Optum Rx Drug Pipeline Insights Report™

Spring 2024

Optum Rx®

Fidanacogene elaparvovec (Brand name to be determined)

[Back to Contents]

Expected FDA decision: 2Q 2024

Fidanacogene elaparvovec will treat adults with moderately-severe to severe hemophilia B.

Key points

Why this drug matters: It could reduce and, in some cases, eliminate the need for chronic and as-needed clotting factor replacement therapy.

Estimated cost: Pricing not yet determined, but a competitor costs $3.5 million per treatment.

Trial notes: Significantly reduced the need for clotting factor replacement therapy, but the durability of response and long-term safety are unknown.

Route of administration: One-time intravenous infusion.

Manufacturer: Pfizer

Condition

Hemophilia B is an inherited bleeding disorder in which blood does not clot properly. It affects just under 5,000 people (primarily males) in the U.S. This genetic mutation causes low levels of **factor IX (FIX), a key component in the clotting process, causing bleeding episodes.**

Hemophilia B is classified as mild, moderate or severe based upon the activity level of FIX. In mild cases, bleeding symptoms may occur after surgery, injury or dental procedure. In some moderate, and most severe cases, bleeding may occur unexpectedly or after a minor injury. Roughly half of patients affected by hemophilia B have a severe form of the disease.

The standard of care for patients with hemophilia B is to receive routine (or **prophylactic**) infusions of FIX replacement therapy to prevent and control bleeding. The total lifetime cost per patient for FIX prophylaxis is estimated between $21 million and $23 million for those with severe and moderately severe hemophilia B.[1]

Clinical profile

Fidanacogene elaparvovec is a gene therapy that provides a naturally occurring version of the FIX coagulation gene. This healthy variant produces 8–12 times more clotting activity, and is sent directly to the liver intravenously to allow patients to produce their own FIX.[2]

Trials

Fidanacogene elaparvovec was evaluated in a Phase 3 study of adult male patients with moderately-severe to severe hemophilia B. The goal was to compare the annualized bleeding rate before and after fidanacogene elaparvovec.

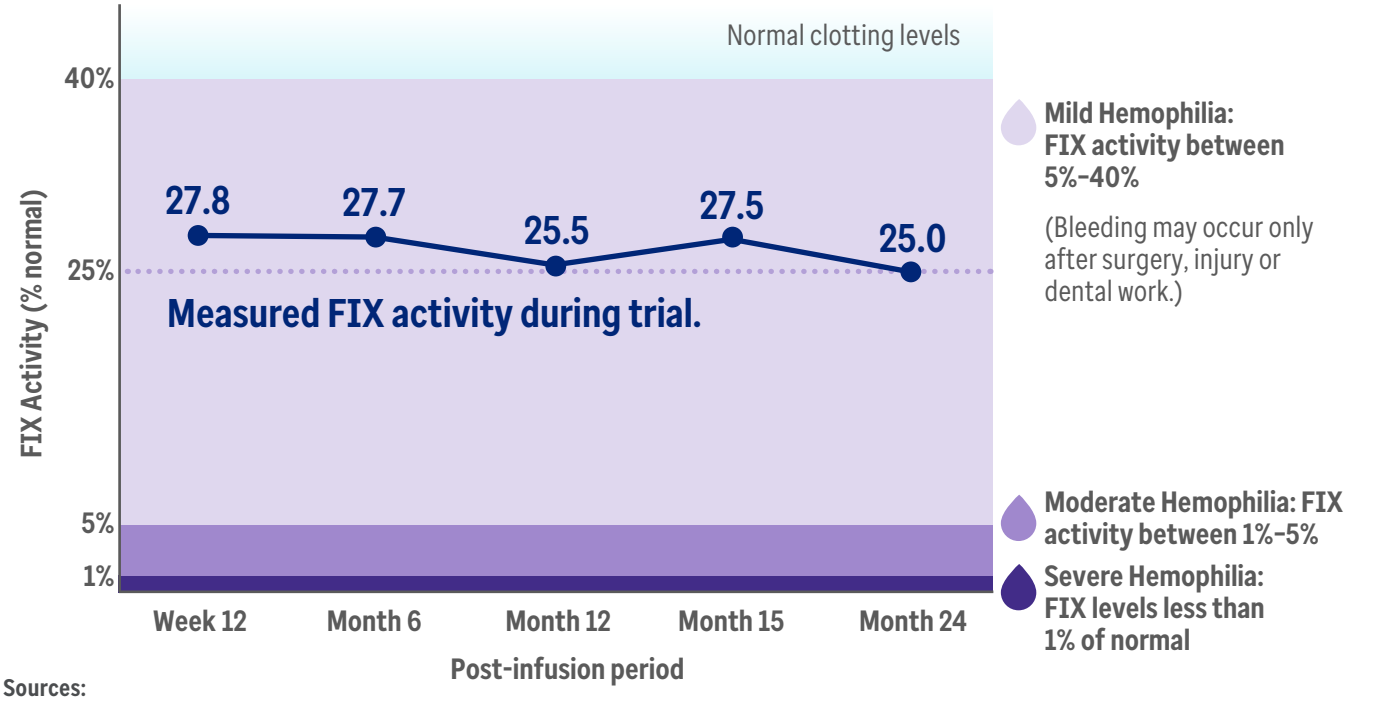
Participants were monitored during six months of routine FIX prophylaxis therapy, then stopped their prophylaxis therapy. They then received one dose of fidanacogene elaparvovec.

In the 12 months following treatment with fidanacogene elaparvovec, patients experienced a 71% reduction in annualized bleeding rate vs. the pre-treatment period.

Fidanacogene elaparvovec *(continued...)*

[Back to Contents]

In the graph below, participants saw FIX activity rise from the moderate or severe levels (<5% FIX) to the mild category, at a range which does not typically feature spontaneous bleeding. This graph depicts the increased FIX activity up to 24 months after infusion of fidanacogene elaparvovec:



Sources:

1. Highlights From the 31st Congress of ISTH. Efficacy and Safety of Fidanacogene Elaparvovec in Adults With Moderately Severe or Severe Hemophilia B: Results From the Phase 3 BENEGENE-2 Gene Therapy Trial. Accessed February 6, 2024.
2. NORD – National Organization for Rare Disorders. Hemophilia B. Last updated: September 20, 2023.

You can access an in-depth discussion of safety and trial data here (p. 1).

Competitive environment

In November 2022, the FDA approved Hemgenix® (etranacogene dezaparvovec), the first gene therapy for hemophilia B. While the efficacy of fidanacogene elaparvovec appears similar to Hemgenix, cross-trial comparisons are difficult.

The biggest questions for fidanacogene elaparvovec (and Hemgenix) are whether their effects are durable, and if they are safe long term. Sustained efficacy is particularly important with gene therapies because of the high cost per dose.

Both fidanacogene elaparvovec and Hemgenix significantly reduced the need for FIX replacement therapy in trials, which can be burdensome and very costly for severe patients. But neither drug fully eliminated the risk of bleeding events, and their ability to increase FIX activity may fade over time.

Trial participants will continue to be monitored until 2029 to evaluate efficacy and safety, and for a total of 15 years to assess long-term safety.[3]

For reference, the Wholesale Acquisition Cost (WAC) for Hemgenix is $3.5 million for a one-time dose.

mRNA-1345 (Brand name to be determined)

[Back to Contents]

Expected FDA decision: April 2024

mRNA-1345 prevents respiratory syncytial virus (RSV)-associated disease in adults aged 60 years or older.

Condition

RSV is a common respiratory virus that usually causes mild, short-term, cold-like symptoms. However, some patients may develop severe RSV infection, which may result in hospitalization. Each year, it is estimated that between 60,000 to 120,000 older adults in the U.S. are hospitalized, and 6,000 to 10,000 die due to RSV infection.

Infants, young children and elderly adults are most at risk for severe RSV infection.

Clinical profile

The mRNA vaccine transmits genetic material with instructions to make copies of a specific spike protein found on the surface of RSV. The immune system reacts by producing antibodies that target this specific protein. If a real RSV virus invades, the body will recognize the RSV spike protein and attack the virus, killing it before it can cause a serious infection.[4]

Key points

Why this drug matters: RSV infection is a significant driver of sickness and death in at-risk patients, particularly the elderly. mRNA-1345 will be the third treatment to join this class since mid-2023, but offers a different approach than existing RSV vaccines.

Estimated cost: Pricing not yet determined, but existing RSV vaccines cost $280 and $295 for a single dose.

Trial notes: Efficacy for mRNA-1345 may be similar to existing RSV vaccines during one RSV season; however, longer-term data is lacking for the Moderna vaccine.

Route of administration: Intramuscular injection.

Manufacturer: Moderna

Trials

The efficacy of mRNA-1345 was evaluated in a Phase 3 study of 35,541 adults aged 60 years or older. Patients received one dose of mRNA-1345 or placebo.

At 112 days, the mRNA-1345 vaccine was 83.7% effective in preventing RSV-associated lower respiratory tract disease with at least two signs or symptoms. It was similarly effective (82.4%) against lower respiratory tract disease with at least three signs or symptoms.[5]

Vaccine efficacy was 68.4% against a different cluster of symptoms (RSV-associated acute respiratory disease).[6]

You can access an in-depth discussion of safety and trial data here (p. 3).

Competitive environment

In 2023, the FDA approved the first preventative vaccines for RSV infection in older adults: GSK's Arexvy® and Pfizer's Abrysvo™.

While it is difficult to compare across clinical trials, the efficacy of mRNA-1345 appears similar to Arexvy and Abrysvo during one RSV season. However, long-term data is lacking for the Moderna vaccine so the need for revaccination is not yet known.

mRNA-1345 *(continued...)*

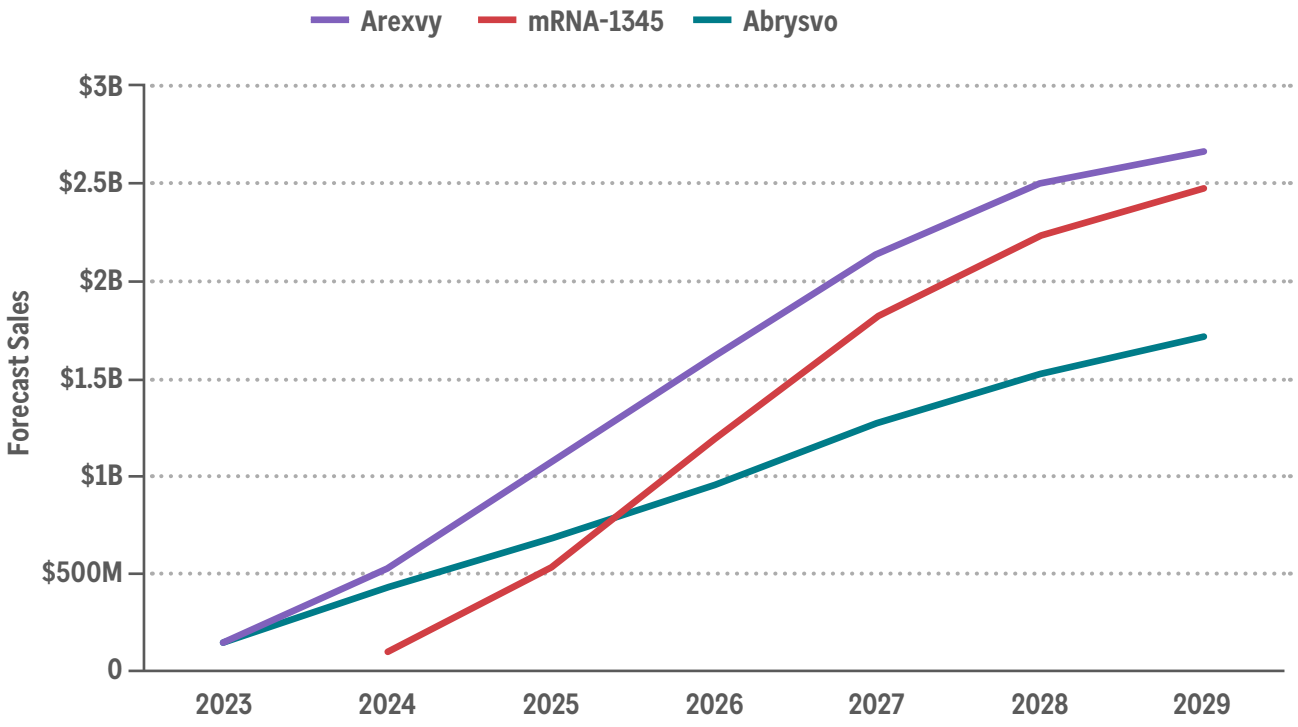
[Back to Contents]

mRNA-1345's initial use will be limited to patients 60 years and older. By comparison, Abrysvo is approved for that group, plus pregnant individuals to provide protection for newborns and young infants. Arexvy is also approved for patients 60 years and older – and could be approved for use in patients as young as 50 years by the end of 2024.

For reference, the WAC for Arexvy and Abrysvo are $280 and $295, respectively, for a one-time dose.

This graph shows estimated sales for the three competitor vaccines through 2029.

Forecast sales: RSV vaccines



Adapted from Precision Vaccinations. $9 Billion RSV Vaccine Market Share Battle Begins. Published July 24, 2023.

Ensifentrine (Brand name to be determined)

[Back to Contents]

Expected FDA decision: June 26, 2024

Ensifentrine is intended as a maintenance treatment for patients with chronic obstructive pulmonary disease (COPD).

Condition

COPD is a group of chronic lung diseases that block airflow, causing shortness of breath, as well as other breathing-related problems, including emphysema and chronic bronchitis.

In 2022, 11.7 million people were diagnosed with COPD, chronic bronchitis, or emphysema. The American Lung Association estimates that COPD was the sixth overall leading cause of death in the U.S. in 2021.[7]

COPD severity is graded by stages based on several factors, including a test called **forced expiratory volume (FEV-1),** the amount of air a person can force out of their lungs in one second. A mild case of COPD might show 80% FEV-1 compared to normal, while a very severe case might be less than 30% of normal.[8]

Key points

Why this drug matters: It will provide a novel add-on therapy to patients requiring additional treatment to manage their COPD.

Estimated cost: Pricing not yet determined, but the wholesale acquisition cost for a related treatment (Breztri Aerosphere®) is approximately $7,600 per year.

Trial notes: Demonstrated significant improvements in lung function. However, studies did not include all combinations of medications, and specifically excluded patients receiving dual or triple therapies.

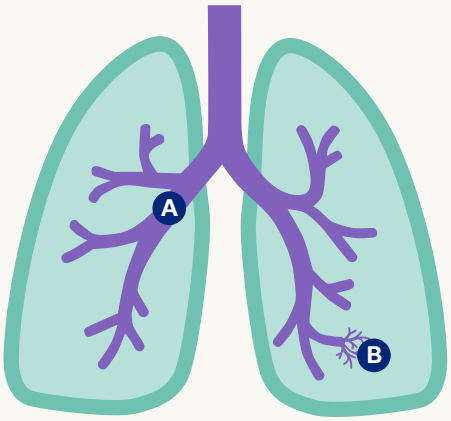
Route of administration: Inhaled solution via nebulizer.

Manufacturer: Verona Pharma

The left side of the illustration below (marked A) depicts how chronic bronchitis affects the large tubes (bronchi) that connect the trachea (windpipe) to the right and left lungs.[9]

The right (marked B), shows how emphysema damages the air sacs in the lungs (alveoli), creating large, open areas. This reduces the surface area of the lungs and limits the amount of oxygen that reaches the blood.[10]

Chronic Obstructive Pulmonary Disease (COPD)



A. Chronic Bronchitis

At left (A), chronic bronchitis affects the large tubes (bronchi) that connect the trachea (windpipe) to the right and left lungs. The bronchi become blocked with mucus and other debris.[9]

B. Emphysema

At (B), emphysema damages the air sacs in the lungs (shown as small branches). This reduces the surface area of the lungs and limits the amount of oxygen that reaches the blood.[10]

Ensifentrine *(continued...)*

[Back to Contents]

Clinical profile

Ensifentrine is an inhaled medication that targets two lung enzymes – one that affects the heart and circulatory system, and one that affects the lungs, especially the bronchial tubes.[11] Ensifentrine acts as an inhibitor to block those enzymes to ease inflammation, widen airways, and remove mucus and trapped particles from the airways.[12]

Trials

Ensifentrine was evaluated in trials that enrolled more than 1,500 adults with moderate to severe COPD. Participants were randomized to receive either ensifentrine or placebo twice daily for 24 weeks. Some patients continued to use a currently approved bronchodilator, while others did not.[13]

Ensifentrine users experienced significant improvements in lung function compared to placebo after 12 weeks in each trial, meeting the primary endpoint.[14]

This image shows the change from baseline at Week 12 in the average forced expiratory volume test. As noted, the values show the increase over expected levels of exhaled air:

Average increase of breath volume in 1 second (FEV1) with ensifentrine vs placebo at week 12:

ENHANCE 1	ENHANCE 2
+87 mL	+94 mL

Source: American Journal of Respiratory and Critical Care Medicine. Ensifentrine, a Novel Phosphodiesterase 3 and 4 Inhibitor for the Treatment of Chronic Obstructive Pulmonary Disease: Randomized, Double-Blind, Placebo-controlled, Multicenter Phase III Trials (the ENHANCE Trials). Published August 15, 2023.

You can access an in-depth discussion of safety and trial data here (p. 9).

Competitive environment

The current standard of care for treatment of COPD includes inhaled short- and long-acting bronchodilators and corticosteroids. These are taken via inhaler or nebulizer. When symptoms persist, there are limited treatment options available, creating an unmet need. It's estimated that up to 50% of COPD patients continue to have symptoms despite their current treatment.

Ensifentrine would provide a novel add-on therapy to patients who require additional treatment to manage their COPD.

Ensifentrine is expected to be the first of several novel treatments for COPD over the next two to three years. Most notably, Sanofi/Regeneron's Dupixent® (dupilumab), which is currently approved for allergic diseases such as eczema, asthma and nasal polyps, could be approved for COPD in mid-2024. Dupixent would compete with ensifentrine as an add-on treatment for severe COPD.

Ensifentrine was not studied in all possible combinations of medications that could be used to treat COPD. For instance, the trials specifically excluded patients who were on two long-acting bronchodilators.

The use of ensifentrine could be limited initially since it will only be available via nebulizer. Verona is developing a dry powder inhaler and metered-dose inhaler, which would be more convenient than using a nebulizer, but it is unknown when those formulations could be on the market.

Ensifentrine is also being evaluated for several other diseases, including cystic fibrosis, non-cystic fibrosis bronchiectasis and asthma.

For reference, the WAC for Breztri Aerosphere is approximately $7,600 per year. In contrast, Dupixent is over $40,000 per year. [15]

References

Unless otherwise specified, all citation taken from RxOutlook®1st Quarter 2024.

1. Journal of Medical Economics. Adult lifetime cost of hemophilia B management in the US: payer and societal perspectives from a decision analytic model. Published March 2, 2021. Accessed March 6, 2024.
2. Hemophilia News Today. Fidanacogene elaparvovec for hemophilia. Last updated Jan. 8, 2024. Accessed March 14, 2024.
3. ibid.
4. Yale Medicine. Comparing the COVID-19 Vaccines: How Are They Different? Published October 5, 2023. Accessed February 15, 2024.
5. New England Journal of Medicine. Efficacy and Safety of an mRNA-Based RSV PreF Vaccine in Older Adults. Published December 14, 2023. Accessed February 22, 2024.
6. ibid.
7. American Lung Association. COPD Trends Brief: Mortality; COPD Trends Brief: Prevalence. Accessed February 15, 2024.
8. Healthline. FEV1 and COPD: How to Interpret Your Results. Updated March 3, 2023. Accessed February 15, 2024.
9. John Hopkins Medicine. Chronic Bronchitis. Accessed March 7, 2024.
10. Mayo Clinic. Emphysema. Accessed March 7, 2024.
11. Cleveland Clinic. Phosphodiesterase Inhibitors. Last reviewed June 8, 2022. Accessed March 7, 2024.
12. COPD News today. Benefits of ensifentrine for COPD seen among subgroups of patients. Published October 23, 2023. Accessed February 15, 2024.
13. ibid.
14. ibid.
15. Optum Rx drug pipeline insights report. Published Summer 2023. Accessed March 8, 2024.

Optum

optum.com/optumrx