAL CONFERENCE ON ANTIMICROBIAL RESEARCH

OCTOBER 1ST TO 3RD SPAIN / MADRID OTHER SPECIALTIES

- Antimicrobial natural products
- Antimicrobial microbes
- Bacteriophages
- Biofilms
- Non-antibiotic biocides
- Antimicrobial materials science and surface chemistry
- Antimicrobials in consumer products
- Antimicrobial chemistry
- Antimicrobial physics
- Techniques and Methods
- Clinical and medical microbiology, infectious diseases and antimicrobials. Public health
- Strengthening of innate immune system as antimicrobial strategy
- Antimicrobial resistance. Mechanisms of action of antimicrobial agents
- Attenuation of virulence as antimicrobial strategy

Contact: Aurora Solano , Formatex Research Center
Phone: 011-34-924-258-615 Fax: 011-34-924-263-053
Email: info@icar-2014.org
http://www.icar-2014.org/

Asia

8TH INTERNATIONAL ROYAN TWIN CONGRESS ON REPRODUCTIVE BIOMEDICINE & STEM CELLS BIOLOGY & TECHNOLOGY

SEPTEMBER 3RD TO 5TH IRAN / TEHRAN GENETICS

Royan International Twin Congress is a forum only for the scientists, researchers and practitioners to exchange and share their knowledge and ideas. Therefore, all participants are appreciated for respecting the non-political atmosphere of the congress.
Contact: Leila Daliri, M.Sc. , Congress Secretariat Executive Manager , Royan Institute
Phone: 011-98-21-2356-2756 Fax: 011-98-21-2356-2178
Email: info@royancongress.com
http://www.royancongress.com/index.aspx

Asia

8TH ANNUAL CONFERENCE OF INTERNATIONAL LIVER CANCER ASSOCIATION (ILCA)

SEPTEMBER 5TH TO 7TH JAPAN / KYOTO GASTROENTEROLOGY, ONCOLOGY

LCA is honoured to be bringing its 8th Annual Conference to beautiful Kyoto, and to give liver cancer experts in all discipline the opportunity to exchange the latest basic and clinical science through transversal and multidisciplinary approach to the field of liver cancer. The multidisciplinary programs of ILCA 2014 will feature:

- State-of-the-Art Lectures offered by distinguished colleagues within the field
- Symposia focusing on the cutting edge advancements on the research and treatment levels, incorporating a truly international panel of speakers
- General Sessions and e-Poster Viewing Tours that will deliver the latest breaking research from among the abstracts submitted to the conference
- Luncheon Workshops offered by the most knowledgeable HCC experts in highly interactive sessions
- Industry Exhibition
- Networking Breaks and Reception
- Simultaneous Translation (English to Japanese)
- Plus! Consensus Workshop on Clinical Trial Design

Contact: ILCA
Phone: 011-32-2-789-2345 Fax: 011-32-2-743-1550
Email: info@ilca-online.org
http://www.ilca2014.org/

Asia

2014 TISSUE ENGINEERING INTERNATIONAL REGENERATIVE MEDICINE SOCIETY (TERMIS) ASIA PACIFIC

SEPTEMBER 24TH TO 27TH SOUTH KOREA / DAEGU GENETICS, OTHER SPECIALTIES

TERMIS-AP has positioned itself as a premier conference in the rapidly growing field of Regenerative Medicine. TERMIS-AP 2014 consists of various themes to provide a comprehensive coverage of diverse topics on current regenerative medicine under a main theme of .Transformation for future healthcare.. It will be a great honor for us to have you on the TERMIS-AP 2014, and your participation will definitely grace the conference.
TERMIS-AP 2014 will be an excellent stage to interact among the participants and lead to a fruitful interdisciplinary discussion. We will feature many opportunities to enhance interactions between students, academics and professionals from around the globe. In addition, it will provide a well-balanced program that includes special sessions in concert with both traditional and core topics. We welcome proposals of special topics that reflect recent and regional interests; these should be suggested at an early stage in the development of the technical program.
Contact: , TERMIS-AP 2014 Secretariat
Phone: 011-82-53-746-9969 Fax: 011-82-53-742-9007
Email: info@termis-ap2014.org
http://www.termis.org/

Asia

2014 WORLD CONGRESS OF INTERNAL MEDICINE (WCIM 2014)

SEPTEMBER 24TH TO 27TH SOUTH OCTOBER 24TH TO 28TH SOUTH KOREA / SEOUL INTERNAL MEDICINE

Join 32nd World Congress of Internal Medicine 2014 in Seoul, South Korea. The congress will be held in COEX (Convention and Exhibition Center), Seoul from October 24th to 28th. Through this course, you will extend multidisciplinary collaboration, share cutting-edge technologies, encourage young professionals, create a new paradigm and bridge the gap between advanced and less developed nations, subsequently leading the world health policy into the right path.
Contact: Secretariat, WCIM 2014
Phone: 011-82-2-566-2229 Fax: 011-82-2-6254-8049
Email: wcim2014@intercom.co.kr
http://www.wcim2014.org/

BRIEF SUMMARY

ESOMEPRAZOLE STRONTIUM

delayed-release capsules 49.3 mg

For oral use only

Rx Only

BRIEF SUMMARY of Prescribing Information

INDICATIONS AND USAGE

Treatment of GERD in Adults: Esomeprazole strontium is indicated for the short-term treatment (4 to 8 weeks) for healing and symptomatic resolution and maintenance (controlled studies do not extend beyond 6 months) of confirmed erosive esophagitis (EE), the short-term treatment (4 to 8 weeks) of heartburn and other symptoms associated with GERD in adults. **Risk Reduction of NSAID-Associated Gastric Ulcer in Adults, *H. pylori* Eradication to Reduce the Risk of Duodenal Ulcer Recurrence in Adults, and Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome in Adults.**

CONTRAINDICATIONS

Esomeprazole strontium is contraindicated in patients with known hypersensitivity to proton pump inhibitors (PPIs). Hypersensitivity reactions, e.g., angioedema and anaphylactic shock, have been reported with esomeprazole use. For information about contraindications of antibacterial agents (clarithromycin and amoxicillin) indicated in combination with esomeprazole strontium, refer to the **CONTRAINDICATIONS** section of their package inserts.

WARNINGS AND PRECAUTIONS

Concurrent Gastric Malignancy: Symptomatic response to therapy with esomeprazole strontium does not preclude the presence of gastric malignancy.

Atrophic Gastritis: Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole, of which esomeprazole is an enantiomer.

***Clostridium difficile* Associated Diarrhea:** Published observational studies suggest that PPI therapy like esomeprazole strontium may be associated with an increased risk of *Clostridium difficile* associated diarrhea. This diagnosis should be considered for diarrhea that does not improve. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. *Clostridium difficile* associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents. For more information specific to antibacterial agents (clarithromycin and amoxicillin) indicated for use in combination with esomeprazole strontium, refer to **WARNINGS** and **PRECAUTIONS** sections of those package inserts.

Interaction with Clopidogrel: Avoid concomitant use of esomeprazole strontium with clopidogrel. Clopidogrel is a prodrug. Inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. The metabolism of clopidogrel to its active metabolite can be impaired by use with concomitant medications, such as esomeprazole, that inhibit CYP2C19 activity. Concomitant use of clopidogrel with 40 mg esomeprazole reduces the pharmacological activity of clopidogrel. When using esomeprazole strontium, consider alternative anti-platelet therapy.

Bone Fracture: Several published observational studies suggest that PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines.

Hypomagnesemia: Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI. For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.

Concomitant Use of esomeprazole strontium with St. John's Wort or Rifampin: Drugs which induce CYP2C19 or CYP3A4 (such as St. John's Wort or rifampin) can substantially decrease esomeprazole concentrations. Avoid concomitant use of esomeprazole strontium with St. John's Wort or rifampin.

Interactions with Diagnostic Investigations for Neuroendocrine Tumors: Serum chromogranin A (CgA) levels increase secondary to drug-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumors. Providers should temporarily stop esomeprazole treatment before assessing CgA levels and consider repeating the test if initial CgA levels are high. If serial tests are performed (e.g., for monitoring), the same commercial laboratory should be used for testing, as reference ranges between tests may vary.

Concomitant Use of esomeprazole strontium with Methotrexate: Literature suggests that concomitant use of PPIs with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration a temporary withdrawal of the PPI may be considered in some patients.

ADVERSE REACTIONS

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of esomeprazole strontium has been established from adequate and well-controlled studies of esomeprazole magnesium.

Adults: The safety of esomeprazole magnesium was evaluated in over 15,000 patients (aged 18 to 84 years) in clinical trials worldwide including over 8,500 patients in the United States and over 6,500 patients in Europe and Canada. Over 2,900 patients were treated in long-term studies for up to 6-12 months. In general, esomeprazole magnesium was well tolerated in both short and long-term clinical trials.

The safety in the treatment of healing of erosive esophagitis was assessed in 4 randomized comparative clinical trials, which included 1,240 patients on 22.3 mg of esomeprazole magnesium (equivalent to 20 mg of esomeprazole), 2,434 patients on 44.6 mg of esomeprazole magnesium (equivalent to 40 mg of esomeprazole), and 3,008 patients on 20 mg of omeprazole daily. The most frequently occurring adverse reactions (≥1%) in all three groups were headache (5.5%, 5%, and 3.8%, respectively) and diarrhea (no difference among the three groups). Nausea, flatulence, abdominal pain, constipation, and dry mouth occurred at similar rates among patients taking esomeprazole magnesium or omeprazole. Additional adverse reactions that were reported as possibly or probably related to esomeprazole magnesium with an incidence <1% are listed below by body system:

Body as a Whole: abdomen enlarged, allergic reaction, asthenia, back pain, chest pain, substernal chest pain, facial edema, peripheral edema, hot flushes, fatigue, fever, flu-like disorder, generalized edema, leg edema, malaise, pain, rigors; **Cardiovascular:** flushing, hypertension, tachycardia; **Endocrine:** goiter; **Gastrointestinal:** bowel irregularity, constipation aggravated, dyspepsia, dysphagia, dysplasia GI, epigastric pain, eructation, esophageal disorder, frequent stools, gastroenteritis, GI hemorrhage, GI symptoms not otherwise specified, hiccup, melena, mouth disorder, pharynx disorder, rectal disorder, serum gastrin increased, tongue disorder, tongue edema, ulcerative stomatitis, vomiting; **Hearing:** earache, tinnitus; **Hematologic:** anemia, anemia hypochromic, cervical lymphadenopathy, epistaxis, leukocytosis, leukopenia, thrombocytopenia; **Hepatic:** bilirubinemia, hepatic function abnormal, SGOT increased, SGPT increased; **Metabolic/Nutritional:** glycosuria, hyperuricemia, hyponatremia, increased alkaline phosphatase, thirst, vitamin B12 deficiency, weight increase, weight decrease; **Musculoskeletal:** arthralgia, arthritis aggravated, arthropathy, cramps, fibromyalgia syndrome, hernia, polymyalgia rheumatica; **Nervous System/Psychiatric:** anorexia, apathy, appetite increased, confusion, depression aggravated, dizziness, hypertonia, nervousness, hypoesthesia, impotence, insomnia, migraine, migraine aggravated, paresthesia, sleep disorder, somnolence, tremor, vertigo, visual field defect; **Reproductive:** dysmenorrhea, menstrual disorder, vaginitis; **Respiratory:** asthma aggravated, coughing, dyspnea, larynx edema, pharyngitis, rhinitis, sinusitis; **Skin/Appendages:** acne, angioedema, dermatitis, pruritus, pruritus ani, rash, rash erythematous, rash maculo-papular, skin inflammation, sweating increased, urticaria; **Special Senses:** otitis media, parosmia, taste loss, taste perversion; **Urogenital:** abnormal urine, albuminuria, cystitis, dysuria, fungal infection, hematuria, micturition frequency, moniliasis, genital moniliasis, polyuria; **Visual:** conjunctivitis, vision abnormal.

Endoscopic findings that were reported as adverse reactions include: duodenitis, esophagitis, esophageal stricture, esophageal ulceration, esophageal varices, gastric ulcer, gastritis, hernia, benign polyps or nodules, Barrett's esophagus, and mucosal discoloration.

In two placebo-controlled studies, 710 patients were treated symptomatic GERD and the most common adverse reactions possibly or probably related to esomeprazole magnesium were diarrhea (4.3%), headache (3.8%), and abdominal pain (3.8%). **Combination Treatment with Amoxicillin and Clarithromycin:** In clinical trials using combination therapy with esomeprazole magnesium plus amoxicillin and clarithromycin, no additional adverse reactions specific to these drug combinations were observed. Adverse reactions that occurred were limited to those observed when using esomeprazole magnesium, amoxicillin, or clarithromycin alone. The most frequently reported drug-related adverse reactions for patients who received triple therapy for 10 days were diarrhea (9.2%), taste perversion (6.6%), and abdominal pain (3.7%). No treatment-emergent adverse reactions were observed at higher rates with triple therapy than were observed with esomeprazole magnesium alone. For more information on adverse reactions with amoxicillin or clarithromycin, see their package inserts, refer to **ADVERSE REACTIONS** sections.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of esomeprazole magnesium. Because these 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. These reports are listed below by body system: **Blood and Lymphatic:** agranulocytosis, pancytopenia; **Eye:** blurred vision; **Gastrointestinal:** pancreatitis, stomatitis, microscopic colitis; **Hepatobiliary:** hepatic failure, hepatitis with or without jaundice; **Immune System:** anaphylactic reaction/shock; **Infections and Infestations:** GI candidiasis; *Clostridium difficile* associated diarrhea; **Metabolism and nutritional disorders:** hypomagnesemia; **Musculoskeletal and Connective Tissue:** muscular weakness, myalgia, bone fracture; **Nervous System:** hepatic encephalopathy, taste disturbance; **Psychiatric:** aggression, agitation, depression, hallucination; **Renal and Urinary:** interstitial nephritis; **Reproductive System and Breast:** gynecomastia; **Respiratory, Thoracic, and Mediastinal:** bronchospasm; **Skin and Subcutaneous Tissue:** alopecia, erythema multiforme, hyperhidrosis, photosensitivity, Stevens-Johnson syndrome, toxic epidermal necrolysis (some fatal).

DRUG INTERACTIONS

Interference with Antiretroviral Therapy: Concomitant use of atazanavir and nelfinavir with PPIs is not recommended. Coadministration of atazanavir with PPIs is expected to substantially decrease atazanavir plasma concentrations and may result in a loss of therapeutic effect and the development of drug resistance. Coadministration of saquinavir with PPIs is expected to increase saquinavir concentrations, which may increase toxicity and require dose reduction. Omeprazole, of which esomeprazole is an enantiomer, has been reported to interact with some antiretroviral drugs. The clinical importance and the mechanisms behind these interactions are not always known. Increased gastric pH during omeprazole treatment may change the absorption of the antiretroviral drug. Other possible interaction mechanisms are via CYP2C19. *Reduced concentrations of atazanavir and nelfinavir:* For some antiretroviral drugs, such as atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole. Following multiple doses of nelfinavir (1250 mg, twice daily) and omeprazole (40 mg daily), AUC was decreased by 36% and 92%, C_{max} by 37% and 89% and C_{min} by 39% and 75%, respectively for nelfinavir and M8. Following multiple doses of atazanavir (400 mg, daily) and omeprazole (40 mg, daily, 2 hr before atazanavir), AUC was decreased by 94%, C_{max} by 96%, and C_{min} by 95%. Concomitant administration with omeprazole and drugs such as atazanavir and nelfinavir is therefore not recommended. *Increased concentrations of saquinavir:* For other antiretroviral drugs, such as saquinavir, elevated serum levels have been reported, with an increase in AUC by 82%, in C_{max} by 75%, and in C_{min} by 106%, following multiple dosing of saquinavir/ritonavir (1000/100 mg) twice daily for 15 days with omeprazole 40 mg daily coadministered days 11 to 15. Clinical and laboratory monitoring for saquinavir toxicity is recommended during concurrent use with esomeprazole. Dose reduction of saquinavir should be considered from the safety perspective for individual patients.

Drugs for Which Gastric pH Can Affect Bioavailability: Esomeprazole inhibits gastric acid secretion. Therefore, esomeprazole may interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (e.g. ketoconazole, atazanavir, iron salts, and erlotinib can decrease, while the absorption of drugs such as digoxin can increase during treatment with esomeprazole. Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects increased the bioavailability of digoxin by 10% (30% in two subjects). Esomeprazole is an enantiomer of omeprazole. Coadministration of digoxin with esomeprazole is expected to increase the systemic exposure of digoxin. Patients may need to be monitored when digoxin is taken concomitantly with esomeprazole.

Effects on Hepatic Metabolism/Cytochrome P-450 Pathways: Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. *In vitro* and *in vivo* studies have shown that esomeprazole is not likely to inhibit CYPs 1A2, 2A6, 2C9, 2D6, 2E1, and 3A4. No clinically relevant interactions with drugs metabolized by these CYP enzymes would be expected. Drug interaction studies have shown that esomeprazole does not have any clinically significant interactions with phenytoin, quinidine, clarithromycin, or amoxicillin. Although drug interaction studies have not shown that esomeprazole has a clinically significant interaction with warfarin, post-marketing reports of changes in prothrombin measures have been received among patients on concomitant warfarin and esomeprazole therapy. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with PPIs and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time. Esomeprazole may potentially interfere with CYP2C19, the major esomeprazole metabolizing enzyme. Coadministration of esomeprazole 30 mg and diazepam, a CYP2C19 substrate, resulted in a 45% decrease in clearance of diazepam. Clopidogrel is metabolized to its active metabolite in part by CYP2C19. Concomitant use of esomeprazole 40 mg results in reduced plasma concentrations of the active metabolite of clopidogrel and a reduction in platelet inhibition. Avoid concomitant administration of esomeprazole strontium with clopidogrel. When using esomeprazole strontium, consider use of alternative anti-platelet therapy. Omeprazole acts as an inhibitor of CYP2C19. Omeprazole, given in doses of 40 mg daily for one week to 20 healthy subjects in a cross-over study, increased C_{max} and AUC of cilostazol by 18% and 26% respectively. C_{max} and AUC of one of its active metabolites, 3,4-dihydrocilostazol, which has 4-7 times the activity of cilostazol, were increased by 29% and 69% respectively. Coadministration of cilostazol with esomeprazole is expected to increase concentrations of cilostazol and its above mentioned active metabolite. A dose reduction of cilostazol from 100 mg twice daily to 50 mg twice daily should be considered. Concomitant administration of esomeprazole and a combined inhibitor of CYP2C19 and CYP3A4, such as voriconazole, may result in more than doubling of the esomeprazole exposure. Dose adjustment of esomeprazole is not normally required. However, in patients with Zollinger-Ellison's Syndrome, who may require higher doses up to 240 mg/day, dose adjustment may be considered. Drugs known to induce CYP2C19 or CYP3A4 or both (such as rifampin) may lead to decreased esomeprazole serum levels. Omeprazole, of which esomeprazole is an enantiomer, has been reported to interact with St. John's Wort, an inducer of CYP3A4. In a cross-over study in 12 healthy male subjects, St. John's Wort (300 mg three times daily for 14 days) significantly decreased the systemic exposure of omeprazole in CYP2C19 poor metabolisers (C_{max} and AUC decreased by 37.5% and 37.9%, respectively) and extensive metabolisers (C_{max} and AUC decreased by 49.6 % and 43.9%, respectively). Avoid concomitant use of St. John's Wort or rifampin with esomeprazole strontium.

Interactions with Investigations of Neuroendocrine Tumors: Drug-induced decrease in gastric acidity results in enterochromaffin-like cell hyperplasia and increased Chromogranin A levels, which may interfere with investigations for neuroendocrine tumors.

Tacrolimus: Concomitant administration of esomeprazole and tacrolimus may increase the serum levels of tacrolimus.

Combination Therapy with Clarithromycin: Coadministration of esomeprazole, clarithromycin, and amoxicillin has resulted in increases in the plasma levels of esomeprazole and 14-hydroxyclarithromycin. Concomitant administration of clarithromycin with other drugs can lead to serious adverse reactions due to drug interactions [see **WARNINGS** and **PRECAUTIONS** in prescribing information for clarithromycin]. Because of these drug interactions, clarithromycin is contraindicated for coadministration with certain drugs [see **CONTRAINDICATIONS** in prescribing information for clarithromycin].

Methotrexate: Case reports, published population pharmacokinetic studies, and retrospective analyses suggest that concomitant administration of PPIs and methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate. However, no formal drug interaction studies of methotrexate with PPIs have been conducted.

SPECIFIC POPULATIONS

Pregnancy: ***Pregnancy Category C:*** There are no adequate and well controlled studies of esomeprazole strontium delayed-release capsules in pregnant women. Teratogenicity was not observed in an embryofetal developmental study in rats with either esomeprazole strontium or esomeprazole magnesium at equimolar oral doses up to 280 mg esomeprazole/kg/day (about 57 times the daily maximum recommended human dose (MRHD) of 40 mg on a body surface area basis). When administered as either the strontium or magnesium salt, changes in bone morphology and physeal dysplasia were observed in pre- and postnatal developmental toxicity studies in rats at doses equal to or greater than 138 mg esomeprazole/kg/day (approximately 33.6 times the daily MRHD of 40 mg on a body surface area basis). Because of the observed effect at the high doses of esomeprazole strontium on developing bone in rat studies, esomeprazole strontium should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Limited published data indicate that esomeprazole and strontium are present in human milk. Because of the effect of esomeprazole strontium observed at high doses on developing bone in rat studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: The safety and effectiveness of esomeprazole strontium delayed-release capsules have not been established in pediatric patients. Strontium is known to compete with calcium for intestinal absorption and is incorporated into bone. Use in pediatric patients is not recommended because adequate safety studies have not been performed.

Geriatric Use: No overall differences in safety and efficacy were observed between the elderly and younger individuals, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Use in Patients with Renal Impairment: No dosage adjustment is necessary in patients with mild to moderate renal impairment. The pharmacokinetics and safety of strontium in patients with severe renal impairment has not been studied and, therefore, use in this patient population is not recommended.

OVERDOSAGE

A single oral dose of esomeprazole at 510 mg/kg (about 103 times the human dose on a body surface area basis), was lethal to rats. The major signs of acute toxicity were reduced motor activity, changes in respiratory frequency, tremor, ataxia, and intermittent clonic convulsions. The symptoms described in connection with deliberate esomeprazole overdose (limited experience of doses in excess of 240 mg/day) are transient. Single doses of 80 mg of esomeprazole were uneventful. Reports of overdosage with omeprazole in humans may also be relevant. Doses ranged up to 2,400 mg (120 times the usual recommended clinical dose). Manifestations were variable, but included confusion, drowsiness, blurred vision, tachycardia, nausea, diaphoresis, flushing, headache, dry mouth, and other adverse reactions similar to those seen in normal clinical experience (see omeprazole package insert - **ADVERSE REACTIONS**). No specific antidote for esomeprazole is known. Since esomeprazole is extensively protein bound, it is not expected to be removed by dialysis. In the event of overdosage, treatment should be symptomatic and supportive. As with the management of any overdose, the possibility of multiple drug ingestion should be considered. For current information on treatment of any drug overdose contact a Poison Control Center at 1-800-222-1222.

Please see package insert for full prescribing information.

More detailed information is available upon request.
For more information about esomeprazole strontium contact:
Amneal Pharmaceuticals at 1-877-835-5472.
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WKMJ
WORLD KOREAN MEDICAL JOURNAL

World Korean Medical Journal (WKMJ) is a bi-monthly journal, which better support the community. WKMJ introduces the emerging issues and new trends of healthcare industry while also providing the best therapeutic products and medical devices available in the US market. WKMJ is delivered throughout 11 countries in the world: Korea, Brazil, China, Japan, Paraguay, Canada, Australia, Singapore, UK, France and Germany

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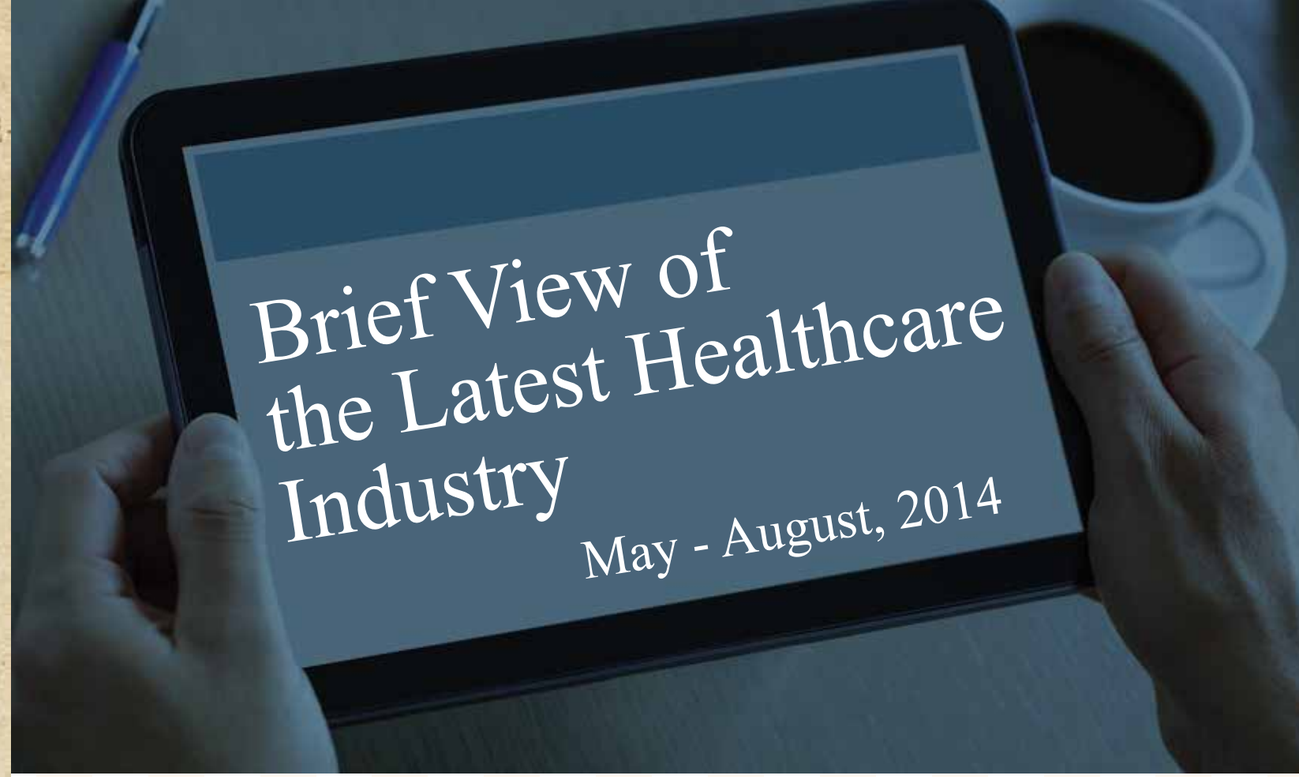

June

1) Ipca and Oncobiologics Create Strategic Biosimilars Partnership

Ipca Laboratories Ltd., India and Oncobiologics, Inc., USA announced today the creation of a two-part alliance for the development, manufacture and commercialization of biosimilar monoclonal antibody products. Under the first part of the agreement, Ipca will in-license and commercialize biosimilar products for the India and associated markets. These products will be developed by Oncobiologics to US FDA and EU regulatory standards for global commercialization. Initial manufacturing will occur in the USA by Oncobiologics and later by Ipca in India.
http://www.pharmpro.com/news/2014/06/ipca-and-oncobiologics-create-strategic-biosimilars-partnership

2) Cheap Drug Greatly Boosts Prostate Cancer Survival

A cheap, decades-old chemotherapy drug extended life by more than a year when added to standard hormone therapy for men whose prostate cancer has widely spread, doctors reported Sunday.
Men who received docetaxel, sold as Taxotere and in generic form, lived nearly 58 months versus 44 months for those not given the drug, a major study found.
http://www.pharmpro.com/news/2014/06/cheap-drug-greatly-boosts-prostate-cancer-survival

3) Worldwide Pharma Industry Marketing Investment Flat in 2013

Cegedim Strategic Data (CSD) has released results on pharmaceutical marketing investments for full year 2013.
Worldwide, industry investment in pharmaceuticals sales force and marketing channels remained flat in 2013, at just under [Eur]85 billion constant US dollars. Notably, the leading 10 multinationals ranked by promotional expenditure, all reduced investment during the 12 months to December 2013.
http://www.pharmpro.com/news/2014/06/worldwide-pharma-industry-marketing-investment-flat-2013

June

16) Ranbaxy Decision Shows Why FDA Reluctant to Rely on European Inspections

The European Medicines Agency (EMA) Thursday said it was lifting a ban on a Ranbaxy Laboratories plant in India whose products the FDA also has banned and is not ready to accept.
http://www.fiercepharma.com/story/ranbaxy-decision-shows-why-fda-reluctant-rely-european-inspections/2014-06-06

17) FDA Panel Advises Against More Clinical Trials for Opioid Constipation Drugs

An FDA panel advised the agency against requiring more large clinical studies for the cardiovascular risks of drugs that treat opioid-induced constipation, relieving drugmakers like AstraZeneca ($AZN), Salix Pharmaceuticals ($SLX) and others from bearing the burden of further clinical safety trials.
http://www.fiercepharma.com/story/fda-panel-advises-against-more-clinical-trials-opioid-constipation-drugs/2014-06-12

18) After 4-year Benicar Review, FDA Slaps Aside Heart-Risk Worries

The FDA finally wrapped up its review of Benicar safety. After four years of sifting data, the agency says it found “no clear evidence” that Daiichi Sankyo’s blockbuster blood pressure drug increased the risk of heart attack. But the agency will require new safety-related data on Benicar’s official label.
http://www.fiercepharma.com/story/after-4-year-benicar-review-fda-slaps-aside-heart-risk-worries/2014-06-25

19) Researchers Link Brain Gene to Kidney Cancer

A gene known to control brain growth and development is heavily involved in promoting clear cell renal cell carcinoma, the most common form of kidney cancer, researchers from Mayo Clinic in Florida are reporting.
http://www.dddmag.com/news/2014/06/researchers-link-brain-gene-kidney-cancer

July

1) FDA Outlines Expectations for Drug Compounders, Including Outsourcing Facilities

The U.S. Food and Drug Administration issued several policy documents regarding compounded drug products for human use, as part of the agency’s continuing effort to implement the compounding provisions of the Drug Quality and Security Act (DQSA), enacted in November 2013. The policy documents consist of a draft interim guidance, a proposed rule, a final guidance, and two revised requests for nominations for the bulk drug substances lists.
http://www.pharmpro.com/news/2014/07/fda-outlines-expectations-drug-compounders-including-outsourcing-facilities

2) Hospira Completes Acquisition of Orchid’s API Manufacturing and R&D Facility

Hospira has completed the acquisition of an active pharmaceutical ingredient (API) manufacturing facility and an associated research and development (R&D) facility from Orchid Chemicals & Pharmaceuticals Ltd., an Indian pharmaceuticals company, for approximately $218 million, after settling prior advances of approximately $30 million.
http://www.pharmpro.com/news/2014/07/hospira-completes-acquisition-orchids-api-manufacturing-and-r-d-facility

3) Missouri Governor Vetoes Health Navigator Limits

Missouri Gov. Jay Nixon vetoed legislation Monday that would have limited who could work in the state as a health insurance guide and blamed a national conservative group for injecting an error into the model legislation.
http://www.pharmpro.com/news/2014/07/missouri-governor-vetoes-health-navigator-limits

4) WHO: Basic Hygiene Can Help Prevent MERS Spread

A World Health Organization official on Thursday urged millions of Muslims making the pilgrimage to Mecca, Saudi Arabia, to exercise basic hygiene as mass gatherings pose risks of spreading the Middle East respiratory syndrome.
http://www.pharmpro.com/news/2014/07/who-basic-hygiene-can-help-prevent-mers-spread

5) Salix Pharmaceuticals to Combine with Cosmo Technologies to Form Salix Pharmaceuticals, plc

Salix Pharmaceuticals, Ltd. and Cosmo Pharmaceuticals S.p.A. today announced a definitive merger agreement under which Salix will combine with Cosmo Technologies Limited (“Cosmo Tech”), a subsidiary of Cosmo. Under the terms of the agreement, Salix will become a wholly-owned subsidiary of Irish domiciled Cosmo Tech.
http://www.pharmpro.com/news/2014/07/salix-pharmaceuticals-combine-cosmo-technologies-form-salix-pharmaceuticals-plc

6) Compounding Pharmacy Oversight Changes Signed

Gov. Deval Patrick on Thursday signed a law he said would address a “gray area” between state and federal oversight of the pharmacies.
The measure includes new licensing and labeling requirements and steps up fines for violations of state rules.
It also reorganizes the board that oversees pharmacies and requires the board’s inspectors to be trained in sterile and non-sterile compounding practices.
http://www.pharmpro.com/news/2014/07/compounding-pharmacy-oversight-changes-signed

July

7) Galderma Finalizes Major Expansion in Aesthetic and Corrective Dermatology in the U.S. and Canada

Galderma S.A. announced that it has gained full rights to distribute Restylane, Perlane, Emervel, Sculptra and Dysport from Valeant Pharmaceuticals International, Inc. The expansion into aesthetic and corrective dermatology in the U.S. and Canada completes Galderma's global skin health footprint and extends its leadership in aesthetic medicine worldwide.
http://www.pharmpro.com/news/2014/07/galderma-finalizes-major-expansion-aesthetic-and-corrective-dermatology-us-and-canada

8) FDA Designates Opioid Overdose Treatment for Fast Track Development Program

The Fast Track program of the FDA is designed to expedite the development and review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. Fast Track-designated drugs ordinarily qualify for priority review, thereby expediting the FDA review process. AntiOp and the FDA may also be able to employ additional tools to expedite the FDA review process such as "rolling submission," whereby AntiOp may submit portions of the new drug application (NDA) in a staged NDA submission process.
http://www.pharmpro.com/news/2014/07/fda-designates-opioid-overdose-treatment-fast-track-development-program

9) Anthera Pharmaceuticals Acquires Sollpur for Exocrine Pancreatic Insufficiency From Eli Lilly

Anthera Pharmaceuticals today announced that it has acquired Sollpura (liprotamase), a novel investigational Pancreatic Enzyme Replacement Therapy ("PERT") from Eli Lilly and Company.
http://www.pharmpro.com/news/2014/07/anthera-pharmaceuticals-acquires-sollpur-exocrine-pancreatic-insufficiency-eli-lilly

10) LEO Pharma and KLOX Technologies Strike Global Dermatology Deal

LEO Pharma A/S and KLOX Technologies Inc. (KLOX) have entered into a worldwide license and joint venture agreement, excluding Canada, to further develop and commercialize KLOX's BioPhotonic technology platform in dermatology, which includes a CE approved treatment for moderate to severe acne. LEO Pharma will also make an equity investment in KLOX.
http://www.pharmpro.com/news/2014/07/leo-pharma-and-klox-technologies-strike-global-dermatology-deal

11) FDA Weighs Cancer Risk of Fibroid Removal Devices

Surgeons developed the technique as an alternative to traditional surgery, which requires a larger incision that often results in more bleeding and longer hospital stays. But the FDA convened a two-day meeting this week after concluding that the risk of accidentally spreading undetected cancer to other organs may be far more common than previously thought.
http://www.pharmpro.com/news/2014/07/fda-weighs-cancer-risk-fibroid-removal-devices

12) Chiltern Acquires Ockham - Companies Merge Operations

Chiltern and Ockham, two full-service contract research organizations (CROs), today announce that Chiltern has acquired 100% of Ockham and that the companies will merge their operations.
http://www.pharmpro.com/news/2014/07/chiltern-acquires-ockham-companies-merge-operations

July

13) CDC Director Admits Safety Problems at Germ Labssourcing Facilities

He director of the Centers for Disease Control and Prevention acknowledged Wednesday that systemic safety problems have for years plagued federal public health laboratories that handle dangerous germs such as anthrax and bird flu..
http://www.pharmpro.com/news/2014/07/cdc-director-admits-safety-problems-germ-labs

14) Teva Completes Acquisition of Labrys

The acquisition of Labrys brings to Teva LBR-101, a fully humanized monoclonal antibody that binds to calcitonin gene-related peptide (CGRP), which is currently in Phase IIb clinical trials for prevention of chronic and episodic migraine. Teva's acquisition of LBR-101 complements the recent acquisition of ZECUITY ®, a novel iontophoretic patch that delivers sumatriptan via the skin for the acute treatment of migraine, and positions Teva to compete for leadership in the treatment and prevention of migraine.
http://www.pharmpro.com/news/2014/07/teva-completes-acquisition-labrys

15) FDA Warns of Compounded Drug Recall by Texas Firm

The agency says FDA inspectors recently uncovered unsanitary conditions at Unique Pharmaceuticals' plant in Temple, Texas. The inspections revealed production problems in several lots of drugs that were supposed to be sterile.
http://www.pharmpro.com/news/2014/07/fda-warns-compounded-drug-recall-texas-firm

16) Agents Get Subsidized 'Obamacare' Using Fake IDs

Undercover investigators using fake identities were able to secure taxpayer-subsidized health insurance under President Barack Obama's health care law.
http://www.pharmpro.com/news/2014/07/agents-get-subsidized-obamacare-using-fake-ids

17) Study: 10M Have Gained Coverage Through Health Law

A new study estimates that more than 10 million adults gained health insurance by midyear as the coverage expansion under President Barack Obama's law took hold in much of the country.
http://www.pharmpro.com/news/2014/07/study-10m-have-gained-coverage-through-health-law

18) Obama Wants Limits on US Company Mergers Abroad

Staking out a populist stand ahead of the midterm elections, President Barack Obama on Thursday demanded "economic patriotism" from U.S. corporations that use legal means to avoid U.S. taxes through overseas mergers.
http://www.pharmpro.com/news/2014/07/obama-wants-limits-us-company-mergers-abroad-0

19) FDA Gives OK to Purdue Pharma's Targiniq ER

The Food and Drug Administration has approved Purdue Pharma's Targiniq ER, an opioid painkiller with abuse-deterrent properties.
The FDA said Wednesday that Targiniq ER (oxycodone hydrochloride and naloxone hydrochloride extended-release tablets) is the second extended-release/long-acting opioid analgesic with approved labeling describing its abuse-deterrent capabilities.
http://www.chaindrugreview.com/suppliernews-archives/2014-07-21/fda-gives-ok-to-purdue-pharmas-targiniq-er

July

20) Metastatic Brain Tumor Treatment Could Be on the Horizon

A new Cincinnati Cancer Center (CCC) study, published in the advance online edition of the journal Oncotarget, provides hope that previously studied SapC-DOPS could be used for treatment of brain cancer that has spread.
http://www.dddmag.com/news/2014/07/metastatic-brain-tumor-treatment-could-be-horizon

21) EU Regulator: Morning-After Pill OK for All Women

A commonly used morning-after pill is suitable for use by heavier women, the European Medicines Agency said Thursday after a review of the evidence sparked by the French manufacturer's declaration that the drugs didn't work in women weighing more than 80 kilograms (176 pounds).
http://www.dddmag.com/news/2014/07/eu-regulator-morning-after-pill-ok-all-women

22) FDA Approves Malignant Hyperthermia Drug

U.S. Food and Drug Administration (FDA) has approved Ryanodex (dantrolene sodium) for injectable suspension indicated for the treatment of malignant hyperthermia (MH), along with the appropriate supportive measures. MH is an inherited and potentially fatal disorder triggered by certain anesthesia agents in genetically susceptible individuals.
http://www.dddmag.com/news/2014/07/fda-approves-malignant-hyperthermia-drug

23) Reoviruses: The Discovery of Their Potential in Cancer Therapeutics

Reoviruses are benign viruses with an important property: they are oncolytic, meaning they are capable of infecting and destroying many kinds of cancer cells. The story of how this discovery was made is an exciting one.
http://www.dddmag.com/articles/2014/07/reoviruses-discovery-their-potential-cancer-therapeutics

24) Roche Buying Seragon for Up to $1.7B

Roche Holding AG said its U.S.-based biotech company Genentech has agreed to acquire American biotechnology firm Seragon Pharmaceuticals Inc. for up to $1.725 billion in cash and contingency payments.
http://www.dddmag.com/news/2014/07/roche-buying-seragon-17b

25) House Passes Bill to Speed FDA's Sunscreen Approvals

The House passed legislation Monday to require the Food and Drug Administration to speed approval of new types of sunscreen in the wake of a regulatory backlog that has stalled their introduction.
http://www.skinandallergynews.com/news/news/single-article/house-votes-to-speed-sunscreen-approvals/66eb81090b9f2782c98d3d99ee997307.html

August

1) Johnson & Johnson Recalls Laparoscopic Surgery Power Morcellators

Johnson & Johnson's Ethicon division, the manufacturer of laparoscopic power morcellators, announced that it is recalling all of the devices they have manufactured. According to news reports, J&J is getting out of the power morcellator business. Doctors and hospitals have expressed concerns about the risk of laparoscopic power morcellators spreading cancer during laparoscopic uterine fibroid removal.
http://fortworth.legalexaminer.com/medical-devices-implants/johnson-johnson-recalls-laparoscopic-surgery-power-morcellators/

2) U.S. Ebola Virus Patient Being Treated in Atlanta Faces Crucial Days

An American infected with Ebola in Liberia was being treated and monitored in the U.S. on Sunday, as doctors worked to provide care in what will be a crucial few days in his attempt to recover from the deadly disease.
http://online.wsj.com/articles/cdc-chief-seeks-to-allay-ebola-fears-1407081530

3) Low T Side Effects Androderm Patch Death Lawsuit

The family of Alvin Harris, from Virginia has recently filed a wrongful death lawsuit against Androderm patch manufacturers. The plaintiffs claim that warnings about the risk of heart attacks, strokes and blood clots side effects with the testosterone replacement therapy were insufficient.
http://fortworth.legalexaminer.com/fda-prescription-drugs/low-t-side-effects-androderm-patch-death-lawsuit/


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