Defence's AccuTOX Published in the Prestigious Journal of Translational Medicine Its Peer Study with Preclinical Data on AccuTOX as an Anti-Cancer Molecule

Vancouver, British Columbia--(Newsfile Corp. - June 6, 2024) - Defence Therapeutics Inc. (CSE: DTC) (OTCQB: DTCFF) (FSE: DTC) ("Defence" or the "Company"), a Canadian biopharmaceutical company developing novel immune-oncology vaccines and drug delivery technologies, is please to announce the publication of a peer-reviewed study on the anticancer properties of its unconjugated AccuTOX®, one of Defence's lead products engineered to treat established solid tumors. The study, which was published in the prestigious *Journal of Translational Medicine*, is entitled, "**Local delivery of AccuTOX® synergises with immune-checkpoint inhibitors at disrupting tumor growth**", and can be directly accessed at the following address: **http://10.1186/s12967-024-05340-2**

The Accum® platform was initially designed to accumulate biomedicines in target cells by inducing endosomal-to-cytosol escape. Interestingly however, the use of unconjugated Accum® was observed to trigger cell death in a variety of cancer cell lines; a property further exploited in the development of Accum®-based anti-cancer therapies. Despite the impressive pro-killing abilities of the parent molecule, some cancer cell lines exhibited resistance. This prompted us to test additional Accum® variants, which led to the identification of the AccuTOX® molecule. From that perspective, AccuTOX® holds many advantages over the parent Accum® entity: i) it exhibits enhanced killing potency while retaining the innate function of endosomal-to-cytosol escape, ii) the molecule can be easily manufactured, iii) it can be linked to antibodies as an in situ cleavable anticancer molecule (to increase its specificity), and iv) it is highly versatile, as it targets multiple intracellular pathways that are highly relevant to cancer growth and progression.

"This study presents insights of how the unconjugated AccuTOX® molecule works. More specifically, we demonstrate that AccuTOX® displays improved killing efficiency, triggers immunogenic cell death and production of toxic byproducts while inducing endosomal breaks. Moreover, AccuTOX® enhances cancer cell visibility to the immune system. It is very rare to have a drug capable of fighting cancer at multiple fronts simultaneously." says Dr. Rafei, the Chief Scientific Officer of Defence Therapeutics.

The key highlights of the AccuTOX® study are:

- AccuTOX® is therapeutically superior to parent Accum® (both *in vitro* and *in vivo*)
- The molecule induces cell death of various murine and human cancer cell lines (T-cell lymphoma, colon, melanoma, lung and breast)
- AccuTOX® triggers the intracellular production of reactive oxygen species and disrupts endosomal membranes
- Following contact with AccuTOX®, cancer cells die through a process called immunogenic cell death
- The compound leads to similar responses in both male and female animals with no apparent toxicity
- AccuTOX® enhances antigen presentation (tumor becomes visible to immune cells)

- Intratumoral administration of AccuTOX® to lymphoma, melanoma or breast cancer synergises with common immune-checkpoint inhibitors leading to efficient tumor growth control

"In addition to providing an important validation of the antitumoral properties of unconjugated AccuTOX®, this compound represents currently the lead core technology at Defence as the same molecule can be used to generate three different lines of therapies with distinct modes of action (anti-cancer injectable, cell-based vaccine and as a payload for ADCs). This unique versatility could pave the path for additional lines of investigations, and it represents a "one solution for three major problems" at once," said Mr. Plouffe, Chief Executive Officer of Defence Therapeutics.

In summary, unconjugated AccuTOX® could be used as an anti-cancer molecule. The triggered effects are interesting and unexpected as the induction of immunogenic cell death brings an additional immune component to the equation, which may turn a "cold" into a "hot" tumor with increased infiltration of immune cells as shown in the published study. With FDA clearance to initiate a Phase I trial, Defence recently submitted a CTA application to Health Canada to widen the scope of clinical testing.

Marketing:

Defence has entered into an agreement with Martin City Studios LLC, where Martin City Studios will produce two audio interviews with Defence's CSO, Dr. Moutih Rafei, with Ellis Martin to be aired on Money Talk Radio and The Ellis Martin Report. Martin City Studios is a company headquartered in New Mexico, United States, dedicated to audio interviews. The cost of the services is $6,500 (U.S.). Martin City Studios does not currently hold any common shares in the company. Martin City Studios and the Company are unrelated and unaffiliated entities. Martin City Studios will be producing an audio interview segment featuring the Company to be updated and aired across Martin City Studios' platforms (as well as posted on the VoiceAmerican.com's Business Channel and Martin City Studios' YouTube channel). A recording of the interviews will be shared when available.

About Defence:

Defence Therapeutics is a publicly-traded clinical-stage biotechnology company working on engineering the next generation vaccines and ADC products using its proprietary platform. The core of Defence Therapeutics platform is the ACCUM® technology, which enables precision delivery of vaccine antigens or ADCs in their intact form to target cells. As a result, increased efficacy and potency can be reached against catastrophic illness such as cancer and infectious diseases.

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