ISA2GO: NOVEL IMMUNOTHERAPY FOR THE TREATMENT OF CANCER AND INFECTIOUS DISEASES

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Immune Oncology

**Organization**: ISA Pharmaceteuticals BV
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**Brief summary:**
Towards clinical PoC of Synthetic Long Peptides in HPV16+ Cervical Cancer and validation of a paradigm shifting personalized SLP immunotherapy.

**Project / initiative description (context and objectives):**
ISA's SLP immunotherapeutics have been designed to trigger optimal killer T cell-mediated immune responses that are capable of killing the diseased cells expressing pathogenic antigens without affecting the healthy tissues. ISA Pharmaceuticals develops its SLP and SLP-AMPLIVANT therapeutics as monotherapy or in combination with chemotherapeutics as well as with immune-modulatory compounds, enabling the development of best-in-class immunotherapeutics as a vital, specific component of combinatorial cancer immunotherapy.

The focus of the company is to obtain clinical proof-of-concept of the ISA101 based immunotherapy in HPV16 positive cancer by progressing clinical development towards pivotal phase and, in parallel, leverage its vast amount of manufacturing and clinical experience to establish a personalized SLP immunotherapy process targeting mutation derived neo-antigens on a patient-by-patient basis.

ISA is seeking investors to lead/complement anticipated funding round allowing the company to reach value inflection point for the ISA101 and deliver validation of the paradigm shifting on-demand personalized SLP immunotherapy.

**Description of the existing or potential collaboration:**

1. Strategic relationship with the Leiden University Medical Center (NL)
2. Clinical collaborations with, amongst others, LUMC (NL), UMCG (NL), University Hospital Gent (BE), University Hospital Leuven (BE) for the CervISA trial and MD Andersson Cancer Centre for the combination trial with nivolumab from BMS.
3. Technology evaluation agreement with SNBL (JP), evaluating ISA101 in a nasal formulation.
4. Several research collaborations with national and international research institutes covering HBV, PRAME and AMPLIVANT projects.
5. Soon to be announced strategic partnerships and collaboration regarding the personalized SLP immunotherapy development.
ISA101 (Human Papilloma Virus, HPV)

ISA101 consists of 13 synthetic long peptides (25-35 amino acids long) derived from the E6 and E7 oncogenic proteins of the HPV 16 virus. This strain is responsible for 50% of human cervical cancers and cervical intra-epithelial neoplasias and more than 85% of HPV-positive head and neck cancers, anal cancers and premalignant HPV-induced anal lesions (termed anal intra-epithelial neoplasia, or AIN). It is administered either subcutaneously or intradermally.

With its ISA101 immunotherapeutic, ISA Pharmaceuticals is targeting the gap between preventive HPV vaccines and standard cancer treatments. The combined total market opportunity addressed by an immunotherapeutic against HPV16 amounts to a multi-billion dollar market annually.

ISA101 is currently in clinical development in advanced and recurrent cervical cancer, incurable HPV16-positive solid tumors and anal intraepithelial neoplasia (AIN). Clinical proof-of-concept has been established in vulvar intraepithelial neoplasia (VIN), a pre-cancerous disease caused by HPV.

Personalized SLP Immunotherapies Targeting Tumor Neo-antigens

In a recent Nature paper (Gubin et al, Nov 2014) it was shown that SLP’s are also effective in targeting mutant neo-antigens in a pre-clinical lung cancer model. This opens a path towards personalized immunotherapies targeting high mutation frequency malignancies such as lung cancer and melanoma. ISA has invested in latest generation peptide synthesis equipment fit for this purpose and is preparing to start clinical development of personalized SLP immunotherapies.

Societal benefits:

High risk HPV infection

HPV infection are associated with the development of dysplastic tissue and pre-malignant cells, which have the potential to subsequently become malignant. The majority of the malignant HPV induced lesions are associated with HPV16 (50-95%). Due to the incomplete vaccination and preventive screening campaigns, the annual incidence of anogenital dysplasia and related cancers, including Head & Neck remains an unmet need worldwide.

While off-the-shelf immune-therapeutics work well in virus-induced cancers, addressing non-viral cancers requires antigens specific to the tumor. Particularly cancers with high mutational load and resistance to standard treatment, such as lung cancer, bladder cancer and melanomas, are likely to be targeted effectively with a mix of SLPs derived from neo-antigens that induce T-cells which exclusively target the malignant cells.

As a pioneer in immunotherapy, ISA is well positioned to explore the field of personalized SLP immunotherapies. These will bring the large and unmet cancer indications within reach of being effectively treated at acceptable costs and will achieve a paradigm shift in the development of future immunotherapies and treatment of cancer in general. For the personalized immunotherapy, ISA aims to adopt a specialized fee-for-service model, delivering on-demand GMP grade unique mixtures of SLP’s.

Planned schedule:

1) Obtain clinical proof of concept of the ISA101 based immunotherapy in cancer by progressing clinical development towards pivotal phase

- Finalizing current phase 1/2 trial (Q3-2016) and two extensions (resp. Q3-2016 and Q2-2017) providing clinical safety and immune response data regarding the optimal dose and combination regimen for the randomized Phase II study;
- Obtaining objective and outstanding clinical efficacy results in cancer through a randomized Phase 2 clinical trial of an optimal ISA101 regimen for the treatment of cervical carcinoma (Q1-2017 – 2019);
- Facilitating the proof of concept combination study in head and neck, anal and cervical cancer using Nivolumab and ISA101 in close collaboration with BMS and MD Andersson Cancer Center (Texas, USA) (initiated in Q4-2015);
- Facilitating an additional proof of concept study in head and neck with a competitor CPB in close collaboration with pharma-partner and a renowned US-institute (planned in 2H-2016):?

2) Establish personalized SLP® immunotherapy program targeting mutation derived neo-antigens

- Establish strategic relationships with key partners in the process chain, e.g. clinical centers, genome/exome sequencing facility, bioinformatics
- Establish a GMP production unit by the end of 2016;
- Initiate a clinical first clinical study in an appropriate indication to establish proof-of-principle early 2017.

What are you expecting from BIOVISION Catalyster?

1 Visibility
2 Meeting potential partners
3 International reach
4 Other