MEDIA UPDATE

Novartis announces positive results from year two of the Phase III trial of Beovu® in diabetic macular edema

- Results from year two of the Phase III KESTREL clinical trial confirmed year one findings, with an overall favorable benefit-risk profile for Beovu® (brolucizumab) 6 mg in patients with visual impairment due to diabetic macular edema (DME)\(^1,2\)

- Beovu showed visual acuity gains that were consistent with year one, and sustained average reductions in central subfield thickness at year two (week 100)\(^1\)

- More Beovu patients experienced resolution of intraretinal and/or subretinal fluid versus aflibercept at year two\(^1\)

- Of Beovu patients who completed the first 12-week dosing interval following the loading phase, 70% remained on 12-week dosing through year two, showing the potential for DME patients to receive fewer injections versus aflibercept\(^1\)

Basel, December 9, 2021 — Novartis today announced the first interpretable results from year two (week 100) of the Phase III KESTREL study. KESTREL assessed the safety and efficacy of Beovu® (brolucizumab) 6 mg in patients with visual impairment due to diabetic macular edema (DME). Results from year two confirmed the visual acuity gains, fluid reduction findings and safety profile from year one, while addressing the burden of frequent treatments for DME patients\(^1,2\).

Results from year two of KESTREL were consistent with those seen at year one, including maintenance of best-corrected visual acuity (BCVA) and sustained reductions in central subfield thickness (CSFT)\(^1,2\). Additionally, numerically fewer Beovu patients had intraocular fluid and/or sub-retinal fluid (IRF/SRF) versus patients treated with aflibercept\(^1\). CSFT is a key indicator of fluid in the retina, and fluid is a key marker of disease activity\(^3,4\).

More than 40% of Beovu patients were maintained on 12-week dosing intervals, and 70% of patients who completed the first 12-week cycle after loading remained on 12-week dosing through year two, showing the potential for Beovu to offer fluid resolution in more DME patients with fewer injections versus aflibercept\(^1\).

“With an average age at diagnosis of 48 years, DME primarily affects working-age adults, which means managing their vision, in addition to multiple comorbidities related to diabetes, may result in loss of work productivity and employment instability\(^5,6\),” said Dr. David M Brown MD, Director of Research, Retina Consultants of Texas. “The extended dosing and fluid resolution observed in year two of the KESTREL clinical trial suggest Beovu has the potential to help appropriate patients more conveniently and effectively manage their disease with dosing intervals every 12 weeks after an initial loading phase.”
Further details of year-two findings from the KESTREL trial, along with findings from KITE*, another pivotal Phase III trial of Beovu in DME, will be presented at upcoming medical congresses.

About the KESTREL year two safety results
In KESTREL (NCT03481634), rates of intraocular inflammation (IOI) were 4.2% for Beovu 6 mg, 5.3% for Beovu 3 mg and 1.1% for aflibercept; retinal vasculitis (RV) rates were 0.5% for Beovu 6 mg, 1.6% for Beovu 3 mg and 0% for aflibercept. Rates of retinal vascular occlusion (RO) were 1.6% for both Beovu 6 mg and 3 mg versus 0.5% for aflibercept. The majority of IOI events were manageable and resolved without any clinical complications. There were no vascular events reported in year two (weeks 52-100). No new RV events were reported during year two of KESTREL. Of the four new RO events reported during year two (two in Beovu 6 mg, one in Beovu 3 mg and one in aflibercept), none were associated with IOI or RV.

Brolucizumab 6 mg is the commercialized dose of Beovu in wet age-related macular degeneration (AMD). Novartis is committed to bringing Beovu 6 mg to DME patients and has submitted data from KESTREL and KITE (NCT03481660), to global health authorities in H2 2021.

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.

KESTREL and KITE involved 926 total patients in 36 countries. 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 at the start of the studies. 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 for the remainder of the study. At week 72 of KITE, Beovu patients dosed every 12 weeks could be extended to dosing every 16 weeks, and patients dosed every eight weeks could be extended to every 12 weeks.

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. DME is the 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.

Consistently high blood sugar levels associated with diabetes can damage small blood vessels in the eye, causing them to leak fluid. This damage leads to an excess of vascular endothelial growth factor (VEGF). VEGF is a protein that stimulates the growth of blood vessels. At elevated levels in DME, VEGF stimulates the growth of abnormal, leaky blood vessels. The resulting accumulation of fluid (known as edema) in the macula can lead to vision impairment or even vision loss. The macula is the area of the retina responsible for sharp, central vision. 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.

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. 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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