Theratechnologies Preclinical Data Presentation at AACR 2024 Highlights Versatility and Flexibility of SORT1+ Technology™ Oncology Platform

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- *Novel camptothecin-peptide conjugates are well tolerated and associated with significant tumor regression in colorectal cancer and triple-negative breast cancer xenograft models*
- *SORT1 gene silencing results in drastic decrease in peptide-drug conjugate uptake which supports a SORT1-mediated internalization process*
- *Poster presentation broadens evidence supporting potential utility of platform-derived peptide-drug conjugates alone or in combination in numerous SORT1-positive tumors*

MONTREAL, April 08, 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 presented preclinical data that highlight the versatility and flexibility of the Company’s SORT1+ Technology™ platform. In a poster session at the 2024 annual meeting of the American Association for Cancer Research (AACR) in San Diego, Calif., researchers reported that Theratechnologies’ investigational camptothecin-peptide conjugates are well tolerated and associated with significant tumor regression in colorectal cancer (CRC) and triple-negative breast cancer (TNBC) xenograft models. The study also demonstrated synergistic anti-tumor efficacy and good tolerability with the combination of two peptide drug conjugates with different payloads.

“The preclinical data presented at AACR add to the sizeable body of evidence supporting the potential utility of the SORT1+ Technology™ platform as an engine for the development of novel peptide-drug conjugates to treat various types of cancer,” said Christian Marsolais Ph.D., Senior Vice President and Chief Medical Officer at Theratechnologies. “In addition to our lead peptide-drug conjugate, sudocetaxel zendusortide, these latest data highlight the promising tolerability and anti-tumor effects of our investigational camptothecin-peptide conjugates, further demonstrating the versatility and flexibility of the platform. We welcome discussions with potential partners who are interested in the further development of these innovative therapies.”

The SORT1+ Technology™ platform relies on the use of a novel, proprietary peptide called TH19P01, which can be conjugated (attached) to numerous well-characterized anticancer drugs. Theratechnologies designed TH19P01 to interact with and be transported by the scavenger receptor sortilin (SORT1), which is involved in protein internalization, sorting, and trafficking, and is expressed in multiple tumor types. Targeting SORT1 with platform-derived peptide-drug conjugates (PDCs) leads to receptor-mediated internalization (endocytosis) of anticancer agents. Once inside cancer cells, active drug is released from the peptide and exerts its cytotoxic effect directly on the cancer cell.

In the poster presented at AACR, the investigators noted that SORT1 gene silencing inhibits camptothecin-conjugate uptake in human HT-29 colorectal adenocarcinoma cells. This observation suggests that these PDCs enter cancer cells via a SORT1-mediated internalization process.

The investigators also described the preclinical effects of three PDCs – TH2101, TH2205, and TH2310 – that have a cytotoxic payload of SN-38, the active metabolite of irinotecan, an anticancer agent that is derived from the Chinese tree *Camptotheca acuminate*. In addition, the poster summarized the activity of another PDC, TH2303, which carries an exatecan payload, a structural analog of camptothecin. Compared to unconjugated irinotecan, the exatecan- and SN-38-conjugates exerted greater anti-proliferative activities against CRC cells in mice. In two different CRC xenograft models, as well as in the TNBC xenograft model, TH2303 was associated with increased tumor growth inhibition and greater tolerability compared to unconjugated exatecan or irinotecan.

In another experiment described in the poster, the combination of two SORT1-targeting PDCs – sudocetaxel zendusortide (TH1902) and TH2101, which have a synergistic anti-tumor effect at reduced doses, led to increased tumor growth inhibition and some complete responses in the HT-29 xenograft model, compared to either PDC administered alone. The combination also was well tolerated.

“The significant tumor regression following combination therapy is notable because the HT-29 xenograft model is known for its resistance to multiple cytotoxic drugs,” commented Prof. Borhane Annabi, Chair in Cancer Prevention and Treatment in the Chemistry Department at the Université du Québec à Montréal. “That observation, along with the impressive anticancer efficacy of the camptothecin-peptide conjugates when administered alone, underscores the potential feasibility of this approach in treating various tumor types.”

A copy of the AACR poster, as well as a second poster presented at the conference, which reinforces existing data for the Company’s lead investigational PDC sudocetaxel zendusortide (TH1902) in activating anti-PD-L1 immunotherapy tumor cell-killing in SORT+1 cancers, can be found at the Theratechnologies website.

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 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 development of multiple PDCs, including, without limitation, camptothecin-peptide conjugates and sudocetaxel zendusortide, their use and the potential benefits to be derived from their use. 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’s Phase 1 clinical trial using sudocetaxel zendusortide will be successful, that signs of efficacy will be observed in such Phase 1 clinical trial and no untoward side effects will be reported, and that the findings observed from the preclinical work conducted on new PDCs will be replicated into human subjects. 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 strong efficacy results from the Phase 1 clinical trial using sudocetaxel zendusortide, the reporting of adverse side effects from the use of sudocetaxel zendusortide leading to a halt of the clinical trial, and that the findings observed from preclinical work conducted on new PDCs are not observed when those are administered into human subjects. 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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