MEDIA UPDATE

Results from real-world data and post-hoc analysis of Novartis Beovu® pivotal trials presented at AAO 2020

- Initial findings on patient characteristics and event likelihood provide insights related to Beovu use in wet AMD\(^1,2\)

- Follows establishment of multi-disciplinary expert coalition and Novartis commitment to sharing data and findings with ophthalmology community

- Despite existing therapies, significant unmet need still exists for wet AMD patients; data shows around half of patients have unresolved fluid, with a third requiring monthly injections\(^3,4\)

Basel, November 13, 2020 — Novartis today reported initial findings from a coalition convened to answer key questions related to treatment with Beovu\(^\circledR\) (brolucizumab) for adults with wet age-related macular degeneration (AMD). Analyses of US real-world and Phase III data presented at the American Academy of Ophthalmology (AAO) 2020 Annual Meeting identified baseline patient characteristics potentially associated with the incidence of inflammation-related adverse events that may occur following treatment with Beovu\(^1,2\). Novartis has a comprehensive program of work underway examining the root cause and potential risk factors for these events, as well as identifying mitigation strategies and treatment protocols.

In the analysis of data from the IRIS Registry, including 12,000 patients treated with Beovu, the highest observed risk for experiencing retinal vasculitis (RV) and/or retinal vascular occlusion (RO) in the six months after first treatment with Beovu was prior intraocular inflammation (IOI) and/or prior RO in the 12 months before first Beovu injection\(^1\). Against an observed overall RV/RO risk rate of 0.46% for all Beovu-treated patients in the registry, this increased to 3.97% in individuals with prior IOI and/or RO\(^1\).

“We are pleased to share these findings that underscore the importance of carefully examining a patient for active ocular inflammation before injecting Beovu and throughout the course of treatment,” said Marcia Kayath, Global Head of Medical Affairs and Chief Medical Officer, Novartis Pharmaceuticals. “Even with the great advancements made in treating wet AMD, data shows 50% of patients have unresolved fluid and a third require monthly injections, highlighting the persistent unmet need that Beovu may help address\(^3,4\).”

In a post-hoc unmasked assessment of the Phase III HAWK and HARRIER data, there was an observed trend toward increased incidence of RV/RO in patients with treatment emergent (boosted/induced) anti-drug antibodies (ADAs)\(^2\). Further analyses of the data presented and additional data collection are ongoing.
Novartis has five presentations at the congress including results from a post-hoc HAWK and HARRIER analysis showing Beovu is associated with greater and sustained reduction in Pigment Epithelial Detachments and Subretinal Hyper-reflective Material compared with aflibercept. Novartis also sponsored a symposium including description of US real-world wet AMD patient case studies with Beovu.

Beovu is now approved in more than 50 countries, including in the US, EU, UK, Japan, Canada and Australia, based on the results of the HAWK and HARRIER clinical trials. Novartis is confident that Beovu continues to represent an important treatment option for patients with wet AMD, with an overall favorable benefit/risk profile.

About Beovu (brolucizumab)
Beovu (brolucizumab, also known as RTH258) is the first advanced humanized single-chain antibody fragment (scFv) approved for clinical use. Single-chain antibody fragments are highly sought after in drug development due to their small size, enhanced tissue penetration, rapid clearance from systemic circulation and drug delivery characteristics.

The proprietary innovative structure results in a small molecule (26 kDa) with potent inhibition of, and high affinity to, all VEGF-A isoforms. Beovu is engineered to deliver a high concentration of drug, thus providing more active binding agents. In preclinical studies, Beovu inhibited activation of VEGF receptors through prevention of the ligand-receptor interaction. Increased signaling through the VEGF pathway is associated with pathologic ocular angiogenesis and retinal edema. Inhibition of the VEGF pathway has been shown to inhibit the growth of neovascular lesions and suppress endothelial cell proliferation and vascular permeability.

About the HAWK and HARRIER studies
With more than 1,800 patients across nearly 400 centers worldwide, HAWK (NCT02307682) and HARRIER (NCT02434328) are the first global head-to-head trials in patients with wet AMD that prospectively demonstrated efficacy of Beovu at week 48 using an innovative q12w/q8w regimen, with a majority of patients on q12w immediately following the loading phase. Both studies are 96-week prospective, randomized, double-masked multi-center studies and part of the Phase III clinical development of Beovu. The studies were designed to compare the efficacy and safety of intravitreal injections of brolucizumab 6 mg (HAWK and HARRIER) and 3 mg (HAWK only) versus aflibercept 2 mg in patients with wet AMD. The most common adverse events (≥5% of patients) with Beovu were vision blurred, cataract, conjunctival hemorrhage, vitreous floaters and eye pain.

About the coalition
In early 2020, following post-marketing reports of vasculitis, Novartis initiated a review of post-marketing safety case reports and together with an external review committee confirmed a safety signal of uncommon adverse events termed as “retinal vasculitis” and/or “retinal vascular occlusion” that may result in severe vision loss. As a result, Novartis initiated worldwide label updates to reflect this adverse event information.

Novartis is dedicated to examining the root causes and potential risk factors associated with these adverse events and has convened a fully dedicated team of Novartis research, drug development and medical specialists, who are working with an external team of top global experts to thoroughly investigate risk factors and identify mitigation strategies and treatment protocols.

About wet age-related macular degeneration
Wet AMD is the leading cause of severe vision loss and legal blindness in people over the age of 65 in North America, Europe, Australia and Asia, impacting an estimated 20 million people worldwide. Wet AMD occurs when abnormal blood vessels form underneath the
macula, the area of the retina responsible for sharp, central vision\textsuperscript{21,22}. These blood vessels are fragile and leak fluid, disrupting the normal retinal architecture and ultimately causing damage to the macula\textsuperscript{21,22}.

Early symptoms of wet AMD include distorted vision (or metamorphopsia) and difficulties seeing objects clearly\textsuperscript{23}. Prompt diagnosis and intervention are essential\textsuperscript{24}. As the disease progresses, cell damage increases, further reducing vision quality\textsuperscript{24}. This progression can lead to a complete loss of central vision, leaving the patient unable to read, drive or recognize familiar faces and potentially depriving them of their independence\textsuperscript{24,25}. Without treatment, vision can rapidly deteriorate\textsuperscript{26}.

\section*{About Novartis in ophthalmology}
At Novartis, our mission is to discover new ways to improve and extend people's lives. In ophthalmology, we develop and deliver life-changing medicines and therapies for diseases and conditions from front to back of the eye, enabled by data and transformative technologies. Our ophthalmic solutions reach more than 150M people per year, from premature infants to the elderly.

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\section*{About Novartis}
Novartis is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world’s top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding
innovative ways to expand access to our latest treatments. About 110,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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