Optum Rx drug pipeline insights report

Summer 2022

Optum Rx®

Drugs to Watch: Summer 2022

From Sumit Dutta, Chief Medical Officer at Optum Rx

Greetings and welcome to this edition of the OptumRx Drug Insights report. We have chosen to highlight four key pipeline drugs with an expected FDA decision in the third quarter of 2022. These drugs reflect cutting edge technologies and are often used in smaller target populations.[1]

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The share of revenue that drug companies devote to research and development has nearly doubled compared to 2000. That's more than other knowledge-based industries, such as semiconductors, technology hardware, and software.[2]

The result is not only a growing number of new drugs approved by the Food and Drug Administration (FDA), but a growing number of complex specialty drugs. Many are biologic drugs based on living cells, which are costly to develop, hard to imitate, and frequently have high prices.[3]

For example, we look at two gene therapy drugs from bluebird bio. Both products target ultra-rare orphan conditions with an unmet need. Within a 24 hour span this June, an FDA advisory panel voted to recommend approval for both drugs. While the FDA is not bound by these recommendations, it usually follows the panel's recommendations.[4]

The first drug is **elivaldogene autotemcel** (brand name Skysona™). Skysona is in development to treat cerebral adrenoleukodystrophy (CALD) in young boys. The second is **betibeglogene autotemcel** (brand name Zynteglo™), to treat beta-thalassemia patients dependent on blood transfusions.

The FDA is expected to decide this fall on both gene therapies. If both receive full FDA approval, the number of gene therapies for sale in the U.S. grows from two to four.

Drug overview

Other drugs in this report include:

Teclistamab, a novel antibody for treatment of relapsed or refractory multiple myeloma.

Deucravacitinib, for treatment of adults with moderate-to-severe plaque psoriasis, which affects approximately six million people in the U.S. It is one of four novel psoriasis therapies facing approval by the end of this year.

The following drugs have either already been recently approved, ahead of expected FDA approval date, or are still considered to be on track for approval this summer:

Please refer here for additional technical background and supplemental sources.

Teclistamab: Brand name to be determined. Expected FDA decision: August 29, 2022.

Teclistamab is a novel drug to treat relapsed or refractory multiple myeloma.

Multiple myeloma is a cancer of plasma cells in the bone marrow. The American Cancer Society estimates 34,470 new cases will be diagnosed with over 12,600 deaths in the U.S. during 2022.

Teclistamab is a **bispecific** antibody that targets both B-cell maturation antigen (BCMA) and CD3, a T-cell receptor. BCMA is expressed at high levels on multiple myeloma cells. Teclistamab redirects CD3-positive T-cells to kill BCMA-expressing myeloma cells.[5]

Performance in trials

An ongoing study (MajesTEC-1) enrolled patients who had relapsed or refractory myeloma after at least three therapy lines. Patients received a weekly subcutaneous injection of teclistamab.[6]

Based on a median follow-up of 14.1 months, the overall response rate was 63% with 30.4% of patients experiencing a complete response or better.[7]

Common adverse events included cytokine release syndrome (CRS), low white blood cell count, anemia, and low platelet levels.[8] CRS can occur when your immune system responds to infection or immunotherapy drugs more aggressively than it should.[9]

You can access an in-depth discussion of safety and trial data here (p. 15).

Competitive environment

Teclistamab (administered subcutaneously) would join three similar therapies that target BCMA for relapsed or refractory multiple myeloma. They are Blenrep® (belantamab mafodotin), which is administered intravenously, and two CAR-T cell therapies approved this year: Carvykti® (ciltacabtagene autoleucel) and Abecma® (idecabtagene vicleucel).

Trial results included patients previously exposed to these three existing treatments. Indirectly, teclistamab appears more effective than Blenrep, while being less effective versus the CAR-T cell therapies. However, it appears that the CAR-T cell therapies see higher rates of CRS and neurotoxicity than teclistamab.

We lack late-stage trial data for teclistamab and robust overall survival data.

No prices have been announced for teclistamab. For reference, the Blenrep wholesale acquisition cost is approximately $17,000 per 21 days.

Deucravacitinib: Brand name to be determined. Expected FDA decision: September 10, 2022.

Deucravacitinib is a novel oral drug being evaluated to treat adults with moderate-to-severe plaque psoriasis.

Plaque psoriasis is a chronic skin disease caused by an immune system dysfunction. Plaque psoriasis affects approximately six million people in the U.S.

We have been following deucravacitinib as part of our broader emphasis on the psoriasis marketplace. (*See Industry trend to watch* in *our previous edition*.)

Clinical profile

Deucravacitinib is a novel tyrosine kinase 2 (TYK2) inhibitor. By selectively targeting TYK2, deucravacitinib helps regulate overproduction of immune inflammatory compounds in immune-mediated diseases such as psoriasis.[10]

Trial data

Trial results for deucravacitinib were released in 2021 (POETYK PSO-1 and POETYK PSO-2). Both studies evaluated patients with moderate-to-severe plaque psoriasis using two standard psoriasis outcome measures: PASI75 and the sPGA.

Psoriasis Area and Severity Index (PASI) is a standard benchmark primary endpoint in clinical trials of psoriasis. PASI75 reflects a 75% reduction in the PASI score. A score of 0 or 1 on the Static Physician Global Assessment (sPGA) is another commonly used psoriasis outcome metric.[11]

Results indicate that deucravacitinib outperformed placebo and Otezla® (apremilast) at 16 and 24 weeks on the PASI75 and sPGA scales. Otezla is an existing oral treatment for plaque psoriasis.

In May 2022, Bristol Myers Squibb released results for the POETYK PSO long-term extension (LTE) trial. It showed that clinical efficacy was maintained through up to two years of treatment.[12]

The most common adverse events with deucravacitinib use were colds and upper respiratory infection.

You can access an in-depth discussion of safety and trial data here (p. 8).

Competitive environment

While deucravacitinib would provide a first-in-class oral treatment for a condition with limited oral options, it is still entering a crowded marketplace. Injectable biologics are commonly used with high response rates in patients with moderate-to-severe plaque psoriasis. Immunosuppressants such as methotrexate and cyclosporine have historically been used, but their place in therapy is limited due to safety concerns. Otezla, an oral phosphodiesterase 4 (PDE4) inhibitor, has been available since 2014 and has a safer adverse event profile vs. historical oral treatments but its use has been limited because injectable biologics are more effective.

While it was not compared directly against injectable biologics, deucravacitinib demonstrated superior efficacy vs. Otezla and was associated with numerically lower rates of discontinuations due to adverse events.

Since deucravacitinib was not compared in head-to-head studies against injectable biologics and indirectly, response rates are generally lower, the likely place in therapy will be similar to Otezla. That is, used in patients requiring systemic therapy, but who should not take or are unwilling to be treated with injectable biologics.

The initial use for deucravacitinib will be limited to the indication of plaque psoriasis. However, deucravacitinib is in development for psoriatic arthritis, ulcerative colitis, Crohn's disease, and lupus.

Due to similarities to the Janus kinase (JAK) inhibitor class, there are some theoretical safety concerns with TYK2 inhibitors such as deucravacitinib. But no major safety signals have been reported in the deucravacitinib studies.

For reference, Otezla wholesale acquisition cost is approximately $48,000 per year.

Betibeglogene autotemcel: Brand name Zynteglo™. Expected FDA decision: August 19, 2022.

Zynteglo is the first of two drugs we are profiling from bluebird bio. It is a gene therapy for transfusion-dependent beta-thalassemia.

Beta-thalassemia is caused by genetic mutations in cells that carry oxygen throughout the body. This disorder may produce classic signs of anemia and may be life-threatening if left untreated.

Current treatment for severe beta-thalassemia is mainly regular, life-long red blood cell transfusions. Patients also need iron chelation therapy to address excess levels of iron in the body due to the repeated blood transfusions.

Stem cell transplantation from a matched donor, ideally a sibling, is currently the only possible cure. However, stem cell transplants carry their own risks, and fewer than 25% of patients have access to a suitable match.[13]

There are an estimated 3,000 patients with beta-thalassemia in the U.S. About half of them are dependent on blood transfusions.

Clinical profile

Zynteglo is manufactured outside of the body using the patient's own bone marrow stem cells. An engineered viral vector is added to the stem cells that includes functional copies of the gene that these patients lack (β-globin). The modified stem cells are then re-infused back into the patient following chemotherapy conditioning.[14]

Trial data

The efficacy of Zynteglo was established in a Phase 3 study in patients 50 years or younger with transfusion dependent beta-thalassemia (NorthStar-2).

The primary endpoint was transfusion independence at 24 months, without any red blood cell transfusions for 12 months or longer.

Overall, 91% of participants achieved transfusion independence, including 86% in patients who were younger than age 12.

The most common adverse events observed were likely a result of the conditioning chemotherapy required for marrow cell transplantation.

You can access an in-depth discussion of safety and trial data here (p. 10).

Competitive environment

The only other FDA-approved therapy for treatment transfusion dependent beta-thalassemia is Reblozyl® (luspatercept). This is a subcutaneous injection given every three weeks, but only treats the anemia resulting from the disease.

If approved, Zynteglo could cure for beta-thalassemia through a one-time intravenous infusion.

With gene therapies like Zynteglo, secondary malignancies are a concern. Although no cancers were found in the beta-thalassemia trials, the degree of risk for secondary malignancies in real-world practice is uncertain. As noted, there are known risks associated with the chemotherapy conditioning regimen.[15]

Due to the short follow-up time (two years) in the study, the durability of transfusion independence is unclear. Interim analysis of the long-term follow-up study showed that 81% achieved transfusion independence and maintained it through the last follow-up.

The target population for this treatment is extremely small. Bluebird bio estimates approximately 1,500 patients with beta-thalassemia in the U.S. would be eligible.

As a gene therapy, Zynteglo is extremely complex to prepare and administer. For reference, analysts forecast a $2.1 million cost for a one-time dose of Zynteglo.[16]

Elivaldogene autotemcel: Brand Name Skysona™. Expected FDA decision: September 16, 2022.

Skysona is the second drug we are profiling from bluebird bio. It is a gene therapy to treat cerebral adrenoleukodystrophy (CALD) in young boys.

Patients with CALD lack a protein (ALDP) needed to break down fatty acids. This causes toxic acids to build up in the brain and leads to disability and an early death.[17] Most patients with CALD will die within a decade of diagnosis if they are not treated with bone marrow (stem cell) transplantation.

There are approximately 40 patients with CALD in the U.S. per year.

Clinical profile

Skysona uses immature bone marrow cells taken from the patient. These cells are modified by a virus that contains a functional copy of the ALDP gene. When the modified cells are infused back into the patient, they spread through the body and develop into different types of healthy cells, including brain cells, that now produce the ALDP protein.[18]

Trial data

Skysona was evaluated in a Phase 2/3 study in 32 males aged 17 years or younger with early signs of CALD (Starbeam ALD-102). The primary endpoint was survival without any of the six major functional disabilities associated with CALD at 24 months.

Results of this study at month 24 showed 90% of patients were alive and free of major functional disabilities. No evidence of these disabilities through nearly seven years of follow-up was found.

The most common adverse events with Skysona were low levels of red/white blood cells and platelets, nausea, vomiting, and swelling and redness inside the mouth.

You can access an in-depth discussion of safety and trial data here (p. 13).

Competitive environment

The only treatment available to CALD patients is stem cell transplantation, which carries its own risks. The risks are lower for patients with a matching sibling donor. This applies to fewer than 30% of patients with CALD.[19]

If approved, Skysona would be a one-time treatment that may stabilize disease progression and preserve neurological function in patients with early CALD.

With the seven years of follow-up from the long-term study (LTF-304), it is unclear whether the improvement in survival outcomes and neurologic preservation is durable.

For reference, the wholesale acquisition cost for Zolgensma® (onasemnogene abeparvovec), a one-time gene therapy for another ultra-rare condition, spinal muscular atrophy, is $2.125 million.

References

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