## Current status of vaccine and program development

Categories : News, Pharmaceuticals, Processing Technologies

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Defence, a publicly traded biotechnology company, is working to develop the next generation of vaccines, antibody-drug conjugates (ADCs), ADC products and therapeutic procedures to fight cancer using its proprietary AccumTM platform. At the core of the Defence Therapeutics platform is AccumTM technology, which enables precise delivery of pharmacologically relevant proteins to target cells and increases intracellular accumulation to those target cells. As a result, improved efficiency and efficacy against serious diseases such as cancer and infectious diseases can be achieved. With four new patents filed last year, Defence's technologies have an increasing intellectual property portfolio. Research activities conducted by Defence last year and plans for future clinical trials will continue.

#### Core technology development

The core of the Company's technology research is based on overcoming a major and common challenge that limits the efficacy of both vaccines and antibody-drug conjugates ("ADCs"). When the target cell binds and internalizes an antigen or an ADC, the complex becomes entrapped within small intracellular vesicles called endosomes. Over time, these endosomes undergo a maturation process, causing them to degrade before they can perform their respective functions. The company's goal is to use the enhancing AccumTM formulation to improve the intracellular transport of biologic therapeutic agents by triggering their escape to cytosols, thus improving their therapeutic effect.

#### Effective cellular vaccine design.

AccumTM technology is ideally suited for vaccines. More specifically, antigens normally taken up by dendritic cells ("DCs") - the best antigen-presenting cells in our body - are first entrapped in endosomes. As these endosomal organelles mature, the pH decreases (i.e., it goes into the acidic range, I4-5) to trigger the activation of specific enzymes as a means of initiating nonspecific antigen degradation. As a result, the resulting fragments can then pass through the endosomal pores to the cytoplasm where specific antigen degradation occurs by the proteasomal mechanism. Although this process occurs naturally, the generated antigen fragments are often damaged, making them unsuitable for optimal immune stimulation. By using AccumTM technology, the ingested antigens are preserved in their natural state while being transported to the cytoplasm. Thus, proteasomal degradation leads to a higher number of immunogenic and stable peptides on the surface of DCs, which can trigger effective T-cell activation.

In research activities conducted by the company, it was found that adding Accum-bound antigens to allogeneic DCs (AccuVAC-D001) increases the therapeutic effect of the vaccine and achieves a survival rate of 70-80% (compared to the 0-20% achieved by current experimentally tested DC-based vaccines). Following the completion of this study, Defence has signed an agreement with a clean room provider in Canada to conduct trial runs with its DC vaccine. The goal is to complete all required GLP studies by the first quarter of 2022 and conduct a Phase I trial against melanoma in the UK by mid-2022.

# Development of protein-based vaccines for infectious diseases (COVID and HPV).

In parallel, the company has already completed all preclinical activities related to its COVID-19 vaccines. The first vaccine (DTC-PT001) is an injectable delivery form boosted by an adjuvant approved by the U.S.

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Food and Drug Administration (FDA). The data obtained showed a strong and durable production of IgG titers (more than 16 weeks) and achieved high reactivity against all tested variants. Moreover, the immunogenicity of the vaccine was well comparable between rodent (mice) and non-rodent (rabbits) models. In addition, vaccination of hamsters (third model - GLP study) followed by virus exposure resulted in effective protection with no observed side effects.

The second vaccine formulation (DTC-IN003) is a vaccine that blocks transmission to stop infection (as opposed to a vaccine that lowers the pathophysiology of the virus). In this case, the vaccine is administered intranasally with a special adjuvant (designed for intranasal vaccination). This vaccine not only triggered the production of IgAs at the mucosal surfaces (where the virus invades), but systemic immunity was also observed, and the antibodies produced showed cross-reactivity with all variants tested. A GLP challenge study is currently underway, with final results expected in late December 2021.

Another infectious disease vaccine in development at Defence Therapeutics is AccuVAC-PT009 against human papillomavirus (HPV). This vaccine uses a mixture of L1 proteins (from different HPV strains) in combination with AccumTM. This involves testing for the ability to produce antibodies against the HPV virus. The effect of the AccuVAC-PT009 vaccine will be compared to the commercially available Gardasil-9 vaccine in terms of immunogenicity (prophylactic vaccine). In addition, Defence is working on a second HPV-related vaccine, but targeted against cervical cancer (AccuVAC-PT0067). The goal of this vaccine is to modify both E6 and E7 proteins to covalently bind AccumTM and then test the vaccine for its ability to treat previously identified cervical cancer. Results of the preclinical studies will be available in early 2022.

### Effective design of ADCs

One challenge of ADCs is insufficient intracellular accumulation of the chemotherapeutic agent transported for effective tumor killing. Defence demonstrated that AccumTM technology increased the ability of the ADC Kadcyla (T-DM1) to specifically kill breast cancer cells. AccumTMimproved endosomal escape of the ADC Kadcyla while targeting the nucleus. Defence anticipates that AccumTM technology will enable it to increase T-DM1 efficacy. This will allow the treatment to overcome resistance mechanisms such as reducing the number of receptors on the cell surface (thereby limiting the efficacy and transport of T-DM1 within the cell). The company has entered into a strategic collaboration with two European institutions to further develop its Accum-ADCs platform.