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Lilly Will Submit Ruboxistaurin Mesylate (Arxxant(TM)) to FDA for Treatment of Diabetic Retinopathy in 2005

Company Will Not Pursue Submission for Treatment of Symptoms of Diabetic Peripheral Neuropathy

INDIANAPOLIS, Aug 02, 2005 /PRNewswire-FirstCall via COMTEX/ -- Eli Lilly and Company announced today that it has completed a Phase 3 clinical trial in which its investigational drug, ruboxistaurin mesylate (proposed brand name Arxxant(TM), pronounced ark-ZONT) reduced the occurrence of vision loss in patients with diabetic retinopathy (DR). As a result, Lilly believes it is appropriate to submit a new drug application (NDA) to the U.S. Food & Drug Administration (FDA) at the end of 2005 for the treatment of DR, the initial indication for ruboxistaurin.

In addition Lilly is announcing today that two Phase 3 clinical trials to determine the effect of ruboxistaurin on treatment of sensory symptoms associated with diabetic peripheral neuropathy (SDPN) have been completed. In these studies, statistical comparison of the change in sensory symptom scores between the placebo and ruboxistaurin-treated groups did not demonstrate significant differences and did not meet the studies' primary endpoints -- a regulatory requirement for submission. Consequently, these results do not support the NDA filing for SDPN. Importantly, however, no significant safety issues were discovered during these clinical trials that would preclude continued clinical development.

"While we are disappointed in the outcome of the trials for SDPN, we are extremely pleased to be one step closer to providing a possible solution for patients with diabetic retinopathy," said Dr. Steven Paul, Executive Vice President, Science and Technology, Eli Lilly and Company. "If ruboxistaurin is approved by the FDA, it would be the first oral medication for the treatment of this serious complication of diabetes," he added.

Results of these Phase 3 clinical trials will be presented at a future major medical meeting in late 2005 or early 2006. In addition, it is Lilly's policy to publish the results of all clinical trials; however, specific publication plans have not yet been determined.

"Since Lilly has been the industry leader in pioneering diabetes therapies for more than 80 years, we believe in the value of innovation and the need for new treatments for this epidemic disease," said Sidney Taurel, Lilly Chairman, President and Chief Executive Officer. "And ultimately, the results from these studies serve as a reminder of the high risks and high rewards associated with pharmaceutical innovation," he added.

About Diabetic Microvascular Complications

Diabetic retinopathy and diabetic peripheral neuropathy (DPN) are diabetic microvascular complications (DMCs). Nearly 75 percent of all people with diabetes have at least one DMC. And while tight blood glucose control (keeping blood sugar at near-normal levels) lowers the risk of DMCs, there are currently no treatments or medications approved in the United States to target the underlying causes of DR and DPN. Eventually, DR can lead to loss of vision or blindness, and DPN can lead to the amputation of toes, a foot or a leg.

Diabetic retinopathy (DR) is a condition that leads to progressive damage to the small blood vessels of the eye, and can lead to vision loss and possible blindness. According to the World Health Organization and the American Diabetes Association, DR is the leading cause of vision loss in adults of working age (20 to 65 years) in industrialized countries. Ruboxistaurin was studied in a Phase 3 clinical trial of 685 patients with moderately severe to severe, non-proliferative DR. The primary objective of this trial was to test the hypothesis that once-daily oral administration of ruboxistaurin over three years would reduce the occurrence of sustained moderate visual loss (equivalent to doubling of the visual angle, such as a reduction in visual acuity from 20/20 to 20/40) in these patients. This trial demonstrated a statistically significant reduction in this outcome. An ongoing trial to determine the effect of ruboxistaurin on diabetic macular edema (DME, a manifestation of DR) progression in patients with less severe DR is expected to be complete in 2010.

Diabetic peripheral neuropathy (DPN) is a progressive disorder resulting in the deterioration of nerve function, the clinical manifestations of which may include subjective sensory symptoms such as numbness, tingling and pain. Ruboxistaurin was studied in two clinical trials, involving more than 500 patients combined, for the treatment of SDPN. These studies had a duration of one year, and the change in sensory symptom scores was the primary outcome measure. Statistical comparison of the change in sensory symptom scores between the placebo- and ruboxistaurin-treated groups did not demonstrate significant

differences. An ongoing, three-year, placebo-controlled trial evaluating ruboxistaurin for the treatment of nerve dysfunction of diabetic peripheral neuropathy (DPN), scheduled to complete in 2007, will continue. In contrast to the just-completed SDPN trials, change in a composite of objective nerve function measures is the primary outcome measure of the DPN trial.

About Ruboxistaurin

Ruboxistaurin is a specific protein kinase C beta (PKC beta) inhibitor, the first of a new class of compounds being investigated for the treatment of diabetic retinopathy (DR) and diabetic peripheral neuropathy (DPN). In addition, Lilly has recently presented results of a pilot study of ruboxistaurin in patients with diabetic nephropathy (kidney disease or DN) at a major medical meeting. These are the three major diabetic microvascular complications (DMCs) associated with type 1 and type 2 diabetes. Metabolic factors associated with diabetes often lead to damage to the small blood vessels in the eyes, nerves and kidneys, ultimately leading to DMCs. Pre-clinical data show that ruboxistaurin is a specific inhibitor of PKC beta. PKC beta is an enzyme that has been implicated in the underlying process of microvascular damage caused by diabetes.

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 microvascular complications 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. 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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