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MEDIA UPDATE

Novartis announces European Commission approval of Beovu® for people living with diabetic macular edema

- *Diabetic macular edema (DME) is a leading cause of blindness in adults in developed countries; unmet needs in DME include improving fluid resolution in the retina and addressing the burden of frequent treatment schedules*[1,2]
- *Approval is based on year one data from the Phase III KESTREL and KITE trials investigating Beovu (brolucizumab) 6 mg versus aflibercept 2 mg in DME patients*[2]
- *In KESTREL and KITE, Beovu was non-inferior to aflibercept in change in best-corrected visual acuity (BCVA) from baseline and showed potential for fluid resolution in numerically more DME patients*[2]
- *KESTREL and KITE were the first pivotal trials to assess an anti-VEGF on six-week dosing intervals in the loading phase, suggesting Beovu may offer fewer injections from the start of treatment through year one*[2]
- *Beovu is approved for the treatment of wet age-related macular degeneration in more than 70 countries, including in the EU*

Basel, March 31, 2022 — Novartis today announced that the European Commission (EC) has approved Beovu® (brolucizumab) 6 mg for the treatment of visual impairment due to diabetic macular edema (DME). Today's approval in DME represents the second indication for Beovu granted by the EC, which was first approved for the treatment of wet age-related macular degeneration in 2020[3]. The EC decision applies to all 27 European Union (EU) member states as well as Iceland, Norway and Liechtenstein.

The EC approval was based on year one data from the Phase III, randomized, double-masked KESTREL and KITE* studies, which met their primary endpoint of non-inferiority in change in best-corrected visual acuity (BCVA) from baseline versus aflibercept at year one[2]. In both trials, following the loading phase, over half of patients (55.1% in KESTREL and 50.3% in KITE) in the Beovu 6 mg arm remained on a 12-week dosing interval through year one[2]. Aflibercept dosing was aligned to the approved EU label in year one of treatment[2,4]. In aggregate, a numerically lower proportion of patient eyes treated with Beovu had intraretinal fluid, subretinal fluid or both at week 52 versus eyes treated with aflibercept (in KESTREL 60.3% in Beovu arm versus 73.3% in aflibercept arm; in KITE 54.2% versus 72.9%, respectively; testing for statistical significance was not performed)[2].

Per the approved prescribing information, following the loading phase of five doses injected six weeks apart, physicians may individualize treatment for DME patients based on their disease activity, as assessed by vision and fluid-related parameters[3]. In patients without disease activity, physicians should consider 12-week intervals between Beovu treatments; in patients with disease activity, physicians should consider eight-week intervals between treatments[3].

“This approval marks a significant milestone for DME patients, many of whom are of working age and struggle with adherence due to the need to manage multiple comorbidities related to diabetes,” said Jill Hopkins, SVP and Global Development Unit Head, Ophthalmology, Novartis Pharmaceuticals. “KESTREL and KITE were the first pivotal trials to assess an anti-VEGF on six-week dosing intervals in the loading phase, suggesting Beovu may offer fewer injections from the start of treatment through year one.* The EC approval of Beovu in DME may thus help address unmet needs.”

The most common ocular and non-ocular adverse events (≥5%) at year one in KESTREL and KITE were conjunctival hemorrhage, nasopharyngitis and hypertension[2]. Intraocular inflammation (IOI) rates in KESTREL were 4.7% for brolucizumab 3 mg (including 1.6% retinal vasculitis), 3.7% for Beovu 6 mg (including 0.5% retinal vasculitis), and 0.5% for aflibercept 2 mg[2]. IOI rates in KITE were equivalent (1.7%) between the Beovu 6 mg and aflibercept 2 mg arms with no retinal vasculitis reported[2]. Retinal vascular occlusion was reported in KESTREL for brolucizumab 3 mg (1.1%) and 6 mg (0.5%), and in KITE for brolucizumab and aflibercept (0.6% each)[2]. The majority of these events were manageable and resolved with routine clinical care[2]. In KESTREL, the percentage of patients who experienced ≥15 letter loss from baseline at year one was 1.6% for brolucizumab 3 mg, 0% for Beovu 6 mg and 0.5% for aflibercept[2]. In KITE, the percentage of patients who experienced ≥15 letter loss from baseline at year one was 1.1% for Beovu 6 mg and 1.7% for aflibercept[2]. Brolucizumab 6 mg is the commercialized dose of Beovu[3].

Novartis remains committed to bringing Beovu to the patients who may benefit from this important medicine. Regulatory applications for Beovu in DME are under review by the U.S. Food and Drug Administration (FDA) and the Japanese Pharmaceuticals and Medical Devices Agency (PMDA). Discussions with additional health authorities regarding Beovu are ongoing.

*Aflibercept dosing was aligned to the approved EU label in year one of treatment

About the KESTREL and KITE clinical trials
KESTREL and KITE are global, randomized, double-masked, Phase III, two-year studies comparing the safety and efficacy of Beovu and aflibercept in the treatment of patients with visual impairment due to DME[5,6].

KESTREL and KITE involved 926 total patients in 36 countries[5,6]. In the loading phase of both trials, patients in the Beovu arms were treated every six weeks for a total of five doses; patients in the aflibercept arms were treated every four weeks for a total of five doses, in line with its label[5,6]. In the first year of the study, following the loading phase, patients in the Beovu arms were subsequently treated every 12 weeks, with those demonstrating disease activity moved to dosing every eight weeks[5,6]. After the loading phase, patients in the aflibercept arms were treated every eight weeks[5,6].

About diabetic macular edema (DME)
DME is a common microvascular complication in patients with diabetes that may have a debilitating impact on visual acuity, eventually leading to blindness[1]. DME is a leading cause of blindness in adults in developed countries, affecting 12% of patients with type 1 diabetes and 28% of those with type 2 diabetes[1].

Consistently high blood sugar levels associated with diabetes can damage small blood vessels in the eye, causing them to leak fluid[1]. This damage leads to an excess of vascular

endothelial growth factor (VEGF)[1,7]. VEGF is a protein that stimulates the growth of blood vessels[1,7]. At elevated levels in DME, VEGF stimulates the growth of abnormal, leaky blood vessels[1,7]. The resulting accumulation of fluid (known as edema) in the macula is a key marker of disease activity and can lead to vision loss[1,7]. The macula is the area of the retina responsible for sharp, central vision[1,7]. Early symptoms of DME include blurry or wavy central vision and distorted color perception, although the disease can also progress without symptoms at early stages[7,8].

About Beovu (brolucizumab) 6 mg
Beovu (brolucizumab, also known as RTH258) 6 mg is approved for the treatment of wet age-related macular degeneration (AMD) in more than 70 countries, including in the US, EU, UK, Japan, Canada and Australia[3,9-12]. In March 2022, Beovu was also approved by the European Commission (EC) to treat diabetic macular edema (DME), applying to all 27 European Union member states as well as Iceland, Norway and Liechtenstein. Additional trials, which study the effects of brolucizumab in patients with wet AMD, diabetic macular edema (DME), and proliferative diabetic retinopathy (PDR), are currently ongoing.

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.

**Kite Pharma, Inc. is neither a sponsor of nor associated with Novartis' KITE trial.*

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About Novartis
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References

1. Romero-Aroca P. Managing diabetic macular edema: The leading cause of diabetes blindness. World J Diabetes. 2011;2(6):98-104.
2. Brown D, Wolf S, Garweg JG, et al. Brolucizumab for the treatment of visual impairment due to diabetic macular edema: 52-week results from the KESTREL & KITE studies. Presented at: The Association for Research in Vision and Ophthalmology (ARVO) 2021 Annual Meeting. May 2021.
3. Beovu [summary of product characteristics] Basel, Switzerland. Novartis: 2020.
4. Eylea [summary of product characteristics] Berlin, Germany. Bayer AG: 2014.
5. Data on file. KESTREL clinical trial protocol (CRTH258B2301). Novartis, 2021.
6. Data on file. KITE clinical trial protocol (CRTH258B2302). Novartis, 2021.
7. National Eye Institute. Macular Edema. Available at: https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/macular-edema. Accessed March 2022.
8. National Eye Institute. Diabetic Retinopathy. Available at: https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/diabetic-retinopathy. Accessed March 2022.
9. Beovu [US prescribing information] East Hanover, NJ. Novartis: 2020.
10. Pharma Japan. National Health Insurance Pricing. Available at: https://pj.jiho.jp/sites/default/files/pj/document/2020/05/New%20Drugs%20to%20Be%20Added%20to%20NHI%20Price%20List%20on%20May%2020_1.pdf. Accessed March 2022.
11. Canadian Agency for Drugs and Technologies in Health. CADTH Canadian Drug Expert Committee Recommendation. Available at: https://cadth.ca/sites/default/files/cdr/complete/SR0632%20Beovu%20-%20CDEC%20Final%20Recommendation%20%E2%80%93%20May%2025%2C%202020_for%20posting.pdf. Accessed March 2022.
12. Beovu [prescription medicine decision summary] Australia. Novartis: 2020.

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