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Ruboxistaurin Reduced Vision Loss in Patients With Moderate to Severe Non-Proliferative Diabetic Retinopathy in a New Study

- Once Daily, Oral Investigational Therapy Reduced Sustained Moderate Vision Loss Over Three-Year Period -

INDIANAPOLIS, Nov 13, 2006 /PRNewswire-FirstCall via COMTEX News Network/ -- Eli Lilly and Company (NYSE: LLY) today announced results from a three-year phase 3 clinical trial in which ruboxistaurin mesylate (proposed brand name Arxxant(TM), pronounced ark-ZONT) reduced the risk of sustained moderate vision loss by 40 percent when compared to placebo in patients with moderate to severe non-proliferative diabetic retinopathy (DR).(1)

The study findings were recently published online in the in press version of Ophthalmology [<http://www.ophsource.org/periodicals/ophtha/inpress>] and will be published in the print version of the December 2006 issue of Ophthalmology.

Diabetic retinopathy (DR) occurs when diabetes damages the small blood vessels in the retina, a part of the eye that is needed for vision. This damage can lead to vision loss and possible blindness. DR affects an estimated 4.1 million Americans age 40 and older, with 899,000 having a vision- threatening form of the disease,(2) and it is the leading cause of blindness among working-age adults.(3) Yet blindness is only a part of the story. Even moderate vision loss can lead to difficulties in reading, driving, employment, and mobility as well as an increased risk of accidental injuries.(4,5,6)

Study Details

Vision loss (measured in the study as sustained moderate vision loss or SMVL) occurred in only 5.5 percent of patients treated with ruboxistaurin compared to 9.1 percent of patients treated with placebo, equaling a 40 percent relative risk reduction (P=0.034) over three years.(1) Vision loss (SMVL) was defined as a three-line loss on a standard eye chart that was sustained for at least 6 months.(1)

This multi-center, 36-month, placebo-controlled, double-masked, phase 3 clinical trial, labeled protein kinase C-diabetic retinopathy study 2 (PKC- DRS2), involved 685 patients randomized at 70 clinical sites to either placebo (n=340) or 32 mg per day of ruboxistaurin (n=340).(1) PKC-DRS2 examined whether ruboxistaurin could reduce the risk of long-term, or sustained moderate vision loss caused by non-proliferative diabetic retinopathy.(1) Patients had moderate to severe nonproliferative diabetic retinopathy at the start of the study.(1) Mean visual acuity was better in the ruboxistaurin- treated patients after 12 months. Baseline-to-endpoint visual improvement of greater than or equal to 15 letters was more frequent (4.9% versus 2.4%) and greater than or equal to 15 letter worsening was less frequent (6.7% versus 9.9%) in ruboxistaurin-treated patients compared with placebo (P=0.005). The beneficial effect of ruboxistaurin was not accompanied by a reduction in the progression of study patients from non-proliferative to proliferative diabetic retinopathy.

Patient discontinuations due to adverse events were not statistically different between treatment groups (n=9, 2.6% placebo; n=16, 4.6% ruboxistaurin).(1) There were 36 patient deaths (n=22, 6.5% placebo; n=14, 4.1% ruboxistaurin), none of which were considered by the investigator or sponsor to be related to study drug. There was no consistent pattern of adverse events to suggest a causal relationship between ruboxistaurin and any spontaneously reported adverse event.

About Diabetic Retinopathy

Diabetic retinopathy is a relatively common microvascular complication in individuals with diabetes that can lead to debilitating vision loss.(7) In the United States, 55 people will go blind every 24 hours as a result of diabetic retinopathy.(8) For persons with type 1 diabetes, the crude prevalence of diabetic retinopathy is about 80 percent.(9)

Non-proliferative diabetic retinopathy (NPDR) occurs when the small blood vessels in the retina are damaged.(6) In the most advanced or proliferative stage of diabetic retinopathy (PDR), new blood vessels grow abnormally from the back of the eye(6) and they may subsequently cause severe vision loss.(6)

Vision loss in patients with DR results predominantly from either the consequences of PDR or diabetic macular edema (DME)

that involves the center of the macula (the area of the retina that allows sharp vision). DME occurs when the macula swells with fluid.

About Ruboxistaurin

Ruboxistaurin is an investigational therapy for the treatment of moderate to severe non-proliferative diabetic retinopathy. It works by limiting the overactivation of protein kinase C beta (PKC beta), a naturally occurring enzyme that has been linked to the development of diabetic retinopathy. It is the first of a new class of compounds being investigated for the treatment of moderate to severe non-proliferative diabetic retinopathy.

Lilly submitted a new drug application (NDA) to seek approval from the U.S. Food and Drug Administration (FDA) for ruboxistaurin for the treatment of moderate to severe non-proliferative diabetic retinopathy in February 2006. Lilly received an approvable letter from the FDA in August 2006. The FDA has indicated it will require efficacy data from an additional Phase 3 study before it will consider approving the molecule. Lilly has decided to appeal the FDA's decision and has recently begun discussions with the agency.

Lilly's Leadership in Diabetes

Through a long-standing commitment to diabetes care, Lilly provides patients with breakthrough treatments that enable them to live longer, healthier and fuller lives. Since 1923, Lilly has been the industry leader in pioneering therapies to help health care professionals improve the lives of people with diabetes, and research continues on innovative medicines to address the unmet needs of patients.

About Lilly

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers -- through medicines and information -- for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com.

This press release contains forward-looking statements about the potential of the investigational compound ruboxistaurin for the treatment of diabetic retinopathy and reflects Lilly's current beliefs. However, as with any pharmaceutical product under development, there are substantial risks and uncertainties in the process of development and regulatory review. There is no guarantee that the product will receive regulatory approvals, or that the regulatory approval will be for the indication(s) anticipated by the company. In particular, there can be no assurance that the company's appeal of the FDA's decision will be successful. There is also no guarantee that the product will prove to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

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