NHF News Briefs

July 6 – July 12, 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.

July 9, 2018
WSJ.com

When Three Brothers with a Blood Disorder Lost Their Jobs, the EEOC Sued

Contractor firm says it let Texas refinery workers go as part of larger 'reduction in force'

By Lauren Weber

Five years ago, Anthony, Drew and Raymond West were called into their supervisor's office and let go from their jobs performing heavy-duty maintenance work at an oil refinery in Beaumont, Texas.

"We kind of knew it was gonna happen, but then again we were all shocked," said Raymond West, age 26, the youngest of the brothers.

The Wests were employed for a contract-worker firm, Signature Industrial Services LLC, and were contracted to do work for Exxon Mobil Corp. Their Signature supervisor had been instructed to let them go because of their medical condition, hemophilia A, according to a lawsuit filed in February by the Equal Employment Opportunity Commission that charged Signature with violating the Americans with Disabilities Act.

Contracting firms like Signature deliver flexibility and cost savings to companies that don't want to take on the long-term liabilities of permanent employees. Contracting firms supply extra workers when business demand increases; those same people may be dropped quickly when demand slumps. The firms compete to win contracts from price-conscious corporate clients.

Big companies are accustomed to absorbing costs such as rising health insurance premiums, which they spread across a large workforce. But experts say that, as large firms outsource work to small companies that often operate with thin margins, there's little capacity for those smaller firms to soak up the costs.

Signature said in a filed response to the suit that the brothers were let go for nonmedical reasons as part of a larger "reduction in force." The company didn't provide details about a broader layoff in the documents. "Signature Industrial Services is committed to providing equal employment opportunities for all workers," the company's attorney said in a statement. Exxon declined to comment on the case.

On Monday, the brothers, the EEOC and Signature are scheduled to gather for a mediation session.

Contracting firms in the oil-and-gas industry "are under constant pressure to get their prices down, and the easiest way is to look for ways to cut material and labor costs," said Andrew Thomas, a former oil and gas lawyer who now runs the Energy Policy Center at Cleveland State University.

Signature's owners learned in June 2012, when their prior health insurance contract was expiring, that their payments could rise steeply due to the Wests' hemophilia, according to the EEOC's complaint. Signature executives asked David White, Signature's project manager at the refinery, to let the brothers go and he refused, the agency alleged.

“You don’t let somebody go because of insurance purposes or high risk or anything else. I don’t believe in that. It’s not right,” Mr. White said in an interview. He said that Signature managers told him to lay off the West brothers because of their impact on the company’s premiums, and added that the West brothers were “good workers, no doubt, very good workers.”

After Mr. White left the company, Signature executives ordered the Wests’ direct supervisor to let the brothers go, according to the EEOC complaint. Told he would lose his job if he defied the order, that manager complied in July 2013, the complaint said.

“It’s never kept me from doing any of my jobs,” Anthony West said of his hemophilia, a gene mutation that makes it difficult for blood to clot, causing people with slight injuries to bleed profusely. Mr. West, age 33, had received a promotion a few months earlier. “I thought I was safe,” he said.

The energy sector relies heavily on contract workers, with about 47% of labor spending paid to an outside workforce, according to a recent report from SAP Fieldglass, which makes software that tracks clients’ use of external workers. Around the time the Wests were let go, Exxon had more than 1,000 contractors working alongside 2,000 direct employees, according to a press report from 2013. Over the last 20 years, Exxon’s workforce has shrunk by almost 40%, from 114,900 in 1997 to 69,600 in 2017.

After they were let go, the West brothers looked for other work. For two years, Anthony took short-term stints with other contract-services firms, but the work was often far from home and kept him away from his wife and three children for long stretches, he says. Now he works in operations for Exxon as a direct employee.

Today, Raymond West makes chemicals as a process operator for a specialty chemical maker. Drew West is a boilermaker and pipefitter for a contracting firm in Dayton, Texas.

“Everyone is entitled to work,” Anthony said. “It just hurt knowing I was let go because of a blood condition I had since I was born.”

July 9, 2018
Prnewswire.com

BioMarin Partners with Believe Limited for 'Breaking Through!' Musical Theater Intensive

First-of-Its-Kind Musical to Help Empower the Bleeding Disorder Community to Find and Use their Voices through the Power of Music

BioMarin Pharmaceutical Inc. today announced an exclusive partnership with Believe Limited to produce the 'Breaking Through!' musical theater intensive. The first-of-its-kind program is a three-day music workshop for the bleeding disorders community and is designed to provide young adults with powerful education on the healing and therapeutic power of the arts and self-expression. The musical workshop, directed by hemophilia advocate and Believe Limited CEO Patrick James Lynch, will be held from November 9 – November 12, 2018 and will culminate in a Broadway-style performance for local bleeding disorder community members, family and friends.

Twenty-five young adults from across the country will be selected for the workshop to be held in New York City to learn and perform a six-song musical about the psychosocial and general health aspects of being a young person with a bleeding disorder. The songs and material will be custom written by composers and lyricists based on ideas shared directly from the participants during the application process. High school students in the U.S. with hemophilia, who are carriers of hemophilia, who have von Willebrand disease, who have another rare factor deficiency, or who have a sibling living with a bleeding disorder are invited to audition.1

Renowned vocal coach and director of UK Haemophilia Society choir Paul Russell will work with the selected high school students as the musical director. In addition to musical performance, trained facilitators will conduct breakout sessions for the participants on the impact of breathing and relaxation pain management, the psychosocial benefits of and the therapeutic value of self-expression in the arts.

"The 'Breaking Through!' musical theater intensive is a groundbreaking effort to empower young people in the bleeding disorder community who want to better understand how the arts and artistic expression can improve their health outcomes, and really, their lives in general," said Lynch. "We're breaking through the barriers created by a bleeding disorder mentally, emotionally and imaginatively with the arts. Our community does an incredible job of working to inspire our young people to participate in physical activity, but I believe it's as important to connect young people to the health and wellness benefits that the arts and self-expression offers as well."

"BioMarin is proud to support the next generation of the bleeding disorder community by creating a positive and impactful experience to allow teens to express the aspects of bleeding disorders that are often overlooked, as well as raise awareness of their impact on patient lives," said Hank Fuchs, M.D., President, Worldwide Research and Development at BioMarin.

Submissions are open now through September 1, 2018. Nominate a high school student, apply or read more information here.

About Hemophilia A

Hemophilia A, also called factor VIII (FVIII) deficiency or classic hemophilia, is a genetic disorder caused by missing or defective factor VIII, a clotting protein. Although it is passed down from parents

to children, about 1/3 of cases are caused by a spontaneous mutation, a new mutation that was not inherited. Approximately 1 in 10,000 people is born with Hemophilia A. People living with the disease are not able to form blood clots efficiently and are at risk for excessive bleeding from modest injuries, potentially endangering their lives. People with severe hemophilia often bleed spontaneously into their muscles or joints. The standard of care for the 43 percent of individuals with hemophilia A who are severely affected is a prophylactic regimen of Factor VIII infusions two to three times per week. Even with prophylactic regimens, many people still experience spontaneous bleeding events that result in progressive and debilitating joint damage.

About Believe Limited

Believe Limited is an award-winning boutique agency focused on creating educational, inspirational and deeply impactful digital content, live events, podcasts and more for rare disease communities, with a deeply-rooted focus in hemophilia and bleeding disorders. Our work has been honored by the National Hemophilia Foundation (NHF), Hemophilia Federation of America (HFA) and the WEBBYs. To learn more about our content and programming, please visit www.BelieveLTD.com.

About BioMarin

BioMarin is a global biotechnology company that develops and commercializes innovative therapies for people with serious and life-threatening rare disorders. The company's portfolio consists of six commercialized products and multiple clinical and pre-clinical product candidates.

For additional information, please visit www.BMRN.com. Information on BioMarin's website is not incorporated by reference into this press release.

July 11, 2018
Fda.gov

Statement from FDA Commissioner Scott Gottlieb, M.D. on Agency's Efforts to Advance Development of Gene Therapies

Once just a theory, gene therapies are now a therapeutic reality for some patients. These platforms may have the potential to treat and cure some of our most intractable and vexing diseases. The policy framework we construct for how these products should be developed, reviewed by regulators, and reimbursed, will help set the stage for the continued advancement of this new market. Last year, we announced our comprehensive policy framework for regenerative medicine, including a draft guidance that describes the expedited programs, such as the breakthrough therapy designation, and the regenerative medicine advanced therapy (RMAT) designation, that may be available to sponsors of these therapies. Today, we're unveiling a complementary framework for the development, review and approval of gene therapies.

In the past 12 months, we've seen three separate gene therapy products approved by the FDA. This reflects the rapid advancements in this field. An inflection point was reached with the development of vectors that could reliably deliver gene cassettes in vivo, into cells and human tissue. In the future, we expect this field to continue to expand, with the potential approval of new treatments for many debilitating diseases. These therapies hold great promise. Our new steps are aimed at fostering developments in this innovative field.

Gene therapies are being studied in many areas, including genetic disorders, autoimmune diseases, heart disease, cancer and HIV/AIDS. We look forward to working with the academic and research communities to make safe and effective products a reality for more patients. But we know that we still have much to learn about how these products work, how to administer them safely, and whether they will continue to work properly in the body without causing adverse side effects over long periods of time. In contrast to traditional drug review, some of the more challenging questions when it comes to gene therapy relate to product manufacturing and quality, or questions about the durability of response, which often can't be fully answered in any reasonably sized pre-market trial. For some of these products, we may need to accept some level of uncertainty around these questions at the time of approval. For example, in some cases the long-term durability of the effect won't be fully understood at the time of approval. Effective tools for reliable post-market follow up, such as required post-market clinical trials, are going to be one key to advancing this field and helping to ensure that our approach fosters safe and innovative treatments.

Even when there may be uncertainty about some questions, we need to make certain we assure patient safety and adequately characterize the potential risks and demonstrated benefits of these products. In part because of the added questions that often surround a new technology like gene therapy, these products are initially being aimed at devastating diseases, many of which lack available therapies, including some diseases that are fatal. In such cases of devastating diseases without available therapies, we've traditionally been willing to accept more uncertainty to facilitate timely access to promising therapies. In such cases, drug sponsors are generally required to conduct post-marketing clinical trials, known as phase 4 confirmatory trials, to confirm clinical benefit of the drug. This is the direction Congress gave the FDA by creating vehicles like the accelerated approval pathway.

When it comes to novel technologies like gene therapy, the FDA is steadfastly committed to a regulatory path that maintains the agency's gold standard for assuring safety and efficacy. As we

develop this evidence-based framework, we're going to have to modernize how we approach certain aspects of these products in order to make sure our approach is tailored to the unique challenges created by these new platforms.

Today, we're taking a step toward shaping this modern structure for the regulation of gene therapy. The agency is issuing a suite of six scientific guidance documents intended to serve as the building blocks of a modern, comprehensive framework for how we'll help advance the field of gene therapy while making sure new products meet the FDA's gold standard for safety and effectiveness.

These policies are part of our efforts to communicate the steps we're taking to provide clear recommendations to sponsors and researchers, so that we can better support innovation. The documents are being issued in draft form so that we can solicit public input on these new policies. As with all draft guidances, all of the comments we receive will be carefully considered prior to finalizing these documents. We're committed to working with stakeholders to bring novel treatments to the market while ensuring the safety of patients.

Disease Specific Gene Therapy Guidances

Today we're issuing three new draft guidance documents on the development of gene therapy products for specific disease categories. These are the first three disease-specific guidances that the agency is issuing for gene therapy products. Our new commitment to develop disease-specific guidance documents reflects the increasing activity in this field, and its growing importance to advancing public health.

Human Gene Therapy for Hemophilia: Gene therapy products for hemophilia are now being developed as single-dose treatments that may enable long-term production of the missing or abnormal coagulation factor in patients. This may reduce or eliminate the need for coagulation factor replacement. To define the proper development pathway for such products, we're issuing a new draft guidance on gene therapy products that are targeted to the treatment of hemophilia. Once finalized, this new guidance will provide recommendations on the FDA's current thinking on clinical trial design and preclinical considerations to support the development of these gene therapy products. Among other elements, the draft guidance provides recommendations regarding surrogate endpoints that could be used by sponsors pursuing accelerated approval of gene therapy products that are intended for treatment of hemophilia.

Human Gene Therapy for Retinal Disorders: Another area of fast-paced activity is gene therapy products targeted to the treatment of retinal disorders. The Human Gene Therapy for Retinal Disorders guidance, once finalized, will assist those developing gene therapy products for a wide variety of retinal disorders affecting both adult and pediatric patients. Gene therapy products currently undergoing clinical trials in the United States for retinal disorders are commonly delivered by intravitreal injections (into the fluid portion of the eye), or by subretinal injections (beneath the retina). In some cases, the gene therapy products are encapsulated in a device to be implanted within the eye. This new guidance document will focus on issues that are specific to gene therapies for retinal disorders. The document provides recommendations related to product development, preclinical testing, and clinical trial design for such products.

Human Gene Therapy for Rare Diseases: Rare diseases are those that affect fewer than 200,000 people in the United States. The National Institutes of Health reports that nearly 7,000 rare diseases affect more than 25 million Americans. About 80 percent of rare diseases are caused by a single-gene defect,

and about half of all rare diseases affect children. Since most rare diseases have no approved therapies, there is a significant unmet need. The Human Gene Therapy for Rare Diseases guidance, once finalized, will provide recommendations on preclinical, manufacturing and clinical trial design for all phases of the clinical development program for these types of gene therapies. The information is intended to assist sponsors in the design of clinical development programs, where there may be limited study population size, potential feasibility and safety issues, as well as issues relating to the interpretation of effectiveness.

Guidances on Manufacturing Gene Therapies

Today, we're also providing new and comprehensive updates to three existing guidances that address manufacturing issues related to gene therapy. These updates reflect input from many stakeholders. We encourage additional feedback on these documents during the comment period.

The first draft guidance, Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs), provides sponsors with recommendations on how to provide sufficient CMC information to assure safety, identity, quality, purity and strength/potency of investigational gene therapy products. The guidance applies to human gene therapies and to combination products that contain a human gene therapy in combination with a drug or device. In addition, this guidance is organized to follow the structure of the FDA guidance on the Common Technical Document.

The second draft guidance, Testing of Retroviral Vector-Based Gene Therapy Products for Replication Competent Retrovirus (RCR) during Product Manufacture and Patient Follow-up, provides additional recommendations regarding the proper testing for RCR during the manufacture of retroviral vector-based gene therapy products, as well as during the follow-up monitoring of patients who've received retroviral vector-based gene therapy products. Specifically, the draft guidance recommends the identification and amount of material to be tested. The guidance also provides advice on general testing methods.

The third draft guidance, Long Term Follow-Up After Administration of Human Gene Therapy Products, provides recommendations regarding the design of long-term follow-up (LTFU) observational studies for the collection of data on delayed adverse events following administration of a gene therapy product. Because of some of the additional uncertainty intrinsic to a novel platform like gene therapy -- including questions related to the durability of the treatment effects as well as the theoretical potential for off-target effects if the genes do not insert correctly -- there's an increased need for robust long term follow-up of patients in the post-market period. This guidance describes product characteristics, patient-related factors, and the preclinical and clinical data that should be considered when assessing the need for LTFU observations and describes the features related to effective post-market follow up.

Once finalized, these draft guidances will replace previous guidances issued by the FDA in April 2008 (CMC) and November 2006 (RCR and LTFU).

The field of gene therapy has progressed rapidly since these guidances were first issued. Therefore, the FDA is updating these guidances to provide sponsors with the agency's most up-to-date thinking.

Our goal is to help promote safe and effective product development in this field. We'll continue to work with the product sponsors to help make the development and approval of these innovative gene

therapies more efficient, while putting in place the regulatory controls needed to ensure that the resulting therapies are both safe and effective. We'll also make full use of our expedited programs such as breakthrough therapy designation and regenerative medicine advanced therapy designation whenever possible.

Gene therapy represents one of the most promising opportunities for developing highly effective and even curative treatments for many vexing disorders. Some of these products are almost certainly going to change the contours of medical practice, and the destiny of patients with some debilitating diseases.

Our goal is to help these innovations advance in a framework that assures the safety and effectiveness of these resulting treatments, and continues to build peoples' confidence in this novel area of medicine.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

July 12, 2018
Globenewswire.com

Catalyst Biosciences Announces Multiple Presentations at the Scientific and Standardization Committee Meeting of the International Society on Thrombosis and Haemostasis

Catalyst Biosciences, Inc., a clinical-stage biopharmaceutical company focused on developing novel medicines to address hematology indications, today announced the presentation of two posters at the 64th Annual Scientific and Standardization Committee (SSC) Meeting of the International Society on Thrombosis and Haemostasis (ISTH) being held in Dublin on July 18-21, 2018.

The posters, presented by Dr. Howard Levy, chief medical officer of Catalyst, entitled: "Phase 2 Trial of Subcutaneously Administered Novel FVIIa Variant, Marzeptacog alfa (activated), in Hemophilia A or B with Inhibitors: Pharmacokinetics, Pharmacodynamics, Safety and Efficacy" and "Phase 1/2 Trial of Single and Multiple Dose Subcutaneously Administered Factor IX Variant CB2679d/ISU304: Pharmacokinetics and Safety," will discuss the current clinical data from Catalyst's hemophilia programs.

Dr. Levy said, "We look forward to sharing interim data from our Factor VIIa program demonstrating the efficacy of subcutaneously (SQ) administered marzeptacog alfa (activated) for the treatment of hemophilia A or B with inhibitors. We will also provide an update on our SQ Factor IX CB 2679d program for the treatment of hemophilia B."

Poster presentations

Presentation Title:	Phase 2 Trial of Subcutaneously Administered Novel FVIIa Variant, Marzeptacog alfa (activated), in Hemophilia A or B with Inhibitors: Pharmacokinetics, Pharmacodynamics, Safety and Efficacy
Presenter:	Howard Levy, M.B.B.Ch., Ph.D., M.M.M.
Abstract Number:	PB196
Session:	Poster Session #1
Date/Time:	Wednesday, July 18, 2018 from 5:00-6:30 p.m. IST
Presentation Title:	Phase 1/2 Trial of Single and Multiple Dose Subcutaneously Administered Factor IX Variant CB2679d/ISU304: Pharmacokinetics and Safety
Presenter:	Howard Levy, M.B.B.Ch., Ph.D., M.M.M.
Abstract Number:	PB159
Session:	Poster Session #1
Date/Time:	Wednesday, July 18, 2018 from 5:00-6:30 p.m. IST

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

Conference Call Details
The management team will host a conference call for investors on Wednesday July 18, 2018, at 8:30 a.m. EDT to discuss the Factor VIIa and Factor IX clinical data. Conference call, webcast and post-conference call replay details are as follows:

Domestic: +1.877.425.9470
International: +1.201.389.0878
Conference ID: 13681615
Webcast: http://public.viavid.com/index.php?id=130521

A replay will be available two hours after completion of the call through August 1, 2018:
Domestic: +1.844.512.2921
International: +1.412.317.6671
Replay ID: 13681615

About Catalyst
Catalyst is a clinical-stage biopharmaceutical company developing novel medicines to address hematology indications. Catalyst is focused on the field of hemostasis, including the subcutaneous prophylaxis of hemophilia and facilitating surgery in individuals with hemophilia. For more information, please visit www.catalystbiosciences.com.

Forward-Looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statement of historical fact, included in this press release regarding our strategy, the efficacy of subcutaneously administered marzeptacog alfa (activated), potential uses and benefits of CB 2679d and marzeptacog alfa (activated), and development plans for these product candidates are forward-looking statements. Actual results or events could differ materially from the plans, intentions, expectations and projections disclosed in the forward-looking statements as a result of various important factors, including, but not limited to, the risk that trials and studies may be delayed and may not have satisfactory outcomes, that ongoing or future trials will not replicate the results from earlier human trials or from prior animal studies, that potential adverse effects may arise from the testing or use of the Company's products, including the generation of antibodies, the risk that costs required to develop or manufacture the Company's products will be higher than anticipated, competition and other factors that affect our ability to establish collaborations on commercially reasonable terms and other risks described in the "Risk Factors" section of the Company's Annual Report on Form 10-K for the year ended December 31, 2017, filed with the Securities and Exchange Commission on March 19, 2018, along with our other filings with the Securities and Exchange Commission. The Company does not assume any obligation to update any forward-looking statements, except as required by law.