NHF NewsBriefs

August 10 – 16, 2018

This report includes selected news items from the past week on issues of concern to the bleeding disorders community. It is designed to help keep NHF national and local leadership and staff informed of the latest information from the news media. It will be distributed by email on Thursday of each week, covering important news items from the previous seven days. Subjects covered will include hemophilia, other bleeding disorders, gene therapy, hepatitis, HIV/AIDS, and others.

Medical Dialogues *(India)
August 10, 2018

DU Cancels Medical Admission of Hemophilia Patient, Associations See Red

By Geeta Sharma

(Editors Pick/Medical Education—New Delhi, India) -- **The cancellation of admission** of a student suffering from Hemophilia A at the University College of Medical Sciences (UCMS) by the Delhi University has had the Hemophilia Federation (India) on the alert. The body has written to the Directorate General of Health Services (DGHS) terming the practice of recertification as 'wrong'. A similar point of view was also expressed by the National Thalassemia Welfare Society that demanded that the DGHS to pass directions to medical colleges to stand by the certification provided for the disability by the Directorate.

The above reiteration by the Societies came in the face of the Faculty of Medical Science (FMS) of DU declaring Mahesh Kumar, a dental student at UCMS, battling haemophilia A, ineligible under the persons with disability category and cancelling his admission on August 2.

A patient of Haemophilia A, Mahesh Kumar had to face the pain of withdrawal of admission, despite the Safdarjang Hospital and Vardhman Mahavir Medical College(one of four designated certification centres)certifying him for admission to medical/dental courses under the all-India quota. The certification granted to him was that of "suffering from severe haemophilia A" with 40-50% disability. Further, still, a certificate from the Army Hospital R&R, Delhi Cantt had also marked his disability at 70%.

Interestingly, the UCMS disability quota student Mahesh Kumar's admission had been "cancelled by a medical board constituted by FMS at Maulana Azad Medical College without any physical examination" state media reports.

The Thalassemia Society emphasized that the Delhi University was not empowered to either reverse or annul the reservation and eligibility criteria for persons with benchmark disability under the Act.

"This unnecessary board assessment for candidates with haematological disabilities is unjustified, causes harassment to the candidates and also not in compliance with the DGHS guidelines," it said.

The President, Hemophilia Federation (India), Vikash C Goyal speaking to the TOI termed the incident as discriminatory Mr. Goyal reaffirmed that DGHS, is the final authority in this case and was disturbed due to the cancellation of the certificate rendered by it, by the FMS, which resulted in admission cancellation.

According to Kumar's father, Bhoop Singh Gurjar, a havildar with Indian Army, "Twenty-two days after the admission, we were asked to come for the verification of the disability and we submitted the certificates. On August 3, a day after his admission was cancelled, I reached Delhi from Kolkata and was told by the college that it has received a communication from FMS that Mahesh is ineligible."

"My son was not physically examined, so how can the university override the disability certificate given by a body which regulates medical education in India?" he said to the Indian Express

S K Dogra, Deputy Registrar, FMS told TOI that medical colleges set up their own medical boards after admissions for certificate verification. "The decision was communicated to MAMC after post-admission verification by the medical board," he said.

The DGHS however, denied any instruction having been issued for a repeat medical examination. "The direction has been that all admissions should be on the basis of certification by the four designated centres. If MAMC had set up a separate board, hope that is within the MCI guidelines," the body reaffirmed.

Dr S Ramji, Dean MAMC, commented: "Admissions are done by Delhi University, not by the college."

Student Mahesh Kumar further claimed that an application had also been submitted to MAMC by him for a medical examination and certification as a government certificate is required to apply for the NEET exam. However, he did not hear from the college he confirmed.

Prnewswire.com
August 8, 2018

Sangamo Announces Positive Preliminary Data from the Phase 1/2 Alta Study Evaluating SB-525 Gene Therapy for Hemophilia A

(Richmond, CA)-- **Sangamo Therapeutics**, Inc. today announced positive preliminary data from the Phase 1/2 clinical trial evaluating SB-525, a cDNA gene therapy candidate for Hemophilia A (the "Alta study"). SB-525 is being developed as part of a global collaboration between Sangamo and Pfizer Inc. for the development and commercialization of potential gene therapy programs for Hemophilia A.

The Alta study is an open-label, dose-ranging clinical trial designed to assess the safety and tolerability of SB-525 in up to 20 adult subjects with severe Hemophilia A. To date, five patients have been treated at three dose levels. A sixth patient is scheduled for treatment later this month. During the initial dose escalation phase, this study enrolls two patients per dose cohort.

Preliminary Observations

- In the Alta study, SB-525 has been generally well tolerated to date with no treatment-related serious adverse events and no use of tapering courses of oral steroids.
- The fifth patient in the study, the first at the third dose level, was treated in June and has achieved therapeutic Factor VIII activity levels.*
- A dose dependent effect has been observed in the study, with patients in the second dose cohort reporting reduced use of factor replacement.

Sangamo and Pfizer expect to present detailed data from the Alta study at a hematology conference in the fourth quarter.

"We have made good progress with dose escalation in this study and are encouraged by the safety and tolerability profile to date and by the attainment of therapeutic Factor VIII activity levels in the first patient in the third dose cohort," said Edward Conner, MD, Chief Medical Officer of Sangamo. "We look forward to generating additional data to assess the consistency and sustainability of the Factor VIII expression observed."

About SB-525

SB-525 comprises a recombinant adeno-associated virus (rAAV) vector carrying a Factor VIII gene construct driven by a proprietary, synthetic, liver-specific promoter. The U.S. Food and Drug Administration has granted Orphan Drug and Fast Track designations to SB-525, which also received Orphan Medicinal Product designation from the European Medicines Agency.

Hemophilia A is a rare blood disorder caused by a genetic mutation resulting in insufficient activity of Factor VIII, a blood clotting protein the body uses to stop bleeding. There are approximately 16,000 patients in the U.S. and more than 150,000 worldwide with Hemophilia A.

About Sangamo

Sangamo Therapeutics is focused on translating ground-breaking science into genomic therapies that transform patients' lives using the Company's platform technologies in genome editing, gene therapy, gene regulation and cell therapy. For more information about Sangamo, visit www.sangamo.com.

Forward-Looking Statements

This press release contains forward-looking statements regarding Sangamo's current expectations. These forward looking statements include, without limitation, statements related to the potential for SB-525 to treat Hemophilia A, the expectation of generating additional data to assess the consistency and sustainability of the FVIII expression observed, the importance of consistency and sustainability of Factor VIII expression, and Sangamo's expectation that it will present detailed data from the Alta study at a hematology conference in the fourth quarter of 2018, and other statements that are not historical fact. These statements are not guarantees of future performance and are subject to certain risks, uncertainties and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, risks and uncertainties related to the completion of the Alta study, the fact that the preliminary observations from the Alta study are based on preliminary data from only the first five patients in the study and that these preliminary data may not be representative of final results after all patients are treated in the study and all data are collected and analyzed; whether the final results from the Alta study will validate and support the safety and efficacy of SB-525, including the risk that the observed therapeutic Factor VIII activity levels and reduced use of factor replacement in the Alta study to date may not be maintained or replicated, Sangamo's reliance on Pfizer and other third-parties to meet their clinical and manufacturing obligations, and the ability to maintain strategic partnerships. Further, there can be no assurance that the necessary regulatory approvals will be obtained or that Sangamo and its partners will be able to develop commercially viable product candidates. Actual results may differ from those projected in forward-looking statements due to these and other risks and uncertainties that exist in Sangamo's operations and business environments. These risks and uncertainties are described more fully in Sangamo's Quarterly Report on Form 10-Q for the quarter ended March 31, 2018, as filed with the Securities and Exchange Commission. Forward-looking statements contained in this announcement are made as of this date, and Sangamo undertakes no duty to update such information except as required under applicable law.

SOURCE Sangamo Therapeutics, Inc.

Related Links *http://www.sangamo.com*

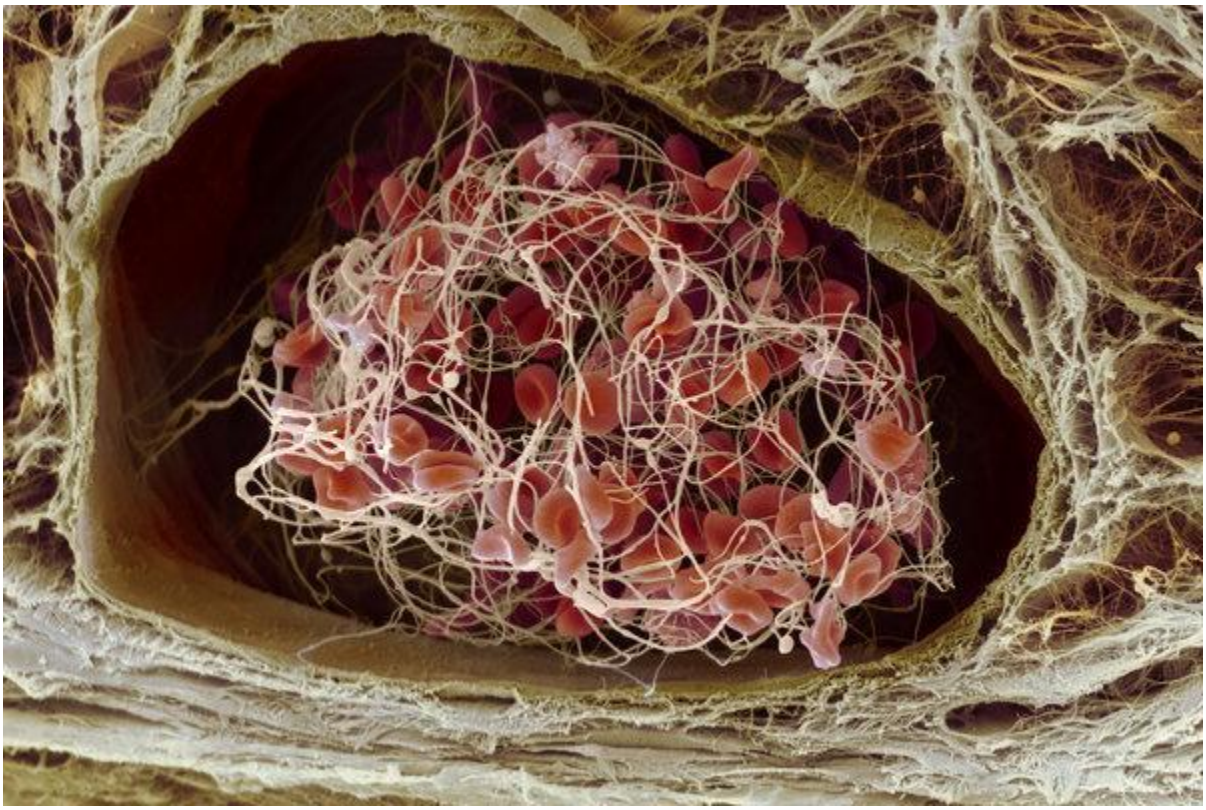
*Epidemiological data indicate that Factor VIII activity above 12% of normal is associated with substantial reduction or elimination of spontaneous bleeds and factor usage. Den Uijl IE et al Haemophilia 2011; 17(6):849-53

The New York Times
August 13, 2018

They Thought Hemophilia Was a 'Lifelong Thing.' They May Be Wrong.

Experimental gene therapies have yielded promising results in early trials. But the drugs have left some patients worried that success will not last.

By Gina Kolata



A colored scanning electron micrograph of a blood clot. Hemophilia is defined by an inability to form blood clots, leading to uncontrolled bleeds and chronic pain.
[CreditSteve Gschmeissner/Science Source]

(*Health)* --**Scientists are edging closer to defeating a longtime enemy of human health: hemophilia, the inability to form blood clots.**

After trying for decades to develop a gene therapy to treat this disease, researchers are starting to succeed. In recent experiments, brief intravenous infusions of powerful new treatments have rid patients — for now, at least — of a condition that has shadowed them all their lives.

There have been setbacks — years of failed clinical trials and dashed hopes. Just last week, a biotech company reported that gene therapy mostly stopped working in two of 12 patients in one trial. But the general trajectory has been forward, and new treatments are expected by many experts to be approved in a few years.

No one is saying yet that hemophilia will be cured. Currently the gene therapy — which uses a virus to deliver a new gene to cells — can only be used once. If it stops working, the patients lose the benefits.

For now, "we are anticipating that this is a once-in-a-lifetime treatment," **said Dr. Steven Pipe,** director of the hemophilia and coagulation disorders program at the University of Michigan and a lead investigator of a clinical trial conducted by the biotech company BioMarin.

The successful treatments are so recent it is hard to say how long they will last. But for the few patients who have been through the clinical trials successfully, life after treatment is so different that it's something of a shock.

There are 20,000 hemophilia patients in the United States who lack one of two proteins needed for blood to clot. It's a genetic condition, and the gene for blood clotting sits on the X chromosome. Virtually all people with hemophilia are men.

Those most severely affected must inject themselves every couple of days with the missing proteins, clotting factor VIII or factor IX. The shots keep hemophiliacs alive, but levels of clotting proteins drop between injections. Even with regular injections, people with hemophilia risk uncontrolled bleeding into a muscle or joint, or even the brain. They must be extremely careful. Once bleeding begins, a joint may bulge as the joint space fills with blood. When the bleeding stops, the joint may be damaged.

Even a routine flight is risky, said **Mark Skinner**, a 57-year-old attorney in Washington with hemophilia who is a past president of the World Federation of Hemophilia. "Carrying luggage around, you can twist the wrong way and immediately trigger a bleed," he said. "Or you can get hit with a cart going down the aisle."

People with hemophilia often are taught as children to avoid most sports and to find professions that will not require much physical activity. Many move to cities to gain easier access to treatment. They may change jobs to get insurance needed to cover medical bills for hospitalizations and surgeries that can reach $1 million a year, plus an average of $250,000 to $300,000 a year for the clotting proteins. (The shots alone can cost as much as $1 million per year.)

Despite their vigilance, most with severe disease eventually develop permanent joint damage from bleeds, often leading to surgery for ankle fusion or hip or knee replacements at an early age. Most live with chronic pain from past bleeds.

For older patients, there is an additional complication. The clotting proteins used in the 1980s were contaminated with H.I.V. and hepatitis C. Nearly everyone with hemophilia got infected.

Now, though, researchers see the start of a new era.

“It’s a really optimistic time,” said Dr. Lindsey A. George, a hematologist at the Children’s Hospital of Philadelphia and a principal investigator for Spark Therapeutics, one of several companies developing gene therapies for hemophilia.

Imperfect successes

The goal of gene therapy is to reduce or eliminate patients’ need for injections with clotting factor and to reduce the number of bleeds. The gene to be inserted depends on whether the patient has hemophilia A, caused by a mutation in the gene for factor VIII, or hemophilia B, caused by a mutation in the gene for clotting factor IX.

Although the symptoms are the same with both forms of the disease, hemophilia A is by far the most common.

A handful of biotech companies are now rushing to get their gene therapies to market. Spark, with gene therapy for hemophilia B, and BioMarin, another biotech company, with a similar treatment for hemophilia A, are starting large, final-phase clinical trials. (Pfizer is taking over the development of the Spark drug.) Results from the two companies’ preliminary trials were not perfect.

Patients in Biomarin’s hemophilia A trial got, on average, normal or above normal levels of factor VIII in their blood, but in the second year, those levels dropped to a median of 46 percent. It’s not clear why.

Patients in Spark’s hemophilia B trial only reached on average 35 percent of normal blood levels of factor IX. But those levels have remained steady for the two years they have been followed.

The good news is that those levels are sufficient for blood to clot, because normal levels are more than people need. After dreaming of a cure for decades, some treated patients are trying to adjust to newfound freedom.

John Brissette, 39, a computer user interface designer in Hanover, Mass., said hemophilia A always dominated his life. He spent childhood yearning to be active like other kids. But bleeds into his joints put him on crutches for days at a time or forced him to keep his arm in a sling.

He would be out of school for a week, then back, then out again with yet another bleed. He was embarrassed by nosebleeds that would not stop. As an adult, he had to have his damaged ankle bones fused. His elbow, after numerous bleeds over the years, gives him chronic pain.

Foreseeing more pain and injuries in the years to come, Mr. Brissette began seeking out gene therapy clinical trials. Eventually, he enrolled in a Spark trial. (The company has an experimental hemophilia A drug, too.)

He received a single infusion on April 19. His blood levels of factor VIII rose from zero to as high as 30 percent of normal and so far have stayed there.

“I have not had a single bruise. I have not had a single bleed,” Mr. Brissette said.

He has not given himself a shot of clotting factor since the procedure.

But he is still struggling to let go of a lifetime of wariness. As he tries to do work around the house or run around with his children, he is unable to shake the dread that he will bleed.

“I’ve become a very cautious person,” Mr. Brissette said.

Bill Konduros, left, and his brother, Jay, have lived with hemophilia most of their lives. Since receiving an experimental gene therapy, they have struggled to shed their wariness of what had been dangerous physical activity. [CreditIan Willms for The New York Times]

A lucky mutation

At first, hemophilia seemed ideal for gene therapy.

Normal blood levels of clotting proteins range widely, from 50 percent to 150 percent of average. A gene therapy for the disease would not have to provide much to be effective for patients. And researchers knew just which genes to insert into patients’ liver cells. The genes for hemophilia A and B were isolated in the early 1980s.

But the research proved difficult, and the first positive result was reported just a decade ago by scientists at University College London. They treated ten patients with hemophilia B and managed to increase their blood levels of factor IX to between 2 percent to 6 percent of normal.

In those patients, clotting proteins have persisted at those levels ever since.

Then scientists stumbled upon an unexpected bonanza. They found a man in Padua, Italy, who had a genetic mutation that made cells churn out as much as 12 times the usual amounts of factor IX. Investigators realized that they could put the mutated gene into a virus and use it to insert the mutated gene into the cells of patients with hemophilia B.

The advantage was that they would not have to use so much virus — and the lower the dose, the less likely the immune system would attack.

"We dropped the dose four-fold," said Dr. Kathy High, a hematologist who is president of Spark.

"Our first patient was a 23-year-old nurse. His level of factor IX rose to around 30 percent and has remained there for two years," she said. The nurse has not needed to inject factor IX and has had no bleeds, she added.

But hemophilia A has been more daunting.

The viruses used to carry modified genes into patient cells are called adeno-associated viruses. They cannot carry a large gene, and the gene for factor VIII, needed to treat hemophilia A, is enormous. After 15 years of effort, investigators finally discovered they could reduce the gene to a manageable size by slicing out portions that turned out not to be needed.

No longer are scientists and patients dazzled by a treatment that raises blood clotting factor levels merely to 6 percent of average. "My thinking has evolved," said Mr. Skinner of the World Hemophilia Foundation. The results that companies are reporting now "really seemed unimaginable" just a few years ago, he added.

'On high alert'

Bill Konduros, 59, owner of a machine shop who lives in Mississauga, Ontario, and his brother, Jay Konduros, 54, a baker in Cambridge, Ontario, had assumed that constant vigilance and increasing disability was their lot in life. Hemophilia would be "a lifelong thing," said Jay Konduros. Then the brothers joined Spark's gene therapy trial for hemophilia B.

The actual infusion of the experimental drug was anticlimactic, Jay Konduros recalled. He walked into a hospital in Philadelphia, sat in a chair and had an intravenous drip for half an hour. That was it.

Now levels of factor IX in Jay Konduros's blood are around 50 percent. Bill, who also joined the trial, has levels closer to 75 percent. Neither has required any factor IX since their gene therapy.

Both struggle to accept the fact that, for the moment, their lives are very different.

“When I hit myself or strain a muscle or twist, I immediately revert to thinking like a hemophiliac,” Bill Konduros said. “You go on high alert. Is the ache spreading? Is it throbbing?”

One day in May, Jay fell, landing on his forearms. Both wrists hit hard on concrete, and he struck the left side of his thigh, already damaged from previous bleeds. He took a few deep breaths and told himself, “You will be O.K., you will be O.K.”

He worried, anticipating disaster. That night he stretched. He examined himself. Nothing seemed damaged. He woke up in wee hours of the morning and nervously examined himself again.

He was fine. He waited three days to call his brother and tell him: He was now a normal person who had a minor fall.

“You hear a lot of things described as miracles or miraculous,” Bill said. “I guess I would say this truly is.”

Gina Kolata writes about science and medicine. She has twice been a Pulitzer Prize finalist and is the author of six books, including “Mercies in Disguise: A Story of Hope, a Family's Genetic Destiny, and The Science That Saved Them.”

A version of this article appears in print on Aug. 14, 2018, on Page D1 of the New York edition with the headline: Subduing Hemophilia.

Reuters.com
August 15, 2018

Express Scripts Staking Out Million-dollar Gene Therapies

By Caroline Humer and Deena Beasley

(Business News)//--**Express Scripts Holding** Co built a multi-billion enterprise pressuring drug companies to lower their prices for U.S. patients. Now it is quietly building a side business: getting paid to help drug companies dispense a new generation of high-priced drugs.

Express Scripts is in talks with biotechnology companies Biomarin Pharmaceutical Inc, Spark Therapeutics Inc and Bluebird Bio Inc., to have its specialty pharmaceutical business exclusively distribute their new hemophilia therapies when they are expected to become available in 2019 and 2020, Chief Medical Officer Steve Miller told Reuters in an interview.

Biomarin, Spark and Bluebird confirmed to Reuters that they were speaking to payers - a group generally defined as pharmacy benefit managers, health plans and government agencies- about pricing models for future therapies. Analysts project those drugs could top $1 million to $1.5 million in price.

Rather than rail against the drugs' expected high prices, Miller echoes the familiar drug company argument that the potentially curative therapies will likely be worth the high cost if they supplant the hundreds of thousands of dollars in annual medical costs to treat ailments such as hemophilia, which affects about 20,000 people in the United States alone.

"Even if they charge $1 million, that's a great deal," Miller said. "So there are going to be some gene therapies where it is very clear that everyone who has that disease should get it."

By working closely with biotech companies, Miller says it can help their expensive therapies succeed commercially. To manage any potential conflicts of interest, he said Express Scripts separates its benefits management and specialty pharmacy businesses.

The move into hemophilia builds on exclusive rights Express Scripts already has to distribute Spark's Luxturna - an $850,000 treatment for a rare genetic disorder that, left untreated, causes children to go blind. It has a similar deal with Biogen Inc (BIIB.O) on Spinraza, he told Reuters. The drug costs $750,000 the first year and treats the rare condition spinal muscular atrophy that often kills babies within months of their birth. Spark and Biogen confirmed the agreements.

The company also helps manage one of the most expensive gene-based cancer treatments on the market: the $475,000 Novartis AG (NOVN.S) gene-based cancer therapy Kymriah - a personalized treatment that requires a long hospital stay. Novartis confirmed the arrangement to Reuters.

Those deals put Express Scripts in a vastly different role than its traditional business managing prescription drug claims for the employees of its corporate and government clients, a business Cigna Corp found so valuable that it agreed in March to acquire Express Scripts for $52 billion.

Patients usually know Express Scripts and other pharmacy benefit managers (PBMs) as the name on the insurance card they present at the pharmacy counter when picking up a prescription. That card activates discounts the benefits managers have negotiated with drug companies to lower prices, usually through rebates. PBMs make money by taking a cut of the rebates, and the rest goes to their clients.

Express Scripts, which negotiates the prescription payments for 80 million people in the United States, competes with UnitedHealth Group Inc's, Optum and CVS Health Corp.
These companies are usually among the most vocal critics of the pharmaceutical industry's pricing practices, publicly calling out companies and specific products for their high cost.

But the pharmacy benefits businesses themselves are facing growing criticism from U.S. regulators, lawmakers, drugmakers, and President Trump, who say they act as unnecessary middlemen and end up helping drive up prices for payers.

Billionaire activist investor Carl Icahn mounted a proxy campaign to stop the deal on expectations the Trump Administration would end the rebates it relies on for profits. But he abandoned his efforts after two shareholder advisory groups came out in favor of the deal.

GROWTH vs CONFLICTS

As the PBM fight plays out publicly, Express Scripts has been expanding its low-profile specialty pharmacy business - which dispenses drugs that usually aren't sold through drugstores because they require special handling. By using its own pharmacy instead of outsiders, Express Scripts is able to hold onto more of the profits along the drug distribution chain.

Specialty pharmacy is one of Express Script's fastest growing businesses and accounts for about a third of its sales and profits, ISI Evercore analyst Ross Muken said. The company earned $4.1 billion last year on total revenue of more than $100 billion - it does not break out financial information for specialty pharmacy.

Many of the newest, most advanced medicines - including gene-based therapies and personalized cancer treatments - will be dispensed through specialty pharmacies, and Express Scripts is pitching biotech companies for exclusive arrangements.

By working as both the manufacturer's partner who gets paid for each sale, and the pharmacy benefit manager responsible for negotiating the best price for its traditional corporate and government clients, Express Scripts is open to questions about being conflicted, industry sources and experts say.

"One could view this role as being a wonderfully catalytic: that they can help balance the views and interests of all the parties by being in this middle facilitating role. Or one could view that they have created a situation where internally they have multiple conflicts of interest, and can they manage them properly?" said Mark Trusheim, strategic director of a group of international payers and providers formed by the Massachusetts Institute of Technology to study gene therapy pricing models.

Express Scripts says it saves money for payers on Luxturna by cutting out the hospital pharmacy mark- up, which is 6 percent for the government Medicare program and more for commercial business – or at least $60,000 on a $1 million drug.

Miller said the company has a firewall between its specialty pharmacy business, which serves the drugmakers, and its businesses negotiating on behalf of his clients, the payers.

"Our PBM treats our specialty pharmacy as they treat any other pharmacy in our pharmacy network," he said. "So they are not privy to their acquisition prices or anything else, and the specialty pharmacy is not privy to the contracts that the PBM has with their payer clients or anything else."

Beyond potential conflict concerns, there is risk in whether the gene therapies will ever make it to the public.

Spark on Aug. 7 said two patients in a small trial had an adverse immune response to an experimental hemophilia gene therapy and its shares lost more than a quarter of their value. And last month, U.S. regulators put Biogen's gene therapy program for spinal muscular atrophy on hold, but no details were disclosed.

Editing by Elyse Tanouye and Edward Tobin

Viivhealthcare.com
August 15, 2018

ViiV Healthcare Reports Positive 48-week Results for First Pivotal, Phase III study for Novel, Long-acting, Injectable HIV-treatment Regimen

ATLAS study meets primary endpoint, showing similar efficacy of a once-a-month, investigational, injectable two-drug regimen of cabotegravir and rilpivirine compared to a standard of care, daily, oral three-drug regimen

(London, UK) **-- ViiV Healthcare** today announced positive headline results from its global, phase III ATLAS study of a long-acting, injectable two-drug regimen (2DR) for the treatment of HIV. ATLAS (Antiretroviral Therapy as Long-Acting Suppression) was designed to establish if HIV-1-infected adult participants who had maintained viral suppression for at least six months, on a daily oral regimen comprised of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a third agent, maintained similar rates of viral suppression upon switching to the investigational, two-drug, long-acting, injectable regimen of cabotegravir and rilpivirine, compared with continuing the three-drug oral regimen.

The study showed long-acting cabotegravir and rilpivirine, injected once a month, had similar efficacy to a standard of care, daily, oral three-drug regimen at Week 48. The injectable treatment regimen met the primary endpoint for non-inferiority (the proportion of participants with plasma HIV-1 RNA ≥50 copies per milliliter [c/mL] using the FDA Snapshot algorithm at Week 48). Overall safety, virologic response and drug resistance results for the injectable regimen were consistent with results from the phase II LATTE and LATTE-2 studies.**[1],[2]**

John C. Pottage, Jr., MD, Chief Scientific and Medical Officer of ViiV Healthcare, said**:** "This novel approach is another step towards potentially reducing the treatment burden for people living with HIV. The data from ATLAS suggest a long-acting, injectable 2DR of cabotegravir and rilpivirine may offer an alternative to daily, oral three-drug therapy for people who have previously achieved viral suppression. If approved, this regimen would give people living with HIV one month between each dose of antiretroviral therapy, changing HIV treatment from 365 dosing days per year, to just 12."

Detailed results from the study will be presented at an upcoming scientific meeting. Headline results from FLAIR, a second pivotal trial designed to evaluate a long-acting, injectable regimen of cabotegravir and rilpivirine in treatment-naïve individuals, are expected later this year.**[3]**

This investigational, long-acting, injectable regimen is being co-developed as part of a collaboration with Janssen Sciences Ireland UC and is not approved by regulatory authorities anywhere in the world.

Notes to editors

About ATLAS (NCT02951052)
The ATLAS study is part of ViiV Healthcare's innovative clinical trial programme for two-drug regimens. The study includes 618 men and women living with HIV and is being conducted at research centres in Argentina, Australia, Canada, France, Germany, Italy, Mexico, Russia, South Africa, South Korea, Spain, Sweden, and the United States.
ATLAS is a phase III, open-label, active-controlled, multicentre, parallel-group, non-inferiority study designed to assess the antiviral activity and safety of a two-drug regimen of long-acting, injectable cabotegravir and rilpivirine dosed every four weeks compared to continuation of current oral anti-retroviral therapy (ART) of two nucleoside reverse transcriptase inhibitors (NRTIs) plus an integrase strand transfer inhibitor (INI), non-nucleoside reverse transcriptase inhibitor (NNRTI), or protease inhibitor (PI) among virally-suppressed individuals. The primary endpoint for ATLAS is the proportion of participants with plasma HIV-1 RNA ≥50 c/mL per the FDA Snapshot algorithm at Week 48 (Missing, Switch, or Discontinuation = Failure, Intent-to-Treat Exposed [ITT-E] population). Subjects were required to be virally-suppressed for six months or greater, on first or second regimen, with no prior failure.
For further information please see **https://clinicaltrials.gov/ct2/show/NCT02951052**.

About cabotegravir
Cabotegravir is an investigational integrase inhibitor (INI) and is not approved by regulatory authorities anywhere in the world. Cabotegravir is being developed by ViiV Healthcare for the treatment and prevention of HIV and is currently being evaluated as a long-acting formulation for intramuscular injection and also as a once-daily oral tablet for use as a lead-in, to establish the tolerability of cabotegravir prior to long-acting injection.

About rilpivirine
Edurant® (rilpivirine) is a once daily non-nucleoside reverse transcriptase inhibitor (NNRTI) used for the treatment of human immunodeficiency virus (HIV-1) infection in combination with other antiretroviral agents in antiretroviral treatment-naïve adult patients with a viral load ≤ 100,000 HIV RNA copies/mL. Long-acting rilpivirine is not approved by regulatory authorities anywhere in the world.
Rilpivirine was developed by Janssen Sciences Ireland UC, one of the Janssen Pharmaceutical Companies of Johnson & Johnson. Rilpivirine is approved in the U.S. and E.U. as Edurant® as a 25mg tablet taken once-a-day and is always taken with a meal. The most common side effects of Edurant include: depression, headache, trouble sleeping (insomnia) and rash.

About EDURANT® (Rilpivirine) EDURANT® (rilpivirine) is a prescription HIV medicine that is used with other antiretroviral medicines to treat Human Immunodeficiency Virus-1 (HIV-1) in patients:

- Who have **never** taken HIV medicines before, **and**
- Who have an amount of HIV in their blood (called "viral load") that is no more than 100,000 copies/mL. Your healthcare professional will measure your viral load

EDURANT® should be taken in combination with other HIV medicines. Your healthcare professional will work with you to find the right combination of HIV medicines
It is important that you remain under the care of your healthcare professional during treatment with EDURANT®

EDURANT® is not recommended for patients less than 12 years of age
EDURANT® does not cure HIV infection or AIDS. You should remain on your HIV medications without stopping to ensure that you control your HIV infection and decrease the risk of HIV-related illnesses. Ask your healthcare professional about how to prevent passing HIV to other people.

Please read Important Safety Information below, and talk to your healthcare professional to learn if EDURANT® is right for you.
Important Safety Information

Can EDURANT® be taken with other medicines? EDURANT® may affect the way other medicines work and other medicines may affect how EDURANT® works and may cause serious side effects. If you take certain medicines with EDURANT®, the amount of EDURANT® in your body may be too low and it may not work to help control your HIV infection, and the HIV virus in your body may become resistant to EDURANT® or other HIV medicines that are like it. To help get the right amount of medicine in your body, you should always take EDURANT® with a meal. A protein drink alone does not replace a meal.

Do not take EDURANT® if:

- Your HIV infection has been previously treated with HIV medicines
- You are taking any of the following medicines:
  - Anti-seizure medicines: carbamazepine (Carbatrol®, Equetro®, Tegretol®, Tegretol-XR®, Teril®, Epitol®), oxcarbazepine (Trileptal®), phenobarbital (Luminal®), phenytoin (Dilantin®, Dilantin-125®, Phenytek®)
  - Anti-tuberculosis (anti-TB) medicines: rifampin (Rifater®, Rifamate®, Rimactane®, Rifadin®), rifapentine (Priftin®) Proton pump inhibitor (PPI) medicine for certain stomach or intestinal problems: esomeprazole (Nexium®, Vimovo®), lansoprazole (Prevacid®), omeprazole (Prilosec®, Zegerid®), pantoprazole sodium (Protonix®), rabeprazole (Aciphex®)
  - More than 1 dose of the steroid medicine dexamethasone or dexamethasone sodium phosphate
  - John’s wort (Hypericum perforatum)

Especially tell your doctor if you take:

- Rifabutin (Mycobutin®), a medicine to treat some bacterial infections. Talk to your doctor or pharmacist about the right amount of EDURANT® you should take if you also take rifabutin
- Medicines used to treat HIV
- An antacid medicine that contains aluminum, magnesium hydroxide, or calcium carbonate. Take antacids at least 2 hours before or at least 4 hours after you take EDURANT®

- Medicines to block acid in your stomach, including cimetidine (Tagamet®), famotidine (Pepcid®), nizatidine (Axid®), or ranitidine hydrochloride (Zantac®). Take these medicines at least 12 hours before or at least 4 hours after you take EDURANT®
- Any of these medicines (if taken by mouth or injection): clarithromycin (Biaxin®), erythromycin (E-Mycin®, Eryc®, Ery-Tab®, PCE®, Pediazole®, Ilosone®), fluconazole (Diflucan®), itraconazole (Sporanox®), ketoconazole (Nizoral®), methadone (Dolophine®), posaconazole (Noxafil®), telithromycin (Ketek®), voriconazole (Vfend®)

This is not a complete list of medicines. Before starting EDURANT®, be sure to tell your healthcare professional about all the medicines you are taking or plan to take, including prescription and nonprescription medicines, vitamins, and herbal supplements.
Before taking EDURANT®, also tell your healthcare professional if you have had or currently have liver problems (including hepatitis B or C), have ever had a mental health problem, are pregnant or planning to become pregnant, or breastfeeding. It is not known if EDURANT® will harm your unborn baby.
You and your healthcare professional will need to decide if taking EDURANT® is right for you. Do not breastfeed if you are taking EDURANT®. You should not breastfeed if you have HIV because of the chance of passing HIV to your baby
What are the possible side effects of EDURANT®? EDURANT® can cause serious side effects including:

- Severe skin rash and allergic reactions. Call your doctor right away if you get a rash. Stop taking EDURANT® and seek medical help right away if you get a rash with any of the following symptoms: severe allergic reaction causing swelling of the face, eyes, lips, mouth, tongue, or throat (which may lead to difficulty swallowing or breathing); mouth sores or blisters on your body; inflamed eye (conjunctivitis); fever; dark urine; or pain on the right side of the stomach area (abdominal pain)
- Depression or mood changes. Tell your doctor right away if you have any of the following symptoms: feeling sad or hopeless, feeling anxious or restless, have thoughts of hurting yourself (suicide), or have tried to hurt yourself
- Liver problems. People with a history of hepatitis B or C virus infection or who have certain liver function test changes may have an increased risk of developing new or worsening liver problems during treatment. Liver problems were also reported during treatment in some people without a history of liver disease. Your healthcare professional may need to do tests to check liver function before and during treatment
- Changes in body shape or body fat have been seen in some patients taking HIV medicines. The exact cause and long-term health effects of these conditions are not known
- Changes in your immune system (immune reconstitution syndrome).
- Your immune system may get stronger and begin to fight infections. Tell your healthcare professional right away if you start having any new symptoms of infection
- Other common side effects of EDURANT® include depression, headache, trouble sleeping (insomnia), and rash.

This is not a complete list of all side effects. If you experience these or other symptoms, contact your healthcare professional right away. Do not stop taking EDURANT® or any other medications without first talking to your healthcare professional.

You are encouraged to report side effects of prescription drugs to the FDA.
Visit **www.fda.gov/medwatch,** or call 1-800-FDA-1088. You may also report side effects to Janssen Products, LP at 1-800-JANSSEN (1-800-526-7736).

Click here for full US prescribing information.
Click here for the EU Summary of Product Characteristics.

About ViiV Healthcare
ViiV Healthcare is a global specialist HIV company established in November 2009 by GlaxoSmithKline (LSE: GSK) and Pfizer (NYSE: PFE) dedicated to delivering advances in treatment and care for people living with HIV and for people who are at risk of becoming infected with HIV. Shionogi joined as a shareholder in October 2012. The company's aim is to take a deeper and broader interest in HIV/AIDS than any company has done before and take a new approach to deliver effective and innovative medicines for HIV treatment and prevention, as well as support communities affected by HIV.
For more information on the company, its management, portfolio, pipeline, and commitment, please visit **www.viivhealthcare.com**.

Cautionary statement regarding forward-looking statements
ViiV Healthcare Limited, the global specialist HIV company, is majority owned by GlaxoSmithKline plc, with Pfizer Inc. and Shionogi Limited. GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described under Item 3.D 'Principal risks and uncertainties' in the company's Annual Report on Form 20-F for 2017.

About GSK
GSK – one of the world's leading research-based pharmaceutical and healthcare companies – is committed to improving the quality of human life by enabling people to do more, feel better and live longer. For further information please visit **www.gsk.com**.

[1] Margolis D A et al. Cabotegravir plus rilpivirine, once a day, after induction with cabotegravir plus nucleoside reverse transcriptase inhibitors in antiretroviral-naive adults with HIV-1 infection (LATTE): a randomised phase 2b dose-ranging trial. The Lancet Infectious Diseases. Published online July 2015. Available at: **http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(15)00152-8/abstract**

[2] Margolis, D. et al. Long-acting intramuscular cabotegravir and rilpivirine in adults with HIV-1 infection (LATTE-2):96-week results of a randomised, open-label, phase 2b, non-inferiority trial. The Lancet. July 2017. Published online: **http://dx.doi.org/10.1016/S0140-6736(17)31917-7** Last accessed August 2018

[3] Study to evaluate the efficacy, safety, and tolerability of long-acting intramuscular cabotegravir and rilpivirine for maintenance of virologic suppression following switch from an integrase inhibitor in HIV-1 infected therapy naïve participants. Available at:
https://clinicaltrials.gov/ct2/show/NCT02938520?term=FLAIR+Cabotegravir&rank=1.

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Catalyst Biosciences (CBIO) Reports Updated Positive Interim Data from Phase 2/3 Study of Subcutaneous MarzAA

(FDA, Management Comments) --**Catalyst Biosciences, Inc**., a clinical-stage biopharmaceutical company focused on developing novel medicines to address hematology indications, today announced updated positive interim data from its Phase 2/3 study of subcutaneous prophylactic **Factor VIIa** (FVIIa) variant marzeptacog alfa (activated) (MarzAA), being developed for the treatment of hemophilia A or B with inhibitors.

The data will be delivered in an oral presentation today at the 2018 Hemophilia Drug Development Summit being held on August 15-16 in Boston.

"The ongoing study of subcutaneous MarzAA for the treatment of hemophilia A or B with inhibitors continues to demonstrate positive interim results, as reflected in the clinical update provided at this year's Hemophilia Drug Development Summit," said Nassim Usman, Ph.D., chief executive officer of Catalyst. "We have not observed any bleeds or anti-drug antibodies in the two additional subjects who most recently completed dosing with 30 µg/kg MarzAA, as well as in the previously reported individual who completed 50 days of dosing with 60 µg/kg MarzAA. The data from these three individuals support the efficacy of MarzAA to reduce annualized bleed rates after daily subcutaneous injections. Importantly, to date we have not observed any injection site reactions nor any anti-drug antibodies after more than 200 subcutaneous doses of MarzAA."

Dr. Howard Levy, chief medical officer of Catalyst, will present the updated interim results from the MarzAA Phase 2/3 trial in which five of up to 12 subjects have been enrolled. Since initial interim data was announced at the ISTH conference in July 2018, in which one subject with a historic annualized bleed rate (ABR) of 26.7 had completed the trial with no bleeds after 50 days of treatment with 60 µg/kg MarzAA, two additional subjects have now completed the trial. One of these subjects, who has a historic ABR of 16.6, had no bleeds during treatment with 30 µg/kg MarzAA for 50 days. No ADAs have been detected to date, with safety data for the final 10 days of dosing still being collected for this subject. The second subject, who has a historic ABR of 15.9, had no bleeds during treatment with 30 µg/kg MarzAA for 44 days. No ADAs have been detected to date.

A copy of the presentation materials can be accessed on the Events and Presentations section of the Catalyst website once the presentation concludes.

About the FVIIa Phase 2/3 Trial

Marzeptacog alfa (activated) (MarzAA) is a potent, subcutaneous Factor VIIa therapy being developed for prophylaxis in hemophilia A or B with inhibitors. The Phase 2/3 open-label, subcutaneous efficacy trial in individuals with hemophilia A or B with inhibitors will evaluate the ability of MarzAA to eliminate, or minimize, spontaneous bleeding episodes. The primary endpoint is a reduction in annualized bleed rate that will be compared with each individual's

recorded historical annualized bleed rate as the control. The trial will enroll up to 12 individuals with hemophilia and an inhibitor across approximately ten clinical trial sites globally. MarzAA has been granted orphan drug designation by the U.S. Food and Drug Administration (FDA) for routine prophylaxis to prevent bleeding episodes in individuals with hemophilia A or B with inhibitors.

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