Theratechnologies Data Presentations at AACR 2023 Showcase Potential of Sudocetaxel Zendusortide as a Single Agent and in Combination with other Anticancer Therapies

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- *Preclinical data suggests that sudocetaxel zendusortide can induce immune cell infiltration in "cold" tumors and improve efficacy for PD-L1 checkpoint inhibitor*
- *Additional in vivo data demonstrate significant activity of sudocetaxel zendusortide against SORT1+ triple-negative (TNBC) and HER2+ breast cancers*
- *High expression of SORT1 in multiple solid tumor types further supports rationale for targeted therapy with sudocetaxel zendusortide*

MONTREAL, April 18, 2023 (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 presented preclinical data that demonstrate the potential utility of its lead investigational peptide drug conjugate (PDC) candidate, sudocetaxel zendusortide (TH1902) -- both as a single agent and in combination with other anticancer therapies -- in targeting tumors that express the sortilin (SORT1) receptor. The new data were presented in poster sessions at the 2023 annual meeting of the American Association for Cancer Research (AACR) in Orlando, Fla.

In two separate posters presented at AACR, sudocetaxel zendusortide demonstrated increased anti-cancer efficacy in combination with programmed cell death-ligand 1 (PD-L1) checkpoint inhibitor therapy in a melanoma mouse model; and as a single agent against SORT1-positive TNBC or HER2+ breast cancer models, resulting in complete tumor regression. Furthermore, sudocetaxel zendusortide generated superior activity in comparison to a combination of Herceptin and docetaxel in the HER2+ Herceptin-resistant tumor model. A third poster showed high expression of SORT1 in multiple tumor types, compared to healthy tissues, bolstering the rationale for SORT1 inhibition as a potential therapeutic approach.

"It's particularly exciting to see in the melanoma animal model that using the SORT1 receptor with sudocetaxel zendusortide in combination with immunotherapy shows greater tumor inhibition and longer survival compared to immunotherapy alone," said Christian Marsolais, Ph.D., Senior Vice President and Chief Medical Officer of Theratechnologies. "Collectively our three AACR poster presentations reinforce the potential of sudocetaxel zendusortide, on its own and in combination, to enable targeted delivery of anticancer therapy. We look forward to further characterizing this novel investigational agent as we seek partners and advance our clinical development program."

Induction of immune cell infiltration and improvement of anti-tumoral activity of anti-PD-L1 checkpoint inhibitor

In the first AACR poster, researchers reported that sudocetaxel zendusortide induces immune cell infiltration and potentiates the anti-tumoral activity of anti-PD-L1 therapy in a melanoma mouse model. Surprisingly, in this non-immunogenic, or "cold," tumor type, immunohistochemistry (IHC) analysis showed a net increase in total leukocyte infiltration within sudocetaxel zendusortide-treated tumors compared with docetaxel-treated tumors, especially with regard to marked increases in tumor-infiltrating lymphocytes and tumor-associated macrophages. Researchers also observed elevated cytotoxic T and natural killer cells in the sudocetaxel zendusortide-treated tumors.

Next, the researchers halved the doses of sudocetaxel zendusortide and docetaxel and combined each agent with an anti-PD-L1 checkpoint inhibitor. Notably, sudocetaxel zendusortide alone showed greater tumor growth inhibition than docetaxel, anti-PD-L1 or anti-PD-L1/docetaxel combination. In addition, the sudocetaxel zendusortide/anti-PD-L1 combination significantly increased tumor growth inhibition and median survival over either anti-PD-L1 or sudocetaxel zendusortide as single agents (21 days compared to 2.5 and 12.5 days, respectively). The investigators attributed the superior anticancer activity of sudocetaxel zendusortide over docetaxel, in part, to the modulation of infiltrating immune cells within the tumor microenvironment.

"Our data are the first to demonstrate that immune cell infiltration patterns could play a pivotal role in the sudocetaxel zendusortide-associated anti-tumoral response," commented Dr. Marsolais. "Given that preclinical results showed a statistically significant improvement in the efficacy of an anti-PD-L1 inhibitor for tumors treated with sudocetaxel zendusortide in contrast to docetaxel, we are hopeful that further research with combination therapy may also lead to improved clinical outcomes."

Breast cancer data

The second AACR poster reported high expression of SORT1 in several TNBC and HER2-positive breast cancer cell lines as well as in more than 60-75% of cases from commercial breast cancer tissue microarrays. Researchers further observed that SORT1 is involved for both cell surface recognition and internalization of the peptide, TH19P01, without payload. Fluorescence microscopy showed rapid uptake and co-localization of both TH19P01 and sudocetaxel zendusortide in the late endosomal and lysosomal compartments at the perinuclear region, indicating that both compounds are internalized through a receptor-mediated endocytosis (a cellular process in which substances are brought into the cell) pathway.

In a murine MDA-MB-231 TNBC tumor model, weekly administration of sudocetaxel zendusortide at a dose (35 mg/kg) equivalent to the maximally tolerated dose (MTD) of docetaxel (15 mg/kg) led to complete and sustained tumor regression, while docetaxel only inhibited tumor growth by half. Furthermore, in mice bearing HER2-positive breast tumor tissue grafts, sudocetaxel zendusortide induced complete tumor regression, unlike docetaxel, Herceptin and Herceptin/docetaxel combination.

Based on the demonstrated high anticancer properties of sudocetaxel zendusortide against SORT1-positive TNBC and Herceptin-resistant HER2-positive breast cancer models, as well as its higher tolerability compared to docetaxel, the researchers concluded that sudocetaxel

zendusortide can be a promising avenue for further evaluation in the treatment of patients with SORT1-positive breast cancers.

SORT1 expression data

To better understand SORT1 expression, the Theratechnologies research team used IHC to screen 19 cancer tissue microarrays with 1394 evaluable cancer cores. They scored each cancer core using an H-score ranging from 0 to 300, whereby a score of 0 indicates no cell staining for SORT1 and a score of 300 corresponds to strong SORT1 staining in all cells. The table below summarizes the percentage of cancer cores with moderate to high SORT1 expression (defined as H-score ≥ 100) as well as the average H-score for each cancer type evaluated:

Cancer type	No. evaluable cores	% with H-score ≥ 100	Average H-score
Endometrial	94	90	197
Thyroid	108	92	188
Melanoma	155	83	184
Bladder	118	81	156
Testis	40	100	116
Lung	152	58	112
• Small cell lung	*44*	*95*	*183*
• Non-small cell lung	*108*	*43*	*82*
Small intestine	54	63	102
Eye	26	46	83
Cervix	376	38	75
Prostate	150	39	71
Liver	121	23	52

Results of the three presentations at AACR 2023 validate and build upon previous reports on the pattern and prevalence of SORT1 expression in common tumor types, underscoring the promise of SORT1 as a target for the delivery and internalization of anticancer therapeutic agents.

Full posters can be found on Theratechnologies' website.

About Immunotherapy in Cold and Hot Tumors

Immunotherapies have significantly improved the treatment of cancer. Researchers continue to explore the power of the body's own 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 (GBM) are cold tumors, and are largely treated with traditional therapies like radiation and chemotherapy. As a result, much research has been done to understand how to turn cold tumors hot by reversing the suppressive microenvironment surrounding cold tumors and attracting more of the right anti-tumor lymphocytes.

About SORT1+ Technology™ and Sudocetaxel Zendusortide (TH1902)

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.

Sudocetaxel zendusortide (TH1902) is currently Theratechnologies' lead investigational 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. Sudocetaxel zendusortide is currently being evaluated in a Phase 1 clinical trial, although patient recruitment was voluntarily paused on December 1, 2022. In alignment with this decision, the FDA placed the trial on partial clinical hold. The Company is currently preparing a protocol amendment, which includes recommendations from the Scientific Advisory Committee meeting held in March 2023.

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 peptides through our SORT1+ Technology™ platform, and of its lead investigational peptide sudocetaxel zendusortide in enabling targeted delivery of anticancer therapy, the potential treatment of cancer, including potentially in combination with other anticancer therapies, using sudocetaxel zendusortide, and the filing of an amended protocol with the FDA to resume the Phase 1 clinical trial using 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. Certain assumptions made in preparing the Forward-Looking Statements include that results from our pre-clinical trial will be replicated into humans during clinical trials into human, if any, sudocetaxel zendusortide will prove safe and effective and will be approved by regulatory authorities for the treatment of cancer, and we will resume our Phase 1 clinical trial using sudocetaxel zendusortide. 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, the impossibility to demonstrate the safe and effective use of sudocetaxel zendusortide and other PDC in our clinical trials, the impossibility to resume the Phase 1 clinical trial using sudocetaxel zendusortide if the FDA does not approve the amendments to our Phase 1 clinical trial protocol, the incapacity of the Company to obtain positive results from the continuous development of its SORT1+ Technology™ platform, and the incapacity to find a partner for the development of our SORT1+ Technology™ platform. 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.sedar.com 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 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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