THE COALITION FOR HEMOPHILIA B

WINTER 2024

HEMOPHILIA B NEWS

NATIONAL NONPROFIT ORGANIZATION

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WOMEN'S RETREAT

FAMILY MEETINGS ON THE ROAD

EMPOWERING WOMEN, TOGETHER: REFLECTIONS FROM THE 2024 WOMEN'S FALL RETREAT

MEETINGS ON THE ROAD: EMPOWERING THE HEMOPHILIA B COMMUNITY ACROSS THE U.S.

MEET AND GREET WITH KIM: A LEADER DEDICATED TO ADVOCACY AND COMMUNITY

LADY J AND THE MAGIC OF THE BLUES AN INTERVIEW WITH THE JACQUELINE MADDIX

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THE COALITION FOR HEMOPHILIA

MISSION

TO MAKE QUALITY OF LIFE THE FOCAL POINT OF TREATMENT FOR PEOPLE WITH HEMOPHILIA B AND THEIR FAMILIES THROUGH EDUCATION, EMPOWERMENT, ADVOCACY, AND OUTREACH.

EMPOWERING WOMEN, TOGETHER: REFLECTIONS FROM THE 2024 WOMEN'S FALL RETREAT

BY ERICA GARBER

Held at the Hilton Alpharetta in Georgia November 14-17, the Coalition for Hemophilia B's ***2024 Women's Fall Education & Empowerment Retreat*** brought together women from across the country to rest, reflect, and reimagine what it means to live boldly with—and alongside—hemophilia B.

From the moment attendees checked in, the tone was one of community, with the hugs, tears, and laughter that come along with any gathering of old and new friends. Thursday evening opened with two concurrent roundtable sessions led by women from the community. Jennifer DeGlopper and Ashley Zebley facilitated a powerful conversation among diagnosed women and those seeking answers, sharing their journeys from misdiagnosis to empowerment. Their honesty created space for others to speak openly, and several in the room described feeling seen and supported fully for the first time.

In the next room, Mandy Aberegg and Danelie Rivera hosted the caregivers' roundtable, welcoming mothers, daughters, sisters, and partners to share the unique emotional weight of caregiving. Their thoughtful questions and calm presence encouraged an honest, affirming dialogue. Laughter and tears filled both rooms and as the evening ended, one participant shared, "I didn't realize how much I needed this space." It was a powerful start to a wonderful weekend of education and connection.

Friday's highlight was the morning visit to Old Rucker Park Farm. From blending herbal teas to exploring the lush landscape, the group spent time immersed in




























nature, connecting in new ways. Catherine Canadeo led a beautiful, grounding Sisterhood Circle of Unity on the farm's lawn—reminding each participant to nurture the soul behind the roles they carry every day.

Expert-led sessions allowed attendees to learn, reflect, and share throughout the weekend. Daysi Fardales gave two highly engaging sessions that helped ground attendees in the power of communication at home and when seeking care. In her session *Family Connection* workshop, participants explored how to strengthen communication across generations and within caregiving dynamics, especially when navigating disclosure at work, school, and in social settings. Through role-play and real-life scenarios, women had a chance to reflect on how they advocate for themselves and their families.

In her second session, *Shared Decision Making*, she offered practical tools for becoming an active partner in care. The session emphasized the importance of asking questions, understanding treatment options, and confidently navigating conversations with providers. Both sessions left participants feeling better equipped to speak up, ask for what they need, and involve their loved ones in a more empowered way.

Natalie Sayer's session on navigating the unknown offered calm, reflective tools to manage anxiety and overwhelm. Participants walked away with practical language and approaches they could use immediately, whether facing medical uncertainty or day-to-day stress. Her workshop paired beautifully with Jeanette Jones' session, which tackled the often-overlooked topic of menopause. This was the first time for many to speak openly about symptoms, treatment questions, and the need for more tailored support.

Tiffany Pringle brought lightness and laughter to the retreat with her session on the healing power of joy. Her energy was contagious, reminding the group that joy is not a luxury—it's a necessity. Later that day, Corazon Tierra returned to lead a *Community Dance* workshop that welcomed all levels and body types. Participants left feeling grounded, empowered, and deeply connected to themselves and one another.

Throughout the weekend, attendees participated in wellness-focused activities—creating space for creativity and personal reflection. The wellness weekend culminated with a moving and memorable group performance led by Corazon Tierra. Her final session blended dance, storytelling, and reflection—reminding us how powerful it can be to inhabit our bodies entirely. For many women in the room, this was more than just movement—it was healing.

Corazon guided participants through expressive exercises that gave space for joy, release, and connection. In a year where many have carried so much, her closing message was clear: our bodies hold our stories, and we can honor them through movement. Laughter and rhythm filled the room as women moved together, grounded in sisterhood and shared strength. It was a powerful reminder of how much is possible when women gather with intention and care.

The retreat ended with creativity and celebration. Attendees reflected on their hopes and connections during Erica Garber's A*natomy of Hope and Connection*, followed by a final night dinner and a high-energy 80s dance party—complete with costumes, karaoke, and an unbelievable lip sync battle none of us will soon forget.

These educational, emotional, and joyful moments offered more than just information. They created a space where women felt seen, supported, and uplifted. We are incredibly grateful to Pfizer for making this retreat possible and their continued commitment to uplifting women and caregivers in our community. Your support helped create an experience that will stay with us for a long time.

Alhemo® is a prescription medicine used for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults and children 12 years of age and older with hemophilia A with Factor 8 inhibitors or hemophilia B with Factor 9 inhibitors. It is not known if Alhemo® is safe and effective in people using Alhemo® while receiving ongoing immune tolerance induction. It is not known if Alhemo is safe and effective for hemophilia A and B with and without inhibitors in children younger than 12 years of age.

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[a]Store in refrigerator before first use. After first use, Alhemo® can be stored at room temperature below 86 °F (30 °C) or in a refrigerator at 36 °F to 46 °F (2 °C to 8 °C) for up to 4 weeks.

IV=intravenous.

Important Safety Information

What is the most important information I should know about Alhemo®?

- **It is important to follow the daily dosing schedule of Alhemo® to stay protected against bleeding.** This is especially important during the first 4 weeks of treatment to make sure a correct maintenance dose is established. Use Alhemo® exactly as prescribed by your healthcare provider (HCP). **Do not** stop using Alhemo® without talking to your HCP. If you miss doses or stop using Alhemo®, you may no longer be protected against bleeding
- **Your HCP may prescribe bypassing agents during treatment with Alhemo®.** Carefully follow your HCP's instructions regarding when to use on-demand bypassing agents, and the recommended dose and schedule for breakthrough bleeds

Do not use Alhemo® if you are allergic to concizumab-mtci or any of the ingredients in Alhemo®.

Before using Alhemo®, tell your HCP about all of your medical conditions, including if you:

- Have a planned surgery. Your HCP may stop treatment with Alhemo® before your surgery. Talk to your HCP about when to stop using Alhemo® and when to start it again if you have a planned surgery
- Are pregnant or plan to become pregnant. It is not known if Alhemo® may harm your unborn baby

  Females who are able to become pregnant
  - Your HCP may do a pregnancy test before you start treatment with Alhemo®.
  - You should use an effective birth control (contraception) method during treatment with Alhemo® and for 7 weeks after ending treatment. Talk to your HCP about birth control methods that you can use during this time
- Are breastfeeding or plan to breastfeed. It is not known if Alhemo® passes into your breast milk. Talk to your HCP about the best way to feed your baby during treatment with Alhemo®

Tell your HCP about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your HCP and pharmacist when you get a new medicine.

How should I use Alhemo®?

- Change (rotate) your injection site with each injection. **Do not** use the same site for each injection
- To determine the right maintenance dose for you, your HCP will do a blood test to check the amount of Alhemo® in your blood. Your HCP may do additional blood tests during treatment with Alhemo®
- Do not share your Alhemo® pens and needles with another person, even if the needle has been changed. You may give another person an infection or get an infection from them
- **If you miss a dose of Alhemo® during the first 4 weeks of treatment,** contact your HCP right away. Your HCP will tell you how much Alhemo® to inject

What are the possible side effects of Alhemo®?

Alhemo® may cause serious side effects, including:

- **Blood clots (thromboembolic events).** Alhemo® may cause blood clots to form in blood vessels, such as in your arms, legs, heart, lung, brain, eyes, kidneys, or stomach. You may be at risk for getting blood clots during treatment with Alhemo® if you use high or frequent doses of factor products or bypassing agents to treat breakthrough bleeds, or if you have certain conditions. Get medical help right away if you have any signs and symptoms of blood clots, including: swelling, warmth, pain, or redness of the skin; headache; trouble speaking or moving; eye pain or swelling; sudden pain in your stomach or lower back area; feeling short of breath or severe chest pain; confusion; numbness in your face; and problems with your vision
- **Allergic reactions.** Alhemo® can cause allergic reactions, including redness of the skin, rash, hives, itching, and stomach-area (abdominal) pain. Stop using Alhemo® and get emergency medical help right away if you develop any signs or symptoms of a severe allergic reaction, including: itching on large areas of skin; trouble swallowing; wheezing; pale and cold skin; dizziness due to low blood pressure; redness or swelling of lips, tongue, face, or hands; shortness of breath; tightness of the chest; and fast heartbeat

The most common side effects of Alhemo® include: bruising, redness, bleeding, or itching at the site of injection, and hives.

Please see Brief Summary of Prescribing Information on the following page.

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- Visit www.novo-pi.com/alhemo.pdf to obtain FDA-approved product labeling
- Call 1-888-668-6732

What is the most important information I should know about Alhemo®?
- **It is important to follow the daily dosing schedule of Alhemo® to stay protected against bleeding.** This is especially important during the first 4 weeks of treatment to make sure a correct maintenance dose is established. Use Alhemo® exactly as prescribed by your healthcare provider. **Do not** stop using Alhemo® without talking to your healthcare provider. If you miss doses, or stop using Alhemo®, you may no longer be protected against bleeding.
- **Your healthcare provider may prescribe bypassing agents during treatment with Alhemo®.** Carefully follow your healthcare provider's instructions regarding when to use on-demand bypassing agents, and the recommended dose and schedule for breakthrough bleeds.

See **"How should I use Alhemo®?"** for more information on how to use Alhemo®.

What is Alhemo®?

Alhemo® is a prescription medicine used for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults and children 12 years of age and older with hemophilia A with factor VIII inhibitors or hemophilia B with factor IX inhibitors.

It is not known if Alhemo® is safe and effective in people using Alhemo® while receiving ongoing Immune Tolerance Induction (ITI).

It is not known if Alhemo® is safe and effective for hemophilia A and B with and without inhibitors in children younger than 12 years of age.

Do not use Alhemo® if you are allergic to concizumab-mtci or any of the ingredients in Alhemo®.

Before using Alhemo®, tell your healthcare provider about all of your medical conditions, including if you:
- have a planned surgery. Your healthcare provider may stop treatment with Alhemo® before your surgery. Talk to your healthcare provider about when to stop using Alhemo® and when to start it again if you have a planned surgery.
- are pregnant or plan to become pregnant. It is not known if Alhemo® may harm your unborn baby. **Females who are able to become pregnant**
  - Your healthcare provider may do a pregnancy test before you start treatment with Alhemo®.
  - You should use an effective birth control (contraception) during treatment with Alhemo® and for 7 weeks after ending treatment. Talk to your healthcare provider about birth control methods that you can use during this time.
- are breastfeeding or plan to breastfeed. It is not known if Alhemo® passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby during treatment with Alhemo®.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I use Alhemo®?
- Use Alhemo® exactly as prescribed by your healthcare provider.
- Your healthcare provider will provide instructions for stopping (discontinuing) your current treatment when switching to Alhemo®.
- Inject Alhemo® 1 time a day.
- **Your healthcare provider should show you or your caregiver how to use Alhemo® before you use it for the first time.**
- Alhemo® is given as an injection under the skin (subcutaneous injection) by you or a caregiver.
- Ask your healthcare provider if you need to use a different injection technique. For example, children and people who are lean may need to inject into a pinched fold of skin to avoid injecting too deep (into the muscle).
- Change (rotate) your injection site with each injection. **Do not** use the same site for each injection.
- You will inject a larger dose (a loading dose) of Alhemo® on your first day of treatment. Then your healthcare provider will prescribe a dose to inject 1 time a day until your maintenance dose is established.
- To determine the right maintenance dose for you, your healthcare provider will do a blood test to check the amount of Alhemo® in your blood. Your healthcare provider may do additional blood tests during treatment with Alhemo®.
- Your healthcare provider will prescribe your dose based on your weight. If your weight changes, tell your healthcare provider.

How should I use Alhemo®? (cont'd)
- Your healthcare provider will provide information on the treatment of breakthrough bleeding during your treatment with Alhemo®.
- Do not share your Alhemo® pens and needles with another person, even if the needle has been changed. You may give another person an infection or get an infection from them.
- **If you miss a dose of Alhemo® during the first 4 weeks of treatment,** contact your healthcare provider right away. Your healthcare provider will tell you how much Alhemo® to inject.
- **If you miss a dose of Alhemo® after your daily maintenance dose is established:**
  - For 1 missed dose, continue your normal daily dose.
  - For 2 to 6 missed doses, give 2 doses as soon as you remember. Then continue your normal daily dose the next day.
  - For 7 or more missed doses, contact your healthcare provider right away as you will need to receive a new loading dose before continuing your normal daily dose.
  - If you are unsure about how much to Alhemo® to inject, contact your healthcare provider.

What are the possible side effects of Alhemo®?

Alhemo® may cause serious side effects, including:
- **Blood clots (thromboembolic events).** Alhemo® may cause blood clots to form in blood vessels, such as in your arms, legs, heart, lung, brain, eyes, kidneys, or stomach. You may be at risk for getting blood clots during treatment with Alhemo® if you use high or frequent doses of factor products or bypassing agents to treat breakthrough bleeds, or if you have certain conditions. Get medical help right away if you have any signs and symptoms of blood clots, including:
  - swelling, warmth, pain, or redness of the skin
  - headache
  - trouble speaking or moving
  - eye pain or swelling
  - sudden pain in your stomach or lower back area
  - feeling short of breath or severe chest pain
  - confusion
  - numbness in your face
  - problems with your vision
- **Allergic reactions.** Alhemo® can cause allergic reactions, including redness of the skin, rash, hives, itching, and stomach-area (abdominal) pain. Stop using Alhemo® and get emergency medical help right away if you develop any signs or symptoms of a severe allergic reaction, including:
  - itching on large areas of skin
  - trouble swallowing
  - wheezing
  - pale and cold skin
  - dizziness due to low blood pressure
  - redness or swelling of lips, tongue, face, or hands
  - shortness of breath
  - tightness of the chest
  - fast heartbeat

The most common side effects of Alhemo® include:
- bruising, redness, bleeding, or itching at the site of injection
- hives

These are not all the possible side effects of Alhemo®.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Alhemo®?
- **Before first use:**
  - Store unused Alhemo® pens in the refrigerator between 36°F to 46°F (2°C to 8°C).
- **After first use:**
  - Store the Alhemo® pen in the refrigerator between 36°F to 46°F (2° to 8°C) or at room temperature below 86°F (30°C) for up to 28 days.
  - Write the date of first use in the space provided on the carton.
  - Throw away (discard) the Alhemo® pen 28 days after first opening even if some medicine is left in the pen.
- Store Alhemo® with the cap on and keep it in the original carton to protect from light.
- Do not store Alhemo® in direct sunlight and keep away from direct heat.
- When stored in the refrigerator, do not store the pen directly next to the cooling element (the part that cools the refrigerator).
- Do not freeze Alhemo®.
- Do not use Alhemo® if it has been frozen or if it has been stored above 86°F (30°C).

Keep Alhemo® and all medicine out of the reach of children.

More detailed information is available upon request.

Available by prescription only.

For information contact: Novo Nordisk Inc., 800 Scudders Mill Road, Plainsboro, New Jersey 08536, USA, 1-888-668-6444

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 US24AHM00199 January 2025

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MEETINGS ON THE ROAD: EMPOWERING THE HEMOPHILIA B COMMUNITY ACROSS THE U.S.

BY JENNIFER DEGLOPPER

A Journey of Learning, Connection, and Fun

What happens when education, wellness, and community come together? A day filled with energy, insight, and lasting connections. The *Meetings on the Road* (MOR) events are taking place across the U.S., bringing resources, engaging discussions, and a sense of empowerment to the hemophilia B community.

This season, our journey took us to Columbus, OH; Chicago, IL; Denver, CO; Anaheim, CA; Birmingham, AL; and Richmond, VA. And the adventure isn't over! Next stops: St. Louis, MO, and San Antonio, TX. (Register now at hemob.org/upcoming-events.)

A Full-Day Immersive Experience

Each event begins with a welcoming atmosphere—attendees check-in, enjoy breakfast, and explore the Exhibit Hall, setting the stage for a day of learning and camaraderie. After opening remarks from The Coalition for Hemophilia B, the real adventure begins.

This year's *Meetings on the Road* featured an exciting Sherlock Holmes-inspired theme, where attendees put their problem-solving skills to the test. From the start, teams were formed by opening pre-mailed envelopes and discovering their partners for the day. The event started with an interactive puzzle hunt, riddles, and mystery-solving games designed to unite people through collaboration and fun. Each challenge layered onto the next—unlocking clues, decoding messages, and racing against time in a true detective-style experience.

Following the thrilling team-building session, attendees took a moment to shake off the tension and get moving with music and motion. Dr. Robert Friedman led an energizing session designed to boost mood, reduce stress, and set a positive tone for the rest of the day.

From there, participants engaged in dynamic discussions about treatment advancements. A CSL speaker presented *An Exciting Path Option for Patients*, exploring gene therapy through clinical data and firsthand








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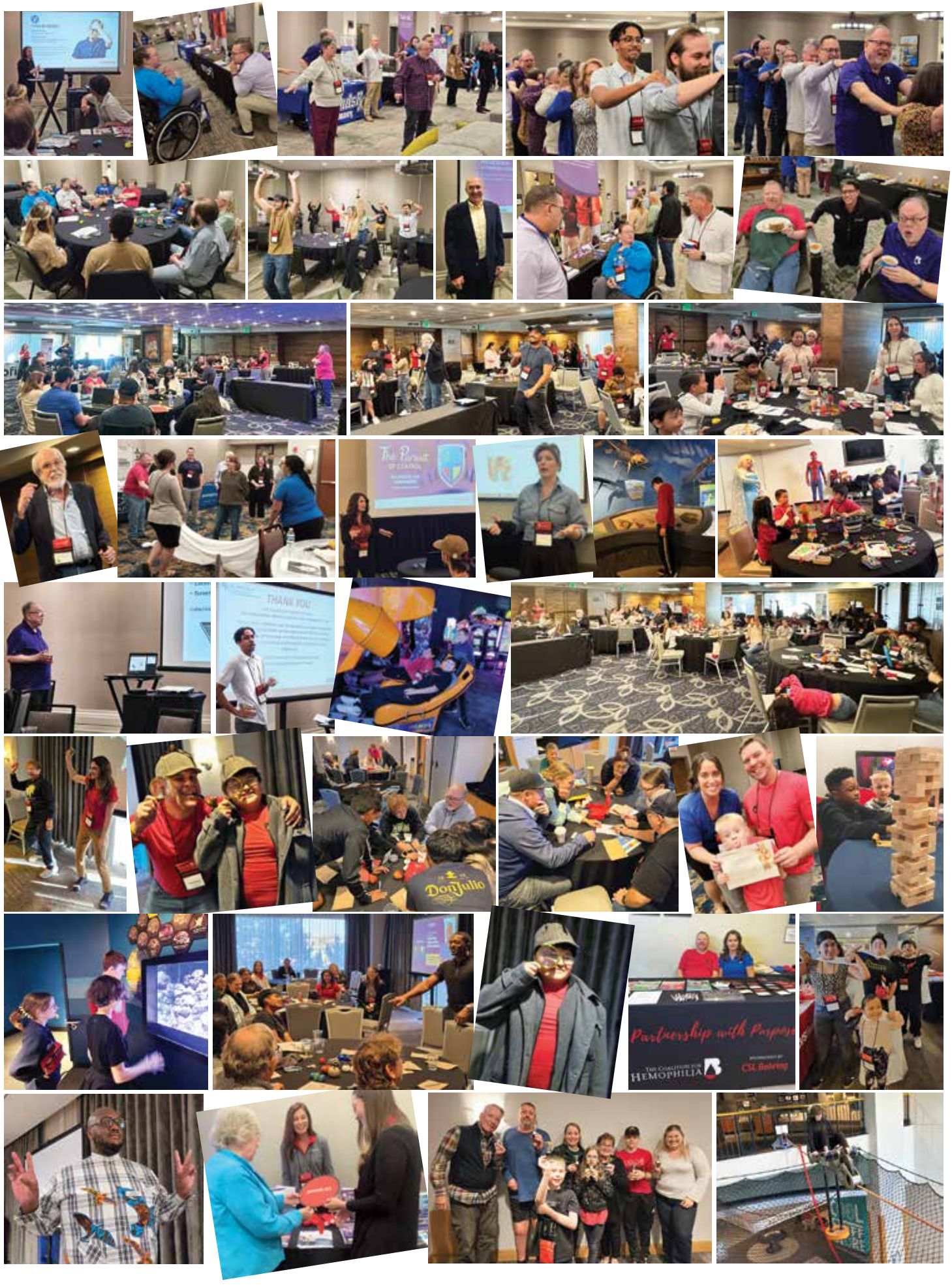
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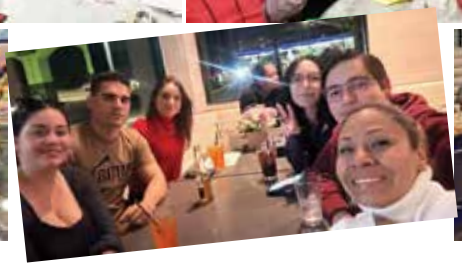

patient experiences. Later, a rotating lineup of expert hematologists—including Dr. Clark at select locations—led an in-depth discussion on the evolving hemophilia B treatment landscape.

More Than Just Learning—A Full Family Experience

While education and advocacy were at the heart of the event, connection and fun played a considerable role. Participants didn't just sit and listen—they worked together, laughed, and built lasting friendships.

The *Meetings on the Road* events welcomed entire families, ensuring that adults and children had a meaningful experience. Kids embarked on special adventure-filled trips, giving them their own exciting activities while parents and caregivers participated in workshops and discussions.

The event also included the *Thrive* session, providing essential guidance on nutrition, stress management, and overall well-being—empowering attendees to take charge of their health beyond treatment.

Gratitude for an Unforgettable Journey

Each event left participants with new friendships, fresh knowledge, and a renewed sense of empowerment. The Coalition for Hemophilia B extends a heartfelt thank you to the expert speakers and the fantastic volunteers who made these events possible. Their dedication and enthusiasm created an engaging, welcoming, and impactful experience.

If you haven't joined us yet, don't miss your chance! The Meetings on the Road are headed next to St. Louis, MO, and San Antonio, TX, with even more cities to be announced soon.

Ready to be part of this incredible journey? Register today at hemob.org/upcoming-events!

A special thank you to CSL Behring for their generous sponsorship, making these events a reality for the hemophilia B community.

CSL Behring

Correction:

In the Fall 2024 issue of Hemophilia B News, we stated that Dr. Danielle Nance is working toward establishing the first adult treatment center in Arizona. This statement was incorrect.

We wish to clarify that Arizona has two established, federally funded Hemophilia Treatment Centers (HTCs) providing comprehensive care for both pediatric and adult patients with bleeding disorders:

1. Arizona Hemostasis & Thrombosis Center at the University of Arizona has been a federally funded HTC since 1978. The center serves over 500 patients and offers a full spectrum of care through a multidisciplinary team that includes adult and pediatric hematologists, a nurse practitioner, a nurse coordinator, a social worker, a physical therapist, a data manager, and a patient financial counselor. The center also provides access to subspecialty care and a Level 1 trauma center.
2. Phoenix Children's Hospital has provided comprehensive care for pediatric and adult patients for over 20 years as a federally funded HTC.

We deeply regret the error and acknowledge the exceptional work these centers have done for decades to serve the Arizona bleeding disorders community. We apologize for any confusion our statement may have caused.

Thank you to Mary Lou Damiano, RN, M.Ed., Program Director of the Arizona Hemostasis & Thrombosis Center, for bringing this to our attention.

CONTROVERSY OVER ISTH HEMOPHILIA TREATMENT GUIDELINES

BY DR. DAVID CLARK

A controversy over a set of clinical treatment guidelines has been raging for over a year now, but you probably haven't heard about it. Unfortunately, it has the potential to negatively affect your treatment. We published a piece about the controversy in the Hemophilia News section of the summer newsletter, but the headline was mistakenly dropped, making it look like it was just part of the preceding article. Here is the summer newsletter report, followed by an update.

New ISTH Clinical Guidelines for Hemophilia Treatment – Summer 2024 Newsletter

6/19/24 The ISTH has released the "International Society on Thrombosis and Haemostasis Clinical Practice Guideline for Treatment of Congenital Hemophilia A and B Based on the Grading of Recommendations Assessment, Development, and Evaluation Methodology." The guideline has caused a lot of controversy in the hemophilia treatment community. It differs in several aspects from the "WFH Guidelines for the Management of Hemophilia," 3rd edition, published in August 2020. The WFH guideline was consensus-based and developed by a large panel of hemophilia treaters according to how they actually treat hemophilia. The ISTH document used the GRADE method (Grading of Recommendations Assessment, Development, and Evaluation methodology), which evaluates the scientific reliability of the information on which the guidelines are based. These give different answers.

The ISTH report tells us that most of the methods used to treat hemophilia have not been rigorously tested according to the highest scientific standards. That's true, and we know it. However, that doesn't mean that your medical treatment is deficient. As explained by Mannucci in an accompanying article in the same issue of the Journal of Thrombosis and Haemostasis, in the GRADE method, the gold standard results from randomized clinical trials (RCTs).

While some hemophilia studies are done using RCTs, most are not. That's not surprising in a small field like hemophilia B. RCTs are expensive, time-consuming, and usually require more significant numbers of subjects – things that aren't always available to us. Instead, hemophilia treaters rely more on another important tool that science gives us - scientific reasoning, plus their own experience. The doctors know, even without studies, that getting factor IX into your bloodstream will help minimize your bleeding, and there are lots of ways to do that to accommodate the variations from patient to patient.

The ISTH report only makes two recommendations for hemophilia B (11 for A). The first is that prophylaxis is recommended over on-demand treatment. We've been assuming this to be valid for a long time (based on scientific reasoning and small non-RCT studies), but it's nice to have it confirmed (although with only "moderate-certainty evidence," according to ISTH).

The other recommendation for hemophilia B is that prophylaxis can be carried out using plasma-derived products, standard half-life recombinant products, or extended half-life (EHL) recombinant products. This is where the potential trouble comes in. According to ISTH, there is not enough scientific evidence to determine which of these three types of products is better, so they can't recommend one over another. This is one of the ways that science operates, which seems to mystify laypeople. ISTH is not saying there is no difference between the three product types; they're just saying that since the studies haven't been done, they can't say whether there is a difference.

Within the scientific/medical community – we understand what this means. The problem is when something like this gets out into the general population and is misunderstood. You can imagine an insurance company reading the ISTH report and assuming it says there is no difference among the three types of products: "Hooray! This is what we've been waiting for. The ISTH, the most prestigious international organization for hemostasis, says there is no difference. We can quit paying for those expensive EHL products and just give everyone cheaper plasma-derived products. We'll save tons of money!"

People fear the same could also be true in countries with national health plans that offer just one or a limited number of products for the country's entire hemophilia B population.

ISTH has written its report very carefully to prevent that misunderstanding, but in a society that doesn't understand or value science, it doesn't always work.

We'll just have to see what happens. [Rezende SM et al., J Thromb Haemost, online ahead of print 6/19/24; see also Mannucci PM, J Thromb Haemost, online ahead of print 6/19/24 and Ainle FN et al., J Thromb Haemost, online ahead of print 6/20/24]

Background and Update

The draft guidelines were given to the hemophilia community for comment in October 2023, with over 400 comments received. In a 5/3/24 statement on its website, the World Federation of Hemophilia (WFH) states, "The ISTH guidelines risk setting hemophilia treatment back 30 years." And further: "These ISTH guidelines may impede patient access to products that can improve outcomes in countries of all socioeconomic strata and thereby harm patients and reverse health equity gains."

The Medical and Scientific Advisory Council (MASAC) of the National Bleeding Disorders Foundation (NBDF) also stated in MASAC Document #288: "The draft ISTH guidelines for hemophilia treatment do not support the changed treatment paradigm in hemophilia. They are counterproductive toward reaching the goal of zero bleeds, and work against the goals of shared decision making and improved patient-centered outcomes." ISTH went ahead and published the guidelines on 6/20/24 in their Journal of Thrombosis and Haemostasis.

Criticism of the ISTH guidelines has continued with three recent articles in the WFH's journal Haemophilia. A group of 44 treaters and other leaders in the hemophilia community, and also on behalf of 14 hemophilia organizations worldwide, published a critical appraisal of the ISTH recommendations. Their conclusion is noteworthy: "These recommendations may mislead healthcare professionals, payers, and governments and therefore cannot serve the patient community well. They set back the advances made in haemophilia care because they overlook important available evidence and do not guide clinical practice to contemporary standards."

They point out that ISTH focused only on annualized bleeding rates (ABRs) and overlooked the benefits of high trough levels and maintenance of healthy joints, as well as the ability of the patient to participate in normal activities and enjoy a high quality of life. They also point out the lack of community consensus in developing the ISTH guidelines and that the three people with hemophilia who were originally on the ISTH panel developing the guidelines dropped out and would not allow their names to be included in the final publication. [Albisetti M et al., Haemophilia, online ahead of print 12/6/24]

Albisetti et al. also point out that the GRADE methodology used by ISTH is not applicable for rare diseases where RCTs are difficult to conduct. In fact, ISTH used a modified GRADE method that takes this into account in their own 2021 guidelines on the treatment of von Willebrand Disease, a less rare disorder. The other Haemophilia paper addresses this in more detail.

Their conclusion is also noteworthy: "The puristic approach taken in the ISTH Guideline development process, without consideration of accepted adaptations to GRADE implementation, created a missed opportunity for progressing haemophilia care, leading to guideline recommendations that have been widely deemed invalid and obsolete by expert healthcare professionals and by those living with the condition, the very people who are expected to implement or bear the impact of the recommendations. Lessons learnt from this comparative analysis should guide future guideline development and encourage collaboration to further advance haemophilia." [Skinner M et al., Haemophilia, online ahead of print 12/9/24]

The European Association for Haemophilia and Allied Disorders (EAHAD) also published a commentary pointing out that guidelines are only recommendations. They state: "Indeed, meticulous observations and progressive understanding of disease pathophysiology have resulted in significant treatment advances that would not merit an RCT today." In other words, based on our knowledge today, RCTs would not provide us with anything better than we already have. [Chowdary P et al., Haemophilia, online ahead of print 12/6/24]

We don't know why ISTH did this and whether insurance companies and ministries of health that control which products are available to hemophilia patients will try to restrict care based on the ISTH guidelines. However, the outpouring of criticism against the ISTH guidelines should help provide strong support against product restrictions. Hopefully, as Dr. Mannucci says in his commentary, this will all turn out to simply be a "storm in a teacup."

IMPORTANT SAFETY INFORMATION

What is HEMGENIX?

HEMGENIX®, etranacogene dezaparvovec-drlb, is a one-time gene therapy for the treatment of adults with hemophilia B who:

- Currently use Factor IX prophylaxis therapy, or
- Have current or historical life-threatening bleeding, or
- Have repeated, serious spontaneous bleeding episodes.

HEMGENIX is administered as a single intravenous infusion and can be administered only once.

What medical testing can I expect to be given before and after administration of HEMGENIX?

To determine your eligibility to receive HEMGENIX, you will be tested for Factor IX inhibitors. If this test result is positive, a retest will be performed 2 weeks later. If both tests are positive for Factor IX inhibitors, your doctor will not administer HEMGENIX to you. If, after administration of HEMGENIX, increased Factor IX activity is not achieved, or bleeding is not controlled, a post-dose test for Factor IX inhibitors will be performed.

HEMGENIX may lead to elevations of liver enzymes in the blood; therefore, ultrasound and other testing will be performed to check on liver health before HEMGENIX can be administered. Following administration of HEMGENIX, your doctor will monitor your liver enzyme levels weekly for at least 3 months. If you have preexisting risk factors for liver cancer, regular liver health testing will continue for 5 years post-administration. Treatment for elevated liver enzymes could include corticosteroids.

What were the most common side effects of HEMGENIX in clinical trials?

In clinical trials for HEMGENIX, the most common side effects reported in more than 5% of patients were liver enzyme elevations, headache, elevated levels of a certain blood enzyme, flu-like symptoms, infusion-related reactions, fatigue, nausea, and feeling unwell. These are not the only side effects possible. Tell your healthcare provider about any side effect you may experience.

What should I watch for during infusion with HEMGENIX?

Your doctor will monitor you for infusion-related reactions during administration of HEMGENIX, as well as for at least 3 hours after the infusion is complete. Symptoms may include chest tightness, headaches, abdominal pain, lightheadedness, flu-like symptoms, shivering, flushing, rash, and elevated blood pressure. If an infusion-related reaction occurs, the doctor may slow or stop the HEMGENIX infusion, resuming at a lower infusion rate once symptoms resolve.

What should I avoid after receiving HEMGENIX?

Small amounts of HEMGENIX may be present in your blood, semen, and other excreted/secreted materials, and it is not known how long this continues. You should not donate blood, organs, tissues, or cells for transplantation after receiving HEMGENIX.

Please see full prescribing information for HEMGENIX at HEMGENIX.com.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

You can also report side effects to CSL Behring's Pharmacovigilance Department at 1-866-915-6958.

BRIEF SUMMARY OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use HEMGENIX safely and effectively. See full prescribing information for HEMGENIX.

HEMGENIX® (etranacogene dezaparvovec-drlb) suspension, for intravenous infusion
Initial U.S. Approval: 2022

----------INDICATIONS AND USAGE----------

HEMGENIX is an adeno-associated virus vector-based gene therapy indicated for the treatment of adults with Hemophilia B (congenital Factor IX deficiency) who:

- Currently use Factor IX prophylaxis therapy, or
- Have current or historical life-threatening hemorrhage, or
- Have repeated, serious spontaneous bleeding episodes.

----------CONTRAINDICATIONS----------

None.

----------WARNINGS AND PRECAUTIONS----------

- Infusion reactions: Monitor during administration and for at least 3 hours after end of infusion. If symptoms occur, slow or interrupt administration. Re-start administration at a slower infusion once resolved.
- Hepatotoxicity: Closely monitor transaminase levels once per week for 3 months after HEMGENIX administration to mitigate the risk of potential hepatotoxicity. Continue to monitor transaminases in all patients who developed liver enzyme elevations until liver enzymes return to baseline. Consider corticosteroid treatment should elevations occur.
- Hepatocellular carcinogenicity: For patients with preexisting risk factors (e.g., cirrhosis, advanced hepatic fibrosis, hepatitis B or C, non-alcoholic fatty liver disease (NAFLD), chronic alcohol consumption, non-alcoholic steatohepatitis (NASH), and advanced age), perform regular (e.g., annual) liver ultrasound and alpha-fetoprotein testing following administration.
- Monitoring Laboratory tests: Monitor for Factor IX activity and Factor IX inhibitors.

----------ADVERSE REACTIONS----------

The most common adverse reactions (incidence ≥5%) were elevated ALT, headache, blood creatine kinase elevations, flu-like symptoms, infusion-related reactions, fatigue, malaise and elevated AST.

To report SUSPECTED ADVERSE REACTIONS, contact CSL Behring at 1-866-915-6958 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------USE IN SPECIFIC POPULATIONS----------

No dose adjustment is required in geriatric, hepatic, or renal impaired patients.

Based on November 2022 version

HEMGENIX is manufactured by uniQure Inc. and distributed by CSL Behring LLC.
HEMGENIX® is a registered trademark of CSL Behring LLC.

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ADVOCACY NEWS

THE COALITION ATTENDS PFIZER ADVOCACY MEETING

BY JAMES ROMANO

In early December 2024, the Coalition for Hemophilia B was invited to attend the Pfizer Rare Disease Advocacy Collaborative. Erica Garber and James Romano represented the Coalition.

The two-day event brought together advocacy leaders from significant Rare Disease Advocacy Groups (NORD, the Every Life Foundation, and Global Genes; Bleeding Disorder Patient Groups (NBDF, HFA, and the Coalition) as well as other rare disease community organizations such as groups from the Sickle Cell Community and the Amyloidosis Community.

The purpose of the meeting was to meet and understand the Pfizer Team and to discuss health policy in the aftermath of the election.

The first day was devoted to introductions to the Pfizer Staff at the Pfizer Headquarters. More than 30 individual staff members were on hand for discussions, presentations, and fellowship with attendees. Mr. Bert Bruce, U.S. President, Rare Disease, at Pfizer, ran the first day.

Each brand team for the disease community spoke. Dr. Burcu Turiakan Diener, VP for the US Gene Therapy department, discussed gene therapy in the hemophilia community. At the end of the first day, there was an interesting discussion on the diversity of Pfizer and its staff, which is essential to rare communities such as the Sickle Cell Community.

The second day was devoted to federal policy. Pfizer reviewed the election outcomes and the status of important patient legislation such as The Safe Step Act and The Help Copays Act. There was a discussion on dealing with Congress and the new Administration

led by representatives of NORD and The Every Life Foundation.

Eboni Morris, formerly of the Hemophilia Federation and now with Pfizer, led a state discussion. Finally, Melissa Bishop Murphy, Senior Director of State Government Affairs, discussed Pfizer's Multicultural Health Equity Collective.

The Coalition for Hemophilia B looks forward to partnering with Pfizer on important advocacy issues and engaging with them to improve treatment access for those with hemophilia B.

NEW YEAR'S RESOLUTION VS NEW YEAR'S REDISCOVERY

BY CATHERINE CANADEO

For some, the past year may have been a personal triumph, a roller coaster of events and emotions—or perhaps both. Setting rigid New Year's resolutions can feel limiting and discouraging. Instead, one of the best ways to move forward is to establish SMART (specific, measurable, achievable, relevant, and time-bound) goals as periodic check-ins.

Rediscovering your "why" helps you stay motivated and focused on achieving these goals. Remember, as long as you continue living your fullest and healthiest life, there's no need to adopt an all-or-nothing approach to your ambitions.

The new year is a time for revitalizing, recharging, resetting, and rejuvenating my life. To simplify this journey, I focus on four major cornerstones: food, body, emotional well-being, and spiritual growth. The key is to keep it simple and avoid overwhelming yourself—take things one day at a time.

Cornerstone One: Food

The first cornerstone is food. The food you eat is crucial to your wellness journey because it directly impacts your body. Healthy, nourishing foods energize and revitalize you, while unhealthy options often leave you feeling sluggish and bloated. Wholesome food makes you feel good on the inside and enhances your outward appearance, reflecting the vitality within

Cornerstone Two: Body

Your body is your home—where you live, play, relax, learn, grow, and exist. A home should feel cozy, safe, secure, and loved, and that's the same feeling we all deserve to have in our bodies. You can cultivate this sense of comfort through various means, including exercise and daily practices that nourish your body. These habits help you stay present as a whole person and foster a sense of active well-being through self-awareness and care.

Cornerstone Three: Emotional Well-Being

Chronic stress—whether personal, professional, or physical—can significantly affect your health. Negative emotions can manifest in unexpected ways, such as bloating, inflammation, digestive disorders, sleep disturbances, weight gain, hormonal imbalances, cardiovascular issues, and even autoimmune disorders. Nurturing your emotional well-being is essential to build a deeper connection with yourself. This means processing, feeling, and resolving your emotions in a healthy way. Remember: *Self-care* = *Self-sustainability* = *Self-love*.

Cornerstone Four: Spiritual Growth

Spiritual growth isn't solely about religion; it's about connecting with your inner spirit. It's about embracing your true, authentic self and becoming more centered and peaceful. When you connect with yourself on this level, you stop taking your imperfections, real or perceived, so seriously. You become more grounded, compassionate, loving, and grateful for the gift of life and the people you cherish.

Creating Your Rediscovery

What inspired you this past year? What gave you a sense of purpose and passion? Reflect on these moments and write them down in categories—spiritual, personal, and professional. Focus on your intentions and introduce a new habit, pattern, or experience each week by taking small, manageable steps. Step out of your comfort zone, as that's where growth and creativity flourish. Rewiring your brain this way brings joy, fun, and fulfillment into your life.

Aspire to reach your full potential and let your beautiful energy shine with grace and gratitude. Rediscover your sense of worth, value, confidence, and, most importantly, self-love. By doing so, you become the best version of yourself and bring positivity and love to those around you.

LADY J AND THE MAGIC OF THE BLUES

AN INTERVIEW WITH THE JACQUELINE MADDIX

BY RENAE BAKER

We first met under larger-than-life guitars hanging from a glass dome among tropical foliage in a section of the Gaylord Opryland Hotel called "Delta." It was the inaugural Beats program, and Jacqueline "Lady J" Maddix attended.

I was intrigued by her smokey voice, sage smile, and the venerable command of the space she held around her. She adapted for her song, "Hootchie Cootchie (Wo) Man," by legendary Mississippi bluesman Willie Dixon.

Way up the Mississippi River from the actual Delta where the genre was crystallized into its famous form, Jacqueline has been a prominent pacemaker of sorts, keeping the pulse of the Blues strong in the Twin Cities via her varied career as a TV and radio personality, MC, bandleader, historian, and author.

For over 30 years, she has hosted her radio show, Songs of the Soul. Stream it Tuesdays from 4:00 pm-6:00 pm CST at https://kfai.org/program/songsofthesoul.

In addition to "Lady J," Maddix is known by many monikers such as Shemu, Root Worker, Blues Storyteller, and "High Priestess of the Blues." She owns them all with both power and humility. The most important name to which she answers is "Mom" to Christoper and David. Her story, as she says, "just weaves together."

Born in Minneapolis in 1954, Jacqueline grew up with three sisters and two brothers. "Little Ray" had hemophilia B. "My sisters were freaked out every time they saw a bleed," Jacqueline remembers. "Me? I just dove right in to see where the bleeding was coming from. I was always right there with my mom, taking care of Ray. Little did we know I was in training to take care of my two sons."

When Jacquie was 13, Raymond died at age eight of a head injury. "This was in the 1960s, even before plasmapheresis. Mountains of whole blood wouldn't have been enough to stop that bleed." Jacquie holds up an old black-and-white family photo. I see a little boy who I think looks just like Christopher. "If I could squish Christopher and David together, you'd have my brother Ray."

As far as they know, Jacquie is the only one of her sisters who carries hemophilia. "When I was younger, even a mosquito bite would just bleed and bleed." She was tested twice, and both times was told she didn't have a bleeding disorder. But that was over 30 years ago. She wonders what a test today might show.

Jacqueline's husband, Stanley, was in the Marine Corps, and the family moved with him to Tennessee and California, but Jacqueline craved coming home to the Twin Cities and the world-class hospital that gave great care to children with hemophilia. After four years of active military duty, they brought the boys back home to Minnesota. A couple of years later, Stanley wanted to return to military life. Jacqueline felt called to stay in the Twin Cities where she could best tend to the boys' medical care. The couple divorced.

Jacquie took a reception job at the University Hospital, where her voice was heard over the louder speakers. Her voice drew exhortations to go into radio. So, she enrolled in broadcasting school. Her first media job was writing and typing the news into a teleprompter for the on-air personality at CBS affiliate WCCO TV, Dave Moore. Jacquie experienced racism and sexism at the station, but Moore was her protector. "He took a liking to me at a time when many people had issues with a black woman talking into their earpiece and giving them time cues." That positive experience helped her learn to write.

"I always loved writing. I thought myself a poet. I've written poems that were published, which led to my being able to write songs," Jacquie says.

The station had cable access and allowed its members to take cameras out on the streets and tape news content. Jacqueline would go to local blues clubs, tape, edit, and turn them into news stories. "That led me to be on the radio."

In 1994, they would go to local blues clubs, tape, edit, and start the aforementioned blues radio show on Minnesota's KFAI radio station. On her show, she interviews and promotes musicians. She also became a contributing writer to the Twin City Blues News and MN Blues on Stage publications. Because of her local celebrity, she is often called upon to MC concerts and blues events, where she tells her listeners the backstories of blues classics. Eventually, someone said, "You know, you should be singing. Everybody already knows and loves you; you should start your own band!"

"And so I did! Everything I've tried to do that's not blues-related never flourishes. Anything that I do that's connected with the music survives. People think I chose the blues, but the blues chose me."

"I used to run the jams here in town, so it's nice to come out to the jams and be 'the old jam lady!'" She laughs. Her deep research into and sharing of the origins of African American people and blues music in "true indigenous storyteller fashion of the blues" earned her respect. In 2015, Lady J was inducted into the Minnesota Blues Hall of Fame as a true blues historian.

In 2012, Jacqueline first put "pencil to paper" to begin writing *Root Wisdom from the Elders' Circle*, which was published in 2021. According to its forward, her mission in writing the book was to "allow ancestral knowledge of old and current times to speak for itself through her life experiences." One review stated, "In the book, she shares sacred stories of transformation. Through her journey into her healing work, she identified Blues music as the carrier of her capacity for endurance."

What she hopes readers of her book will take away is that "We are all one people, and we are all coming back together again to become one people. If people respond to that idea, maybe some hatred and divisiveness will end." When her sons were diagnosed with hemophilia B with an inhibitor, Jacquie was told that was very unusual for African Americans and that they probably wouldn't live past the age of five. But this tribal medicine woman used music and "Mama laying on of hands" to heal. Are the blues about suffering? "That is someone else's interpretation of the blues," Lady J smiles.

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marstacimab-hncq
injection | 150 mg/mL

For routine prophylaxis in patients 12 years and older with hemophilia A or B without inhibitors

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Not actual size.

It's here—a once-weekly subcutaneous prophylactic treatment, now approved for eligible **patients with hemophilia B without inhibitors**

What is HYMPAVZI?
HYMPAVZI is a prescription medicine used to prevent or reduce the frequency of bleeding episodes in adults and children 12 years of age and older with hemophilia A without factor VIII inhibitors or hemophilia B without factor IX inhibitors.

It is not known if HYMPAVZI is safe and effective in children younger than 12 years old.

IMPORTANT SAFETY INFORMATION

Important: Before you start using HYMPAVZI, it is very important to talk to your healthcare provider about using factor VIII and factor IX products (products that help blood clot but work in a different way than HYMPAVZI). You may need to use factor VIII or factor IX medicines to treat episodes of breakthrough bleeding during treatment with HYMPAVZI. Carefully follow your healthcare provider's instructions regarding when to use factor VIII or factor IX medicines and the prescribed dose during your treatment with HYMPAVZI.

Before using HYMPAVZI, tell your healthcare provider about all of your medical conditions, including if you:
- have a planned surgery. Your healthcare provider may stop treatment with HYMPAVZI before your surgery. Talk to your healthcare provider about when to stop using HYMPAVZI and when to start it again if you have a planned surgery.
- have a severe short-term (acute) illness such as an infection or injury.
- are pregnant or plan to become pregnant. HYMPAVZI may harm your unborn baby.

  Females who are able to become pregnant:
  - Your healthcare provider will do a pregnancy test before you start your treatment with HYMPAVZI.
  - You should use effective birth control (contraception) during treatment with HYMPAVZI and for at least 2 months after the last dose of HYMPAVZI.
  - Tell your healthcare provider right away if you become pregnant or think that you may be pregnant during treatment with HYMPAVZI.
- are breastfeeding or plan to breastfeed. It is not known if HYMPAVZI passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription medicines, over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of HYMPAVZI?
HYMPAVZI may cause serious side effects, including:
- **blood clots (thromboembolic events).** HYMPAVZI may increase the risk for your blood to clot. Blood clots may form in blood vessels in your arm, leg, lung, or head and can be life-threatening. Get medical help right away if you develop any of these signs or symptoms of blood clots: swelling or pain in arms or legs; redness or discoloration in your arms or legs; shortness of breath; pain in chest or upper back; fast heart rate; cough up blood; feel faint; headache; numbness in your face; eye pain or swelling; trouble seeing
- **allergic reactions.** Allergic reactions, including rash and itching have happened in people treated with HYMPAVZI. Stop using HYMPAVZI and get medical help right away if you develop any of the following symptoms of a severe allergic reaction: swelling of your face, lips, mouth, or tongue; trouble breathing; wheezing; dizziness or fainting; fast heartbeat or pounding in your chest; sweating

The most common side effects of HYMPAVZI are injection site reactions, headache, and itching.

These are not all the possible side effects of HYMPAVZI. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

Please see Important Facts about HYMPAVZI on the next page or at www.HYMPAVZI.com

Pfizer

IMPORTANT FACTS

HYMPAVZI™
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Important information: Before you start using HYMPAVZI, it is very important to talk to your healthcare provider about using factor VIII and factor IX products (products that help blood clot but work in a different way than HYMPAVZI). You may need to use factor VIII or factor IX medicines to treat episodes of breakthrough bleeding during treatment with HYMPAVZI. Carefully follow your healthcare provider's instructions regarding when to use factor VIII or factor IX medicines and the prescribed dose during your treatment with HYMPAVZI.

What is HYMPAVZI used for?

HYMPAVZI is a prescription medicine used to prevent or reduce the frequency of bleeding episodes in adults and children 12 years of age and older with hemophilia A without factor VIII inhibitors or hemophilia B without factor IX inhibitors.

It is not known if HYMPAVZI is safe and effective in children younger than 12 years old.

What should I tell my healthcare provider before using HYMPAVZI?

Tell your healthcare provider about all your medical conditions, including if you:

- have a planned surgery. Talk to your healthcare provider about when to stop using HYMPAVZI and when to start it again if you have a planned surgery.
- have a severe short-term (acute) illness such as an infection or injury.
- are pregnant or plan to become pregnant. HYMPAVZI may harm your unborn baby.
  - **Females who are able to become pregnant:**
    - Your healthcare provider will do a pregnancy test before you start your treatment with HYMPAVZI.
    - You should use effective birth control (contraception) during treatment with HYMPAVZI and for 2 months after the last dose of HYMPAVZI.
    - Tell your healthcare provider right away if you become pregnant or think that you may be pregnant during treatment with HYMPAVZI.
- are breastfeeding or plan to breastfeed. It is not known if HYMPAVZI passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription medicines, over-the-counter medicines, vitamins, and herbal supplements.

How should I use HYMPAVZI?

See the detailed "Instructions for Use" that comes with your HYMPAVZI for information on how to inject a dose of HYMPAVZI, and how to properly throw away (dispose of) used HYMPAVZI prefilled syringe or HYMPAVZI prefilled pen.

- Use HYMPAVZI exactly as prescribed by your healthcare provider.
- Your healthcare provider will provide information on the treatment of breakthrough bleeding during your treatment with HYMPAVZI. **Do not** use HYMPAVZI to treat breakthrough bleeding.

What warnings should I know about HYMPAVZI?

HYMPAVZI may cause serious side effects, including:

- **blood clots (thromboembolic events).** HYMPAVZI may increase the risk for your blood to clot in blood vessels in your arm, leg, lung, or head and can be life-threatening. Get medical help right away if you develop any of these signs or symptoms of blood clots:
  - swelling or pain in arms or legs
  - redness or discoloration in your arms or legs
  - shortness of breath
  - pain in chest or upper back
  - fast heart rate
  - cough up blood
  - feel faint
  - headache
  - numbness in your face
  - eye pain or swelling
  - trouble seeing
- **allergic reactions.** Allergic reactions, including rash and itching have happened in people treated with HYMPAVZI. Stop using HYMPAVZI and get medical help right away if you develop any of the following symptoms of a severe allergic reaction:
  - swelling of your face, lips, mouth, or tongue
  - trouble breathing
  - wheezing
  - dizziness or fainting
  - fast heartbeat or pounding in your chest
  - sweating

The most common side effects of HYMPAVZI are injection site reactions, including:

- itching
- swelling
- hardening
- redness
- bruising
- pain

Headache and itching were also common side effects. A serious side effect of swelling in the legs happened in one patient in the clinical trial.

These are not all of the possible side effects of HYMPAVZI. Call your doctor for medical advice about side effects. For more information, ask your doctor.

This information is not comprehensive. How to get more information:

- Talk to your health care provider or pharmacist
- Visit www.HYMPAVZI.com to obtain the FDA-approved product labeling
- Call 1-888-HYMPAV-Z

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Pfizer

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LET'S PLAY NINE: 2023 AWARDEE UPDATE

BY SHELLY FISHER

Whether you're young or young at heart, there's something undeniably special about the game of golf. Unlike team sports, a golfer sets out with only his clubs, some tees, and favorite golf balls as his teammates, hoping to stay in the fairway, avoid the rough, and get a good read on the lie of the green.

There can be some conferring of club choice and approach among the friends riding in your golf cart or a caddie, if you have one, but ultimately, the golfer alone makes the ultimate decision on strategy. If it sounds a lot like life, that's because it is, and it's making a significant impact in the lives of preteens and teens with hemophilia B.

Recipients of the *Let's Play Nine Golf Scholarships* the Coalition for Hemophilia B offers to young golf enthusiasts with hemophilia B ages 7-19 can purchase golf lessons or clubs. In addition to providing an avenue for those young golfers already playing and excelling at the game, this scholarship is intended to foster a love of golf and encourage anyone interested in learning more about the sport. Please join us in congratulating our 2023 scholarship recipients! Let's find out where the game has taken them so far!

Ben continues to be an avid golfer and plays whenever he gets the chance at his local chapter on a course called the Fox Den. He loves Top Golf and thinks his coach, Golf Pro Evan, is "super cool." He felt that the CHB scholarship was "amazing" and elaborated on just what it meant to him to receive it. "Learning how to hit a ball and start learning the basic rules of golf made me feel so special. Many of my friends are on football and soccer teams, and golf helped me feel like I belonged somewhere, too! I even get to go golfing now with my cousin and my aunt!" Ben likes golf because "it helps me focus and use my big muscles," and he says his mom sees that he is "confident and happy" when he plays. He also has a special message for his mom: "I just wish she would take me to the range more so I can WHACK balls super far!" Ben's mom added, "I will never find words to express how thankful we are for the CHB."

For the past three years, Brayden has participated in the summer youth golf program through the Northern Ohio Hemophilia Foundation and enjoys playing at Fox Den. "Coach Rick has been great in teaching me the fundamentals of the game." The soon-to-be ninth grader also hits the driving range anytime he can and hopes to be on his high school team next year. Brayden was honored and excited to be awarded the CHB's scholarship and "a nice set of clubs" because golf "is a great way for me to stay physically active in a safe environment with my hemophilia. It's a sport that can last a lifetime." Brayden also likes the laid-back aspect of golf and shared his thoughts on why. "Being outdoors helps reduce stress and anxiety, and I enjoy focusing on the game in a relaxed environment."

Fifteen-year-old Brock is driving about 250 yards with the brand new King Cobra Aerojet driver he received thanks to the CHB scholarship, and as a result, he has placed in several tournaments this spring. Though he credits the club he received thanks to the CHB scholarship, Brock also shared that he "plays his own game and tries to focus on his swing." Brock enjoys the challenge of picking the

right club, reading the greens, "hitting the ball just right," and choosing the right strategy. He also shared that pushing the golf cart and walking the courses has improved his physical fitness and flexibility, giving him a lot of mental freedom to feel relaxed. Golf has also allowed Brock to make friends he can trust to be good sportsmen.

Collin is also still in the game and plays junior courses in Oklahoma City. While he doesn't have a coach yet, he takes advantage of all advice from his "PawPaw," a former Pinehurst Junior Champion. "I'm looking forward to my PawPaw visiting at the end of September so he can give me some more lessons." In his own words, he plays golf because "it's fun, teaches me patience, how to work hard and have discipline, make new friends, and make a lot more memories with my PawPaw." Winning the scholarship and getting his own set of clubs was uniquely special to Collin and his family since his grandfather is a retired golf professional living with hemophilia B who encourages Collin to live life at its fullest.

Hannah, a regular player at her local club, Buffalo Golf Club, participated in golf lessons all last summer and a junior tournament. "It just had one girl competing against me, and we had a great time!" She credits the scholarship for helping her get clubs sized just for her, making the game more enjoyable and making longer drives. She is also getting better at her irons.

New to the game of golf, Zak took his new clubs to the local golf course several times to hit balls on the range, and it inspired his parents to get clubs of their own. As a result, they now play as a family. Excited to win a set of new clubs from CHB, Zak plans to spend a lot of time on the course this summer, and his mom is already visiting with the coaches at his high school next school year. He shared this about golf, "I just love hitting the golf balls at the driving range with my family. I have invited my cousins to come along with us. They enjoy it just as much as I do. It's been a great opportunity for a family-friendly, fun, and relaxing activity we can all do together."

Though he's a full-time freshman in college, Andrew can't wait to get back on the course and have some fun. "I enjoy playing golf, knowing I have it all the time I want. It helps me relax my mind." He was glad he signed up for the scholarship and said, "It means a lot how caring (the CHB) are and how nice they are the whole time."

To the sponsors who made the stories of these young golfers possible, The Coalition for Hemophilia B would like to extend a heartfelt expression of gratitude: CSL BEHRING, MEDEXUS, NOVO NORDISK, CVS HEALTH, and THE WINGMAN FOUNDATION. Your generosity's impact is infinite in its possibilities and the lifelong pursuit of a time-honored and treasured pursuit-the game of golf.

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women & girls with hemophilia

articles to support, educate, and empower

Generations of Hemophilia, One Unstoppable Advocate: Debbie Murray

BY JENNIFER DEGLOPPER

Debbie Murray, 56, has lived a life deeply intertwined with hemophilia. Growing up, she witnessed it firsthand through her father, who lived with the disorder. For her family, hemophilia was simply part of everyday life.

The condition has been present across generations in her family tree: two great-uncles who passed away young from bleeds, a cousin from her father's generation who died as a toddler due to a bleed, another cousin who succumbed to hepatitis C around the age of 65, and yet another who died of HIV at just 30 years old. One cousin required a liver transplant due to hepatitis B. Debbie's father also passed at 65 from hepatitis C. Now, hemophilia continues in her family through herself, her sister, her son, her granddaughter, and her grandson.

Looking back on her childhood, Debbie sees how hemophilia affected her even then, long before her formal diagnosis. She recalls nights spent in tears from the relentless pain in her legs and ankles. Life on the family farm was active, and injuries, like hurting her elbow, took an unusually long time to heal. However, as a girl, her pain was often dismissed as drama.

When she began menstruating, the heavy bleeding, clots, and flooding seemed normal to her, simply because she didn't know otherwise. At the age of 17, Debbie underwent a tonsillectomy—a harrowing ordeal that left her vomiting blood and bleeding for days. She required three blood transfusions and was left anemic, yet her condition was dismissed as nothing unusual.

Throughout her life, more signs of hemophilia emerged. She experienced ongoing joint pain, excessive bleeding after dental procedures, and hemorrhaging during the births of her children. Her son's birth was particularly traumatic, as doctors struggled to stop the bleeding. Yet Debbie, focusing on her son's health and hemophilia diagnosis, put her own symptoms on the back burner.

Debbie had known since her early 20s that her Factor IX levels were abnormal—consistently ranging between 25 and 30 when tested before surgeries—but no provider had taken action. Her abnormal levels were noted, then dismissed, and she was sent off to undergo procedures

without any preventive treatment.

At the age of 35, Debbie underwent gallbladder surgery, which became a turning point. Complications lead to a hematoma that went untreated despite her repeated warnings about her low factor IX levels. The incident resulted in permanent nerve damage to her right leg. Seeking better care, she began looking for a hematologist who could help her prevent future complications.

Debbie spent two decades fighting for proper treatment. Doctors told her she would only need factor for a major procedure—something as extreme as open-heart surgery—despite her previous complications during gallbladder surgery.

Years later, when she returned to her home city, she received a dose of factor in 2019—but her care remained inadequate. That same year, she was finally diagnosed with hemophilia B. Even then, she was given only a single dose before surgery and denied any treatment to manage post-operative bleeding.

To make matters worse, she was expected to make the six-hour round trip to her treatment center each time she needed factor, with no option to store it at home—despite her extensive experience administering it, both as a patient and a registered nurse.

Still, Debbie pressed on, searching for a provider who would take her seriously. She was seen at another treatment center, but her doctor dismissed the idea that women might need factor. Another hematologist told her there was no literature supporting prophylactic treatment for women, that it was too expensive, and that her insurance likely wouldn't cover it—all of which turned out to be completely false. Once Debbie secured prior authorization, her insurance had no issue approving it.

She explored other options, but the barriers remained. Another center about six hours from home wasn't accepting new patients. And another – five hours away, was even more discouraging. When she inquired about care for women with hemophilia, the clinic's secretary bluntly told her that women couldn't have the condition. That conversation made it painfully clear: this was not the right place for her.

Her search eventually led her to see Dr. Danielle Nance—a specialist who became the first doctor to truly listen and fully recognize the extent of her condition. Dr. Nance identified signs of untreated bleeds just by looking at Debbie's left knee, which had long been a source of pain and limited mobility.

As she's grown older, Debbie has shifted her focus toward advocating for women and girls with bleeding disorders. Her determination

has only grown stronger as she watches her granddaughter, who also has hemophilia, deal with joint damage at just 13 years old due to inadequate treatment. Debbie has made it her mission to raise awareness, fight for better care, and ensure no other woman or girl feels dismissed or ignored. Along the way, she has found a supportive community of women who understand her struggles. Their camaraderie has been a source of strength and comfort.

Debbie recently appeared on a local TV station to raise awareness about women and girls living with hemophilia in honor of World Hemophilia Day, April 17, 2025. She has also been profiled on the website *Hemophilia News Today* and is an active voice on social media, regularly speaking out to educate and advocate for better care.

Beyond her advocacy work, Debbie treasures time with her family, including her husband of 36 years, Don, and their beloved grandchildren. She loves to travel, particularly to warm destinations, and enjoys spending time near the ocean. Her hobbies include gardening, kayaking, attending hockey and baseball games, and going to rock concerts—though she'll occasionally attend a country concert, too. She also loves crafting, reading, and cake decorating, having made wedding cakes for both her son and daughter. At home, Debbie is surrounded by her pets, including two dogs, two cats, and four bunnies, who have their own dedicated room in her house.

Debbie finds inspiration in her mother, who suffered a stroke when Debbie was just a baby. Despite significant mobility challenges, her mother has shown unwavering resilience and determination throughout her life. At nearly 81, she remains a powerful role model for Debbie, exemplifying the strength to overcome adversity.

Debbie's advice for women in the hemophilia community:

"Advocate for yourself fearlessly. Knowledge, connection, and persistence are key. Seek out reliable information, attend conferences, and lean on the support of the bleeding disorders community. If a doctor isn't listening or providing adequate care, don't settle—keep looking until you find one who does. You deserve to be heard, believed, and treated with respect. Never settle for less."

SHARE YOUR STORY

Are you ready to share your story and help others? Whether you have an incredible career, an extraordinary family, or a tale of triumph, we want to hear from YOU! You will collaborate with an in–house writer to help you communicate your story in a compelling and meaningful way. The best part is that no previous writing experience is necessary! To add your voice and share your insights with The Coalition for Hemophilia B, please contact us at contact@hemob.org.

Supporting our community is the foundation of **what we do**

That's why Novo Nordisk goes beyond offering a broad range of treatments and is dedicated to providing educational resources and one-on-one support!

We have **resources** for people living with:

- **Hemophilia A**
- **Hemophilia B**
- **Hemophilia A with inhibitors**
- **Hemophilia B with inhibitors**
- **Glanzmann's thrombasthenia when platelets don't work**
- **Factor VII deficiency**
- **Factor XIII A-subunit deficiency**

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HEMOPHILIA LANDSCAPE *UPDATES*

BY DR. DAVID CLARK

Cancer in People with Hemophilia and HIV Infection

10/31/24 A group in Japan looked at cancer in hemophilia patients infected with HIV, the AIDS virus. In data from 64 HIV-treatment centers, they found 328 patients with both hemophilia and HIV infection of which 35 developed cancers over the 8-year study period. The rationale for the study is that there had been no surveys of hemophilia/HIV patients during the time period since the development of antiretroviral therapy (ART) for HIV infection and direct-acting antivirals (DAAs) for hepatitis C. The study did not include cancers that are a direct result of AIDS, such as Kaposi's Sarcoma.

The 35 patients (seven or 20% with hemophilia B) had a median age of 51. Six percent reported heavy alcohol consumption and 18% were current smokers. All but one were co-infected with hepatitis C. The most common cancers were liver cancer (41% of patients) followed in order by colon cancer (14%), malignant lymphoma (9%), tongue cancer (6%) and papillary thyroid cancer (6%).

Metastasis (spread of cancer to other tissues) had occurred in 29% of the patients. After treatment 68% of the patients had complete remission, but 18% died.

The results suggest that all forms of cancer are about twice as common in hemophilia patients infected with HIV than in the general population. Liver cancer was about 23 times more common in these patients, possibly because of co-infection with hepatitis C, which is known to increase the risk. Interestingly, the percentage of heavy drinkers was relatively low at 6%, so the incidence of liver cancer could be even higher in other cultures that tend to drink more heavily. The incidence of colon cancer was only about 1.3 times that in the general population.

Papillary thyroid cancer was found in two of the 35 patients (6%). This is a fairly rare cancer, so finding it at all is surprising. The reason is unknown. The study also found that all of the cancers tended to occur in younger-than-expected patients. The authors conclude: "These findings emphasize the importance of cancer screening and preventive measures even in younger [patients with hemophilia and HIV] because early detection is crucial for addressing the elevated risk."

[Koga M et al., Glob Health Med, 6(5) 316-323, 2024]

Impact of Natural Variation in Clotting Factor Levels on Bleeding in Hemophilia

12/7/24 Why do two hemophilia patients with the same factor levels bleed differently? That's one of the big questions in hemophilia. One possibility is that the levels of other clotting factors and anticoagulants vary from person to person. We've seen from the work on rebalancing agents that varying the levels of anticoagulants can have a significant effect on clotting behavior. The same is probably true of the levels of the other clotting factors. At ASH, a group from the University of North Carolina explored that question.

In laboratory experiments with donated plasma, the researchers varied the levels of a number of clotting factors and inhibitors and found that indeed, the levels of many of those components significantly affected clotting times. They found that factors VIII and IX had the strongest correlation between clotting time and factor level, as might be expected since their absence causes hemophilia. Factor XII was next followed by factor XI, two clotting factors we don't talk about much. Factors XI and XII work near the beginning of the pathway that ends with factors VIII and IX activating factor X. They also found that levels of C1 esterase inhibitor, an inhibitor of both factors XI and XII had a significant effect, as would be expected. [ASH abstract 1202]

Epilepsy and Intracranial Hemorrhage

11/22/24 Intracranial hemorrhage (ICH) or bleeding in the brain is a serious complication of hemophilia. Even with the improved treatments available today, ICH still occurs in up to 11% of hemophilia patients, and also accounts for up to 18% of deaths in those patients. ICH is also one of the major causes of epilepsy, in general. However, there have been few studies of epilepsy as a complication of hemophilia. A group from Japan looked at the characteristics of epilepsy in five pediatric patients with hemophilia (3 As; 2 Bs) at their hospital. Four patients with epilepsy had a history of ICH, while the fifth patient had no clinical episodes but did show evidence of ICH revealed by MRI imaging studies. This represented about 10% of their total patients, which is consistent with the "up to 11%" stated above. Four patients had severe hemophilia, and all were less than two years of age.

In four patients ICH was identified before they were diagnosed with hemophilia. After diagnosis they were treated with factor concentrates or Hemlibra® (for the hemophilia A patients) and had no further episodes of ICH. Epilepsy was subsequently identified in two of the patients but was not diagnosed until several years after their ICH. The rate of epilepsy was significantly higher in the patients with ICH than in the other patients with hemophilia but no ICH. Except for epilepsy, no statistically significant neurological complications were observed in the five patients with ICH, although other studies have reported developmental delays and paralysis after ICH. This suggests that epilepsy can occur without additional neurological complications.

This was a small study but it points out that epilepsy is a complication that should be recognized in patients with hemophilia. It also shows the importance of early diagnosis since treatment can potentially reduce the incidence of ICH. Finally, imaging studies are important for patients with hemophilia and epilepsy, even in those without obvious clinical episodes of ICH. [Eguchi Y et al., Cureus, 16(11) e74261, 2024]

Ehlers-Danlos, Factor IX and Vitamin C

9/23/24 A few years ago, Kim Phelan pointed out to me that we seem to have a higher-than-expected number of members who have both Ehlers-Danlos Syndrome (EDS) and hemophilia B. I couldn't tell her why at the time, but recent research may be pointing to a cause. EDS is a connective-tissue disorder that is thought to be caused by mutations in the genes for collagen. Collagen is the main structural protein of the body. Our skin, bones and ligaments are made of collagen. The structural framework of our organs is made of collagen. Our blood vessels have a collagen framework that makes them strong. A common feature of EDS is being "double-jointed." Because of a mutated collagen gene, the ligaments (connective tissue) that hold the joints together ends up being stretchier, so the joint can bend further than normal.

We've also been learning that factor IX accumulates inside the walls of blood vessels where it binds to a type of collagen called collagen IV. That "extravascular" factor IX, factor IX residing outside the bloodstream, seems to be important for good clotting. Studies have shown that even if you have <1% of normal factor IX activity in your blood, you can still have fairly good clotting if there is enough factor IX inside the walls of the blood vessels. We don't know why this extravascular factor IX is important for clotting or how it does whatever it does, so this is a subject of much research interest.

EDS patients can have bleeding problems. One reason seems to be that the collagen mutations make the blood vessels weaker so they break more easily. However, that doesn't account for all their bleeding issues. Another idea is that a mutated collagen IV might lose its ability to bind factor IX, and thus the ability to let factor IX do whatever it does inside the blood vessel walls to promote clotting.

So, can any of this help us understand the "bleeding disorder of unknown cause" (BDUC) that predominantly affects women. These are people who don't clot properly but whose bleeding disorder isn't hemophilia A or B or any other known clotting factor deficiency, von Willebrand disease, a platelet disorder or anything else that we know. With the above background, a group of Danish researchers looked at BDUC and found that it is frequently associated with EDS and related connective tissue disorders.

Secondly, they also looked at vitamin C levels in people with BDUC. Vitamin C is something of an enigma. It was popularized years ago by Nobel prize winner Linus Pauling as kind of a cure-all. It probably isn't that, but one thing we know is that it is involved in the production of collagen. The researchers found that vitamin C levels were, in fact, lower in the BDUC/EDS patients. They propose a study of vitamin C supplementation in BDUC patients.

This is an exciting area of research. In addition to helping BDUC patients, findings could also help us understand hemophilia better. We know that about 15% of hemophilia patients don't fit into our current model of how clotting works, and this could shed some light on that. There is obviously a gap, probably several gaps, in our understanding of clotting that need to be filled in order to help BDUC patients and other patients with problematic bleeding disorders. Science often proceeds slowly, but at least we're on the way. [Leinøe E et al., Haemophilia, online ahead of print 9/23/24]

Bone Mineral Density and Hemophilia

We know that people with hemophilia have lower bone mineral density (BMD), which can lead to osteoporosis. We just don't know why. Two recent studies have looked at two different aspects of this condition.

11/12/24 A group from Germany looked to see whether there is a correlation between hemophilia severity and BMD. In 255 patients with hemophilia from a single treatment center, they found that 63% showed reduced BMD. The data were collected by dual x-ray absorptiometry (DXA) scans of the patient's femoral neck (the top of the thigh bone where it goes into the hip joint) and the lumbar (lower) spine. They found significantly lower BMD in patients with severe hemophilia than in mild patients. Moderate hemophilia patients were in between with BMDs not significantly different from either the severe or mild patients. Previous research has suggested that joint damage affects BMD and the results here were in agreement.

Interestingly, they found that the fracture risk in the patients with osteoporosis was actually lower than in the general population, although other studies have

shown the opposite. This concurs with a previous study that suggested than hemophilia patients have few bone fractures despite osteoporosis. The study showed little effect of HIV or HCV (hepatitis C virus) infection on BMD, although other studies have shown an effect. They also found that about 19.2% of subjects had a vitamin D deficiency, compared with 30.8% of the male German population. Vitamin D is important for bone health. The authors suggest routine screening for low BMD in hemophilia patients starting at age 30. [Ransmann P et al., Res Pract Thromb Haemost, online ahead of print 11/12/24]

10/23/24 A group of Italian researchers studied the effects of clotting factors on bone cells. Bone cells include osteoblasts, which continuously produce new bone, and osteoclasts, which continuously break down bone (resorption). Bone is continuously being formed and broken down, so the balance between the activities of these two cell types is important for bone health.

Their results showed that factor VIII, von Willebrand factor, activated factor X and thrombin can inhibit bone breakdown, which presumably leads to stronger bone. They found that activated factor IX had no effect on bone breakdown, which is in contrast to an animal study that showed that IX-deficient mice show reduced BMD and osteoporosis. This suggests that factor IX might have an effect on another part of the bone production/resorption process, rather than directly on bone cells. It has been suggested in other studies that factor IX does not have a direct effect. Instead, factor IX may help increase production of thrombin which then affects bone cells. [Battafarano G et al., Sci Reports, online ahead of print 10/23/24]

Characteristics of Hemophilia in Women

12/8/24 We don't know much about bleeding in women with hemophilia. They are estimated to comprise about one-third of all hemophilia patients but data in registries shows a proportion less than 10%. Thus, there is a lot of missing information which leads to inappropriate management and represents a healthcare disparity. A group at Yale did a retrospective analysis of patients from their center to help fill the gap in knowledge.

Using the ISTH classification scheme, female patients were classified as "carriers" if their factor levels were 40% or greater and as "women with hemophilia" if their levels were less than 40%. [Note that women have been reported to have bleeding issues even with levels into the 60+% range. In the US, 50% is considered the lower limit of the normal range while in the rest of the world, 40% is the lower limit of normal.] The subjects included women with either hemophilia A, B or C (factor XI deficiency), but here, we'll concentrate on the 16 women who either have hemophilia B or are carriers.

The average age at diagnosis was 16 years. 89% had mild hemophilia with 11% moderate or severe. 89% of the women with hemophilia B were treated at hemophilia treatment centers (HTCs), and 86% of the carriers. Common manifestations in the entire group (107 subjects with A, B or C) were easy bruising (53% of the group), heavy menstrual bleeding (46%), iron deficiency anemia (45%) and epistaxis (nosebleed, 25%). Post-partum hemorrhage was reported in 10% of the group and miscarriage in 33%. About 42% of the B carriers used clotting factor treatment as did 67% of the Bs with hemophilia. Anti-fibrinolytics (like Amicar) were used by 57% of the B carriers and 67% of the Bs with hemophilia.

The authors conclude that the study highlights the significant bleeding issues in females with hemophilia as well as in carriers, and that those issues are much worse than in the general population. They point out substandard care for carriers and women with hemophilia, especially concerning reproductive care. They advocate for higher inclusion of women in hemophilia registries and clinical studies. [ASH abstract 2584]

12/8/24 A similar study from the University of Pittsburgh focused only on hemophilia B. Their group of 129 subjects included 89 Amish women who all share the same factor IX mutation. They found a low correlation of bleeding with factor IX level with an R2-value of 0.16. That means that only about 16% of the observed bleeding cases could be explained by factor level, which is consistent with other studies of bleeding in females.

One of the surprising findings was that they saw the same high variability between factor level and bleeding rate in the Amish women, who are a fairly homogeneous population. This all suggests that we are really missing one or more factors that affect bleeding in women, and possibly in men, too. They also found a high prevalence of iron deficiency with 93% of the subjects with ferritin (the protein that carries iron around the bloodstream) levels below 50 ng/ml. They recommend routine ferritin screening in women regardless of factor level. [ASH abstract 2586]

History of Hemophilia in Women

12/13/24 Where did the idea that hemophilia doesn't affect women come from? Now we know. A group of Canadian hemophilia treaters has just published a study on the history of hemophilia in women. The culprit was a German physician named Christian

Friedrich Nasse (1778 – 1851). In 1820, he published Nasse's Law which states, "women of bleeding families, although they marry men from normal families, carry the disease over from their own fathers to their children, and yet never suffer from the disease themselves." Not a hypothesis, not a conjecture, not a theory, but a full-blown law!

We can't just blame Nasse, though. He has had plenty of support from his colleagues for 200 years. Reading this article is fascinating, but also depressing. It details 200 years of men's arrogance and their prejudice against and mistrust of women. The article is open access (free) and easy for the lay person to read. See the reference at the end of this report.

The authors of the study identified nine different eras in the history, starting with the 1800s – 1920. Another physician, John Conrad Otto did write, "when the cases shall become more numerous, it may perhaps be found that the female sex is not entirely exempt." In 1886, we see the first report of an affected woman. That case was heavily disputed at the time and largely dismissed, but re-evaluation of the same patient 50 years later proved it to be correct.

By the 1920 – 1940 era, as knowledge of genetics increased, researchers realized that a woman with two affected X-chromosomes (homozygous) could have hemophilia and the race was on to find one. They looked at hemophilia families and found a lot of women with bleeding issues. However, the focus at the time seemed to be on preventing these women from having children rather than a concern for the women's own health. Ostler's 1935 textbook on medicine states, "The women of bleeder families should not marry or marrying, they should not bear children. Males may marry safely."

Things started to get better in the 1940 – 1960 era when we could actually measure factor levels in patients, but there was still prejudice and mistrust against women. A 1956 article reported, "However, such women [from hemophilia families] are of course likely to be acutely aware of bleeding phenomena and may exaggerate otherwise unremarkable symptoms." Maybe it's the doctors who need to be made more aware of bleeding phenomena! Science advances, so prejudice has to take a new tack.

The article goes on through six more eras up until the present day. The story is slowly getting better, but the authors still report for the present day, "However in parallel with advances, we see other reports that females affected by hemophilia continue to be undertreated, experience ongoing symptom dismissal, have limited access to specialized care and are excluded from most major clinical trials." Science doesn't seem to be the problem here. [Chaigneau M et al., J Thromb Haemost, online ahead of print 12/13/24. The easiest way to find a copy is to use the DOI identifier. Just Google: "DOI:10.1016/j.jtha.2024.12.004"]

RIXUBIS® [Coagulation Factor IX (Recombinant)] Important Information

What is RIXUBIS?

RIXUBIS is an injectable medicine used to replace clotting factor IX that is missing in adults and children with hemophilia B (also called congenital factor IX deficiency or Christmas disease).

RIXUBIS is used to control and prevent bleeding in people with hemophilia B. Your healthcare provider may give you RIXUBIS when you have surgery. RIXUBIS can reduce the number of bleeding episodes when used regularly (prophylaxis).

Detailed Important Risk Information for RIXUBIS® [Coagulation Factor IX (Recombinant)]

Who should not use RIXUBIS?

You should not use RIXUBIS if you

- are allergic to hamsters
- are allergic to any ingredients in RIXUBIS.

Tell your healthcare provider if you are pregnant or breastfeeding because RIXUBIS may not be right for you

What should I tell my healthcare provider before using RIXUBIS?

You should tell your healthcare provider if you

- have or have had any medical problems
- take any medicines, including prescription and non-prescription medicines, such as over-the-counter medicines, supplements or herbal remedies
- have any allergies, including allergies to hamsters

What should I tell my healthcare provider before using RIXUBIS? (cont'd)

- are breastfeeding. It is not known if RIXUBIS passes into your milk and if it can harm your baby
- are pregnant or planning to become pregnant. It is not known if RIXUBIS may harm your unborn baby
- have been told that you have inhibitors to factor IX (because RIXUBIS may not work for you).

What are the possible side effects of RIXUBIS?

Allergic reactions may occur with RIXUBIS. Call your healthcare provider or get emergency treatment right away if you get a rash or hives, itching, tightness of the throat, chest pain or tightness, difficulty breathing, lightheadedness, dizziness, nausea, or fainting.
Some common side effects of RIXUBIS were unusual taste in the mouth and limb pain.

Tell your healthcare provider about any side effects that bother you or do not go away.

Your body may form inhibitors to factor IX. An inhibitor is part of the body's defense system. If you form inhibitors, it may stop RIXUBIS from working properly. Consult with your healthcare provider to make sure you are carefully monitored with blood tests for development of inhibitors to factor IX.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see RIXUBIS Important Facts on the following page and discuss with your healthcare provider.

RIXUBIS
[COAGULATION FACTOR IX (RECOMBINANT)]
MOVING FORWARD

Important facts about RIXUBIS®:

RIXUBIS
[COAGULATION FACTOR IX (RECOMBINANT)]

This leaflet summarizes important information about RIXUBIS. Please read it carefully before using this medicine. This information does not take the place of talking with your healthcare provider.

What is RIXUBIS used for?

RIXUBIS is a medicine used to replace clotting factor (Factor IX) that is missing in people with hemophilia B. Hemophilia B is also called congenital factor IX deficiency or Christmas disease. Hemophilia B is an inherited bleeding disorder that prevents blood from clotting normally. RIXUBIS is used to prevent and control bleeding in people with hemophilia B. Your healthcare provider may give you RIXUBIS when you have surgery. RIXUBIS can reduce the number of bleeding episodes when used regularly (prophylaxis).

Who should not use RIXUBIS?

You should not use RIXUBIS if you
- are allergic to hamsters
- are allergic to any ingredients in RIXUBIS

Tell your healthcare provider if you are pregnant or breastfeeding because RIXUBIS may not be right for you.

What should I tell my healthcare provider before using RIXUBIS?

You should tell your healthcare provider if you
- have or have had any medical problems
- take any medicines, including prescription and non-prescription medicines, such as over-the-counter medicines, supplements or herbal remedies
- have any allergies, including allergies to hamsters
- are breastfeeding. It is not known if RIXUBIS passes into your milk and if it can harm your baby
- are pregnant or planning to become pregnant. It is not known if RIXUBIS may harm your unborn baby
- have been told that you have inhibitors to factor IX (because RIXUBIS may not work for you).

What is the most important information I should know about RIXUBIS?

Allergic reactions have been reported with RIXUBIS. Stop using the product and call your healthcare provider or get emergency treatment right away if you get a rash or hives; rapid swelling of the skin or mucous membranes; itching; tightness of the throat; chest pain or tightness; wheezing; difficulty breathing; low blood pressure; lightheadedness; dizziness; nausea; vomiting; tingling, prickling, burning, or numbness of the skin; restlessness; or fainting.

Your body may form inhibitors to factor IX. An inhibitor is part of the body's defense system. If you form inhibitors, it may stop RIXUBIS from working properly. Consult with your healthcare provider to make sure you are carefully monitored with blood tests for the development of inhibitors to factor IX.

The use of factor IX containing products has been associated with the development of blood clots. Talk to your doctor about your risk for potential complications and whether RIXUBIS is right for you.

What are the possible side effects of RIXUBIS?

Some common side effects of RIXUBIS were unusual taste in the mouth, limb pain, and atypical blood test results. Tell your healthcare provider about any side effects that bother you or do not go away. These are not all the side effects possible with RIXUBIS. You can ask your healthcare provider for information that is written for healthcare professionals.

Consult with your healthcare provider to make sure your factor IX activity blood levels are monitored so they are right for you.

You should be trained on how to do infusions by your healthcare provider or hemophilia treatment center. Many people with hemophilia B learn to infuse their RIXUBIS by themselves or with the help of a family member.

Call your healthcare provider right away if your bleeding does not stop after taking RIXUBIS.

Medicines are sometimes prescribed for purposes other than those listed here. Do not use RIXUBIS for a condition for which it is not prescribed. Do not share RIXUBIS with other people, even if they have the same symptoms that you have.

The risk information provided here is not comprehensive. To learn more, talk about RIXUBIS with your healthcare provider or pharmacist. The FDA-approved product labeling can be found at https://www.shirecontent.com/PI/PDFs/RIXUBIS_USA_ENG.pdf or by calling 1-877-825-3327.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

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Takeda

HEMOPHILIA LANDSCAPE EMERGING THERAPIES

BY DR. DAVID CLARK

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There is a huge amount of new product development happening in hemophilia B. The potential new products can be separated into three categories: 1) improved factor products, 2) rebalancing agents, and 3) gene therapy. These updates are divided into those three categories. Within each category, the entries are generally listed in order of the names of the organizations developing the product.

A number of the items below were presented at the American Society of Hematology (ASH) annual meeting on December 7 – 10, 2024, in San Diego. Copies of the abstracts (summaries) for the presentations are available for free at https://www.hematology.org/meetings/annual-meeting/abstracts.

IMPROVED FACTOR PRODUCTS

These are improved versions of the factor products that most people with hemophilia B are currently using, and they also include products for inhibitor treatment. The improvements include longer half-lives and delivery by subcutaneous injection. This section also contains updates on some of the current products on the market.

CSL Reports on Real-World Use of Idelvion®

12/5/24 CSL Behring markets Idelvion®, an extended half-life recombinant factor IX product for treating hemophilia B. At ASH, they discussed interim results from their ongoing ORPHEE study in France that follows a group of hemophilia B patients using Idelvion® for routine prophylaxis, one-time use for surgery, or on-demand treatment. In 77 patients on prophylaxis, including 62 severes, they found an annualized bleed rate (ABR) of 0.5 (range 0.0 – 1.9) for all bleeds and zero (0.0 – 0.7) for spontaneous bleeds. The average weekly consumption of factor IX was 43 (35.5 – 53.0) IU/kg. Among 43 patients who had previously been treated with Alprolix, 21 patients were able to increase their infusion interval from 7 days to 14 days. Thirty-three (77%) of those 43 patients reduced their weekly factor IX consumption from 59.95 to 42.5 IU/kg. All patients maintained good bleed protection. [Volot P et al., Eur J Haematol, online ahead of print 12/5/24]

HEMA Shows Sevenfact® Reduces Pain from Bleeding Episodes in Inhibitor Patients

12/9/24 HEMA Biologics distributes Sevenfact®, an activated factor VII treatment for hemophilia A and B patients with inhibitors made by LFB, a French pharmaceutical company. An international group of researchers who had participated in the PERSEPT 1 study supporting licensure of the product did an after-the-fact analysis of the effect of Sevenfact® treatment on pain.

For 468 bleeding episodes in five adolescents and 22 adults, they observed pain relief at 12 hours after the initial infusion, with further pain decreases observed at 24 hours. Using a 100-point pain scale, they found pain scores ranging from 26.5 to 45.3 before treatment. At 12 hours after the initial infusion the scores had dropped to 1.1 to 11.2. At 24 hours, the mean pain scores again decreased, falling to values varying from 0.0 to 3.8. [ASH abstract 3972]

SeraGene Reports on siRNA Targeting Plasminogen

12/9/24 SeraGene Therapeutics, a Canadian company, is developing siPLG, a silent interfering RNA (siRNA) treatment to inhibit the production of plasminogen to promote clot formation. Fibrinolysis is the process that breaks down a clot during the healing process. Fibrinolysis begins at the same time that clot formation begins. Fibrinolysis starts slowly but continues throughout the healing process. In a person with a normal clotting system, the clotting process overwhelms the fibrinolysis process at first so that a good clot can be formed to stop bleeding. However, in a person with hemophilia, even a small amount of fibrinolysis during clot formation can be too much of an obstacle to clot formation.

The enzyme that breaks down the clot is called plasmin. Its precursor, plasminogen, binds to the fibrin in a growing clot. Binding to the clot changes the shape of plasminogen and makes it susceptible to several other enzymes in the clotting system that can activate it to form plasmin. People with hemophilia often use tranexamic acid (Cyklokapron or Lysteda) or

aminocaproic acid (Amicar) to treat minor bleeds. Those molecules bind to plasminogen and keep it from being activated to form plasmin. Inhibiting plasmin formation protects the growing clot from immediate degradation. This is often enough to allow the formation of an adequate clot, especially in people with milder forms of hemophilia.

SeraGene's siPLG doesn't inhibit plasmin formation; it keeps plasminogen from being made in the first place. This is similar to how fitusiran, a rebalancing agent under development, keeps antithrombin from being made. To make any protein, a cell makes a messenger RNA (mRNA) template of the gene for that protein. That mRNA is then secreted from the cell's nucleus and taken up by the protein-producing mechanism in the central part of the cell. siRNAs bind to the mRNA to interfere with the production of the protein.

At ASH, SeraGene reported on experiments with siPLG in non-human primates (NHPs), following up on previous experiments in hemophilic dogs. Using an intravenous infusion of siPLG contained in lipid nanoparticles, they found that they could eliminate 70% of plasminogen production without producing symptoms of plasminogen deficiency (plasminogen has other jobs in the body besides clot breakdown). They also found that clots produced by the treated NHPs had improved stability, suggesting that the method might help in hemophilia. These results support the continued development of siPLG. [ASH abstract 3959]

Staidson Reports on Factor X Activator for Inhibitor Treatment

12/7/24 Staidson, a Chinese biotech, is developing STSP-0601(bemiltenase alfa) to treat A and B patients with inhibitors. Bemiltenase, which is purified from the venom of the Siamese Russell's Viper snake, is a known molecule that activates factor X. Russell's Viper venom has been used for decades in laboratory assays of factor X and other clotting factors. Staidson has purified bemiltenase from the venom and used it to create a clinical-use product with a half-life similar to that of NovoSeven®. Activated factor VII products like NovoSeven® work by directly activating factor X in the clotting cascade, bypassing the factor VIII/IX steps that normally activate factor X.

Their Phase I study in 70 patients with 334 bleeding events found good bleeding protection at two different doses of STSP-0601. They found no serious adverse events, although four (out of 37) subjects in the higher dose group experienced signs of thrombosis. The results are encouraging, and the development of STSP-0601 will continue. [ASH abstract 1213]

REBALANCING AGENTS

Rebalancing agents tweak the clotting system to restore the balance so the blood clots when it should and doesn't clot when it shouldn't. The clotting system is a complex system of clotting factors that promote clotting, plus anticoagulants that inhibit clotting. In a person without a bleeding disorder, the system is in balance, producing clots as needed. In hemophilia, with the loss of some clotting factor activity, the system is unbalanced; there is too high a level of anticoagulant activity keeping the blood from clotting. Rebalancing agents mainly reduce or inhibit the activity of anticoagulants in the system. Most of these agents help restore clotting in people with hemophilia A or B, with or without inhibitors.

Centessa Halts Development of SerpinPC

11/12/24 Centessa Pharmaceuticals has been developing SerpinPC, a rebalancing agent that inhibits activated protein C, an anticoagulant. The product was being tested in several Phase II clinical studies with good results. However, Centessa has decided to discontinue the project for two main reasons. First, with Hympavzi™ and Alhemo® recently licensed and Fitusiran on the verge of licensure, the rebalancing agent field is rapidly filling up with more high-powered companies that would be a challenge to market against. Second, Centessa has products in development for other rare diseases that they can now give more attention to. They will probably try to sell or license SerpinPC to another company. [Centessa 3rd Quarter Financial Report 11/12/24]

Novo's Alhemo® Licensed in the US for Inhibitor Patients

12/20/24 Novo Nordisk has been developing Alhemo® (concizumab), an inhibitor of the anticoagulant tissue factor pathway inhibitor (TFPI), as a rebalancing agent. Concizumab is a daily subcutaneous injection for treating hemophilia A and B patients, with or without inhibitors. The FDA has now approved Alhemo® for treating hemophilia A and B patients 12 years or older, but only for those with inhibitors. This approval should represent a significant advance in treatment for inhibitor patients, who currently suffer from few good treatment options. [Novo press release 12/20/24]

There are now two rebalancing agents approved in the US, Alhemo® and Pfizer's Hympavzi™, both anti-TFPI agents. A third, Sanofi's fitusiran, which limits antithrombin production, is also expected to be licensed this spring. Pfizer and Novo took different paths to licensure. Pfizer first focused on non-inhibitor patients, possibly to make sure they were first to market, an important goal in pharmaceutical development. Novo, already known as a supplier of inhibitor treatment products because of their

NovoSeven®, instead focused first on the smaller inhibitor market. Both products will probably be licensed for both inhibitor and non-inhibitor patients in the near future.

11/6/24 Novo has now published the complete Phase III study data analysis for patients without inhibitors. An accompanying editorial was also published in the print edition of The Lancet. [Chowdary P et al., The Lancet, online before print 11/6/24, corrected 12/3/24. Editorial: Mancuso ME, The Lancet, 11(12), e880-e881, 2024]

12/8/24 At ASH, Novo reported the results for patients in the lead-in study before receiving Alhemo® treatment. Companies often employ lead-in studies in a small field like hemophilia, where it is difficult to get enough patients to provide a separate control (comparison) group for studies. The study subjects become their own control group. They will be followed, for instance, for six months while they are on their previous treatment. That produces enough data to act as a baseline for comparison with the new treatment results.

The study included 231 patients from 109 clinical centers in 33 countries: 138 subjects without inhibitors (70 As; 68 Bs) and 80 subjects with inhibitors (49 As; 31 Bs). Most subjects had severe hemophilia. For subjects without inhibitors, the average ABR for on-demand patients was 21.5 for hemophilia A and 10.5 for hemophilia B. For non-inhibitor patients on prophylaxis, the respective ABRs were 4.7 and 2.2. For patients with inhibitors, the average ABRs were 15.2 (As) and 9.3 (Bs) for on-demand treatment and 10.3 and 12.4 for prophylaxis, respectively.

Physical activity levels were similar for all patients, but those for Bs with inhibitors were the lowest. Average Hemophilia Joint Health Scores (HJHS) were lowest (better) for patients on prophylaxis: 16.2 for the As and 8.8 for the Bs. For on-demand treatment, the average scores were 25.1 for As and 31.0 for Bs. Interestingly, HJHS scores were similar for Bs with inhibitors, whether on prophylaxis (23.7) or on-demand treatment (22.3). Before therapy with Alhemo® was started, these data provided a good snapshot of the condition of the "typical" severe hemophilia patient. [ASH abstract 2585]

12/9/24 Novo continued reporting their study data in another session, looking at inhibitor patients with or without target joints. Patients with target joints had an average ABR of 10.6 pre-treatment, which declined to 1.7 after 32 weeks on Alhemo®. Patients without target joints had an average ABR of 9.0 pre-treatment, which was reduced to 0.9 after 32 weeks on Alhemo®. By the 56-week cutoff, 92% of target joints had resolved (no longer a target joint). Low ABRs continued on Alhemo®, and there were no new safety issues. [ASH abstract 715]

12/9/24 Rebalancing agents work for both hemophilia A and B, and it is probable that they could also help patients with other rare bleeding disorders, including bleeding of unknown cause. A group from Spain and the Netherlands looked at the use of Alhemo® in such cases. Starting with a group of 247 patients who had experienced bleeding episodes, they identified 47 patients with bleeding disorders of unknown cause (BDUC). The others had identifiable bleeding causes such as hemophilia or platelet disorders.

In those 47 patients (14 men and 30 women), only three patients did not respond to Alhemo® or factor VIIa. Interestingly, they found that many of the patients had high tissue factor pathway inhibitor (TFPI) levels in their blood. Thus, high TFPI levels may be implicated in some BDUC cases, and Alhemo®, which inhibits TFPI, may be a suitable treatment for these patients. [ASH abstract 3977]

Pfizer Presents New Studies on Hympavzi™

Pfizer markets Hympavzi™ (marstacimab), an inhibitor of the anticoagulant tissue factor pathway inhibitor (TFPI), which was recently approved as a rebalancing agent. Hympavzi™ is a once-weekly subcutaneous injection delivered via a pre-filled syringe or auto-injector pen for treating hemophilia A and B patients without inhibitors. The product is expected to work equally well for inhibitor patients but has not yet been licensed for that indication. At ASH, they presented the results of three studies.

12/7/24 They reported on the safety of Hympavzi™ in their Phase III licensure study. In 116 patients, both As and Bs without inhibitors, treated for approximately 12 months, hemoglobin and hematocrit (the proportion of red blood cells in your blood) either remained stable or improved. Fibrinogen levels in most patients showed a slight decrease, as did platelet counts, but they remained in the normal range. Most patient's liver function tests remained stable, although two patients developed hyperbilirubinemia, an increase in the protein bilirubin in the blood, which suggests a breakdown of red blood cells. These and other laboratory test abnormalities were not considered clinically significant or reported as adverse events. [ASH abstract 1210]

12/7/24 They also reported on the effect of patient weight on the dose of Hympavzi™. Using patient data from the Phase II and III studies, they did computer analyses that showed that Hympavzi™ could be dosed on a weight-independent basis in most patients. All patients could be treated with the same dose regardless

of their weight. Annualized bleeding rate (ABR) appears independent of dose, and no thromboembolic events were observed in any patient. The likely explanation is that Hympavzi™ is already at its concentration of maximum effectiveness even at the lower doses, so the additional product does not make much difference. [ASH abstract 1215]

12/9/24 A third study examined the nature of bleeds encountered during Hympavzi™ prophylaxis. In the same group of subjects examined above, at baseline (before starting to receive Hympavzi™), 69.5% of the subjects had one or more target joints. A target joint experiences repeated bleeds. The usual definition is a joint with at least three spontaneous bleeds within six months. The total number of bleeds during the six-month lead-in period before Hympavzi™ treatment was 1312, of which 1114 were treated with factor. The total bleeds during the twelve-month treatment period was 687, of which 504 were treated. Most bleeds were spontaneous and occurred in joints rather than soft tissue. The most common sites of joint bleeds were the foot/ankle, elbow, and knee. [ASH abstract 716]

Sanofi Provides Updates on Firusiran

Sanofi is developing fitusiran, a silent interfering RNA treatment that inhibits the production of antithrombin (AT), an anticoagulant. Fitusiran is a monthly subcutaneous injection for treating hemophilia A and B patients, with or without inhibitors. Approval is currently pending in the US, and a decision is expected from the FDA in late March 2025.

12/6/24 Sanofi has published their Phase II clinical study results, which spanned the changeover from a fixed-dose regimen to a dosing strategy based on the patient's actual AT levels. The change occurred after thrombotic events occurred in some patients on the fixed-dose regimen. In those patients, the fixed-dose apparently led to too-low AT levels, which predisposed the patients to thrombosis (too much clotting). They observed that the median ABRs were comparable for the fixed-dose (ABR: 0.70) and AT-based (0.87) doses. [Pipe SW et al., Blood Adv, online ahead of print 12/6/24]

12/7/24 All of the rebalancing agents still leave the possibility of experiencing breakthrough bleeds. Determining the best method for treating those bleeds is essential for all the products. Breakthrough bleeds must all be treated with clotting factor or bypassing agent (for inhibitor patients); additional doses of the rebalancing agent are ineffective and could lead to thrombosis. In addition, with the clotting factor/anticoagulant balance in the clotting system modified, lower doses of clotting factor or bypassing agent (for inhibitor patients) may be required to treat the bleed while again preventing thrombosis. At ASH, Sanofi presented the results of a study on treating breakthrough bleeds for patients on fitusiran. They found that most breakthrough bleeds could resolve with one reduced dose of clotting factor or 1 – 2 doses of bypassing agent for inhibitor patients. [ASH abstract 128]

12/8/24 Although AT is the major inhibitor of thrombin, and thus of clotting, there are other thrombin inhibitors in plasma whose action becomes more important when AT levels are reduced. These include heparin cofactor II (HCII), α-1-protease inhibitor (α1PI), and α-2-macroglobulin (α2M). Laboratory studies at the University of North Carolina presented at ASH showed that HCII and α1PI only had minimal effect on thrombin generation at low levels of AT, while α2M appeared to play a dominant role. Therefore, the activity of α2M has to be included in models used to predict the effects of fitusiran. [ASH abstract 2577]

12/8/24 Doses of the rebalancing agents do not correspond directly to levels of clotting factors. For instance, with fitusiran, what level of residual AT in a hemophilia B patient would give bleeding protection comparable to a 100% factor IX level? This is another question that the producers of rebalancing agents have to explore. At ASH, Sanofi presented an updated mathematical model developed to answer that question.

Sanofi had previously developed a model for hemophilia A that was unique in that it included the effects of α-2-macroglobulin (α2M), a protein that, like antithrombin, can inactivate thrombin and thus inhibit clotting. As described in the above study, at reduced AT levels, the effects of α2M become more pronounced and can't be neglected. With the model's success for hemophilia A, Sanofi has modified it to predict clotting in hemophilia B patients on fitusiran. The model shows that the clotting produced at reduced AT levels of 15 – 35% is equivalent to that produced by factor IX levels of 20 – 40%. The results from the patients in the clinical studies support these results. [ASH abstract 2590]

Vega Therapeutics Developing a Protein S Inhibitor as a Rebalancing Agent

12/9/24 Vega Therapeutics was spun out of its parent company, Star Therapeutics, to develop a rebalancing agent to treat bleeding disorders. Vega's lead candidate, VGA039, an inhibitor of the anticoagulant protein S, has been shown in preclinical studies to promote clotting in various bleeding disorders. Because a number of companies are already targeting their rebalancing agents toward hemophilia, Vega decided to look at von Willebrand Disease (vWD). Since VGA039 could also work for hemophilia B, we'll continue to follow its progress.

At ASH, Vega reported their Phase Ia clinical study looking at increasing doses of VGA039. They reported results in six vWD patients receiving two different doses of VGA039. The product was well-tolerated with no adverse events, thrombotic reactions, or injection site reactions. They saw increased thrombin generation at both doses, suggesting the VGA039 should increase clot formation with weekly subcutaneous dosing. Further studies are being planned. [ASH abstract 3981]

GENE AND CELL THERAPY

Gene therapy is the process of inserting new, functional factor IX genes into the body to allow it to produce its own factor IX. Cell therapy is the transplantation of whole cells modified to perform a specific function, such as producing factor IX.

Be Bio Reports on Phase I/II Gene Therapy Study

12/8/24 Be Biopharma is developing BE-101, a cell therapy for hemophilia B in which a patient's B cells are genetically modified to produce factor IX. The treatment involves harvesting B cells from the patient's bloodstream and then modifying them in the laboratory to contain a factor IX gene. They plan to use the higher-activity Padua gene, which is also used in most other gene therapies. The modified B cells are then transplanted back into the patient's bloodstream. The modified B cells are expected to engraft permanently in the bone marrow, where they will continuously produce factor IX. They described their Phase I/II clinical study at ASH to test the product.

The Phase I/II study will have two parts. Part 1 will be a dose-escalation study to find the optimum dose to produce a factor IX level of 15% or higher in up to 18 subjects with severe or moderately severe hemophilia B. Part 2 will then treat up to six patients at the selected dose to look further at safety and factor IX production. Future studies will include adolescents and additional doses. The duration of this initial study is 52 weeks. The study is now recruiting patients. [ASH abstract 2593.1]

Biocad Starts Phase III Study of Russian Gene Therapy

11/27/24 Biocad, a Russian biotech, is developing ANB-002, an AAV5-based gene therapy for hemophilia B. After successful Phase I/II studies, they have permission from the Russian Ministry of Health to conduct a Phase III study. They include subjects with risk factors that may diminish the effectiveness of the gene therapy, such as antibodies to AAV5 and/or a history of hepatitis B. They hope to be able to reach more patients, many of whom have been unable to receive gene therapy. No further information is available at this time. [GXP News article, 11/27/24]

Chinese Group Studies Activated Factor X Production with Gene Therapy

9/10/24 A group in China is studying gene therapy to produce activated factor X (FXa) for treating hemophilia A or B patients with inhibitors. Inhibitor patients have developed antibodies (inhibitors) against factor VIII or IX, which prevents them from being treated with normal clotting factor products. These patients are often treated with bypassing agents such as activated factor VII (FVIIa), which directly activates factor X, bypassing the factor VIII/IX step in the clotting cascade.

Why don't we use FXa directly instead of FVIIa to activate FX? One good reason is that FXa only has a half-life of about 2.7 seconds in the bloodstream! However, several longer-acting factor X molecules have been developed recently and have shown good efficacy and safety in clinical studies. The Chinese group is exploring using one of these longer half-life FXa molecules as a gene therapy to produce FXa in the body continuously.

The issue they are trying to solve is that we don't know what would happen if an inhibitor patient were given the current factor VIII or IX gene therapies. If a hemophilia B inhibitor patient were given factor IX gene therapy, their liver would start cranking out factor IX into their bloodstream. However, their immune system would also start producing antibodies against factor IX. There could be a "war" between the liver-producing factor IX and the immune system trying to eliminate that factor IX.

We don't know which would win, but if the immune reaction becomes strong enough, the resulting inflammation could cause a lot of damage. However, note that some animal data suggests that gene therapy might actually tolerize the patient toward factor IX, but we don't know for sure. An FXa gene therapy could potentially help an inhibitor patient without the danger.

The researchers have shown that their method works in hemophilic mice with inhibitors. The gene therapy significantly improved clotting in the mice. Interestingly, they also showed that if they injected their gene therapy into the joints of the mice, they could induce FXa production within the joint and alleviate the occurrence of synovitis. [Zhang F et al., Gene Therapy, online ahead of print 9/10/24]

CSL Reports on the Cost-Effectiveness of Hemgenix®

12/2/24 CSL Behring markets Hemgenix®, a gene therapy for hemophilia B that is delivered by an adeno-associated virus (AAV) vector and uses the Padua high-activity factor IX gene. A recent publication looked at the cost-effectiveness of Hemgenix® compared to conventional factor IX prophylaxis. Using a computer simulation, the authors found that the $3.5 million product led to a lifetime cost savings of $11 million compared to factor IX prophylaxis.

The study also predicted that patients would receive an additional 0.64 quality-adjusted life-years (QALYs). QALYs are used in economic evaluations and insurance programs to determine the value of treatments. One QALY is equivalent to one year of life in perfect health. Therefore, the additional 0.64 QALY would correspond to 0.64 years longer life or to one year of longer life at 64% of perfect quality of life, or any combination in between. [Sarker J et al., Appl Health Econ Health Policy, online ahead of print 12/2/24]

11/18/24 Gene therapy has not taken off as much as the companies had hoped, and some companies are rethinking their commitment to gene therapy. CSL is part of this trend and has decided to shut down its gene and cell therapy R&D lab in Pasadena, CA. Some gene and cell therapy R&D staff will relocate to CSL's lab in Waltham, MA. These changes will have no impact on Hemgenix®. [Fierce Biotech article, 11/18/24]

Indian Researchers Developing Lipid Nanoparticle-Delivered Gene Therapy

11/9/24 A group of researchers in India is developing a gene therapy delivered by lipid nanoparticles (LNPs) rather than AAV viruses. The AAV virus particles that deliver all three current hemophilia gene therapies, two for hemophilia B and one for hemophilia A, are plagued by interactions with the immune system. One of the immune system's main jobs is to defend the body against viruses.

When a patient gets an infusion of AAV-based gene therapy, their immune system goes to work immediately to fight off that potential "infection." The three licensed treatments get around this by infusing so many viral particles that the immune system is overwhelmed. This allows some virus particles to make it to the liver, where they can deposit their genes into liver cells. The immune system creates antibodies against the AAV virus but can't make enough antibodies to eliminate all of the virus particles. However, those antibodies persist in the circulation, precluding the gene therapy's re-dosing.

The huge number of virus particles assaulting the liver trigger additional immune reactions, including inflammation. Inflammation is a sledgehammer. It destroys healthy cells as well as virus particles. Inflammation basically works on the principle that it destroys everything, hoping that there is enough healthy tissue left over to let the body recover. With gene therapy, the liver often becomes inflamed, requiring corticosteroids to tamp down the inflammation before part of the liver is affected. This works in most patients, but we don't know the long-term consequences, if any.

A more straightforward method may be to use LNPs to deliver the new gene. LNPs are already successfully used to deliver the two COVID mRNA vaccines. LNPs usually do not trigger the immune system. The walls of the body's cells are made of lipids, so the LNPs look to the immune system just like another cell. The problem is that LNPs have a low efficiency of transfection (like infection; inserting their payload, in this case a new gene, into cells) and also don't target any specific type of cell. The Indian group is trying to change that.

They have added galactose molecules to the outside of their LNPs so the LNPs will tend to bind to certain receptors on liver cells. So far, they have tried twelve different galactose-based molecules, looking at their ability to combine with liver cells in the laboratory. They found one of those modified LNPs that appears to transfect liver cells efficiently. They showed that when those LNPs were filled with the high-activity Padua factor IX gene, transfected liver cells showed good expression of factor IX.

Thus, the use of LNPs could be a significant improvement over the use of AAV for gene therapy. This work is at an early stage, and there will be obstacles to overcome, as usual, but this approach appears promising. [Lohchania B et al., Pharmaceutics, 16, 1427, 2024]

SonoThera Exploring Acoustic Methods for Gene Delivery

12/7/24 SonoThera is developing ultrasound-mediated gene delivery (UMGD) as a non-viral gene therapy method. The method, called sonoporation, uses ultrasound (high-frequency sound waves) to create pores in cell walls to allow molecules to enter the cell. Experiments with mice showed that they can produce significant factor VIII or IX expression. The method is re-doseable, so they can go back in with additional factor genes, if it is desired to further increase the factor levels. They saw no safety or tolerability issues. [ASH abstract 2232]

Note that other research groups have also looked at sonoporation as a gene delivery method with similar results. SonoThera is the first we've seen that proposes to develop this into a clinical treatment. [ASH abstract 2232]

GENE THERAPY CAREGIVERS EVENT: INSIGHTS AND EXPERIENCES

BY ALYSHA MCCABE

This past October and November, CSL Behring brought together individuals with hemophilia B, their caregivers, and medical professionals for two evenings of shared stories, learning, and support. These sessions, designed to offer valuable insights into gene therapy, focusing on Hemgenix®, allowed participants to hear directly from field experts and those who have undergone the treatment themselves. These gatherings allowed participants to connect, ask questions, and learn from real-life experiences.

Andrea Buxton, a Family Nurse Practitioner (FNP-C) from the Hemophilia Outreach Center, started the event on October 10th by sharing her extensive experience with hemophilia B and gene therapy. Her clinical expertise and hands-on experience with gene therapy made her an excellent speaker for those considering or currently navigating the path of gene therapy for hemophilia B. During her presentation, she discussed the treatment journey, eligibility criteria, and the support available to patients and caregivers as they explore gene therapy options.

On November 14th, Betsy Koval, a Patient Navigator from CSL, provided an informative and comprehensive overview of gene therapy, focusing on its potential to transform the treatment landscape for hemophilia B. She detailed the three key approaches to gene therapy and expertly discussed the science behind how gene therapy works in a way that felt accessible for caregivers to understand. Additionally, Betsy walked caregivers through the entire gene therapy process, from what to expect from a consultation to after treatment.

Hemgenix® is a one-time gene transfer therapy that delivers a functional copy of the factor IX gene to the liver, where it helps produce the factor IX protein necessary for blood clotting. This innovative treatment could potentially eliminate the need for routine infusions of factor IX, providing long-term benefits for eligible patients.

Following the expert speakers, Michael, a hemophilia B community member who received Hemgenix® at age 23, shared his experience with gene therapy. Michael's journey with hemophilia B and his decision to undergo gene therapy provided an inspiring and relatable perspective for those considering this treatment. Michael shared his story openly and humbly, resonating deeply with the event participants.

One key takeaway from both evenings was the importance of communication. Caregivers were encouraged to engage openly with their healthcare providers, emphasizing that understanding the treatment process and its potential benefits and risks is essential. Many caregivers expressed how helpful it was to hear directly from someone who had been through the process. "Hearing Michael's experience made it feel more approachable."

The events also featured discussions about how to prepare for conversations with family members who might not fully understand or support the idea of gene therapy. Many caregivers expressed concerns about how to approach these difficult conversations. The sessions offered practical advice on bringing up gene therapy, discussing its potential benefits, and ensuring that everyone involved feels informed and heard.

Ultimately, these events were about more than just understanding gene therapy—they were about building a sense of community and empowering patients, caregivers, and families to take the next step in their treatment journey confidently. By hearing Michael's story and asking questions that were personal and relevant to their own experiences, participants gained a deeper understanding of the potential of Hemgenix® and the available support.

Both events ended on a note of optimism, with caregivers and patients encouraged to continue their discussions with their medical teams, seek out resources, and connect with others in the hemophilia community. The support, knowledge, and shared experiences from these events will help many make informed decisions about their or their loved ones' care moving forward.

Thank you, CSL Behring, for making these impactful events possible. Your support has helped the hemophilia B community gain valuable insights into gene therapy, empowering them to make informed decisions.

CSL Behring

STRENGTH IN CONNECTION:
A VIRTUAL COMMUNITY FOR THOSE 50 & OVER

BY MARTA THOMAS

Aging with a bleeding disorder presents unique challenges, but no one has to navigate it alone. We created *Strength in Connection*, a virtual support program for individuals 50 and older with hemophilia B. This one-of-a-kind program brings together participants from across the United States, fostering community, connection, and shared experiences—all from the comfort of home.

A Holistic Approach to Aging Well

Through Strength in Connection, participants engage in informative and interactive sessions to promote strength, balance, and well-being. Our programming includes:

- Strength Training & Balance Exercises – Maintain mobility and prevent injuries.
- Kinesiology & Movement Science – Learn expert techniques for moving safely with a bleeding disorder.
- Health & Wellness Education – Gain insights on aging well, joint health, and staying active.
- Interactive & Nostalgic Games – Stimulate the mind and bring back cherished memories.
- Open Conversations & Peer Support – A safe space to share experiences, challenges, and encouragement.

Expert-Led Sessions for Health & Wellness

Our recent events featured two outstanding speakers, each bringing valuable expertise and practical guidance:

October 16 – "Restore Your Posture" with Douglas Stringham, MS, LAT, ATC

Doug, a specialist in athletic training and total health education, shared actionable techniques to improve posture, reduce discomfort, and enhance movement. His session focused on ergonomics, alignment principles, and breathing techniques, inspiring participants to make minor but meaningful adjustments for better overall health.

November 20 – "Balancing After 50: Fall Prevention" with Dr. Michael Zolotnitsky

Dr. Zolotnitsky, a physical therapist and advocate for individuals with bleeding disorders, led an insightful fall prevention and balance training session. His targeted exercises for strengthening the hips and stability systems gave attendees practical strategies to reduce fall risk and stay active. His approachable style and deep expertise made a lasting impact on the group.

More Than a Program—A Lifeline

Strength in Connection is more than just a program—it's a lifeline. It bridges the gap for those who may feel isolated due to age, mobility, or health challenges, offering friendship, support, and encouragement.

We are proud to provide this opportunity and to see the bonds and connections that have formed. Whether you're looking for practical health tips, fun activities, or a welcoming community that understands your journey, Strength in Connection is here for you.

Thank you, Sanofi, for your generous support in making these inspiring events possible. Join us for our next session and experience the power of connection, strength, and support!

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As it has for the past decade, our community continues to motivate and inspire us. That's why we look forward to a future filled with possibility, backed by the community support that unites and raises us all.

CONNECT WITH A CoRe

Sanofi Community Relations and Education (CoRe) Managers provide information about ALPROLIX, treatment options, and more.

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MEET AND GREET WITH KIM: A LEADER DEDICATED TO ADVOCACY AND COMMUNITY

BY ALYSHA MCCABE

Our CEO, Kim Phelan, has been a pillar of the hemophilia B community, a trusted advocate, a hands-on leader, and a cherished friend to so many families. Despite her role, Kim remains deeply involved with families, watching children grow and ensuring every voice in the community is heard.

Building Connections Through Advocacy and Support

This past October, Kim hosted two virtual ***Meet and Greet with Kim*** sessions for parents and caregivers, providing a space to discuss pressing issues, share experiences, and explore ways we can better support families through advocacy and education. These gatherings were significant, as they allowed new families to connect with seasoned members, fostering an environment of support, mentorship, and shared wisdom.

During the sessions, Kim emphasized a key message:

- Advocacy matters—speaking up is crucial for yourself or a loved one.
- Be prepared—if you struggle to advocate for yourself, write everything down and bring a trusted supporter to stand beside you.
- Empower yourself—knowing your rights and understanding available resources make all the difference.

The evening was insightful and uplifting, filled with warm conversations, strong connections, and even some fun games, sparking laughter and friendly competition.

Looking Ahead: More Advocacy-Focused Events

As our community faces new challenges, Kim and our team are committed to continuing these critical conversations. Plans are already in motion to host more advocacy-focused events, ensuring every individual and family has the tools, support, and confidence to navigate their journey.

Kim's dedication to the community goes beyond leadership; it's personal. She cherishes every opportunity to spend time with families, listen to their needs, and create meaningful change. We are grateful for her unwavering passion and leadership. Stay tuned for upcoming events!

PARENTING SUPPORT:
WHEN THE PARENT IS ALSO THE PATIENT - TAKING CARE OF YOURSELF FIRST

BY MARTA THOMAS

The recent session, *When the Parent is Also the Patient: Tips to Take Care of Yourself and Your Child with a Bleeding Disorder,* on November 6th, provided a safe and welcoming space for parents navigating the complexities of parenting while managing their health.

The evening began with a warm introduction from Carrie Koenig, setting a positive and supportive tone for the session. Dr. Nance captivated the audience with her compassionate and practical insights into balancing the demands of personal health and caregiving. She shared her extensive expertise in blood disorders, emphasizing the importance of self-care and its direct impact on a parent's ability to care for their child effectively.

Throughout her presentation, Dr. Nance provided actionable self-care strategies, such as prioritizing spa days, taking vacations, and simply allowing oneself time to relax. She encouraged participants to embrace small joys and to carve out moments of peace amidst life's challenges. Her message resonated deeply with attendees, many of whom related to balancing their needs with those of their children.

The session also included a heartfelt discussion, where parents shared their personal experiences and practical tips for self-care. The open dialogue fostered a sense of community and understanding as participants realized they were not alone in their journeys. From setting boundaries to scheduling downtime, the group's collective wisdom enhanced the session's value.

As the evening progressed, the conversation transitioned into informal discussions, allowing parents to connect on a personal level. These moments of shared laughter and encouragement underscored the importance of community in navigating life with a bleeding disorder.

Thank you, Sanofi, for making this invaluable event possible and providing a supportive space for parents to balance their health with caregiving.

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A NIGHT FOR HOLIDAY FAMILY FUN!

BY ALYSHA MCCABE

T'was the night for festive family fun when over 20 families gathered with CHB on Thursday, December 5th, for a ***Holiday Family Fun*** event filled with laughter and excitement. The evening started with participants contributing words for a super-silly mad-lib parody of "T'was the Night Before Christmas," setting the tone for a lighthearted and joyful night.

The fun continued as teams were formed to tackle three thrilling rounds of Mad Gabs, where they worked together to decipher seemingly random phrases into holiday-themed expressions. The room buzzed with energy and laughter as teams raced to figure out the puzzling words. The excitement didn't stop there—three rounds of Kahoot Trivia followed, with all questions centered around holiday themes, sparking friendly competition and even more fun. The event brought the community together in a heartwarming way, creating memories that will last long after the holidays.

HOLIDAY FUN FEST BRINGS CHEER TO THE B HUB COMMUNITY

BY ALYSHA MCCABE

The B Hub community kicked off the season with this year's ***Holiday Fun Fest***, a chance to share traditions, laughter, and creativity with friends near and far. Throughout December, we hosted 14 holiday-themed livestream events in the B Education Hub—a digital platform designed to deliver critical health information and foster meaningful connections within the hemophilia B community. It's a space where members come together to learn, share, and support one another, and this event was a perfect example of what makes the B Hub such a special place. The *Holiday Fun Fest* highlighted how vibrant and welcoming this community is—a place where members of all ages and backgrounds can come together to learn, share, and grow.

Festive story-times with Erica Garber sparked curiosity and connection as we explored holiday traditions around the world and celebrated themes of joy, self-acceptance, and cultural pride. Santa even came to town for two special story-times, spreading magic and cheer as he shared a holiday classic with children and families. Creative challenges with Corazon Tierra and Laura Echandi brought out our artistic sides with colorful piñatas, handmade paper stars, choreography, holiday dance, and cherished food traditions shared across the community.

Music played a significant role, too. A live jam session with Wayne Cook and Shelby Smoak filled the week with rhythm and fun, while Jacquie Maddix hosted an uplifting Old School Christmas Radio Hour, spinning songs that inspired joy, nostalgia, and connection. Rocky Williams kept us laughing with his holiday-themed comedy, and members took to the feed to showcase their talents, share memories, and even try out some frosty dance moves.

From heartfelt stories to lighthearted moments, the Holiday Fun Fest was about more than just activities. It was a celebration of the connections that make this community unique—a chance to learn from each other, share a little holiday cheer, and remind ourselves of the joy of coming together.

Thank you to everyone who joined in the fun and made this event one to remember! If you haven't already, join us in the B Education Hub—we can't wait to see you there for future events!

GINGERBREAD DECORATING!

BY ROCKY WILLIAMS

On Saturday, December 14th, our community gathered for an event packed with holiday magic and creative flair! The ***Gingerbread House Decorating and Trivia*** celebration was a holly, jolly highlight of the season, bringing together families and friends to celebrate the most wonderful time of the year.

From transforming gingerbread houses into dazzling, frosting-filled masterpieces to singing our favorite holiday tunes, the event was a tree-mendous success! Attendees joined in on lively games like "This or That," cracked their way through trivia rounds, and brought their A-game to epic Kahoot showdowns that had everyone on the edge of their seats!

This event wasn't just about fun but about bringing our community closer together and creating unforgettable memories. And let's not forget the friendly competition! A big round of Santa-plause for our winners:

1st Place: The Beaty Family

2nd Place: The Dockham Family and the Stielper Family

3rd Place: The Haralson Family

A huge thank you to everyone who joined us and made the event so special. We're also incredibly grateful to our wonderful sponsors, Medexus Pharma and Paragon Hemophilia, whose generous support made this event truly unforgettable and snow much fun!

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WOMEN'S VIRTUAL WINTER RETREAT

BY MARTA THOMAS

This past December, we were thrilled to host the ***2024 Women's Winter Education & Empowerment Retrea***t, a weekend dedicated to fostering sisterhood, learning, and personal growth. With an inspiring lineup of expert speakers and engaging activities, attendees left empowered and recharged for the year ahead.

The retreat began on Friday, December 6th, with a warm welcome from Kim Phelan, CEO of the Coalition for Hemophilia B. Kim set the tone for the weekend by celebrating the strength and resilience of women within our community. This was followed by an empowering message from Sanofi, highlighting their continued commitment to our cause.

The evening's first session, *Your Future in Focus*, led by Vanessa Harris, was a creative and inspiring start to the retreat. Vanessa guided participants in crafting visual guides to map their goals and dreams, providing practical tools for turning intentions into reality. The hands-on activity left attendees with a tangible reminder of the future they are building.

The night concluded with Shonda Joshua leading *Chit Chat and Chocolate*, a heartfelt session filled with laughter and shared experiences. The fun continued into the *Opening Night Pajama Party*, featuring Bingo, lively conversations, and music, creating the perfect blend of relaxation and connection.

On Saturday, December 7th, the retreat began with Makenzie Sledd's morning rejuvenation session, designed to awaken the body with gentle exercises focused on balance and movement. Later, Catherine Canadeo presented *Unwrapping Peace*, sharing strategies for navigating holiday stress and creating meaningful moments of joy and balance.

The day's highlights included the *Arty Tea Party*, led by Erica Garber, where attendees enjoyed tea and crafted aromatic slime, blending creativity with sensory exploration. Alexandra Boria's *Building Your Advocacy Toolkit* provided attendees with the tools to advocate effectively for themselves and others within the hemophilia community. At the same time, Lee Kim's *Art of Human Curiosity and Genuine Connections* inspired participants to nurture authentic relationships through curiosity and exploration.

Saturday's finale, *Primal Screaming Therapy* with Tina Saachi, offered a powerful emotional release, helping participants heal and transform past pain into personal strength. The day ended with a festive and interactive

Saturday Night Event, combining a tropical holiday escape room and a scavenger hunt.

The retreat closed on Sunday, December 8, with sessions emphasizing self-expression and support. Makenzie Sledd returned for another rejuvenating morning session, followed by Alexandra Boria's *Women, Girls, and Hemophilia*, which addressed the unique challenges faced by women in the community. The final session, *Being Seen, Heard, and Valued*, led by Karen Boyd and David Rushlow, created a safe space for participants to explore authenticity and connection in their relationships.

The weekend ended with parting moments led by Erica Garber, leaving attendees with a renewed sense of community and commitment to supporting one another. This retreat was a testament to the strength and unity of women coming together to learn, grow, and thrive.

Thank you, Sanofi, for making this empowering retreat possible and for your continued commitment to the women in our community. Your support helped create a space for connection, learning, and renewal, leaving attendees inspired and recharged for the year ahead.

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GENE THERAPY SUPPORT NETWORK: A PRIVATE SPACE FOR MEN WITH HEMOPHILIA B 18 AND OVER

BY LAUREN ROBINSON

For men with hemophilia B who are curious about gene therapy or actively considering it, finding a safe and supportive space to discuss the process is essential. That's why we offer a private support group exclusively for men aged 18 and older, moderated by someone who has personally undergone gene therapy.

Our ***Gene Therapy Support Network*** events, held virtually on Zoom, bring together individuals who want to hear real-life experiences from those who have been through the process. These gatherings have provided a unique opportunity for participants to ask questions, share thoughts, enjoy a few laughs, and maybe even some dance moves!

A Community of Shared Experiences

During these support events, participants had the chance to hear from over six men who have undergone gene therapy, offering firsthand insight into the journey. This private space creates a sense of community, allowing attendees to connect with others who share their concerns and curiosity about gene therapy.

Key Topics Discussed

Throughout the sessions, a wide range of important topics were covered, including:

- Financial responsibility for treatment
- Family planning and life after gene therapy
- Ongoing care and monitoring post-treatment
- Emotional and mental well-being during the process

Participants gained honest and valuable perspectives about the experiences, emotions, and challenges of choosing gene therapy by discussing these key areas.

Why This Group Matters

Deciding to undergo gene therapy is deeply personal, and having a support network to lean on can make all the difference. This group offers a judgment-free zone where individuals can ask specific questions, process their thoughts, and connect with peers who truly understand what they're going through.

Stay tuned for future *Gene Therapy Support Network* events! If you or someone you know is considering gene therapy and would like to join our next session, we encourage you to reach out. You don't have to navigate this journey alone; support is here.

We are incredibly grateful to CSL Behring for their sponsorship, which has made these sessions possible.

CSL Behring

UPCOMING EVENTS

For more information and to register: hemob.org/upcoming-events

MAY 13, 2025 • VIRTUAL
Gene Therapy Rap Session
Meet with a hemophilia B member on gene therapy

MAY 17, 2025
SAN ANTONIO, TX
Meeting on the Road
Connect with your hemophilia B community!

MAY 20, 2025 • VIRTUAL
Product Landscape Updates
Understand your treatment options with Dr. David Clark!

MAY 29, 2025 • VIRTUAL
Gene Therapy Rap Session
Meet with a hemophilia B member on gene therapy

MAY 29–JUNE 1, 2025
TULSA, OK
Men's Education & Empowerment Retreat
A unique experience, during which men are given a safe space to share their journey with others and gain support

JUNE 3, 2025 • VIRTUAL
Survive & Thrive, Mental Health
Tools for Wellness, Support in Community

JUNE 10, 2025 • VIRTUAL
Gene Therapy Rap Session
Meet with a hemophilia B member on gene therapy

JUNE 17, 2025 • VIRTUAL
Foro Latino de Hemofilia B
Potenciar las voces latinas en la hemofilia B

JUNE 26–29, 2025
STONE MOUNTAIN, GA
Women's Education & Empowerment Retreat
A unique experience, during which women are given a safe space to share their journey with others and gain support

JULY 2, 2025 • VIRTUAL
Gene Therapy Rap Session
Meet with a hemophilia B member on gene therapy

JULY 8, 2025 • VIRTUAL
Strength in Connection, 50+ Series
Aging well, together in hemophilia B

JULY 16–20, 2025 • NASHVILLE, TN
The Beats
Calling all musicians ages 13+ for an incredible experience this summer! All skill levels are welcome to apply! *Ages 13-14 must be accompanied by a parent

JULY 24, 2025 • VIRTUAL
Hemophilia B Product Landscape
Understand your treatment options with Dr. David Clark!

AUG 5, 2025 • VIRTUAL
Gene Therapy Rap Session
Meet with a hemophilia B member on gene therapy

AUG 16, 2025
CHARLOTTE, NC
Meeting on the Road
Connect with your hemophilia B community!

AUG 26, 2025 • VIRTUAL
Gene Therapy Rap Session
Meet with a hemophilia B member on gene therapy

SEPT 6, 2025 • MILWAUKEE, WI
Meeting on the Road
Connect with your hemophilia B community!

SEPT 13, 2025 • SAN DIEGO, CA
Meeting on the Road
Connect with your hemophilia B community!

SEPT 16, 2025 • VIRTUAL
Gene Therapy Rap Session
Meet with a hemophilia B member on gene therapy

SEPT 23, 2025 • VIRTUAL
Hemophilia B Product Landscape
Understand your treatment options with Dr. David Clark!

SEPT 18-21, 2025
STONE MOUNTAIN, GA
Men's Education & Empowerment Retreat
A unique experience, during which men are given a safe space to share their journey with others and gain support

SEPT 27, 2025
MINNEAPOLIS, MN
Meeting on the Road
Connect with your hemophilia B community!

SEPT 30, 2025 • VIRTUAL
Gene Therapy Rap Session
Meet with a hemophilia B member on gene therapy

OCT 4, 2025 • PORTLAND, ME
Meeting on the Road
Connect with your hemophilia B community!

OCT 16, 2025 • VIRTUAL
Gene Therapy Rap Session
Meet with a hemophilia B member on gene therapy

OCT 18, 2025 • PHOENIX, AZ
Meeting on the Road
Connect with your hemophilia B community!

OCT 23, 2025 – VIRTUAL
From Newborn to Empty Nest: Parenting Support
Understanding phases of childhood, one milestone at a time

OCT 25, 2025 • PITTSBURG, PA
Meeting on the Road
Connect with your hemophilia B community!

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>
> SHANNON L. ALDER

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The Coalition for Hemophilia B is a national nonprofit serving the hemophilia B community for 30 years.

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SCAN ME

For information, contact Kim Phelan, 917-582-9077, kimp@hemob.org

MEET DANIEL:
He's managing life with hemophilia B and dreaming of managing the Houston Astros!

BY SHELLY FISHER

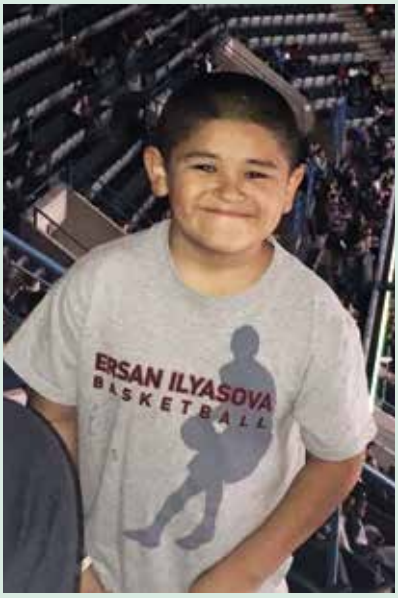
Daniel was in between classes and a visit to the dining hall when I got the opportunity to visit with him. As a sophomore majoring in sports management, he shared his passion for baseball, family dedication, and dream to one day manage the Houston Astros. Halfway into making that dream a reality, Daniel will no doubt be a name that we ultimately hear loud and clear in the world of sports.

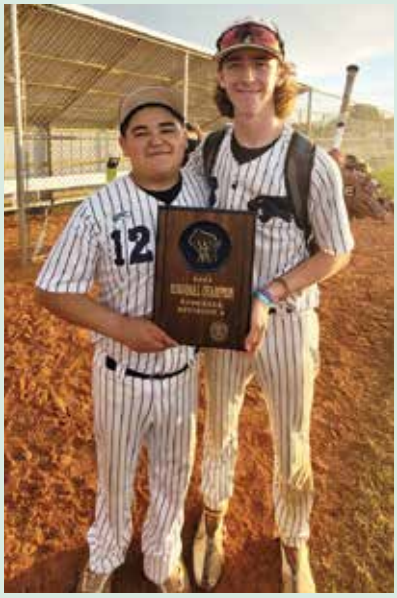
Choosing his university with practicality, Daniel doesn't mind the hour-and-a-half drive to the University of Wisconsin-Parkside because it allows him to be closer to his family while pursuing his academic goals and participating in a club that honors his Latino heritage.

Though he managed many different teams in high school, he shared that he was enjoying a new experience– managing his university's track team and doing all of the filming. Daniel told me he also finds time to participate as a member at large in a Latinos Unidos club and believes in their mission to help Latino students grow and learn while observing their cultural heritage.

Unsurprisingly, he shared that his current favorite class is Ethics and Issues in Sports Management because it allows him a deeper dive into his major amidst all of the recommended basics. In addition, he confided that the professor happened to be his favorite teacher this semester. "He gives us a great idea of what it's like in the sports world because he has experience."

With his keen sense of management and foresight,





Daniel was already looking ahead to his internship with a professional league near the university and hoping for a paid internship with a clubhouse. He also plans to obtain an eventual master's degree at the University of Texas for additional certifications in his field.

Daniel is no stranger to the sports world. Growing up in a family with a mom and sisters who love collegiate volleyball and the Texas Longhorns, he quickly found his favorite in baseball. After playing in his local league through the coach pitch level, he took a break due to the type of head bleeds he was experiencing at that time, but he knew he still had a lot to offer the sports arena. "I have a very intelligent brain when it comes to baseball or sports."

After some encouragement from the sports enthusiasts in his family, he pursued team management while in high school. Managing his school's football team for 2 years, the baseball team for 5 years, and the wrestling team for 4 years fueled his love for athletic competition, and he found his niche in supporting coaches and teams. He credits two of his coaches, Tom Davey and John Jrolf, with making him feel like a part of the team and not treating him any differently after finding out about his hemophilia diagnosis. "They helped push me and mold me into how I am going into this industry and how I want to work in sports. I want to make an impact on a team, and I know that I can do that."

Since then, he has realized his pursuits in clubhouse operations also include scouting and upper-level management. Though he takes some heat from his Wisconsin friends, he is proud to proclaim that his all-time favorite team is the Houston Astros, and Daniel hopes to support their management in some way once he graduates. With a brain wired for baseball, he follows the Houston Astros closely and already has some management suggestions for them.

Daniel said his friends would describe him as generous, likable, easy to talk to, and funny. Though most of the students in his friend group commute to the university, a typical day would involve attending classes, eating in the dining hall, and hanging out with them at a pool hall named The Den.

After a routine procedure at birth involving a heel prick, Daniel was tested and diagnosed with hemophilia B. It was unexpected, as Daniel was the 4th sibling in his family. "My mom had to learn a lot more to take care of me, which definitely changed our lives. I am so grateful to her for going through everything with me and supporting me all the way."

Having recently attended his first Coalition for Hemophilia B event in Chicago, he is looking forward to more and hoping one will be held near a ballfield. "You meet more kids who share your disorder, connect and grow friendships, and learn more about your disorder. You also see friends you have met in the past who are spread out all over the country."

Daniel had sound advice for anyone who has recently been diagnosed. "Don't let it bring you down. There are new ways to help with medicine. Keep your head up. Take your medicine. Go to events and meet people. See hemophilia B as an opportunity and take that opportunity to grow."

There's nothing like meeting a fellow Astros fan from the University of Wisconsin-Parkside but meeting one with specific management advice for the team is a whole other experience! If anyone from the Astros ball club reads this, you might want to look Daniel up! I know I will watch for his name in the sports world, not if but when he joins the game!

MEET ADAM: DEDICATED STUDENT, HISTORY BUFF, AND FORREST GUMP FAN!

BY SHELLY FISHER

An eighth grader with a goal to make all A's, Adam was celebrating improvement in his grades when we visited, and he shared his thoughts on all things middle school, cooking class, his love of history, and the important people in his life.

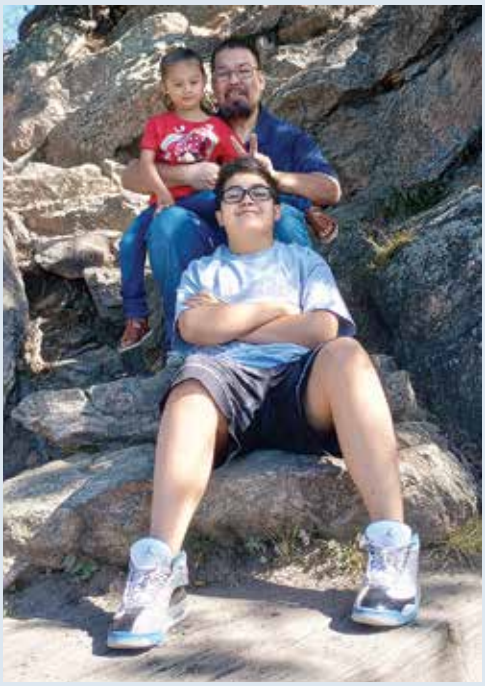
Adam told me his schedule included a STEM class, English, math, and science, but cooking and history were his favorites. "I love learning about history, the samurais, and the continental army when they were fighting against the British. I like history because it shows an aspect of history and tells a story, so it doesn't get lost in the past."

When asked what his cooking specialties were, he said, "Sugar cookies," but he shared that he wasn't quite ready to take over the making of his mom's famous tacos and carne asada.

The budding historian felt his friends would describe him as outgoing, humorous, and the friend that everyone goes to for conversation. Though talkative in class, he also shared that he is focused and always listens to his teacher. When he is not studying, you can find Adam pursuing the same type of entertainment as most students his age. He enjoys playing Minecraft, Call of Duty, and Grand Theft Auto.

After starting to crawl at eight months, Adam's mother noticed bruises all over his legs. A doctor diagnosed him with severe hemophilia B with an inhibitor and connected her with a specialist. With no family history of bleeding disorders, his mother pursued testing and found that she was a carrier.

Early in their journey, while learning more about Adam's condition, she encountered difficulty finding his veins to administer Factor IX, so he had a port implanted to facilitate his transfusions. However, during his first time receiving Factor IX using his port, he began coughing, and even though his mother communicated that this was not normal, the nurse continued the transfusion. After she left the room, Adam's lips began to swell, and both his parents realized he was having an allergic reaction to the factor IX medication. After a trip to the emergency room and an administration of Benadryl, Adam got some relief. Still, unfortunately, the entire event was replayed again



the next day when he had to get his infusion, which confirmed an allergic reaction to factor IX.

Because Adam is the only patient with an inhibitor and allergy at their hematologist's practice, his care and treatment were especially important. His family is grateful to their hematologist, Dr. Wong, and Adam added, "He's there to listen to me and help me."

This middle schooler also appreciates his family supporting him throughout his journey with hemophilia B. He said his mom is the "listener" and the "researcher," while his dad hangs out with him and administers his medication.

Adam and his family have also become involved in The Coalition for Hemophilia B. They had the best time at a recent meeting on the road! The event was super engaging and an awesome way to connect with others in the hemo B community. Adam is excited and can not wait to join CHB and see everyone at the symposium later this year in Orlando.

When asked if he had a favorite movie, Adam responded immediately with "Forrest Gump." His mother shared that the family relates to the famous line, "life is like a box of chocolates, you never know what you're going to get," because spontaneous bleeds in Adam's elbows and ankles keep life "interesting" each night, and they never know what they will wake up to some mornings.

When asked what advice he would give someone with a new hemophilia B diagnosis, he had great advice, which applies to life in general. "Keep on going. It gets easier and harder at the same time, but you will get through it." Well said, Adam.

B inspired!

Stories and artwork from teens in the Hemophilia B Community

Winter 2024

IN THIS ISSUE:

- MEET ADAM: DEDICATED STUDENT, HISTORY BUFF, AND FORREST GUMP FAN!
- MEET DANIEL: HE'S MANAGING LIFE WITH HEMOPHILIA B AND DREAMING OF MANAGING THE HOUSTON ASTROS!

MEET ADAM!

MEET DANIEL!

WANTED: TEEN CONTENT CREATORS!

Calling all content creators! If you have a heart for tweens/teens and a drive for content creation, then we would love for you to volunteer your time and talents with us. The Coalition for Hemophilia B is currently accepting volunteers to collaborate on a new section of the newsletter just for those special 11–18 year olds in our community.

No experience required as we have a team ready to polish your brilliant ideas for publication. If you have ideas for topics, events, and new sections, let's work on this together – reach out to rockyw@hemob.org for your next steps!