DEAR FRIENDS—

One of our guiding principles since our founding has been to provide the tools and education patients and their families need to make informed decisions about their bleeding disorder. This annual special edition of Dateline Federation is a product of our focus on that principle. We hope you find this tool helpful in your journey navigating treatment options and emerging therapies and a conversation starter for you and your medical providers.

It was 17 years ago when I was choosing a treatment option for my newborn son with severe hemophilia A. The overwhelming feeling remains vivid. It was a confusing and scary process, despite having wonderful support from the staff at our local Hemophilia Treatment Center. I was a mom, unsure of how to even spell hemophilia at that point, just wanting to make the right call for my baby’s health. But, I didn’t know what questions to ask, what specifics to consider or even what our options were. At that time, little did I know that the number of treatment options for bleeding disorders would nearly double before my son even graduated high school and that novel treatment options beyond a recombinant clotting factor would become readily accessible.

As patients, we have the right to know our options. But it is our responsibility to educate and empower ourselves about our disorder. From our community’s history we know that patients and their families look to advocacy organizations such as HFA to provide the facts and information needed. HFA remains committed to being a trusted source of information for you. Furthermore, we are steadfast in our commitment to ensure a safe blood supply and transparency around treatment options and their efficacy.

We’re continually evaluating the educational content we produce, always looking for ways to improve the resources we create for families. This product guide and list of emerging therapies has evolved over the past five years in an effort to create a tool that is useful. Our team is currently exploring ways to dive deeper into the topics you see in these pages, including an overview of products by disorder, access issues in insurance coverage and a look at the future of gene therapy and other new novel treatments.

As always, we want to hear from you to know if these are topics you want us to focus on, with the possibility of HFA hosting a multi-day online event focused on treatment options. What do you think is missing from the current tools and resources available to you and your family around treatment options and emerging therapies? Who do you want to hear from: doctors, researchers, manufacturers? Contact us at info@hemophiliafed.org; we’d love to hear from you.

Our legacy as a community of informed, engaged, educated and empowered advocates demands we always continue to gain the knowledge we need to move forward toward improved treatments and outcomes for everyone. Let this resource be a launching point for you.

Sonji Wilkes

Hemophilia Mom
VP, Policy & Advocacy

DATELINE FEDERATION < www.hemophiliafed.org
**COVID-19 VACCINES DON’T STOP EMERGING THERAPY OPTIONS FOR THOSE WITH BLEEDING DISORDERS**

By HFA STAFF WITH SCIENTIFIC REVIEW BY DR. DAVID CLARK AND DR. LISA HENSLEY

Many people have questions about the COVID-19 vaccines. This article will answer one primary question: Can getting vaccinated for COVID-19 cut off treatment options for emerging bleeding disorder treatments and therapies? Of the three vaccines currently available in the United States, the Pfizer and Moderna vaccines use messenger ribonucleic acid (mRNA) technology while the Johnson & Johnson vaccine uses a viral vector.

**HOW THESE VACCINES WORK**

The virus that causes COVID-19 is called SARS-CoV-2, which is a coronavirus. Coronaviruses have protein spikes sticking out of them that allow the virus to attach to and enter cells. All three vaccines use that spike protein to help our bodies develop an immune response to prevent illness.

In the case of the mRNA vaccines, when you get the shot, mRNA goes into cells and sends “instructions” to the cells to create the spike protein. By itself, the spike protein will not cause COVID-19 — it’s just one piece of the virus. The mRNA lasts in your system for about 24 hours and then starts to degrade, but your cells will continue to express the spike proteins for a few days. Your immune system recognizes those spike proteins as foreign and starts creating an immune response against them. The first dose of the vaccine starts this process and provides some protection. The second dose raises and refines that protection to about 95% and helps the effects of the vaccine last longer.

The refinement is like the second time you play an opponent in a sport: Even if they change some of their strategy, you are better able to handle them.

The Johnson & Johnson vaccine works differently, using something called a “viral vector.” A viral vector is created when scientists test a nonpathogenic virus, (that doesn’t make humans sick) and alter it to do something different. For the vaccine, Johnson & Johnson took an adenovirus and replaced part of the DNA in it with the SARS-CoV-2 spike protein. When you get the shot, the adenovirus enters your cells, giving them the genetic instructions to make the spike protein. Once those spike proteins start appearing on the surfaces of your cells, your immune system recognizes them as foreign and builds an immune response against them. As with the mRNA, the viral vector does not replicate well, so it also degrades out of the body.

Johnson & Johnson vaccine requires only one dose at this time.
SO, LET’S BUST SOME MYTHS:

**MYTH 1**
Getting an mRNA vaccine will prevent you from being able to receive future bleeding disorder treatments that use mRNA.
There is no evidence that having an mRNA vaccine will close off access to future bleeding disorder treatments that use mRNA. The mRNA from the vaccine goes in and gives instructions to make the SARS-CoV-2 spike protein and then is degraded in about 24 hours.

**MYTH 2**
Getting a viral vector vaccine will prevent you from being able to receive future bleeding disorder gene therapy treatments.
There is no evidence that having a gene therapy vaccine made from an adenovirus will close off access to future gene therapy bleeding disorder treatments that use AAV.

**MYTH 3**
Getting an mRNA vaccine will change your DNA.
Getting an mRNA vaccine does not create any permanent genetic changes. mRNA is a piece of genetic code that goes in, gives instructions to your cells, and, in the case of the vaccine mRNA, starts leaving your system in about 24 hours. It’s generally gone in about three days. In addition, the vaccine mRNA works on the outer part of muscle cells without going into the cells’ nuclei, which is where your genes/DNA are located.

**MYTH 4**
The vaccines can give you COVID-19.
Because the vaccines only use the SARS-CoV-2 spike protein, there is no way to get COVID-19 from a vaccine.
INFORMED CONSENT: A Process, Not Just a Form

BY HFA STAFF

Patients with bleeding disorders are no strangers to engaging in conversations with medical, research and pharmaceutical staff. Emergency rooms, doctors' offices, pharmaceutical company offices, conference rooms and exhibit halls have all become places to engage in medical discussions. Each of these venues has different, but similar, codes of ethics to follow when engaging in conversations about patients' health, and all require obtaining informed consent before conducting health care intervention or research through a study or trial.

Consent can only be obtained from a mentally competent adult or a legally authorized representative of a mentally incompetent adult. This legal status refers to the capacity of a person to act on their own behalf and their ability to understand the information presented, to appreciate the consequences of acting or not acting on that information, and to make a choice.

PARTICIPATION BY MINORS

A parent or legal guardian provides consent for a minor. However, children 12 and older who are asked to participate in a research project must do so voluntarily and must verbally, assent to the research project. The explanation of the project and the language used must be appropriate to the child. In some localities, even children as young as 7 years old are asked to consent to participate in research studies.

FDA REGULATIONS

Under the U.S. Food and Drug Administration regulations, an Institutional Review Board is an administrative body that has been formally designated to review and monitor biomedical research involving human subjects. The IRB has the authority to approve, require modifications needed to secure approval, or disapprove research. This group review serves an important role in the protection of the rights and welfare of human research subjects. (The local IRB that approves the study can provide more information about consent as it relates to children.)

RESEARCH AND CLINICAL TRIALS

Consent works differently in a hospital setting versus a research/clinical trial setting. In the research/clinical trial setting, the first step to understanding is discovering that a research study or clinical trial exists. Patients may learn about the existence of a research project or clinical trial via mail, telephone, through a friend or during an in-person visit with a doctor.

WHAT SHOULD I ASK?

• Is a written copy of the research procedures available?
• What are the benefits and risks of this research project?
• How will I be informed if there are changes to this project?
• Am I waiving any of my rights by signing this consent form?
• May I ask a person I trust to read this document?
• Will my name and address be kept confidential or will it be shared with others?
• How will my information be stored to protect my privacy?
• May I refuse to participate in this research project?
• What if I change my mind after I agree to participate?
• How do I withdraw my consent after I sign the form?
• If I withdraw my consent and stop participating, what will happen with the information already collected from me?
• Are there negative consequences if I withdraw my consent?
• (In case of pharmaceutical trials) Will I be given the actual medication or a placebo?
• (If English is not your first language) Is the information available in my preferred language?

WHAT HAVE I LEARNED?

• The purpose of the research.
• The name, address and phone number of the Principal Investigator.
• How long I am expected to participate.
• If any of the medications or procedures are experimental.
• The possible risks or discomforts.
• If there are any alternative procedures or courses of treatment.
• If my information and medical records will be kept confidential.
• If I will be paid for my participation.
• The medical treatments available if I get injured.
• Who I can call if I have questions.
• If I am required to participate in this study.
• If there is a penalty if I refuse to participate.
• If there is a penalty if I stop participating at any time.

More than a signature: Informed consent is about your understanding and willingness to participate in a study, not about signing a form.
A LOOK AT FDA’S GENE AND CELL THERAPY FRAMEWORK and its Impact on New Hemophilia Treatments in 2021 and Beyond

BY ANGELA N. JOHNSON, PH.D., RAC, CPGP
SENIOR DIRECTOR OF REGULATORY AFFAIRS AT SIGILON THERAPEUTICS IN CAMBRIDGE, MASSACHUSETTS, AND REGULATORY STRATEGY LECTURER AT NORTHEASTERN UNIVERSITY IN BOSTON

More cell and gene therapy products are being developed and entering clinical trials each year. The U.S. Food and Drug Administration plays a key role in overseeing drug development, including providing guidance and receiving investigational new drug applications or requests to start a new clinical trial submitted by drug developers.

In 2021, there are more than 1,000 cell and gene therapy clinical trials, including more than a dozen in hemophilia. FDA announced it expects more than 200 new requests to start clinical trials based on gene and cell technologies each year. By 2025, FDA expects 10 to 20 new CGT treatments will be approved annually.

Gene therapy treatments for hemophilia have shown potential to eliminate the need for prophylactic factor infusions and injections. Unlike gene therapy, newer technologies such as genetically modified factor-producing cells do not involve changes in patient genetic material and may allow better control of dosing as well as redosing. But many challenges and uncertainties face researchers and drug developers. To help set best practices across the industry, FDA guidance frameworks play an important role in safe and efficient development of CGT products.

WHAT ARE FDA GUIDANCE FRAMEWORKS?
To help the companies developing new drugs, FDA publishes recommendations called guidance documents. Unlike the laws passed by Congress or formal regulations, guidance documents contain FDA expectations and current scientific thinking not required by law. If we think of regulations as the law that requires drug developers to do, we can think of guidance documents as a playbook of how to do it in most, but not all, cases.

Guidance frameworks are groups of related guidance documents, such as those relating to CGT. New guidance creation is an important part of FDA’s ongoing mission to expedite innovations that make medical products more effective, safer and more affordable. Guidance documents are written and published according to a process called Good Guidance Practice, which describes how FDA staff will bring together expert and public feedback in guidance recommendations.

GROWING EXPECTATIONS FOR CGT IN HEMOPHILIA
FDA’s first draft guidance document dedicated to early development of CGT clinical trials — Guidance for Industry: Considerations for the Design of Early-Phase Clinical Trials of Cellular and Gene Therapy Products — was released as a draft in 2013 and finalized in 2015. It discussed many recommendations for manufacturing, testing and patient safety and follow-up.

In 2016, Congress passed the 21st Century Cures Act or Cures Act, which includes provisions designed to expedite and streamline development of innovative new medicines. This law builds on FDA’s existing responsibilities and established regenerative medicine therapies, including gene therapy, cell therapy, products made from tissues and combinations of these products. FDA published guidance in 2017 and updated in 2020 to help industry apply these new regulations that together are referred to as the FDA regenerative medicine framework. Both human gene editing and transfer, as well as genetically modified cells that lead to a sustained factor production in hemophilia, are considered to be regenerative medicine therapies by FDA.

Guidance for developing CGT products specifically for hemophilia was published by FDA in 2018. Then in 2020, it was updated when FDA launched its expanded framework for cell and gene therapies. This framework contained several new guidance documents, including hemophilia CGT. This brought the total number of guidance documents in the framework to 27. In 2021, we can see how the evolution of hemophilia gene and cell therapy has been affected by the development of this framework.

EARLY 2020: FDA LAUNCHES CELL AND GENE THERAPY GUIDANCE FRAMEWORK
On Jan. 28, 2020, FDA launched its landmark guidance framework for CGT products. Updates included improvements to the guidance for hemophilia and...
For the treatment of bleeding episodes in people* with hemophilia A or B with inhibitors

I’M READY TO MOVE ON

Get rapid, predictable, and reliable bleed control with SEVENFACT 225†

Rapid effect: 3 hour
At 3 hours, 84% of mild/moderate bleeding episodes were controlled with a single dose

Predictable‡ response: 84%
At 9 hours, 84% of mild/moderate bleeding episodes treated achieved bleed control after a single dose

Reliable control: 99.5%
At 24 hours, 99.5% of mild/moderate bleeding episodes were resolved

Convenient home use: 98%
98% of bleeding episodes were treated at home

† 225 mcg/kg initial dosing regimen in the clinical trial.
‡ As seen in the clinical trial.

Summary of Selected Safety Information
What is the most important information I should know about SEVENFACT?
The most serious possible side effect of SEVENFACT is abnormal clotting involving blockage of blood vessels, which include stroke, blockage of the main blood vessel to the lung, and deep vein blood clots.
You should know the signs of abnormal clotting and seek medical help immediately if they occur. Signs of clotting in places other than your site of bleeding can include new onset of swelling and pain in limbs, new onset of chest pain, shortness of breath, loss of sensation or motor power, or altered consciousness or speech.

What is SEVENFACT?
SEVENFACT is an injectable medicine used for the treatment and control of bleeding episodes occurring in adults and adolescents 12 years of age and older with Hemophilia A or B with inhibitors. Injecting medicines requires special training; do not attempt to self-infuse unless you have been taught how by your healthcare provider.

Who should not use SEVENFACT (coagulation factor VIIa)?
You should not use SEVENFACT if you are allergic to rabbits, or if you have known allergies to SEVENFACT or any of its components. Seek immediate medical help if you experience hives, itching, rash, difficulty breathing with cough or wheezing, swelling around the mouth and throat, tightness of the chest, dizziness or fainting, or low blood pressure after taking SEVENFACT.
Tell your healthcare provider prior to using SEVENFACT if you have begun treatment of a bleeding episode with another bypassing agent.

What should I tell my healthcare provider before I use SEVENFACT?
Tell your healthcare provider if you are pregnant, are nursing, or plan to become pregnant; if you have had prior blood clots, heart disease or heart failure, abnormal heart rhythms, prior pulmonary clots, or heart surgery; or if you have or have had any other medical conditions.

What are the possible side effects of SEVENFACT?
The most common adverse reactions for SEVENFACT are headache, dizziness, infusion-site discomfort, infusion-site hematoma, and infusion-related reaction and fever. Seek immediate medical help if you have signs of a blood clot or an allergic reaction.

To report SUSPECTED ADVERSE REACTIONS or product complaints, contact HEMA Biologics at 1-855-718-4362. You may also report SUSPECTED ADVERSE REACTIONS to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Patient Product Information on the next page.
SEVENFACT® (recombinant coagulation factor VIII [rFVIII]).

• Are allergic to rabbits.

WHO SHOULD NOT USE SEVENFACT?

You should not use SEVENFACT if you:

• Are having an active infection.

You should know the signs of abnormal clotting (thrombosis) described below and seek medical help immediately if they occur.

• Have certain infections or blood disorders.

• Are allergic to rabbits.

You should not use SEVENFACT if you:

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A Look at the DRUG RECALL PROCESS

BY HFA STAFF

It is important to pay attention when a product is recalled, but with all the different sources of information and the different types of recalls, it can be confusing. Recalls, designed to protect the public’s health, are used as a way to deliver information to consumers in an expeditious manner.

A recall is an action taken by a manufacturer to remove a product (food, drugs, medical devices and cosmetics) from the market, initiated either by the manufacturer or by request from the U.S. Food and Drug Administration. In either case, the manufacturer removes or corrects a product that is in the market and in violation of FDA rules and regulations. In both cases, the FDA considers the recall to be manufacturer initiated.

Alternatively, an FDA-mandated recall, also known as a mandatory recall, occurs when FDA orders a manufacturer to recall a product or mandates recall requirements. The FDA’s role is to oversee the manufacturer’s recall strategy, monitor the recall for effectiveness, and classify the recall.

RECALL CLASSIFICATION

Class I: Includes a health hazard situation in which there is reasonable probability that the use of the product will lead to serious, adverse health consequences or death.

Class II: Includes a potential health hazard situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

Class III: Includes a situation in which use of or exposure to the product is not likely to cause adverse health consequences.

Market withdrawal: When a product has a minor violation that would not be subject to FDA legal action a “market withdrawal” occurs. The product is removed by the firm from the market or the firm corrects the violation.

Medical device safety alert: Released in circumstances in which a medical device may present an unreasonable risk of substantial harm. These situations also are considered recalls in certain cases.

Each FDA recall follows specific timelines and procedures depending upon the circumstances. For example, each recall is initiated with a written order that states the violation, the product, lot and serial numbers to be recalled, and the timeline for the recall. Each recall is unique and requires its own recall strategy developed by the Center Recall Unit. The CRU will consider how far the recall should extend, whether the public needs to be warned and if so, in what geographical area, and the appropriate assessment for recall effectiveness. A recall designated voluntary, requested and mandatory depends on who initiates the process. Based upon the gravity of the situation, FDA will issue a public warning.

RECALL METHODS

Voluntary Recall: Initiation of a Recall by a Manufacturer

Consistent with its responsibility to protect the public health from products that are defective or potentially harmful, a manufacturer may voluntarily initiate a recall. If a recall is manufacturer-initiated, FDA reviews the information provided by the manufacturer, conducts a health hazard evaluation, classifies the recall and then advises the manufacturer in writing of the assigned recall classification. FDA then places the notice of the recall in the FDA Weekly Enforcement Report. Nearly all recalls implemented in the U.S. are begun on a voluntary basis by the anything we can go to get.

If a manufacturer has voluntarily initiated a recall, it is the manufacturer’s responsibility to promptly notify each of its direct accounts. If the recall extends beyond direct accounts, then the direct accounts should be instructed by the recalling manufacturer to contact sub-accounts that may have received the product. Once all the accounts have been informed about the recall, they must promptly follow the recall strategy that was previously put in place for that account.

FDA Mandated Recalls

In urgent situations, FDA may request a recall. The request is directed to the manufacturer that has the primary responsibility for making or marketing the product. Class 1 category recalls are most often requested recalls. It is important to note FDA considers an FDA requested recall to be manufacturer initiated.

The associate commissioner for regulatory affairs approves all recall requests from FDA. A letter outlining the need for a recall is sent to manufacturer. After a recall has begun, the recall is entered in the Recall Enterprise System. The RES is a database used by FDA to submit, update, classify and terminate recalls.

FDA’s authority to issue a mandatory recall is very limited. Subjects of mandatory recalls can include devices, biological products, human tissue intended for transplantation, infant formula, tobacco products and food. FDA also has discretion to order a mandatory recall if it finds that a human cell, tissue or cellular or tissue-based product is a source of dangerous infection to humans or does not adequately protect against communicable disease.
### Recent Recalls of Products Indicated for Treatment of Bleeding Disorders

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Date</th>
<th>Issue</th>
<th>Scope</th>
<th>Action taken</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mononine</td>
<td>CSL Behring</td>
<td>January 21, 2021</td>
<td>Manufacturing deviation that occurred during the filling process.</td>
<td>1 lot in United States; other lots worldwide</td>
<td>Voluntary pharmacy-level recall. Manufacturer stated “patients can continue to use product they may have. Although the potential for safety risk to patients is considered low, it cannot be fully excluded.” Note: Product was discounted in September 2020; product was expected to be available through mid-2021.</td>
<td></td>
</tr>
<tr>
<td>Tranexamic acid</td>
<td>Mylan</td>
<td>September 1, 2020</td>
<td>Some carton/package labels may have been mislabeled as an unrelated product, Amiodarone HCl Injection.</td>
<td>4 lots</td>
<td>Voluntary recall to the hospital/clinic level. Product is exclusively used in inpatient setting.</td>
<td></td>
</tr>
<tr>
<td>Stimate nasal spray</td>
<td>Ferring Pharmaceuticals (Distributor: CSL Behring)</td>
<td>July 21, 2020</td>
<td>Product testing revealed low volume and therefore above-specification concentration of active ingredient</td>
<td>All product worldwide</td>
<td>Voluntary recall (initiated as pharmacy-level recall; subsequently extended to consumer-level). Manufacturer does not anticipate product becoming available before second half of 2023.</td>
<td></td>
</tr>
<tr>
<td>VONVENDI</td>
<td>Takeda</td>
<td>February 25, 2020</td>
<td>Internal manufacturer audit revealed “one step did not proceed as expected.” Manufacturer informed FDA during its regular on-site inspection and received “feedback on how [they] could improve.” Manufacturer subsequently recalled vials from lots manufactured during this period, despite finding no impact on product safety or efficacy.</td>
<td>2 lots, 3425 vials, U.S. only</td>
<td>Voluntary pharmacy level recall.</td>
<td></td>
</tr>
<tr>
<td>Humate-P</td>
<td>CSL Behring</td>
<td>October 15, 2019</td>
<td>Printing misalignment on label could lead to confusion on dosage/potency</td>
<td>Lots of all fill sizes (600, 1200, 2400 Ius)</td>
<td>No recall. Drug information alert issued by manufacturer.</td>
<td></td>
</tr>
<tr>
<td>Hemlibra</td>
<td>Genentech</td>
<td>October 5, 2019</td>
<td>Particulate matter outside specifications found in vials (product deviation, not contamination)</td>
<td>Found in 1 batch during routine inspection</td>
<td>No recall (regulators agreed there was no change in product benefit/risk profile). Genentech notified U.S., European, Canadian and Japanese health authorities in March 2019.</td>
<td></td>
</tr>
<tr>
<td>Hemlibra</td>
<td>Genentech (through contract specialty pharmacy Medvantx)</td>
<td>September 21, 2019</td>
<td>Injection needles of incorrect length included in shipment to patients who receive product through the Genentech Patient Foundation</td>
<td>124 families and 92 health care providers; shipments involved took place over ~2 months</td>
<td>No recall; Genentech notified FDA via standard U.S. drug safety reporting.</td>
<td></td>
</tr>
<tr>
<td>Kogenate FS</td>
<td>Bayer</td>
<td>July 19, 2019</td>
<td>Mislabeling resulted in distribution of wrong product, wrong dosage, post-expiration</td>
<td>2 lots, 900+ vials, distributed over period of 6 months</td>
<td>Class 2 voluntary recall to end user.</td>
<td></td>
</tr>
</tbody>
</table>
CURRENT PRODUCTS AVAILABLE FOR TREATMENT OF BLEEDING DISORDERS

Whether you or your child has just been diagnosed, or you’ve lived with a bleeding disorder for decades, knowledge of treatment options is a key component of being able to advocate for yourself and essential to having informed conversations with health care professionals. To help patients and caregivers with the process of navigating available treatment options, we’ve compiled a comprehensive list of all therapies currently available and approved by the Food and Drug Administration.

Information in this issue should not be interpreted as medical advice. We encourage frequent dialogue with experienced health care professionals regarding your health and the therapies used to treat your bleeding disorder.

43 APPROVED PRODUCTS BY THE NUMBERS:

PRODUCTS BY TYPE

- Recombinant clotting factor (56%)
- Plasma-derived clotting factor (28%)
- Non-factor product (14%)
- Bi-specific antibody (2%)

NUMBER OF PRODUCTS BY INDICATION

- Factor VIII: 23
- Factor IX: 9
- Inhibitor: 4
- vWD: 7
- Rare: 7
- Other: 2

MOST RECENTLY RELEASED PRODUCTS

<table>
<thead>
<tr>
<th>YEAR RELEASED</th>
<th>PRODUCT</th>
<th>INDICATION</th>
<th>MANUFACTURER</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>SEVENFACT</td>
<td>Inhibitor</td>
<td>HEMA Biologics</td>
</tr>
<tr>
<td>2020</td>
<td>Desmopressin Acetate Injection USP (desmopressin acetate)</td>
<td>Factor VIII; vWD</td>
<td>Dr. Reddy’s Laboratories</td>
</tr>
<tr>
<td>2019</td>
<td>Novo Nordisk</td>
<td>Factor VIII</td>
<td>ESPEROCT</td>
</tr>
<tr>
<td>2018</td>
<td>Bayer</td>
<td>Factor VIII</td>
<td>Jivi</td>
</tr>
</tbody>
</table>
**LIST OF APPROVED PRODUCTS**

Detailed product information can be found on the following pages, organized by indication.

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Product Type</th>
<th>Specific Product Type</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advate</td>
<td>Takeda</td>
<td>Factor VIII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adynovate</td>
<td>Takeda</td>
<td>Factor VIII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Afstyla</td>
<td>CSL Behring</td>
<td>Factor VIII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alphanate</td>
<td>Grifols, Inc</td>
<td>Factor VIII/vWD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aphanine SD</td>
<td>Grifols, Inc</td>
<td>Factor IX</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alprolix</td>
<td>Sanofi Genzyme</td>
<td>Factor IX</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amicar</td>
<td>Akorn Pharmaceuticals</td>
<td>Other</td>
<td>Ammoniaproline acid - oral solution and tablets</td>
<td></td>
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<tr>
<td>BeneFIX</td>
<td>Pfizer, Inc.</td>
<td>Factor IX</td>
<td></td>
<td></td>
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<tr>
<td>Coagadex</td>
<td>Bio Products Laboratory USA, Inc</td>
<td>Rare</td>
<td></td>
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<tr>
<td>Corifact</td>
<td>CSL Behring</td>
<td>Factor VIII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyklokapron</td>
<td>Pfizer, Inc.</td>
<td>Factor VIII</td>
<td>(transaminoic acid injection)</td>
<td></td>
</tr>
<tr>
<td>DDAVP (Desmopressin)</td>
<td>Ferring Pharmaceuticals</td>
<td>Factor VIII/vWD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desmopressin Acetate Injection USP</td>
<td>(desmopressin acetate)</td>
<td>Dr. Reddy’s Laboratories</td>
<td>Factor VIII/vWD</td>
<td></td>
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<tr>
<td>Eloctate</td>
<td>Sanofi Genzyme</td>
<td>Factor VIII</td>
<td></td>
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<tr>
<td>Esperoct</td>
<td>Novo Nordisk</td>
<td>Factor VIII</td>
<td></td>
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<tr>
<td>FIBRYGA</td>
<td>Octapharma USA, Inc</td>
<td>Factor VIII</td>
<td>Rare</td>
<td></td>
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<tr>
<td>FEIBA NF</td>
<td>Takeda</td>
<td>Inhibitor</td>
<td></td>
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<tr>
<td>Hemofil M</td>
<td>Takeda</td>
<td>Factor VIII</td>
<td></td>
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<tr>
<td>Humate-P</td>
<td>CSL Behring</td>
<td>Factor VIII/vWD</td>
<td></td>
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<tr>
<td>Idelvion</td>
<td>CSL Behring</td>
<td>Factor IX</td>
<td></td>
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<tr>
<td>IXINITY</td>
<td>Medexus</td>
<td>Factor IX</td>
<td></td>
<td></td>
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<tr>
<td>Jivi</td>
<td>Bayer</td>
<td>Factor VIII</td>
<td></td>
<td></td>
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<tr>
<td>Koate</td>
<td>Kedrion Biopharma</td>
<td>Factor VIII</td>
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<td></td>
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<tr>
<td>Kogenate FS</td>
<td>Bayer</td>
<td>Factor VIII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kovastry</td>
<td>Bayer</td>
<td>Factor VIII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lysteda</td>
<td>Ferring Pharmaceuticals</td>
<td>Factor VIII/vWD</td>
<td>(transaminoic acid tablets)</td>
<td></td>
</tr>
<tr>
<td>NovoSeven RT</td>
<td>Novo Nordisk</td>
<td>Factor VIII</td>
<td></td>
<td></td>
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<tr>
<td>Obizur</td>
<td>Takeda</td>
<td>Rare</td>
<td></td>
<td></td>
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<tr>
<td>Profilnine</td>
<td>Grifols, Inc</td>
<td>Factor IX</td>
<td></td>
<td></td>
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<tr>
<td>RiaSTAP</td>
<td>CSL Behring</td>
<td>Rare</td>
<td></td>
<td></td>
</tr>
<tr>
<td>REBIVYN</td>
<td>Novo Nordisk</td>
<td>Factor IX</td>
<td></td>
<td></td>
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<tr>
<td>Recombinate</td>
<td>Takeda</td>
<td>Factor VIII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rixibis</td>
<td>Takeda</td>
<td>Factor IX</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SEVENFACT</td>
<td>HEMA Biologics</td>
<td>Factor VIII</td>
<td>Inhibitor</td>
<td></td>
</tr>
<tr>
<td>Stimate</td>
<td>CSL Behring</td>
<td>Factor VIII/vWD</td>
<td>(Desmopressin Nasal Spray)</td>
<td></td>
</tr>
<tr>
<td>Treten</td>
<td>Novo Nordisk</td>
<td>Rare</td>
<td></td>
<td></td>
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<tr>
<td>Vonvendi</td>
<td>Takeda</td>
<td>vWD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wilate</td>
<td>Octapharma USA, Inc</td>
<td>Factor VIII/vWD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xyntha</td>
<td>Pfizer, Inc.</td>
<td>Factor VIII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xyntha/Xyntha Solofuse</td>
<td>Pfizer, Inc</td>
<td>Factor VIII</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HOW TO NAVIGATE OUR PRODUCT CHARTS**

The pages that follow contain a comprehensive and exhaustive list of products that are approved by the Food and Drug Administration for treatment of a bleeding disorder. For ease of navigation, the charts are published in sections by indication (Factor VIII, Factor IX, Inhibitor, VWD, Rare or Other), with each containing the following categories of information:

- **Product**: Name used to market and sell the therapy.
- **Manufacturer**: Company that produces and sells the therapy.
- **Product Type**: Indicated method used to create product.
- **Specific Product Type**: Detailed classification of product type, if applicable.
- **Half Life**: Amount of time a product stays intact in the bloodstream until its efficacy is halved.
- **FDA Approved**: Year the product was approved for treatment by FDA.
- **Indications**: Bleeding disorder type/factor deficiency the therapy is intended to treat.

We’ve made every effort to ensure the accuracy of the information in this list by using information directly from manufacturers and publicly available information from websites, such as FDA. We do not encourage community members to use one product over another, and we strongly urge you to discuss your treatment options with qualified medical professionals.

Content in this issue is current as of March 2021. Given the fast-paced environment that manufacturers and governmental agencies work within, some information could have changed since going to print. Please refer to manufacturers’ or the FDA’s websites for the most up-to-date information.
<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Product Type</th>
<th>Specific Product Type</th>
<th>Half-Life</th>
<th>FDA Approval Date</th>
<th>Indications</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advate</td>
<td>Takeda</td>
<td>Recombinant clotting factor</td>
<td>Antihemophilic factor (recombinant)</td>
<td>Adults (&gt;16 years): 12.0 ± 4.2 hrs; 12 to &lt;16 yrs: 12.0 ± 2.9 hrs; 5 to &lt;12 yrs: 11.2 ± 3.5 hrs; 2 to &lt;5 yrs: 9.5 ± 1.8 hrs; 1 month to &lt;2 yrs: 8.7 ± 1.4 hrs</td>
<td>2003</td>
<td>Factor VIII</td>
<td></td>
</tr>
<tr>
<td>Adynovate</td>
<td>Takeda</td>
<td>Recombinant clotting factor</td>
<td>Antihemophilic factor (recombinant), PEGylated</td>
<td>18 years: 14.69 ± 3.79 hrs; 12 to &lt;18 years: 13.43 ± 4.05 hrs; 6 to &lt;12 years: 12.4 ± 1.67 hrs; &lt;6 years: 11.8 ± 2.43 hrs. Overall 1.3-1.5 half-life extension compared to ADVATE</td>
<td>2015</td>
<td>Factor VIII</td>
<td></td>
</tr>
<tr>
<td>Afstyla</td>
<td>CSL Behring</td>
<td>Recombinant clotting factor</td>
<td></td>
<td>After single dose of 50 IU/kg: Adults (&gt;18 years): 14.2 hours (mean); Adolescents (&lt;12 to &lt;18 years): 14.3 hours (mean); Children (&lt;6 to &lt;6 yrs): 10.4 hours (mean); (&gt;6 to &lt;12 years): 10.2 hours (mean)</td>
<td>2016</td>
<td>Factor VIII</td>
<td></td>
</tr>
<tr>
<td>Alphanate</td>
<td>Grifols, Inc</td>
<td>Plasma-derived clotting factor</td>
<td></td>
<td>17.9</td>
<td>1978</td>
<td>Factor VIII; vWD</td>
<td></td>
</tr>
<tr>
<td>Cyklokapron (tranexamic acid injection)</td>
<td>Pfizer, Inc.</td>
<td>Non-factor product</td>
<td>Antifibrinolytic agent</td>
<td>2 hours¹</td>
<td>1986</td>
<td>Factor VIII; Factor IX</td>
<td>f-terminal elimination phase g-indicated for short-term use (two to eight days) to reduce or prevent hemorrhage and reduce the need for replacement therapy during and following tooth extraction. Prescribing Information at <a href="http://www.pfizermedicalinformation.com/en-us/patient">www.pfizermedicalinformation.com/en-us/patient</a></td>
</tr>
<tr>
<td>DDAVP (Desmopressin)</td>
<td>Ferring Pharmaceuticals</td>
<td>Non-factor product</td>
<td>Intravenous injection-factor catalyst /factor booster/factor precipitator</td>
<td></td>
<td>1978</td>
<td>Factor VIII; vWD</td>
<td></td>
</tr>
<tr>
<td>Desmopressin Acetate Injection USP (desmopressin acetate)</td>
<td>Dr. Reddy’s Laboratories</td>
<td>Non-factor product</td>
<td>Intravenous injection-factor catalyst /factor booster/factor precipitator</td>
<td></td>
<td>2020</td>
<td>Factor VIII; vWD</td>
<td></td>
</tr>
<tr>
<td>Eloctate</td>
<td>Sanofi Genzyme</td>
<td>Recombinant clotting factor</td>
<td></td>
<td>19.7 hours (17.4, 22.0) in adults Pediatric: 12 to 17 years: 16.4 hours (14.1, 18.6) 6 to 11 years: 14.9 hours (12.0, 17.8) 1 to 5 years: 12.7 hours (11.2, 14.1)</td>
<td>2014</td>
<td>Factor VIII</td>
<td>PK parameters were determined after a single 50 IU/KG dose.</td>
</tr>
<tr>
<td>ESEROCT</td>
<td>Novo Nordisk</td>
<td>Recombinant clotting factor</td>
<td></td>
<td>22 hours (mean) fixed dosing regimen of one injection every four days for adolescents or adults, or every three to four days in children.</td>
<td>2019</td>
<td>Factor VIII</td>
<td></td>
</tr>
<tr>
<td>HEMLIBRA</td>
<td>Genentech</td>
<td>Bi-Specific Antibody</td>
<td>Therapeutic bi-specific antibody</td>
<td>26.9 +/- 9.1 days (mean +/- SD)</td>
<td>2017</td>
<td>Factor VIII; Inhibitor</td>
<td>2017 for inhibitors, 2018 for non-inhibitors. Additional route of delivery information: humanized, monoclonal, subcutaneous injection</td>
</tr>
<tr>
<td>Hemofil M</td>
<td>Takeda</td>
<td>Plasma-derived clotting factor</td>
<td>Antihemophilic factor (human) method m, monoclonal Purified</td>
<td>14.8 ± 3.0 hrs</td>
<td>1966</td>
<td>Factor VIII</td>
<td></td>
</tr>
<tr>
<td>Product</td>
<td>Manufacturer</td>
<td>Product Type</td>
<td>Specific Product Type</td>
<td>Half-Life</td>
<td>FDA Approval Date</td>
<td>Indications</td>
<td>Notes</td>
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</tr>
<tr>
<td>Humate-P</td>
<td>CSL Behring</td>
<td>Plasma-derived clotting factor</td>
<td></td>
<td>12.2 hours (mean) in Hemophilia A; 10-11 hours (median) for VWD</td>
<td>1986</td>
<td>Factor VIII; vWD</td>
<td></td>
</tr>
<tr>
<td>Jivi</td>
<td>Bayer</td>
<td>Recombinant clotting factor</td>
<td>Antihemophilic factor (recombinant), PEGylated-acl</td>
<td>17.9 hours</td>
<td>2018</td>
<td>Factor VIII</td>
<td>Extended half-life</td>
</tr>
<tr>
<td>Koate</td>
<td>Kedrion Biopharma</td>
<td>Plasma-derived clotting factor</td>
<td></td>
<td>16.1</td>
<td>1974</td>
<td>Factor VIII</td>
<td></td>
</tr>
<tr>
<td>Kogenate FS</td>
<td>Bayer</td>
<td>Recombinant clotting factor</td>
<td>Antihemophilic factor (recombinant)</td>
<td>Adults: 13.74 hours Children: 10.7 hours</td>
<td>1993</td>
<td>Factor VIII</td>
<td></td>
</tr>
<tr>
<td>Kovaltry</td>
<td>Bayer</td>
<td>Recombinant clotting factor</td>
<td>Antihemophilic factor (recombinant)</td>
<td>0 to &lt;6 yrs: 12.1 hours 6 to &lt;12 yrs: 12.0 hours 12 to 17 yrs: 14.4 hours 18 yrs: 14.2 hours</td>
<td>2016</td>
<td>Factor VIII</td>
<td></td>
</tr>
<tr>
<td>Novoeight</td>
<td>Novo Nordisk</td>
<td>Recombinant clotting factor</td>
<td></td>
<td>Adults/adolescents—One Stage Clotting Assay: 10.8 hours; Chromogenic Assay: 12.0 hours; Pediatrics—One Stage Clotting Assay: 0-&lt;6 yo - 7.7 hours, 6-&lt;12 yo - 8.0 hours; Chromogenic Assay: 0-&lt;6 yo - 10.0 hours, 6-&lt;12 yo - 9.4 hours</td>
<td>2013</td>
<td>Factor VIII</td>
<td></td>
</tr>
<tr>
<td>NUWIQ</td>
<td>Octapharma USA, Inc.</td>
<td>Recombinant clotting factor</td>
<td>Antihemophilic recombinant clotting factor</td>
<td>171 +/- 11.2 hrs. (Adults); 13.1 +/- 2.6 hrs. (6-&lt;12 yrs.); 11.9 +/- 5.4 hrs. (2-5 yrs.)</td>
<td>2015</td>
<td>Factor VIII</td>
<td>NUWIQ is a recombinant FVIII produced in human cells without chemical modification or protein fusion.</td>
</tr>
<tr>
<td>Recombinate</td>
<td>Takeda</td>
<td>Recombinant clotting factor</td>
<td>Antihemophilic factor (recombinant)</td>
<td>14.6 ± 4.9 hrs</td>
<td>1992</td>
<td>Factor VIII</td>
<td>Half-life 11.2 ± 2.5 vs Advate</td>
</tr>
<tr>
<td>Stimate (Desmopressin Nasal Spray)</td>
<td>CSL Behring</td>
<td>Non-factor product</td>
<td>Nasal spray</td>
<td>3.3-3.5 hours</td>
<td>1994</td>
<td>Factor VIII; vWD</td>
<td></td>
</tr>
<tr>
<td>Wilate</td>
<td>Octapharma USA, Inc.</td>
<td>Plasma-derived clotting factor</td>
<td></td>
<td>VWF: 15.8 hours; FVIII: 19.6 hours</td>
<td>2009</td>
<td>Factor VIII; vWD</td>
<td>Prophylaxis trial underway</td>
</tr>
<tr>
<td>Xyntha</td>
<td>Pfizer, Inc.</td>
<td>Recombinant clotting factor</td>
<td></td>
<td>11.2 ± 5.0 hours**</td>
<td>2008</td>
<td>Factor VIII</td>
<td>a-Results from 30 previously treated patients (PTPs) 12 to 60 years old, who received a single infusion of 50 IU/ kg XYNTHA. b-Compared to adults, the half-life of XYNTHA is shorter in children and the clearance (based on per kg body weight) is approximately 40% higher in children. Prescribing Information at <a href="http://www.pfizermedicalinformation.com/en-us/patient">www.pfizermedicalinformation.com/en-us/patient</a></td>
</tr>
<tr>
<td>Xyntha/Xyntha Solofuse</td>
<td>Pfizer, Inc.</td>
<td>Recombinant clotting factor</td>
<td></td>
<td>11.2 ± 5.0 hours**</td>
<td>2008</td>
<td>Factor VIII</td>
<td>a-Results from 30 previously treated patients (PTPs) 12 to 60 years old, who received a single infusion of 50 IU/ kg XYNTHA. b-Compared to adults, the half-life of XYNTHA is shorter in children and the clearance (based on per kg body weight) is approximately 40% higher in children. Prescribing Information at <a href="http://www.pfizermedicalinformation.com/en-us/patient">www.pfizermedicalinformation.com/en-us/patient</a></td>
</tr>
<tr>
<td>Product</td>
<td>Manufacturer</td>
<td>Product Type</td>
<td>Specific Product Type</td>
<td>Half-Life</td>
<td>FDA Approval Date</td>
<td>Indications</td>
<td>Notes</td>
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</tr>
<tr>
<td>Alphanine SD</td>
<td>Grifols, Inc</td>
<td>Plasma-derived clotting factor</td>
<td></td>
<td>50 IU/KG: ADULTS - 86.52 Hrs (37.2%); PEDIATRIC - 12 to 17 years: 80 hours (15%); 6 to 11 years: 72 hours (23%); 2 to 5 years: 68 hours (24%); 100 IU/KG: ADULTS - 97 Hrs (35%); PEDIATRIC - 12 to 17 years: 94 hours (24%)</td>
<td>1990</td>
<td>Factor IX</td>
<td></td>
</tr>
<tr>
<td>Alprolix</td>
<td>Sanofi Genzyme</td>
<td>Recombinant clotting factor</td>
<td></td>
<td>2014 Factor IX</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BeneFIX</td>
<td>Pfizer, Inc.</td>
<td>Recombinant clotting factor</td>
<td></td>
<td>18.8 ± 5.4 hours (range 11 to 36 hours)</td>
<td>1997</td>
<td>Factor IX</td>
<td></td>
</tr>
<tr>
<td>Cyklokapron</td>
<td>Pfizer, Inc.</td>
<td>Non-factor product</td>
<td>Antifibrinolytic agent</td>
<td>2 hours†</td>
<td>1986</td>
<td>Factor VIII; Factor IX</td>
<td></td>
</tr>
<tr>
<td>Idelvion</td>
<td>CSL Behring</td>
<td>Recombinant clotting factor</td>
<td></td>
<td>After single dose of 50 IU/kg: Adults: 104 hours; Adolescents (12 to &lt;18 years): 87 hours (mean); Children (0 to &lt;6 years): 90 hours (mean); and (6 to &lt;12 years): 93 hours (mean)</td>
<td>2016</td>
<td>Factor IX</td>
<td></td>
</tr>
<tr>
<td>IXINITY</td>
<td>Medexus</td>
<td>Recombinant clotting factor</td>
<td></td>
<td>24 hours</td>
<td>2015</td>
<td>Factor IX</td>
<td>Pediatric trial underway</td>
</tr>
<tr>
<td>Profilnine</td>
<td>Grifols, Inc</td>
<td>Plasma-derived clotting factor</td>
<td></td>
<td>1990 Factor IX</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>REBINYN</td>
<td>Novo Nordisk</td>
<td>Recombinant clotting factor</td>
<td></td>
<td>Single Dose: ≥ 6 years = 69.6 hours; 7-12 years old = 76.3 hours; 13-17 years old = 89.4 hours; ≥ 18 years old = 83.0 hours. Steady state: 13 - 17 years old 103.1 hours; ≥ 18 years old = 114.9 hours†</td>
<td>2017</td>
<td>Factor IX</td>
<td>Limitations of Use: REBINYN® is not indicated for routine prophylaxis in the treatment of patients with hemophilia B. REBINYN® is not indicated for immune tolerance induction in patients with hemophilia B</td>
</tr>
<tr>
<td>Rixibis</td>
<td>Takeda</td>
<td>Recombinant clotting factor</td>
<td>Coagulation factor IX (recombinant)</td>
<td>≥ 12 years = 25.7 ± 1.5 hrs; 6 - &lt;12 years = 23.2 ± 1.6 hrs; &lt;6 years = 27.7 ± 2.7 hrs</td>
<td>2013</td>
<td>Factor IX</td>
<td></td>
</tr>
</tbody>
</table>
## INHIBITOR

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Product Type</th>
<th>Specific Product Type</th>
<th>Half-Life</th>
<th>FDA Approval Date</th>
<th>Indications</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEIBA NF</td>
<td>Takeda</td>
<td>Plasma-derived clotting factor</td>
<td>Anti-inhibitor coagulant complex</td>
<td>Peak thrombin generation at 15 to 30 minutes with thrombin generation returning to baseline value 8 to 12 hours, half-life is approximately 4 - 7 hours</td>
<td>1986</td>
<td>Inhibitor</td>
<td>Prophylaxis indication 2013. Plasma-Derived Clotting Factor containing primarily non-acti-vated FII, FIX and FX and acti-vated FVII, and small amounts of FVIII antigen</td>
</tr>
<tr>
<td>HEMLIBRA</td>
<td>Genentech</td>
<td>Bi-specific antibody</td>
<td>Therapeutic bi-specific antibody</td>
<td>26.9 +/- 9.1 days (mean +/- SD)</td>
<td>2017</td>
<td>Factor VIII; Inhibitor</td>
<td>2017 for inhibitors, 2018 for non-inhibitors. Additional route of delivery information: humanized, monoclonal, subcutaneous injection</td>
</tr>
<tr>
<td>NovoSeven RT</td>
<td>Novo Nordisk</td>
<td>Recombinant clotting factor</td>
<td></td>
<td>Hemophilia A or B — Adolescents/Adults (15-63 yrs): 2.9-31 hours; Pediatrics (2-12 yrs): 2.6 hours FVII Deficiency — Adolescents/Adults (20-43 yrs): 2.8-3.1 hours</td>
<td>1999</td>
<td>Inhibitor; Rare</td>
<td>Received FDA approval in April 2020. Now available as of January 2021.</td>
</tr>
<tr>
<td>SEVENFACT</td>
<td>HEMA Biologics</td>
<td>Recombinant clotting factor</td>
<td>Recombinant factor VII</td>
<td>Hemophilia A or B—Adolescents/Adults (15-63 yrs): 2.9-31 hours; Pediatrics (2-12 yrs): 2.6 hours. FVII Deficiency—Adolescents/Adults (20-43 yrs): 2.8-3.1 hours</td>
<td>2020</td>
<td>Inhibitor</td>
<td></td>
</tr>
</tbody>
</table>

## vWD

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Product Type</th>
<th>Specific Product Type</th>
<th>Half-Life</th>
<th>FDA Approval Date</th>
<th>Indications</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alphanate</td>
<td>Grifols, Inc</td>
<td>Plasma-derived clotting factor</td>
<td></td>
<td>17.9</td>
<td>1978</td>
<td>Factor VIII; vWD</td>
<td></td>
</tr>
<tr>
<td>DDAVP (Desmopressin)</td>
<td>Ferring Pharmaceuticals</td>
<td>Non-factor product</td>
<td>Intravenous injection-factor catalyst/factor booster/factor precipitator</td>
<td>1978</td>
<td>Factor VIII; vWD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desmopressin Acetate</td>
<td>Dr. Reddy’s Laboratories</td>
<td>Non-factor product</td>
<td>Intravenous injection-factor catalyst/factor booster/factor precipitator</td>
<td>2020</td>
<td>Factor VIII; vWD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humate-P</td>
<td>CSL Behring</td>
<td>Plasma-derived clotting factor</td>
<td></td>
<td>12.2 hours (mean) in Hemophilia A; 10-11 hours (median) for VWD</td>
<td>1986</td>
<td>Factor VIII; vWD</td>
<td></td>
</tr>
<tr>
<td>Stimate (Desmopressin</td>
<td>CSL Behring</td>
<td>Non-factor product</td>
<td>Nasal spray</td>
<td>3.3-3.5 hours</td>
<td>1994</td>
<td>Factor VIII; vWD</td>
<td></td>
</tr>
<tr>
<td>Vonvendi</td>
<td>Takeda</td>
<td>Recombinant clotting factor</td>
<td>von Willebrand factor (recombinant)</td>
<td>For 50IU/kg mean hours (SD) 22.6 (5.34)</td>
<td>2015</td>
<td>vWD</td>
<td></td>
</tr>
<tr>
<td>Wilate</td>
<td>Octapharma USA, Inc.</td>
<td>Plasma-derived clotting factor</td>
<td></td>
<td>VWF: 15.8 hours; FVIII: 19.6 hours</td>
<td>2009</td>
<td>Factor VIII; vWD</td>
<td>Prophylaxis trial underway</td>
</tr>
<tr>
<td>Product</td>
<td>Manufacturer</td>
<td>Product Type</td>
<td>Specific Product Type</td>
<td>Half-Life</td>
<td>FDA Approval Date</td>
<td>Indications</td>
<td>Notes</td>
</tr>
<tr>
<td>---------------</td>
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<td>------------------------------------------------------------</td>
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<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Coagadex</td>
<td>Bio Products Laboratory USA, Inc.</td>
<td>Plasma-derived</td>
<td>Lyophilized powder for solution for intravenous injection</td>
<td>Patients 12 years and older: 30.3 hours</td>
<td>2015</td>
<td>Rare</td>
<td>The half-life in children &lt; 12 years has not been evaluated. However, incremental recovery (IR) in children &lt;12 years of age has been assessed and is significantly lower than in patients 12 years and older, translating to larger dosing requirements in this age group, as per the approved dosing recommendations in the Coagadex label. In a phase 3 study in children aged &lt;12 years diagnosed with moderate or severe hereditary FXD, the mean IR was significantly lower in younger (0–5 years) than in older (6–11 years) children (1.53 vs 1.91 IU/dL, per IU/kg; p = 0.001). In the overall population of children 0–11 years, mean IR was 1.74 IU/dL per IU/kg. In patients 12 years and older, IR has been assessed to be significantly higher at 2.04 IU/dL per IU/kg.</td>
</tr>
<tr>
<td>Contact</td>
<td>CSL Behring</td>
<td>Plasma-derived</td>
<td></td>
<td>6.6 hours by Berichrom Assay method (mean)</td>
<td>2011</td>
<td>Rare</td>
<td></td>
</tr>
<tr>
<td>FIBRYGA</td>
<td>Octapharma USA, Inc.</td>
<td>Plasma-derived</td>
<td></td>
<td>75.9 hours (mean)</td>
<td>2017</td>
<td>Rare</td>
<td></td>
</tr>
<tr>
<td>NovoSeven RT</td>
<td>Novo Nordisk</td>
<td>Recombinant</td>
<td></td>
<td>Hemophilia A or B—Adolescents/Adults (15-63 yrs): 2.9-3.1 hours; Pediatrics (2-12 yrs): 2.6 hours; FVII Deficiency—Adolescents/Adults (20-43 yrs): 2.8-3.1 hours</td>
<td>1999</td>
<td>Inhibitor; Rare</td>
<td></td>
</tr>
<tr>
<td>Obizur</td>
<td>Takeda</td>
<td>Recombinant</td>
<td>Antihemophilic factor (recombinant), porcine sequence</td>
<td>Patients may vary in their pharmacokinetic (e.g., half-life, in vivo recovery) and clinical responses</td>
<td>2014</td>
<td>Rare</td>
<td></td>
</tr>
<tr>
<td>RiaSTAP</td>
<td>CSL Behring</td>
<td>Plasma-derived</td>
<td></td>
<td>78.7 hours (mean)</td>
<td>2009</td>
<td>Rare</td>
<td></td>
</tr>
<tr>
<td>Tretten</td>
<td>Novo Nordisk</td>
<td>Recombinant</td>
<td></td>
<td>Adults: 5.1 hrs Pediatrics: 7.1 hrs</td>
<td>2013</td>
<td>Rare</td>
<td></td>
</tr>
<tr>
<td>Amicar</td>
<td>Akorn Pharmaceuticals</td>
<td>Non-factor product</td>
<td>Oral Solution and Tablets</td>
<td>n/a</td>
<td>1998</td>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>Lysteda</td>
<td>Ferring Pharmaceuticals</td>
<td>Non-factor product</td>
<td>Tablet</td>
<td>n/a</td>
<td>1986</td>
<td>Other</td>
<td>Tablet/650mg</td>
</tr>
</tbody>
</table>
We’re counting down the days for HFA hugs to resume

Until then, we’re here for you and your family at www.hemophiliafed.org
A TUMULTUOUS YEAR, Few Changes for Treatment Options

BY HFA STAFF

Our last product guide hit the presses in early April 2020, right as the coronavirus caused the world to come to a screeching halt. At the time, many assumed a few weeks of lockdowns would control the virus. Yet here we are a year later, with almost everything we considered to be a temporary change now seemingly a normal part of life. More than 30.5 million cases were confirmed in the U.S., taking the lives of more than 550,000 people. Amidst the tragedy and suffering, the scientific and medical communities responded in heroic ways. From frontline workers to the teams implementing a testing network that conducted more than 376 million tests, the response to the pandemic demonstrated the potential that exists when we work together.

In just 10 months, the pharmaceutical industry, using years of work and research findings, was able to create, research, manufacture and begin distributing vaccines that have been proven safe and effective at preventing death from COVID-19. Since January, more than 200.5 million doses of vaccine have been delivered to states, with about 2.9 million doses administered per day on average.

Routine medical procedures and treatments were upended during the pandemic, and people living with a bleeding disorder saw changes to systems that were permanent fixtures in their lives. With many hospitals and Hemophilia Treatment Centers closed for anything but COVID-19 treatment, community members were forced to change their routines. One mom of a 3-year-old boy with hemophilia shared that she began to use her local pediatrician’s office to assist with infusions on a weekly basis, instead of driving into the city to visit the HTC, which was in a large hospital. A mom of a teenage son with hemophilia shared a positive experience with their Annual Comp Clinic, now taking place as a telehealth visit. This process, which previously lasted hours in person, has been shortened substantially. Through telehealth, medical providers still provided high-quality individual care, even going so far as to measure joint range of motion over the video screen.

While the world was changing fast in almost every other sense, the list of treatment options available for bleeding disorders experienced a quiet year with no major changes. Though, this year’s list does reflect some edits:

- **Desmopressin Acetate Injection—new product addition**—Launched for FVIII in May 2020 by Dr. Reddy’s Laboratories, this drug is a generic version of DDAVP. DDAVP is the licensed/trademark name owned by Ferring Pharmaceuticals.
- **Wilate—new indication listed for Factor VIII**—This product, manufactured by Octapharma, has been available for treatment of vWD since 2009 but was approved for treatment of Factor VIII in October 2019. This was not reflected on our product charts last year by omission.
- **Mononine—removed from available products**—CSL Behring announced in 2020 that it would no longer be distributing or manufacturing this factor IX treatment, saying, “Over time, patients have transitioned from older therapies to newer, next generation treatment options, and very few patients currently remain on MONONINE in the U.S.”

The future of treatment for bleeding disorders remains an exciting topic for our community. In our emerging therapies charts, you’ll find 53 clinical trials currently underway, investigating the efficacy and safety of 30 investigational therapeutic products. While these things don’t happen overnight, years of research have led to this moment in which our community could see several product approvals in the next few years, some that could drastically affect the way people with a bleeding disorder receive care.

Let’s make today brilliant.

Takeda is here to support you throughout your journey and help you embrace life’s possibilities. Our focus on factor treatments and educational programs, and our dedication to the bleeding disorders community, remain unchanged. And our commitment to patients, inspired by our vision for a bleed-free world, is stronger than ever.

bleedingdisorders.com
US Food and Drug Administration’s Drug Approval Process

What is a drug, as defined by FDA?
A drug is any product that is intended for the use in the diagnosis, cure, mitigation, treatment or prevention of disease and is intended to affect the structure or any function of the body.

PRE-CLINICAL
Drug Sponsor’s Discovery and Screening Phase:

1. Animals Tested
   Sponsor must test new drug on animals for toxicity. Multiple species are used to gather basic information on the safety and efficacy of the compound being investigated/researched.

2. IND Application
   The sponsor submits an Investigational New Drug application to FDA based on the results from initial testing. This application includes the drug’s composition and manufacturing specifications and offers a plan for testing the drug on humans.

3. Phase 1
   20-80 healthy volunteers: The typical number of healthy volunteers used in Phase 1; this phase emphasizes safety. The goal in this phase is to determine what the drug’s most frequent side effects are and, often, how the drug is metabolized and excreted.

4. Phase 2
   100s of patients: The typical number of patients used in Phase 2; this phase emphasizes effectiveness. The goal is to obtain preliminary data on whether the drug works in people who have a certain disease or condition. For controlled trials, patients receiving the drug are compared with similar patients receiving a different treatment — usually a placebo or a different drug. Safety continues to be evaluated, and short-term side effects are studied.

5. Phase 3
   1000s of patients: The typical number of patients used in Phase 3. These studies gather more information about safety and effectiveness, study different populations and different dosages, and use the drug in combination with other drugs.

Drug Developed
Drug sponsor develops a new drug compound and seeks to have it approved by FDA for sale in the United States.

At the end of Phase 2, FDA and sponsors discuss how large-scale studies in Phase 3 will be conducted.

FDA’s requirement for the number of patients needed to conduct a study/trial does change based on the size of the patient population being studied. For bleeding disorder studies/trials, counts are significantly reduced and sometimes can be fewer than 10 patients for Phase I trials. By Phase III, trials may include more than 100 people.

The objective: Have a statistically relevant sample size from which to draw conclusions.

For example, 200 trial participants in a hemophilia study is 1% of the U.S. hemophilia population, whereas 1% of the U.S. diabetic population in a diabetes study trial would equal 291,000 participants.
FDA meets with a drug sponsor prior to submission of a new drug application.

The drug sponsor formally asks FDA to approve a drug for marketing in the United States by submitting an NDA. An NDA includes all animal and human data and analyses of the data, as well as information about how the drug behaves in the body and how it is manufactured.

After an NDA is received, FDA has 60 days to decide whether to file it so it can be reviewed. If FDA files the NDA, an FDA review team is assigned to evaluate the sponsor’s research on the drug’s safety and effectiveness.

FDA reviews the drug’s professional labeling and ensures appropriate information is communicated to health care professionals and consumers.

Because it’s not possible to predict all of a drug’s effects during clinical trials, monitoring safety issues after drugs get on the market is critical. The role of FDA’s post-marketing safety system is meant to detect serious unexpected adverse events and take definitive action when needed.

Once FDA approves a drug, the post-marketing monitoring stage begins. The sponsor (typically the manufacturer) is required to submit periodic safety updates to FDA.

FDA’s MedWatch voluntary system makes it easier for physicians and consumers to report adverse events. Usually, when important new risks are uncovered, the risks are added to the drug’s labeling and the public is informed of the new information through letters, public health advisories and other educational means. In some cases, the use of the drug might be substantially limited. And in rare cases, the drug might need to be withdrawn from the market.
CLINICAL STUDIES:
HOW DO THEY WORK?

BY HFA STAFF WITH SOURCING FROM THE NATIONAL INSTITUTES OF HEALTH’S NATIONAL LIBRARY OF MEDICINE

A clinical study involves research using human volunteers (also called participants) that is intended to add to medical knowledge. There are two main types of clinical studies: clinical trials (also called interventional studies) and observational studies.

In a clinical trial, participants receive specific interventions according to the research plan or protocol created by the investigators. These interventions may be medical products, such as drugs or devices; procedures; or changes to participants’ behavior, such as diet. Clinical trials may compare a new medical approach to a standard one that is already available, to a placebo that contains no active ingredients or to no intervention. Some clinical trials compare interventions that are already available to each other.

When a new product or approach is being studied, it is not usually known whether it will be helpful, harmful or no different than available alternatives (including no intervention). The investigators try to determine the safety and efficacy of the intervention by measuring certain outcomes in groups of participants according to a research plan or protocol. Participants may receive interventions (which can include medical products such as drugs or devices) or procedures as part of their routine medical care, but participants are not assigned to specific interventions by the investigator (as in a clinical trial). For example, investigators may observe a group of older adults to learn more about the effects of different lifestyles on cardiac health. Investigators assess health outcomes in groups of participants who receive interventions, but participants are not assigned to specific interventions by the investigator as they would be in a clinical trial.

WHO CONDUCTS?
Every principal investigator, who is often a medical doctor, leads a clinical study.临床研究团队可能包括医生、护士、社会工作者和其他医疗专业人士。

Clinical studies can be sponsored, or funded, by pharmaceutical companies, academic medical centers, voluntary groups and other organizations, in addition to federal agencies. Doctors, other health care providers and other individuals can also sponsor research.

WHO PARTICIPATES?
Some studies seek participants who have the illnesses or conditions that will be studied while other studies are looking for healthy participants. Some studies are limited to a predetermined group of people who are asked by researchers to enroll.

WHO’S ELIGIBLE?
The factors that allow someone to participate in a clinical study are called inclusion criteria. The factors that disqualify someone from participating are called exclusion criteria. Criteria are listed in the study protocol. Factors are based on characteristics such as age, gender, the type and stage of a disease, previous treatment history and other medical conditions.

WHERE?
Studies take place in hospitals, universities, doctors’ offices and community clinics, depending on who is conducting the study.

LENGTH?
The length of a clinical study varies, depending on what is being studied. Participants are told how long the study will last before they enroll.

PROTECTIONS?
Informed consent is a process used by researchers to provide potential and enrolled participants with information about a clinical study. It protects participants and provides enough information for a person to understand the risks of potential benefits of and alternatives to the study. (See page 10 for more information on informed consent.)

Institutional Review Boards
Each federally supported or conducted clinical study and each study of a drug, biological product or medical device regulated by FDA must be reviewed, approved and monitored by an institutional review board. An IRB is made up of doctors, researchers and members of the community, who make sure the study is ethical and the rights and welfare of participants are protected.

Relationship to Usual Health Care
While enrolled in a clinical study, participants continue to see their usual health care providers who work with the research team to make sure the study will not conflict with other medications or treatments.

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HOW DO THEY WORK?

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INTERESTED IN PARTICIPATING?

Anyone interested in participating in a clinical study should know as much as possible about the study and feel comfortable asking the research team questions about the study, the related procedures and any expenses. The following questions may be helpful during such a discussion:

- What is being studied and how long will it last?
- Why do researchers believe the intervention being tested might be effective?
- What will I have to do and is hospitalization required?
- Who will know which intervention I receive during the trial? Will I know? Will members of the research team know?
- How do the possible risks, side effects and benefits of this trial compare with those of my current treatment?
- What tests and procedures are involved?
- Who will pay for my participation and will I be reimbursed for other expenses?
- What type of long-term follow-up care is part of this trial?
- If I benefit from the intervention, will I be allowed to continue receiving it after the trial ends?
- Will results of the study be provided to me? Who will oversee my medical care while I am participating in the trial?
- What happens if I am injured during the study?

THE FIVE PHASES OF A CLINICAL TRIAL

EARLY PHASE 1 (FORMERLY LISTED AS “PHASE 0”):
Exploratory study involving very limited human exposure to the drug, with no therapeutic or diagnostic goals. Examples would include screening studies and microdose studies.

PHASE 1:
Studies that are usually conducted with healthy volunteers and that emphasize safety. The goal is to find out what the drug’s most frequent and serious adverse events are and, often, how the drug is metabolized and excreted.

PHASE 2:
Studies that gather preliminary data on effectiveness, as in whether the drug works in people who have a certain disease or condition. For example, participants receiving the drug may be compared to similar participants receiving a different treatment, usually an inactive substance, called a placebo, or a different drug. Safety continues to be evaluated and short-term adverse events are studied.

PHASE 3:
Studies that gather more information about safety and effectiveness by studying different populations and different dosages, and by using the drug in combination with other drugs.

PHASE 4:
Studies occurring after FDA has approved a drug for marketing. These include post-market requirement and commitment studies that are required of, or agreed to by, the study sponsor. These studies gather additional information about a drug’s safety, efficacy or optimal use.

EARLY PHASE 1:

Creating a path for advancement in hemophilia gene therapy research

“It’s an exciting time in hemophilia. I’m grateful to be in a position to help people understand gene therapy research. With access to that knowledge, you can help make the right decision for yourself.”

Guillermo Campillo,
Senior Patient Education Liaison

Advance your knowledge about gene therapy. Be informed. Feel empowered.
Learn more about investigational gene therapy for hemophilia at HemophiliaForward.com.
For residents of the U.S. only

Scan here to stay connected

Hemophilia Forward is sponsored by Spark Therapeutics, Inc.
1-855-SPARKTX | Sparktx.com
Within the past decade alone, medical research and scientific advancements have reshaped the way the bleeding disorders community looks at treatment. Discussions of a cure, or long-lasting, one-time treatment options no longer seem so far-fetched, but they are instead very likely outcomes of a scientific breakthrough.

Numerous companies and research teams are evaluating their products and therapies through the Food and Drug Administration’s clinical trial process right now.

Whether you or your child has just been diagnosed, or you’ve lived with a bleeding disorder for decades, knowledge of approved treatment options and emerging therapies is a key component of being able to advocate for yourself and essential to have informed conversations with health care professionals.

To help patients and caregivers with the process of navigating emerging therapies, we’ve compiled a comprehensive list of therapies currently undergoing clinical trial through FDA.

Information in this issue should not be interpreted as medical advice. We encourage frequent dialogue with experienced health care professionals regarding your health and the therapies used to treat your bleeding disorder.

### EMERGING THERAPIES UNDERGOING CLINICAL TRIALS FOR TREATMENT OF BLEEDING DISORDERS

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Detailed product information can be found on the following pages, organized by indication.

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**INVESTIGATIONAL THERAPEUTIC PRODUCTS CURRENTLY UNDERGOING CLINICAL TRIAL**

To help patients and caregivers with the process of navigating emerging therapies, we’ve compiled a comprehensive list of therapies currently undergoing clinical trial through FDA.

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**EMERGING THERAPIES UNDERGOING CLINICAL TRIALS FOR TREATMENT OF BLEEDING DISORDERS**

Within the past decade alone, medical research and scientific advancements have reshaped the way the bleeding disorders community looks at treatment. Discussions of a cure, or long-lasting, one-time treatment options no longer seem so far-fetched, but they are instead very likely outcomes of a scientific breakthrough. Numerous companies and research teams are evaluating their products and therapies through the Food and Drug Administration’s clinical trial process right now.

To help patients and caregivers with the process of navigating emerging therapies, we’ve compiled a comprehensive list of therapies currently undergoing clinical trial through FDA.

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Detailed product information can be found on the following pages, organized by indication.
The pages that follow contain a list of emerging therapies that are undergoing clinical trial by the Food and Drug Administration for treatment of a bleeding disorder. For ease of navigation, the charts are published in sections by indication (Factor VIII, Factor IX, Inhibitor, VWD, Rare or Other), with each containing the following categories of information:

- **Investigational Therapeutic Product Name**: Product name used during a research/trial. Usually, this name is changed when a product is approved and brought to market.
- **Phase**: The current stage in the FDA approval process.
- **Indications**: Bleeding disorder type/factor deficiency the therapy is intended to treat.
- **Indication Details**: Detailed classification of indication, if applicable.
- **Type**: Method used to create the product/therapy.
- **Specific Product Type**: Detailed classification of type, if applicable.

We’ve made every effort to ensure the accuracy of the information in this list by using information directly from manufacturers and publicly available information from websites, such as FDA. We do not encourage community members to use one product over another, and we strongly urge you to discuss your treatment options with qualified medical professionals.

Content in this issue is current as of March 2021. Given the fast-paced environment that manufacturers and governmental agencies work within, some information could have changed since going to print. Please refer to manufacturers’ or the FDA’s websites for the most up-to-date information.

### Companies Running the Most Trials

<table>
<thead>
<tr>
<th>Company</th>
<th>Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>SANOFI GENZYMÉ</td>
<td>12</td>
</tr>
<tr>
<td>PFIZER, INC.</td>
<td>6</td>
</tr>
<tr>
<td>BIOMARIN PHARMACEUTICAL</td>
<td>5</td>
</tr>
<tr>
<td>HEMA BIOLOGICS</td>
<td>3</td>
</tr>
<tr>
<td>NOVO NORDISK</td>
<td>3</td>
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<tr>
<td>TAKEDA</td>
<td>3</td>
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<tr>
<td>UNIGURE</td>
<td>3</td>
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</tbody>
</table>

### Clinical Trials by Indication

<table>
<thead>
<tr>
<th>Indication</th>
<th>Trials</th>
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<tbody>
<tr>
<td>FACTOR VIII</td>
<td>25</td>
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<tr>
<td>FACTOR IX</td>
<td>23</td>
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<tr>
<td>INHIBITOR</td>
<td>12</td>
</tr>
<tr>
<td>RARE</td>
<td>2</td>
</tr>
</tbody>
</table>

*Note, one clinical trial can research more than one indication

### Stages of Ongoing Clinical Trials

- **Phase 1**: 6 trials
- **Phase 1/2**: 17 trials
- **Phase 2**: 5 trials
- **Phase 2/3**: 3 trials
- **Phase 3**: 19 trials
- **Phase 3/4**: 1 trial
- **Phase 4**: 1 trial

### How to Navigate Our Emerging Therapies Charts

The pages that follow contain a list of emerging therapies that are undergoing clinical trial by the Food and Drug Administration for treatment of a bleeding disorder. For ease of navigation, the charts are published in sections by indication (Factor VIII, Factor IX, Inhibitor, VWD, Rare or Other), with each containing the following categories of information:

- **Investigational Therapeutic Product Name**: Product name used during a research/trial. Usually, this name is changed when a product is approved and brought to market.
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<table>
<thead>
<tr>
<th>Investigational Therapeutic Product Name</th>
<th>Sponsor</th>
<th>Type</th>
<th>Specific Type</th>
<th>Phase</th>
<th>Indications</th>
<th>Indication Details</th>
<th>Official Title of Study</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 3</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with or without inhibitor, who were previously under factor or BPA prophylactic treatment</td>
<td>A Study of Fitusiran in Severe Hemophilia A and B Patients Previously Receiving Factor or Bypassing Agent Prophylaxis (ATLAS-PK)</td>
<td></td>
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<tr>
<td>TAK-754</td>
<td>Takeda</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 1/2 - Active, not recruiting</td>
<td>Factor VIII</td>
<td>Hemophilia A</td>
<td>Safety and Dose Escalation Study of an Adeno-Associated Viral Vector for Gene Transfer in Hemophilia A Participants</td>
<td></td>
</tr>
<tr>
<td>marstacimab</td>
<td>Pfizer, Inc.</td>
<td>Novel: Non-factor product</td>
<td>Antibody to Tissue Factor Pathway Inhibitor</td>
<td>Phase 3 - FDA Orphan Drug Status (HA), 2016 <a href="http://www.clinicaltrials.gov">www.clinicaltrials.gov</a>; NCT03938792</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Severe hemophilia A or B (Factor VIII or Factor IX activity &lt; 1%) Subjects enrolled as Factor VIII or Factor IX inhibitor patients must have a positive inhibitor test result (above the upper limit of normal) at the local laboratory and must receive a bypass agent as primary treatment for bleeding episodes</td>
<td>An Open-Label Study in Adolescents and Adult Severe (Coagulation Factor &lt;1%) Hemophilia A or B Patients or without Inhibitors: Comparing Standard Treatment to PF-06741086 Prophylaxis</td>
<td></td>
</tr>
<tr>
<td>giroctocogene fitelparvovec</td>
<td>Pfizer, Inc.</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 3- FDA Orphan Drug Status, Fast Track status, Regenerative Medicine Advanced Therapy Designation; NCT04370054</td>
<td>Factor VIII</td>
<td>Moderately severe to severe hemophilia A adult subjects (FVIII:C &lt;1%) who have completed at least 6 months of routine prophylaxis with FVIII products in the lead-in study C0371004</td>
<td>Study to Evaluate the Efficacy and Safety of PF-07055480 in Moderately Severe to Severe Hemophilia A Adults (AFFINE)</td>
<td>Novel therapeutic modality consisting of genetically modified allogeneic cells encapsulated in small molecule modified alginate spheres designed to avoid immune rejection by the host organism.</td>
</tr>
<tr>
<td>SIG-001</td>
<td>Sigilon Therapeutics, Inc</td>
<td>Cell Therapy</td>
<td>Non-viral based encapsulated cell therapy</td>
<td>Phase 1.2 - FDA Orphan Drug Status (HA), 2019. Recruiting (NCT04546628)</td>
<td>Factor VIII</td>
<td>FVIII</td>
<td>A Phase 1, 2 Open-Label, Dose-Escalation, Safety, Tolerability, and Efficacy Study of SIG-001 in Adult Patients with Severe or Moderately Severe Haemophilia A without Inhibitors</td>
<td></td>
</tr>
<tr>
<td>giroctocogene fitelparvovec</td>
<td>Pfizer, Inc.</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 1/2 - FDA Orphan Drug Status, Fast Track status, FDA Regenerative Medicine Advanced Therapy Designation: July, 2019 NCT03060120; Trial was fully transitioned from Sangamo to Pfizer as of December 2019</td>
<td>Factor VIII</td>
<td>Severe hemophilia A (FVIII:C &lt;1%) with &gt;150 documented exposure days and no history of inhibitors who are negative for neutralizing antibodies</td>
<td>A Phase 1/2, Open-Label, Adaptive, Dose-Ranging Study to Assess the Safety and Tolerability of SB-525 (Recombinant AAV2/6 Human Factor B Gene Therapy) in Adult Subjects With Severe Hemophilia A</td>
<td></td>
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<tr>
<td>SB-FIX</td>
<td>Sangamo Therapeutics</td>
<td>Gene Therapy</td>
<td>Genome Editing</td>
<td>Phase 1 - IND cleared. Orphan drug designation by FDA</td>
<td>Factor VIII</td>
<td>Severe IX</td>
<td>A Phase I, Open-Label, Ascending Dose Study to Assess the Safety and Tolerability of AAV2/6 Factor IX Gene Therapy Via Zinc Finger Nuclease (ZFN) Mediated Targeted Integration of SB-FIX in Adult Subjects With Severe Hemophilia B</td>
<td>Active, not recruiting</td>
</tr>
<tr>
<td>Investigational Therapeutic Product Name</td>
<td>Sponsor</td>
<td>Type</td>
<td>Specific Type</td>
<td>Phase</td>
<td>Indications</td>
<td>Indication Details</td>
<td>Official Title of Study</td>
<td>Notes</td>
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<tr>
<td>SB-525</td>
<td>Sangamo Therapeutics</td>
<td>Gene Therapy</td>
<td></td>
<td>Phase 1/2 - IND cleared. Orphan drug designation by FDA and EMA. Fast track from FDA</td>
<td>Factor VIII</td>
<td>Severe VIII</td>
<td>A Phase 1/2, Open-Label, Adaptive, Dose-Ranging Study to Assess the Safety and Tolerability of SB-525 (Recombinant AAV2/6 Human Factor VIII Gene Therapy) in Adult Subjects With Severe Hemophilia A</td>
<td>Active, not recruiting. Sangamo Therapeutics, in partnership with Pfizer</td>
</tr>
<tr>
<td>concizumab</td>
<td>Novo Nordisk</td>
<td>Novel: Investigational factor product</td>
<td>Anti-TFPI</td>
<td>II - NCT03196284</td>
<td>Factor VIII; Factor IX</td>
<td>Congenital VIII and IX with inhibitors</td>
<td>A Trial Evaluating the Efficacy and Safety of Prophylactic Administration of Concizumab in Haemophilia A and B Patients With Inhibitors (explorer™4)</td>
<td></td>
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<tr>
<td>concizumab</td>
<td>Novo Nordisk</td>
<td>Novel: Investigational factor product</td>
<td>Anti-TFPI</td>
<td>II - NCT03196297</td>
<td>Factor VIII; Factor IX</td>
<td>Congenital VIII and IX</td>
<td>A Trial Evaluating Efficacy and Safety of Prophylactic Administration of Concizumab in Patients With Severe Haemophilia A Without Inhibitors (explorer™5)</td>
<td></td>
</tr>
<tr>
<td>giroctocogene fitelparvovec, fidanacogene elaparvovec</td>
<td>Pfizer, Inc.</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 3 - NCT0358716</td>
<td>Factor VIII; Factor IX</td>
<td>Severe hemophilia A adult subjects (FVIII:C &lt;1%) who are negative for nAb to AAV vector SB-525 capsid (AAV6) and moderately severe to severe hemophilia B (FIX:C &lt;2%) who are negative for nAb to AAV vector Spark-100, prior to the respective therapeutic phase 3 gene therapy studies</td>
<td>Six Month lead-in Study to Evaluate Prospective Efficacy and Safety Data of Current FIX Prophylaxis Replacement Therapy in Adult Hemophilia B Subjects (FIX:C&lt;2%) or Current FIX VIII Prophylaxis Replacement Therapy in Adult Hemophilia A Subjects (FIX:C&lt;1%)</td>
<td></td>
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<tr>
<td>NNC0365-3769 A (Mim8)</td>
<td>Novo Nordisk</td>
<td>Novel: Non-factor product</td>
<td>Coagulation factor VIII mimetic antibody</td>
<td>II - NCT04204408</td>
<td>Factor VIII; Inhibitor</td>
<td>Hemophilia A with or without inhibitors</td>
<td>Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single and Multiple Subcutaneous Doses of NNC0365-3769 (Mim8) in Healthy Subjects and in Subjects With Hemophilia A With or Without Factor VIII Inhibitors</td>
<td>clinicaltrials.gov/ct2/show/NCT04204408?tem=mim8&amp;draw=2&amp;rank=1</td>
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<tr>
<td>valoctocogene roxaparvovec</td>
<td>BioMarin Pharmaceutical Inc.</td>
<td>Gene Therapy</td>
<td>AAV Vector-Mediated Gene Transfer Therapy</td>
<td>Phase 3 - Orphan Drug Designation from FDA; Breakthrough Therapy Designation from FDA and EMA; Priority Medicines (PRIME) status from EMA, BLA filed to FDA Q4 2019; MAA validated by EMA Q4 2019.</td>
<td>Factor VIII</td>
<td>Severe Hemophilia A</td>
<td>J02 - A Phase 3 Open-Label, Single-Arm Study To Evaluate The Efficacy and Safety of BMN 270, an Adeno-Associated Virus Vector-Mediated Gene Transfer of Human Factor VIII at a dose of 4E13 vg/kg in Hemophilia A Patients with Residual FVIII Levels &lt; 1 IU/dL</td>
<td>Active, not enrolling</td>
</tr>
<tr>
<td>BAY2599023 (DTX201)</td>
<td>Bayer</td>
<td>Gene Therapy</td>
<td></td>
<td>Phase 1/2 - Recruiting</td>
<td>Factor VIII</td>
<td>Severe Hemophilia A</td>
<td>A Phase 1/2 Open-label Safety and Dose-finding Study of BAY2599023 (DTX201), an Adeno-associated Virus (AAV) hu37-mediated Gene Transfer of B-domain Deleted Human Factor VIII, in Adults With Severe Hemophilia A</td>
<td>Bayer in collaboration with Ultragenyx Pharmaceuticals</td>
</tr>
<tr>
<td>SubQ-8</td>
<td>Octapharma USA, Inc.</td>
<td>Novel: Investigational factor product</td>
<td>Human-cl rhFVIII and Recombinant human von Willebrand Factor fragment dimer</td>
<td>Phase 1, Phase 2 - VIII</td>
<td>Factor VIII</td>
<td>VIII</td>
<td>Safety and Pharmacokinetics of Subcutaneous Injection of OCTA101 in Adult Patients With Severe Hemophilia A</td>
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<tr>
<td>Investigational Therapeutic Product Name</td>
<td>Sponsor</td>
<td>Type</td>
<td>Specific Type</td>
<td>Phase</td>
<td>Indications</td>
<td>Indication Details</td>
<td>Official Title of Study</td>
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<tr>
<td>AAV2/8-HLP-FVIII-V3</td>
<td>St. Jude Children’s Research Hospital</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 1</td>
<td>Factor VIII</td>
<td>VIII</td>
<td>GO-8: Gene Therapy for Haemophilia A Using a Novel Serotype 8 Capsid Pseudotyped Adeno-associated Viral Vector Encoding Factor VIII-V3</td>
<td></td>
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<tr>
<td>Efanesoctocog Alfa (BIVV001)</td>
<td>Sanofi Genzyme</td>
<td>Novel: Investigational factor product</td>
<td>rFVIIIFc-XTEN</td>
<td>Phase 1 Phase 2</td>
<td>Factor VIII</td>
<td>VIII</td>
<td>A Phase 1/2a, Open-Label, Dose-Escalation Study to Determine the Safety, Tolerability, and Pharmacokinetics of a Single Intravenous Injection of rFVIIIFc-VWF-XTEN (BIVV001) in Previously Treated Adults With Severe Hemophilia A</td>
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<tr>
<td>Efanesoctocog Alfa (BIVV001)</td>
<td>Sanofi Genzyme</td>
<td>Novel: Investigational factor product</td>
<td>rFVIIIFc-XTEN</td>
<td>Phase 1 Phase 2</td>
<td>Factor VIII</td>
<td>VIII</td>
<td>A Phase 1, Open-Label, Single-Site, Safety, Tolerability, and Pharmacokinetics Study of Repeat Doses of BIVV001</td>
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<tr>
<td>Efanesoctocog Alfa (BIVV001)</td>
<td>Sanofi Genzyme</td>
<td>Novel: Investigational factor product</td>
<td>rFVIIIFc-XTEN</td>
<td>Phase 3</td>
<td>Factor VIII</td>
<td>VIII</td>
<td>A Phase 3 Open-Label, Multicenter Study of the Safety, Efficacy, and Pharmacokinetics of Intravenous Recombinant Coagulation Factor VIII Fc-von Willebrand Factor-XTEN Fusion Protein (rFVIIIFc-VWF-XTEN; BIVV001) in Previously Treated Patients ≥ 12 Years of</td>
<td></td>
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<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 3</td>
<td>Factor VIII; Factor IX</td>
<td>Hemophilia A and hemophilia B without inhibitor, who were previously under factor on demand treatment</td>
<td>ATLAS-A/B: A Phase 3 Study to Evaluate the Efficacy and Safety of Fitusiran in Patients With Hemophilia A or B, Without Inhibitory Antibodies to Factor VIII or IX</td>
<td></td>
</tr>
<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 1</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with or without inhibitor</td>
<td>A Phase 1 Single-ascending and Multiple-ascending Dose, Safety, Tolerability and Pharmacokinetics Study of Subcutaneously Administered ALN-AT3SC in Healthy Adult Volunteers and Hemophilia A or B Patients (Moderate or Severe Hemophilia)</td>
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</tr>
<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 1 Phase 2</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with or without inhibitor, who completed Phase 1 study</td>
<td>An Open-label Extension Study of an Investigational Drug, Fitusiran, in Patients With Moderate or Severe Hemophilia A or B</td>
<td></td>
</tr>
<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 3</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with inhibitor, who were previously under BPA on demand treatment</td>
<td>ATLAS-INH: A Phase 3 Study to Evaluate the Efficacy and Safety of Fitusiran in Patients With Hemophilia A or B, With Inhibitory Antibodies to Factor VIII or IX</td>
<td></td>
</tr>
<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 2/3</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with inhibitor, pediatric patients 1-11 years of age</td>
<td>Fitusiran Prophylaxis in Male Pediatric Subjects Aged 1 to Less Than 12 Years With Hemophilia A or B (ATLAS-PEDS)</td>
<td></td>
</tr>
<tr>
<td>SPK-8016</td>
<td>Spark Therapeutics, Inc.</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 1, Phase 2</td>
<td>Factor VIII</td>
<td>VIII</td>
<td>Dose-finding Study of SPK-8016 Gene Therapy in Patients With Hemophilia A to Support Evaluation in Individuals With FVIII Inhibitors</td>
<td></td>
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<tr>
<td>SCT800</td>
<td>Sinocelltech Ltd.</td>
<td>Recombinant clotting factor</td>
<td>Recombinant VIII</td>
<td>Phase 4</td>
<td>Factor VIII</td>
<td>Moderate to Severe VIII</td>
<td>A Multicenter, Open Extension Trial to Evaluate Safety and Efficacy of Recombinant Human Coagulation Factor VIII (SCT800) During Long Term Treatment in Previously Treated Patients With Severe Hemophilia A</td>
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<tr>
<td>Investigational Therapeutic Product Name</td>
<td>Sponsor</td>
<td>Type</td>
<td>Specific Type</td>
<td>Phase</td>
<td>Indications</td>
<td>Indication Details</td>
<td>Official Title of Study</td>
<td>Notes</td>
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<tr>
<td>SCT800</td>
<td>Sinocelltech Ltd.</td>
<td>Recombinant clotting factor</td>
<td>Recombinant VIII</td>
<td>Phase 3</td>
<td>Factor VIII</td>
<td>Severe VIII</td>
<td>A Multicenter Phase III Uncontrolled Open-label Trial to Evaluate Safety and Efficacy and Pharmacokinetics of Recombinant Human Coagulation Factor VIII (SCT800) in Previously Treated Paediatric Patients With Severe Haemophilia A.</td>
<td>Recruiting by invitation</td>
</tr>
<tr>
<td>valoctocogene roxaparvovec</td>
<td>BioMarin Pharmaceutical Inc.</td>
<td>Gene Therapy</td>
<td>AAV Vector-Mediated Gene Transfer Therapy</td>
<td>Phase 1/2</td>
<td>Factor VIII</td>
<td>Severe Haemophilia A</td>
<td>205 - A Phase 1/2 Safety, Tolerability and Efficacy Study of BMN 270, an Adeno-Associated Virus Vector-Mediated Gene Transfer of Human Factor VIII in Hemophilia A Patients with Active or Prior Inhibitors</td>
<td>Active and Enrolling</td>
</tr>
<tr>
<td>valoctocogene roxaparvovec</td>
<td>BioMarin Pharmaceutical Inc.</td>
<td>Gene Therapy</td>
<td>AAV Vector-Mediated Gene Transfer Therapy</td>
<td>Phase 3 - Orphan Drug Designation from FDA; Breakthrough Therapy Designation from FDA and EMA; Priority MEdicines (PRIME) status from EMA; BLA filed to FDA Q4 2019; MAA validated by EMA Q4 2 019</td>
<td>Factor VIII</td>
<td>Severe Haemophilia A</td>
<td>303 - A Phase 3b, Single Arm, Open-Label Study to Evaluate the Efficacy and Safety of BMN 270, an Adeno-Associated Virus Vector-Mediated Gene Transfer of Human Factor VIII, with Prophylactic Corticosteroids in Hemophilia A Patients</td>
<td></td>
</tr>
<tr>
<td>valoctocogene roxaparvovec</td>
<td>BioMarin Pharmaceutical Inc.</td>
<td>Gene Therapy</td>
<td>AAV Vector-Mediated Gene Transfer Therapy</td>
<td>Phase 3 - Orphan Drug Designation from FDA; Breakthrough Therapy Designation from FDA and EMA; Priority MEdicines (PRIME) status from EMA; BLA filed to FDA Q4 2019; MAA validated by EMA Q4 2 019</td>
<td>Factor VIII</td>
<td>Severe Haemophilia A</td>
<td>701 - A Prospective, Observational Study Evaluating Seroprevalence and Rate of Seroconversion of Antibodies against Adeno-associated Virus (AAV) Serotypes and Exploratory Vectors in Subjects with Hemophilia A in the United States</td>
<td>Active and Enrolling</td>
</tr>
<tr>
<td>valoctocogene roxaparvovec</td>
<td>BioMarin Pharmaceutical Inc.</td>
<td>Gene Therapy</td>
<td>AAV Vector-Mediated Gene Transfer Therapy</td>
<td>Phase 3 - Orphan Drug Designation from FDA; Breakthrough Therapy Designation from FDA and EMA; Priority MEdicines (PRIME) status from EMA; BLA filed to FDA Q4 2019; MAA validated by EMA Q4 2 019</td>
<td>Factor VIII</td>
<td>Severe Haemophilia A</td>
<td>301 - A Phase 3 Open-Label, Single-Arm Study To Evaluate The Efficacy and Safety of BMN 270, an Adeno-Associated Virus Vector-Mediated Gene Transfer of Human Factor VIII at a dose of 6E13 vg/kg in Hemophilia A Patients with Residual FVIII Levels ≤ 1 IU/dL</td>
<td>Active, not enrolling</td>
</tr>
<tr>
<td>Efanesoctocog Alfa (BIVV001)</td>
<td>Sanofi Genzyme</td>
<td>Novel: Investigational factor product</td>
<td>rFVIIIc-XTEN</td>
<td>Phase 3</td>
<td>Factor VIII</td>
<td>VIII</td>
<td>A Phase 3 Open-label, Multicenter Study of the Long-term Safety and Efficacy of Intravenous Recombinant Coagulation Factor VIII Fc-von Willebrand Factor-XTEN Fusion Protein (rFVIIIc-VWF-XTEN; BIVV001) in Previously Treated Patients With Severe Hemophilia</td>
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<tr>
<td>Efanesoctocog Alfa (BIVV001)</td>
<td>Sanofi Genzyme</td>
<td>Novel: Investigational factor product</td>
<td>rFVIIIc-XTEN</td>
<td>Phase 3</td>
<td>Factor VIII</td>
<td>VIII</td>
<td>A Phase 3 Open-label, Multicenter Study of the Safety, Efficacy, and Pharmacokinetics of Intravenous Recombinant Coagulation Factor VIII Fc-von Willebrand Factor-XTEN Fusion Protein (rFVIIIc-VWF-XTEN; BIVV001) in Previously Treated Pediatric Patients &lt;12</td>
<td></td>
</tr>
<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 3</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with or without inhibitor, who completed Phase 3 studies</td>
<td>Long-term Safety and Efficacy Study of Fitusiran in Patients With Hemophilia A or B, With or Without Inhibitory Antibodies to Factor VIII or IX (ATLAS-OLE)</td>
<td></td>
</tr>
<tr>
<td>Investigational Therapeutic Product Name</td>
<td>Sponsor</td>
<td>Type</td>
<td>Specific Product Type</td>
<td>Phase</td>
<td>Indications</td>
<td>Indication Details</td>
<td>Official Title of Study</td>
<td>Notes</td>
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<tr>
<td>AAV5-hFIXco-Padua/AMT-061</td>
<td>uniQure</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 2B - Breakthrough Designation; 1/30/17</td>
<td>Factor IX</td>
<td>IX</td>
<td>Phase IIb, Open-label, Single-dose, Single-arm, Multi-center Trial to Confirm the Factor IX Activity Level of the Serotype 5 Adeno-associated Viral Vector Containing the Padua Variant of a Codon-optimized Human Factor IX Gene (AAVS-hFIXco-Padua, AMT-061)</td>
<td></td>
</tr>
<tr>
<td>AAV5-hFIXco-Padua/AMT-061</td>
<td>uniQure</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 3 - Breakthrough Designation; 1/30/17</td>
<td>Factor IX</td>
<td>IX</td>
<td>Phase III, Open-label, Single-dose, Multi-center, Multinational Trial Investigating a Serotype 5 Adeno-associated Viral Vector Containing the Padua Variant of a Codon-optimized Human Factor IX Gene (AAVS-hFIXco-Padua, AMT-061) Administered to Adult Subjects</td>
<td>Licensed to CSL Behring for Commercialization (pending government approval), Trial on Clinical Hold FDA, Dec. 2020</td>
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<tr>
<td>AMT-060 (AAVS-hFIX)</td>
<td>uniQure</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase I, Phase 2 - Breakthrough Designation; 1/30/17</td>
<td>Factor IX</td>
<td>IX</td>
<td>A Phase I/II, Open-label, Uncontrolled, Single-dose, Dose-ascending, Multi-centre Trial Investigating an Adeno-associated Viral Vector Containing a Codon-optimized Human Factor IX Gene (AAVS-hFIX) Administered to Adult Patients With Severe or Moderately Severe Hemophilia B</td>
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<tr>
<td>concizumab</td>
<td>Novo Nordisk</td>
<td>Novel: investigational factor product</td>
<td>Anti-TFPI</td>
<td>II - NCT03196284</td>
<td>Factor VIII; Factor IX</td>
<td>Congenital VIII and IX with inhibitors</td>
<td>A Trial Evaluating the Efficacy and Safety of Prophylactic Administration of Concizumab in Haemophilia A and B Patients With Inhibitors (explore™4)</td>
<td></td>
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<tr>
<td>concizumab</td>
<td>Novo Nordisk</td>
<td>Novel: investigational factor product</td>
<td>Anti-TFPI</td>
<td>II - NCT03196297</td>
<td>Factor VIII; Factor IX</td>
<td>Congenital VIII and IX</td>
<td>A Trial Evaluating Efficacy and Safety of Prophylactic Administration of Concizumab in Patients With Severe Haemophilia A Without Inhibitors (explore™5)</td>
<td></td>
</tr>
<tr>
<td>fidanacogene elaparvovec</td>
<td>Pfizer, Inc.</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 2 - FDA Breakthrough Designation: July, 2016 FDA Orphan Drug Designation: September, 2015 <a href="http://www.clinicaltrials.gov">www.clinicaltrials.gov</a>; NCT03307980</td>
<td>Factor IX</td>
<td></td>
<td>Moderately severe to severe hemophilia B (FIX:C&lt;2%) with &gt;50 exposure days and no history of inhibitors who have previously received PF-06838435 and completed the CO371005 study</td>
<td>Long-term Safety and Efficacy Study and Dose-Escalation Substudy of PF-06838435 in Individuals With Hemophilia B</td>
</tr>
<tr>
<td>Investigational Therapeutic Product Name</td>
<td>Sponsor</td>
<td>Type</td>
<td>Specific Product Type</td>
<td>Phase</td>
<td>Indications</td>
<td>Indication Details</td>
<td>Official Title of Study</td>
<td>Notes</td>
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<tr>
<td>fidanacogene elaparvovec</td>
<td>Pfizer, Inc.</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 3 - FDA Breakthrough Designation: July, 2016 FDA Orphan Drug Designation: September, 2015 <a href="http://www.clinicaltrials.gov">www.clinicaltrials.gov</a>; NCT03861273</td>
<td>Factor IX</td>
<td>Moderately severe to severe hemophilia B (FIX:C&lt;2%) and no history of inhibitors who completed 6 months of routine Factor IX prophylaxis therapy during the lead in study (CO371004) and have &gt;50 documented exposure days to a FIX protein product such as recombinant, plasma-derived or extended half-life FIX product</td>
<td>A Study to Evaluate the Efficacy and Safety of Factor IX Gene Therapy With PF-06838435 in Adult Males With Moderately Severe to Severe Hemophilia B (BENEGENE-2)</td>
<td></td>
</tr>
<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 3</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with or without inhibitor, who were previously under factor or BPA prophylactic treatment</td>
<td>A Study of Fitusiran in Severe Hemophilia A and B Patients Previously Receiving Factor or Bypassing Agent Prophylaxis (ATLAS-PPX)</td>
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<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 3</td>
<td>Factor VIII; Factor IX</td>
<td>Hemophilia A and hemophilia B without inhibitor, who were previously under factor on demand treatment</td>
<td>ATLAS-A/B: A Phase 3 Study to Evaluate the Efficacy and Safety of Fitusiran in Patients With Hemophilia A or B, Without Inhibitory Antibodies to Factor VIII or IX</td>
<td></td>
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<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 1 Phase 2</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with or without inhibitor, who completed Phase 1 study</td>
<td>An Open-label Extension Study of an Investigational Drug, Fitusiran, in Patients With Moderate or Severe Hemophilia A or B</td>
<td></td>
</tr>
<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 3</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with inhibitor, who were previously under BPA on demand treatment</td>
<td>ATLAS-INH: A Phase 3 Study to Evaluate the Efficacy and Safety of Fitusiran in Patients with Hemophilia A or B, With Inhibitory Antibodies to Factor VIII or IX</td>
<td></td>
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<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 2/3</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with inhibitor, pediatric patients 1-11 years of age</td>
<td>Fitusiran Prophylaxis in Male Pediatric Subjects Aged 1 to Less Than 12 Years With Hemophilia A or B (ATLAS-PEDS)</td>
<td></td>
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<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 3</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and Hem B with or without inhibitor, who completed Phase 3 studies</td>
<td>Long-term Safety and Efficacy Study of Fitusiran in Patients With Hemophilia A or B, With or Without Inhibitory Antibodies to Factor VIII or IX (ATLAS-OLE)</td>
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<tr>
<td>Investigational Therapeutic Product Name</td>
<td>Sponsor</td>
<td>Type</td>
<td>Specific Product Type</td>
<td>Phase</td>
<td>Indications</td>
<td>Indication Details</td>
<td>Official Title of Study</td>
<td>Notes</td>
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<tr>
<td>giroctocogene fitelparvovec, fidancagene elaparvovec</td>
<td>Pfizer, Inc.</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 3 - NCT0358716</td>
<td>Factor VIII; Factor IX</td>
<td>Severe hemophilia A adult subjects (FVIII:C &lt;1%) who are negative for nAb to AAV vector SB-525 capsid (AAV6) and moderately severe to severe hemophilia B (FIX:C &lt;2%) who are negative for nAb to AAV vector Spark-100, prior to the respective therapeutic phase 3 gene therapy studies</td>
<td>Six Month lead-in Study to Evaluate Prospective Efficacy and Safety Data of Current FIX Prophylaxis Replacement Therapy in Adult Hemophilia B Subjects (FIX:C&lt;2%) or Current FVIII Prophylaxis Replacement Therapy in Adult Hemophilia A Subjects (FIX:C&lt;1%)</td>
<td>6-month lead-in study (phase 3)</td>
</tr>
<tr>
<td>masrtacimab</td>
<td>Pfizer, Inc.</td>
<td>Novel: Non-factor product</td>
<td>Antibody to Tissue Factor Pathway Inhibitor</td>
<td>Phase 3 - FDA Orphan Drug Status (HA), 2016 <a href="http://www.clinicaltrials.gov">www.clinicaltrials.gov</a>; NCT03938792</td>
<td>Factor VIII; Factor IX; inhibitor</td>
<td>Severe hemophilia A or B (Factor VIII or Factor IX activity &lt; 1%) Subjects enrolled as Factor VIII or Factor IX inhibitor patients must have a positive inhibitor test result (above the upper limit of normal) at the local laboratory and must receive a bypass agent as primary treatment for bleeding episodes</td>
<td>An Open-Label Study in Adolescent and Adult Severe (Coagulation Factor &lt;1%) Hemophilia A or B Patients with or without inhibitors Comparing Standard Treatment to PF-06741086 Prophylaxis</td>
<td></td>
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<tr>
<td>Marzeptacog alfa (activated)</td>
<td>Catalyst Biosciences</td>
<td>Recombinant clotting factor</td>
<td>Recombinant FVIIa variant</td>
<td>Phase 2/3</td>
<td>Factor IX</td>
<td>VIII or IV with inhibitors</td>
<td>Open Label Phase 2/3 Study of Coagulation Factor VIIa Variant Marzeptacog Alfa (Activated) in Adult Subjects With Hemophilia A or B with inhibitors.</td>
<td></td>
</tr>
<tr>
<td>MOD-5014</td>
<td>OPKO Biologics</td>
<td>Novel: Investigational factor product</td>
<td>Long-acting Recombinant Vila</td>
<td>Phase 1</td>
<td>Factor IX</td>
<td>VIII, IX with inhibitors</td>
<td>A Phase 1, Randomized, Single-blind, Placebo-controlled, Single Dose, Dose-escalated Study to Assess the Safety, Pharmacokinetic and Pharmacodynamic Profile of Subcutaneous Administration of a Long-acting Recombinant Factor Vila in Healthy Adult Males</td>
<td></td>
</tr>
<tr>
<td>scAAV2/8-LPi-hFixXco</td>
<td>St. Jude Children's Research Hospital</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 1</td>
<td>Factor IX</td>
<td>IX</td>
<td>An Open Label Dose-Escalation Study Of A Self Complementary Adeno-Associated Viral Vector (scAAV 2/8-LPi-hFixXco) For Gene Transfer in Hemophilia B</td>
<td></td>
</tr>
<tr>
<td>TAK-748</td>
<td>Takeda</td>
<td>Gene Therapy</td>
<td>Gene Transfer</td>
<td>Phase 1/2 - Suspended (Reevaluation of development strategy)</td>
<td>Factor IX</td>
<td>Hemophilia B</td>
<td>A Phase 1/2 Study of SHP648, an Adeno-Associated Viral Vector for Gene Transfer in Hemophilia B Subjects</td>
<td></td>
</tr>
<tr>
<td>Investigational Therapeutic Product Name</td>
<td>Sponsor</td>
<td>Type</td>
<td>Specific Product Type</td>
<td>Phase</td>
<td>Indications</td>
<td>Indication Details</td>
<td>Official Study Title</td>
<td>Notes</td>
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<tr>
<td>Coagulation FVIIa (Recombinant) Eptacog Beta or LR769</td>
<td>HEMA Biologics</td>
<td>Recombinant clotting factor</td>
<td>Coagulation VIIa, Recombinant, non-biosimilar</td>
<td>Phase 3b - Finalizing CSR</td>
<td>Inhibitor</td>
<td>Treatment of bleeding, Congenital VIII or IX with inhibitors: birth to &lt;12 years</td>
<td>PERSEPT 2 --NCT02348680 A Phase III Study on the Safety, Pharmacokinetics, and Efficacy of Coagulation Factor VIIa (Recombinant) in Congenital Hemophilia A or B Pediatric Patients from birth to &lt;12 years old with inhibitors to Factor VIII or IX</td>
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<tr>
<td>Coagulation FVIIa (Recombinant) Eptacog Beta or LR769</td>
<td>HEMA Biologics</td>
<td>Recombinant clotting factor</td>
<td>Coagulation VIIa, Recombinant, non-biosimilar</td>
<td>Phase 3 - Finalizing CSR</td>
<td>Inhibitor</td>
<td>Prevention of excessive bleeding, Congenital VIII or IX with inhibitors: elective surgery or other invasive procedures</td>
<td>PERSEPT 3 --NCT023548143 A Phase 3 Study of the Safety and Efficacy of Coagulation Factor VIIa (Recombinant) for the Prevention of Excessive Bleeding in Congenital Hemophilia A or B Patients With Inhibitors to Factor VIII or IX undergoing Elective Surgery</td>
<td></td>
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<tr>
<td>Coagulation FVIIa (Recombinant) Eptacog Beta or LR769</td>
<td>HEMA Biologics</td>
<td>Recombinant clotting factor</td>
<td>Coagulation VIIa, Recombinant, non-biosimilar</td>
<td>Phase 1b - Open access published link: <a href="https://onlinelibrary.wiley.com/doi/pdf/10.1111/hae.13357">https://onlinelibrary.wiley.com/doi/pdf/10.1111/hae.13357</a></td>
<td>Inhibitor</td>
<td>Dose Ranging Study for VIII or IX with inhibitors: ≥12 years</td>
<td>Dose-Ranging Study (N=15) Phase Ib Study Design Dose escalation, pharmacokinetics, safety and in vivo pharmacodynamics Ducore, et al. 2017 NCT01708564</td>
<td></td>
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<tr>
<td>Dalcinacog alfa (CB 2673d/ ISU304)</td>
<td>Catalyst Biosciences</td>
<td>Recombinant clotting factor</td>
<td>Recombinant IX</td>
<td>Phase 1/2</td>
<td>Inhibitor</td>
<td>IX</td>
<td>A Phase 1, Open-label, Multi-center, Dose-escalation Study to Investigate the Safety, Pharmacokinetics and Pharmacodynamics of ISU304 in Previously Treated Hemophilia B Patients</td>
<td></td>
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<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 3</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with or without inhibitor, who were previously under factor or BPA prophylactic treatment</td>
<td>A Study of Fitusiran in Severe Hemophilia A and B Patients Previously Receiving Factor or Bypassing Agent Prophylaxis (ATLAS-PPX)</td>
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<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 1</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with or without inhibitor</td>
<td>A Phase 1 Single-ascending and Multiple-ascending Dose, Safety, Tolerability and Pharmacokinetics Study of Subcutaneously Administered ALN-AT3SC in Healthy Adult Volunteers and Hemophilia A or B Patients (Moderate or Severe Hemophilia)</td>
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<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 1 Phase 2</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with or without inhibitor, who completed Phase 1 study</td>
<td>An Open-label Extension Study of an Investigational Drug, Fitusiran, in Patients With Moderate or Severe Hemophilia A or B</td>
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<tr>
<td>Fitusiran/SAR439774</td>
<td>Sanofi Genzyme</td>
<td>Novel: Non-factor product</td>
<td>RNAi</td>
<td>Phase 3</td>
<td>Factor VIII; Factor IX; Inhibitor</td>
<td>Hemophilia A and hemophilia B with inhibitor, who were previously under BPA on demand treatment</td>
<td>ATLAS-INH: A Phase 3 Study to Evaluate the Efficacy and Safety of Fitusiran in Patients with Hemophilia A or B, with Inhibitory Antibodies to Factor VIII or IX</td>
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<tr>
<td>Investigational Therapeutic Product Name</td>
<td>Sponsor</td>
<td>Type</td>
<td>Specific Product Type</td>
<td>Phase</td>
<td>Indications</td>
<td>Indication Details</td>
<td>Official Study Title</td>
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<tr>
<td>MOD-5014</td>
<td>OPKO Biologics</td>
<td>Novel: Investigational factor product</td>
<td>Long-acting Recombinant Vila</td>
<td>Phase 1, Phase 2</td>
<td>Rare</td>
<td>Moderate to Severe VIII or IX with or without inhibitors</td>
<td>A Phase I/2a, Open-Label, Multi-center, Dose Escalation Study to Assess the Safety, Pharmacokinetics (PK) and Pharmacodynamics (PD) Profile of a Long Acting Recombinant FVila (MOD-5014) in Adult Men With Hemophilia A or B</td>
<td></td>
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<tr>
<td>TAK-755</td>
<td>Takeda</td>
<td>Novel: Investigational factor product</td>
<td>Recombinant ADAMTS13</td>
<td>Phase 3 - Recruiting</td>
<td>Rare</td>
<td>Congenital/hereditary TTP</td>
<td>A Study of Prophylactic and On-demand Treatment of Congenital Thrombotic Thrombocytopenic Purpura (cTTP) With BAX 930 (rADAMTS13)</td>
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</table>

No clinical trials of investigational therapeutic products for treatment of vWD were reported.

No clinical trials of investigational therapeutic products for treatment of other bleeding disorders were reported.
We’re counting down the days for HFA hugs to resume

Until then, we’re here for you and your family at www.hemophiliafed.org

Connected to what matters.

Our admiration for the hemophilia community knows no bounds. It pushes us to discover, advocate, and support you in ways big and small. So more moments like this are possible.

Let’s connect.

rareblooddisorders.com
@HemophiliaCoRes
1-855-SQZHEME

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MAT-US-20190001-06-09-2020
Connected to you.

As Community Relations & Education Managers, our work with the hemophilia community is deeply personal. It unites us in our efforts to help educate and support you and your family.

Reach out to your local CoRe to learn more. rareblooddisorders.com
†@HemophiliaCoRes | 1-855-SGZHEME