

## TAXOTERE® (DOCETAXEL) GRANTED FDA APPROVAL TO TREAT LOCALLY ADVANCED HEAD AND NECK CANCER PRIOR TO CHEMORADIOTHERAPY AND SURGERY

BRIDGEWATER, NJ – OCTOBER 1, 2007 – Sanofi-aventis announced that the U.S. Food and Drug Administration (FDA) has approved Taxotere® (docetaxel) Injection Concentrate in combination with cisplatin and 5-fluorouracil for induction therapy of locally advanced squamous cell carcinoma of the head and neck (SCCHN) before patients undergo chemoradiotherapy and surgery.

The FDA based its approval on the results of the phase III randomized, open-label, international trial, TAX 324, which established the efficacy and safety of the Taxotere-based regimen in significantly improving survival.

### Approval Based on Clinical Trial Tax 324

Among patients treated with Taxotere-based therapy (TPF, n=251) overall survival was significantly improved compared to patients receiving just cisplatin and 5-fluorouracil (PF, n=243); the relative risk of death was 30% lower (HR 0.70; p=0.0058). Patients treated with TPF had a longer median overall survival of 70.6 months vs. 30.1 months for patients receiving PF only, representing a more than three year improvement in median OS for patients treated with TPF. The probability to survive three years was 62% in the TPF arm compared to 48% in the PF arm.

“The TAX 324 trial found that the addition of Taxotere to standard induction chemotherapy significantly improved patient survival, adding years to patients’ lives,” noted clinical investigator Marshall Posner, MD, Medical Director of the Head and Neck Oncology Program at Dana-Farber Cancer Institute in Boston. “The approval of Taxotere to be given in combination with other standard chemotherapy as the first step in a therapeutic sequence followed by chemoradiotherapy and surgery is a significant advancement in treatment for patients with locally advanced head and neck cancer.”

All patients entering TAX 324 had tumors of the oropharynx, larynx, hypopharynx or oral cavity that either could not be removed, were considered potentially operable but unlikely to be cured with surgery, or could not be removed in order to preserve organ function. Participants in the trial had either stage III or IV SCCHN with no distant metastases.

Patients were treated every three weeks for three cycles with either TPF (Taxotere 75 mg/m<sup>2</sup> plus cisplatin 100 mg/m<sup>2</sup> and 5-fluorouracil 1000 mg/m<sup>2</sup> a day for four days) or PF (intravenous cisplatin 100 mg/m<sup>2</sup> followed by 5-fluorouracil 1000 mg/m<sup>2</sup> a day for five days), the standard therapy. Both groups of patients were then

given weekly chemotherapy (carboplatin) together with radiation therapy for seven weeks, followed by surgery for those patients identified as candidates. The study was designed primarily to evaluate overall survival. Secondary endpoint included progression-free survival, response rates, toxicity, quality of life and clinical benefits.

Overall, the incidence of grade 3/4 toxicity was 65% in the Taxotere arm (TPF) compared to 62% in the group receiving cisplatin and fluorouracil (PF). Patients treated with TPF had more febrile neutropenia (12% vs 7%), neutropenic infection (12% vs 8%), and grade 3/4 neutropenia (84% vs. 56%), dizziness (4% vs. 2%), alopecia (4% vs 1%) and diarrhea (7% vs. 3%) than those in the PF group. Patients in the PF group had more grade 3/4 thrombocytopenia (11% vs. 4%), stomatitis (27% vs. 21%), lethargy (10% vs. 5%) and vomiting (10% vs. 8%). The incidence of other grade 3/4 events was similar between the two groups, such as nausea, anorexia and constipation.

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