SPECIAL ISSUE

Get Involved

HEMAWARE

The Bleeding Disorders Magazine | NATIONAL BLEEDING DISORDERS FOUNDATION | hemaware.org

For people with hemophilia, actively participating in health care decisions is more important than ever.

Austin Caldwell, 25, of Mooresville, North Carolina, has hemophilia A

Power to the Patient

In this special issue of **HemAware**, you'll read about why it's important for **people with hemophilia** to be active participants in managing **their bleeding disorder.** You'll also learn how **being involved with an advocacy organization can provide much-needed support and guidance,** as well as bring about important policy changes that **will improve care for everyone** in the community.

BY DONNA BEHEN
PHOTOGRAPHY BY KEVIN TITUS & ERIC WILLIAMS

"At that age, I didn't really know what empowerment was, but now looking back at that experience, I realize that it really empowered me."

Austin Caldwell

Austin Caldwell vividly remembers

involved in managing his hemophilia. "I was 8 years old and dining room table and taught me how to self-infuse," recalls walked me through all of the steps, and I was really proud I

Caldwell, a project manager who lives in Mooresville, North Carolina, says being able to self-infuse had an immediate effect on his quality of life. "It made such a difference because I could do more, and I didn't have to wake up at 5 a.m. anymore so my nurse could come and infuse me before I left for school at 7:15."

"At that age, I didn't really know what empowerment was, but now looking back at that experience, I realize that it really empowered me," he says.

AN EXCITING TIME FOR HEMOPHILIA CARE

Today, being an empowered patient with hemophilia — educating yourself about your options, and actively participating in health care decisions and managing your condition — is more important than ever, says Courtney D. Thornburg, M.D., a hematologist at Rady Children's Hospital in San Diego.

"As the number of treatment options has increased and the goals of hemophilia care have changed, patient empowerment is a really critical issue for people with hemophilia," she says. "It's a very exciting time, but in order for people to decide what's right for them, they need to have the knowledge and skills necessary to have meaningful discussions with their health care team."

The pace of advancement in hemophilia treatments is another reason why patients should be more actively involved, says Brendan Hayes, the National Bleeding Disorders Foundation's senior director of education, innovative therapies.

"There is a tremendous amount of innovation right now, and it's happening very quickly," she says. "So it's important that people stay on top of all their options, weigh the pros and cons, and make educated and informed decisions based on that information."

THE SHARED DECISION-MAKING APPROACH

More and more providers today are embracing a new approach to patient care called shared decision-making, which is based on the idea that a patient's lived experience, personal preferences, and lifestyle are as important to plotting a course of treatment as a provider's knowledge of the treatments themselves.

In the past, Thornburg says, "doctors tended to follow the golden rule: I should treat others the way I would want to be treated." Today, it's all about following the platinum rule, which is to treat others the way *they* would want to be treated. "We as clinicians are not just presuming that we know what the patient wants," she adds.

"The really cool thing about shared decision-making is that all kinds of things get factored into a treatment decision," Hayes says. "It's things like: What are my goals? What are my preferences? What stage of life am I in? All of these quality-of-life issues are really critical."

For some people, adapting to the shared decision-making model can be difficult because they may not feel comfortable asking questions or expressing their opinion with their providers, Hayes says. "It's going to feel uncomfortable at first, but it's a muscle that you need to work, and you'll get better at it with every interaction," she says.

DO YOUR OWN RESEARCH ... BUT TREAD CAREFULLY

Learning more about your blood disorder is a key component in becoming more empowered, and community-based organizations such as NBDF, the Hemophilia Federation of America, and the World Federation of Hemophilia are good sources for reputable educational materials.

"The benefit of doing online research is that you can take your time and really delve into the material, you can talk about it with friends and family or other peers with

the first time he felt actively

my home health nurse sat me down at our Caldwell, 25, who has hemophilia A. "She was able to hit my vein on my first try."

BETTER TOGETHER Providers like hematologist Courtney D. Thornburg, M.D., encourage patients like Austin Caldwell to take an active role in health care decisions.

3 KEY THINGS YOUR DOCTOR WANTS TO KNOW

Hematologist Courtney D. Thornburg, M.D., says these questions are integral to the shared decision-making process:

WHAT ARE YOUR PRIORITIES AND GOALS?

From there, your health care team can help you decide whether there are any new treatment options or ways to optimize your current therapy that can enable you to reach those goals.

HOW DO YOU LIKE TO LEARN?

Do you prefer face-to-face conversations, printed handouts, webinars, podcasts, or something else? Your health care team can help you learn about your treatment options in a way that's most comfortable for you.

WHO ELSE SHOULD BE PART OF THE CONVERSATION?

If you want your spouse or someone else close to you to be involved in the decision-making process, your doctor needs to know which trusted partners to engage.

hemophilia, and then take it back to your hemophilia treatment center to discuss with your health care team," Thornburg says.

"All of the content on the NBDF website is extremely well vetted," Hayes says. "We have physicians review everything to ensure it's medically accurate, and we regularly update the site." She particularly recommends the Innovative Therapies section of the website as well as the Steps for Living website, which includes information on novel treatments.

"We strive to make the Steps for Living content accessible to as many people as possible, so a lot of the material is bite-sized information that's easy to understand, and all of it has been translated into Spanish, too," Hayes says.

If you find information about hemophilia care elsewhere on the internet, such as social media or message boards, you should always take it back to your health care team rather than just "blindly trusting the information or following advice," Thornburg advises.

"You might find information that's based on one particular patient who might have had a bad experience that could be a lot different from what the majority of people have experienced," she says. "On the other hand, you could have false hope if you read a bunch of stories about people who had a great experience with a treatment without understanding that not everyone may respond as well."

MAKE THE MOST OF YOUR APPOINTMENTS

The ideal clinic visit is one where you feel fully comfortable sharing your goals, priorities, and concerns with your health care team, Thornburg says.

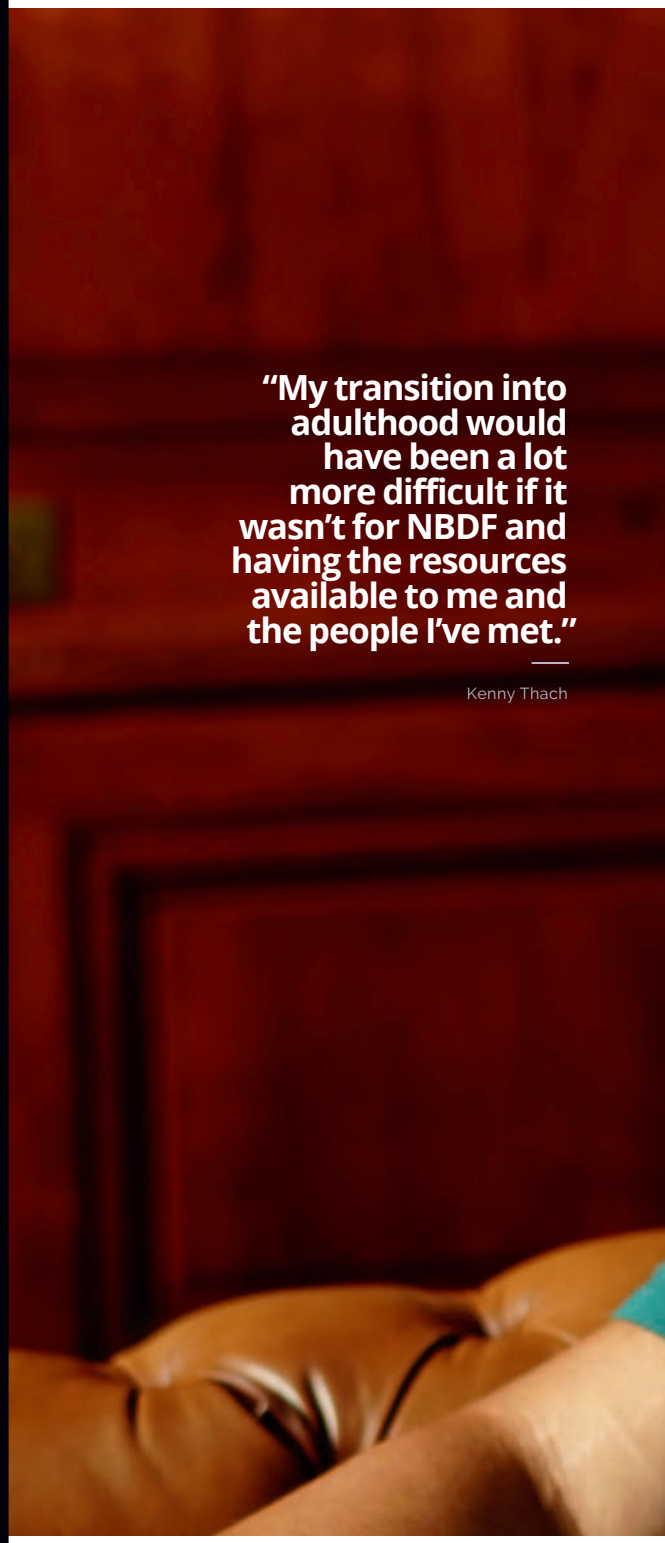
"It's your right to speak up for yourself and say, 'Yes, I'm happy with my treatment, so let's keep doing this,' or 'I don't think I'm doing as well as I could be doing, so let's talk about what we could change,'" she says.

When you're faced with information that is complicated or confusing, "help me understand ..." is a good way to launch a conversation, Hayes says. She also recommends not going in empty-handed.

"The best thing to do is to take a list of questions so that you're fully prepared. Your provider should be excited to see that you've done some homework and that you really want to learn. You're taking ownership of your own health care, which is what shared decision-making is all about."

After his positive experience with taking charge of his infusions at a young age, Caldwell has continued to play an active role in his own care. Now, when he meets with his hematologist for his yearly appointments, the visits feel like an equal collaboration.

"When I talk to my doctor, I feel comfortable advocating for myself and telling him what I think is best for me, but I'm also interested in what he has to say, so it's definitely 50-50," Caldwell says. "It's a relaxed conversation, which is so beneficial."



ADVOCACY GROUPS SUPPORT

BY MATT MORGAN
PHOTOGRAPHY BY NICOLE LOEB

Connect and Serve

PEOPLE WITH CHRONIC CONDITIONS AND HELP BRING ABOUT POLICY CHANGES THAT IMPROVE CARE, BUT THEY CAN'T DO IT WITHOUT YOU

Kenny Thach's family learned he had

baby teeth came out and his gums would not stop bleeding. disorder and helped to explain the mysterious bumps and that his path to advocacy began.

His younger brother developed serious, long-term complications from his own bleeding disorder as an infant, and that became the family's focus throughout much of Thach's childhood.

At a young age, he learned to advocate for his brother, translating for his mother at doctor appointments and helping her fill out paperwork and figure out insurance forms.

"I was doing things a regular kid should not be doing, you wouldn't think," he says. "But it helped me mature at a very fast rate and really understand my bleeding disorder, and it allowed me to learn of all the opportunities that come with it. I was getting involved in something bigger than myself."

FIRST STEPS TO ADVOCACY

Thach's connection to an advocacy organization for his bleeding disorder came at an opportune time in his life, in his midteens. He had just become too old to attend the Hole in the Wall Gang Camp in Ashford, Connecticut, which was founded by Paul Newman for children with serious illnesses.

His nurse practitioner at the Yale Hemophilia Center in New Haven, Emily Bisson, suggested he try a camp put on by the New England Hemophilia Association, or NEHA, a chapter of the National Bleeding Disorders Foundation.

"At family camp, I was able to feel like I had a place of belonging, that I was able to be around people who knew me," Thach says. "I didn't have to talk about my bleeding disorder if I didn't want to. It was very comforting. I was hooked."

Camps are one way that people can get involved with an advocacy group, says Bill Robie, director of state government relations at NBDF who helps oversee public policy for the foundation. Since 1969, NBDF's summer camps have provided children with bleeding disorders a typical camp experience under the caring watch of counselors and staff.

LOVED ONES are often the first advocates for someone with a bleeding disorder, as Kenny Thach experienced.

CHAPTER EVENTS provide an outlet for people to learn more about their conditions and connect with others.

severe hemophilia A when his

His mother took him for testing, which revealed the bleeding bruises he would get as a baby. It wasn't long after that, really,

PEOPLE'S VOICES are needed to tell personal stories that move legislators into action at the state and national levels.

SUMMER CAMPS give children with bleeding disorders a typical camp experience under the caring watch of counselors.

TRAINING ADVOCATES

After a few years of attending NEHA events, Thach was approached by Bisson along with Rich Pezzillo, who is the chapter's executive director, and Heather Case, NEHA's camp director at the time, about joining NBDF's National Youth Leadership Institute, or NYLI.

Launched in 2002, NYLI provides leadership opportunities for adults ages 18 to 24 in the bleeding disorders community. It includes in-person training, webinars, and year-round communication to encourage participants to grow personally, effect change, and positively influence others.

"NYLI is a wonderful program," Robie says. "It's fairly unique from what I've seen from other disease groups. We're training people within the community to develop careers that will serve the community as they go forward."

Through NYLI, Thach went to Washington, D.C., for NBDF's Washington Days, an annual event where hundreds of advocates from all over the country gather to receive advocacy training and then meet with legislators on Capitol Hill to discuss issues important to the NBDF community.

MAKING VOICES HEARD

Frequently, those issues center on policies related to medical coverage.

"People with chronic diseases often have high-cost therapies. It's a daily reality of their lives," Robie says. "And they're vulnerable to any policy changes or practices with health care and insurance — which drugs are covered, which services are covered, how much patients have to pay out of pocket. Advocacy organizations are critical in making sure that people with chronic conditions are protected and they can access the services and medications they need."

People's stories are critical in appealing to the national and state legislators who make and change policies, so this is where getting involved in an advocacy organization can be instrumental.

"I'm a lobbyist. My expertise is in understanding the policymaking process and understanding advocacy. But I don't have a chronic disease," Robie says. "Ultimately, if we don't

"Our state chapters offer a lot of opportunities. Most of them don't have very big staff, so any volunteers they can get are helpful."

Bill Robie, NBDF

hear from patients, we're not able to address their concerns. The moment I bring a patient in who has a very personal story, who's impacted by something, that's really what gets a legislator's attention."

For example, when Robie visited with state legislators in Tennessee, he invited a family of four to join him to help illustrate the impact that managing a chronic condition had on them.

"I can talk about how expensive their medication is all day long," Robie says. "But when the mother has an annual statement of benefits that shows the medication costs were $1.2 million for her two boys, that makes it real for the legislator."

Simply by lending their time and their story to an advocacy organization, these people are empowering themselves and others.

STATE AND LOCAL OPPORTUNITIES

Involvement in an advocacy organization doesn't necessarily require trips to the nation's capital. It can be done at the state and local levels, too.

For many families dealing with a chronic condition, the first point of contact with an advocacy group is attending a chapter event. NBDF has 52 chapters across the U.S. and in Puerto Rico to drive the organization's initiatives at the local level. Chapters host advocacy days, educational retreats, summer camps, and fundraising events such as walks.

"Meeting people at chapter events — people in your community who are living close to you — is really helpful and powerful," says Lena Volland, director of education for NBDF. "Every chapter normally puts on fantastic local events, and people can not only gain information there but also meet with other people who are in the bleeding disorders community. And that's always such a good connection to make, with other people who are walking on the same path or who are going through a similar situation."

Some people choose to deepen their involvement and serve on a chapter's advocacy or fundraising committee. "Our state chapters offer a lot of opportunities," Robie says. "Most of them don't have very big staff, so any volunteers they can get are helpful. Not everybody might want to serve on the board immediately, but they'll get involved and probably at some point will be asked to serve in a more serious capacity."

GIVING AND RECEIVING

Since first connecting with NBDF through his local chapter's family camp, Thach has continued to stay involved in that program. He has been head counselor for his age group for the past six years and has served on the counselor leadership team. In 2023, he was part of the camp committee.

Besides giving to the group, he has also received. Thach, like many adults with a bleeding disorder, has had to navigate the challenges of maintaining his care into adulthood.

"NBDF allowed me to gain the skills to learn how to transition into my adult care more efficiently in terms of looking at insurance policies, knowing what to look for, and knowing the verbiage and the vocabulary associated with it," he says. "My transition into adulthood would have been a lot more difficult if it wasn't for NBDF and having the resources available to me and the people I've met."

In addition to summer camps for children, NBDF chapters host events, such as men's retreats, that support people as they transition out of pediatric care. NBDF's Own Your Path is a six-month, app-based program that gives eligible adults ages 18 to 29 the information they need to manage their bleeding disorders, including access to a health coach.

Thach is open to taking on more responsibilities within NBDF at the state or national level, but at 26 years old, he doesn't want to get ahead of himself. For now, he's balancing bleeding disorders advocacy with his personal aspirations, including his career as a scientist and his professional goal to contribute to the hemophilia field.

"It's really just giving back," he says. "The way I see it, I'm doing what I do to create a better life for the next generation."

HEMAWARE Executive Editor: Ilana Ostrin, iostrin@hemophilia.org. Senior Editors: Brett Spitale, bspitale@hemophilia.org; Neil Frick, MS, nfrick@hemophilia.org. Advertising Sales: Tom Corcoran, thomascorcoranjr@yahoo.com, 215.275.6420. Contributing Staff Associate: Angelina Wang. MANIFEST Managing Editor: Donna Behen, donna.behen@manifest.com. Senior Editor: Matt Morgan. Creative Director: John Lanuza. Art Director: Angela Koch. Senior Photo Editor: Leah Rudolfo. The National Bleeding Disorders Foundation is grateful to BioMarin for sponsoring this special issue. *HemAware* (ISSN 1088-7008) is published by the National Bleeding Disorders Foundation (NBDF), 1230 Avenue of the Americas, 16th Floor, New York, NY 10020, 212.328.3700, toll free 800.42.HANDI, fax 212.328.3777.

IS GENE THERAPY RIGHT FOR YOU?

BioMarin is here to help you learn what all the buzz is about—from curiosity to eligibility and beyond.

We'll help you find out how to get started and learn what questions to ask your healthcare team.

Ask your healthcare team about eligibility testing today.

BIOMARIN

~~DAYS~~
~~WEEKS~~
~~MONTHS~~

YEARS WITHOUT PROPHYLAXIS IS POSSIBLE

Results are based on 112 people whose data were collected for at least 6 months before receiving ROCTAVIAN and compared with their data over a 3-year follow-up period.*

90 out of 112 people responded to ROCTAVIAN and were able to stop and stay off continuous prophylaxis.†‡

*The 3-year follow-up period began 5 weeks or more after administration and consists of a median follow-up of 3 years with a range of 1.7 to 3.7 years. Median is the middle number in a list of numbers arranged from smallest to largest. Range shows the lowest and highest numbers in a list.

†ROCTAVIAN was studied in 112 people whose data were collected for at least 6 months before their infusion (rollover population) and 22 people who immediately received their infusion (directly enrolled population). ROCTAVIAN worked for 80% (90/112) of people in the rollover population and 68% (15/22) of people in the directly enrolled population throughout the 3-year follow-up period. Andrew was part of the directly enrolled population.

‡Prophylaxis is defined as the ongoing use of Factor VIII or another treatment to prevent bleeds.

What is ROCTAVIAN?

ROCTAVIAN is a one-time gene therapy used for the treatment of adults with severe hemophilia A who do not have antibodies to the virus, AAV5 which is determined by a blood test.

Important Safety Information

Do not take ROCTAVIAN if you have an active infection or if you have a long-term infection that is not controlled by the medicines you take, have scarring of the liver (significant liver fibrosis or cirrhosis), are allergic to mannitol (an inactive ingredient in ROCTAVIAN).

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

ROCTAVIAN may cause serious side effects during the infusion and afterward:

- During and in the hours following the infusion, tell your doctor or nurse immediately about any symptoms you experience, including hives or other rashes, itching, sneezing, coughing, difficulty breathing, runny nose, watery eyes, tingling throat, nausea (feeling sick), diarrhea, low blood pressure, rapid heartbeat, light-headedness (near-fainting), fever, chills, or shivering. Talk to your doctor about what to do if you experience any side effects after you leave the infusion
- Before and regularly following administration of ROCTAVIAN, your doctor will perform blood tests to check your liver health. Make sure you obtain these blood tests during the specified time your doctor instructs you to. Based on your liver test results, you may need to take corticosteroids or another medicine for a period of time (several months or longer) to help decrease liver enzyme levels, which may cause side effects while you receive them. Talk to your doctor about these side effects and what you need to do to improve and maintain your liver's health

ROCTAVIAN™

(valoctocogene roxaparvovec-rvox)

Suspension for intravenous infusion

Get started with eligibility testing today

Visit ROCTAVIAN.com

- Patients with active Factor VIII inhibitors should not take ROCTAVIAN. Following administration your doctor will monitor you for inhibitors and you will have regular factor level testing. Talk to your doctor if you start bleeding following ROCTAVIAN, in order for your doctor to assess the need for additional tests or treatments
- Depending on your risk factors, an improvement in Factor VIII levels may mean an increased possibility of unwanted blood clots (so called "thromboses," in either veins or arteries). You and your doctor should discuss your risk factors before and after treatment and how to recognize symptoms of unwanted clots and what to do if you think you may have one
- ROCTAVIAN can insert itself into the DNA of human body cells. The effect that insertion may have on those cells is unknown, but such events may contribute to a theoretical risk of cancer. There have been no reported cases of cancer caused by treatment with ROCTAVIAN. Your doctor may perform regular monitoring if you have pre-existing risk factors for developing liver cancer. In the event of cancer, your doctor may send a sample to BioMarin Pharmaceutical Inc. for further testing

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 the brief summary of the Patient Information on the next page and Prescribing Information at ROCTAVIAN.com.

BIOMARIN

Brief Summary of Patient Information

What is ROCTAVIAN?

ROCTAVIAN is a one-time gene therapy used for the treatment of adults with severe hemophilia A who do not have antibodies to the virus, AAV5 which is determined by a blood test. ROCTAVIAN uses a modified virus, called a vector, to deliver a working copy of the Factor VIII gene to liver cells to enable your body to produce clotting factor on its own, which helps the blood to clot and prevents or reduces the occurrence of bleeding. The modified virus does not contain viral DNA and does not cause disease in humans.

Do not take ROCTAVIAN if you:

- Have an active infection or if you have a long-term infection that is not controlled by the medicines you take
- Have scarring of the liver (significant liver fibrosis or cirrhosis)
- Are allergic to mannitol (an inactive ingredient in ROCTAVIAN)

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

ROCTAVIAN may cause serious side effects during the infusion and afterward:

- During and in the hours following the infusion, tell your doctor or nurse immediately about any symptoms you experience, including hives or other rashes, itching, sneezing, coughing, difficulty breathing, runny nose, watery eyes, tingling throat, nausea (feeling sick), diarrhea, low blood pressure, rapid heartbeat, light-headedness (near-fainting), fever, chills, or shivering. Talk to your doctor about what to do if you experience any side effects after you leave the infusion
- Before and regularly following administration of ROCTAVIAN, your doctor will perform blood tests to check your liver health. Make sure you obtain these blood tests during the specified time your doctor instructs you to. Based on your liver test results, you may need to take corticosteroids or another medicine for a period of time (several months or longer) to help decrease liver enzyme levels, which may cause side effects while you receive them. Talk to your doctor about these side effects and what you need to do to improve and maintain your liver's health
- Patients with active Factor VIII inhibitors should not take ROCTAVIAN. Following administration your doctor will monitor you for inhibitors and you will have regular factor level testing. Talk to your doctor if you start bleeding following ROCTAVIAN, in order for your doctor to assess the need for additional tests or treatments
- Depending on your risk factors, an improvement in Factor VIII levels may mean an increased possibility of unwanted blood clots (so called "thromboses," in either veins or arteries). You and your doctor should discuss your risk factors before and after treatment and how to recognize symptoms of unwanted clots and what to do if you think you may have one
- ROCTAVIAN can insert itself into the DNA of human body cells. The effect that insertion may have on those cells is unknown, but such events may contribute to a theoretical risk of cancer. There have been no reported cases of cancer caused by treatment with ROCTAVIAN. Your doctor may perform regular monitoring if you have pre-existing risk factors for developing liver cancer. In the event of cancer, your doctor may send a sample to BioMarin Pharmaceutical Inc. for further testing

What should I tell my doctor before I get ROCTAVIAN?

Talk to your doctor about the following:

- **Your medical conditions including:**
  - — Any general risk factors for unwanted blood clots and for cardiovascular disease
  - — If your immune system's ability to fight infections is reduced
  - — If you have inhibitors or a history of inhibitors to Factor VIII
- **All medicines you take or new medicines you plan to take,** including prescription and nonprescription drugs, vitamins, herbal supplements, and vaccines
- If you have a female partner that plans to become pregnant within 6 months of treatment

What should I avoid after taking ROCTAVIAN?

- Avoid alcohol use for the first year. Talk to your doctor about how much alcohol may be acceptable after the first year
- You and any female partner must prevent becoming pregnant for 6 months. Discuss with your doctor which methods of contraception are suitable
- Do not donate semen for at least 6 months after treatment
- Do not donate blood, organs, tissues, or cells

What are the possible side effects of ROCTAVIAN?

- **The most common side effects of ROCTAVIAN are:**
  - — Nausea, fatigue, headache, infusion-related reactions, vomiting, and abdominal pain
  - — Changes to laboratory results from blood tests that measure your liver health and other ways your body is responding to ROCTAVIAN

What other information should I know before getting ROCTAVIAN?

- **Receiving gene therapy again in the future:** ROCTAVIAN is a one-time treatment. Currently, treatment with ROCTAVIAN means you cannot receive another gene therapy for hemophilia
- **Hemophilia treatment registry:** After treatment with ROCTAVIAN, you will be asked to enroll in a 15-year registry to help study the long-term safety of the treatment and how well it continues to work
- **Understanding the risks and benefits of ROCTAVIAN:** While the majority of patients experience a benefit from ROCTAVIAN, the treatment response and duration may vary. Some patients do not experience a benefit from ROCTAVIAN. It is not possible to predict if and how much a patient may benefit. After administration, your doctor will monitor your lab tests and talk to you about whether you can stop prophylaxis, whether you should start prophylaxis again, and whether and how you should treat any surgeries, procedures, injuries, or bleeds

Talk to your doctor about the potential risks and benefits of ROCTAVIAN. Whether a patient experiences a benefit or not, the risks discussed here and with your doctor still apply.

These are not all the possible side effects of ROCTAVIAN. Talk to your doctor for medical advice about side effects. You may report side effects to BioMarin Pharmaceutical Inc. at 1-866-906-6100 or FDA at 1-800-FDA-1088.

Please see additional safety information in the Prescribing Information and Patient Information at ROCTAVIAN.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.

Manufactured by
BIOMARIN®
BioMarin Pharmaceutical Inc.
105 Digital Drive, Novato, CA 94949

AN INTERVIEW WITH

DR MARK REDING

Dr. Mark Reding, Director of the Center for Bleeding and Clotting Disorders at University of Minnesota Medical Center in Minneapolis, talks about gene therapy.

Tell me a little bit about yourself.

I was born and raised in South Dakota. As an undergraduate, I wasn't sure what I wanted to do, but I liked science and wanted to stay in school as long as possible (mostly to avoid making a career path decision). Medical school seemed like a good way to do that. I came to the University of Minnesota for medical school in 1988, and 35 years later I am still at the same institution.

When did you first become interested in gene therapy research, and why?

I spent a few years in the lab during my fellowship and early in my faculty career. We were studying the immune response to Factor VIII and why some people make inhibitor antibodies and others don't. At that time, we knew that gene therapy was coming, and we were curious about the potential of it.

How have you seen the concept of gene therapy progress over the years?

When the first gene therapy clinical trials started in the mid to late 1990s, this approach had already been in preclinical development for about 20 years. At that time, we thought this treatment would be a clinical option in the near future and not take another 25 years.

GENE THERAPY ELIGIBILITY CONSIDERATIONS

How do you decide who is a good candidate for gene therapy?

I think we need to keep a very open mind here. There are many things that impact an individual's eligibility for gene therapy. And moving forward with this treatment option includes careful consideration and collaboration between the patient and the hemophilia healthcare team. We now have many good treatment options for hemophilia, and the reasons why gene therapy may be a good option for one individual may be different than for another.

When considering candidates, how do you think beyond those potentially "ideal" candidates?

I don't think we can really define an "ideal" candidate. There are many factors to consider, and this is a good example of how the approach of "shared clinical decision-making" can be extremely helpful in coming to the right decision.

How can people learn more about these treatment options?

There are many resources out there, but I believe the best place to start is at their hemophilia treatment center (HTC). The HTC team should be well equipped to help those considering gene therapy and to connect them to resources to help navigate this process.

AN INTERVIEW WITH

DR MARK READING

TREATMENT-RELATED CONSIDERATIONS

What do you think people should know about eligibility testing for gene therapy?

One thing to remember is that eligibility testing might also include checking for the presence of antibodies against the vector, as results would have an impact on the decision to move forward or not.

How would you advise people considering gene therapy to better understand insurance coverage, out-of-pocket costs, and manufacturer-supported services?

The best place for people to start is at the HTC. Their HTC team should be very experienced in these areas and have the ability to make connections with outside resources if needed.

What are the potential concerns you see with gene therapies?

You would need to talk to your doctor about the safety of any gene therapy treatment. But one immediate concern for someone considering gene therapy is that we do not yet have the ability to predict how well a person will respond and the durability of some gene therapy treatments.

Do you see gene therapy for hemophilia becoming more mainstream?

As we continue to figure out the high degree of variability in individual responses to therapy, as well as questions about durability, over time, I believe gene therapy has the potential to become more mainstream.

How does health equity impact your treatment decisions for gene therapy?

In my view, we are obligated to do everything we can to ensure that everyone has the same access to treatment for their bleeding disorder, including gene therapy.

What most excites you about gene therapy for hemophilia?

I am excited about the possibilities that gene therapy may offer for those in other parts of the world where access to the currently available therapies is still very limited.

IF YOU COULD PROVIDE
ONE WORD
TO DESCRIBE
GENE THERAPY,
WHAT WOULD IT BE?

PROGRESS.

A CANDID INTERVIEW WITH ANDREW.

MY ROCTAVIAN EXPERIENCE.

We sat down with Andrew, who was part of the ROCTAVIAN clinical trial and helped make the FDA approval possible.

ROCTAVIAN is a one-time gene therapy used for the treatment of adults with severe hemophilia A who do not have antibodies to the virus, AAV5 which is determined by a blood test. Do not take ROCTAVIAN if you have an active infection or if you have a long-term infection that is not controlled by the medicines you take, have scarring of the liver (significant liver fibrosis or cirrhosis), are allergic to mannitol (an inactive ingredient in ROCTAVIAN).

Before ROCTAVIAN

Tell me a little bit about yourself.

Well, first off, I'm an adult living with severe hemophilia A. I'm also a father to an adventurous toddler, and I've been married for almost 6 years. I teach high school history and enjoy jogging and other outdoor activities.

Why did you decide to participate in the ROCTAVIAN clinical trial?

At the age of 27, I had my prophylaxis regimen down, but I decided to do it for the hemophilia A community.

How did you first learn about ROCTAVIAN gene therapy?

I first learned about ROCTAVIAN through my nurse at my hemophilia treatment center (HTC). She was my caretaker nurse who gave me infusions when I was young.

What questions did you ask yourself and/or your care team?

My internal question was, 'Is this going to be an option for me?' After talking with my care team and my family, I believed that it was worth it to myself and to others to give it a try. Once I understood the safety concerns, I was ready to do it. The only other consideration was between my wife and I because doing the trial would mean waiting to have a baby.*

*You and your female partner must use an effective form of birth control for 6 months after ROCTAVIAN to prevent pregnancy, and you should not donate semen.

During ROCTAVIAN

What was your experience like on infusion day?

I remember everything about my infusion day. My wife was by my side the whole time, went with me, and sat right next to me. For me, the infusion itself was about 4 hours, and my doctors monitored me throughout and continued to check on me afterwards.†

†Temporary infusion-related reactions may occur during, or shortly after, treatment. Some of the reactions may include:

- Hives or other rashes
- Itching, sneezing, coughing, difficulty breathing, runny nose, watery eyes, tingling throat
- Nausea (feeling sick), diarrhea
- Low blood pressure, rapid heartbeat, light-headedness (near-fainting)
- Fever, chills, shivering

Where did you go for your follow-up, and was it different than your dosing location?

I traveled to Michigan to be dosed, but my follow-up regimen and blood draws were all done at my local HTC. This was great for me because I was able to plan around the schedule. In the first 6 months after gene therapy, the follow-up appointments are fairly frequent, once per week, and I was honestly curious to see where my Factor VIII levels were each week.‡

‡**Follow-up schedule:** First 6 months: weekly; Next 6 months: every 1 to 2 weeks; Year 2: Every 3 months; After Year 2: Every 6 months.

When did you notice ROCTAVIAN was working?

The first sign for me that it was working was about 3 to 4 weeks after I had received ROCTAVIAN. I cut myself while I was shaving and immediately ran to the fridge to get factor, but before I could even get to the other room, the bleeding had stopped.§

§ROCTAVIAN did not work for everyone. Some patients did not respond to treatment or lost response to treatment. It is not possible to predict if and how much you may benefit from ROCTAVIAN. After taking ROCTAVIAN, your doctor will monitor your lab tests and talk to you about whether you can stop prophylaxis, whether you should start prophylaxis again, and whether and how you should treat for any surgeries, procedures, injuries, or bleeds. Individual Factor VIII levels produced and durability of levels reached can vary.

Depending on your risk factors, an improvement in Factor VIII levels may mean an increased possibility of unwanted blood clots (also called "thromboses," in either veins or arteries). You and your doctor should discuss your risk factors before and after treatment and how to recognize symptoms of unwanted clots and what to do if you think you may have one.

After ROCTAVIAN

Why would you encourage others to get tested to see if they're eligible for gene therapy for hemophilia?

I really got excited about ROCTAVIAN after I started doing more research and talking to more doctors about it. I truly believe it deserves consideration, and if others are interested, they should talk to their doctor and check for eligibility.

Since your one-time infusion of ROCTAVIAN, have you had to resume ongoing prophylaxis after you stopped?

With ROCTAVIAN I was able to make my own Factor VIII and stop and stay off continuous prophylaxis through 3 years.‖¶

‖Individual results may vary. Before ROCTAVIAN, the average annualized bleeding rate (ABR) was 5.4. After ROCTAVIAN, the average ABR dropped to 2.6.

¶13 out of 112 people (12%) returned to continuous prophylaxis after ROCTAVIAN, with a median start time at 2.3 years with a range of 0.1 to 3.3 years. An ABR of 35 was added to account for the periods when these people were on prophylaxis.

Do you consider yourself a role model for the gene therapy or hemophilia community?

I don't know that I would necessarily consider myself a role model, but a big part of why I decided to be a part of the clinical trial was for the hemophilia community. I just hope that the data and the positive experience I've had can encourage more people to consider gene therapy for hemophilia A.

How would you feel, and what would you do, if this all stopped working tomorrow?

I would feel grateful for the 3 years I had without prophylaxis.#

#90/112 people responded to ROCTAVIAN and were able to stop and stay off continuous prophylaxis. ROCTAVIAN worked for 80% (90/112) of people in the rollover population and 68% (15/22) of people in the directly enrolled population throughout the 3-year follow-up period. Prophylaxis is defined as the ongoing use of Factor VIII or another treatment to prevent bleeds.

The 3-year follow-up period began 5 weeks or more after administration and consists of a median follow-up of 3 years with a range of 1.7 to 3.7 years. Median is the middle number in a list of numbers arranged from smallest to largest.

ROCTAVIAN was studied in 112 people whose data were collected for at least 6 months before their infusion (rollover population) and 22 people who immediately received their infusion (directly enrolled population). In the rollover population, the average Factor VIII level was 34%, with a range of 0 to 291.4 at Year 3. Results were measured using a one-stage test, which is one way to measure Factor VIII levels. Range shows the lowest and highest numbers in a list. Andrew was part of the directly enrolled population.

ROCTAVIAN can insert itself into the DNA of human body cells. The effect that insertion may have on those cells is unknown, but such events may contribute to a theoretical risk of cancer. There have been no reported cases of cancer caused by treatment with ROCTAVIAN. Your doctor may perform regular monitoring if you have pre-existing risk factors for developing liver cancer. In the event of cancer, your doctor may send a sample to BioMarin Pharmaceutical Inc. for further testing.

INSPIRED

WHAT'S THE **ONE WORD** YOU WOULD USE **TO DESCRIBE YOUR GENE THERAPY EXPERIENCE?**

BIOMARIN

ROCTAVIAN™ (valoctocogene roxaparvovec-rvox)
Suspension for intravenous infusion

Indication and Important Safety Information

What is ROCTAVIAN?

ROCTAVIAN is a one-time gene therapy used for the treatment of adults with severe hemophilia A who do not have antibodies to the virus, AAV5 which is determined by a blood test. ROCTAVIAN uses a modified virus, called a vector, to deliver a working copy of the Factor VIII gene to liver cells to enable your body to produce clotting factor on its own, which helps the blood to clot and prevents or reduces the occurrence of bleeding. The modified virus does not contain viral DNA and does not cause disease in humans.

Do not take ROCTAVIAN if you:

- Have an active infection or if you have a long-term infection that is not controlled by the medicines you take
- Have scarring of the liver (significant liver fibrosis or cirrhosis)
- Are allergic to mannitol (an inactive ingredient in ROCTAVIAN)

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

ROCTAVIAN may cause serious side effects during the infusion and afterward:

- During and in the hours following the infusion, tell your doctor or nurse immediately about any symptoms you experience, including hives or other rashes, itching, sneezing, coughing, difficulty breathing, runny nose, watery eyes, tingling throat, nausea (feeling sick), diarrhea, low blood pressure, rapid heartbeat, light-headedness (near-fainting), fever, chills, or shivering. Talk to your doctor about what to do if you experience any side effects after you leave the infusion
- Before and regularly following administration of ROCTAVIAN, your doctor will perform blood tests to check your liver health. Make sure you obtain these blood tests during the specified time your doctor instructs you to. Based on your liver test results, you may need to take corticosteroids or another medicine for a period of time (several months or longer) to help decrease liver enzyme levels, which may cause side effects while you receive them. Talk to your doctor about these side effects and what you need to do to improve and maintain your liver's health
- Patients with active Factor VIII inhibitors should not take ROCTAVIAN. Following administration your doctor will monitor you for inhibitors and you will have regular factor level testing. Talk to your doctor if you start bleeding following ROCTAVIAN, in order for your doctor to assess the need for additional tests or treatments
- Depending on your risk factors, an improvement in Factor VIII levels may mean an increased possibility of unwanted blood clots (so called "thromboses," in either veins or arteries). You and your doctor should discuss your risk factors before and after treatment and how to recognize symptoms of unwanted clots and what to do if you think you may have one
- ROCTAVIAN can insert itself into the DNA of human body cells. The effect that insertion may have on those cells is unknown, but such events may contribute to a theoretical risk of cancer. There have been no reported cases of cancer caused by treatment with ROCTAVIAN. Your doctor may perform regular monitoring if you have pre-existing risk factors for developing liver cancer. In the event of cancer, your doctor may send a sample to BioMarin Pharmaceutical Inc. for further testing

What should I tell my doctor before I get ROCTAVIAN?

Talk to your doctor about the following:

- **Your medical conditions including:**
  - Any general risk factors for unwanted blood clots and for cardiovascular disease
  - If your immune system's ability to fight infections is reduced
  - If you have inhibitors or a history of inhibitors to Factor VIII
- **All medicines you take or new medicines you plan to take,** including prescription and nonprescription drugs, vitamins, herbal supplements, and vaccines
- If you have a female partner that plans to become pregnant within 6 months of treatment

What should I avoid after taking ROCTAVIAN?

- Avoid alcohol use for the first year. Talk to your doctor about how much alcohol may be acceptable after the first year
- You and any female partner must prevent becoming pregnant for 6 months. Discuss with your doctor which methods of contraception are suitable
- Do not donate semen for at least 6 months after treatment
- Do not donate blood, organs, tissues, or cells

What are the possible side effects of ROCTAVIAN?

- **The most common side effects of ROCTAVIAN are:**
  - Nausea, fatigue, headache, infusion-related reactions, vomiting, and abdominal pain
  - Changes to laboratory results from blood tests that measure your liver health and other ways your body is responding to ROCTAVIAN

What other information should I know before getting ROCTAVIAN?

- **Receiving gene therapy again in the future:** ROCTAVIAN is a one-time treatment. Currently, treatment with ROCTAVIAN means you cannot receive another gene therapy for hemophilia
- **Hemophilia treatment registry:** After treatment with ROCTAVIAN, you will be asked to enroll in a 15-year registry to help study the long-term safety of the treatment and how well it continues to work
- **Understanding the risks and benefits of ROCTAVIAN:** While the majority of patients experience a benefit from ROCTAVIAN, the treatment response and duration may vary. Some patients do not experience a benefit from ROCTAVIAN. It is not possible to predict if and how much a patient may benefit. After administration, your doctor will monitor your lab tests and talk to you about whether you can stop prophylaxis, whether you should start prophylaxis again, and whether and how you should treat any surgeries, procedures, injuries, or bleeds

Talk to your doctor about the potential risks and benefits of ROCTAVIAN. Whether a patient experiences a benefit or not, the risks discussed here and with your doctor still apply.

These are not all the possible side effects of ROCTAVIAN. Talk to your doctor for medical advice about side effects. You may report side effects to BioMarin Pharmaceutical Inc. at 1-866-906-6100 or FDA at 1-800-FDA-1088.

Please see additional safety information in the Prescribing Information and Patient Information at ROCTAVIAN.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.

Manufactured by
BioMarin Pharmaceutical Inc.
105 Digital Drive, Novato, CA 94949

One-to-one treatment support

BIOMARIN RARECONNECTIONS™ IS WITH YOU RIGHT FROM THE START

FINANCIAL NAVIGATION SUPPORT

- **Understand potential out-of-pocket** costs associated with one-time ROCTAVIAN gene therapy
- **Navigate the insurance process** and learn about coverage options to gain access to gene therapy
- **Identify potential financial assistance options,** including co-pay support for commercially insured patients*
- **Educate and work with your healthcare provider's office** on insurance coverage requirements for access to gene therapy

LAB SUPPORT

For qualified commercially insured patients:

- **Mobile blood draw services** for pre-infusion eligibility testing and post-infusion follow-up†
- **Walk-in lab support** (eg, Quest Patient Service Center) for pre-infusion eligibility and post-infusion follow-up†

BioMarin Rare Connections™

1-833-ROCTAVIAN

Learn how **BioMarin RareConnections™** can help you before, during, and after ROCTAVIAN treatment.

BIOMARIN-RARECONNECTIONS.COM

ROCTAVIAN™
(valoctocogene roxaparvovec-rvox)
Suspension for intravenous infusion

BIOMARIN

*Valid only for those patients with commercial prescription insurance coverage for products who meet eligibility criteria. Offer not valid for prescriptions, administration, or related labs reimbursed, in whole or in part, by any federal, state, or government-funded insurance programs (for example, Medicare, Medicare Advantage, Medigap, Medicaid, VA, DoD, or TRICARE), for cash-paying patients, where product, administration, or related labs are not covered by patient's commercial insurance, where patient's commercial insurance plan reimburses them for the entire cost of their prescription drug, administration, and/or related labs, or where prohibited by law or by the patient's health insurance provider. Patients who are residents of certain states (MA or RI) are not eligible for drug administration co-pay support. Patients who are residents of certain states (MI, MN, or RI) are not eligible for laboratory services co-pay support. If at any time a patient begins receiving prescription drug, administration, or related lab coverage under any such federal, state, or government-funded healthcare program, patient will no longer be able to use the BioMarin Co-Pay Assistance Program and patient must notify BioMarin RareConnections at 1-833-ROCTAVIAN (1-833-762-8284) to stop participation. Patients may not seek reimbursement for the value of the out-of-pocket expense amount covered by the Program from any third-party payer, whether public or private. The Program is valid ONLY for qualifying patients residing in the 50 US states or in Puerto Rico with commercial insurance who have a valid prescription for an FDA-approved indication for the qualifying BioMarin therapy. This program is not health insurance. Offer may not be combined with any other rebate, coupon, or offer. Co-payment assistance under the Program is not transferable. BioMarin Pharmaceutical Inc. reserves the right to rescind, revoke, or amend the Program without notice. Patient/caregiver certifies responsibility for complying with applicable limitations, if any, of any commercial insurance and reporting receipt of program rewards, if necessary, to any commercial insurer. The Program is subject to termination or modification at any time. Some restrictions apply.

†Mobile blood draw services and walk-in lab support for blood draws related to ROCTAVIAN gene therapy are for commercially insured patients only. These services are not available to residents of certain states (MI, MN, RI). Some restrictions apply.