



## **Threshold Pharmaceuticals Presents Encouraging Data From Clinical Trials of TH-302 for Solid Tumors**

REDWOOD CITY, Calif., May 30, 2009 (GlobeNewswire via COMTEX News Network) -- Threshold Pharmaceuticals, Inc. (Nasdaq:THLD) today announced clinical trial results related to its clinical stage hypoxia-activated prodrug, TH-302. The results were presented at the American Society for Clinical Oncology (ASCO) being held May 29 to June 2, 2009, at the Orange County Convention Center in Orlando, FL.

"The results from these studies are encouraging to us and to our advisors. The monotherapy trial demonstrated an attractive safety profile for TH-302 with minimal evidence of myelosuppression and, as previously reported, signs of therapeutic activity in small cell lung cancer and metastatic melanoma. In the combination therapy trials, TH-302 appears to be safely combined with labeled doses and schedules of gemcitabine, docetaxel, pemetrexed, and doxorubicin. Additionally, we have observed partial responses in combination with all four chemotherapies with some patients experiencing durable responses extending out over six months," said John Curd, M.D., Threshold's president and chief medical officer. "Though these clinical trials are in an early stage of development with a relatively small number of patients, we remain hopeful that TH-302 may provide an additional treatment option for patients living with cancer."

### **Monotherapy Results**

Results from thirty-one patients in a Phase 1 clinical trial evaluating the safety and preliminary efficacy of TH-302 in patients with advanced solid tumors are being presented at a poster session on May 30, 2009. The clinical trial was designed with an initial accelerated titration design followed by a standard dose escalation schema. The trial has completed the dose escalation component, reached the maximum tolerated dose (MTD) and is currently enrolling patients in the expansion phase of the trial at the MTD.

As previously reported, efficacy signals have been observed in two patients enrolled in this Phase 1 trial. One patient with refractory small cell lung cancer metastatic to the liver had a partial response (PR), as judged by RECIST (Response Evaluation Criteria In Solid Tumors), at their initial response assessment. The patient had received two cycles of TH-302 at 480 mg/m<sup>2</sup> and discontinued from the trial after treatment delay, unrelated to therapy, and disease progression. An additional patient with melanoma metastatic to the lung and liver had a RECIST PR after two cycles of TH-302 at 670 mg/m<sup>2</sup>. Fifty-eight percent of these 31 patients, who had previously failed a median of 3 prior therapies, achieved stable disease (SD) or better.

The first dose limiting toxicities for TH-302 were reported in the 670 mg/m<sup>2</sup> cohort: one patient developed grade 3 perianal and rectal ulcers that were considered related to study drug and a second patient developed grade 3 oral mucositis with dehydration. An intermediate dose of 575 mg/m<sup>2</sup> was evaluated and determined to be the MTD. Since nausea and vomiting increased at higher doses of TH-302, standard anti-emetic prophylaxis was recommended at doses that exceed 240 mg/m<sup>2</sup>. Skin and mucosal adverse events increased with dose, therefore there was an increase in dose delays or reductions at higher doses. Adverse events of grade 3 or greater were reported in 17 (55%) patients. Hematologic toxicity has been minimal with grade 2 neutropenia reported in two patients, grade 2 thrombocytopenia reported in one patient, and worsening anemia and lymphopenia in 14 (45%) and 20 (65%) patients, respectively.

In the expansion phase of the trial, which includes weekly doses of TH-302 at the MTD of 575 mg/m<sup>2</sup> the drug continues to be tolerated. There have been no new unexpected adverse events, with one of the 9 additional patients treated at the MTD of 575 mg/m<sup>2</sup> having a dose limiting toxicity (DLT) of grade 3 cheilitis (inflammation of the lips). The initial activity seen in small cell lung cancer and malignant melanoma was further supported by an additional PR in each indication in the initial patients treated in the dose expansion. Thus far, 2 of 5 patients with small cell lung cancer and 2 of 2 patients with metastatic melanoma in the monotherapy trial have achieved a RECIST criteria PR. Dosing once every three weeks is also being evaluated in this trial and dose escalation is ongoing. To date there has been one case of pancytopenia (a reduction in the number of red and white blood cells, as well as platelets) at 670 mg/m<sup>2</sup> and one DLT of grade 3 fatigue in the initial patient dosed at 940 mg/m<sup>2</sup>.

### **Combination Therapy Results**

The combination therapy results refer to two clinical trials, 402 and 403, that are investigating TH-302 in combination with four different chemotherapy regimens.

The 402 trial is a Phase 1/2, three arm, multicenter, dose escalation and dose expansion trial to determine the safety, efficacy and pharmacokinetics of TH-302 in combination with gemcitabine or docetaxel or pemetrexed in patients with advanced solid tumors. The trial was initiated in August 2008. The trial is expected to include up to 102 patients. The trial will include a dose

escalation phase followed by expansion at the MTD within four specific indications with 12 patients treated in each indication. To date, 30 patients in the dose-escalation phase have been assessed for response.

In the TH-302 plus gemcitabine arm, TH-302 is administered intravenously for 30 to 60 minutes on days 1, 8 and 15 of a 28 day cycle. Gemcitabine is dosed according to its package insert (1000 mg/m<sup>2</sup> on days 1, 8 and 15 of the 28 day cycle). Eleven patients have had tumor assessments, 3 of whom had a PR in the following cancers: ovarian, esophageal and pancreatic. The ovarian response was confirmed, meaning that the RECIST criteria PR was maintained through a subsequent assessment at least 28 days later; the esophageal and pancreatic PRs were unconfirmed. There are 6 patients with SD, 5 of whom have ongoing SD lasting for 3 to 8 cycles of chemotherapy.

In the TH-302 plus docetaxel arm, TH-302 is administered intravenously on days 1 and 8 of a 21 day cycle. Docetaxel is dosed according to its package insert (75 mg/m<sup>2</sup> on day 1 of the 21 day cycle). Nine patients have had tumor assessments, 2 of whom had a PR in non-small cell lung cancer and anal cancer with both confirmed and ongoing. There are 5 patients with SD, 3 of whom have ongoing SD lasting for 4 to 5 cycles.

In the TH-302 plus pemetrexed arm, TH-302 is administered intravenously on days 1 and 8 of a 21 day cycle. Pemetrexed is dosed according to its package insert (500 mg/m<sup>2</sup> on day 1 of the 21 day cycle). Ten patients have had tumor assessments, 2 of whom had a PR, both in non small cell lung cancer with both confirmed and ongoing after over six months on treatment. There are 5 patients with SD, 3 of whom have ongoing SD lasting for 5 to 9 cycles.

The 403 trial is a Phase 1/2, multicenter, dose escalation trial to determine the safety, efficacy and pharmacokinetics of TH-302 in combination with doxorubicin in patients with advanced soft tissue sarcoma. The trial was initiated in September 2008. The trial will include up to 36 patients (12-24 in the dose escalation arm). TH-302 is administered intravenously on days 1 and 8 of a 21 day cycle. Doxorubicin is dosed according to its package insert (75 mg/m<sup>2</sup> on day 1 of the 21 day cycle). Three patients have had tumor assessments, 2 of whom had a PR, one confirmed and one awaiting confirmation. The third patient has ongoing SD for 4 cycles.

In general, hematologic toxicity was higher than might be expected if chemotherapy was administered by itself, but was generally well tolerated and not dose limiting. Skin and mucosal toxicities were TH-302 dose dependent with a trend for increased frequency and greater severity at higher doses. Although these skin and mucosal toxicities have been bothersome in some patients and resulted in dose reductions or delays in therapy, these events have been reversible with an improvement in symptoms between cycles and following dose reductions. Investigations have been initiated to better understand and treat, or prevent, these toxicities.

A copy of the monotherapy poster presented at ASCO may be obtained by calling the Company.

#### About Threshold Pharmaceuticals

Threshold is a biotechnology company focused on the discovery and development of drugs targeting Tumor Hypoxia, the low oxygen condition found in microenvironments of most solid tumors. This approach offers broad potential to treat most solid tumors. By selectively targeting tumor cells, we are building a pipeline of drugs that hold promise to be more effective and less toxic to healthy tissues than conventional anticancer drugs. For additional information, please visit our website ([www.thresholdpharm.com](http://www.thresholdpharm.com)).

#### Forward-Looking Statements

Except for statements of historical fact, the statements in this press release are forward-looking statements, including statements regarding Threshold's product candidates, clinical trial results and plans, and potential therapeutic uses and benefits of our product candidates. These statements involve risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. Potential risks and uncertainties include, but are not limited to, Threshold's ability to enroll and complete its current and anticipated clinical trials, the time and expense required to conduct such clinical trials and analyze data, the possibility that results from these trials will not be confirmed, potential adverse side effects, issues arising in the regulatory or manufacturing process and the results of such clinical trials (including product safety issues and efficacy results). Further information regarding these and other risks is included under the heading "Risk Factors" in Threshold's Quarterly Report on Form 10-Q, which was filed with the Securities Exchange Commission on May 7, 2009 and is available from the SEC's website ([www.sec.gov](http://www.sec.gov)) and on our website ([www.thresholdpharm.com](http://www.thresholdpharm.com)) under the heading "Investors." We do not intend to update any forward-looking statement made in this news release.

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