FDA approves Lucentis (ranibizumab injection) for treatment of diabetic macular edema
First major treatment advance in more than 25 years for sight-threatening condition

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that Lucentis (ranibizumab injection) was approved by the U.S. Food & Drug Administration (FDA) for treatment of diabetic macular edema (DME), an eye condition in people with diabetes that causes blurred vision, severe vision loss and sometimes blindness. Diabetes is now the leading cause of new cases of blindness in American adults,¹ and DME is estimated to affect more than 560,000 Americans with the disease.²

Lucentis is the first and only FDA-approved medicine for DME, a condition for which the standard of care has not changed significantly in more than 25 years. To date, the standard of care in the U.S. for DME has been laser surgery, which slows the rate of vision loss and helps stabilize vision, but has demonstrated only limited ability to restore lost vision.³

“For the first time, Americans with diabetic macular edema will have access to an FDA-approved medicine shown to help many patients rapidly regain substantial amounts of lost vision,” said Hal Barron, M.D., chief medical officer and head, Global Product Development. “We developed Lucentis to treat diseases of the eye and are pleased to have received this third U.S. indication to help a new population of people whose eyesight may be affected by diabetes.”

“This approval is an important advancement in the fight against blindness for people with diabetes,” said David M. Brown MD, Retinal Specialist at The Methodist Hospital, Houston Texas, and clinical trial investigator. “Now that it will be available, Lucentis therapy can begin to make a difference in the lives of our patients with DME.”

Lucentis 0.5 mg once monthly was first approved by the FDA for treatment of wet age-related macular degeneration (AMD) in 2006 and for macular edema following retinal vein occlusion (RVO) in 2010. Lucentis 0.3 mg once monthly was approved for DME, and physicians can order immediately with shipments
expected to begin August 15.

**Lucentis Efficacy in DME**

The approval of Lucentis in DME was based on Genentech’s Phase III trials, RIDE and RISE, two identically-designed, parallel, double-masked, three-year clinical trials, which were sham-treatment controlled for 24 months. A total of 759 patients were randomized into three groups to receive monthly treatment with 0.3 mg Lucentis (n=250), 0.5 mg Lucentis (n=252) or sham injection (control group, n = 257). Primary outcomes were evaluated at 24 months and have been published in *Ophthalmology*.4

In the studies, treatment with Lucentis demonstrated improved clinical outcomes including substantial visual gain for many DME patients. Results showed patients who received 0.3 mg Lucentis experienced significant, early (Day 7) and sustained (24 months) improvements in vision:

- More patients who received Lucentis were able to read at least three additional lines (15 letters) on the eye chart at 24 months: RIDE: 34 percent in the 0.3 mg group versus 12 percent in the control group; RISE: 45 percent, 0.3 mg versus 18 percent, control (primary endpoint)
- Patients who received Lucentis had average vision gains exceeding two lines (10 letters) on the eye chart at 24 months: RIDE: 10.9 letters, 0.3 mg versus 2.3 letters, control; RISE: 12.5 letters, 0.3 mg versus 2.6 letters, control
- Significant gains in average vision were observed 7 days after the first treatment
- Patients who received Lucentis were significantly more likely to maintain their vision (lose < 15 letters on the eye chart) at 24 months: RIDE: 98 percent, 0.3 mg versus 92 percent, control; RISE: 98 percent, 0.3 mg versus 90 percent, control

For all time points comparing 0.3 mg Lucentis to control through month 24 p < 0.01.

Vision improvements observed in patients treated with Lucentis at 24 months were maintained with continued treatment through 36 months.

**Lucentis Safety in DME**

The benefit/risk profile of Lucentis was favorable in patients with DME through 36 months in the clinical trials. Pooled safety analysis of RIDE and RISE at 24 months showed:
• The ocular safety of Lucentis in patients with DME was generally consistent with that established in patients with wet AMD and RVO (through 36 months).

• The most common ocular events occurring at a higher rate in patients receiving 0.3 mg Lucentis compared to the control groups included conjunctival hemorrhage (bleeding under the lining of the eye): 47 percent, 0.3 mg versus 32 percent, control; eye pain: 17 percent, 0.3 mg versus 13 percent, control; foreign body sensation in eyes: 10 percent, 0.3 mg versus 5 percent, control; vitreous floaters: 10 percent, 0.3 mg versus 4 percent, control; and increased eye pressure: 18 percent, 0.3 mg versus 7 percent, control.

Although uncommon, trends toward increased rates of arteriothromboembolic events (ATEs) such as vascular death, deaths of unknown cause, nonfatal heart attacks and nonfatal strokes, have been observed in prior studies of Lucentis in other diseases.

• Rates of these events were similar among DME patients receiving 0.3 mg Lucentis and the control groups at 24 months at 5.6 percent, 0.3 mg versus 5.2 percent, control. The rate of ATE events at 36 months was 10.8 percent for patients in the 0.3 mg treatment group (control period ended at 24 months).

• The rate of stroke in DME patients at 24 months was 1.2 percent, 0.3 mg versus 1.6 percent, control. The rate of stroke at 36 months was 2.0 percent for patients in the 0.3 mg treatment group.

Pooled analyses also showed the rate of fatal events (death from any cause) in patients treated in the DME trials was low, and many causes of death were not unusual for patients with advanced diabetes complications. However, a potential relationship between the events and intravitreal use of VEGF inhibitors cannot be excluded. The rate of fatalities at 24 months was 2.8 percent, 0.3 mg versus 1.2 percent, control. The rate of fatalities at 36 months was 4.4 percent for patients in the 0.3 mg treatment group.

About DME

DME is swelling of the macula, the central part of the retina responsible for sharp, central vision. DME begins with diabetes, which can cause damage to blood vessels in the eye over time. When this happens, a patient is said to have diabetic retinopathy, the most common diabetic eye disease. The damaged blood vessels can leak blood and fluid, causing swelling and blurred vision, severe vision loss and sometimes blindness.

Nearly 26 million Americans have diabetes, which has become the leading cause of new cases of blindness in adults aged 20-74. Among Americans aged 40 years and older, more than 4.2 million have diabetic
retinopathy, according to the 2005–2008 National Health and Nutrition Examination Survey (NHANES). A subsequent analysis estimates that 560,500 have DME. It has also been estimated that up to 10 percent of people with diabetes will get DME during their lifetime.

**About Lucentis**

Lucentis is a prescription medicine for the treatment of patients with wet AMD, macular edema following RVO, and DME.

Lucentis is a recombinant humanized monoclonal antibody fragment (lacking a Fc region). Lucentis is the first VEGF inhibitor specifically designed for use in the eye to bind to and inhibit VEGF-A, a protein that is believed to play a critical role in the formation of new blood vessels (angiogenesis) and the hyperpermeability (leakiness) of the vessels.

In wet AMD, these new blood vessels grow under the retina and leak blood and fluid, causing rapid damage to the macula. Lucentis administered monthly in wet AMD clinical trials demonstrated an improvement in vision of three lines or more on the study eye chart in up to 41 percent of patients at two years. Nearly all patients (90 percent) treated monthly with Lucentis in those trials maintained (defined as losing < 15 letters) vision.

In RVO, angiogenesis and hyperpermeability can lead to macular edema, the swelling and thickening of the macula. Lucentis administered at 0.5 mg monthly in RVO clinical trials demonstrated the following average vision gains for patients at six months: Patients with branch-RVO experienced an average gain of 18.3 letters on the study eye chart (compared to 7.3 letters for the control group) and patients with central-RVO experienced an average gain of 14.9 letters on the study eye chart (compared to 0.8 letters for the control group).

Lucentis has been rigorously studied in multiple retinal diseases in 27 clinical trials involving more than 10,500 patients worldwide.

Outside the U.S., Lucentis has received regulatory approval for treatment of visual impairment due to DME in more than 75 countries, for treatment of wet AMD in more than 100 countries and for treatment of RVO in more than 70 countries.
Lucentis was discovered by Genentech and is being developed by Genentech and Novartis for diseases or disorders of the eye. Genentech retains commercial rights in the U.S. and Novartis has exclusive commercial rights for the rest of the world.

About Roche
Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world’s largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche’s personalized healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2011, Roche had over 80,000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 42.5 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: www.roche.com.

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References: