



Theratechnologies Announces Publication in *Frontiers in Immunology* that Deepens Understanding of Sudocetaxel Zendusortide (TH1902) Molecular Mechanism of Action

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- *Publication pinpoints triggering of cGAS/STING pathway to activate immune defense mechanisms, as well as potentiation of anti-PD-L1 immune-mediated tumor cell killing, in triple-negative breast cancer xenograft model*
- *Weekly administration of single agent sudocetaxel zendusortide demonstrated superior tumor growth inhibition and immune cell infiltration compared to docetaxel in “cold” murine tumor model*
- *Preclinical results suggest new approaches for broadening immunotherapy utilization in combination with sudocetaxel zendusortide*

MONTREAL, Feb. 20, 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 the publication of a peer-reviewed article in *Frontiers in Immunology* that enhances understanding of the molecular mechanism of action of sudocetaxel zendusortide (also known as TH1902) as a potential anticancer treatment. Sudocetaxel zendusortide is an investigational, first-in-class peptide-drug conjugate (PDC) that targets the sortilin receptor (SORT1) and expedites the internalization and delivery of the cytotoxic payload (docetaxel) directly into cancer cells.

The article, “**Sudocetaxel Zendusortide (TH1902) triggers the cGAS/STING pathway and potentiates anti-PD-L1 immune-mediated tumor cell killing**” appears in the “Cancer Immunity and Immunotherapy” section of the February (Volume 15) issue of the journal. It reports on preclinical research in which sudocetaxel zendusortide induced complete and prolonged tumor regression in a triple-negative breast cancer (TNBC)-derived xenograft tumor model and demonstrated tumor regression associated with growth inhibition and immune cell infiltration in a “cold” murine (syngeneic) tumor model. Additionally, combining sudocetaxel zendusortide with an anti-PD-L1 checkpoint inhibitor led to increases in tumor growth inhibition and median animal survival.

“The results published in *Frontiers in Immunology* demonstrate that sudocetaxel zendusortide exerts its antitumor activity, in part, through modulation of the immune tumor microenvironment,” said Christian Marsolais, Ph.D., Senior Vice President and Chief Medical Officer at Theratechnologies, and one of the paper’s co-authors. “Our findings reinforce that combining this novel peptide-drug conjugate with anti-PD-L1 checkpoint inhibitor therapy may yield improved clinical outcomes, with potentially profound implications for patients across various cancer types.”

“An important aspect of our research is the activation of an antitumor immunity process through involvement of the cGAS/STING pathway, a key regulator in the cancer-immunity cycle,” commented Prof. Borhane Annabi, Chair in Cancer Prevention and Treatment in the Chemistry Department at the Université du Québec à Montréal, and a co-author of the *Frontiers in Immunology* paper. “Although the animal tumor model we worked with is considered a non-immunogenetic, or ‘cold’ tumor model, we observed a net increase in leukocyte infiltration within sudocetaxel zendusortide-treated tumors, especially for tumor-infiltrating lymphocytes and tumor-associated macrophages. This realization supports the rationale for further exploration of the combination of sudocetaxel zendusortide with immunotherapy.”

The article can be accessed online [here](#).

About Immunotherapy in Cold and Hot Tumors

Immunotherapies have significantly improved the treatment of cancer. Researchers continue to explore the power of the immune system to find and destroy cancer cells. “Hot” tumors show signs of inflammation, meaning the tumor has already been infiltrated by immune cells rushing to fight the cancerous cells. Only a few types of cancers are considered to be hot. “Cold” tumors have not yet been infiltrated with T cells. This signals that the immune response is not working, making it difficult to provoke an immune response with immunotherapies. Most cancers of breast, ovary, prostate, pancreas, and brain (e.g., glioblastoma [GBM]) are cold tumors, and are largely treated with traditional therapies like radiation and chemotherapy. As a result, researchers have sought to understand how to turn cold tumors hot by reversing the suppressive microenvironment surrounding cold tumors and by attracting more of the “right” anti-tumor lymphocytes.

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. As 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 in individuals with advanced ovarian cancer.

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 [X](#) (formerly 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 combination of sudocetaxel zendusortide with anti-PD-L1 checkpoint inhibitor therapy which may yield improved clinical outcomes, the potential treatment of various types of cancer with sudocetaxel zendusortide, the development of PDCs resulting from the SORT1+ Technology™ platform and our estimates regarding the expression of SORT1 in various types of cancer. 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 results observed in pre-clinical testing will be replicated into humans, sudocetaxel zendusortide will be able to treat various types of cancer, the Company will be successful in developing additional PDCs from the SORT1+ Technology™ platform and positive safety and efficacy results will be observed from the current Phase 1 clinical trial studying sudocetaxel zendusortide. 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 inability of sudocetaxel zendusortide to demonstrate efficacy results when used in human subjects, limitations in the types of cancer for which sudocetaxel zendusortide could be used and limitations in the capacity of the Company to develop new PDCs. We refer current and potential investors to the "Risk Factors" section of our Annual Information Form dated February 27, 2023, available on SEDAR+ at www.sedarplus.ca and on EDGAR at www.sec.gov as an exhibit to our report on Form 40-F dated February 28, 2023, 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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