Optum Rx drug pipeline insights report

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Optum Rx®

Drugs to Watch: Fall 2022

From Sumit Dutta, Chief Medical Officer at Optum Rx

Welcome to our latest summary of important new pharmaceutical products. In this edition, we highlight three key pipeline drugs with an expected U.S. Food and Drug Administration (FDA) decision by the end of the fourth quarter of 2022.

Two of the three drugs discussed have an orphan drug designation, while the third was granted priority review designation. We are seeing an increase of new orphan drugs and expect this trend to continue, if not accelerate. This is important since orphan drugs are priced more than 30 times higher than non-orphan drugs. Almost 40% of new orphan drugs coming to market cost more than $100,000 per year, while cell and gene therapies can cost much more.[1]

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Drug overview

Sparsentan is an orphan drug being reviewed to treat immunoglobulin A (IgA) nephropathy, a kidney disease also known as Berger's disease.

Etranacogene dezaparvovec is a new gene therapy with orphan status for hemophilia B. It will be the first gene therapy approved for hemophilia B administered as a one-time infusion directly into the bloodstream.

Pegcetacoplan will treat geographic atrophy, a late-stage form of an eye condition known as age-related macular degeneration. Recently accepted for FDA review, a decision is expected before the end of November.[2]

Please refer here for additional technical background and supplemental sources.

Sparsentan: Brand name to be determined.
Expected FDA decision: November 17, 2022

Sparsentan is under review for the treatment of immunoglobulin A (IgA) nephropathy (also known as Berger's disease).

IgA is an immune system antibody that attacks pathogens and fights infections. In IgA nephropathy, this antibody collects in the kidneys, causing inflammation and gradual damage to kidney tissues.[3]

Kidney function decline in IgA nephropathy is associated with an excess of endothelin A and angiotensin II. Both are vasoconstrictors that cause a narrowing of blood vessels and an increase in pressure in the kidney.

Over time, IgA nephropathy can lead to end-stage kidney disease (ESKD) and the need for dialysis. IgA nephropathy is one of the most common kidney diseases, affecting more than 100,000 people in the U.S. Travere Therapeutics estimates approximately 30,000 to 50,000 cases are addressable with sparsentan at launch.

Clinical profile

Sparsentan combines two blocking mechanisms in one molecule that reduce the activity of endothelin type A and angiotensin II.[4]. This helps reduce inflammation and blood pressure in the kidneys.

Trial data

Sparsentan is being evaluated in the ongoing PROTECT study, a randomized, double-blind, active-control trial in adults with IgA nephropathy. Patients were randomized to receive sparsentan or irbesartan, an angiotensin II receptor blocker (ARB) used to treat IgA nephropathy.

The primary efficacy endpoint is change in proteinuria (high level of protein in the urine), which is associated with the kidney damage from IgA nephropathy. At week 36, patients receiving sparsentan achieved a mean reduction in proteinuria of 49.8% compared to 15.1% for irbesartan-treated patients.

A secondary endpoint is rate of change in estimated glomerular filtration rate measuring the level of kidney function to determine the kidney disease stage. This study is ongoing and topline results from this endpoint analysis are expected in the second half of 2023.

You can access an in-depth discussion of safety and trial data here (p. 5).

Competitive environment

There is an unmet need for effective IgA nephropathy treatments. Sparsentan would potentially be the first non-steroidal drug approved for treatment of IgA nephropathy.

Unlike many other orphan conditions, there are established alternative treatments for IgA nephropathy. In the pivotal trial, sparsentan demonstrated promising improvements in proteinuria vs. a standard of care treatment option. The current standard of care includes:

- Off-label use of angiotensin-converting enzyme (ACE) inhibitors like lisinopril, and ARBs like irbesartan. These can help prevent progression of the disease by reducing proteinuria and lowering blood pressure.
- Corticosteroids are also used to reduce inflammation, but they work by weakening the immune system, which may lower someone's ability to fight infections.[5]

The PROTECT study included patients with persistent proteinuria and active ACE inhibitor or ARB treatment. In practice, sparsentan could be reserved as a second-line therapy after inadequate response to these drugs. There is also limited drug safety information and no current efficacy data showing improvements in kidney function.

Finally, sparsentan is also in development for focal segmental glomerulosclerosis, another rare kidney disease with a high unmet need.

The wholesale acquisition cost for Tarpeyo® (budesonide), a corticosteroid approved for IgA nephropathy, is approximately $172,000 per year.

Etranacogene dezaparvovec: Brand name to be determined. Expected FDA decision: November 24, 2022.

Etranacogene dezaparvovec is a new gene therapy to treat adult patients with moderately-severe-to-severe hemophilia B.

Hemophilia is an inherited bleeding disorder primarily affecting males, in which the blood does not clot properly. There are two major types of hemophilia: A and B. People with hemophilia B have low levels of the clotting factor IX (FIX). Current treatment includes replacement therapy to supply missing clotting factor from an external source.

FIX replacement therapy has a high treatment burden and is extremely costly. A 2021 study analyzed patients with severe and moderately-severe hemophilia B. Lifetime FIX replacement costs ranged $21 to $23 million dollars, depending on the type of treatment.[6]

30,000 to 33,000 males with hemophilia A and B live in the U.S.[7] Hemophilia B is less prevalent than hemophilia A, affecting approximately 6,000 males.[8]

Clinical profile

Hemophilia B is caused by mutations in the FIX gene, which governs production of clotting FIX. Etranacogene dezaparvovec uses a modified adeno-associated virus 5 (AAV5) to deliver a highly functional version of the FIX gene to liver cells, where the enhanced FIX genes will reproduce.

Trial data

Efficacy of etranacogene dezaparvovec was evaluated in an open-label, single-arm study in 54 patients with severe or moderately-severe adult hemophilia B requiring FIX replacement.

After establishing a baseline annualized bleeding rate, patients received a single administration of etranacogene dezaparvovec. The primary endpoint was annualized bleeding rate from month 7 to month 18 after infusion.

Adjusted annualized bleeding rate for all bleeds was reduced 64% and the rate for all FIX-treated bleeds was reduced 77% over months 7 to 18. 98% of patients treated with a full dose of etranacogene dezaparvovec discontinued use of prophylactic FIX replacement.

You can access an in-depth discussion of safety and trial data here (p. 7).

Competitive environment

The current standard of care for patients with severe hemophilia B is chronic FIX prophylactic treatment. As noted, lifetime costs for this treatment are extremely high. If approved, etranacogene dezaparvovec would be the first one-time gene therapy for hemophilia B and reduce, and in some cases eliminate, the need for chronic and as-needed FIX replacement therapy.

Sustained efficacy is especially important with gene therapies because of the high projected cost for a one-time dose. In trials, etranacogene dezaparvovec significantly reduced the need for FIX replacement therapy, but the durability of response is unknown.

Of the estimated 6000 hemophilia B cases in the U.S., the manufacturer is targeting moderate-to-severe hemophilia B patients, representing approximately 60% of all patients. This narrows the total addressable market substantially.[9]

Other hemophilia B gene therapies in development could be available in 2024 to 2025. Some eligible patients could wait until data is available for these competitors and not to be early adopters for etranacogene dezaparvovec.

No price has been announced, but currently approved gene therapies have been expensive. For reference, the wholesale acquisition cost for Zolgensma® (onasemnogene abeparvovec-xioi), a gene therapy for spinal muscular atrophy, is approximately $2.1 million for a one-time dose. Similarly, Zynteglo (betibeglogene autotemcel), a gene therapy for beta-thalassemia, has a $2.8 million wholesale acquisition cost.

Pegcetacoplan: Brand name to be determined. Expected FDA decision: November 26, 2022.

Pegcetacoplan is under review for the treatment of geographic atrophy (GA), an eye disease that causes vision loss in the center of the field of vision.[10]

Geographic atrophy is an aggressive form of dry (as opposed to wet) age-related macular degeneration (AMD).[11] Geographic atrophy is a leading cause of blindness that affects more than 1 million people in the U.S.[12]

Persons most at-risk for AMD include those who are age 55 and older. In addition, people who have a family history of AMD, are Caucasian or who smoke are also at-risk.[13]

There are no FDA-approved treatments for geographic atrophy.[14]

Clinical profile

Pegcetacoplan is designed to regulate the complement cascade, part of the body's immune system. Excessive activation of the complement cascade results in destruction of healthy cells in the eye, which can lead to several retinal diseases, including geographic atrophy. Pegcetacoplan may slow the growth of geographic atrophy lesions by regulating the complement cascade.[15]

Pegcetacoplan is administered via intravitreal injection, which places a medication directly into the space in the back of the eye called the vitreous cavity.[16]

Trial data

Pegcetacoplan was evaluated in 1,258 patients in two Phase 3 studies: OAKS and DERBY. Each tested monthly or every-other-month eye injections of pegcetacoplan.[17]

- At month 18, both studies showed that pegcetacoplan reduced GA lesion growth with monthly and every-other-month treatment compared to baseline.
- OAKS: Monthly (22%; $p<0.0001$); every-other-month (16%; $p=0.0018$).
- DERBY: Monthly (13%; $p=0.0254$); every-other-month treatment (12%; $p=0.0332$).

Full trial results have not been published, but readers can view the top line results here.

Competitive environment

There is no FDA-approved treatment for geographic atrophy and existing treatments for wet AMD have not been effective for geographic atrophy. Over the next few years, this is likely to change significantly. In addition to pegcetacoplan (Apellis Pharmaceuticals), at least 10 harmaceutical makers have products for geographic atrophy in development.[18]

Some analysts believe that avacincaptad pegol from Iveric bio is the closest competitor to pegcetacoplanin terms of performance and time to market. While it is difficult to compare trial results, the reductions in geographic atrophy lesion growth for avacincaptad pegol appear favorable compared to pegcetacoplan.[19]

Iveric bio expects topline data for a second Phase 3 clinical trial to be available in the third quarter of 2022.[20]

By 2032, pegcetacoplan is anticipated to generate more than $900 million in revenue in the U.S., while avacincaptad pegol could generate more than $1 billion.[20]

References

All references, unless otherwise indicated: Optum Rx. Rx Outlook. 3rd Quarter, 2022. Published August 22, 2022. Accessed August 22, 2022.

1. Institute for Clinical and Economic Review. The Next Generation of Rare Disease Drug Policy: Ensuring Both Innovation and Affordability. Published April 7, 2022. Accessed August 22, 2022.

2. Apellis Pharmaceuticals, Inc. Apellis Announces FDA Acceptance and Priority Review of the New Drug Application for Pegcetacoplan for the Treatment of Geographic Atrophy (GA). Posted July 19, 2022. Accessed August 20, 2022.

3. Mayo Clinic. IgA nephropathy (Berger's disease). Published July 21, 2021.

4. BioSpace. Travere Therapeutics Announces Orphan Drug Designation for Sparsentan for the Treatment of IgA Nephropathy. Published: Jan 12, 2021. Accessed August 24, 2022.

5. WebMD. Tarpeyo 4 Mg Capsule, Delayed Release Glucocorticosteroids - Uses, Side Effects, and More. Accessed August 25, 2022.

6. Journal of Medical Economics. Adult lifetime cost of hemophilia B management in the US: payer and societal perspectives from a decision analytic model. Published online March 2, 2021. Accessed August 23, 2022.

7. Centers for Disease Control and Prevention (CDC). A New Study of Hemophilia Occurrence Finds Many More Cases in the United States. Page last reviewed: July 17, 2020. Accessed August 22, 2022.

8. National Institutes of Health. StatPearls. Hemophilia. Last Update: June 11, 2022. Accessed August 22, 2022.

9. Seeking Alpha. uniQure: Betting on Hemophilia-B Cure. Published January 18, 2022. Accessed August 23, 2022.

10. Apellis Pharmaceuticals, Inc. Apellis Announces FDA Acceptance and Priority Review of the New Drug Application for Pegcetacoplan for the Treatment of Geographic Atrophy (GA). Posted July 19, 2022. Accessed August 20, 2022.

11. Delve Insight. Dry AMD Market: Pegcetacoplan or Zimura, Which Therapy Will Dominate the Market? Published May 27, 2022. Accessed August 26, 2022.

12. Apellis Pharmaceuticals, Inc. Apellis Announces FDA Acceptance and Priority Review of the New Drug Application for Pegcetacoplan for the Treatment of Geographic Atrophy (GA). Posted July 19, 2022. Accessed August 20, 2022.

13. National Eye Institute. Age-Related Macular Degeneration (AMD). Last updated June 22, 2021.

14. Apellis Pharmaceuticals, Inc. Apellis Announces FDA Acceptance and Priority Review of the New Drug Application for Pegcetacoplan for the Treatment of Geographic Atrophy (GA). Posted July 19, 2022. Accessed August 20, 2022.

15. Apellis Pharmaceuticals, Inc. Understanding Geographic Atrophy. Accessed August 26, 2022.

16. American Society of Retina Specialists. Intravitreal Injections. Accessed August 22, 2022.

17. Apellis Pharmaceuticals, Inc. Apellis Announces Pegcetacoplan Showed Continuous and Clinically Meaningful Effects at Month 18 in Phase 3 DERBY and OAKS Studies for Geographic Atrophy (GA). Published March 16, 2022. Accessed August 22, 2022.

18. Delve Insight. Dry AMD Market: Pegcetacoplan or Zimura, Which Therapy Will Dominate the Market? Published May 27, 2022. Accessed August 26, 2022.

19. IVERIC bio, Inc. Iveric Bio Announces Presentation of Post-Hoc Analysis at Macula Society from GATHER1 Clinical Trial of Zimura® in Patients with Geographic Atrophy. Published June 10, 2022. Accessed August 26, 2022.

20. ibid.

21. Delve Insight. Dry AMD Market: Pegcetacoplan or Zimura, Which Therapy Will Dominate the Market? Published May 27, 2022. Accessed August 26, 2022.

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