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<Note to Editor>

Background Information

Lenticular opacity was observed in a high-dose group of a 13-week safety preclinical study in rats which ran in parallel with the Phase I study. Eisai immediately suspended the phase I clinical study, reported to the FDA and received an order of clinical hold from the FDA. No medical issues were observed in subjects who received E2012 in the phase I study in an examination which was conducted at the point when the study was suspended. Lenticular opacity was not observed in a 13-week safety study in monkeys. Additionally, lenticular opacity was not observed in the single dose administration at maximum tolerated dosing and 4-week administration in high doses as well as in their long term follow-up examination in rats. Eisai conducted an additional 13-week multiple dosing study in rats to reevaluate repeatability and recoverability potential and examined the no adverse effective level, the mechanism causing lenticular opacity, and an exploratory marker. Examination of follow-up data from the Phase I study was also conducted. After submitting these data to the agency on February 29, 2008, Eisai received the response from the FDA.