SPRING 2023

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FSIG Connection

News from the Fabry Support & Information Group

'I am life, beauty and power'

Animator with Fabry advocates during Rare Disease Week

COURTESY OF WES BURIAN

Wes Burian, art director for "Kung Fu Panda" and other animated films, delivers his speech at the RARE Artist awards in Washington, D.C.

By Wes Burian
FSIG Contributor

Fabry disease is not something that we the affected usually associate with ability, agency or power. However, my recent time spent in Washington, D.C., as one of 600 attendees of Rare Disease Week (Feb. 27 distinct reminder that we are all able to make a difference, we all have choices and we all have some kind of power—simply by being willing to tell our story—because we all matter. We all matter.

I had the opportunity to attend Rare Disease Week because I was recognized as a 2022 Awardee by the EveryLife Foundation's RARE Artist Program (everylifefoundation.org/rare-artist) for an art piece I entered entitled "Sprout." When I submitted it, I didn't even know when or what Rare Disease Day was.

50TH ISSUE

Rare Disease Day is observed the world over in many countries on the last day in February every year, which in a leap year is the rarest day of the year. Every year, hundreds of patient advocacy groups for rare diseases coordinate on this day to bring visibility to the one in 10 people who has a rare disease in the United States.

During my week, I attended the Rare Disease Day conference at the National Institutes of Health and the Rare Disease Legislative Advocates' conference on Capitol Hill. This culminated

See ARTIST, Page 4

FSIG conference brings insight, bestows awards

By Lisa Bacon
FSIG Programs Director

There's just something special about getting together with other Fabbers—especially when we can be surrounded by some of the leading medical minds in treatment of our disease!

The 10th annual FSIG Expert Fabry Conference was held Feb. 25-27 at Rosen Shingle Creek in Orlando, Florida. We gathered together both adults and teens (as well as children!) to learn from the speakers and engage with one another. The speakers included Dr. Jefferies, Dr. Joseph Ray, Dawn Laney and Dr. Rob Hopkin.

See CONFERENCE, Page 2

WELCOME

Dear Friends,

Welcome to the 50th edition of FSIG Connection.

It's amazing to me looking back over the past two decades at how far we have come. I think the first newsletter went out to fewer then 35 people in the United States, and now we distribute to over 2,000—with many going around the globe!

When we started this newsletter, there was no treatment. Now there are four globally, with one being a biosimilar—and more expected. Right from the start gene therapy was discussed, and now it is in clinical trials.

Knowledge has increased and treatment has improved lives. What is yet to come? Let's keep finding out together.

Jack

Jack Johnson, Executive Director

CONFERENCE: continued from page 1

Emcee Rob makes introductions to attendees.

Christeen Moburg from Sangamo signs in for the sponsor game.

Boys enjoy balloon fun in the kids area, where an onsite babysitting company provided care and games.

Representatives from sponsor Rare Patience Voice greet attendees.

The whole gang! Everyone who participated in the conference gathers for a group photo.

Daniel from uniQure stands with ladies from FIN.

FSIG CONFERENCE

CONFERENCE SPONSORS

DIAMOND
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Sanofi

SILVER
Sangamo

GOLD
4DMT
Amicus

PARTNER
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Attendees visit the sponsor tables, including Sanofi and Chiesi.

RECOGNITION

FEFC BEST CAREGIVER AWARD
John Humphrey
Nominated by Crystal Monday

FEFC BEST DOCTOR AWARD
Bruce Barshop MD
Nominated by Steve Gormley

FEFC MEDICAL PROFESSIONAL AWARD
Dawn Christiansen
Carrie Cox
Crystal Davis
Nominated by Tami & Britney Lence


The Fabry 101 Roundtable discussion, led by Dawn Laney.

ARTIST: continued from page 1

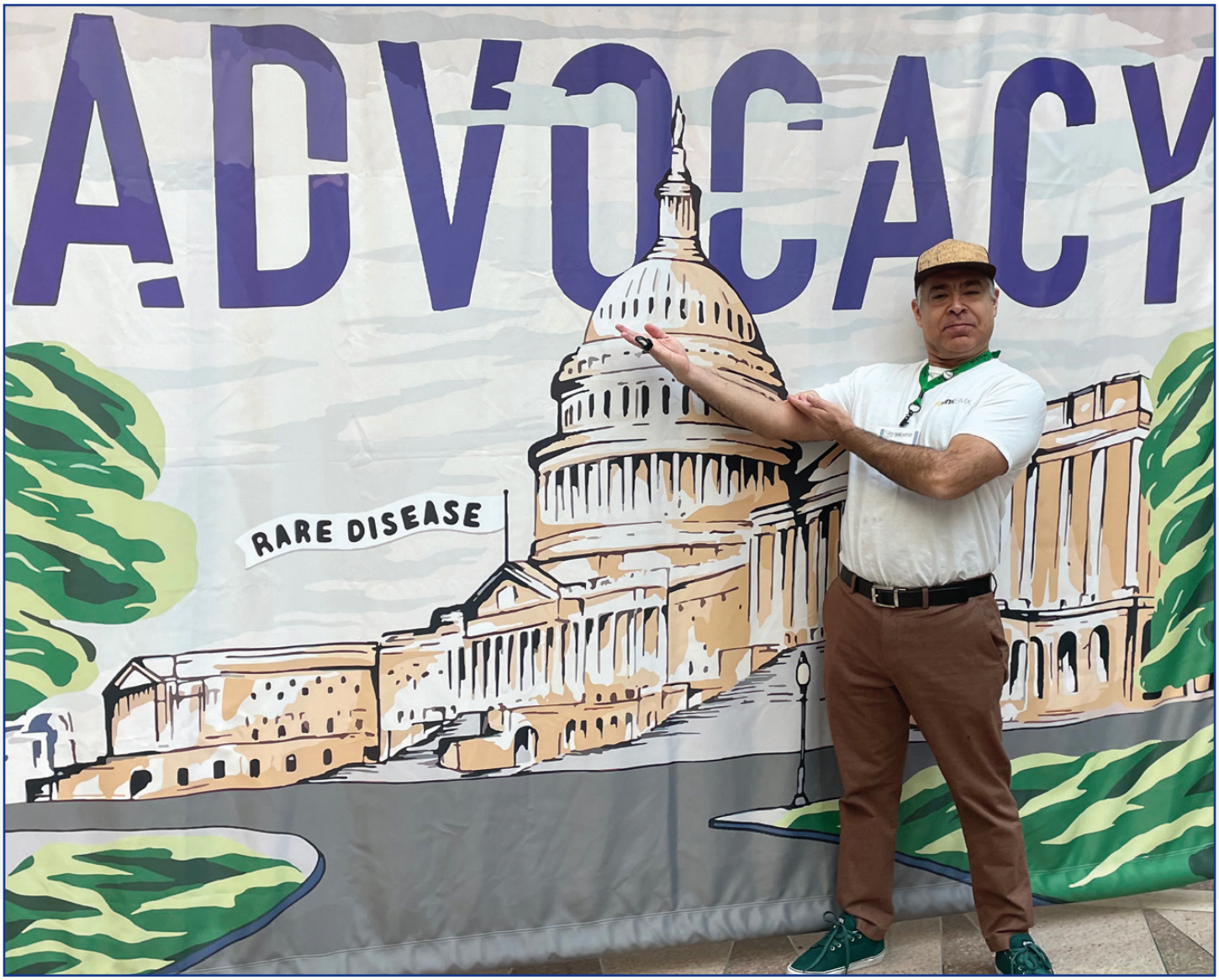
in meetings with my senators and congressional representatives from Oregon, where I represented the Fabry community in telling my story and my daughter's story.

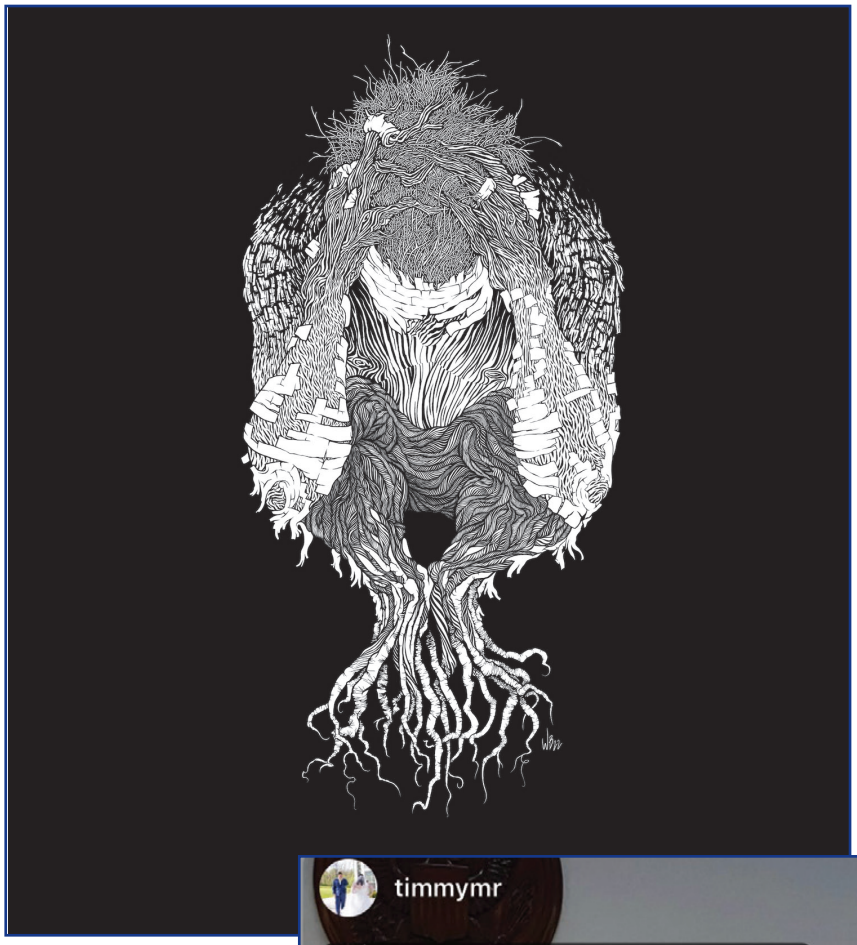
I asked for their support of specific legislation that is before both House and Senate right now called the BENEFIT Act, which would mandate the FDA show how patient experience data from clinical trials is used when considering approval of new drugs. Being in a gene therapy clinical trial for my Fabry disease currently, this issue is of particular passion to me. As patients, I think our experience matters just as much as the numbers and data charts by which we are more often evaluated—and valued.

I believe art has the power to cut directly through some barriers that words can't penetrate. During my meetings with the legislators, I wore a shirt with my art on the front. In this way, I hoped to communicate what it feels like to have this disease that so often is not shown by the way I look on the outside. From feedback I have received, it was a very effective communication method.

Yes, sometimes I am curled up in my bed, in pain or too exhausted to move. Sometimes I suppose now I am in my senator's office, being the expert on what it's like to have Fabry disease and telling them we matter, and then I'm back in bed again, in agony. I'd never imagined myself as an advocate, but being a part of Rare Disease Week, I realized any of us can be. Anyone can attend Rare Disease Week and be part of the RDLA conference too. Maybe next year you should consider joining me!

I want to leave you with the speech I delivered [sidebar, next page] at the reception for the RARE Artist awards held during Rare Disease Week, because it's my story. The most important fact I learned during that week is that our unique strength and power to be advocates is in our stories.





COURTESY OF WES BURIAN

Wes Burian's winning artwork, "Sprout," is shown above. At right is a post showing Burian with his creation while giving the speech shown in the blue box for Rare Disease Week in Washington, D.C.

WES'S SPEECH

My name is Wes and I'm an artist. This is my drawing and that's what it feels like to be me. I have a rare disease called Fabry disease. It doesn't really matter if you know the clinical definitions and manifestations of Fabry right now because by taking the time to see my art you have now learned what I most long for you to know about it.

In what seems now like a previous existence, I had a 20-year career I loved as an art director and department head at a prominent animation studio in Hollywood. I was responsible for creating the look of a panda named Po who does Kung Fu, and many other characters, heroes, villains, during a career that was eventually claimed six years ago by the stalking villain in my own genes when I was forced to give it up and go onto full-time disability.

I was so lost, and during that first painful year I used to struggle to walk down an arroyo near my house. An arroyo, for those who aren't desert dwellers, is a dry desert canyon formed by massive, rushing, eroding floods that come tumbling out of the mountains during the stormy season, uprooting trees and all manner of vegetation in their path.

Over the course of these months, I began to see my body in the twisted, broken, rotted trees that had been carried in froth and turmoil down the canyon to new places of rest where I met them in peace. As I spent time walking alongside them I started to appreciate their unique shapes and amazing textures and I heard their stories. Soon I couldn't tell if I was seeing death or life any more. I couldn't tell if I was seeing withering … or unfurling. Was I seeing weakness or was that strength?

I started to see wisdom. Painful wisdom that can't be learned any other way. I saw hope. Hope in the beauty of a new becoming.

This is me. I am loss, pain and damage and at the same time I am life, beauty and power. I have something important to say, not in spite of my disease but because of it.

These RARE artists are my new peers—they have unique wisdom to give to make this country and this world a better place for everybody. Fellow artists and non-artists alike, we have the power to share our stories and connect with each other and hold each other and experience the undoing and the flourishing at the same time. We can be hope to one another.

Galafold users adhering, enjoy quality of life gains

By Lindsey Shapiro, PhD
FabryDiseaseNews.com

(Jan. 19, 2023) Adults with Fabry disease exhibited high levels of adherence to at-home Galafold (migalastat) treatment over a two-year period, according to a recent study.

Patients also reported a stable quality of life, with reductions in pain and physical limitations over time—all of which are factors that can influence the likelihood a person will take their treatment as prescribed, according to authors.

The main barrier to taking the medication was forgetfulness, "which should be addressed by attending physicians to maintain therapy adherence in the long run," the researchers wrote.

The study, "Patient reported quality of life and medication adherence in Fabry disease patients treated with migalastat: A prospective, multicenter study," was published in the journal *Molecular Genetics and Metabolism*.

Galafold is an approved chaperone therapy from Amicus Therapeutics that is designed to restore alpha-gal A activity in patients carrying certain types of disease-causing mutations. It essentially works by attaching to the unstable or dysfunctional alpha-gal A, stabilizing it, and partially restoring its function.

Galafold is taken orally, every other day, with a two-hour interval to any food intake. While oral self-administration offers convenience compared with other treatments, such as enzyme replacement therapies that are given as into-the-vein infusions at healthcare facilities, it also can be associated with poor medication adherence.

Not only can this directly influence its effectiveness, but poor adherence to the pricey medication can contribute to a high burden on the healthcare system.

Read full story: bit.ly/FabryAdherence

Early start on Fabrazyme shows strongest outcomes

By Joana Vindeirinho, PhD
FabryDiseaseNews.com

(Dec. 15, 2022) Male patients with Fabry disease who started treatment with Fabrazyme (agalsidase beta) at an earlier age had a slower decline in kidney function compared with older patients with more severe disease, according to a study assessing data from the Fabry Registry.

Continued treatment in female and male Fabry patients younger than 30 led to a modest decline in kidney function, stable heart-related parameters, and some improvements in self-reported symptoms after at least 2.5 years of follow-up.

"The greater decline in [kidney function] among older ... males [with severe kidney disease] may suggest a benefit of earlier treatment," the research team wrote. "The findings emerging from this comprehensive analysis of clinical outcomes substantially contribute to bridging the gap in understanding the clinical outcomes associated with agalsidase beta [Fabrazyme] treatment among pediatric, adolescent, and young adult patients with this complex genetic disorder."

Read full story: bit.ly/FabryEarly

Heart, kidney declines may be undiagnosed in Fabry

By Patricia Inácio, PhD
FabryDiseaseNews.com

(Feb. 2, 2022) A long clinical history of cardiac alterations, including heart valve impairments, without an apparent cause and accompanied by kidney dysfunction may be a sign of undiagnosed Fabry disease, a case report suggests.

Heart disease is common with Fabry disease. In fact, a hallmark is the enlargement and excessive thickness of the heart's left lower pumping chamber (left ventricle).

"The lessons from this case are that the constellation of unexplained progressive LV [left ventricle] wall thickness or LV hypertrophy [enlargement], valvular abnormalities, and multiorgan involvement should trigger the differential diagnosis of [Fabry disease]," the researchers wrote.

Researchers at the Naval Military Medical University, China described the case of a 54-year-old man who was hospitalized due to swelling in both legs and abdominal distension, symptoms that had lasted for more than a year, but worsened in the last three months.

Read full story: bit.ly/Heart-Kidney

Have you been screened for lymphedema? 1/10 affected

By Marisa Wexler, MS
FabryDiseaseNews.com

(Feb. 16, 2023) More than one in 10 people with Fabry disease have a form of swelling called lymphedema, a recent study reported that highlighted the importance of screening for this type of swelling, which often goes unrecognized.

"Strategies to identify lymphedema in a timely manner can facilitate effective treatment and minimize the associated morbidity," the researchers wrote in the study, "Prevalence of lymphedema among Anderson-Fabry disease patients: A report from the Fabry registry," which was published in Molecular Genetics and Metabolism.

Lymphedema is caused by the buildup of lymph, the protein-rich fluid that normally drains through body tissues before being recycled back into the bloodstream. This type of swelling has been reported in patients with Fabry, but there's not much data about how common it is, leading scientists in the U.S. to analyze data from the Fabry Registry (NCT00196742), an observational study sponsored by Sanofi that's tracking the clinical outcomes of Fabry among thousands of patients. The registry is recruiting participants at hundreds of sites worldwide.

Read full story: bit.ly/FabryLymphedema

Man on dialysis & ERT develops problems in brain blood vessels

By Steve Bryson, PhD
FabryDiseaseNews.com

(Aug. 12, 2022) A man with Fabry disease undergoing long-term dialysis to support kidney function and receiving enzyme replacement therapy (ERT) experienced recurrent complications related to blood vessels in his brain, a case study reported.

While further investigation into such cases is needed, the researchers recommended that Fabry patients with end-stage kidney disease who also are on ERT receive long-term follow-up to monitor for unexpected blood vessel events.

In this report, researchers based at the Nagoya University, in Japan, described the case of a man with Fabry who experienced cerebrovascular complications during ERT while on peritoneal dialysis for 10 years.

Read full story: bit.ly/DialysisERT

Heart disease, other symptoms could be signs of late-onset Fabry disease

By Patricia Inácio, PhD
FabryDiseaseNews.com

(Aug. 19, 2022) Left ventricular hypertrophy (LVH)—a condition when the walls of the heart's left pumping chamber (left ventricle) become thickened—accompanied by damages to peripheral nerves and hearing impairments could be signs of late-onset Fabry disease, according to a case report.

"This case serves as a potent reminder to pay meticulous attention to 'red flags' accompanying LVH," its authors wrote.

In this report, researchers at the Albany Medical Center, New York, describe the case of patient with late-onset Fabry whose initial symptoms were LVH, which makes it harder for the heart to pump blood efficiently.

The patient was in his 50s and had been examined in the hospital by the cardiology team two years before after showing an abnormal swelling in the legs and shortness of breath during physical activity.

Read full story: bit.ly/LateOnset

Study finds good vision in Fabry patients despite eye changes

By Steve Bryson, PhD
FabryDiseaseNews.com

Despite disease-related eye changes, visual acuity — the sharpness of a person's vision, with 20/20 denoting perfect clarity of sight — was "good" in children and adults with Fabry disease, a study showed.

Eye involvement was not associated with disease severity in adults with Fabry, and overall vision-related quality of life also was reported as good.

Researchers noted that opacities or scarring in the eye lens or cornea, the transparent layer on the eye surface, may suggest Fabry disease in children.

"Early ophthalmological signs could be a clue to help early [Fabry] diagnosis," the team wrote. The study, "Visual outcome, ocular findings, and visual quality of life in patients with Fabry disease," was published in the journal *Ophthalmic Genetics*.

An estimated 90% of people with Fabry have corneal opacities — brown, grey, or yellowish streaks that appear on the cornea. At first, they may appear cloudy over the cornea but become more streak-like with time. Blood vessels in the eyes also may look twisted and/or slightly enlarged.

Although corneal opacities do not seem to affect vision, they are considered important for early diagnosis and disease monitoring. As such, additional knowledge of eye abnormalities in Fabry patients may help with diagnosis and avoid treatment delays.

To that end, researchers at the Karolinska Institutet, in Sweden, conducted a detailed eye examination of 26 people with Fabry disease to investigate visual disease, outcomes, and vision-related quality of life.

Participants included 16 males, ages 5–57, and 10 females, ages 30–63 years. Enzyme replacement therapy was prescribed to 12 male and five female patients, and one male and one female were receiving Galafold (migalastat).

Read full story: bit.ly/EyeChanges

FSIG

FSIG is a support group dedicated to dispensing information and encouraging mutual self-help as a means of emotional support.

FSIG was formed in 1996 by two Fabry patients and supportive family members with the hope that their particular understanding of this disease, combined with experience gathering information and working with doctors could benefit others.

FSIG is a nonprofit, tax-exempt organization and relies on charitable contributions to provide services to those with Fabry disease, their families and supportive others. Donations may be sent to the address below.

Please feel free to make copies of the FSIG Newsletter to share with your family, friends and others. We encourage anyone interested in FSIG or the newsletter to contact us so we can make sure you receive the next issue.

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Ups, downs for gene therapy

4D-310 boosts heart health in trial

By Steve Bryson, PhD | FabryDiseaseNews.com

(Jan. 2, 2023) One year after treatment with 4D-310, an experimental gene therapy for Fabry disease, measures of heart health have improved in the first three participants in a clinical trial, according to new data announced by the therapy's developer, 4D Molecular Therapeutics (4DMT).

"Utilizing a novel vector invented at 4DMT with the goal of achieving increased delivery and transduction within the heart in humans, 4D-310 is designed to enable [GLA gene] expression and disease correction directly within cardiomyocytes [heart cells]," said Eric Adler, MD, a professor at the University of California at San Diego and trial investigator.

4DMT is currently conducting two Phase 1/2 clinical trials testing 4D-310 in patients with Fabry disease: one is being run in the U.S., the other in Taiwan and Australia. According to the company, a total of six patients have so far been given the gene therapy across the two studies.

All six patients received a dose of 10 trillion vector genomes per kilogram of body weight. Participants also received immune-suppressing corticosteroids to help prevent an immune response against the viral vector that could diminish the therapy's efficacy or cause side effects.

As of late 2022, one-year data was available for three of the patients, all of whom participated in the U.S. trial. Results showed that two of the three patients experienced improvements in peak VO2, a measure of how well the heart and lungs can provide oxygen to body tissues during exercise.

Before treatment with 4D-310, two of the three patients had abnormally low scores on the Kansas City Cardiomyopathy Questionnaire (KCCQ), a measure of heart health-related quality of life. Scores improved in both of these patients after one year. In the third patient, scores were normal at the study's start and remained stable after one year.

Read full story: bit.ly/Heart4D-310

ST-920 gene therapy leading to long-term benefits in STAAR trial

By Marisa Wexler, MS
FabryDiseaseNews.com

(Oct. 21, 2022) One-time treatment with ST-920 (isaralgagene civaparvovec), an experimental gene therapy being developed by Sangamo Therapeutics, continues to be generally well-tolerated among people with Fabry disease, according to new data from the Phase 1/2 STAAR clinical trial.

Trial data show that the gene therapy leads to long-term increases in activity of the alpha-GalA enzyme. Fabry disease is caused by genetic mutations that impair the functionality of this enzyme, leading to a toxic accumulation of certain fatty molecules such as lyso-Gb3 in cells.

ST-920 uses a viral vector to deliver a healthy copy of the gene encoding the alpha-GalA enzyme to cells in the liver. These cells can "read" this gene to produce a functional enzyme that is secreted into the blood and pumped out to the rest of the body.

"The constant production of [alpha]-Gal A should lead to a reduction and potentially the clearance of Fabry disease substrates such, as globotriaosylsphingosine (lyso-Gb3), from target organs," according to the researchers.

Read full story: bit.ly/STAARtrial

Freeline halts FLT190 gene therapy work, cuts jobs

Press Release

(April 4, 2023) Freeline Therapeutics today reported financial results for the full year ended December 31, 2022, and provided a corporate update.

"While we remain encouraged by the data on FLT190 in Fabry disease, we have paused its development and are further streamlining the organization to extend our cash runway and focus on FLT201 in Gaucher disease," said Michael Parini, Freeline's CEO.

Streamlining Organization to Extend Cash: RunwayFreeline is restructuring to align with its focus on FLT201, increase efficiencies and reduce operating expenses. The company has proposed to reduce its workforce by nearly 30 percent, bringing its headcount to approximately 65 employees. In addition to reducing headcount related to FLT190, Freeline is proposing to make cuts across the organization to further streamline, while maintaining core capabilities and ensuring the ability to drive enrollment in the GALILEO-1 trial of FLT201.

Net Loss: Net loss was $89.0 million, or $1.50 per share, for the year ended December 31, 2022.

Learn more: bit.ly/flt190halt

Oral Venglustat lowers Gb3 with no signs of disease

By Lindsey Shapiro, PhD
FabryDiseaseNews.com

(Dec. 2, 2022) Daily treatment with the investigational oral therapy venglustat in men with Fabry disease led to significant reductions in globotriaosylceramide (Gb3 or Gl-3)—the fatty molecule that accumulates to toxic levels in the disease—and no signs of disease progression.

That's according to up to three years of data from a small Phase 2a clinical trial (NCT02228460) and its extension study (NCT02489344).

"The totality of data from these studies indicates the potential value of venglustat for the long-term treatment of Fabry disease," the researchers wrote, noting that larger, longer studies are needed to confirm these findings. The safety and efficacy of venglustat is being further assessed in adults with Fabry in two currently recruiting placebo-controlled Phase 3 clinical trials: PERIDOT (NCT05206773) and CARAT (NCT05280548).

The PERIDOT trial is investigating venglustat's effects on abdominal and nerve damage-related pain, while CARAT will evaluate the treatment's therapeutic effects in left ventricular hypertrophy, a heart condition seen in some Fabry patients. Both are sponsored by Sanofi-Genzyme, which is developing venglustat.

The company-funded Phase 2 study, "Venglustat, an orally administered glucosylceramide synthase inhibitor: assessment over 3 years in adult males with classic Fabry disease in an open-label Phase 2 study and its extension study," was published in *Molecular Genetics and Metabolism*.

In Fabry, a deficiency in the alpha-galactosidase A enzyme prevents the appropriate breakdown of certain fatty molecules. These molecules, especially Gb3, then accumulate in cells, disrupting the function of the body's tissues.

A standard Fabry treatment is enzyme replacement therapy, which works to provide a working version of the missing enzyme, restoring the body's ability to break down Gb3.

In contrast, venglustat is a substrate reduction therapy. Instead of working to supply the enzyme needed to digest the fatty molecules, it acts to prevent the generation of the molecules in the first place. It does so by suppressing an enzyme that's needed for their synthesis.

The Sanofi-sponsored Phase 2a trial enrolled 11 men (median age 24 years; range of 18–37 years) with Fabry disease at eight treatment centers in the U.S., the U.K., France, Poland, and Russia. Participants, who had not previously received any Fabry disease-specific therapy, took oral venglustat (15 mg) once per day for 26 weeks, or about six months.

Read full story: bit.ly/venglustat

Novel ERT ISU303 from South Korea shows promise in small trial

By Marisa Wexler, MS
FabryDiseaseNews.com

(Oct 28, 2022) ISU303, an experimental enzyme replacement therapy for Fabry disease, showed a good safety profile and some promising signs of efficacy in a small clinical trial in Asia, according to researchers.

The "results suggest that ISU303 is safe and effective and [may be an] alternative ERT for [Fabry disease]," the researchers wrote.

The study, titled "A phase II, multicenter, open-label trial to evaluate the safety and efficacy of ISU303 (Agalsidase beta) in patients with Fabry disease," was published in the journal *Medicine*.

ISU303 is a novel agalsidase beta form of ERT that is being developed by the Korean company ISU Abxis. It is produced using a Chinese hamster ovary cell line, in a similar manner to Fabrazyme.

This clinical trial enrolled 10 people with Fabry disease at centers in South Korea. Among the patients, seven were men, three were women, and the average age was 33. Eight patients had received previous ERT with Fabrazyme, while the other two were newly diagnosed and had not been on enzyme replacement therapy before.

The participants were treated with ISU303 for six months. The therapy was administered via infusions every other week, with each infusion lasting 4–6 hours. Nine patients completed the study; one withdrew early due to an unexpected pregnancy.

At the start of the study, the average level of Gb3 in participants' blood was 8.1 micrograms per milliliter (ug/mL). After 22 weeks (about 5.5 months) of treatment with ISU303, the level decreased significantly to 4.09 ug/mL. Gb3 levels below 9.9 ug/mL are considered normal.

Average levels of Gb3 in urine also decreased significantly following ISU303 treatment. Levels of a related molecule called lyso-Gb3 did not change significantly in blood or urine.

Read full story: bit.ly/ISU303Trial

European agency gives thumbs-up to PRX-102

Press Release

(Feb. 24, 2022) Chiesi Global Rare Diseases, a business unit of the Chiesi Group established to deliver innovative therapies and solutions for people affected by rare diseases, and Protalix BioTherapeutics, Inc. (NYSE American:PLX) (TASE:PLX), a biopharmaceutical company, announced today that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending marketing authorization for PRX-102 (pegunigalsidase alfa), the first and only pegylated enzyme for the treatment of adult patients with Fabry disease.

"Chiesi and our partners at Protalix are deeply committed to people living with Fabry disease and their families, many of whom experience unmet medical needs," said Giacomo Chiesi, Head of Chiesi Global Rare Diseases. "Our deepest gratitude to all the individuals with Fabry disease who have participated in clinical trials. Thanks to them, PRX-102 has been extensively studied during the clinical development program, providing the data for the CHMP's evaluation and positive opinion regarding a positive benefit-risk profile for PRX-102. We look forward to advancing towards approval and launch in Europe and will continue our mission to deliver this potential new treatment option to people living with Fabry disease around the world."

PRX-102 is a novel recombinant human α-Galactosidase-A (α-Gal-A) enzyme being investigated as an enzyme replacement therapy (ERT) for the treatment of Fabry disease. The positive CHMP opinion was based on a marketing authorization application (MAA) that includes positive data from a comprehensive set of preclinical, clinical and manufacturing studies evaluating PRX-102. The clinical development program includes the completed Phase 3 BALANCE, BRIDGE, and BRIGHT clinical trials, the Phase 1/2 clinical trial, and ongoing related extension studies that combined represent more than 400 years of exposure to PRX-102. PRX-102 has been studied in more than 140 patients, consisting of both ERT-naïve and ERT-experienced patients, and includes a head-to-head trial versus agalsidase beta.

Read full story: bit.ly/CHMP-Opinion

PROTALIX ISSUES LETTER

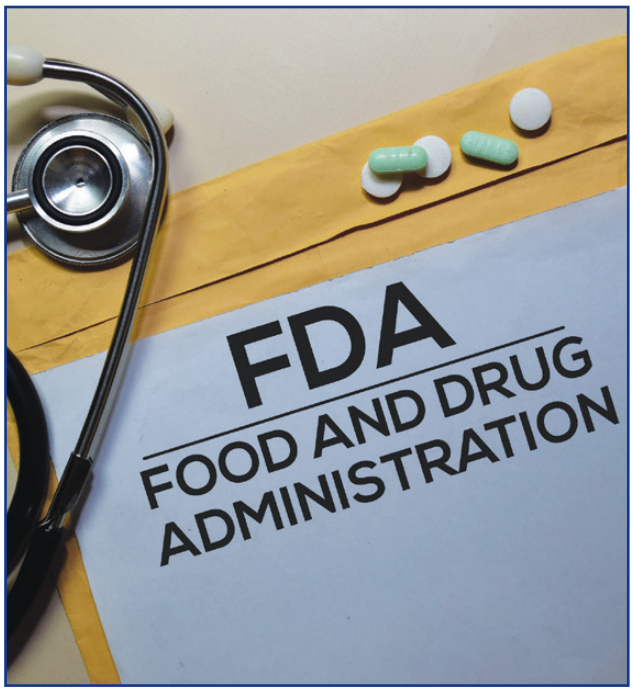
Dear Shareholders,

2022 was a strong year for Protalix, and I would like to take a moment to reflect on the significant progress we have made. Together with our development and commercialization partner, Chiesi, we executed on key regulatory milestones with the submission of marketing authorization applications in the United States and the European Union for PRX–102 for the treatment of adult patients with Fabry disease, bringing us one step closer to the potential approval and commercialization of this important treatment option.

I continue to be immensely grateful to our team and our partners for their steadfast dedication to bringing PRX–102 to patients. I am proud of our accomplishments in 2022, highlighted below, and look forward to continued success in 2023 as we continue to work towards meaningful, value-adding milestones and transformational catalysts.

Read full story: bit.ly/protaletter

FDA grants orphan drug status to AceLink's AL01211



By Marisa Wexler, MS
FabryDiseaseNews.com

(Sept. 9, 2022) AL01211, a once-daily oral therapy being developed by AceLink Therapeutics for Fabry disease, has been granted an orphan drug designation by the U.S. Food and Drug Administration.

The FDA gives this designation to investigational treatments with the potential to improve care for rare diseases that affect fewer than 200,000 people in the U.S. The designation gives AceLink, as the therapy's developer, certain incentives including tax credits, fee waivers, and the potential for seven years of market exclusivity if the FDA ultimately approves the treatment.

AL01211 is designed to block the activity of GCS, or glucosylceramide synthase, which is an enzyme that facilitates the first step in the production of glycosphingolipids, a diverse group of biologically active fatty molecules. Fabry disease is caused by genetic mutations that result in an abnormal buildup of certain glycosphingolipids, particularly globotriaosylceramide (Gb3), inside cells.

By blocking the activity of GCS, AL01211 is designed to reduce this toxic buildup, ultimately slowing disease progression. According to AceLink, the investigational therapy has high potency against GCS and other pharmacological properties that are expected to allow for once-daily oral dosing. Of note, the therapy is unable to cross the blood-brain barrier, meaning it will not get into the brain or spinal cord if administered systemically. *Read full story: bit.ly/OrphanStatus*

FDA slaps hold on 4D's Fabry gene therapy trial

By Marisa Wexler, MS
FabryDiseaseNews.com

(Feb. 9, 2023) The U.S. Food and Drug Administration (FDA) has placed a hold on the 4D-310 clinical program, an experimental gene therapy for Fabry disease being developed by 4D Molecular Therapeutics (4DMT).

The hold was disclosed in a filing submitted by 4DMT to the Securities and Exchange Commission earlier this month. The FDA's decision, which comes less than a month after 4DMT announced it would stop enrolling participants in ongoing trials, is "consistent with the company's plans" for 4D-310, according to 4DMT.

4DMT is running two Phase 1/2 trials of 4D-310 in people with Fabry disease: one in the U.S. (NCT04519749) and another in Taiwan and Australia (NCT05629559). As of January, six participants had been dosed across both.

Fabry disease is caused by mutations in the GLA gene, resulting in the toxic buildup of fatty molecules inside cells. 4D-310 is designed to deliver a healthy copy of the gene to cells to stop this process. It uses an engineered viral vector to deliver its genetic cargo to cells. Three of the six participants developed a typical hemolytic uremic syndrome (aHUS), a rare disorder marked by the destruction of red blood cells, low platelet counts, and kidney damage. One of the three aHUS cases was considered a dose-limiting toxicity event, meaning the tested dose was likely too toxic to be used in clinical practice. In all three cases, aHUS resolved within two to four weeks.

In the trials, the participants received immune-suppressing corticosteroids to reduce immune-related side effects. According to 4DMT, future trials are planned to use a different immune-suppressing regimen consisting of a combination of rituximab and sirolimus, which is expected to lower the risk of aHUS and toxicity-related events.

In accordance with instructions from the FDA, 4DMT is continuing to collect clinical data from the six patients treated so far. The company plans to present detailed data from the trial, including safety findings and treatment effects on heart health, at a scientific conference later this month.

Read full story: bit.ly/4D-FDA

BRIEFS

Since 2018, 10% of FDA approved drugs had trials that missed primary endpoints

(Feb. 13, 2023) According to a research letter published in *JAMA Internal Medicine*, about 10% of drugs approved by the US Food and Drug Administration between 2018 and 2021 had pivotal trials with null findings.

"Our findings underscore the complexity of regulatory decision-making, as exemplified by evidence of effectiveness despite a null primary end point finding," wrote James L. Johnston, MD, of the department of medicine at Brigham and Women's Hospital in Boston, along with his colleagues, in their research letter. "For other drugs, the evidence of efficacy was less clear."

Read full story: bit.ly/EndpointsMissed

Rare disease advocates win victory over state's 'harmful' accelerated approval proposal

(Sept. 28, 2022) In a huge victory for the rare disease community, the Centers for Medicare and Medicaid Services (CMS) approved the Oregon Health Plan's 1115 Demonstration Waiver without the provision that would have permitted the state to exclude coverage for prescription drugs approved using the accelerated approval pathway, reports Every Life Foundation.

The approved waiver provides several expanded health services for the residents of Oregon, including continuous enrollment in Medicaid to limit the disruption of services for some children and adults and expanded programs to address social determinants of health within the state.

The accelerated approval pathway allows FDA to use a surrogate endpoint (also called a biomarker) to evaluate the safety and efficacy of therapies for serious conditions with unmet needs.

Read full story: bit.ly/RDC-Victory

Help improve treatment—join the Fabry Registry!

By Eric Rice &
Michelle Hackenberry
Data Registry Services LLC
The Fabry Disease Registry is sponsored by Genzyme, a Sanofi Company.

What is the Fabry Registry?
The Fabry Disease Registry* is a global resource dedicated to improving the understanding of the variability and progression of Fabry disease. Any person with a confirmed diagnosis of Fabry disease is eligible to participate, regardless of disease type, treatment status or treatment choice. The Registry's mission is to increase the understanding of Fabry disease to improve outcomes for patients with this disorder.

How Does It Benefit Me?
The data collected in the Registry is part of an ongoing observational study and it allows researchers and physicians to continually update their treatment options and the management of your disease. In short:

Better Data=
Better Research=
Better Treatment!

Additionally, if you are participating in the Registry through Data Registry Services, we provide you with easy and free access to all your current and historical health records in one location.

How Can I Participate?
Data Registry Services is making Registry participation as easy as possible for all interested individuals.

- No cost to you
- You keep your current physician and it does not influence your current treatment
- Your information is secure and de-identified prior to being added to the Registry
- We collect all your records from your health care providers, no additional work for you

Reach out to us directly and we will facilitate the process. It is simple and free. We will send you an informational packet and schedule a short meeting. With a couple of signatures you will be enrolled in the Fabry Registry and you will be contributing to a better understanding and better long term management and treatment of Fabry disease.

You may already be enrolled, or you may think you are enrolled, if you are not sure, reach out to us and we can get you the answer in short order!

Data Registry Services prides itself in ensuring that all patients, regardless of their treatment location, have access to participation in the Fabry Disease Registry. We would love to help get you on board!

Register today at: DataRegistryServices.com

Patients can now access all their health records digitally

By Melissa James
FSIG Contributor

Under United States legistlation that took effect in October, health care organizations are required to give patients unfettered access to their full health records in digital format. That means no more long delays, fuzzy faxed documents, or high charges for printing.

The new federal rules, which were passed under the 21st Century Cures Act, were created to shift the balance of power—ensuring patients can not only access their data, but choose with whom to share it.

As pointed out on the Stat News website, "It is the jumping-off point for a patient-mediated data economy that lets consumers in health care benefit from the fluidity they've had for decades in banking: they can move their information easily and electronically, and link their accounts to new services and software applications.

Even with the rules now in place, health data experts said change will not be fast or easy. Providers and other data holders—who have dug in their heels at every step—can still withhold information under certain exceptions. And many questions remain about protocols for sharing digital records, how to verify access rights, and even what it means to give patients all their data. Does that extend to every measurement in the ICU? Every log entry? Every email? And how will it all get standardized?"

Long story short, it will take time for providers and other data holders to fully comply, the site explains, especially since enforcement remains spotty and unclear under the new rules.

Read full story: bit.ly/RecordsAccess

HEALTH BRIEFS

Hospital accuses Fabry boy's parents of abuse, takes custody

(Nov. 8 2022) A Florida family was unexpectedly separated while on a trip to Boston for a medical check-up for their 5-year-old son. Michael Seklecki Sr., the father of two boys, accused Boston Children's Hospital of medically kidnapping not just 5-year-old Mikey but also 3-year-old Noah.

Seklecki and his wife were accused of medical child abuse, Munchausen by proxy and doctor shopping, according to a press release. The family spent thousands of dollars traveling from their Florida residence to Boston to seek expert advice on Mikey's illness. He had suffered from chronic, severe gastrointestinal complications, and the family began traveling to Boston Children's Hospital regularly for appointments in November of 2021. His medical team in Florida was unable to provide a diagnosis or treatment plan.Under the care of Dr. Samuel Nurko at BCH, Mikey was diagnosed with colon sigmoid dysmotility, according to the release.

After being referred to genetics for further testing, Mikey was diagnosed with Fabry disease. The family returned to Florida to being treatment after BCH refused to do immediate treatments. BCH instead wanted to wait six months to see how the condition improved.

Once back in Florida, the family met with the medical team there and those providers disagreed with the treatment timeline provided by BCH. They started the life-saving treatment immediately instead of waiting for six months to pass.

Read full story: bit.ly/fabrykidnap

Biopsy key for detection of early kidney involvement in females

(Nov. 1, 2022) Patients with Fabry disease face progressive decline in kidney function, as well as disorders of the nervous system and the heart. Disease progression may be stopped or mitigated with specific therapy, but results depend significantly on early initiation of treatment.

Elena Emanuela Rusu and colleagues in Romania conducted a retrospective study to examine clinical and histologic aspects of renal involvement in untreated female patients diagnosed with Fabry disease by genetic test between 2015 and 2021 in a single center. Results of the study were reported at the European Renal Association 59th Congress.

Read full story: bit.ly/KidneyBiopsy

Hydroxychloroquine side effects, Fabry symptoms may overlap

(Oct. 14, 2022) Rare side effects caused by hydroxychloroquine, a medication used to prevent malaria and to treat several autoimmune diseases, may mimic some symptoms of Fabry disease, a case series suggests.

Hydroxychloroquine (HCQ) toxicity was associated with heart, kidney and muscle problems, as observed in Fabry disease. "A thorough investigation should be performed in these cases to properly elucidate the cause followed by the appropriate targeted therapy," the researchers wrote. In this report, researchers at the University of Colorado Denver and University of Nebraska Medical Center, described the cases of three women who experienced rare side effects with HCQ and compared their symptoms to those linked with Fabry disease.

Read full story: bit.ly/SymptomOverlap

Cheaper hearing aids now in stores thanks to Biden-Harris Administration

Press Release

(Oct. 17, 2022) To lower the price of hearing aids and expand access, President Biden's Executive Order on Promoting Competition in the American Economy called on the Food and Drug Administration (FDA) to make hearing aids available over the counter, without a prescription. That is now reality.

Starting today, hearings aids are now on store shelves across the country—for thousands of dollars less than they previously cost.

Specifically, today, under a final rule issued by the FDA, adults with mild-to-moderate hearing loss can buy hearing aids at a store or online without a prescription, exam, or audiologist fitting. FDA estimates this could lower average costs by as much as $3,000 per pair—providing significant breathing room for the nearly 30 million Americans with hearing loss, including nearly 10 million adults under age 60.

Retailers across the country are now selling over-the-counter hearing aids. Options available today or coming soon include:

- Starting today, Walgreens is selling hearings aids at stores nationwide and online for $799 per pair. Comparable models sold by specialists range from $2,000 to $8,000 a pair.
- Starting today, CVS will start selling over-the-counter hearing aids on CVS.com, with varying options on model and price point.

Full release also includes details on Walmart, Best Buy & Hy-Vee prices and structure.

Read full story: bit.ly/CheaperHearingAids

HEALTH COSTS

Employers use patient assistance programs to offset their own costs

(Dec. 6, 2022) There's a strategy that employers are using to deal with the high cost of drugs prescribed to treat conditions such as arthritis, psoriasis, cancer, and hemophilia: Those employers are tapping into dollars provided through programs they have previously criticized: patient financial assistance initiatives set up by drugmakers, which some benefit managers have complained encourage patients to stay on expensive brand-name drugs when less expensive options might be available.

Now, though, employers, or the vendors and insurers they hire specifically to oversee such efforts, are seeking that money to offset their own costs. Drugmakers object, saying the money was intended primarily for patients. But some benefit brokers and companies like SaveOnSP say they can help trim employers' spending on insurance—which, they say, could be the difference between an employer offering coverage to workers or not.

It's the latest twist in a long-running dispute between the drug industry and insurers over which group is more to blame for rising costs to patients. And patients are, again, caught in the middle.

Read full story: bit.ly/OffsetDrugCosts

Prices for hundreds of drugs have outpaced inflation

(Nov. 1, 2022) The AARP reports that list prices on more than 1,200 prescription drugs rose faster than inflation between July 2021 and July 2022, rising on average 31.6 percent, according to a new report the Department of Health and Human Services (HHS) says illustrates the need for a key provision of the Inflation Reduction Act.

Under the new law, pharmaceutical companies that raise the price of their products more than the rate of general inflation will have to pay Medicare a rebate for those outsize price hikes. The provision is designed to help reduce the size and frequency of prescription drug price increases, according to HHS. Price tracking that will be used to assess rebates began on Oct. 1.

"In recent years, prescription drug prices have skyrocketed, but thanks to the Inflation Reduction Act, America's families will soon start seeing relief," HHS Secretary Xavier Becerra said in a statement.

Using data aggregated by the web-based analytical tool AnalySource, HHS's Office of Health Policy examined all prescription drug price increases that occurred in January and July of 2022. The two months, the office notes, historically account for most of the drug price increases that occur each year.

Among its key findings:

- The list price of more than 3,000 drugs increased in January and/or July of 2022, a greater number than in January and July of 2021.
- The average price increase was nearly $150 per drug (10 percent) in January 2022, and it was $250 (7.8 percent) in July 2022.
- There were 1,216 products whose price increases during the 12-month period from July 2021 to July 2022 exceeded the inflation rate of 8.5 percent for that time period. The average price increase for these drugs was 31.6 percent.
- The sharpest percentage price hike (over 1,000 percent) was for fluconazole, an antifungal medication. The wholesale package price increased from $2 to $24 or more.
- The largest list price increase, however, was for two cancer medications, Tecartus and Yescarta. Each saw its wholesale package price climb from $399,000 to $424,000.

Read full story: bit.ly/DrugsInflation

A look at how medical debt is ruining credit for patients

(Oct. 6, 2022) NPR ran an article about how earlier in 2022, three national credit agencies announced new policies to deal with medical debt, which left consumer advocates celebrating. They thought it would provide relief for patients like Penelope Wingard, a woman whose story they highlighted.

But it turns out the changes aren't enough to help her or many other Black and low-income patients, who are often the ones hit hardest by medical debt. Under the new policies, Equifax, Experian and TransUnion will remove from credit reports any paid debts or individual bills that were less than $500 and had gone to collections, even if unpaid. This doesn't wipe out what people owe, but the idea is to remove the black mark of collections from their credit so they can more easily reach milestones like qualifying for a car or home loan.

The changes, which go into full effect in 2023, are expected to benefit an estimated 16 million Americans. But a federal report released this summer suggests those may not be the people who need it most.

"Although the credit reporting companies have trumpeted this as a big change, the fact is they're just removing the small stuff," says Ryan Sandler, a co-author of the report and senior economist with the Consumer Financial Protection Bureau. "They're not maybe doing as good of a thing as their press releases would like you to believe."

Read full story: bit.ly/med-debt

Trump-era health care rule breaks law, hurting patients

(Oct. 24, 2022) Among Americans who take prescription drugs, reported Newsweek, a quarter struggle to afford their medication. For those who are in poor health or have low incomes, the portion is even higher.

These days, the rising cost of everyday goods and services is forcing more people to face difficult decisions and ask themselves: How can I pay for utilities, the groceries, or the medicine that's keeping me alive?

Now imagine that someone offers you financial assistance for the express purpose of paying for your medicine—problem apparently solved. But in a cruel twist, your health insurer pockets that assistance, without counting it toward your annual deductible or out-of-pocket maximum.

That's why the HIV+Hepatitis Policy Institute, the Diabetes Leadership Council, and the Diabetes Patient Advocacy Coalition filed suit in federal court, challenging the Trump-era federal government rule that allows insurers and pharmacy benefit managers to carry out this harmful practice.

Read full story: bit.ly/RuleBreakingLaw

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