April 2017 - ISSUE 13

# WKMJ

World Korean Medical Journal

## Cover Story
## Inspirational Korean Healthcare Leader

Dr. Larry Kwak, Vice President of Translational Research & Developmental Therapeutics at City of Hope National Medical Center

## Entrepreneur Interview

Mario Pennisi, Chief Executive Officer at Life Sciences Queensland

## Biopharmaceutical Report

Legislation to Force Payer Coverage of Abuse-Deterrent Opioids Faces Resistance

Western CAR-Ts Face Chinese Development Hurdles Due to Regulatory Uncertainty

# HOLY NAME MEDICAL CENTER

IT'S NOT JUST OUR JOB TO SERVE EVERY MEMBER OF OUR COMMUNITY.
IT'S OUR MISSION.

1,000 PHYSICIANS
LEADING-EDGE MEDICAL & SURGICAL SPECIALTIES
CULTURALLY SENSITIVE, COMPASSIONATE CARE

EMERGENCY CARE CENTER • REGIONAL CANCER CENTER • CARDIAC AND STROKE CARE
MINIMALLY INVASIVE SURGERY • BREAST CENTER • ASIAN LIVER CENTER
ASIAN DIABETES CENTER • DIALYSIS CENTER • INPATIENT SERVICES
CENTER FOR SLEEP MEDICINE • CENTER FOR PHYSICAL REHABILITATION • ORTHOPEDIC CENTER
MULTIPLE SCLEROSIS CENTER • RADIOLOGY SERVICES • HOME HEALTH CARE
HOSPICE AND PALLIATIVE CARE • MATERNAL/CHILD HEALTH SERVICES • PAIN MANAGEMENT SERVICES
KOREAN MEDICAL PROGRAM • CHINESE MEDICAL PROGRAM • FILIPINO MEDICAL PROGRAM

Holy Name Medical Center
Asian Health Services

718 Teaneck Road, Teaneck, NJ 07666 | www.holyname.org | For Asian Health Services, call 201-833-3399


**S-Vision Architecture and S-Vue Probe**

Consisting of the newly developed S-Vision Architecture and S-Vue probe, RS80A offers the state-of-the-art technologies for outstanding images.

## EXPERIENCE A TRULY PREMIER ULTRASOUND

RS80A increases professionalism and confidence with accurate results using advanced technologies developed by Samsung, while simultaneously enhancing user convenience and providing an effective work environment.

## RS80A

**PREMIUM AT ITS BEST**

Scan code or visit
www.samsungmedison.com
to learn more

* RS80A's approvals/registrations may differ by countries.

SAMSUNG
SAMSUNG MEDISON

*Peeking through wooden fence: Christian (4), a boy who resides in a small town of N.J., is waiting for spring to come.*

# OUR EDITORIAL BOARDS




PUBLICATION W MEDICAL STRATEGY GROUP

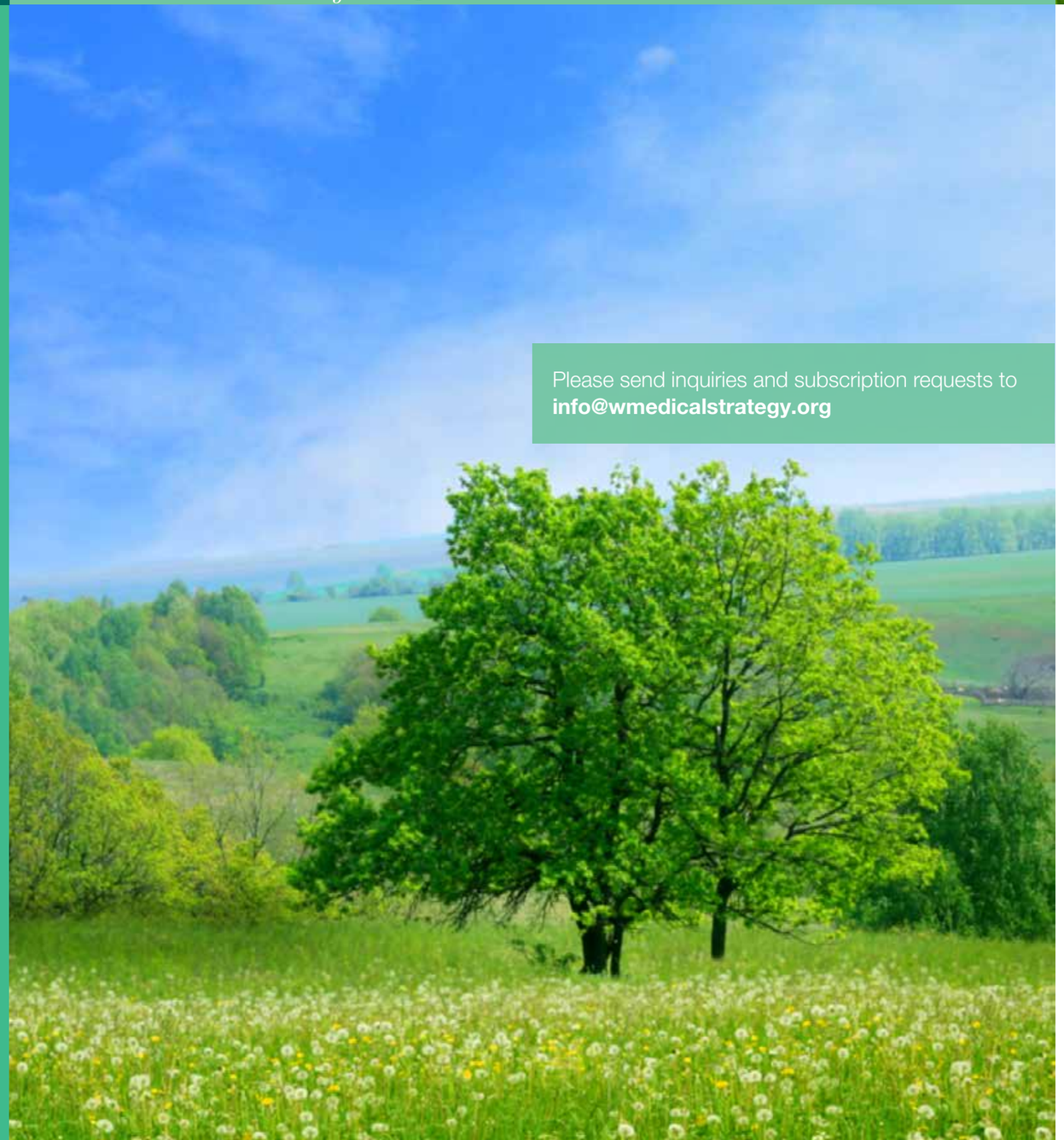
SECRETARIAT STAFF Yisun Yuk / Yeereum Chung / Katie Lee / Sangji Lee / Eunie Kim / Minhye Park / Justin Brown / Sophia Emerson

MAIN OFFICE 210B Sylvan Ave., Englewood Cliffs NJ 07632 Tel. 201.402.1400 Fax. 201.430.2472
Email. info@wmedicalstrategy.org (Sophia Emerson)

MEDIA PARTNERS PharmAsia News, BioPharm Insight, DailyPharm, BioCentury

World Korean Medical Journal is published bi-monthly by W Medical Strategy Group, 210B Sylvan Ave., Englewood Cliffs, NJ 07632. Tel. 201.402.1400, Fax. 201.430.2472, Email. info@wmedicalstrategy.org, Website www.wmedicalstrategy.org. Please send inquiries, subscription requests and address changes to the above address.

WKMJ
World Korean Medical Journal
W K M J 1 3 t h I s s u e W K M J 1 3 t h I s s u e W K M J 1 3 t h I s s u e W K M J 1 3 t h I s s u e W K M J 1 3 t h I s s u e W K M J 1 3 t h I s s u e W K M J 1 3 t h I s s u e



Please send inquiries and subscription requests to
**info@wmedicalstrategy.org**

# TABLE OF CONTENTS


## Cover Story
Dr. Larry Kwak, Vice President of Translational Research & Developmental Therapeutics at City of Hope National Medical Center

## Entrepreneur Interview
Mario Pennisi, Chief Executive Officer at Life Sciences Queensland

## Biopharmaceutical Report
Legislation to Force Payer Coverage of Abuse-Deterrent Opioids Faces Resistance

Western CAR-Ts Face Chinese Development Hurdles Due to Regulatory Uncertainty

# FROM THE PUBLISHER

Year 2017 is becoming a dawn of new era for two nations in the Pacific Rim, South Korea and the U.S. What nearly happened with President Richard Nixon in the U.S. history has finally happened in South Korea as President Park Geun-hye was impeached on March 2017. The country slipped into a political whirlwind building up to a presidential election in May. The upcoming election in Korea may signal a new path in government-industry relations, as well as physician-medical industry relations, with ever more enhanced transparency and scrutiny. In the U.S., Trump tried to repeal and replace the Affordable Care Act, but it did not happen as there was no viable replacement plan, but just rhetoric and ideology. There will be continued evolution of healthcare in both countries and hopefully it will be a positive change.

In this issue, we feature a very distinguished Korean American Physician Larry Kwak, MD, PhD, a leading oncologist named as Time Magazine's 100 Most Influential people in 2010. We remember an incident where Dr. Kwak was a keynote speaker in the Korean American Medical Association Hawaii meeting in 2014, when two hurricanes disrupted his travel. Despite the harsh circumstances, he still made it to the meeting and showed his perseverance and dedication which he emphasized in the interview. Dr. Kwak has done and continues to push the envelope in translational tumor research and has worked its way to actual treatments. He has worked at National Cancer Institute, then moved to the MD Anderson Cancer Center where he met his mentor, Dr.Waun Ki Hong, who was featured in the last issue of WKMJ, and he was recently recruited to the City of Hope in Los Angeles. He is truly a medical celebrity in city of Los Angeles and I was proud to see his picture on the billboards of LA. He was also selected for the highest honor in Korean Medicine with the Ho-Am Prize. Despite his many successes and achievements, he is a very humble and dedicated family man. He has many scientific publications but also contributed to society with a book on raising children with his wife Ruth. Immunology is a topic that is very complex and difficult but he makes it simple for everyone to understand and it is truly one of his many gifted skills. Dr. Kwak's scientific contributions are pivotal in the War on Cancer and he has won battles with the translational research in immuno-oncology with cancer vaccine.

The entrepreneur interview is with Mario Pennisi of Life Science Queensland (LSQ) of Australia. Despite the fact that the country is isolated and does not have a large population compared to its size, Australia has the world's 13th largest economy and has a role and influence in international affairs including medicine. Australia also is an advanced medical country which has much to offer in life sciences activities in both research and commercial opportunities. LSQ CEO Pennisi has a global view of Life Science and wants to leverage the opportunities in Australia with the rest of the world. Surely there are unique opportunities and challenges but also innovation and novelty from a continent country.

The world is changing with great advances, such as Watson computer entering medicine and coming of self-driving cars, but there are geo-political instabilities, and old and new challenges. However, we must go on and hope for the better during these challenging times and we must remember two of the most important attributes in medicine, patience and hope, and also take action when you can.

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



# FROM THE EDITOR-IN-CHIEF

Weekly meeting held every Monday has been a core part of our company culture since day one. While the meeting agenda has shifted as time passed by, the goal of providing everyone to discuss, connect and learn remains the same. Inspiring words and optimistic view points from greatest thinkers of all time are often shared in our weekly meeting to discuss upon: "Being good is easy, what is difficult is being just (Victor Hugo)", "Nothing great in the world has ever been accomplished without passion (Georg Wilhelm Friedrich Hegel)", "The most beautiful thing we can experience is the mysterious (Albert Einstein)".

Interviewing with Dr. Larry Kwak gave me similar experience as reading quotes from the great minds; encourage to achieve goals, share affection and motivation to endure hard work. In the 13th edition of WKMJ, we have interviewed a physician leader in therapeutic world, who had been named as one of Time Magazine's 100 Most Influential People in 2010, Dr. Larry Kwak.

Dr. Kwak, the key leader of the Hematologic Malignancies and Stem cell Transplantation Institute, shared his great professional and family stories with us, and revealed his precious ideas of how to be successful. As he put it, "we all have a universal calling; namely, to enhance the welfare of others". Dr. Larry Kwak's story brought warmth to me like a soft spring breeze.

For the Entrepreneur Interview, we featured Mr. Mario Pennisi CEO of LSQ, Life Science Queensland, an organization which plays a role as the gateway for life science companies located in Queensland, Australia. Life Sciences Queensland Limited (LSQ) is an active Australian industry group that was established to assist those entities that use R & D across the Life Sciences as part of their business endeavors. I have long history of personal and professional relationship with Mario over decades. I always enjoyed his expertise, insights, great personality, and friendship. I am glad to share his story with our readers.

Addition to these two major articles, we have rich selection of articles which will bring amusement of reading to our readers.

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

# WKMJ RECAP OF THE LAST ISSUE


Cover Story

## Inspirational Korean Healthcare Leader "Dr. Waun Ki Hong, Division Head of Cancer Medicine at The University of Texas MD Anderson Cancer Center"

Dr. Waun Ki Hong is the Division Head and Professor at The University of Texas MD Anderson Cancer Center, an American Cancer Society Professor, and a Samsung Distinguished University Chair in Cancer Medicine. A national and international leader in medical oncology, Dr. Hong is a foremost authority on the treatment and prevention of head and neck cancer and lung cancer. Dr. Hong is also one of the founders of cancer chemoprevention and pioneered a new paradigm for cancer – the possibility that it can be prevented or delayed. Additionally, he was the main architect and principal investigator for BATTLE, the first successful biopsy-driven trial in lung cancer. To read more about Dr. Hong's establishments and how his contributions impacted current and future of cancer researches, please read 12th issue of WKMJ.

Entrepreneur Interview

## Mark Paxton, Chief Executive Officer at Rx-360

Mark Paxton, the first CEO of Rx-360, served as a Regulatory Counsel in the FDA CDER Office of Compliance prior to joining Rx-360 where he was responsible for assisting in the development of supply chain security policies, both domestically and internationally. RX-360 is the international pharmaceutical supply chain consortium dedicated to protecting patient safety. To learn more about Rx-360 and the importance of audit programs offered, please refer to issue 12.

Biopharmaceutical Report I

## Politicizing Science

While the FDA reform provisions in the 21st Century Cures Act give the agency backing to carefully advance some of its long-term objectives, an analysis of the bill's details suggests that when it comes to NIH, at best the legislation is a missed opportunity to make meaningful changes at the world's largest biomedical funding agency, leaving long-term problems untouched. At worst, Cures will be a step backward that will politicize research and skew grant-making toward flashy, short-term translational science projects. To read more, please refer to issue 12.

Biopharmaceutical Report II

## Humira Biosimilar Unlikely to Reach the Market Before 2020

The numerous biosimilars for AbbVie's (NYSE:ABBV) Humira (adalimumab) are unlikely to reach the market prior to Amgen's (NASDAQ:AMGN) approved biosimilar, Amjevita, and certainly not before 2020. AbbVie's patent estate for Humira is far too complex and Amgen has enough of a head start advantage with its approval and ongoing litigation that is likely another biosimilar could surpass it to market. Further, legal experts agreed it is more likely a Humira biosimilar would reach the market in 2022. To find out about the details, please read issue 12.


## Since. 1983

It has been a 30 years of the craftmanship that first to start
and striving for the best preventive medicine practice
and professional comprehensive medical examinations.
It includes followings.

- Provides one-stop service from examination to treatment.
- Comprehensive Medical Exam/ National Health Insurance Examination/ Industrial Special Screening Examination
- Notified Center for Immigration Examinations, Student Visa Examinations, Work Visa Examinations
- Bioequivalence tests, Agency for Human Subject Right and Research
- Contracted for partnership with most of Prestige University Hospitals in Korea.

의료법인 하나로 의료재단
Hanaro Medical Foundation
TEL : +82-2-590-1111
URL : www.hanaromf.com

H A N A R O  M E D I C A L  F O U N D A T I O N

www.enzychem.com

PLAG
록피드
SAFETY QUALITY
HEALTH RIGHTS

# ROCKPID®

The world first patented functional health food that modulates immunity
PLAG in ROCKPID® has an immune modulating and immune balancing activity
Hematopoietic, Anti-inflammatory and Anti-metastasis Efficacies
Fulfills the popularization of deer antlers through state-of-the-art sciences and innovative technologies

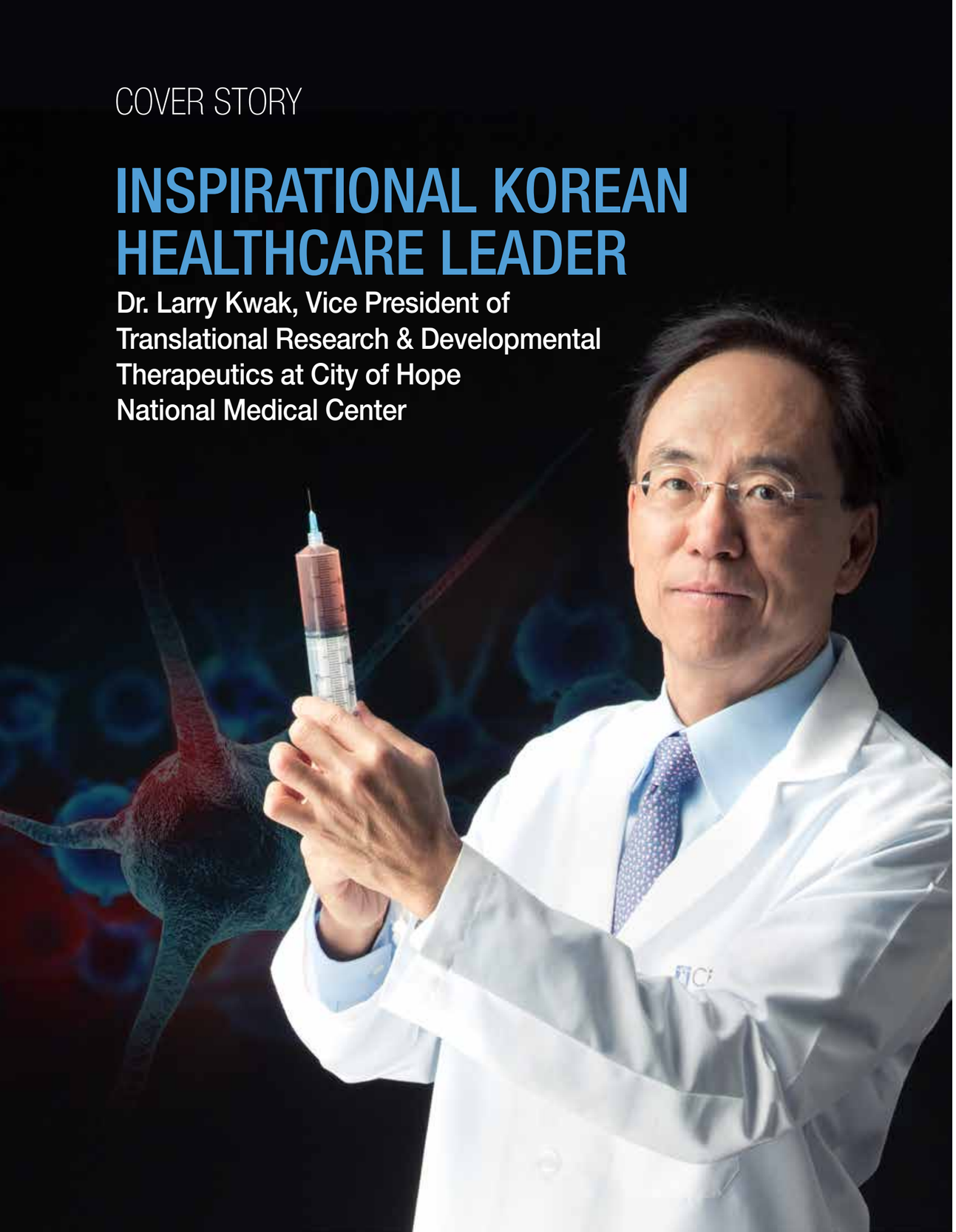
*Purchase is available @ www.thepowerfood.com*


## Inquiry

Email: expert@enzychem.com  Tel: 1-800-611-9701

# INSPIRATIONAL KOREAN HEALTHCARE LEADER

## Dr. Larry Kwak, Vice President of Translational Research & Developmental Therapeutics at City of Hope National Medical Center

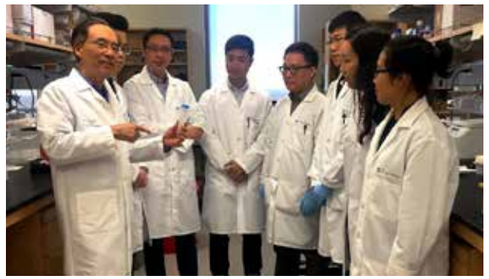


COVER STORY

**1. Dr. Kwak, you are a world-renowned physician and cancer research scientist. What was the reason for attending medical school? What motivated you to become a physician?**

- I give a lot of credit to my family background. I have a wonderful Korean heritage of service to mankind. My maternal grandfather, Oh Chung Soo, was the first Korean to graduate from Massachusetts Institute of Technology (MIT) in 1927, and he later returned to Korea to serve in the government as Minister of Commerce. My parents were both educators. My father, Kwak No Whan, came to the U.S.A. to earn his Ph.D. degree in Physics, and my mother, Oh Chang Sook, came to the U.S.A. for undergraduate college on a piano performance scholarship. As a child, my parents encouraged me to pursue a profession in which I could enhance the welfare of mankind and also instilled in me the values of hard work and motivation.

I became interested in medical research at a very young age. Actually, it was a pivotal experience during a summer high school internship. I was given a job doing some menial tasks in a hospital clinical laboratory. But my mentor, a pathologist, would invite me into his office every day after work and show me slides under the microscope of cancer cells. Interspersed with those cancer cells were normal immune cells and he would challenge me to think about why those cells – the normal immune cells – were there and if they could one day be harnessed to fight cancer. That exposure sparked my interest in cancer research. From that point on, my education and training were aimed towards that ultimate goal of being able to make discoveries in the laboratory as a scientist and then as a physician to be able to walk over to the clinic and offer those cutting edge treatments to patients.



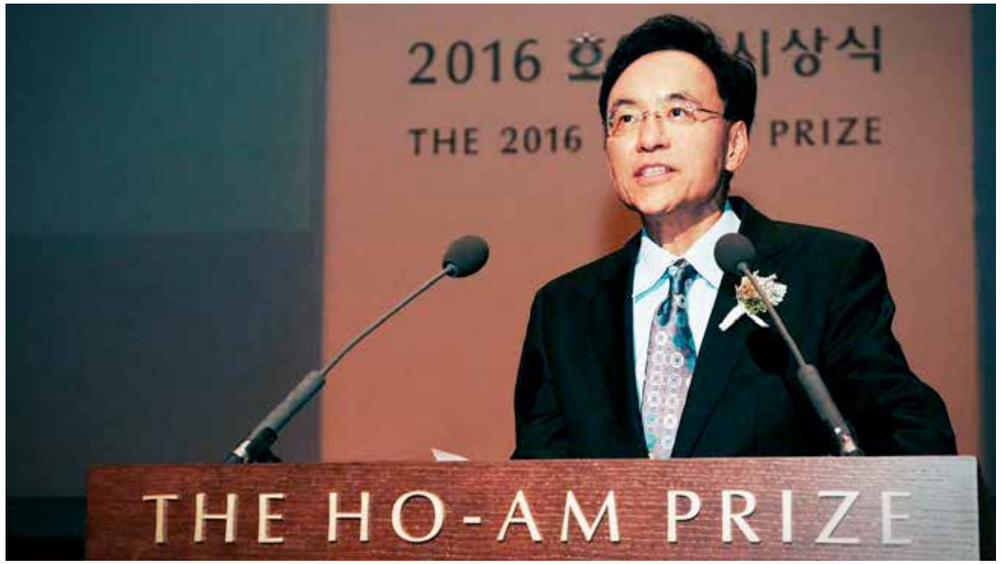
*Dr. Kwak with his laboratory scientists and postdoctoral fellows at City of Hope*

> **“being able to make discoveries in the laboratory as a scientist and then as a physician to offer those cutting edge treatments to patients”**

**2. During more than 20 years of commitment in oncology research, you may have gone through various obstacles; can you share some of the most difficult moments in your career?**

- My first job was at age thirty-four after I finished my M.D. and Ph.D. degrees and clinical residency and subspecialty oncology fellowship at Stanford. I was offered a position to lead my own research program at the National Cancer Institute. It was a wonderful decade at the National Cancer Institute– that’s where some of the earliest discoveries were made by my laboratory in developing one of the first cancer vaccines. We optimized it in laboratory animals and then ultimately were able to take it to patients through the different phases of clinical trials, starting with phase 1 and eventually to phase 3 clinical trial, the last phase in clinical development for a drug, which was ultimately positive.

But it was during the early ground breaking pivotal work 20 years ago that we encountered obstacles to the idea of harnessing the immune system. When we first tested cancer vaccines in the traditional phase 1 clinical trial model; i.e., in patients with advanced cancer burdens, they failed to show any real effectiveness, and this generated many naysayers in the oncology community. But we went back to the drawing board, and testing in mice, we observed that the most effective setting for vaccines was against a minimal cancer burden. In other words, when we combined chemotherapy first, to shrink 90% of the cancer, then gave the vaccine to mop up the remaining microscopic cancer cells, most of the mice were cured. When this principle of combining chemotherapy with the vaccine was




*Dr. Kwak delivering Ho-Am prize acceptance speech in Seoul, South Korea*

then applied to lymphoma patients, the length of their remissions was doubled on average, compared with chemotherapy alone, with some patients staying in remission for 15 years after receiving the vaccine.

So, to me, this is the true meaning of the Ho-Am Prize in Medicine - perseverance. My wife and I traveled to Seoul at the end of May last year to accept the award. And with several Nobel laureates in the audience, it was this message of faith and persistence that I shared to describe my journey in my acceptance speech.

**3. We see that you have been named as one of Time Magazine's 100 Most Influential People in 2010 along with former President Barack Obama and Steve Jobs, to name a few. This list includes people who are recognized for affecting the world. Can you share with our readers some of the major achievements and outcomes you have accomplished during your professional life?**

- First, I need to tell you a funny story: I remember receiving an email from the Time Corporation and I didn't open it right away, because I get a lot of emails and I thought it was a form of spam. And frankly I'd never heard of the Time 100, but I did end up opening it a few days later and I ran it by our communications department. They said "Oh my goodness, this is a major thing and you should definitely go accept it." So my wife and I both attended the ceremony in New York City - there were so many famous people there (including three other persons of Korean heritage, including Yuna Kim). They actually roll out a red carpet there at the Lincoln Center. Adam Sandler was in line in front of us and the paparazzi were all there snapping his photo; the cameras were going off all the time. And then it was our turn. Our host said, "This is Dr. Larry Kwak" and everything stopped and you could hear everybody whispering, "Who's that, who's that?" And then a few seconds later all the cameras just started going off again- it turns out that it didn't matter who it was after all!

I was honored for my 20 year-long commitment to the science of cancer vaccines. I was fortunate to be recognized, as I think a major component of any recognition is the right timing. I've been working in this field of cancer immunotherapy for most of my life, and just now we're starting to see the fruits of these labors. Specifically, we now have treatments which are actually approved by the FDA in this field and it has opened up a whole new area of cancer research (known as Immuno-Oncology) which is very promising. So I was fortunate that the committee recognized some of my early work as seminal. I was involved in the beginning and was one of the scientists whose research set the groundwork for the successes that we're seeing today in the clinic.

**4. Dr. Kwak, you are the Vice President and Associate Director for Translational Research and Developmental Therapeutics at City of Hope. What are your key roles, responsibilities, and principles of leading in one of the most comprehensive cancer centers? Also what are the long-term goals and visions that you hope to see the City of Hope to achieve?**

- As Vice-President and Associate Director for Translational Research and Developmental Therapeutics, my primary responsibility is to shape the next generation of research and treatments for cancer, in general, and lymphoma and hematologic malignancies, in particular, at City of Hope. In my combined roles as a physician, scientist, and mentor, my vision is to assemble and lead research teams to integrate and accelerate basic discoveries from laboratories to clinical development and first-in-human clinical trials of novel "homegrown" therapeutics, such as next generation cancer immunotherapies. I play a key role in the future direction of City of Hope's precision medicine and teamwork science initiatives.

*The photo of Dr.Kwak and his family*

**5. We see that you are an eminent opinion leader in translational cancer researches. Translational research is a relatively new research discipline which applies findings from basic and fundamental sciences into medical practices. What do you think is the current status, trends, and challenges in translational research? Also, what do you forecast the major changes would be in translational research in the next five years?**

- I'm glad you asked, because translational research is what really energizes me. I like to point out that I've actually been engaging in this discipline long before the term was coined and before it became popular. True translational research is the idea of taking discoveries from the laboratory and applying them directly to patients. Having training and expertise as a scientist and the perspective and compassion of a physician is one path to such a career, but it's not the only way. My passion is to inspire the next generation of young physician-scientists with the same vision to see their own research applied in their lifetime, as well as patients to have faith and courage.

My own professional path has allowed me to experience the personal satisfaction of the first two "d's" in the therapeutics development triad; namely, discovery and development. But to achieve the last "d"; namely, delivery, I believe academic medical centers need to collaborate more with commercial biotech and pharma companies to achieve the ultimate goal of getting innovative therapies out to the general public. For example, in my leadership role at City of Hope, I oversee several resources that are actively collaborating with commercial entities in advancing new therapies and technologies, such as clinical-grade (GMP) manufacturing facilities which have some external clients, and we have recruited several members from industry to our internal committee which makes "go" and "no go" decisions about investment in our own products with commercialization potential.

Here is also where I see a lot of potential in Korea, with the growing excitement and corresponding investment in biotechnology that is taking place now. As a way to give back to my Korean heritage, I have a deep interest in making myself available to provide advice and guidance to the Korean biotechnology community to help catalyze growing collaborations with academic medical centers.

**6. What would be your advice or comments for current medical students as well as those who aspire to become a doctor?**

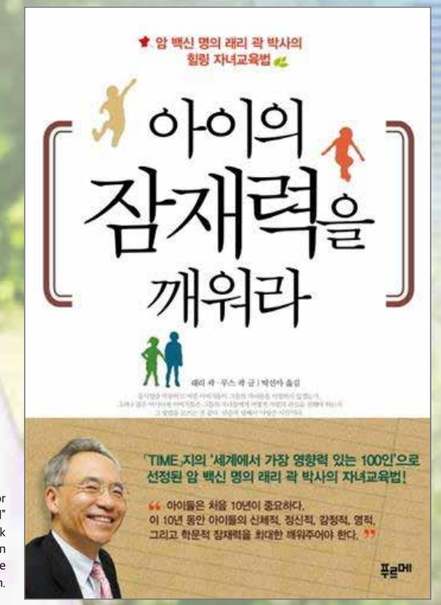
*Dr.Kwak with his family at a family trip*

- Well, I think the wonderful thing about living in America is that you can still be recognized for your achievements, and so the advice that I give when I talk with young people is three things. The first is to make sure that in everything you undertake, you strive for excellence. Aristotle defined excellence as something that you do as a habit, so it's not just a one-time event and it becomes a part of your core values. One component of excellence is the perseverance I spoke of earlier. Unfortunately, perseverance is becoming less popular among young persons – I see it even in my own children; one anecdote is that when I told my family about the TIME100 award, my second son's response was, "Gee, that's great Dad, but who would want to work on the same thing for 20 years?!" Second, seek out wise mentors. It's very difficult to walk any road alone and I look at my own experience beginning with my high school summer internship experience as pivotal. I've had other mentors along the way at every step in my career that have really helped guide me, most recently Dr. Waun Ki Hong, Samsung Distinguished University Chair Emeritus Professor at MD Anderson Cancer Center. Third, especially for young families, my advice is to maintain proper perspective and be committed to your family. Several years ago, my wife and I authored a book (see photo) in Korea focused on the importance of teamwork in parenting. In it, we describe several examples from my own life making intentional choices to be a father that was involved in the lives of my four children. I can still recall deliberately turning off my mobile phone as soon as I arrived home each evening when our children were young to give them my undivided attention until they went to bed.

**7. WKMJ has readers from more than 10 countries globally. Please share your final words with our readers.**

- I feel like the most fortunate person in this world, not only because of a wonderfully supportive wife and family, but also because I believe everyone has a purpose on this Earth, and my God-given, unique design happens to be my occupation. I love my job, because I wake up every morning anticipating that today is another day we might make a laboratory discovery that will make an immediate impact for cancer patients. In other words, I feel like I'm operating in my sweet spot, and I even get paid for it! One of my close friends, who founded a nonprofit leadership training organization, called Xealots, promotes the idea that we all have a universal calling; namely, to enhance the welfare of others. In the medical profession we benefit from having so many choices of primary care or specialties to choose among, so my hope for my fellow physicians of Korean heritage is that we all have maximum impact in our respective spheres of influence. W


*Dr.Larry Kwak and his wife Ruth Kwak at TIME 100 Gala*




Dr. Larry Kwak and his wife Ruth Kwak is an author of the book called "Tap into Children's Potential" which emphasizes the importance of teamwork and communication in parenting to help children reach their full potential through their experience from raising four children.

*Tap into Children's Potential*
*(Larry and Ruth Kwak, PRUME, 364p, 2012)*

## Larry W. Kwak, MD, PhD

Vice President and Cancer Center Associate Director, Translational Research & Developmental Therapeutics
City of Hope National Medical Center

Dr. Kwak is currently a Vice President and Cancer Center Associate Director of Translational Research and Developmental Therapeutics, Dr. Michael Friedman Professor for Translational Medicine, Director of Toni Stephenson Lymphoma Center at City of Hope National Medical Center. Dr. Kwak served as Head of the Vaccine Biology Section, Experimental Transplantation and Immunology Branch, at the National Cancer Institute (NCI) for 12 years. His NCI laboratory is credited with the pioneering bench-to-clinic development of a therapeutic cancer vaccine for B-cell malignancies, which was recently reported as positive in a landmark national Phase III clinical trial. From 2004-2014 Dr. Kwak served as Chairman of the Department of Lymphoma and Myeloma and Co-Director of the Center for Cancer Immunology Research at the University of Texas, M.D. Anderson Cancer Center in Houston, Texas, where he also held the Justin Distinguished Chair in Leukemia Research. Under his leadership, his department successfully captured extensive research support, including large team science grants, such as two SPORE grants in Lymphoma and Multiple Myeloma, respectively, from the NCI and a SCOR program project grant awarded by the Leukemia and Lymphoma Society. A committed physician, scientist, and mentor, his vision is to assemble and lead research teams to integrate basic discoveries from academic laboratories with translational clinical development to first-in-human clinical trials of novel "homegrown" therapeutics, such as next generation cancer immunotherapies. In 2010 Dr. Kwak was named to the TIME100, one of the world's 100 most influential people by TIME magazine, for his 20 year commitment to the science of cancer immunotherapy. In 2016 he was awarded the Ho-Am Prize in Medicine for his pioneering research in cancer immunotherapy.

# W MEDICAL STRATEGY GROUP

W Medical Strategy Group and its global network can lead your business to right solutions. Cruise on board with WMSG's in-depth expertise and accurate insights. We will navigate the world of health care industries to take you where you need to be.

Discover your destinations with us. Let the sailings begin.

**www.wmedicalstrategy.org**


MEDICAL STRATEGY GROUP

**W Medical Strategy Group**
210 (B) Sylvan Ave. Englewood Cliffs, NJ 07632
Tel : (201) 402 – 1400 Fax : (201) 430 – 2472
www.wmedicalstrategy.org


www.drh.co.kr

# DAERIM SAINT MARY'S HOSPITAL

## Health Screening Program & Specialized Care Center

Experience the world class renowned medical services at Daerim St. Mary's Hospital, aim to become the world best.


- The best specialist medical team, the most advanced medical technology and **Impeccable service**
- Optimized medical system for designing the best customized checkup program option for each patient

**Global Healthcare Team**

**Appointment**

08:30am~17:30pm 82-2-831-9003
010-4557-5798 (kakao ID:Daerim8319003)
Hoilday & At night 82-2-829-9222
E-mail : global_healthcare@drh.co.kr

One–Stop Operation

# Kegel·Q

personal exercise monitor and trainer for your pelvic floor muscles

## Kegel Exercise Enhanced by Kegel·Q

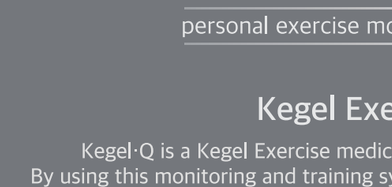
Kegel·Q is a Kegel Exercise medical device with biofeedback for women's urinary incontinence.
By using this monitoring and training system, you can learn, through trial and error, to control your mental and physical processes in order to manage urinary incontinence.

## Main Features & Benefits of Kegel·Q

**Measurement/Recording**
Monitoring Urinary Incontinence
: Measuring and recording the contraction pressure of pelvic floor muscles

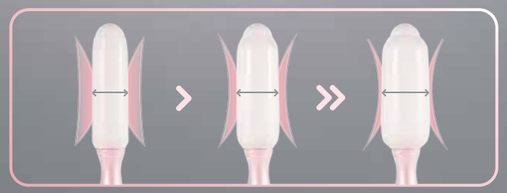
**Exercise**
Training for Urinary Incontinence
: Exercising with 2 (high·low) strengths and 3 levels of effective workout programs

**Audio Guidance**
: Audio guidance while operating for easy to use




## Specially-Designed Probe

- Medical grade silicone for safety
- Even expansion for effective exercise in any position
- Heating mode (98.6°F/37°C) at the human body temp. for comfort and air expansion without stimulation



※ *Multicenter clinical trials are currently recruiting participants at reputable university hospitals in South Korea including Seoul National University Bundang Hospital and these trials are sponsored by Korea Health Industry Development Institute.*

MFDS Registered

**[USA]**
**Oh Pharmaceutical Co., Ltd.**
**9800 Connecticut Dr. Crown Point, IN 46307**
**+1 219 644 3239, info@ohpharma.com**

**[South Korea]**
**UK Ucera Co., Ltd.**
**30, Jeonpa-ro, Manan-gu, Anyang-si, Gyeonggi-do, 14086**
**+82 31 467 2395, kegelq@ucera.com**

# Entrepreneur Interview

## Mario Pennisi, Chief Executive Officer at Life Sciences Queensland

*Mario Pennisi giving a speech at the Innovation-20*

**1. Life Sciences Queensland Limited (LSQ) is an Australian industry-led organization working to assist the growth of individual firms and organizations and to enhance Queensland's national and international reputation as a center of commercial and research excellence in life sciences. Please explain LSQ's strategies, mission, and activities to our readers.**

Life Sciences Queensland Limited (LSQ) is an active Australian industry group that was established to assist those entities that use R&D across the life sciences as part of their business endeavours. Specifically, we are most interested in the outcomes of the R&D.
It seems that this interest is now best described as the role of life sciences innovation in economic development.

Like other peak industry groups, we exist to assist and promote the interests of our members. We do so by identifying and interacting with key international counterparts so that our members and the stakeholders of our counterparts (from across the globe) have opportunity to meet and to explore opportunities to get to know each other – and when the circumstances are appropriate – to work together.

*Mario Pennisi having a conversation with one of the speakers*

Life Sciences Queensland





Our engagement strategy is across a few areas. Once we have identified various stakeholders, we create fora (physical and virtual) to enable them to interact. We work to deliver to them contacts, services and initiatives that they would not do by themselves (because they haven't recognised the need, or they don't have the resources to do it).

Through our constant market outreach activities, we try to identify and/or create opportunities that our members might be able to seize. Where possible and of interest to our members, we arrange and facilitate a co-ordinated approach to business meetings – especially in relation to trade missions (inbound or outbound).

Our high level of activity and interaction positions us well to play a leading role in influencing public policy – and our bipartisan approach generally serves the broadest interests of all our stakeholders.


*Mr. Pennisi presenting at The Australian Bioenergy and Bioproducts Symposium*

**2. We see that LSQ provides diverse products and services to its members. Can you explain what benefits members would receive from working with LSQ?**

LSQ has a dedicated team of professionals who are focused on assisting and representing members to gain opportunities and to leverage the network of capabilities – both from within the membership – and also throughout our international alliances. This assists all stakeholders - and serves to strengthen the alliances that have been established.

In many cases, our members may not be in a position by themselves to seek out the broad range of stakeholders that LSQ has managed to identify and engage.

Also as a highly visible and active advocate for the role of life sciences innovation and the role it plays in economic development, LSQ is a highly regarded and effective voice for industry – representing industry's needs and aspirations to our elected officials - at all levels of government and in a bipartisan manner.

Mario Pennisi with his colleagues during closing ceremony of the Innovation-20

Mr. Pennisi with his colleagues at TABBS event

**3. LSQ is a key channel for building and maintaining a globally competitive sector in Australia. As an entrepreneur, what would you say are the top three priority assets or skill sets needed for to be successful in the global life sciences industry?**

When creating anything, you need to have a clear vision of what you are trying to achieve. You need to recognize what skills you have (either personally or across the stakeholder group) and you must then identify those individuals (or other stakeholder groups) who can complement and help grow your capabilities. This is key because collaboration is essential to establishing and growing any enterprise.

You need to be bold – ask the "what if" questions and be prepared to back yourself (and your partners) to be able to achieve your goals and ambitions.

It is important to learn the lessons from others who have been successful (and even from those who may not have enjoyed success) and use these experiences to inform what you should do.

Above all – get started! Don't wait until it is "perfect" before you start – otherwise you will never start. Also while never loosing sight of the goal, be prepared to "flex and pivot" if that is what is needed. Lastly, never give up.


Mario Pennisi providing congratulatory remark

**4. As a CEO of LSQ what do you think is the most important issue in the life sciences industry? How do you forecast global life sciences industry will be like in the next five years?**

Life sciences innovation is crucial for our survival – as ultimately this is the sector that will deliver the products that will feed, fuel and heal the peoples of the world. Life sciences innovation requires relatively long time frames, can be very expensive, and involves technical risk.

All of these things mean that the life cycle from idea to delivery usually takes several years. Because it does take several years, this invariably means that it will involve a number of political cycles – therefore bipartisan support and stable policy arrangements are crucial to an efficient and effective life sciences sector.

With the recent political changes in a number of jurisdictions around the world, we are seeing that the previous bipartisan support for the knowledge based ecosystem is under extreme pressure as new political leaders try to engage with their constituents in ways that may challenge existing international relationships and global supply chains. These new interactions cause uncertainty and political instability – in turn causing investment in life sciences to be perceived to be riskier.

**5. WKMJ has readers from over 10 countries globally. Please share your final words or thoughts with our readers.**

Life sciences innovation is not for the faint-hearted. You need patience and the ability to work with several (and many) stakeholders at any time – and from all over the world. You will face challenges, from technical, to regulatory, to financial – but those who prevail will bring to the world those outcomes that will feed, fuel and heal the world. The possibilities are endless, and the results priceless. Also remember, never give up! Never give up! Never give up!

Mario Pennisi with his colleagues during award ceremony

## Mario Pennisi

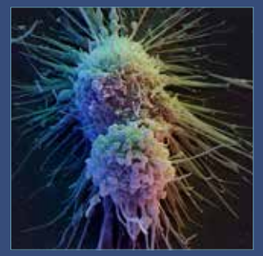
Chief Executive Officer, Life Sciences Queensland

Mario Pennisi is the inaugural CEO of Life Sciences Queensland LSQ. He has been the CEO of LSQ since its establishment in 2005, and has over 20 years' experience in the life sciences industry. Mr. Pennisi has extensive experience in managing commercial operations in the life science industry. In the mid-1990s, in affiliation with US and German-based organisations, he established the first Queensland-based 'central laboratory', servicing international trials in the Asia-Pacific region. He was also a founding member of Queensland's first contract research organisation. Mr. Pennisi has overseen LSQ's growth to become Australia's peak industry group for therapeutic product service providers. LSQ represents over 100 members and it maintains relationships with strategic partners across the Asia Pacific Region and in Europe and North America.

# Biopharma Report

## BIOPHARMACEUTICAL REPORT I

LEGISLATION TO FORCE PAYER COVERAGE OF ABUSE-DETERRENT OPIOIDS FACES RESISTANCE



## BIOPHARMACEUTICAL REPORT II

WESTERN CAR-TS FACE CHINESE DEVELOPMENT HURDLES DUE TO REGULATORY UNCERTAINTY

BIOPHARMA REPORT I

# Legislation to Force Payer Coverage of Abuse-Deterrent Opioids Faces Resistance

Proposed legislation across 23 US states to force payers to increase reimbursement of abusedeterrent (AD) opioids will likely face significant resistance due to state cost implications, most experts said. The state payer- Medicaid- and private payers alike will likely argue that AD opioids do not currently have enough evidence to support the idea that they prevent abuse and addiction, experts added.

Some products approved with AD labelling include Teva Pharmaceuticals' (NYSE:TEVA) Vantrela (hydrocodone bitartrate), Egalet's (NASDAQ:EGLT) Arymo (morphine sulphate), Purdue Pharma's Targiniq ER (oxycodone and naloxone extended-release tablets) and Pfizer's (NYSE:PFE) Embeda (morphine sulfate and naltrexone).

Experts noted action to push any state legislation that would force access to more expensive AD drugs would directly impact the Medicaid budget, as Medicaid is one of the largest payers of opioid products. Thus only a few states at most will implement changes, most experts said. Private payers and patients would also balk at paying more, including higher premiums, as a result of insurers being forced to reimburse AD products, they added.

That said, two other experts were more optimistic on legislation prospects, considering the continued development of AD formulations. But others said only further data of benefit of AD opioids could sway states and payers in favour of increasing access to AD opioids, given abuse likely stems from diversion rather than misuse by the patients who are prescribed opioids.

**State and payer costs prohibitive**

Based on conversations with consultants, it is expected that only a few states will implement very strong legislation to force physicians to prescribe AD opioids, said Nikolaj Sorensen, CEO of Orexo, a Swedish company which markets opioid products for both pain and opioid dependence. The extraordinary cost increase of AD opioids compared to cheap generic formulations is one of the major blocks to passage for most states, explained Sorensen, with one consultant agreeing. AD opioids can cost as much as 10 times their generic equivalent counterparts, noted one pain expert.



> "The extraordinary cost increase of AD opioids compared to cheap generic formulations is one of the major blocks to passage for most states"

One of the biggest hurdles to passage is the costs of AD coverage would be primarily absorbed by Medicaid budgets, with private health insurance companies also affected, explained Sorensen, the consultant and Bob Twillman, executive director, Academy of Integrative Pain Management, Lenexa, Kansas. Medicaid operates annual budgets, so longterm benefits from AD formulations, assuming they prevent overdose and addiction, are not helpful, noted Michael Barnes, chairman, The Centre for Lawful Access and Abuse Deterrence, Washington, DC. Also, there are cost implications to patients with private health insurance in that premiums would likely rise as a result of the increased cost to payers, added Sorensen. A patient with good intentions and who is unlikely to abuse or misuse opioids will object to paying higher premiums so legislation is likely to be unpopular, he noted. Payers will also object to paying more for a product if a patient is not abusing it, he explained.

Private health insurance companies are lobbying against any state legislation, using the argument that AD opioids are being advertised as safe when they still carry risks, which is a powerful and valid argument, said Twillman. Their lobbying is pretty persuasive to prevent legislation passage, he said. However, the legislation is being pushed by AD pharma makers, he added.

In California there was a bill that attempted to mandate at least one AD opioid be placed on formularies with no increased co-pay, however it was rapidly killed, said Jeremy Adler, senior pain management physician assistant, Pacific Pain Medicine Consultants, Oceanside, California. States such as New York and New Jersey vetoed potential legislation in 2016 due to cost and evidence concerns, though new bills may be possible, said Shruti Kulkarni, policy director, The Centre for Lawful Access and Abuse Deterrence, Washington, DC and the consultant. However, without a major political leadership change in New York, New Jersey and California, any new bills are likely to be vetoed again, noted Barnes.

In New Jersey, the governor that vetoed a bill to increase access to AD opioids, noted it would cost the state more than USD 11m each year, and there were limited data supporting the usage of AD opioids to prevent addiction, said the consultant. In Utah, the state Senate requested a cost/benefit analysis study which concluded that AD drugs should be subject to higher cost sharing given that limited data demonstrates the value of AD opioids, said the consultant. The Virginia state Senate has similarly requested a study on AD opioid coverage which is expected to conclude and provide recommendations imminently, he added.

### Limited data for AD opioids

Despite other experts noting the difficulty of legislation passing, Kulkarni said she was more optimistic because the FDA is strongly encouraging generic manufacturers to make AD formulations which could have a positive impact on their uptake. Barnes agreed, adding that whilst at the moment there are only a few products on the market, the approval of more AD drugs would likely help create further competition and increase access. The AD market is growing with some recent FDA approvals such as Vantrela and Arymo, he said. There are also an additional 20-30 AD products in the clinical development pipeline, he said. One thing that would likely help swing the pendulum in favour of AD opioid coverage would be outcomes data showing AD products help reduce overdoses and addiction and thus there may be a better cost/benefit ratio, noted four experts.

However, it may be difficult to get data to demonstrate AD opioids have a significant impact on abuse, as the majority of opioid abuse is as a result of diversion, said Adler. Physicians can assess patient records to determine addiction potential and prescribe AD opioids in those cases, but they cannot prevent medication from being stolen or diverted, he said.

One pain expert and Twillman noted that following Purdue's OxyContin (oxycodone controlled release) change to an AD formulation, data shows its abuse dropped significantly.

OxyContin is the only AD opioid with any real-world data supporting its efficacy in reducing abuse, the pain expert added. Considering the few AD options on the market, the ability to assess their effectiveness is limited, he said. Also, nearly all AD products are long-acting opioids, which account for only 3% of the total prescriptions for opioids, and most abuse occurs with immediate-release opioids, heroin and fentanyl, he explained. W


## Hamish McDougall

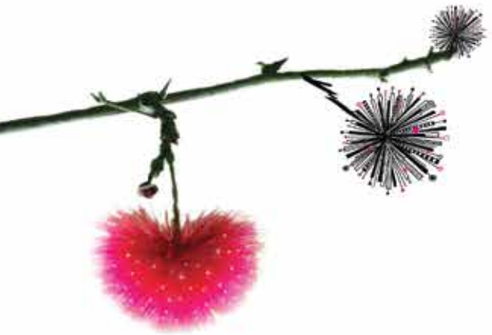
Reporter, London

Hamish has a BSc in Neuroscience from the University of Sussex and is primarily covering the neuroscience indications for BioPharm Insight. Prior to joining us he was assistant commissioning editor for a well-known collection of biomedical journals at Expert Reviews, including Expert Review of Gastroenterology & Hepatology, Expert Review of Clinical Pharmacology and Expert Review of Respiratory Medicine.

## Fiona Barry

Reporter, London

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



# Happy smile and hope after pain

Cancer-free D.K. Lee

D.K. Lee has related to It's A Wig that she will promote to cancer patients about the beauty classes and healing programs she attended. The beauty classes are held at Kyung Hee Medical Center and it is for cancer patients to help them feel more womanly during their hard times. She would like to thank all the people who gave her hope. "Thank you for giving me a second chance to live as a woman. With the hopes and gifts that I have received, it encourages me to work harder to volunteer my time for the people who are fighting against cancer."

Kyung Hee Medical Center patient
D. K. Lee

D.K. Lee attending
beauty classes while chemotherapy treatment

BIOPHARMA REPORT II

# Western CAR-Ts face Chinese Development Hurdles Due to Regulatory Uncertainty

Western-origin chimeric antigen receptor T-cell (CAR-T) therapies being developed in China face an uncertain regulatory landscape at the national level, as well as disparities between hospitals' practices at the local level, experts said.

While regulation of cell therapies like CAR-Ts may fall under Chinese Food and Drug Administration (CFDA) regulations, details of these regulations remain unclear, experts said. However, Ministry of Health-imposed restrictions on commercialization of cell therapies -- put in place after a scandal last year -- appear likely to be lifted, experts said, and potential approval of CAR-Ts in the US may spur the Chinese government to liberalize policies. Meanwhile, widely different hospital-level skillsets and approaches to institutional review board (IRB) approvals mean CAR-T manufacturers must be careful about which centers they use, experts said.

Kite Pharma (NASDAQ:KITE) announced 10 January the formation of a Shanghai-based joint venture (JV), Fosun Pharma Kite Biotechnology, with Fosun Pharmaceutical (SHA:600196), to will license and develop Kite's axicabtagene ciloleucel (axi-cel) in China. The deal gives the JV options to license other Kite CAR-Ts and T-cell receptor (TCR) therapies. Juno Therapeutics (NASDAQ:JUNO) announced 7 April 2016 a similar JV, JW Biotechnology, with Shanghai-based WuXi AppTec.

Analysts have noted recent health care reform developments and a favorable landscape for in-licensing and partnering of foreign cell therapies in China, especially CAR-Ts, describing the Kite-Fosun JV as positing substantial cell therapy development opportunities there.

A Kite spokesperson noted the CFDA has drafted guidelines for cell therapies that are under review, but it does not currently regulate them, and the company has not disclosed timing or other details regarding clinical trials in China. The spokesperson added the 50/50-owned JV will be a separate Chinese company that will manufacture and develop axi-cel there. Juno did not address specific inquiries, and neither Fosun nor WuXi AppTec responded to requests for comment.

**Uncertain regulatory landscape**

A hurdle remaining to be cleared is Ministry of Health-imposed restrictions on commercial use of cell therapies in cancer - though clinical trials are still allowed - following a high-profile scandal last year in which a synovial sarcoma patient died after receiving dendritic cell cytokine-induced killer (DC-CIK) therapy, noted Alex Chang, professor, School of Medicine, Tongji University, Shanghai, and Lung-Ji Chang, Department of Molecular Genetics and Microbiology, University of Florida College of Medicine, Gainesville. Despite being ineffective, the therapies had become widespread in China, leading to many patients being defrauded, Lung-Ji Chang added.

However, based on documentation, the government appears to be moving toward allowing commercialization, said Jianqiang Li, formerly Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, Washington, and now working on a startup in China. Dr Weidong Han, Department of Hematology, Chinese People's Liberation Army Hospital, Beijing, said the government is treating CAR-T development as a priority.

> **"FDA approval of CAR-Ts would be proof of concept for clinical application and could thus spur the Chinese government to open the market faster"**

Draft guidance that the CFDA released for public comment on 16 December 2016 proposed a CFDA-led regulatory framework for stem cell therapy, immune cell therapy and gene editing. The draft guidance has sparked industry debate and indicates the CFDA is gradually establishing a more flexible and pragmatic approach to cell therapy, according to a 20 December press release by Innovative Cellular Therapeutics, a Shanghai-based CAR-T company.

Thus, cell therapy development, which previously fell under the authority of the Ministry of Health, will likely now fall specifically under CFDA oversight, Jianqiang Li said. In general, cell therapies had previously not been regulated much, Lung-Ji Chang said.

FDA approval of CAR-Ts would be proof of concept for clinical application and could thus spur the Chinese government to open the market faster, said Peng Li, principal investigator, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences. This news service previously reported that axi-cel would likely win FDA approval for aggressive nonHodgkin's lymphoma, while acute lymphoblastic leukemia (ALL) data on Novartis' (VTX:NOVN) opened a decent approval path for tisagenlecleucel-T.

But for the moment, there are no specific development regulations for CAR-T, Lung-Ji Chang said, thereby presenting a hurdle to Western CAR-Ts entering the market. For example, it is unclear if initiating a clinical trial would require filing an IND-type application, and who would look at such an application if it was filed, he said.

Given regulatory uncertainties and the greater difficulties of developing drugs in China than in the US, Kite and Juno were smart enough to know it would not be a good idea to try and enter the Chinese market by themselves, Alex Chang said. A lot of companies previously opened research facilities in China when the government opened the pharmaceutical market, but closed them after discovering drug development there was more difficult than anticipated due to unpredictable regulations, Lung-Ji Chang said.

**Hospital practice disparities**

Beyond regulatory hurdles, there are also development disparities in terms of different hospitals' practices during trials, Lung-Ji Chang said. While some will make sure to get IRB approval before starting a study, others will not until after the study has started, he explained, adding some still will not seek IRB approval at all, he explained.

With time, he said, hospitals in China may catch up to international standards and ensure IRB approval before enrolling patients. But until then, companies developing CAR-Ts will have to be very picky about which hospitals they use for clinical trials, he said, adding that even working with CROs in China can sometimes be hectic because they do not do a good enough job facilitating communication between trial sites and sponsors.

Many hospitals have also insisted on doing manufacturing on-site, whereas others do not, Peng Li said. Because of this, he said, the CAR-T development program he is running set up central GMP facilities in Guangzhou and Changsha, as well as smaller facilities at some of the centers.

ClinicalTrials.gov lists one Phase I study (NCT02822326) -- in which he is taking part -- of a CD19-targeting CAR-T in acute leukemia, sponsored by Guangdong General Hospital.

In terms of centers' abilities to handle the toxicities associated with CAR-T and required inpatient care, Peng Li, Lung-Ji Chang and Alex Chang agreed there were significant disparities between some hospitals, with some being exemplary in their treatment of patients and others ill-equipped to handle CAR-T toxicities due to lack of skills, while doctors at other hospitals were too harried to communicate efficiently with sponsors.


Alaric DeArment
Reporter, New York

Alaric DeArment covers cancer drug development for BioPharm Insight. He served as associate editor of Drug Store News from 2008 to 2014, covering branded and generic drugs from development to distribution, retail and specialty pharmacy and regulatory affairs. In 2011-2012, he edited the book Contestation and Adaption: The Politics of National Identity in China. 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. Follow Alaric on Twitter @AlaricD_BPI

# Looking to start a clinical trial?

## Have you seen what Australia has to offer?

- High quality clinical and pre-clinical research capabilities
- Political stability, safe & robust legal and regulatory system
- Quick start-up time of clinical trials
- Preferred location for incorporation in multi-national trials
- State-of-the-art medical research facilities and hospitals
- Strengths in pre-clinical and early clinical development phases
- Strong Government commitment and investment
- Favourable Australian Dollar Exchange Rates
- Access to 45% R&D Tax Credit*

*Contact LSQ to find out how to acces the R&D Tax Credit

LSQ can help you get started.

Contact us now.

info@lsq.com.au
+61 7 3331 3999
www.lsq.com.au
@LSQld

Life Sciences Queensland

# CVH

## Center for Viral Hepatitis

바이러스간염진료센터

- **To promote the awareness of hepatitis B**
- **To screen in high risk population**
- **To facilitate the linkage to care**

**SCREENING**
Get tested and be prepared

**EDUCATION/ RESEARCH**
earn what's new on viral hepatitis

**HEPATITIS EXPERTS**
Find specialists around you

**LINKAGE TO CARE**
Engage yourself to access health care

www.cureHep.org

# FOLLOW THE JOURNEY OF VIREAD

**#1** **Prescribed oral antiviral** according to US prescription data for treatment of CHB[1a]

## COMPLETE RESPONSE RESULTS AT YEAR 1...

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

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

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

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

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

## INDICATION AND USAGE

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

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

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

## IMPORTANT SAFETY INFORMATION

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

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

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

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

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

Viread® 300mg tablets
tenofovir disoproxil fumarate

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

## ...AT 8 YEARS: NO RESISTANCE WAS

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

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

## IMPORTANT SAFETY INFORMATION (cont'd)

### WARNINGS AND PRECAUTIONS

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

### ADVERSE REACTIONS

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

### DRUG INTERACTIONS

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

# DETECTED AT YEAR 1 THROUGH YEAR 8


## NO HBV RESISTANCE DEVELOPED YEAR 1 through YEAR 8

### in clinical trials (Studies 102 and 103)[2,3]*

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

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

## IMPORTANT SAFETY INFORMATION (cont'd)

### DRUG INTERACTIONS (cont'd)

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

### DOSAGE AND ADMINISTRATION

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

### DOSAGE ADJUSTMENT FOR PATIENTS WITH ALTERED CREATININE CLEARANCE

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

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

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

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

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

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

**For more information, visit www.viread.com/hcp**

300 mg 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 therapy, including VIREAD. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including VIREAD. If appropriate, resumption of anti-hepatitis B therapy may be warranted *(See Warnings and Precautions)***

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

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

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

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

**Dosage Adjustment for Adult Patients with Altered Creatinine Clearance**

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

a. Calculated using ideal (lean) body weight.

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

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

**CONTRAINDICATIONS:** None.

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

**Bone Effects**

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

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

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

*Mineralization Defects:* Cases of osteomalacia associated with proximal renal tubulopathy, manifested as bone pain or pain in extremities and which may contribute to fractures, have been reported in association with the use of VIREAD *(See Adverse Reactions)*. Arthralgias and muscle pain or weakness have also been reported in cases of proximal renal tubulopathy. Hypophosphatemia and

## Brief Summary (Cont'd)

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 384 weeks.

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

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

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

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

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

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

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

# Conference Alerts

## North America

### ARVO 2017 Annual Meeting
May 7-11, 2017 | Baltimore, Maryland, USA

***Website: http://www.arvo.org/AM/Default.aspx***
Contact: arvo@arvo.org

The Annual Meeting of the Association for Research in Vision and Ophthalmology (ARVO) is the largest gathering of eye and vision researchers in the world, attracting over 11,000 top eye and vision researchers and clinicians from more than 75 countries to explore cutting-edge basic and clinical science. The Annual Meeting features five days of the most innovative and cutting-edge vision science in every facet of vision research. It will discuss the challenges in bridging gaps in our scientific knowledge, creating effective collaborations and keeping bright young minds engaged in research careers.

### The 7th Annual Traumatic Brain Injury Conference
May 24-25, 2017 | Washington, DC, USA

***Website: http://tbiconference.com/home/***
Contact: enquiries@tbiconference.com

This conference brings together researchers and clinicians from industry, academia, the military and government to present ground-breaking research in a variety of areas related to traumatic brain injury. This event provides a special opportunity for a variety of stakeholders to present original research and analysis aimed at providing a full picture of the progress being made towards better diagnosis, treatment and long-term care for TBI survivors. At this annual event, physicians, nurses, neurosurgeons, scientists, and drug/diagnostic developers from all over the world network and learn from one another.

### American Society of Clinical Oncology 2017 Annual Meeting
June 2-6, 2017 | Chicago, Illinois, USA

***Website: http://am.asco.org***
Contact: customerservice@asco.org

The ASCO Annual Meeting brings together more than 25,000 oncology professionals from a broad range of specialties, making it an excellent venue for exploring the theme of the Meeting — “Science and Society.”

### 5th Global Summit and Medicare Expo on Head and Neck Surgery
June 19-20, 2017 | Philadelphia, Pennsylvania, USA

***Website: http://headnecksurgery.global-summit.com***
Contact: ufs@uniteforsight.org

Head & Neck Surgery 2017 focuses on the area of medicine that deals with disorders and conditions of the ear, nose, and throat region, and related areas of the head and neck. This conference will witness a conglomeration of various arenas in Head and Neck Surgery and as it involves a vast range of medical streams within it, this conference will be an excellent platform for interdisciplinary interactions, to exchange and share knowledge under a single roof.



## Europe

### The 2017 World Congress Integrative Medicine & Health
May 3-5, 2017 | Berlin, Germany

***Website: https://www.ecim-iccmr.org/2017/***
Contact: esim@charite.de

This congress will take place in association with a number of international organizations including the Academic Consortium for Integrative Medicine and Health (ACIMH) in North America and others from around the globe. The main congress topics will include research, clinical care, education, traditional healing systems, and medicine and arts. Researchers, educators, policy makers and clinical providers of Complementary and Alternative Medicine (CAM) are all invited to take part in the conference.

### EuroGUHC 2017 Meeting
May 5-6, 2017 | Lausanne, Switzerland

***Website: http://wp1.euroguch.com/welcome-message/***
Contact: GTito@paragong.com

The EuroGUCH 2017 meeting is the most prestigious conference on adult congenital heart disease in Europe, organized under the auspices of the working group on grown-up congenital heart disease of the European Society of Cardiology. The meeting will cover important and burning topics in adult congenital heart disease and will have an international faculty including many European opinion leaders in the field. Focus will be given on novel therapeutic strategies of anticoagulation, heart failure, pulmonary hypertension and systemic hypertension, novel interventional therapies for valve dysfunction, and arrhythmia, and problems beyond heart disease (including sexuality and depression).

### The 7th International IVI Congress
May 11-13 | Bilbao, Spain

***Website: http://www.ivi2017.com***
Contact: ivi2017@pacifico-meetings.com

The 7th International IVI Congress is a top-level reproductive medicine congresses, addressing cutting edge topics in this continuously evolving field of human reproduction and offering the most reputable international speakers available.systemic hypertension, novel interventional therapies for valve dysfunction, and arrhythmia, and problems beyond heart disease (including sexuality and depression).

## Asia

### 32nd International Conference of Alzheimer’s Disease International
April 26-29, 2017 | Kyoto, Japan

***Website: http://www.adi2017.org***
Contact: adi2017@mci-group.com

The annual conference of Alzheimer’s disease International (ADI) attracts thousands of people with an interest in dementia from over 100 countries around the world. Hosted with a different Alzheimer association around the world each year, in 2017, the conference will be hosted with Alzheimer’s Association Japan (AAJ). The conference is one of the world’s largest and most important conferences on Alzheimer’s disease and dementia, featuring a range of international keynote speakers and a high standard of scientific and non-scientific content; combined this makes it the optimum setting to learn about the latest advances in the treatment of dementia.

### MediWorld – China International Medical Travel Show
May 12-14, 2017 | Shanghai, China

***Website: http://www.chinamediworld.com***
Contact: info@chinamediworld.com

MediWorld - China International Medical Travel Show is a networking and learning event bringing together affluent Chinese health travelers, international hospitals and clinics, referring doctors, medical tourism facilitators, destination tourism organizations, online medical travel platforms, insurers and China’s private hospitals. Meet face-to face with China’s affluent international patients. Identify partners and start a dialogue in networking sessions or private meetings. Learn about international treatment options, what motivates different patient segments, how referrals and decisions are made, the market opportunities and pitfalls to avoid.

# Kinexum


**Kinexum designs, guides and manages strategic and operational solutions to the regulatory, manufacturing, nonclinical and clinical development as well as commercial challenges necessary to bring healthcare products from proof of concept to commercialization.**

Our experts, whether as an individual consultant or as an integrated team, supplement the strengths of large and small organizations to reach high value milestones effectively and efficiently.

Kinexum specializes in crafting creative but sound and integrated solutions across scientific disciplines, therapeutic areas, product modalities and business stages.

## www.Kinexum.com

We would be pleased to assist your organization, please contact us at info@kinexum.com or visit our website for more information.



# Synatura

**Ivy leaf 30% ethanol ext. + Coptis Rhizoma butanol ext.**

## Synatura is...

- *No.1 antitussive & expectorant product in Korea*
- *Synergy effect by combination of natural products*
- *Best choice for inflammatory chronic bronchitis*
- *Proven safety and effect*


**Ahngook Pharmaceutical Co., Ltd**
www.ahn-gook.com




### 1. Fda Approves Regeneron, Sanofi $37,000 Per Year Eczema Drug

The U.S. Food and Drug Administration approved Regeneron Pharmaceuticals Inc and Sanofi SA's drug for moderate-to-severe atopic dermatitis, a product widely seen as the most important future growth driver for the two companies. Sanofi and Regeneron said the drug, Dupixent, will have a list price of $37,000 a year. But while the price before discounts and rebates to insurers is far more expensive than topical medicines and steroids currently used to treat eczema, it is less pricey than other injectable antibody drugs for serious conditions, such as psoriasis, that list for about $50,000 a year. Dupixent is also being developed for severe asthma, where it will compete with a wave of other new biotech medicines, such as GlaxoSmithKline's Nucala, as well as for nasal polyps.

*http://www.reuters.com/article/us-regeneron-fda-eczema-idUSKBN16Z25Z*

### 2. Health Bill Would Add 24 Million Uninsured but Save $337 Billion

The House Republican plan to replace the Affordable Care Act would increase the number of people without health insurance by 24 million by 2026 to 52 million people compared with 28 million projected under current law, while slicing $337 billion off federal budget deficits over that time, the nonpartisan Congressional Budget Office said. The Trump administration immediately denounced the budget office's conclusions. Tom Price, the secretary of health and human services, suggested the report offered an incomplete picture because it did not take into account regulatory steps he intends to take, as well as other legislation that Republicans plan as part of their multistep strategy to repeal and replace the health law.

*https://nyti.ms/2mDeE1g*

### 3. Drugmaker Lilly to Invest $850 Million in U.S. Operations in 2017

The U.S. administration has threatened an import tax, while Trump has attacked some of the world's biggest companies, prompting many to make promises to invest more in the United States. Many companies are also urging Congress to overhaul the U.S. tax system, saying a set of changes Republicans proposed last year will make them more competitive globally and help create U.S. jobs. Eli Lilly and Co said it would invest $850 million in its U.S. operations this year, and is willing to spend more if the U.S. introduces more favorable tax laws. Indianapolis-based Lilly, whose earnings growth resumed in 2015 after three years, has been aggressively developing new drugs.

*http://www.reuters.com/article/us-lilly-investment-idUSKBN16V1I7*

### 4. Activist Investor Sarissa Seeks Innoviva CEO Pay Cut

Hedge fund Sarissa Capital Management LP sought a sharp cut in the compensation of Innoviva Inc's (INVA.O) chief executive, the latest salvo by the activist investor in its proxy fight against the drug company. Sarissa has nominated three directors to Innoviva's board and criticized the company's cost structure, as well as executive compensation, considering that it only manages drug royalties and does not market or sell any products. Sarissa also called for a pay cut for Innoviva's board members. The compensation paid to the company's chief executive, Michael Aguiar, should be reduced to below $500,000 per year, Sarissa said. Sarissa also said the compensation paid to Innoviva's board members should be reduced to below $200,000.

*http://www.reuters.com/article/us-innoviva-sarissa-idUSKBN1711ZZ*

### 5. Amgen Accuses Would-be Copycat Coherus of Stealing its Neulasta Secret

In its new lawsuit, Amgen claims Coherus engineered a "massive conspiracy" to steal its information, according to analysts at Barclays. That conspiracy, Amgen says, included recruiting its employees, who then siphoned off secrets and passed them to Coherus. Coherus allegedly received information on "stolen" USB drives, including "sensitive Amgen standard operating procedures, laboratory notebook pages, validated analytical methods, method development reports, specifications, documents reflecting process optimization work, cost calculators and pricing and contracting strategies," the analysts say. But Coherus "categorically" rejects the allegations, CEO Denny Lanfear said in a statement, and accused Amgen of using the lawsuit to stave off competition.

*http://www.fiercepharma.com/pharma/amgen-takes-to-california-courts-to-allege-trade-secret-theft*

### 6. After Three Defeats and $200M in Damages, J&J Notches Win in St. Louis Talc Litigation

A St. Louis jury spurned plaintiff Nora Daniels' claim that Johnson & Johnson's baby powder caused her ovarian cancer. Eleven out of twelve jurors sided with the pharma giant. J&J's triumph comes after it lost three cases last year, all in St. Louis, to the tune of nearly $200 million all together. A jury awarded $72 million in damages in February, followed by a $55 million decision in May and a $67 million ruling in October. But the company is far from in the clear with its courtroom battles. It's facing thousands of other talc cases in St. Louis, a city whose jury pool is tainted, J&J argues, by millions in ad spending by its opponents. Outside of St. Louis, the drug giant has had more luck. In New Jersey, J&J attorneys convinced a judge to toss two cases, with Goodrich noting in the new statement that "plaintiffs' scientific experts could not adequately support their theories" of a link between talc powder and ovarian cancer.

*http://www.fiercepharma.com/legal/following-three-defeats-j-j-prevails-latest-st-louis-talc-suit*

### 7. Democrats, Sanders Back Massive Pharma Overhaul in 'Landmark' Pricing Legislation

In the wake of the Republicans' failure to repeal and replace the Affordable Care Act last week, Democrats are stepping in with some proposals of their own. A lot of proposals would dramatically reshape the industry. The bill would require drug companies to publicly report development, manufacturing and marketing costs; allow Medicare to negotiate drug prices; tax drugmakers who implement big price hikes; and mandate more reporting by patient assistance groups who receive pharma funds. It also would clear the way for importing cheaper (and safe) meds from Canadian sellers, end the direct-to-consumer advertising tax deduction, outlaw pay-for-delay arrangements that keep generic drugs off the market, and create incentives to bolster generic drug competition.

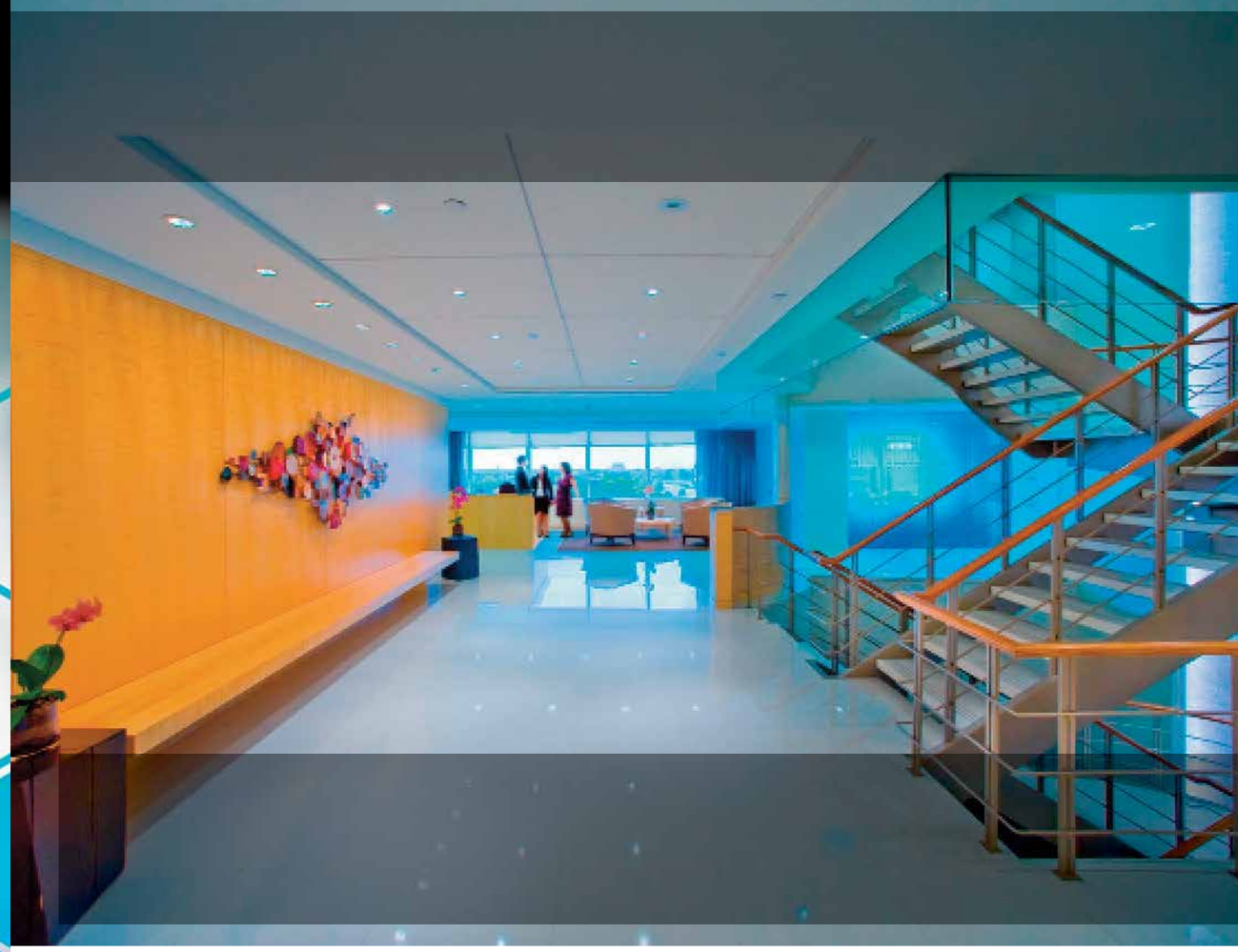
*http://www.fiercepharma.com/regulatory/democrats-sanders-eye-big-pharma-reforms-landmark-legislation*

# A better option for clinical toxicology and pharmacogenetics testing.

Advanced Clinical Laboratory Solutions is an independent clinical laboratory specializing in clinical toxicology and pharmacogenetics that provides convenient, high-quality testing services and accurate, timely test results to patients, physicians and medical centers across the country.

ACLS®
Advanced Clinical Laboratory Solutions, inc

844.225.7522 (844-ACLSLAB) ⬢ www.aclsdiagnostics.com



James V. Aiosa
Paul V. Majkowski
Geoffrey R. Kaiser
Partners

RIVKIN RADLER LLP
ATTORNEYS AT LAW

Driven to Deliver®

Long Island • New York City • New Jersey

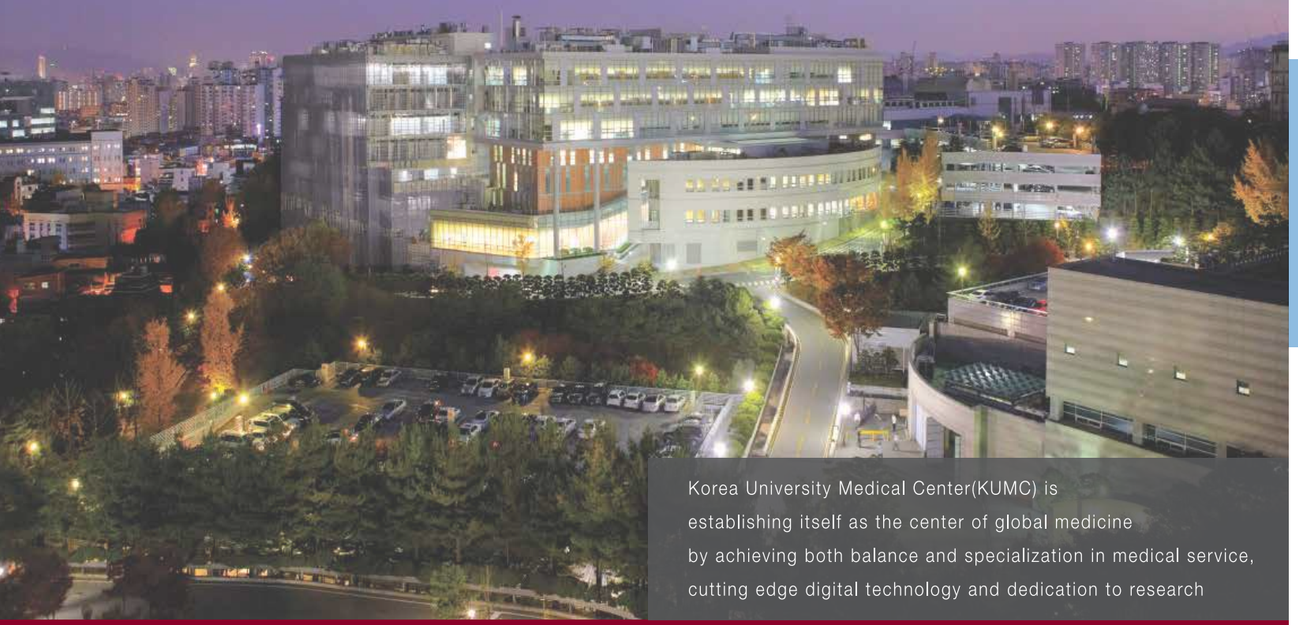
www.rivkinradler.com

www.kumc.or.kr

KU MC KOREA UNIVERSITY MEDICAL CENTER

Patients-centric, R&D-centric

# KOREA UNIVERSITY MEDICAL CENTER



Korea University Medical Center(KUMC) is
establishing itself as the center of global medicine
by achieving both balance and specialization in medical service,
cutting edge digital technology and dedication to research

## “Striving to be the best medical complex”

KUMC sets up the standards of Medicine education, Medical research, Medical service

**College of Medicine**
의과대학
(+82)-2-2286-1139

**College of Health Science**
보건과학대학
(+82)-2-940-2700

**Anam Hospital**
안암병원
(+82)-2-1577-0083

**Guro Hospital**
구로병원
(+82)-2-1577-9966

**Ansan Hospital**
안산병원
(+82)-2-1577-7516

cap ACCREDITED™ LM EQA European Quality Assurance ANAB ACCREDITED

ISO 9001:2008 & KS Q ISO 9001:2008

30th ANNIVERSARY

THIS IS WHO WE ARE

# For Evidence-Based Laboratory Medicine

**Seoul Clinical Laboratories (SCL)**
was established in 1983 as Korea’s first specialized clinical and pathology reference laboratories.
Since then, SCL has taken a leading role in the field of both clinical diagnostic and specialized analytic techniques, and has continuously pursued 3 core values, Service, Quality and Research.
At present, SCL with 24-hour operational system provides full services for about 4,000 clinics and hospitals nationa-wide and is also constructing a global network with Mayo Clinics, Quest Diagnostics, Inc., USA , Mitsubishi Chemical Medience Co., Japan, and Dian Diagnostics, in China.

## Diagnostic Innovations

*We are passionate about developing innovaitve, ground breaking tests, products and tools to enhance patient care, provide value to our clients, and transform information into knowledge and insights.*

## Expertise Across Multiple Disciplines

Six Sigma SCL Quality, Service, Research
Seoul Medical Science Institute
*Seoul Clinical Laboratories*

12, Jangmun-ro 6-gil, Yongsan-gu, Seoul, Korea
Tel : +82-2-790-6500 I Call Center : 82-2-330-2001~3
Website : http://www.scllab.co.kr


# Advancing Therapeutics, Improving Lives.

For more than 25 years, Gilead has worked to develop medicines that address areas of unmet medical need for people around the world.

Our portfolio of medicines and pipeline of investigational drugs include treatments for HIV/AIDS, liver diseases, cancer, inflammatory and respiratory diseases and cardiovascular conditions.

Every day we strive to transform and simplify care for people with life-threatening illnesses.

GILEAD

For more information, please visit www.gilead.com.