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Scancell Holdings plc
("Scancell" or the "Company")

New publication highlights potential of Modi-1 for hard to treat cancers

Modi-1 Phase 1/2 trial expected to start in H1 2021

Scancell Holdings plc, (AIM:SCLP), the developer of novel immunotherapies for the treatment of cancer, is pleased to announce the publication of a peer-reviewed research paper in the *Journal for ImmunoTherapy of Cancer* entitled: "Combination vaccine based on citrullinated vimentin and enolase peptides induces potent CD4-mediated anti-tumor responses".[1] The Company also provides an update on current progress and future plans for a Phase 1/2 clinical trial in patients with solid tumours including triple negative breast cancer, ovarian cancer, renal cancer and head and neck cancer.

Scancell's Moditope® platform represents a completely new class of potent and selective immunotherapy agents based on stress-induced post-translational modifications (siPTM) such as citrullination. The publication describes the first Moditope® vaccine, Modi-1, and its ability to stimulate potent T cell responses that translate into tumour protection in melanoma and ovarian cancer models. The responses were mediated by CD4 T cells and were also able to protect against a second challenge of the tumour confirming the induction of a memory response. The paper also confirms that conjugating the Modi-1 citrullinated peptides to the toll-like receptor-stimulating adjuvant AMPLIVANT®, previously licensed from ISA Pharmaceuticals, allows the therapeutic dose to be reduced by up to 100-fold. The full abstract is detailed below.

In January 2020, the Company provided an update on progress towards initiating the Modi-1 Phase 1/2 clinical trial. This has been advanced further with successful completion of GMP drug substance manufacture for all three of the conjugates that comprise the Modi-1 product. Importantly, the technical challenges reported in January concerning one of the peptide components have been successfully resolved, enabling progression to GMP drug product manufacture and formulation of clinical supplies in Q3 2020.

Formal regulatory-compliant toxicity studies have now been completed, with no evidence of any local or systemic toxicities being reported. In addition to the Scientific Advice meeting held with the Paul-Ehrlich-Institut regulatory authority in 2019, a further successful meeting was held with the UK Medicines and Healthcare products Regulatory Agency in February 2020. The Company continues to progress the necessary processes and documentation required for regulatory submission to start the planned clinical study in the UK in the first half of 2021.

Professor Lindy Durrant, Chief Scientific Officer of Scancell, commented:

"These data further validate the unique mode of action, and long-term protection, of citrullinated Moditope® peptides and their potential as novel immunotherapies for hard to treat cancers, particularly when conjugated with the AMPLIVANT® adjuvant to boost the overall immune response."

Abstract

Background: Stress-induced post-translational modifications occur during autophagy and can result in generation of new epitopes and immune recognition. One such modification is the conversion of arginine to citrulline by peptidylarginine deiminase enzymes.
Methods: We used human leukocyte antigen (HLA) transgenic mouse models to assess the immunogenicity of a citrullinated peptide vaccine by cytokine enzyme-linked immunosorbent spot (ELISpot) assay. Vaccine efficacy was assessed in tumor therapy studies using HLA-matched B16 melanoma and ID8 ovarian models expressing either constitutive or interferon-gamma (IFNγ) inducible Major Histocompatibility Complex (MHC) class II (MHC-II) as represented by most human tumors. To determine the importance of CD4 T cells in tumor therapy, we analyzed the immune cell infiltrate into murine tumors using flow cytometry and performed therapy studies in the presence of CD4 and CD8 T cell depletion. We assessed the T cell repertoire to citrullinated peptides in ovarian cancer patients and healthy donors using flow cytometry.

Results: The combination of citrullinated vimentin and enolase peptides (Modi-1) stimulated strong CD4 T cell responses in mice. Responses resulted in a potent anti-tumor therapy against established tumors and generated immunological memory which protected against tumor rechallenge. Depletion of CD4, but not CD8 T cells, abrogated the primary anti-tumor response as well as the memory response to tumor rechallenge. This was further reinforced by successful tumor regression being associated with an increase in tumor-infiltrating CD4 T cells and a reduction in tumor-associated myeloid suppressor cells. The anti-tumor response also relied on direct CD4 T cell recognition as only tumors expressing MHC-II were rejected. A comparison of different Toll-like receptor (TLR)-stimulating adjuvants showed that Modi-1 induced strong Th1 responses when combined with granulocyte-macrophage colony-stimulating factor (GMCSF), TLR9/TLR4, TLR9, TLR3, TLR1/2 and TLR7 agonists. Direct linkage of the TLR1/2 agonist to the peptides allowed the vaccine dose to be reduced by 10-fold to 100-fold without loss of anti-tumor activity. Furthermore, a CD4 Th1 response to the citrullinated peptides was seen in ovarian cancer patients.
Conclusions: Modi-1 citrullinated peptide vaccine induces potent CD4-mediated anti-tumor responses in mouse models and a CD4 T cell repertoire is present in ovarian cancer patients to the citrullinated peptides suggesting that Modi-1 could be an effective vaccine for ovarian cancer patients.

[1.] Victoria A Brentville, Rachael L Metheringham, Ian Daniels, Suha Atabani, Peter Symonds, Katherine W Cook, Mireille Vankemmelbeke, Ruhul Choudhury, Poonam Vaghela, Mohamed Gijon, Ghislaine Meiners, Willem-Jan Krebber, Cornelis J M Melief, Lindy G Durrant. Combination vaccine based on citrullinated vimentin and enolase peptides induces potent CD4-mediated anti-tumor responses. Journal for ImmunoTherapy of Cancer 2020;8:e000560. doi:10.1136/jitc-2020-000560.

This announcement contains inside information for the purposes of Article 7 of Regulation (EU) 596/2014 (MAR).

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About Scancell

Scancell is developing novel immunotherapies for the treatment of cancer based on its ImmunoBody® and Moditope® technology platforms.

ImmunoBody® vaccines target dendritic cells and stimulate both parts of the cellular immune system. They have the potential to be used as monotherapy or in combination with checkpoint inhibitors and other agents. This platform has the potential to enhance tumour destruction, prevent disease recurrence and extend survival.

- SCIB1, the lead programme, is being developed for the treatment of melanoma. A phase 1/2 clinical trial has so far successfully demonstrated survival data of more than five years.

- SCIB2 is being developed for the treatment of non-small cell lung cancer and other solid tumours. Scancell has entered into a clinical development partnership with Cancer Research UK (CRUK) for SCIB2.

Moditope® represents a completely new class of potent and selective immunotherapy agents based on stress-induced post-translational modifications (siPTM). It stimulates the production of killer CD4 T cells which overcome the immune suppression induced by tumours, allowing activated T cells to seek out

and kill tumour cells that would otherwise be hidden from the immune system. Moditope® alone, or in combination with other agents, has the potential to treat a wide variety of cancers.

- Modi-1 is being developed for the treatment of solid tumours including triple negative breast cancer, ovarian cancer, renal cancer and head and neck cancer.

AvidiMab™ is a patent protected technology platform which increases the avidity of human antibodies by promoting non-covalent Fc-Fc interactions. This modification induces the direct tumour cell killing properties of Scancell's anti-glycan monoclonal antibodies (mAbs) but has broad potential to increase the avidity or potency of any therapeutic monoclonal antibody including those being developed for autoimmune diseases, as well as cancer.

For further details, please see our website: www.scancell.co.uk