IMMATICS PRESS RELEASE

Nature publication reports first-in-human trial for a personalized cancer immunotherapy

Clinical study demonstrates proof-of-concept for active personalized immunotherapy approach in a pioneering multi-center, multi-national study to treat brain cancer

This study is a blueprint for Immatics' highly personalized ACTolog® adoptive cell therapy trial currently treating patients at MD Anderson Cancer Center

Tuebingen, Germany, December 20th, 2018 – The prospect of an actively personalized approach to the treatment of cancer has moved a step closer with the recent publication in *Nature* of data from the phase 1 study GAPVAC-101, testing a novel therapeutic concept tailored to specific characteristics of patients' individual tumors and immune systems. For the first time, the feasibility of such a highly personalized form of immunotherapy has been exemplified in a multi-center, multi-national clinical setting.

To date, glioblastoma, an aggressive form of brain cancer with poor prognosis, and other tumor types have not sufficiently benefited from recent breakthroughs with checkpoint inhibitors due to lack of high mutational load which is thought to be essential for the mode of action of this therapeutic class. Indeed, many tumor types are characterized by a low mutational load and thus only few neoantigens are targetable by the immune system. Such cancers exhibit a high unmet medical need and require additional therapeutic strategies tailored to the features of the patient's individual tumor and appreciating the entire breadth of the cancer target repertoire.

The Glioma Actively Personalized Vaccine Consortium (GAPVAC) approach is a highly personalized method being progressed through the GAPVAC-101 first-in-human clinical trial by a European Union-funded consortium, led by Immatics Biotechnologies GmbH (Tuebingen, Germany) and BioNTech AG (Mainz, Germany).

Fifteen newly diagnosed glioblastoma patients treated at six European centers received two immunotherapies in succession; APVAC1 targeted at non-mutated antigens, followed by APVAC2 preferentially targeted at neo-antigens. Immunotherapy compositions were personalized for each patient based on analysis of the transcriptome, immunopeptidome and mutanome of the individuals' tumors and, for APVAC1, also based on the capability of each patient to mount an immune response. Both immunotherapy types displayed favorable safety and immunogenicity. Non-mutated APVAC1 antigens induced sustained central memory CD8+ T-cell responses, whilst APVAC2 induced T helper cell type 1 (TH1) CD4+ as well as CD8+ T-cell responses against predicted neo-epitopes.

The GAPVAC-101 trial served as a blueprint for the ACTolog® IMA101-101 trial sponsored by Immatics. ACTolog® is the first adoptive cell therapy trial applying the concept of active personalization.

Dr. Harpreet Singh, Chief Scientific Officer of Immatics and President & CEO of Immatics US, said: "We are at a very exciting stage in the evolution of tailor-made cancer treatments based on the diseases of individual cancer patients. The ability to exploit the full repertoire of tumor antigens, including non-mutated and neoantigens, may offer more

effective immunotherapies, especially for tumors with low mutational load. And there is more to come. The next step is to translate the concept of active personalization, successfully demonstrated in this study, into adoptive cell therapies – which we have achieved with the ACTolog® IMA101 clinical trial Immatics is currently running at MD Anderson Cancer Center."

Prof. Hans-Georg Rammensee, Head of the Department of Immunology at the University of Tuebingen, Germany, and Co-Founder of Immatics added: "I am very pleased to see that the concept of active personalization proposed by us more than a decade ago has been applied for the treatment of glioblastoma patients. GAPVAC constitutes the first clinical trial using a combination of personalized mass spectrometry, next-generation sequencing, mRNA microarray, immune repertoire analysis and peptide GMP manufacturing for every patient and delivering these complex logistics in a multi-center multi-national clinical trial."

The approach of personalization of immunotherapies was first proposed by Prof. Hans-Georg Rammensee in 2000. His department was also responsible for the APVAC "on-demand" GMP manufacturing, led by Prof. Stefan Stevanovic, in the GAPVAC trial. The University of Tuebingen also served as one of the six European clinical trial centers treating glioblastoma patients.

Publication reference:

Hilf et al., Actively personalized vaccination trial for newly diagnosed glioblastoma, *Nature* 2018 Advance online publication date: 19th December, 2018 (DOI: 10.1038/s41586-018-0810-y)

About Immatics

Immatics is a clinical-stage biopharmaceutical company active in the discovery and development of T-cell redirecting immunotherapies for the treatment of cancer. The Company's transformative product candidates are – best in class – Adoptive Cell Therapies and Bispecific TCR molecules. These products are directed against tumor targets that have been identified and validated by Immatics' proprietary and world-leading XPRESIDENT® technology. XPRESIDENT® is the most sensitive, unbiased and high-throughput technology capable of identifying targets in virtually any type of cancer and any HLA type. Together with Immatics' powerful TCR discovery technology XCEPTOR®, these two platforms allow a full range of cancer therapies to be developed.

Immatics' pipeline includes T-cell therapy programs based on the proprietary ACTolog®, ACTengine® and ACTallo® approaches, which are developed in collaboration through Immatics US with University of Texas MD Anderson Cancer Center and co-funded by the Cancer Prevention and Research Institute of Texas (CPRIT), and several bispecific TCR and antibody molecules.

Operating from Tuebingen, Munich and Houston, the Company has recognized that novel, better and safer targets are the key to developing future cancer immunotherapies and it is Immatics' mission to deliver the power of T cells to cancer patients.

For regular updates about Immatics, visit www.immatics.com.

About GAPVAC

GAPVAC was launched in 2013 being the first clinical trial at that time designed to create, manufacture and develop actively personalized vaccines (APVACs) tailored to the individual characteristics of the patient's tumor and immune system. It is based on combining latest state-of-the-art technologies, including next-generation sequencing (NGS), high-sensitivity mass spectrometry and innovative immunomonitoring approaches to generate an optimal therapy for the individual patient. The trial was led by chief investigators Prof. Dr. Wolfgang Wick, University of Heidelberg, and Prof. Dr. Pierre-Yves Dietrich, University of Geneva, both internationally recognized experts in the treatment and immunology of brain cancer. The trial was conducted by the GAPVAC consortium supported by a €6 million grant from the European Union Framework 7 (EU FP7) program (number 305061).

About ACTolog® T-cell therapy

The ACTolog® IMA101 phase 1 clinical trial is led by Apostolia Tsimberidou, M.D., Professor at the Department of Investigational Cancer Therapeutics at the University of Texas MD Anderson Cancer Center, and co-funded by the Cancer Prevention and Research Institute of Texas (CPRIT). The ACTolog® concept is based on the principle of endogenous T-cell therapy pioneered by Professor Cassian Yee, M.D. Unlike tumor-infiltrating lymphocytes, ACTolog® T-cell products are generated from peripheral blood cells with defined target selectivity. Utilizing its proprietary antigen discovery platform XPRESIDENT®, Immatics has created a warehouse of eight cancer targets. From this warehouse, the most suitable targets for each patient's tumor are identified by analyzing the tumor biomarkers. Up to four personalized T-cell products are then activated and manufactured for each patient by isolation and enrichment of the patient's endogenous T cells in vitro. Billions of such activated and specific T cells are then re-infused into the cancer patient to attack the tumor. The ACTolog® T-cell products are manufactured at The Evelyn H. Griffin Stem Cell Therapeutics Research Laboratory in collaboration with The University of Texas Health Science Center in Houston (UTHealth).

About the University of Tuebingen

The University of Tübingen is one of eleven universities judged excellent under the German government's Excellence Initiative and ranks well in international comparisons. Tübingen is one of the world's foremost locations for neuroscientific research. Along with translational immunology and cancer research, microbiology and infection research, and molecular plant biology, it makes Tübingen a cutting-edge center of research in the Life Sciences. Further areas of core research are in Machine Learning, Geoscience and Environmental Science; Archaeology and Anthropology; Language and Cognition; and Education and the Media. More than 27,700 students from Germany and around the world are currently enrolled at the University of Tübingen, enjoying a broad spectrum of some 300 different study programs. As part of the German government's Excellence Strategy, the University will host three clusters of excellence: Control of Microorganisms to Fight Infection (CMFI), Image-Guided and Functionally Instructed Tumor Therapies (iFIT) and Machine Learning in Science. https://uni-tuebingen.de/

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