Roctavian Eases Suffering For Adults With Severe Hemophilia A

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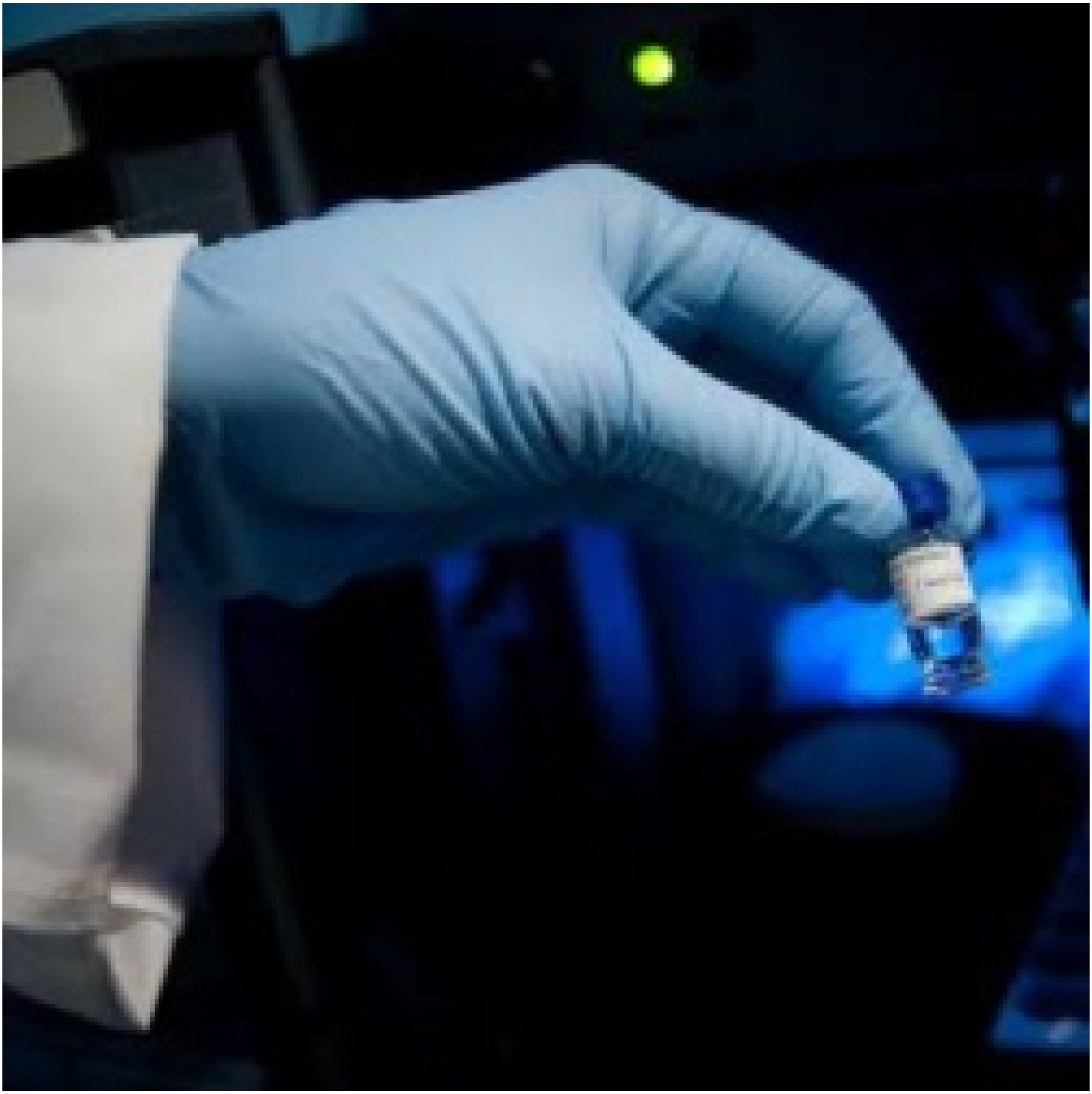
Hemophilia is a rare bleeding disorder in which the blood does not clot properly, resulting in extended bleeding time after an injury or internal bleeding, which may be life threatening. Many individuals with hemophilia become physically or mentally disabled from chronic joint damage due to bleeding. Hemophilia is caused by the blood having little or none of a specific plasma protein, or clotting factor, which is needed for normal clotting.
There are 3 types of hemophilia, based on which clotting factor is low or missing, A and B are the most common:

- Hemophilia A — caused by a deficiency of clotting factor VIII
- Hemophilia B — caused by a deficiency of clotting factor IX
- Hemophilia C — caused by a deficiency of clotting factor XI

Conventional treatment for hemophilia is based on the severity of the condition in each individual, along with their activity level and need for future medical or dental procedures. The main treatment is a preventative clotting factor replacement therapy usually administered several times a week. More recently, a non-factor monoclonal antibody administered every one to four weeks has become available for hemophilia A which provides a more consistent bleed protection. In contrast to conventional therapies which must be administered over and over, a gene therapy for hemophilia A developed using St. Jude intellectual property offers a more permanent solution.

On June 29, 2023, Roctavian (valoctocogene roxaparvovec) was the first gene therapy for adults with severe



hemophilia A to be approved by the FDA. The European Commission had previously approved the gene therapy in August 2022. Roctavian is a single-dose treatment for people with hemophilia A using an adeno-associated viral- (AAV) type vector carrying the Factor VIII gene into liver cells, enabling a persistent increase of their levels of Factor VIII. This has improved their body's ability to control bleeding without regular injections.

The vector used in this treatment was largely developed through pioneering work by St. Jude, the University College London (UCL), and the National Institutes of Health (NIH). The St. Jude work was led by Drs. Andrew Davidoff and John Gray, and the UCL was led by former St. Jude post doc Amit Nathwani. The NIH work (led by Robert Kotin, Jay Chiorini, and their colleagues) focused on a new method of producing AAV vectors in insect cells and the development of the AAV5 vector used in the product itself. At each institution these were also largely the same teams who contributed to **Hemgenix**, a gene therapy for the treatment of adults living with hemophilia B. The technology behind Roctavian was licensed to BioMarin Pharmaceuticals, Inc. in 2013 by St. Jude and with two agreements from NIH in 2013 and 2015, respectively.

The FDA approval for Roctavian was supported by results from BioMarin's pivotal GENEr-8 trial, the longest global

Phase 3 study to date for any gene therapy in hemophilia A. The therapy was shown to be effective in reducing the rate of bleeding in a cohort of 134 patients for at least three years. Participants in the Phase 2 study have been observed for more than five years with evidence of diminishing factor levels over time in some.

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