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With Winrevair Approved, Merck Has A Chance To Execute On CV Strategy

The WAC price of Winrevair is $14,000 per vial

by Jessica Merrill

The activin signaling inhibitor sotatercept was approved by the US FDA for pulmonary arterial hypertension.

Merck & Co., Inc.'s Winrevair (sotatercept) was approved by the US Food and Drug Administration for the treatment of pulmonary arterial hypertension, positioning the company to execute on its ambitious goal of establishing a $10bn cardiovascular franchise by 2030. Winrevair was approved on 26 March, the FDA action date, and represents the first drug approved to address the underlying cause of the disease.

The subcutaneous injection, administered every three weeks, will be priced at a wholesale acquisition cost (WAC) of $14,000 per vial, though dosing is based on weight and the product will be distributed in single-vial or double-vial kits.

Winrevair works by improving the balance between pro- and anti-proliferative signaling to regulate vascular cell proliferation underlying PAH. Winrevair is approved for adults with PAH categorized as World Health Organization (WHO) Group 1 to increase exercise capacity, improve WHO functional class (FC) and reduce the risk of clinical worsening. WHO Group 1 generally refers to PAH and within Group 1 are other subgroups divided by FC, which refers to disease progression.

PAH is a rare and progressive disease; there are roughly 40,000 individuals in the US diagnosed and living with PAH, who are WHO Group 1, according to Merck.

The approval is based on the results of the Phase III STELLAR trial, which compared Winrevair to

placebo in adults with PAH WHO Group 1, FC II and III, and showed the addition of Winrevair to background therapy increased six-minute walk distance from baseline by 41 meters and met eight of nine secondary endpoints. (Also see "*Merck's Sotatercept Hits Phase III Marks In Mid-Stage PAH Patients*" - Scrip, 10 Oct, 2022.)

"We expect utilization to be similar to use in the STELLAR study," Merck said of the early launch trends. Most patients in STELLAR were already receiving background therapy, with 61% of individuals on three therapies and 35% on two background drugs.

"We expect payer mix to be weighted heavily towards Medicare and Medicaid patients with commercially insured patients representing around a third or more of patients," Merck added. Labeling allows for patients and caregivers to administer the drug at home, so that Merck expects the drug will be predominantly dispensed through specialty pharmacies and covered under patients' pharmacy benefit.

Existing treatments for PAH include calcium channel blockers and PDE5 inhibitors like sildenafil or tadalafil, available generically and used off label. Another class of drugs that are approved for PAH are endothelin receptor antagonists like *Johnson & Johnson*'s Opsumit (macitentan), which was approved for PAH patients categorized as WHO Group 1 nearly 10 years ago, and newly approved Opsynvi, which combines macitentan and tadalafil into a single tablet. (Also see "*Actelion's Opsumit Ramps Up As Tracleer Patent Loss Gets Closer*" - Pink Sheet, 17 Feb, 2015.)

Johnson & Johnson's PAH franchise, which also includes the prostacyclin receptor agonist Uptravi (selesipag), generated $3.82bn in 2023.

Analysts have robust expectations for Winrevair. Ahead of the approval, JP Morgan analyst Chris Schott, in a 4 March research note, forecast that sotatercept would generate $400m in 2024, $1.5bn in 2025 and approach $5bn in revenue by 2030.

"We see sotatercept ramping quickly in Class II/III PAH patients given the suboptimal current standard of care and see further opportunities for growth with the launch of an autoinjector over time as well as with potential label expansion to additional patient populations," he said.

Risk Of Bleeding Requires Monitoring

Labeling for Winrevair includes several serious risks that require monitoring, including increased risk of bleeding, but those risks are included in the Warnings section and not in a black box warning. FDA also did not require a risk evaluation and mitigation strategy (REMS).

A risk of increases in hemoglobin that can lead to erythrocytosis requires monitoring of hemoglobin before each dose is administered for the first five doses, or longer if values are unstable, and periodically thereafter. Winrevair may decrease platelet count and lead to severe

thrombocytopenia, which can increase the risk of bleeding. Labeling recommends against initiating treatment if platelet counts are below 50,000/mm^3 and recommends similar monitoring of platelet levels.

Merck's Expansion Strategy

Winrevair is a cornerstone of Merck's portfolio expansion strategy to diversify away from Keytruda (pembrolizumab) as that drug edges closer to the end of its expected exclusivity in 2028. The company has pinned much of that effort on expansion in cardiovascular disease, where Merck has a long heritage but has had a smaller presence more recently. Management outlined a plan to investors in 2022 that targets eight new drug approvals or indications for cardiovascular disease drugs and $10bn in revenue by 2030. (Also see "*Merck & Co Maps Out Route To $10bn Cardiovascular Franchise*" - Scrip, 6 Apr, 2022.)

Merck expects to expand the use of Winrevair to more PAH patients and has Phase III trials ongoing in later-stage patients with class III or IV disease (ZENITH) and in newly diagnosed patients (HYPERION), with completion targeted for 2025 and 2026, respectively, according to clinicaltrials.gov.

The approval of Winrevair comes two and a half years after Merck acquired the drug through the $11.5bn purchase of *Acceleron Pharma, Inc.* in 2021. (Also see "*Merck's $11.5bn Acceleron Buy Partially Fills Future Keytruda Revenue Gap*" - Scrip, 30 Sep, 2021.)