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WAMJ

World Asian Medical Journal

Inspirational Asian Healthcare Leader

DAVID HO

Scientific Director and Chief Executive Officer,
Aaron Diamond AIDS Research Center (ADARC)

BIOPHARMA REPORT I

Novavax's NanoFlu Has Tepid Expert Market Forecasts in Influenza Versus Sanofi's Fluzone

BIOPHARMA REPORT II

Bayer's Finerenone Use Will Face Off With SGLT2 Inhibitors

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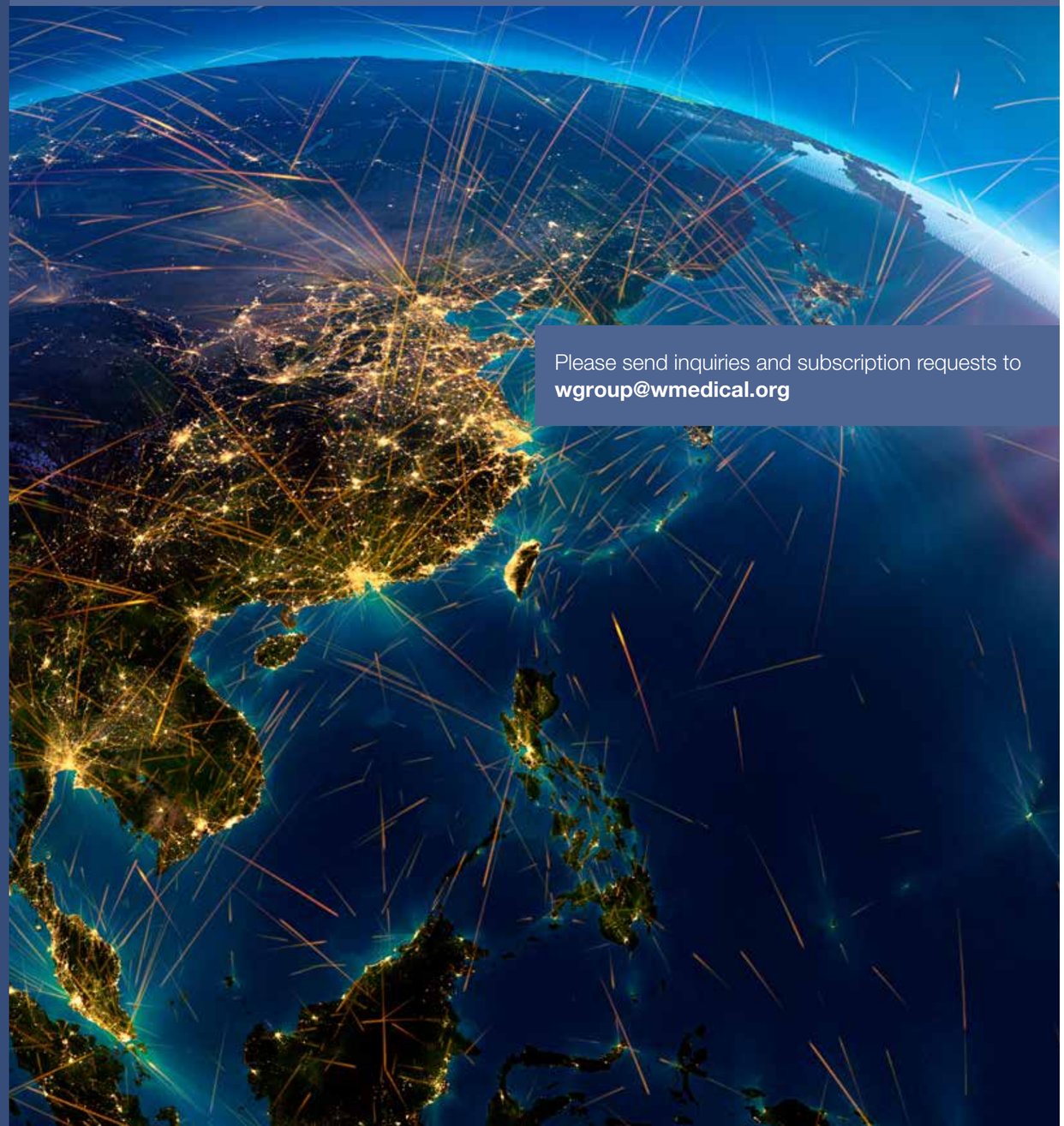

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From the Publisher

Our 20th issue marks the end of 2019 and I hope everyone is well as the holidays are approaching.

I think the keywords of healthcare in year the 2019 were two: Innovation and Collaboration. Innovations have transformed the future of healthcare and medicine, and bio-health collaborations have accelerated such transformation. Combination of the two has led the healthcare industry to date, and it will continue to remain the impetus for growth.

In this issue, we feature one remarkable physician and thought leader who led the state-of-the-art innovation and established an extraordinary collaboration in the area of AIDS/HIV research, Dr. David D. Ho, M.D. He is an Irene Diamond Professor at The Rockefeller University and the Scientific Director and Chief Executive Officer at Aaron Diamond AIDS Research Center. He has dedicated his life to researching the pathogenesis of HIV infection and the dynamics of HIV replication, and he led the development of life-prolonging combination antiretroviral therapy, also known as the "AIDS cocktail". This was a result of his persistent research despite the stigma associated with the disease. Contributing to the accumulation of scientific evidence that adjusted the public's conception about the disease, Dr. Ho sets an example for scientists who wish to take part in medical innovation. His achievements in the areas of AIDS/HIV research are remarkable not only for the results but also for their insights into how we can better serve the patients. His visions and efforts on overcoming unmet medical needs will always remain as a living legacy to inspire and motivate all of us. Dr. Ho's story and achievement show us why innovation in medical treatment is so critical in enhancing the quality of people's lives.

Innovation and collaboration are the same keywords that represent World Asian Medical Journal and our efforts to bringing diversity and new avenues of progress in all branches of healthcare. Through our publications, we try to spread the messages of innovation and invite people to participate in the platform of collaboration.

New trends and issues of the bio-health industry were featured in the articles. Many eminent experts shared their knowledge and insights as authors in this edition. I wish that our readers will find this exciting selection of articles to be helpful and pleasant.

Needless to say, our goal is to connect with one another and provide a forum for readers to develop an integrative perspective in healthcare.

2019 was a great and exciting year. All the editorial boards and staffs of WAMJ wish all our readers festive holidays and a prosperous 2020.

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

From the Editor-in-Chief

Welcome to our 20th issue!

I write these words at the start of the traditional holiday season here in America--a time of thanks, fellowship, and "good will toward men." A fitting time to recognize the talents and dedication of my WAMJ colleagues. The staff does all the hard work of publication— planning, research, writing, layout, etc. Editors merely edit—if that. In WAMJ's case, little is required of the titular editor. Credit for what you have before you goes to those who actually do the work, not me. My thanks and congratulations to our dedicated staff.

One of the great pleasures of serving as WAMJ's Editor-in-Chief is the opportunity to encounter superb minds and noble spirits. One such is the subject of our cover story. David Ho, M.D., Professor of Medicine at The Rockefeller University, has devoted his life and his luminous talent to fighting HIV, first through revolutionary combination anti-retroviral therapy; later by working towards vaccine creation. Relatedly, Dr. Ho has published extensively and garnered honors galore. I leave to others the more thorough discussion these subjects deserve to focus, instead, on Dr. Ho's courage.

Those of us old enough to remember the start of what became the HIV epidemic recall that, for reasons unknown, members of discrete and insular minorities began to develop Pneumocystis carinii pneumonia, previously uncommon, and Kaposi's sarcoma, until then a rare malignancy. Patients tended to come disproportionately from the ranks of IVDUs (intravenous drug users) and homosexuals; hemophiliacs and babies born to infected mothers were also at risk. Little was understood about the disease, except that it carried a mortality rate approaching 100%. Terror reigned. Assembly line workers refused to stand next to other employees suspected of having the disease. Some health professionals refused to care for patients suspected or known to be infected. America closed her doors to persons from endemic areas. While many clergymen were leaders in trying to help the afflicted, some found in the epidemic divine retribution for human sinfulness and an exhortation to repent.

Against this background, Dr. Ho and a small group of researchers began to search for the truth about the disease. In a remarkably short length of time, by historical standards, he and his fellow investigators began to unlock the secrets that would transform HIV infection from a death sentence to a manageable chronic illness. In doing so, they not only saved lives, they caused many to re-examine their own philosophies.

In this season of rejoicing, let us remember the sufferings of the sick, whether with HIV or with other illnesses, and let us honor the contributions of heroic, astute, and dedicated medical scientists, such as Dr. David Ho.

Joseph P. McMenamin, MD, JD, FCLM
Editor in Chief
EVP of W Medical Strategy Group

WAMJ Recap of the Last Issue

COVER STORY
Joanne Liu, M.D., C.M., FRCPC, International President of Médecins Sans Frontières (MSF)

Dr. Joanne Liu is a pediatric emergency physician, associate professor at the University of Montreal, and the International President of Médecins Sans Frontières (MSF), also known as Doctors Without Borders. Having been involved in MSF since 1996, Dr. Liu has worked in conflict zones around the world including Palestine, Central African Republic, and Sudan, providing support for war refugees and victims of natural disasters and epidemics. In MSF, Dr. Liu also helped create the telemedicine project, which connects MSF physicians in 150 remote sites with a pool of medical specialists across the globe. She also helped develop one of the first programs offering comprehensive medical care for survivors of sexual violence in the Republic of Congo. To learn more about Dr. Liu, please refer to issue 19 of WAMJ.

SPECIAL REPORT
In Memory of Dr. Waun Ki Hong, the Physician-Scientist Who Transformed and Redefined Cancer Treatment

This January, the cancer medicine field and the medical community at large lost a legacy. Dr. Waun Ki Hong, past division head and Professor at The University of Texas MD Anderson Cancer Center, past President of the American Association of Cancer Research (AACR), and a Samsung Distinguished University Chair in Cancer Medicine, lived a full and accomplished life before passing in the close presence of family. In the first issue of WAMJ, we commemorated Dr. Hong's lifelong contributions through the Special Report. To read about Dr. Waun Ki Hong's accomplishments during his lifetime, please refer to issue 19 of WAMJ.

BIOPHARMACEUTICAL REPORT I
Both AbbVie's Orilissa and Myovant's Relugolix Expected to Face Similar Payer Scrutiny in Uterine Fibroids

AbbVie's Orilissa for endometriosis-related pain faces difficulties in reimbursement due to the challenges of having to provide adequate evidence to prescribe the drug. Myovant's Relugolix faces the same problem, and they will therefore likely extend to other indications like uterine fibroids. However, there are conflicting opinions on the predicted impact of these drugs. Nonetheless, an AbbVie-sponsored 2-year analysis looked at Orilissa's treatment and found it to be cost-effective, while some find the time period of the analysis to be inadequate. Orilissa is currently the only approved GnRH antagonist, and Relugolix is in two Phase III studies for patients with endometriosis-related pain. To read more about Orilissa and Relugolix, please refer to issue 19 of WAMJ.

BIOPHARMACEUTICAL REPORT III
Is Tau the New Amyloid?

Pharmas are starting to look beyond amyloid to treat Alzheimer's disease and are focusing on tau as the next big target. The question is whether they can pick out the lessons from the amyloid saga to avoid following the same storied path. Tau is considered the next-best chance to β amyloid for AD, driving pharma companies to pile on the same target despite the absence of clinical proof as they did for amyloid. However, the lessons from β amyloid taught tau drug developers that timing the treatment and finding the right population – rather than taking all comers – could dramatically increase their chance of success. To learn more about tau and amyloid for AD treatment, please read issue 19 of WAMJ.

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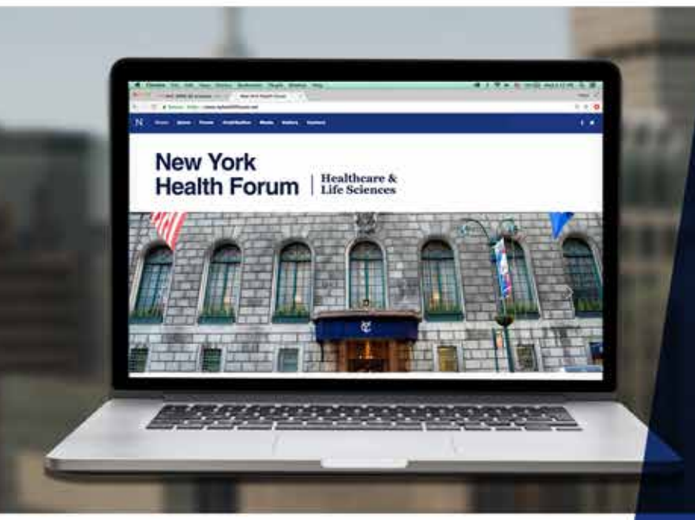

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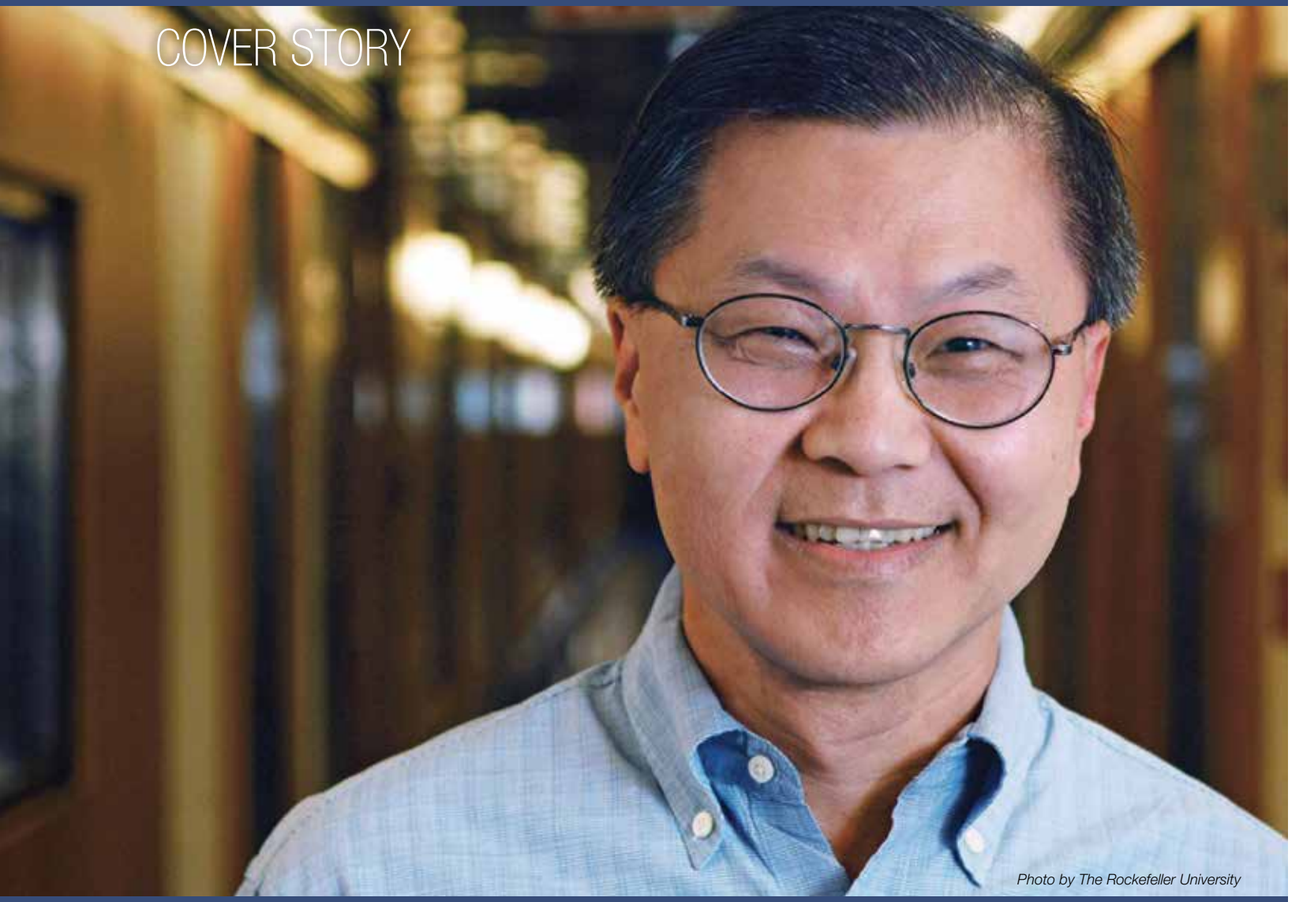


Photo by The Rockefeller University

Inspirational Asian Healthcare Leader

David Ho, M.D.

Scientific Director and Chief Executive Officer, Aaron Diamond AIDS Research Center (ADARC)

Irene Diamond Professor, The Rockefeller University

COVER STORY

1. Dr. Ho, you are a world-renowned physician at the forefront of medical innovation with HIV/AIDS Research. Can you share with our readers what motivated you to attend medical school and become a physician? Also, what event in your career or philosophical reflection drove you to specialize in HIV/AIDS research?

- In 1970, I started in college as a student interested in physics. As I took courses in biology, however, I realized that the life sciences were undergoing a major transformation with a series of important discoveries. Gradually, my interest evolved to focus on biology, with an eye toward diseases affecting human health. This was the reason that upon graduating from Caltech, I entered Harvard Medical School, although my main objective was medical research rather than the practice of medicine. Several years later, while serving as chief medical resident in a hospital on the west side of Los Angeles, I chanced to encounter cases of young gay men who presented to the hospital with a multitude of infections that suggested that their immune systems were severely impaired. In retrospect, these were among the earliest cases of AIDS reported to the CDC in 1981. This medical mystery piqued my scientific curiosity, which I have pursued ever since. Of course, I did not realize then that this nascent disease would ultimately become one of the worst pandemics in human history.

2. We see that you have been devoted to medical research and education for over 30 years. What were some of the most memorable achievements during your professional life? Also, what were the most demanding obstacles you had to overcome during the path of your career, and how did you do it?

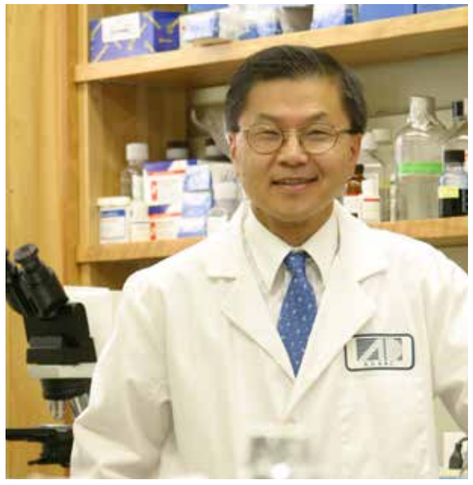
- The most important contribution to AIDS research from my laboratory is the unraveling of the dynamics of HIV in infected persons. Analyzing patient data quantitatively, we were able to shatter the old notion that HIV infection was largely quiescent for a long period of time. Instead, we revealed that HIV was highly dynamic throughout the entire course of infection. Every day, billions and billions of new HIV particles are produced and then removed. Similarly, millions and millions of infected T cells become newly infected, which then die in short order. Associated with this extensive and continuous HIV replication is the rapid destruction of CD4 T cells that are so important in orchestrating our immune systems in fighting pathogens.

Dr. Ho with Irene Diamond, the philanthropist who created the Aaron Diamond AIDS Research Center; 1991

3. You and your colleagues discovered the innovative "AIDS cocktail", a combination antiretroviral therapy. This discovery turned AIDS, a fatal disease with no cure, into a treatable disease with a significantly lower mortality rate. Can you share with our readers the background of this ground-breaking discovery? How did this finding affect the course of your research for HIV/AIDS? What lessons can other researchers learn from your experience, in AIDS and in other disorders?

- From the understanding of HIV dynamics discussed above, we came to understand in great detail that the virus was mutating so rapidly that millions and millions of new variants were being produced each day inside the body of an infected person. Given such high mutation rates, we easily determined that, if the drugs were given individually, mutants would arise each day to continually resist our antiretroviral drugs. Even administering two drugs at a time was relatively easy for HIV to evade. However, our calculations also suggested that if we were to force the virus to make multiple key mutations simultaneously in one viral genome (to resist a combination of three or more drugs), the probability that resistance would develop was exceedingly low. This

realization in 1995 led us to initiate three different trials of combination antiretroviral therapy in patients. Within a few months, we knew that our strategy was correct in that we were able to durably control HIV replication in our patients. We waited a year to be sure the good results could be maintained for that duration. Indeed, by the summer of 1996, I announced our results to the world at the International AIDS Conference held in Vancouver. That became the turning point of the AIDS epidemic when an automatic death sentence was transformed into a manageable disease. Gratifyingly, over 21 million individuals worldwide have benefited from such a treatment strategy.



Dr. Ho in ADARC Lab

4. Especially early on, AIDS research was stymied to some extent by the stigma associated with the behaviors that came to be associated with higher risk for contracting the disease. Was your own work ever hampered by this problem? Can you offer any insights for how to overcome such problems in the care and treatment of other patients likewise stigmatized?

> “That became the turning point of the AIDS epidemic when an automatic death sentence was transformed into a manageable disease”

- It was certainly distressing to witness the stigma and discrimination endured by infected persons. The injustice was suffered at the hands not only of strangers but also of family and friends, and even health care workers. Just imagine dying from a lethal disease while being shunned by your loved ones! At the time, we could rely solely on science to argue that this disease is transmitted only by intimate contact such as sex and sharing of needles, and not by casual contact. It was not easy, but with the passage of time and accumulation of scientific evidence, much of the public (in the US) has become reassured by the lack of casual transmission of HIV. Around the globe, however, many remain ignorant about the basic facts on HIV/AIDS, resulting in persistence of stigma and discrimination against infected persons. Knowledge is power.

Dr. Ho with Dr. Gerald Friedland, Chairman of the Board, Aaron Diamonds AIDS Research Center at the National Portrait Gallery in Washington, D.C. 2017

Dr. Ho with Magic Johnson and Bill Clinton at `The Inaugural Irene Diamond Gala Dinner in 2009

5. As the Scientific Director and CEO of the Aaron Diamonds AIDS Research Center (ADARC), please share with our readers the mission and goal of ADARC. Also, having been involved with the center since 1989, did you witness or initiate any major shifts in how ADARC pursues its goals?

- Our institute came into being in 1989, and we had a singular mission of making scientific contributions that would be meaningful to controlling this epidemic. We have done so by focusing on important scientific topics that could have an impact on the lives of patients. We are now primarily working on how to develop new modalities to block HIV transmission. These include vaccines, antibodies, and long-acting antiretroviral drugs. In addition, while we have good therapies for patients, we still do not have a cure. Thus, the pursuit of curative strategies is another major focus for us. Lastly, starting in January, the Aaron Diamond AIDS Research Center will officially be a part of the Columbia University Vagelos College of Physicians and Surgeons. This transition will mark the second phase of our research institute.

6. You have been involved with the center and at the forefront of this field for three decades. As an eminent opinion leader of HIV/AIDS research, what do you think are current necessities and urgencies in the field? Also, what do you forecast the major changes would be in HIV/AIDS studies in the next 10 years? How does your projection affect your research?

- The answer to this question is partially addressed above. Since this virus continues to spread, with over 1.7 million new infections worldwide each year, we need to come up with some effective ways to block HIV transmission. An effective vaccine is the ultimate solution. However, that task is daunting and likely to require many more years. In the meantime, we need to come up with strategies to contribute to the slowing of HIV spread. Most promising preventive approaches to date include the use of HIV-neutralizing monoclonal antibodies or long-acting anti-HIV drugs. Both of these areas are important to my group. I suspect that we will be making important progress on this front in the coming years.

7. Can you share your final remarks with our readers from around the world? Also, do you have any advice for physicians and healthcare professionals who wish to take part in medical innovation?

- Practicing doctors help patients each day, one at a time. That could be most gratifying. On the other hand, medical scientists could help many patients at once with a major breakthrough that comes once in a decade or a lifetime. That, too, is gratifying, of course. But the greatest reward day to day is the pursuit of new knowledge. One must have the passion, curiosity, and tenacity for solving the unknown and discovering the new. W

Dr. Ho featured as Time Magazine's Man of the Year in 1996

David Ho, M.D.

Scientific Director and Chief Executive Officer, Aaron Diamond AIDS Research Center (ADARC)
Irene Diamond Professor, The Rockefeller University

David Ho, M.D., is a medical doctor and HIV/AIDS researcher who has made many innovative contributions to the understanding and technological treatment of HIV infection. He is the Scientific Director and Chief Executive Officer of the Aaron Diamond AIDS Research Center (ADARC) and the Irene Diamond Professor at The Rockefeller University in New York City. Dr. Ho has been at the forefront of AIDS research for three decades. He has published over 400 papers, enabling the scientific community to understand the mechanism of HIV replication. Dr. Ho pioneered the "AIDS Cocktail" of combination antiretroviral therapy, which allowed the control of HIV replication in patients. He has received numerous honors and awards for his scientific accomplishments. He is the recipient of 12 honorary doctorates, including those from Columbia University and Tsinghua University. Dr. Ho was Time magazine's 1996 Man of the Year, and on January 8, 2001, he was presented with the Presidential Citizens Medal by President Clinton. He received his bachelor of science in physics with highest honors from the California Institute of Technology and an M.D. from the Harvard-MIT Division of Health Sciences and Technology. He completed his residency in internal medicine at Cedars-Sinai Medical Center, UCLA School of Medicine, and his fellowship at Massachusetts General Hospital and Harvard Medical School.

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Biopharma Report

BIOPHARMACEUTICAL REPORT I

NOVAVAX'S NANOFLU HAS TEPID EXPERT MARKET FORECASTS IN INFLUENZA VERSUS SANOFI'S FLUZONE

BIOPHARMACEUTICAL REPORT II

BAYER'S FINERENONE USE WILL FACE OFF WITH SGLT2 INHIBITORS

Novavax's NanoFlu Has Tepid Expert Market Forecasts in Influenza Versus Sanofi's Fluzone

Novavax's (NASDAQ:NVAX) NanoFlu influenza vaccine has garnered lukewarm expert predictions for its market uptake, with experts noting it does not seem to be a major improvement upon **Sanofi's** (EPA:SAN) Fluzone.

Despite high expert and analyst expectations for positive Phase III results and subsequent FDA approval, NanoFlu's similarity to Fluzone in terms of its components is a low bar for market advantage, experts said. NanoFlu's performance in the market will depend on other flu vaccines in the pipeline, with additional stiff competition from the long-entrenched Fluzone, experts added.

A price premium may be warranted if the Phase III demonstrates superiority, but the vaccine may run into higher costs anyway due to its production, experts noted. Novavax needs to offer discounts to secure a spot on the market, one expert said.

Experts expect that results from the Phase III will be consistent with the Phase II, which showed improved immune responses due to NanoFlu's more efficient technology compared to traditional immune vaccine technology. The Phase II and Phase III use the same comparator, further underscoring expert expectations of positive data.

Top-line immunogenicity and safety data for the 2,650-patient, randomized, observer-blinded, active-controlled Phase III trial (NCT04120194) are expected in 1Q20, according to analysts. A 27 June company press release indicated an upcoming licensure and future BLA via the accelerated approval pathway. Novavax did not return requests for comment.

NanoFlu's peak sales were estimated at USD 783m globally, according to one analyst report. Novavax's market cap is USD 111.36m.

Dampened market uptake expectations

As NanoFlu uses the same recombinant hemagglutinin (HA) protein nanoparticle as other flu vaccines, it is not a major improvement over what is already on the market, but rather it a me-too product, said Dr Peter Palese, chair, Department of Microbiology, Icahn School of Medicine, Mount Sinai, New York.

However, NanoFlu is unique in that it is produced in the SF9 insect cell baculovirus system, which is dissimilar to the traditional chicken embryo used for vaccines. While NanoFlu is an improvement in terms of production versus the current vaccines on offer (eggmade trivalent/quadravalent vaccines), that is a low bar for market success, a postdoctoral research scientist said.

Whether or not NanoFlu becomes the future influenza market leader will depend on the success of more revolutionary vaccines moving through Phase I/II trials, the scientist added. NanoFlu's Phase II trial results have not been "mind-blowing", as several candidate vaccines have reported similar results, such as BiondVax's (NASDAQ:BVXV) M-001, he said. BiondVax's website states M-001 leads to an immune response in a wide range of influenza strains.

If M-001 does succeed, it would be the first universal vaccine, said Dr James Cook, clinical professor of Medicine, Division of Infectious Diseases, Loyola University Medical Center, Illinois. This would make it a major competitor for NanoFlu or other investigational vaccines, he added. M-001 has the theoretical advantage of being effective against a wide range of types of influenza and should not have to be reformulated each year to be effective against emerging influenza strains due to its design, said Cook. NanoFlu is likely to face the same problem regarding emerging influenza strains as any other vaccine made of antigens/protein sequences defined by known, circulating influenza strains, said Cook.

These vaccines might be less effective against a new strain that could emerge during the influenza season if that strain has mutations of one or more HA sequences, as occurred at the end of the 2018–2019 influenza season, said Cook.

Even if NanoFlu were to demonstrate superiority versus Fluzone in its Phase III, it would not automatically be a market leader, as Fluzone has been FDA approved since 1987, said Rhonda Simoff, vice president, Strategic Solutions, The American Journal of Managed Care. Fluzone costs USD 17 per 10 dose vial, and NanoFlu cannot be priced any higher than that, said Randy Vogenberg, principal, Institute for Integrated Healthcare and Access Market Intelligence, Greenville, South Carolina.

If NanoFlu does demonstrate superiority in its Phase III, which is designed as a noninferiority trial, it can add on a 25% premium, Simoff added. However, based on public information, it seems likely that NanoFlu will be more expensive than Fluzone to produce, thus leading to a higher sticker price, Vogenberg said. The typical range of drug discounts NanoVax can offer insurers for greater market access is 30–60%, Vogenberg said.

Positive Phase III, FDA approval expected

Experts expect the Phase III results will be positive based on Phase II data showing that NanoFlu demonstrated superiority against Fluzone with a 45% increase against vaccine-homologous virus, A/Singapore ($p<0.001$), 22% increase against a historic drifted virus, A/Switzerland ($p=0.014$) and 42% increase against a forward drifted virus, A/Wisconsin ($p<0.001$).

The Phase III should have consistent results, as the technology used in NanoFlu is more efficient than the traditional immune vaccines technology, said Dr Amesh Adalja, senior scholar, Johns Hopkins Center for Health Security, Baltimore. Because the Phase III noninferiority benchmark will be passed due to the same comparator being used as the Phase II, FDA approval is likely, said Cook.

The trial's 21–28 day primary efficacy endpoint timeframe is relevant to see the peak titer induced by the vaccine, Adjala said. After 28 days, the immune response would be expected to wane, he said.

The saponin-based Matrix-M adjuvant of NovaVax's NanoFlu demonstrated good tolerability in the Phase II, experts agreed, adding they expect a similar safety profile for the Phase III. There may be some mild adverse effects, such as shoulder pain or fever, Palese said, noting this type of vaccine is very unlikely to cause any adverse effects. W

Bernarda Tundzhay
Reporter, London

Bernarda Tundzhay Ahmed is a BSc Medical Physiology graduate from the University of Leicester and a recent MSc Finance and Accounting postgraduate. She has done excessive research in physiology and pharmacology, molecular and cellular pharmacology and neuroscience, mainly focusing on anticonvulsants and dopamine metabolism inhibitors in cocaine addiction treatments.

Happy smile and hope after pain

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

Cancer-free D.K. Lee

D.K. Lee attending
beauty classes while chemotherapy treatment

Bayer's Finerenone Use Will Face Off With SGLT2 Inhibitors

Sodium-glucose cotransporter-2 (SGLT2) inhibitors' growing prominence in diabetic kidney disease (DKD) will likely impede uptake for Bayer's (ETR:BAYN) Phase III mineralocorticoid receptor antagonist (MRA), finerenone, experts noted. While finerenone will likely have an advantage over older drugs within its class, payers are likely to also scrutinize its value-add when combined with SGLT2 inhibitors and may still prefer the less expensive existing versions, they explained. Nonetheless, they added, the lack of standard SGLT2 use and the class being contraindicated for some patients will aid market traction.

SGLT2 inhibitors were not an option for DKD patients when Phase III development started in September 2015 for finerenone, experts acknowledged. Prominent among the SGLT2 inhibitor class is Johnson & Johnson's (NYSE:JNJ) Invokana (canagliflozin), which won FDA approval for DKD on 30 September. Because finerenone will likely not be directly compared to SGLT2 inhibitors, the choice between the two in deciding a patient's regimen will become a factor of cost and payer coverage, two experts said.

Ongoing finerenone studies do not compare the drug to Invokana or any other SGLT2 inhibitor, but subgroup data on the combination of an SGLT2 inhibitor and finerenone will give an indication of the duo's additive efficacy, some experts noted. Yet, they added, a separate randomized trial will likely be required to spur use in this fashion.

Results from Phase III FIDELIO-DKD (NCT02540993), which has a kidney function-focused primary endpoint, are expected in 2Q20, as per an analyst report. The Phase III FIGARO-DKD (NCT02545049), focused on cardiovascular risk analysis, has a primary completion date in June 2021, according to ClinicalTrials.gov. This news service reported earlier today that experts are cautiously optimistic about the chances of FIDELIO and FIGARO achieving success due to encouraging Phase II data.

A second analyst estimated peak sales of USD 1bn for finerenone with a 50% probability of commercial success. Bayer's market cap is EUR 65.84bn (USD 71.17bn). Bayer did not respond to a request for comment.

SGLT2 inhibitors claim space in kidney disease

The new environment for kidney disease is more complicated than when the finerenone trials started, said Dr Mark Cooper, head, Department of Diabetes, Monash University, Melbourne, Australia. Johnson & Johnson won approval for Invokana on the back of the Phase III CREDENCE study (NCT02065791), which was stopped early after an interim analysis indicated the risk of kidney failure and cardiovascular events was lower when patients with type 2 diabetes (T2D) and chronic kidney disease (CKD) received Invokana compared to placebo (Perkovic et al N Engl J Med 2019; 380:2295-2306).

Renal outcomes and cardiovascular mortality data with other SGLT2 inhibitors like AstraZeneca's (LON:AZN) Farxiga (dapagliflozin) and Boehringer Ingelheim's Jardiance (empagliflozin) are expected, but both drugs have been shown to be renoprotective in T2D studies. The Phase III DAPA-CKD trial with Farxiga will complete in November 2020, and Phase III EMPA-KIDNEY with the latter completes in 2022. While

"Because finerenone will likely not be directly compared to SGLT2 inhibitors, the choice between the two in deciding a patient's regimen will become a factor of cost and payer coverage"

FIDELIO and FIGARO were being performed, the renoprotective qualities of Farxiga, Jardiance and Invokana became apparent, along with their ability to target albuminuria, said a FIGARO investigator.

CREDENCE trial results are practice-changing, experts noted. More patients should be treated with SGLT2 inhibitors, and in fact, they should not be used exclusively in diabetic patients where they were first approved, said Dr Jay Wish, professor of Clinical Medicine, Division of Nephrology, Indiana University, Indianapolis. SGLT2 inhibitors are effective regardless of whether a patient has diabetes at least from the cardiovascular risk point of view, agreed a FIDELIO investigator.

However, despite SGLT2 inhibitor efficacy in patients with diabetes and kidney disease or even kidney disease alone, some patients continue to have residual disease, said a second FIGARO investigator and the FIDELIO investigator. Also, while CREDENCE results were significant, SGLT2 inhibitors are still not used in most countries, and the class is contraindicated for some patients, albeit a relatively small part of the population, said Cooper. Invokana is not yet approved in the EU, but in a 22 August press release, Cambridge, UK-based Mundipharma—Invokana's European distributor—said the drug's license extension to treat Stage 2 and 3 CKD patients was accepted by the EMA. Invokana is contraindicated for patients with severe renal impairment, end-stage renal disease or on dialysis and those with a serious hypersensitivity reaction to Invokana.

Hence, there is room for finerenone as a therapy for renal disease, said the second FIGARO investigator. Moreover both classes act by distinct pathways, he added. SGLT2 inhibitors lower blood sugar by causing its excretion through urine, and MRAs block the hormone aldosterone, which regulates sodium and potassium transport, thus impacting the heart

and kidneys. While effective, SGLT2 inhibitors still do not counteract the effects of aldosterone, said the first FIGARO investigator.

Yet, it is hard to predict the efficacy of finerenone combined with an SGLT2 inhibitor, said the second FIGARO investigator. If patients are on SGLT2 inhibitors, their kidney disease progression will have slowed, making it tougher to show an extra benefit with a new drug, Cooper added. Also, MRAs and SGLT2s are both diuretics, and it is not known whether this will have an additive effect when used long-term, he noted.

Since the FIDELIO and FIGARO studies have patients who were on SGLT2 inhibitors, data from this patient subgroup receiving both drugs will give an indication of their interaction, said the second FIGARO investigator. A preplanned analysis will evaluate the impact of patients on SGLT2 inhibitors in addition to finerenone, added the FIDELIO and first FIGARO investigator. The timing

of this analysis has not been stated in trial-related publications. In FIDELIO and FIGARO, 4.5% and 8.3% of patients are on SGLT2 inhibitors, respectively (Bakris et al; Am J Nephrol. 2019 Oct 25:1-12 and Ruilope et al; Am J Nephrol. 2019 Oct 30:1-12.).

While the FIDELIO and FIGARO studies will give an idea about finerenone's additional benefit on top of SGLT2 inhibitors or angiotensin-converting enzyme (ACE) inhibitors, a separate trial would still be needed to establish use of such a combination, said the FIDELIO investigator. Cooper agreed that data from FIDELIO and FIGARO will not be enough to drive the use of a finerenone/SGLT2 inhibitor combination.

Payer considerations for finerenone use

The MRA class is a cornerstone of renal protection, and physicians could likely accept finerenone as a first choice between drugs of that class, said Wish. If the finerenone studies are positive, the drug would be preferred over other MRAs, since it is expected that finerenone will have lower rates of hyperkalemia compared to other MRAs based on the Phase II studies, added Cooper.

Yet, since finerenone will likely be more expensive than other MRAs, physicians may mainly want to use it in CKD patients who receive MRAs but develop side effects, noted Wish. Payers as well may demand that finerenone be an option only after patients have either failed spironolactone or been treated with potassium binders for the hyperkalemia, he added. Physicians are very comfortable using MRAs for kidney disease and they have also been widely used for heart failure, added Cooper.

And while combination data is needed for finerenone/SGLT2 inhibitor use, expense will also be a factor. The challenge is that newer drugs like finerenone and the T2D therapies are expensive, and using the two classes together would be very expensive compared to an older drug like metformin, said the first FIGARO investigator. Ideally, a patient still suffering from albuminuria despite metformin and an SGLT2 inhibitor would benefit from finerenone being added to those two, but the high cost would mean physicians may have to choose between finerenone and an SGLT2 inhibitor, he added. The magnitude of positive data in the finerenone trials compared to CREDENCE may help with the selection, said the first FIGARO investigator. W

Manasi Vaidya

Reporter, New York

Manasi Vaidya joined as a reporter in New York in February 2015 and has covered the drug development space across a number of therapeutic areas, and built an expertise in writing about oncology. While focusing on analysis pieces about ongoing clinical trials, her coverage has also branched out to regulatory issues, pricing and reimbursement and patent litigation. She has covered practice-changing developments from high profile conferences like ASCO and SABC, in addition to FDA regulatory meetings. She previously covered the Asian biotechnology industry for BioSpectrum, a monthly magazine in India, for two years. She has a Masters degree in Science, Health and Environmental Reporting from New York University, and a Masters degree in Biotechnology from Dr. D. Y. Patil University. Her work has appeared in Nature Medicine, Nautilus and Technology Review India.

FOLLOW THE JOURNEY OF VIREAD

COMPLETE RESPONSE RESULTS AT YEAR 1...

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

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® 300 mg 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

38th Annual J.P. Morgan Healthcare Conference

January 13-16, 2020 | San Francisco, California, USA

Website: https://www.jpmorgan.com/global/healthcare-conference

The annual J.P. Morgan Healthcare Conference is the largest and most informative healthcare investment symposium in the industry, brining together industry leaders, emerging fast-growth companies, innovative technology creators, and members of the investment community. The hundreds of companies presenting run the gamut, from start-ups to those with more than $300 billion in market cap, and encompass the entire global healthcare landscape, including pharmaceutical firms, healthcare service providers, profit and not-for-profits, and medical device companies.

International Meeting on Simulation in Healthcare (IMSH)

January 18-22, 2020 | San Diego, California, USA

Website: http://imsh2020.org/
Contact: admin@ssih.org

The International Meeting on Simulation in Healthcare (IMSH) is a scientific conference that explores the latest innovations and best practices in healthcare simulation. IMSH provides the tools and resources healthcare professionals need to advance their skills, impact change in delivery systems and practice, and ultimately, to improve patient safety. Attendees come from all over the world to experience three days of networking, hands-on workshops, plenary speakers, nearly 300 education sessions, and an Exhibit Hall full of the latest products and services.

BIO CEO & Investor Conference

February 10-11, 2020 | New York, New York, USA

Website: https://www.bio.org/events/bio-ceo-investor-conference
Contact: info@bio.org

Now in its 22nd year, the BIO CEO & Investor Conference is one of the largest independent investor conferences focused on established and emerging publicly traded and select private biotech companies. Experience the best of biotech with two days of productive partnering meetings with institutional and early-stage investors, industry analysts, and senior biotechnology executives, in one location.

HIMSS Global Conference & Exhibition

March 9-13, 2020 | Orlando, Florida, USA

Website: https://www.himssconference.org/
Contact: himss@compusystems.com

HIMSS is a global advisor and thought leader supporting the transformation of health through information and technology. As a mission driven non-profit, HIMSS offers a unique depth and breadth of expertise in health innovation, public policy, workforce development, research and analytics to advise global leaders, stakeholders and influencers on best practices in health information and technology. HIMSS delivers key insights, education and engaging events to healthcare providers, governments and market suppliers, ensuring they have the right information at the point of decision.

WHCC20 – The 17th Annual World Health Care Congress

March 29-April 1, 2020 | Washington, D.C., USA

Website: https://www.worldhealthcarecongress.com/
Contact: wcreg@worldcongress.com

WHCC20 brings together global thought leaders and key decision-makers from all sectors of the healthcare. The World Congress offers unique conferences and events in health care, life sciences and pharmaceutical that are unmatched by any other organizer. Through our educationally focused events, we convene CEOs and senior-level executives from all segments of the health care and life sciences industries to exchange ideas, discuss market trends, and explore solutions to the most pressing challenges facing a variety of roles within these organizations.

GHIC 2020 - Global Health & Innovation Conference

April 4-5, 2020 | New Haven, Connecticut, USA

Website: https://www.uniteforsight.org/conference/
Contact: ufs@uniteforsight.org

The Global Health & Innovation Conference is the world's leading and largest global health conference as well as the largest social entrepreneurship conference, with nearly 2,000 professionals and students from all 50 states and more than 55 countries. This must attend, thought-leading conference convenes leaders, changemakers, and participants from all sectors of global health, international development, and social entrepreneurship.

11th Annual CUGH Conference - Global Health in a Time of Worldwide Political Change

April 4-5, 2020 | Washington, D.C., USA

Website: https://www.cugh2020.org/
Contact: info@cugh.org

The theme of the 11th Annual Consortium of Universities for Global Health is "Global Health in a Time of Worldwide Political Change." Over 1,800 scientists, students and implementers from academia, NGOs, government and the private sector will present, learn and collaborate to address some of the pressing challenges the world faces. Attendees will have many opportunities to engage, learn, contribute, and collaborate with each other in a dynamic, inspiring environment.

2020 International Congress on Integrative Medicine and Health

April 28-May 1, 2020 | Cleaveland, Ohio, USA

Website: http://www.icimh.org/#home
Contact: Register@ConferenceSolutionsInc.com

The congress will take place in association with a number of international organizations including Academic Consortium for Integrative Medicine and Health, in association with the International Society for Complementary Research. The mission of the Congress is to improve public health through showcasing advancements in the field of integrative medicine. The main congress topics will include research, policy, education and clinical care.

Conference Alerts

Europe

5th World Congress on Public Health and Nutrition

January 30-February 1, 2020 | Paris, France

Website: https://publichealth.healthconferences.org/

The 5th World Congress on Public Health and Nutrition (Public Health 2020) is one-of-a-kind event showcasing the many facets and diversity of public health and nutrition. Public Health 2020 are expected to attend over 200 public health professionals, nurses and healthcare experts. The theme of the conference "Discovering New Ways to Ameliorate Global Health" will underpin the need for collaboration and cooperation of individuals from a wide range of professional backgrounds.

DIA Europe 2020

March 17-19, 2020 | Brussels, Belgium

Website: https://www.diaglobal.org/en/flagship/dia-europe-2020/about/conference
Contact: https://www.diaglobal.org/en/contact-us

DIA Europe 2020 is the largest and most forward-looking neutral healthcare conference in Europe. This annual healthcare meeting reflects DIA's strategic initiatives across several Thought Leadership streams, including Clinical Development & Operations, Regulatory Science & Operations, Value and Access, Medical Affairs and many others.

IPVC 2020 – 33rd International Papillomavirus Conference

March 23-27, 2020 | Barcelona, Spain

Website: https://ipvconference.org/
Contact: https://ipvconference.org/contact-us/

The 33rd International Papillomavirus Conference & Basic Science, Clinical and Public Health Workshops will gather researchers, clinicians and other health professionals to share knowledge and ideas on papillomaviruses and their associated diseases, from basic science to global health impact.

EuroGUCH 2020

April 17-18, 2020 | Leuven, Belgium

Website: https://kuleuvencongres.be/euroguch2020
Contact: euroguch@kuleuven.be

The 11th Annual European Meeting on Adult Congenital Heart Diseases is one of the most prestigious Meetings in the world, organized by the Working Group on Adult Congenital Heart Disease of the European Society of Cardiology. The scientific program is designed to cover a wide range of ACHD subjects from exercise, pregnancy, arrhythmias, endocarditis, pulmonary hypertension, novel interventional and surgical therapies, and issues beyond heart disease including precision medicine strategies.

Asia

12th Asia Pacific Global Summit on Healthcare

January 27-28, 2020 | Bangkok, Thailand

Website: https://healthcare.global-summit.com
Contact: healthcareasiapacific@asiaconvention.com

Healthcare Asia Pacific 2020 is an uncommon event proposed for Healthcare specialists to support the dispersal and utilization of research disclosures on Healthcare. The theme of the meeting is "Leading Innovation for Better Healthcare and Nursing Systems." The gathering invites speakers from social Healthcare Universities, clinical research associations, expository associations and Healthcare venture to share their investigation experiences on all parts of this rapidly developing field and thusly, giving a show off of the latest Healthcare Techniques.

13th World Congress on Virology and Infectious Diseases

February 24-25, 2020 | Tokyo, Japan

Website: https://virology.conferenceseries.com/asiapacific
Contact: info@scientificmeets.com

Virology Asia 2020 revolves around the theme "Latest and Advanced Therapeutic Approaches of Virology." The Virology Asia 2020 serves as a global platform that brings all eminent research professionals like Virologist, Microbiologists, Biotechnologists, Business dignitaries to discuss and share the knowledge in virology like the new challenges faced, viral replication, cell structure, biochemical aspects of viruses.

PHAR-EAST Asia's Pharma & Biotech Festival

March 31-April 1, 2020 | Singapore, Singapore

Website: https://www.terrapinn.com/exhibition/phar-east/index.stm
Contact: malie.samson@terrapinn.com

Phar-East is a premium closed-door conference held annually in Singapore for the Asian Pharma and Biotech industry. Returning again in March, Phar-East 2020 will continue with the ever-popular conference tracks covering Immunotherapy, Pharma 4.0, Market Access & Pricing through to Biotech Investment and the new Bio-Data stream.

13th Asia Pacific Pediatric Congress

April 29-30, 2020 | Singapore, Singapore

Website: https://pediatrics.pediatricsconferences.com/
Contact: contact@scientificmeets.com

Asian Pediatrics 2020 will be an innovative and informative International conference reflecting the direction of Pediatrics in the 21st century and offers a wide range of diversions to participants of all backgrounds. This Pediatric conference provides an excellent opportunity to discuss the latest developments within the field. The conference runs with the theme "Meeting the Challenges in the field of Neonatology and Perinatology."

LATEST HEALTHCARE INDUSTRY NEWS

Sep – Dec 2019

1. In Stunning Twist, FDA Approves Sarepta's Duchenne Drug It Rejected

The Food and Drug Administration approved Sarepta's Duchenne muscular dystrophy therapy Vyondys 53, four months after rejecting the drug over safety concerns. The decision comes as a major surprise, as Sarepta had given no prior hints that it had resubmitted an application to the agency. Reversing a rejection so quickly is highly unusual. A type of nucleic acid therapy, Vyondys 53 is now conditionally cleared for the roughly 8% of patients with Duchenne who are "amenable" to exon 53 skipping, the mechanism by which the drug works. The FDA's rejection of Vyondys 53 had stirred speculation the agency had done so for political reasons tied to the controversy over Exondys 51.
https://www.biopharmadive.com/news/fda-surprise-approval-sarepta-vyondys-53-duchenne-drug/569015/

2. New Drugs for Sickle Cell Excite but, at ASH, a Recognition That More Is Needed

For decades, a repurposed cancer drug was the only treatment option for the tens of thousands of Americans who suffer from sickle cell disease, an inherited disorder that warps red blood cells to potentially devastating effects. That's since changed, following a Food and Drug Administration approval for Endari in 2017 and then, just last month, for two new drugs from Novartis and Global Blood Therapeutics. The flurry of approvals, along with advancing development for nearly 20 other experimental therapies, is a dramatic change for a sickle cell disease community that hasn't always been a focus for drug developers. The disease more commonly affects black and Hispanic people. Many of those affected are less well off and are covered by government insurance.
https://www.biopharmadive.com/news/sickle-cell-new-drugs-excite-more-needed-ash/568690/

3. Hospital Groups Sue to Block Price-Transparency Rule

Hospital groups sued to block a Trump administration rule forcing them to disclose secret rates, for the first time laying out the industry's legal strategy for defeating the president's central health-policy initiative. The lawsuit filed Wednesday says the rule compelling the hospitals to publish their negotiated rates with insurers violates the First Amendment and goes beyond the statutory intent of the Affordable Care Act. The groups say the disclosure under the rule would be compelled speech in violation of the First Amendment. They are asking for an expedited decision, saying hospitals could otherwise spend needless time and resources preparing for a rule that may be invalidated by the court.
https://www.wsj.com/articles/hospital-groups-sue-to-block-price-transparency-rule-11575460685

4. FTC Puts the Brakes on Illumina's $1.2B Offer for DNA Sequencing Rival PacBio

The Federal Trade Commission has moved to block Illumina's $1.2 billion takeover of its emerging rival, Pacific Biosciences, saying the DNA sequencing giant would substantially be harming competition. The commission also gave its staff clearance to seek temporary restraining orders or federal injunctions, if necessary, to maintain the current business while its complaint is heard by an administrative law judge in a formal hearing. "When a monopolist buys a potential rival, it can harm competition," said Gail Levine, deputy director of the FTC's Bureau of Competition, in a statement. "These deals help monopolists maintain power. That's why we're challenging this acquisition." The FTC has claimed that the acquisition would reduce the combined company's incentives to develop new products and that Illumina and PacBio's rivalry drives them to innovate.
https://www.fiercebiotech.com/medtech/ftc-blocks-illumina-s-1-2b-offer-for-dna-sequencing-rival-pacbio

5. SABCS: 10-Year Study Shows Targeted Radiation Can Be as Effective as Whole-Breast Doses Against Cancer

A decade-long study found patients with early breast cancer may be spared radiation procedures that span the whole breast, and that shorter and less invasive courses of treatment aimed at portions of the breast may be just as effective. After surgery to remove the tumor, patients who received accelerated partial breast irradiation saw similar rates of recurrence to those who received whole breast irradiation, according to the data presented at the San Antonio Breast Cancer Symposium. The study also found that it was unable to reject the idea that lower-dose radiation therapy was less effective compared to whole-breast treatments, with little difference between its two study arms.
https://www.fiercebiotech.com/medtech/sabcs-10-year-study-shows-targeted-radiation-can-be-as-effective-as-whole-breast-doses

6. CVS, Rite Aid Join Lawsuit Over Diabetes Drug Overcharging

CVS Health and Rite Aid joined other pharmacy chains Monday in a lawsuit accusing three drugmakers of squeezing out generic competitors to protect their sales of a diabetes medication, resulting in $2.8 billion in excessive spending. The lawsuit details a series of events that allegedly impeded competitors via notorious "patent games" that policymakers aim to ban. The pharmacy chains allege Assertio Therapeutics paid Lupin Pharmaceuticals to delay its generic version of Glumetza, the extended-release iteration of a drug that has been used to treat Type 2 diabetes since 2002. While Lupin's generic could have entered the market in 2009, the companies settled a related patent lawsuit and kept the competition at bay until 2016.
https://www.modernhealthcare.com/legal/cvs-rite-aid-join-lawsuit-over-diabetes-drug-overcharging

7. UPS Drone Makes First Home Prescription Deliveries for CVS

United Parcel Service Inc. Flight Forward drones have flown prescription medications to the front lawn of a private home and to a retirement center, the UPS unit's first revenue-generating deliveries for drugstore chain CVS Health Corp. UPS and CVS said on Tuesday the deliveries were the first of their kind under an program approved by the U.S. Federal Aviation Administration (FAA). Regulators are still hammering out rules for how the unmanned winged vehicles will operate in U.S. airspace and guidelines are expected in 2021. UPS became the first company to win the broadest FAA certification to operate a drone airline. That permits Flight Forward to collect payment for drone deliveries and to fly as many drones supported by as many operators as necessary to meet customer demand.
https://www.reuters.com/article/us-ups-drones/ups-drone-makes-first-home-prescription-deliveries-for-cvs-idUSKBN1XF2JC

8. Novartis Pivots Shanghai R&D Site From Early Discover to Development

Novartis is calling it curtains on early drug discovery at its R&D site in Shanghai in a companywide move to "rebalance" its discovery and early development efforts. The company plans to add more than 300 new jobs in the coming years but will be bidding adieu to about 150 early discovery personnel. "Our need to better resource early drug development globally, combined with important changes to the drug development and commercialization landscape in China, have converged on the decision to pivot from drug discovery in Shanghai to early drug development," said Jay Bradner, M.D., president of the Novartis Institutes for BioMedical Research (NIBR).
https://www.fiercebiotech.com/biotech/novartis-pivots-shanghai-r-d-site-from-early-discovery-to-development

9. Google's Health Care Ambitions Now Involve Thousands of Patient Records

Google announced a partnership with a large U.S. health care system aimed at modernizing its information system and providing new tools for doctors, in the tech giant's latest foray into the health industry. Google is providing cloud computing services to Ascension, which operates health centers in 21 states, mostly across the South and Midwest. It is also testing the use of artificial intelligence to examine health records and find patterns that Google says might help doctors and other providers. Both companies stressed that their deal is compliant with federal health-privacy law. Unlike most of the data Google collects on individuals, health data is strictly regulated by the federal government. Health care providers are increasingly interested in using data to help manage care and keep patients healthy.
https://www.seattletimes.com/business/googles-health-care-ambitions-now-involve-patient-data-2/

10. Genome Sequencing in Newborns Raises Ethical Issues

In 2014, the National Institutes of Health funded four projects to study the benefits and risks of genomic sequencing for newborns. During the study, the research team felt moral distress about not being able to disclose the information because it wasn't related to a childhood disease, so they approached their institutional review board and asked for permission to disclose it and then told the baby's parents. Ultimately, the study protocol was modified to require all participating families to agree to receive information about adult-onset conditions, too. However, Dr. Lainie Friedman Ross of the MacLean Center addressed that sequencing all or large parts of a baby's genome at birth could reveal genetic variations that increase risk for conditions that occur in childhood or not until adulthood. The conditions could be benign or ultimately be untreatable later.
https://www.reuters.com/article/us-health-newborns-genomics-ethics/genome-sequencing-in-newborns-raises-ethical-issues-idUSKBN1XN2TR

11. Trump Administration Sues Gilead Over HIV Drug Patents

The U.S. government on Wednesday accused Gilead of illegally profiting from taxpayer-funded HIV research, suing the biotech in federal district court for infringing on patents tied to the preventive use of two HIV drugs. The lawsuit escalates a dispute between Gilead and the Department of Health and Human Services, which holds four patents for research done in the 2000s by the Centers for Disease Control and Prevention on pre-exposure prophylaxis HIV treatment. Gilead has refused to license those patents from HHS, the agency said, and in August contested their validity by requesting the U.S. Patent Office review all four patents. Gilead sells two drugs, Truvada and Descovy, for PrEP, expanding the use of which is a major component of the Trump administration's plans to reduce new HIV infections in the U.S.
https://www.biopharmadive.com/news/trump-administration-sue-gilead-prep-hiv-patents-truvada/566834/

12. China Approves Alzheimer's Drug, Inviting Fresh Debate in Field With Few Successes

In a decision likely to stir scientific debate across the world, China's health regulator conditionally approved a new Alzheimer's drug for patients with mild-to-moderate forms of the neurodegenerative disease. The drug, which was developed by the little-known Shanghai Green Valley Pharmaceuticals, will be available throughout China by the end of the year, according to the company and an English statement posted on the website of China's National Medical Products Administration. No new Alzheimer's drug has won approval since 2003 and drugmaker efforts to change that have consistently come up short, making the NMPA's decision notable. But it's not clear how effective Green Valley's drug is, with limited information about the positive trial results reported by the company last year.
https://www.biopharmadive.com/news/china-alzheimers-drug-oligomannate-approval-green-valley/566540/

13. Merck to Lay Off 500 US-Based Commercial Employees

Merck & Co. plans to lay off approximately 500 U.S.-based employees working on sales and commercial teams, the company disclosed Thursday in a regulatory filing and confirmed Friday to BioPharma Dive. Affected employees, who are spread out across the country, will be laid off on Jan. 3, 2020 with separation packages, according to a company statement. Merck has also reduced its U.S. workforce by 40% in the past decade to 25,400 workers at the end of 2018. These newest job cuts appear set to further lower that figure, although a Merck spokesperson noted the pharma is hiring for U.S. oncology-focused jobs. "This is not a new restructuring effort," Merck spokesperson Pamela Eisele said in a statement. Instead, the layoffs are part of "ongoing company-wide efforts to sharpen Merck's focus" on R&D growth opportunities.
https://www.biopharmadive.com/news/merck-500-pharma-layoffs-US-sales-workforce-reductions/565346/

14. Johnson & Johnson's Legal Challenges Mount

Johnson & Johnson, facing lawsuits from more than 100,000 plaintiffs over its product safety and marketing tactics, has taken the aggressive strategy of battling many of the cases in court, and is losing. Juries and judges have ordered the health-products giant to pay billions of dollars in several recent trials over claims that J&J's signature baby powder and certain drugs and medical devices injured people, and that its marketing practices fueled the opioid-addiction epidemic. The number of talc-lawsuit plaintiffs surged to 15,500 as of June 30, from 1,400 in early 2016, the Journal analysis found. Plaintiffs in personal-injury lawsuits over J&J's pelvic mesh devices for women have declined from a peak of more than 55,000 pending in 2017 but still number about 24,800.
https://www.wsj.com/articles/johnson-johnsons-legal-challenges-mount-11571055242

15. Bayer to Back 11 International Startups in Various Digital Health Enterprises

Bayer has signed onto sprawling new collaborations with 11 digital health startups spanning areas such as oncology, ophthalmology, pulmonology, radiology, digital therapeutics and cardiovascular health. The program also paves the way for longer-term collaborations, including commercial development support to bring the digital health products to market, said Zsuzsanna Varga, head of Bayer's G4A program, which is divided into two different pathways. The "Growth Track" grants early-stage startups €75,000 ($82,700 U.S.) for co-creating products, plus co-working space and mentoring at Bayer's pharmaceuticals division headquarters in Berlin. Meanwhile, the "Advance Track" includes startups looking to co-create and execute commercial deals and includes incremental milestone-based payments.
https://www.fiercebiotech.com/medtech/bayer-to-back-11-startups-various-digital-health-enterprises

16. Purdue Pharma, Maker of OxyContin, Files for Bankruptcy

Purdue Pharma, maker of OxyContin, the drug widely seen as igniting the opioid crisis, filed for Chapter 11 bankruptcy on Sunday night, a move at the center of the company's efforts to shield itself and its owners from more than 2,600 federal and state lawsuits. The terms of the filing are expected to be fiercely contested by a group of states that have refused to settle with Purdue and are intent on pursuing the company's owners, the Sacklers, considered one of the wealthiest families in the United States. Restructuring the company through bankruptcy was at the heart of a tentative settlement agreement reached between the company and thousands of cities and counties that have sued it in federal court for its role in the opioid epidemic.

https://www.nytimes.com/2019/09/15/health/purdue-pharma-bankruptcy-opioids-settlement.html

17. Roivant Offloads Biotech Stakes in $3B Alliance With Japanese Pharma

Sumitomo Dainippon Pharma will pay Roivant Sciences $3 billion for its stake in five of the holding company's subsidiaries, and take a more than 10% stake in the parent company founded by unorthodox CEO Vivek Ramaswamy. Through the alliance, Sumitomo Dainippon additionally gains the option to acquire Roivant's stake in six more subsidiaries with up to 25 pipeline projects. The Japanese pharma is looking to replace lost revenue from the looming expiration of U.S. patent expiration on its biggest seller, the antidepressant Latuda, which had sales of more than $1.7 billion in the company's 2018 fiscal year.

https://www.biopharmadive.com/news/roivant-deal-sumitomo-dainippon-3-billion-ramaswamy/562401/

18. Regulatory Barriers Limit Alternative State Drug Payment Models

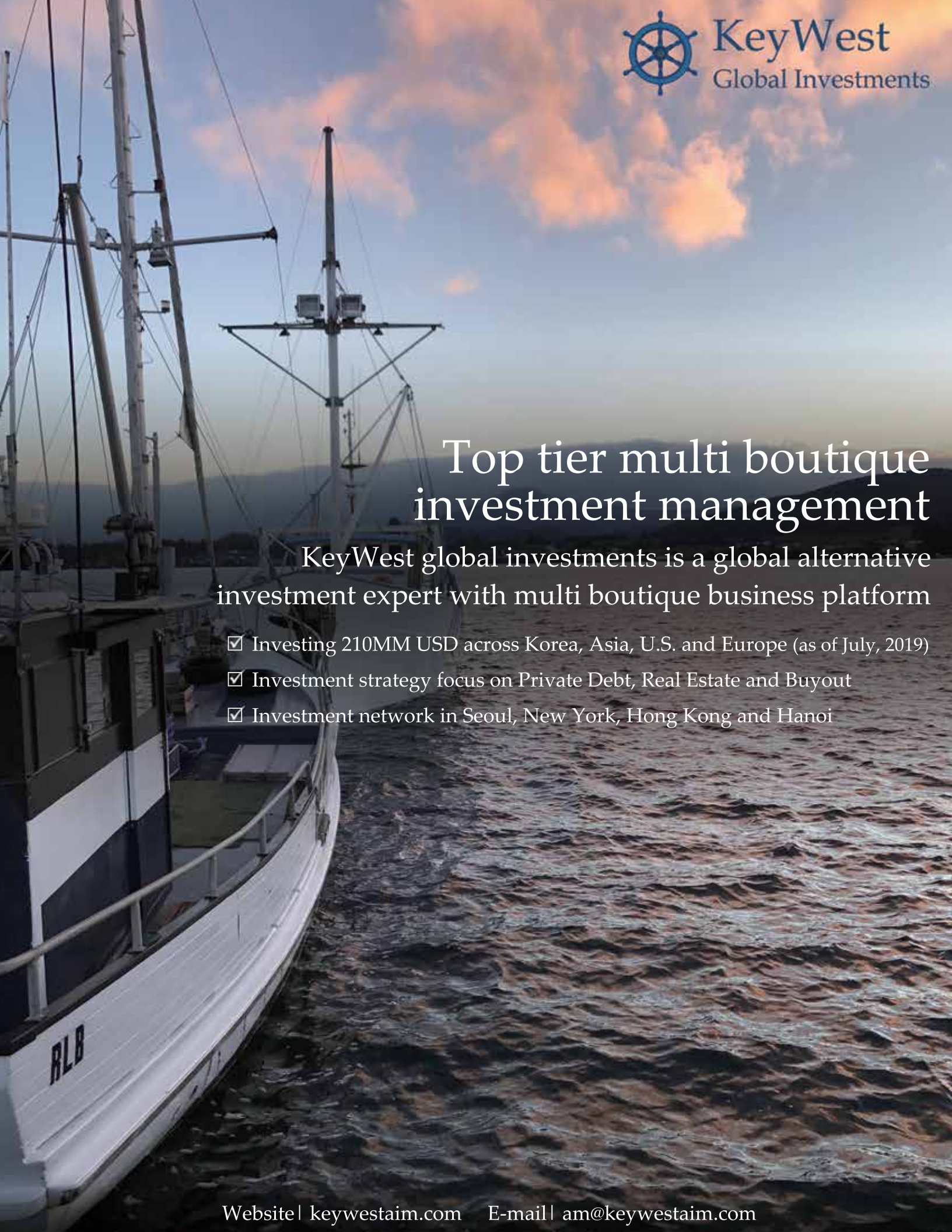
More states are turning to alternative payment models for prescription drugs covered under Medicaid, as they seek to balance increasing costs with public health goals. Despite regulatory and implementation barriers that still impede the spread of outside-the-box approaches, Louisiana's "Netflix" model approach has captured many headlines. The state reached a deal with a subsidiary of drugmaker Gilead in which the state will receive an unlimited supply of its hepatitis C drug Harvoni for a fixed sum each year for five years. Other ideas build incentives into contracts to reward for positive outcomes. Oklahoma, Michigan and Colorado have negotiated outcomes-based contracts with drug manufacturers, in some way reimbursing the drugmaker for how well the drug works.

https://www.biopharmadive.com/news/regulatory-barriers-limit-alternative-state-drug-payment-models/563204/

19. Israel Prepares to Unleash AI on Health Care

Israel is becoming a testing ground for the power of artificial intelligence to improve health care. Digital medical records for the vast majority of Israelis are currently stored in databases maintained by the handful of semipublic HMOs that provide most health care in Israel. While the biggest health-maintenance organizations already leverage their records in partnerships with private companies to develop technology for more advanced health care, Israel's government wants to take such efforts to a new level. And the greater goals, officials say, based largely on the promise of AI technology, are to make health care less expensive, more effective and better tailored to individuals everywhere.

https://www.wsj.com/articles/israel-prepares-to-unleash-ai-on-health-care-11568599261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