Andrew,
ROCTAVIAN
clinical study
participant

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

WHAT IF YOU COULD MAKE YOUR OWN FACTOR VIII?

It's possible with a one-time infusion of ROCTAVIAN

The only approved gene therapy for eligible adults with severe hemophilia A

Individual Factor VIII levels produced and durability of levels reached can vary.

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.

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).

Please see Important Safety Information throughout and in the Prescribing Information and Patient Information.

BIOMARIN®

One-time ROCTAVIAN. Improved bleed control through 3 years.

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

Before ROCTAVIAN, the average annualized bleeding rate (ABR) was 5.4. After ROCTAVIAN, the average ABR dropped to 2.6.†

Three years after his one-time treatment, Andrew is still making his own Factor VIII.

Individual Factor VIII levels produced and durability of levels reached can vary.

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 difference between the lowest and highest numbers in a list. Andrew was part of the directly enrolled population.

*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.

†13 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.

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

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~~DAYS~~ ~~WEEKS~~ ~~MONTHS~~ YEARS WITHOUT PROPHYLAXIS IS POSSIBLE

Meet Andrew: a runner, teacher, and father who is part of the ROCTAVIAN gene therapy clinical study.

Andrew used Factor VIII prophylaxis regularly until he received his one-time treatment of ROCTAVIAN. He worked with his doctor to monitor his levels over the following weeks to see if he could stop treatment.

Andrew was able to stop and stay off continuous prophylaxis throughout a 3-year follow-up period.*

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.

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

Connect with a BioMarin representative today to find out if you're eligible.

Visit ROCTAVIAN.com

What is the most important information I should know about ROCTAVIAN? (cont.)

- 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

Please see Important Safety Information throughout and in the Prescribing Information and Patient Information.

Safety data

Select warnings and precautions:

- 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
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- 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

Most common side effects from the clinical study:

Nausea	Fatigue	Headache
Infusion-related reactions	Vomiting	Abdominal pain

Changes to laboratory results from blood tests that measure your liver health and other ways your body is responding to ROCTAVIAN

The results are based on 134 people from 2 study populations. 112 people were part of a rollover study, collecting baseline data for at least 6 months before their ROCTAVIAN infusion and 22 people were directly enrolled and immediately received ROCTAVIAN.

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Indication and Important Safety Information

What is ROCTAVIAN?

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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:

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Important Safety Information (cont.)

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.

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