

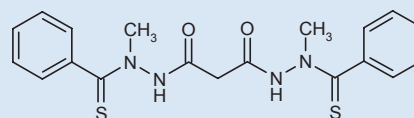
DRUGLINE

MOLECULE OF THE MONTH

*M*olecule of the Month is a regular feature in **DRUG NEWS & PERSPECTIVES** and on Prous Science's website (www.prous.com). One or more drugs, complete with chemical structure (where available), are selected on the basis of criteria that include the originality of the chemical structure, singularity of mechanism of action and progression through the R&D pipeline, as well as for being claimed for a new indication or where current therapies are inexistent or have proved unsatisfactory.

Elesclomol

Synta Pharmaceuticals' **elesclomol** (STA-4783) is a first-in-class small-molecule oxidative stress inducer. Elesclomol induces an oxidative stress response in cancer cells by inducing heat shock protein 70 (Hsp70), thereby inducing apoptosis and enhancing the activity of certain anticancer agents such as paclitaxel. In October, Synta signed a global collaboration agreement with GlaxoSmithKline for the joint development and commercialization of elesclomol. Under the terms of the agreement, the companies will share responsibility for development and commercialization of elesclomol in the U.S. and GSK will have exclusive responsibility for



Elesclomol

development and commercialization of the product outside the U.S. In addition, Synta will also be eligible to receive potential milestone payments for events leading to approval of elesclomol in metastatic melanoma, and further development and regulatory milestones across various indications. Elesclomol was granted fast-track designation by the FDA in 2006 for the treatment of metastatic melanoma.

In a double-blind, randomized, multicenter phase II trial reported last summer at ASCO, 81 patients with metastatic melanoma were randomized to receive paclitaxel (80 mg/m²) plus elesclomol (213 mg/m²) or paclitaxel alone for 3 weeks on a 4-week schedule. Intent-to-treat analysis revealed a median progression-free survival (PFS) of 3.68 and 1.84 months, respectively, for the combination versus paclitaxel alone and a response rate of 15.1% and 3.6%, respectively. Chemotherapy-naïve patients showed an even greater benefit on the combination, with a median PFS of 8.28 and 2.40 months, respectively, for the combination and paclitaxel alone. Moreover, several patients progressing on paclitaxel alone showed a delay in the time to progression when elesclomol was added. Adverse event rates were similar in both treatment groups, the most common events in the combination group being fatigue, alopecia, constipation, nausea, arthralgia, insomnia, diarrhea, anemia and hypoesthesia (O'Day, S. et al., 43rd Annu Meet Am Soc Clin Oncol (ASCO) (June 1-5, Chicago)

2007: Abst 8528; Kirshner, J. et al. 43rd Annu Meet Am Soc Clin Oncol (ASCO) (June 1-5, Chicago) 2007: Abst 14107).

In mid-November, Synta announced that the first patients had been treated in the SYMMETRYSM (Synta Metastatic Melanoma Elesclomol Trial) trial, a global, pivotal phase III clinical trial to evaluate the safety and efficacy of elesclomol in patients with stage IV metastatic melanoma. Synta has also successfully completed the special protocol assessment process, reaching agreement with the FDA on the design, conduct and planned analyses of the trial. The trial is enrolling patients with stage IV metastatic melanoma who have not received prior chemotherapy but who may have already been treated with non-chemotherapeutic agents such as biologics. Approximately 630 patients will be enrolled in the blinded, randomized, controlled study, which will be conducted at approximately 150 centers worldwide. Patients will be randomized (1:1) to elesclomol (213 mg/m²) plus paclitaxel (80 mg/m²) or paclitaxel alone (80 mg/m²) and will receive 3 weekly treatments and 1 week without treatment per each 4-week cycle. If tolerated, treatment will continue until disease progression. The control arm treatment, the combination arm treatment, the doses, the schedule and the primary endpoint of PFS, are the same as in the above phase IIb trial. There are two planned analyses for the primary endpoint of PFS: an interim analysis to assess safety and non-futility will be conducted

