Theratechnologies' Sudocetaxel Zendusortide ASCO 2024 Presentation Demonstrates Signs of Long-Term Efficacy and Manageable Safety Profile in Patients with Solid Tumors

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- *Poster highlights durable disease stabilization lasting beyond treatment completion*
- *Results suggest a unique, multimodal mechanism of action that differs from other cancer therapeutics*
- *Favorable tolerability sets stage for Part 3 (dose optimization) of Phase 1 trial, already underway*

MONTREAL, May 23, 2024 (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 Phase 1 data demonstrating signs of long-term efficacy and a manageable safety profile of its lead investigational peptide drug conjugate (PDC) candidate, sudocetaxel zendusortide (TH1902), in patients with solid tumors. The data will be presented in a poster session on June 1, 9:00 AM-12:00 PM CDT (abstract #3081, poster board #226) at the 2024 American Society of Clinical Oncology (ASCO) annual meeting, which is taking place May 31-June 4, 2024, in Chicago, IL.

In an updated analysis from Parts 1 and 2 of an ongoing Phase 1 clinical trial, sudocetaxel zendusortide induced durable disease stabilization (up to 45 weeks) lasting beyond treatment completion. The results suggest a unique, multimodal mechanism of action distinct from other cancer therapeutics, including induction of immune cell infiltration even in "cold" tumor models, inhibition of vasculogenic mimicry, targeting of chemotherapy-resistant cancer stem cells, and activation of the cGAS/STING immune pathway, among other actions. Additionally, investigators observed an early efficacy signal primarily in female cancers (ovarian cancer, endometrial cancer, triple-negative breast cancer [TNBC]), with seven of 16 participants (44%) achieving a clinical benefit rate (complete response + partial response + stable disease), as confirmed via Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. The poster presentation, which constitutes the first report of long-term efficacy, safety, and pharmacokinetic (PK) data from the Phase 1 study, also suggests that sudocetaxel zendusortide has a manageable safety profile when dosed at 300mg/m^2, with few Grade 3 adverse events (AEs).

"The initial long-term Phase 1 data further validate and expand upon the preliminary evidence of antitumor activity with sudocetaxel zendusortide in individuals with solid tumors," said Ira Winer, M.D., Ph.D., FACOG, a member of the Gynecologic Oncology and Phase 1 Clinical Trials Multidisciplinary Teams at Karmanos Cancer Center and Associate Professor of Oncology at Wayne State University. "It is highly unusual to see such long-lasting disease stabilization even after treatment cessation in patients with advanced disease. These updated data provide an informative baseline as we seek to optimize the dose of this novel peptide-drug conjugate in patients with platinum-resistant ovarian cancer in the next stage of the Phase 1 trial."

Study details

Dr. Winer and colleagues conducted an analysis of the long-term efficacy, safety, and PK of sudocetaxel zendusortide from Parts 1 and 2 of the Phase 1 trial, which seeks primarily to characterize the agent's safety and tolerability. Part 1 (modified intrapatient dose escalation, n=18) included patients with recurrent/refractory advanced tumors (all comers) with no limit on the number of previous therapies, including taxanes. Part 2 (dose expansion, n=18) included patients with cancers with known high expression of the sortilin (SORT1) receptor, including ovarian cancer, endometrial cancer, TNBC, and melanoma. Part 3 (dose optimization) of the Phase 1 trial, in patients with advanced ovarian cancer that is no longer platinum-sensitive, is ongoing.

In a sub-analysis of efficacy in 16 patients with TNBC, ovarian, and endometrial cancers, seven patients exhibited RECIST 1.1-confirmed clinical benefit, with six patients achieving long-term stabilization of disease (up to a maximum of 45 weeks in duration) even after drug discontinuation in some patients. One patient with ovarian cancer had an overall partial response (PR), with a RECIST 1.1-confirmed complete response (CR) in target lesions, and stabilization of disease (SD) in non- target lesions, lasting up to 24 weeks from initiation of treatment. In addition, one patient with endometrial cancer, whose dose was escalated from 60 mg/m^2 to 360 mg/m^2 in Part 1, completed a total of 11 treatment cycles; this patient's disease remained stable throughout eight months of treatment, up to the time of consent withdrawal. All 16 patients had prior exposure to taxane-containing regimens (range: 1-6). The investigators characterized the prolonged stabilization of disease as clinically significant in this heavily pretreated patient population, which typically experiences recurrence during or shortly after treatment discontinuation.

Sudocetaxel zendusortide has a manageable safety profile, with most treatment-related AEs rated as mild to moderate in severity and managed with standard supportive care or dose reductions. Investigators noted that the low number of Grade 3 AEs compares favorably to the published literature for unconjugated docetaxel.

PK measures showed that exposure to free docetaxel was much lower than that for sudocetaxel zendusortide, a finding that may explain the lower incidence and severity of AEs seen with sudocetaxel zendusortide versus docetaxel alone. The maximum concentration (Cmax) of sudocetaxel zendusortide was 30.4 micromolar (µM), compared to 0.58 µM for free docetaxel. The 24-hour area under the curve (AUC_{24}) for sudocetaxel zendusortide was 74.8 nanomoles per hour per liter (h.nmol/mL), versus 3.1 h.nmol/mL for free docetaxel. The free docetaxel/sudocetaxel zendusortide AUC ratio was less than 1% up to 300 mg/m^2, suggesting that most docetaxel remains associated with the peptide over the period of analysis.

"One year after our presentation of preliminary evidence of antitumor activity at the 2023 ASCO annual meeting, the Phase 1 sudocetaxel zendusortide trial continues to yield important information about long-term efficacy, safety, and pharmacokinetics of this promising peptide-drug

conjugate," commented Christian Marsolais, Ph.D., Senior Vice President and Chief Medical Officer at Theratechnologies. "These latest data leave us well positioned for Part 3 of the study, in which we aim to optimize the dose to see further signs of efficacy while limiting toxicity. We look forward to sharing more data from this ongoing trial in the future."

About Sudocetaxel Zendusortide (TH1902) and SORT1+ Technology™

Sudocetaxel zendusortide is a first-of-its-kind sortilin receptor (SORT1)-targeting PDC, and the first compound to emerge from the Company's broader licensed oncology platform. A new chemical entity, sudocetaxel zendusortide employs a cleavable linker to conjugate (attach) a proprietary peptide to docetaxel, a well-established cytotoxic chemotherapeutic agent used to treat many cancers. The FDA granted Fast Track designation to sudocetaxel zendusortide as a single agent for the treatment of all sortilin-positive recurrent advanced solid tumors that are refractory to standard therapy. Sudocetaxel zendusortide is currently being evaluated in a Phase 1 clinical trial.

Theratechnologies has established the SORT1+ Technology™ platform as an engine for the development of PDCs that target SORT1, which is expressed in multiple tumor types. SORT1 is a "scavenger" receptor that plays a significant role in protein internalization, sorting, and trafficking. Expression of SORT1 is associated with aggressive disease, poor prognosis, and decreased survival. It is estimated that SORT1 is expressed in 40% to 90% of endometrial, ovarian, colorectal, triple-negative breast (TNBC), and pancreatic cancers, making this receptor an attractive target for anticancer drug development.

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.sedarplus.ca and on EDGAR at www.sec.gov. Follow Theratechnologies on Linkedin and Twitter.

Forward-Looking Information

This press release contains forward-looking statements and forward-looking information (collectively, the "Forward-Looking Statements") within the meaning of applicable securities laws, that are based on management's beliefs and assumptions and on information currently available to it. You can identify forward-looking statements by terms such as "may", "will", "should", "could", "promising", "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 conduct of Part 3 of the Phase 1 clinical trial using sudocetaxel zendusortide, the data on signs of long-term efficacy of sudocetaxel zendusortide and safety of sudocetaxel zendusortide, and the further development of the Company's lead PDC, sudocetaxel zendusortide. 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 contained in this press release. These assumptions include, without limitation, that the Company will successfully complete Part 3 of the Phase 1 clinical trial, that signs of long-term efficacy and safety will be observed in such Part 3 of the Phase 1 clinical trial and no untoward side effects will be reported, and the further development of the Company's lead PDC, sudocetaxel zendusortide, will continue generating reportable data and will be successful. Forward-Looking Statements assumptions are subject to a number of risks and uncertainties, many of which are beyond the Company's 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, the lack of observation of signs of efficacy and safety results during Part 3 of the Phase 1 clinical trial, the reporting of adverse side effects from the use of sudocetaxel zendusortide leading to a halt of the clinical trial and, eventually, the Company's further development of its lead PDC, sudocetaxel zendusortide, and additional PDCs. We refer current and potential investors to the "Risk Factors" section (Item 3.D) of our Form 20-F dated February 21, 2024, available on SEDAR+ at www.sedarplus.ca and on EDGAR at www.sec.gov under Theratechnologies' public filings. 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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