Theratechnologies TH1902 Study Published in Pharmaceutics Demonstrates Inhibition of Human Sortilin (SORT1)-Positive Ovarian and Triple-Negative Breast Cancer Stem-Like Cells and Tumor Growth

September 12, 2022

- *Researchers report superior anticancer activity against cancer stem-like cells with TH1902, compared to unconjugated docetaxel*
- *First evidence for TH1902 targeting of human breast and ovarian cancer stem-like cells in vitro and in vivo*
- *Paper highlights potential mechanisms by which TH1902 can bypass underlying causes of resistance to docetaxel that can contribute to treatment failure and disease recurrence*

MONTREAL, Sept. 12, 2022 (GLOBE NEWSWIRE) -- Theratechnologies Inc. (“Theratechnologies” or the “Company”) (TSX: TH) (NASDAQ: THTX), a biopharmaceutical company focused on the development and commercialization of innovative therapies, today announced the publication of a preclinical study demonstrating the *in vitro* and *in vivo* efficacy of TH1902, an investigational sortilin (SORT1)-targeted peptide-drug conjugate, in inhibiting ovarian cancer and triple-negative breast cancer (TNBC) stem-like cells’ (CSCs) tumor growth. The study, published as part of the special issue of *Pharmaceutics* “Targeting Drug Resistance and Metastatic Pathways for Cancer Therapy”, reports that TH1902 appears to exert anticancer activity that is superior to unconjugated docetaxel in preclinical models, in part by circumventing the chemoresistance phenotype that is often responsible for treatment failure and cancer recurrence.

SORT1 is a scavenger receptor protein that binds to circulating proteins and peptides prior to their intracellular internalization. It is upregulated in several types of cancer. TH1902, now being investigated across at least eight solid tumor types in a Phase 1 clinical trial, has been shown in preclinical models to recognize and exploit SORT1 function, to efficiently trigger *in vitro* cell death through apoptosis, to inhibit *in vitro* cell cycling by trapping cells into the G2/M phase, and to inhibit *in vivo* growth of CSCs from gynecological cancers including ovarian cancer and TNBC. The *Pharmaceutics* paper provides the first evidence for TH1902 targeting of human breast and ovarian CSCs, both *in vitro* and *in vivo*. The limited ability of docetaxel, a widely used cancer chemotherapeutic agent, to inhibit the growth of CSCs from TNBC and ovarian cancer may be one mechanism of resistance and limit the effectiveness of the drug in controlling tumor growth and spread.

“The development of resistance to chemotherapy is a major obstacle to successful anticancer treatment, and the presence of cancer stem-like cells within tumors is believed to play an important role in that process,” said Dr. Christian Marsolais, Chief Medical Officer, Theratechnologies. “The *Pharmaceutics* publication provides important insights into the ability of TH1902 to inhibit the growth of these cells.”

In the *Pharmaceutics* paper, researchers at Theratechnologies and the Molecular Oncology Laboratory at Université du Québec à Montréal (UQAM) describe the activity of TH1902 against CSCs and its ability to circumvent some of the known resistance phenotypes associated with CSCs. Their findings suggest that TH1902 targets cancer cells overexpressing the sortilin receptor – an effect that is absent in healthy cells. Additionally, at doses equivalent to docetaxel, single-agent TH1902 exhibited superior efficacy against breast and ovarian CSCs, compared to docetaxel alone. Finally, when combined with carboplatin in an ovarian tumor model, the efficacy of TH1902 was also superior to that of paclitaxel- or docetaxel-carboplatin combinations. In TNBC and ovarian CSCs animal models, TH1902 decreased tumor growth by 80%, compared to roughly 35% in docetaxel-treated mouse models.

“Given our enhanced understanding of the association of SORT1 and cancer resistance to chemotherapy, using TH1902 to exploit SORT1 function within cancer stem-like cells may further offer a path to bypassing the chemoresistance phenotype often responsible for cancer recurrence,” stated Dr. Borhane Annabi, Professor of Biochemistry and Chair in Cancer Prevention and Treatment at UQAM. “TH1902 thus appears to offer a promising strategy for targeting cancer cells that exhibit plasticity, metastatic potential, and resistance to chemotherapy.”

The U.S. Food and Drug Administration (FDA) granted TH1902 Fast-Track Designation in February 2021. The basket portion of the Phase 1a/1b trial is currently enrolling at sites across the United States (TH1902 in Patients With Advanced Solid Tumors - Full Text View - ClinicalTrials.gov).

About TH1902 and SORT1+ Technology™

Theratechnologies is currently developing a platform of proprietary peptides called SORT1+ Technology™ for cancer drug development targeting SORT1 receptors. The SORT1 receptor plays a significant role in protein internalization, sorting and trafficking. It is highly expressed in cancer cells compared to healthy tissue, which makes SORT1 an attractive target for cancer drug development. Expression of SORT1 is associated with aggressive disease, poor prognosis and decreased survival. It is estimated that the SORT1 receptor is expressed in 40% to 90% of cases of endometrial, ovarian, colorectal, triple-negative breast and pancreatic cancers.

TH1902 is currently Theratechnologies’ lead investigational peptide-drug conjugate (PDC) candidate for the treatment of cancer derived from its SORT1+ Technology™. It is the company’s proprietary peptide linked to docetaxel – a commonly used cytotoxic agent used to treat many cancers. The FDA granted fast track designation to TH1902 as a single agent for the treatment of all sortilin-positive recurrent advanced solid tumors that are refractory to standard therapy.

About Theratechnologies

Theratechnologies (TSX: TH) (NASDAQ: THTX) is a biopharmaceutical company focused on the development and commercialization of innovative therapies addressing unmet medical needs. Further information about Theratechnologies is available on the Company's website at www.theratech.com, on SEDAR at www.sedar.com and on EDGAR at www.sec.gov.

Forward-Looking Information

This press release contains forward-looking statements and forward-looking information (collectively, “Forward-Looking Statements”), within the meaning of applicable securities laws, that are based on our management’s beliefs and assumptions and on information currently available to our management. You can identify Forward-Looking Statements by terms such as "may", "will", "should", "could", “would”, "outlook", "believe", "plan", "envisage", "anticipate", "expect" and "estimate", or the negatives of these terms, or variations of them. The Forward-Looking Statements contained in this press release include, but are not limited to, statements regarding the development of a treatment for patients with Sortilin positive solid tumors, the development of our SORT1+ Technology™ platform and the conduct and recruitment of patients for the basket trial using TH1902. Although the Forward-Looking Statements contained in this press release are based upon what the Company believes are reasonable assumptions in light of the information currently available, investors are cautioned against placing undue reliance on these statements since actual results may vary from the Forward-Looking Statements. Certain assumptions made in preparing the Forward-Looking Statements include that: the pre-clinical results obtained using TH1902 will be replicated into humans, we will be able to continue recruiting patients to conduct the basket trial using TH1902, no dose limiting toxicities will be observed in patients comprising the basket trial, our manufacturer of TH1902 will be able to supply the required quantity of TH1902 in due time to advance the basket trial, and we will see signs of efficacy of TH1902 in the conduct of the basket trial across all patients forming part of the trial. Forward-Looking Statements assumptions are subject to a number of risks and uncertainties, many of which are beyond Theratechnologies’ control that could cause actual results to differ materially from those that are disclosed in or implied by such Forward-Looking Statements. These risks and uncertainties include, but are not limited to, our inability to recruit patients for the conduct of the basket trial, the observation of adverse safety issues, the lack of demonstration of efficacy in many or in all of the patients forming part of the trial, issues regarding the manufacture and supply of TH1902, and conflicts with third party suppliers in the conduct of our basket trials. We refer current and potential investors to the “Risk Factors” section of our Annual Information Form dated February 23, 2022 available on SEDAR at www.sedar.com and on EDGAR at www.sec.gov as an exhibit to our report on Form 40-F dated February 24, 2022 under Theratechnologies’ public filings for additional risks related to the Company. The reader is cautioned to consider these and other risks and uncertainties carefully and not to put undue reliance on Forward-Looking Statements. Forward-Looking Statements reflect current expectations regarding future events and speak only as of the date of this press release and represent our expectations as of that date. We undertake no obligation to update or revise the information contained in this press release, whether as a result of new information, future events or circumstances or otherwise, except as may be required by applicable law.

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