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Threshold Pharmaceuticals Announces Interim Results from Tarloxotinib Program and its Plans to Focus on Evofosfamide and Earlier-Stage Opportunities

-- Tarloxotinib Primary Interim Response Rate Endpoint Achieved in Patients with Recurrent or Metastatic Squamous Cell Carcinoma of the Skin (SCCS) but not Achieved in Patients with Metastatic Squamous Cell Carcinoma of the Head and Neck (SCCHN) or Advanced EGFR-Mutant, T790M-Negative Non-Small Cell Lung Cancer (NSCLC); Company to Discontinue Investment in its Tarloxotinib Program --

-- Company to Focus on Evofosfamide in Combination with Immune Checkpoint Antibodies in Ongoing Collaboration with The University of Texas MD Anderson Cancer Center; Potential Registration of Evofosfamide in Japan, and IND-Enabling Studies of TH-3424 --

SOUTH SAN FRANCISCO, Calif., Sept. 29, 2016 (GLOBE NEWSWIRE) -- Threshold Pharmaceuticals, Inc. (Nasdaq:THLD), a clinical-stage biopharmaceutical company specializing in the development of novel pharmaceutical products and technologies for the treatment of cancer, today announced interim data from its two Phase 2 proof-of-concept clinical trials of tarloxotinib and outlined its plans to focus company resources on the more clinically-advanced evofosfamide program as well as an earlier-stage anticancer candidate, TH-3424.

"While the response observed in our squamous cell carcinoma of the skin study with tarloxotinib was encouraging, the overall results from the two studies didn't meet the activity thresholds required to move forward the molecule forward despite the promising results seen in preclinical translational studies," said Barry Selick, Ph.D., Chief Executive Officer of Threshold. "As a result, we are making no further investment in this program. Instead, we plan to build on the efforts of our collaborator, Dr. Michael Curran of The University of Texas MD Anderson Cancer Center, to demonstrate the potential therapeutic value of adding evofosfamide to immune checkpoint inhibition, to continue to pursue discussions with Japanese regulatory authorities regarding potential registration pathways for evofosfamide, and to advance TH-3424 through IND-enabling toxicology studies with the goal of reaching the clinic in 2017. We plan to provide additional operational guidance in the fourth quarter of 2016."

About the Tarloxotinib Program
Tarloxotinib bromide (the International Nonproprietary Name, previously known as TH-4000), or "tarloxotinib", is a prodrug designed to selectively release a covalent (irreversible) EGFR tyrosine kinase inhibitor under severe hypoxia, a feature of many solid tumors. The interim results from the two Phase 2 proof-of-concept clinical trials evaluating the efficacy and safety of tarloxotinib are outlined below. Both clinical trials utilized a Simon two-stage design to ensure adequate efficacy as measured by tumor response to justify continued enrollment. Tumor response was evaluated at baseline and every eight weeks using the Response Evaluation Criteria in Solid Tumors (RECIST). As a result, and taking into consideration the totality of the clinical data with tarloxotinib, enrollment in both Phase 2 clinical trials and further development of tarloxotinib will be discontinued.

Tarloxotinib in patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) or skin (SCCS) (TH-CR-602):

- In the first stage of the SCCS arm of the trial, a confirmed partial response was observed in 1 of 7 patients. According to the study design, the response rate was sufficient to expand the trial to evaluate additional patients.
- However, of the 22 SCCHN patients who were assessed, although 8 achieved stable disease, none achieved a confirmed partial response.

Tarloxotinib in patients with EGFR-mutant, T790M-negative, advanced non-small cell lung cancer (NSCLC) (TH-CR-601):

- In the first stage of the trial, a response rate greater than or equal to 4 out of 19 patients was the threshold for expansion and continuation of the trial. Per protocol response is defined as tumor shrinkage (a partial or complete response).
- Although 7 of 21 assessed patients achieved stable disease, no patients achieved a confirmed partial response.

Threshold licensed exclusive worldwide rights to tarloxotinib from the University of Auckland, New Zealand, in September 2014.

About the Evofosfamide Program
Evofosfamide (previously known as TH-302) is an investigational hypoxia-activated prodrug of a bis-alkylating agent that is preferentially activated under severe hypoxic tumor conditions, a feature of many solid tumors. On December 6, 2015, the Company announced the outcomes of two Phase 3 studies (MAESTRO and TH-CR-406/SARC021) of evofosfamide stating that neither study met its primary endpoint. However, the Phase 3 trial (MAESTRO) data demonstrated meaningful improvement in overall survival in a subgroup of 116 patients from Japan, in which the risk of death was reduced by 48 percent for patients on the treatment arm compared to patients on the control arm. In addition, translational data evaluating the role of hypoxia in mediating treatment resistance to cancer immunotherapy conducted at The University of Texas MD Anderson Cancer Center suggests that evofosfamide may play a role in improving the efficacy of "checkpoint antibodies" such as ipilumimab. The Company's evofosfamide efforts are as follows:

- Plan to initiate a Phase I clinical trial with four disease specific expansions of evofosfamide in combination with immune checkpoint antibodies in collaboration with researchers and clinicians at The University of Texas MD Anderson Cancer Center.
- Pursue discussions with Japanese regulatory authorities regarding potential registration pathways for evofosfamide for treatment of pancreatic cancer.

About the TH-3424 Program
TH-3424 is the Company's new, small-molecule drug candidate, discovered at Threshold, being evaluated for the potential treatment of hepatocellular (liver) cancer (HCC), castrate resistant prostate cancer (CRPC), T-cell acute lymphoblastic leukemias (T-ALL), and other cancers expressing high levels of aldo-keto reductase family 1 member C3 (AKR1C3). Tumors overexpressing AKR1C3 can be resistant to radiation therapy and chemotherapy. TH-3424 is a prodrug that selectively releases a potent DNA cross-linking agent in the presence of AKR1C3. Preliminary nonclinical toxicology studies suggested an adequate therapeutic index that the Company believes warrants continued development as follows:

- Continue to conduct Investigational New Drug (IND)-enabling toxicology studies of TH-3424 in collaboration with Ascenta Pharmaceuticals, Ltd.

A comprehensive summary of TH-3424's preclinical profile including biochemical, *in vitro* cell-based, and *in vivo* animal-based characterization of its pharmacological properties was presented at the 2016 Annual Meeting of the American Association for Cancer Research (AACR) in April 2016. Copies of the poster are available at the Company's website at: http://www.thresholdpharm.com/scientific_publications.

As a result of the Company's focus on evofosfamide and TH-3424, Stewart M. Kroll, the Company's Chief Operating Officer, and the members of the biostatistics and data management group will be departing the company. Kristen Quigley, Executive Director of Clinical Operations at Threshold, will retain leadership of all clinical trial operational responsibilities. The Company estimates that it will incur a one-time charge in the fourth quarter of approximately $0.9 million related to the reduction in headcount, including severance, benefits and related costs. This charge is expected to include approximately $300,000 of non-cash expense related to the extension of the post-termination exercise period for the outstanding vested stock options for the affected employees.

About Threshold Pharmaceuticals
Threshold is a clinical-stage biopharmaceutical company focused on the discovery and development of drugs and diagnostic agents targeting tumor hypoxia, the low oxygen condition found in microenvironments of most solid tumors as well as the bone marrows of some hematologic malignancies. This approach offers broad potential to treat a variety of cancers. 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 the Company's website.

Forward-Looking Statements
Except for statements of historical fact, the statements in this press release are forward-looking statements, including all statements regarding the therapeutic potential of evofosfamide and TH-3424; Threshold's plans to focus its resources on evofosfamide and TH-3424; anticipated development activities related to evofosfamide and TH-3424, and the anticipated timing thereof; Threshold's plans to continue to pursue discussions regarding potential registration pathways for evofosfamide in Japan, and the potential for evofosfamide to be approved for marketing in Japan; and Threshold's estimates of the total and non-cash charges it expects to occur in connection with the reduction in employees, and the anticipated timing thereof. 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: the difficulty and uncertainty of pharmaceutical product development, including the risks that the design of, or data collected from, the planned Phase I clinical trial of evofosfamide with immune checkpoint inhibitors may be inadequate to demonstrate safety or sufficient efficacy, or otherwise may be insufficient to support any further development of evofosfamide, and that Threshold's toxicology studies of TH-3424 may not demonstrate sufficient safety to support an investigational new drug application and to further the development of TH-3424 into the clinic; the uncertain and time-consuming regulatory approval process, including the risk that data from the completed MAESTRO clinical trial will not be sufficient to support the approval of evofosfamide for the treatment of patients with pancreatic cancer in Japan; Threshold's need for and the availability of

resources to develop evofosfamide and TH-3424 and to support Threshold's operations, including the risks that Threshold's currently-available resources may be insufficient to further current development plans for evofosfamide and TH-3424 and that Threshold will otherwise need to raise substantial additional capital in order to advance the clinical development of evofosfamide and TH-3424; the risks that Threshold could determine to abandon the development of evofosfamide and TH-3424 as a result of inadequate resources, negative or inconclusive clinical trial or toxicology study results, the failure to obtain regulatory approval of evofosfamide in Japan, or otherwise; and risks related to Threshold's ability to implement the reduction in employees as currently anticipated, the impact of such reduction on Threshold's business and unanticipated charges not currently contemplated that may occur as a result of such reduction. Further information regarding these and other risks is included under the heading "Risk Factors" in Threshold's Quarterly Report on Form 10-Q, which has been filed with the Securities and Exchange Commission on August 1, 2016 and is available from the SEC's website (www.sec.gov) and on our website (www.thresholdpharm.com) under the heading "Investors." We undertake no duty to update any forward-looking statement made in this news release.

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