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Voydeya approved in the US as add-on therapy to ravulizumab or eculizumab for treatment of extravascular haemolysis in adults with the rare disease PNH

Approval of first-in-class, oral, Factor D inhibitor based on results from pivotal ALPHA Phase III trial

Voydeya (danicopan) has been approved in the US as add-on therapy to ravulizumab or eculizumab for the treatment of extravascular haemolysis (EVH) in adults with paroxysmal nocturnal haemoglobinuria (PNH).[1] *Voydeya* is a first-in-class, oral, Factor D inhibitor developed as an add-on to standard-of-care *Ultomiris* (ravulizumab) or *Soliris* (eculizumab) to address the needs of the approximately 10-20% of patients with PNH who experience clinically significant EVH while treated with a C5 inhibitor.[2,3]

The approval by the US Food and Drug Administration (FDA) was based on positive results from the pivotal ALPHA Phase III trial. Results from the 12-week primary evaluation period of the trial were published in *The Lancet Haematology*.[2]

Bart Scott, MD, Professor, Division of Hematology and Oncology at the University of Washington Medical Center, and Professor, Clinical Research Division at Fred Hutchinson Cancer Center, said: "The approval of *Voydeya* offers this small subset of PNH patients an add-on therapy designed to address EVH, while maintaining disease control with *Ultomiris* or *Soliris*. Terminal complement inhibition with *Ultomiris* can address the life-threatening complications of PNH, building on the efficacy and safety of *Soliris* established over nearly 20 years."

Marc Dunoyer, Chief Executive Officer, Alexion, said: "The approval of first-in-class, Factor D inhibitor *Voydeya* marks an important advancement in the treatment of PNH and builds on our leadership and commitment to bring forward innovation in complement science. As the ALPHA trial suggests, dual complement pathway inhibition at Factor D and C5 may be an optimal treatment approach for this subset of patients with EVH, enabling them to continue with proven standard-of-care therapy."

The ALPHA Phase III trial evaluated the efficacy and safety of *Voydeya* as add-on to *Ultomiris* or *Soliris* in patients with PNH who experienced clinically significant EVH. Results showed that *Voydeya* met the primary endpoint of change in haemoglobin from baseline to week 12 and all key secondary endpoints, including transfusion avoidance and change in Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-Fatigue) score.[2]

Results from the ALPHA Phase III trial showed *Voydeya* was generally well tolerated, and no new safety concerns were identified. In the trial, the most common treatment-emergent adverse events were headache, nausea, arthralgia and diarrhoea.[2]

Voydeya has been granted Breakthrough Therapy designation by the US FDA and PRIority MEdicines (PRIME) status by the European Medicines Agency. *Voydeya* has also been granted Orphan Drug Designation in the US, European Union (EU) and Japan for the treatment of PNH. *Voydeya* has been approved in Japan and recommended for approval in the EU. Regulatory reviews are ongoing in additional countries.

Notes

PNH

PNH is a rare, chronic, progressive and potentially life-threatening blood disorder. It is characterised by red blood cell destruction within blood vessels (also known as intravascular haemolysis) and white blood cell and platelet activation, which can result in thrombosis (blood clots).[4-6]

PNH is caused by an acquired genetic mutation that may happen any time after birth and results in the production of abnormal blood cells that are missing important protective blood cell surface proteins. These missing proteins enable the complement system, which is part of the immune system and is essential to the body's defence against infection, to 'attack' and destroy or activate these abnormal blood cells.[4] Living with PNH can be debilitating, and signs and symptoms may include blood clots, abdominal pain, difficulty swallowing, erectile dysfunction, shortness of breath, excessive fatigue, anaemia and dark-coloured urine.[4,7,8]

Clinically Significant EVH

EVH, the removal of red blood cells outside of the blood vessels, can sometimes occur in PNH patients who are treated with C5 inhibitors.[9,10] Since C5 inhibition enables PNH red blood cells to survive and circulate, EVH may occur when these now surviving PNH red blood cells are marked by proteins in the complement system for removal by the spleen and liver.[4,6,11] PNH patients with EVH may continue to experience anaemia, which can have various causes, and may require blood transfusions.[9,10,12,13] A small subset of people living with PNH who are treated with a C5 inhibitor experience clinically significant EVH, which results in continued symptoms of anaemia and may require blood transfusions.[4,7,14,15]

ALPHA

ALPHA is a pivotal, global Phase III trial designed as a superiority study to evaluate the efficacy and safety of *Voydeya* as an add-on to C5 inhibitor therapy *Soliris* or *Ultomiris* in patients with PNH who experience clinically significant EVH. In the double-blind, placebo-controlled, multiple-dose trial, patients were enrolled and randomised to receive *Voydeya* or placebo (2:1) in addition to their ongoing *Soliris* or *Ultomiris* therapy for 12 weeks. A prespecified interim analysis was performed once 63 randomised patients had completed 12 weeks of the primary evaluation period or discontinued treatment as of June 28, 2022. At 12 weeks, patients on placebo plus *Soliris* or *Ultomiris* were switched to *Voydeya* plus *Soliris* or *Ultomiris*, and patients on *Voydeya* plus *Soliris* or *Ultomiris* remained on this treatment for an additional 12 weeks. Patients who completed both treatment periods (24 weeks) had the option to participate in a two-year long-term extension period and continue to receive *Voydeya* in addition to *Soliris* or *Ultomiris*.

The open-label period of the study is ongoing.[2,16]

***Voydeya* (danicopan)**
Voydeya (danicopan) is a first-in-class oral Factor D inhibitor. The medication works by selectively inhibiting Factor D, a complement system protein that plays a key role in the amplification of the complement system response. When activated in an uncontrolled manner, the complement cascade over-responds, leading the body to attack its own healthy cells. *Voydeya* has been granted Breakthrough Therapy designation by the US Food and Drug Administration and PRIority MEdicines (PRIME) status by the European Medicines Agency. *Voydeya* has also been granted Orphan Drug Designation in the US, EU and Japan for the treatment of PNH.

Voydeya is approved in the US as add-on therapy to ravulizumab or eculizumab for the treatment of EVH in adults with PNH.

Voydeya is also approved in Japan for certain adults with PNH in combination with C5 inhibitor therapy.

Alexion is also evaluating *Voydeya* as a potential monotherapy for geographic atrophy in a Phase II clinical trial.

Alexion
Alexion, AstraZeneca Rare Disease, is the group within AstraZeneca focused on rare diseases, created following the 2021 acquisition of Alexion Pharmaceuticals, Inc. As a leader in rare diseases for more than 30 years, Alexion is focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and commercialisation of life-changing medicines. Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its development efforts on haematology, nephrology, neurology, metabolic disorders, cardiology and ophthalmology. Headquartered in Boston, Massachusetts, Alexion has offices around the globe and serves patients in 70 countries.

AstraZeneca
AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on social media @AstraZeneca.

Contacts
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