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Genentech *Tarceva* Trials "On Track" Despite INTACT: Response To *Iressa*

Genentech and OSI Pharmaceuticals are pointing to the dosing regimen in clinical trials of *Tarceva* (erlotinib) as one reason that *Phase III* studies of the EGFR oncologic agent will have a positive outcome despite the negative findings in AstraZeneca's *Phase III* program for *Iressa*.

Although *Iressa* and *Tarceva* both "block the EGFR pathway, there are important differences between the agents and clinical programs including structure, formulation, pharmacokinetics and *Phase III* design and dosing," OSI and Genentech declared Aug. 19. AstraZeneca announced the same day that *Iressa* (ZD1839) showed no benefit as add-on therapy in treatment of non-small cell lung cancer (*see preceding story*).

Genentech and OSI believe that their dosing strategy with *Tarceva* is one point of differentiation. "The dose employed in the alliance's *Phase III* program of 150 mg/day is the apparent maximum tolerated dose for this agent as determined in earlier *Phase I* studies," the companies said. "The choice of dose is based on the belief that this dosing strategy may be clinically important in the use of this agent."

AstraZeneca did not find a clear dose-response relationship for *Iressa* in *Phase II* studies ("The Pink Sheet" May 27, p. 34).

Prilosec OTC Switch Set For Early 2003 Following FDA "Approvable" Letter

AstraZeneca's OTC switch for *Prilosec* (omeprazole) will wait until 2003 after receipt of an "approvable" letter from FDA.

AstraZeneca's OTC marketing partner Procter & Gamble said it expects to launch OTC *Prilosec 1* very early in the new year after addressing the issues identified in the Aug. 8 action letter. The company says FDA wants certain modifications to *Prilosec 1* labeling and a consumer comprehension study.

FDA's comments in the action letter mirror recommendations made by a joint Gastrointestinal Drugs/Nonprescription Drugs Advisory Committee during a June 21 review of the OTC application. The committee voted 16-2 to approve the switch, pending label modifications ("The Pink Sheet" June 24, p. 24).

The committee suggested that the proposed indication – "for prevention of the symptoms of frequent heartburn...only for those who suffer heartburn two or more days a week" – should include the caveat that *Prilosec 1* is inappropriate for acute or episodic use.

OSI and Genentech/Roche have three ongoing *Phase III* trials assessing *Tarceva* in the treatment of non-small cell lung cancer ("The Pink Sheet" Jan. 15, 2001, p. 8).

Two of the *Tarceva Phase III* trials are studying the drug as add-on therapy to standard chemo. The studies are powered to demonstrate a 25% improvement in survival, the companies said. "Accrual was recently completed for" a 1,000-patient, Genentech-sponsored study combining *Tarceva* to carboplatin and paclitaxel. Accrual "is currently on track" for a 1,000-patient, Roche-sponsored trial combining *Tarceva* with Lilly's *Gemzar* (gemcitabine) and cisplatin.

The third *Phase III* trial is assessing the efficacy of *Tarceva* as monotherapy in refractory non-small cell lung cancer patients. "This is the only single agent controlled *Phase III* study of an EGFR targeted agent designed to detect a survival advantage in refractory non-small cell lung cancer," OSI and Genentech noted.

The companies hope for approval of *Tarceva* in mid-2004 ("The Pink Sheet" Jan. 14, p. 29). ♦ ♦

Committee members recommended that labeling advise consumers not to expect immediate relief from a single dose of *Prilosec*. In addition, members suggested that a statement be added to labeling advising consumers how often the 14-day course of therapy can be repeated.

The delay means that omeprazole generics could enter the prescription market before the OTCs are available.

AstraZeneca expects generic competition for *Prilosec* as early as the third quarter ("The Pink Sheet" Aug. 5, p. 35). Omeprazole's composition of matter patent expired in October 2001, and a decision is pending in litigation over secondary omeprazole patents ("The Pink Sheet" June 10, p. 27).

The *Prilosec* switch delay marks the third recent setback for AstraZeneca with a pending NDA. The agency also wants to see additional data on the cholesterol drug *Crestor* (rosuvastatin) prior to approval ("The Pink Sheet" Aug. 12, p. 27). In addition, AstraZeneca's *Phase III* trials of the pending oncologic agent *Iressa* as add-on therapy had a disappointing result (*see related story*, p. 9). ♦ ♦