Phase 3 Study Showed MACUGEN® Improved Vision Over Standard Of Care In Patients With Diabetic Macular Edema

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Patients on MACUGEN Maintained and Expanded Vision Gains Over Two Years

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(BUSINESS WIRE)--Results from a Phase 3 study demonstrate MACUGEN® (pegaptanib sodium) significantly improved vision in patients with diabetic macular edema (DME), a complication of diabetes that is a leading cause of blindness in people of working age.(1) In the study, 37 percent of patients treated with MACUGEN gained two lines, or 10 letters, of vision on the ETDRS eye chart at 54 weeks, compared to 20 percent of patients who received a sham (placebo-like) procedure which consists of anesthesia and a simulated injection in the eye (p=0.0047). The data were presented today at the World Ophthalmology Congress in Berlin by Frank G. Holz, an investigator in the trial and director of the University Eye Hospital at the University of Bonn in Germany.

“These encouraging Phase 3 results demonstrate that MACUGEN has the potential to improve vision in people with DME, a serious complication of chronic diabetes,” said Marla B. Sultan, M.D., M.B.A., global clinical lead for MACUGEN at Pfizer. ”Currently there are no approved pharmaceutical treatments for DME, and when left untreated, about one out of four people with this condition will develop moderate vision loss within three years,” said Dr. Sultan. “Pfizer is pleased to be exploring MACUGEN as a potential treatment option to address this unmet medical need.”

The phase 3 trial met its primary endpoint of the proportion of patients gaining greater than ten letters vs sham at one year. On average, patients treated with MACUGEN gained 5.2 letters of vision at year one compared to 1.2 letters for patients receiving sham ($p < 0.05$). At the end of year two, patients receiving MACUGEN had gained on average 6.1 letters of vision compared to 1.3 letters for patients in the sham arm of the study ($p < 0.01$). All patients enrolled in the study were eligible to receive laser therapy, the current standard of care for DME, beginning at week 18 of the study at the physician's discretion using ETDRS guidelines.

Dr. Paul Mitchell, an investigator in the trial and director of the Centre for Vision Research at the Westmead Millennium Institute for Medical Research in Westmead, Australia, said, "There is a clear need for new treatment strategies for DME. The MACUGEN Phase 3 study in DME, along with other recently published studies, including those new data presented this week in Berlin, sheds light on the potential role of VEGF-inhibition in the management of this sight-threatening disease."

Pfizer plans to submit to the European Medicines Agency a variation to the European Marketing Authorization for MACUGEN to include an indication for DME.

About the Study

Study A5751013 is a multicenter, randomized, sham-controlled, double-masked, comparative Phase 3 trial over two years with an open-label year-three extension. The primary analysis included 260 patients with DME at 56 global sites. The primary objective of the study was to evaluate whether MACUGEN improved vision compared with sham injections in patients with DME, and to assess the safety of MACUGEN in these patients.

In this fully masked study, patients received an injection of 0.3 mg MACUGEN or a sham procedure every six weeks for a total of nine injections in year one. In year two, subjects could receive injections as often as every six weeks based on pre-specified criteria, including visual acuity, clinical examination, optical coherence tomography (OCT) and the opinion of the investigator. Up to three focal or grid laser treatments per year were permitted beginning at week 18, also at the investigator's discretion using ETDRS guidelines, in both arms. There was also an option for patients to be enrolled in an open-label year-three extension.

The primary outcome measure of the study was the proportion of subjects who, after one year, experienced an improvement in vision from baseline of two lines, or 10 letters, on the ETDRS eye chart.

The study also collected data on a number of secondary outcome measures at one and two years, including the proportion of subjects with an improvement in vision at two years, changes in average visual acuity over time, proportion of eyes experiencing a change in the degree of retinopathy, the use of laser photocoagulation therapy, optical coherence tomography (OCT), vision-related quality of life, and safety. Additional results will be submitted for presentation at a future medical meeting.

Overall, MACUGEN was well tolerated, and there were no new or unexpected safety signals in the study. The most common treatment-emergent adverse events occurred in the eye; this includes conjunctival hemorrhage (22%), eye pain (10%), punctate keratitis (11%), and diabetic retinal edema (11%). The incidences of most events were similar between the two treatment groups or in favor of MACUGEN. An increase in intraocular pressure related to the injection procedure was another common treatment-emergent adverse event and was noted in almost 2.5 times more subjects (n=17) treated with MACUGEN than sham (n=7). Cardiac disorders were the most common, serious, treatment-emergent adverse events; these were reported in 6.9% of patients treated with MACUGEN and 5.6% of patients treated with the sham procedure. No deaths were related to the injection procedure or study drug. Adverse events were consistent with those observed in clinical trials of MACUGEN in patients with neovascular age-related macular degeneration (wet AMD) and similar to clinical experience with MACUGEN.

About Diabetic Macular Edema (DME)

Diabetic macular edema (DME) is a common form of diabetic retinopathy, an eye disease caused by damage to the blood vessels of the retina in the back of the eye and the leading cause of blindness among working-age adult populations (20 to 65 years).(2) DME occurs when damaged blood vessels leak fluid into the center of the macula, the area of the retina responsible for sharp, straight-ahead vision. The fluid makes the macula swell and causes blurry vision. When left untreated, 25% of people with DME will develop moderate vision loss within three years.(3) There are no pharmaceutical therapies available today for patients with DME.(4) Currently available treatment options for DME consist of two main types of laser therapy: focal and grid photocoagulation. These therapies have limitations and are generally not used in patients with edema in the center of the macula.

The International Diabetes Federation estimates that 285 million people around the world have diabetes and approximately 14% of people with diabetes have DME. Prevalence of DME increases to 29% for people with diabetes who use insulin for more than 20 years.(4) By 2030, the incidence of diabetes is expected to rise to 438 million worldwide, and the

incidence of diabetes-related eye complications, like DME and diabetic retinopathy, are also expected to continue to increase worldwide.

About MACUGEN

MACUGEN, a selective inhibitor of VEGF-165, is indicated in Europe and the United States for the treatment of neovascular age-related macular degeneration (wet AMD) and is administered in a 0.3-mg dose once every six weeks by intravitreal injection. MACUGEN is a pegylated anti-VEGF aptamer, which binds to vascular endothelial growth factor (VEGF). VEGF is a protein that plays a critical role in angiogenesis (the formation of new blood vessels) and increased permeability (leakage from blood vessels), two pathological processes that contribute to vision loss.

Pfizer Inc. (NYSE: PFE) markets and sells MACUGEN outside of the United States, and Eyetech Inc. markets and sells MACUGEN in the United States.

For full prescribing information about MACUGEN, please visit http://www.medicines.org.uk/emc/document.aspx?documentId=17843.

About Pfizer Ophthalmics

Pfizer Ophthalmics, a division of Pfizer Inc., is committed to preserving sight and eliminating preventable blindness. Pfizer Ophthalmics discovers, develops and provides leading treatments in ophthalmology to support patients who are at risk of blindness or suffering from vision impairment. Pfizer is committed to conducting research in disease areas including age-related macular degeneration, diabetic macular edema, dry eye, glaucoma and elevated intraocular pressure.

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This release contains forward-looking information about a potential additional indication for MACUGEN, including its potential benefits, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development; whether and when the European Medicines Agency will approve the application that may be filed for this additional indication as well as its decisions regarding labeling and other matters that could affect the availability or commercial potential of such additional indication; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2009 and in its reports on Form 10-Q and Form 8-K.

References:

(1) Klein R, Klein BE, Moss SE: Visual impairment in diabetes. Ophthalmology 1984; 91: 1-9

(2) International Diabetes Federation. Facts Sheet Diabetes and Eye Disease. Available at http://www.idf.org/fact-sheet-diabetes-and-eye-disease. Accessed April 14, 2010.

(3) Ibid.

(4) American Academy of Ophthalmology. "Understanding Diabetic Retinopathy. A Science Writers Guide To A Potentially Blinding Disease." 2006;13

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