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PRESS RELEASE

EU-funded consortium led by immatics and BioNTech to advance a novel class of fully personalized therapeutic cancer vaccines into clinical trials for brain cancer

Regulatory authority approves clinical trial for Glioma Actively Personalized Vaccine Consortium (GAPVAC)
First centers to enroll glioblastoma patients opened in Heidelberg and Tuebingen
European Union supports the initiative with a €6 million grant

Mainz, Germany, 14. October 2014 – *immatics* biotechnologies GmbH and BioNTech AG announce today that they are moving a novel concept of fully personalized therapeutic cancer vaccines, **Glioma Actively Personalized VAccine Consortium (GAPVAC)**, into the clinic. The German national authority, the Paul-Ehrlich-Institute (PEI), has approved the start of a phase 1/2 study, GAPVAC-101, which applies for the first time the concept of treating glioblastoma patients based on drugs designed and manufactured for each patient individually according to specific characteristics of their tumor and immune system. The screening of first patients for the trial has commenced at the University Hospital of Heidelberg, Germany, and the University Hospital of

Tuebingen, Germany. The complex manufacturing of the personalized vaccines will be performed by the GMP unit of the University of Tuebingen in close cooperation with the "GMP and Core Services platform" of the German Cancer Consortium (DKTK).

GAPVAC is the first EU-funded initiative aimed at clinically developing biomarker-guided **actively personalized vaccines (APVACs)** to treat patients with glioblastoma. Glioblastoma, an aggressive form of brain cancer with poor prognosis, has a high unmet need and the limited treatments available today have minimal effect on overall survival. The GAPVAC consortium includes 14 organizations in Europe and the United States and is led by *immatics* biotechnologies GmbH (Coordinator) and BioNTech AG (Vice Coordinator). The consortium is supported by a €6 million grant from the European Union Framework 7 (EU FP7) program.

The clinical trial will recruit up to 30 newly diagnosed glioblastoma patients for the phase 1/2 trial and aims to show that APVACs are well tolerated and induce a strong and specific response against cancer, as well as demonstrating the feasibility of this highly innovative approach. Glioblastoma patients will be immunized with two vaccines specifically prepared for each patient. The first vaccine will be a tailored selection of peptides chosen from a pre-manufactured warehouse supplied by consortium partner BCN Peptides (Barcelona) consisting of approx. 70 peptides based on the target profile of the individual cancer tissue and the ability of the individual's immune system to induce a response to the selected targets. The second vaccine will be based on full next-generation sequencing (NGS)-based genetic analysis of the patient and will comprise peptides newly manufactured by consortium partner University of Tuebingen. The latter vaccine will largely target mutations occurring in the cancer but not in healthy tissue. Both actively personalized vaccines will be designed according to

biomarker-guided procedures performed at *immatics* and BioNTech and will be administered in addition to standard chemotherapy after surgery and initial radio-chemotherapy are completed. The clinical trial is being accompanied by an extensive biomarker program involving the Association of Cancer Immunotherapy (CIMT), a non-profit organization dedicated to the advancement of cancer vaccines.

The clinical trial will be led by chief investigator Prof. Dr. Wolfgang Wick, University of Heidelberg, and co-led by Prof. Dr. Pierre-Yves Dietrich, University of Geneva, both internationally recognized experts in the treatment and immunology of brain cancer.

Prof. Dr. Wolfgang Wick, Chair of the Department of Neurooncology at the University of Heidelberg, said: "The trial concept is exactly the right combination of exceptional science and a rigorous protocol for a disease for which over-simplified strategies have failed in the past. The scientific approach in this trial offers the chance for each involved patient to benefit clinically. In addition, we will learn a lot for future efforts in immunotherapy, bridging the precision of genomic medicine and immunotherapy."

Dr. Harpreet Singh, Chief Scientific Officer of *immatics* and Coordinator of the GAPVAC consortium, said: "The start of the GAPVAC clinical trial – based on an entirely new, personalized approach to treating cancer – is the result of the innovative science and the dedication of the excellent consortium members. For the first time, we have translated the specific characteristics of each individual patient's disease into a therapeutic drug candidate for further assessment in the clinic. The project members are driven by the real possibility of developing a truly personalized treatment for patients whose current options are extremely limited. I wish to thank everyone

involved in GAPVAC and look forward to the first results from this exciting collaborative effort."

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Notes to editors:

About the project

GAPVAC was launched in 2013 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 consortium is supported by a €6 million grant from the European Union Framework 7 (EU FP7) program.

About the partners

immatics uses its unique antigen discovery engine XPRESIDENT® to generate a warehouse of tumor-associated peptides (TUMAPs) from which the most suitable for each patient will be selected based on transcriptomic and peptidomic analysis to create the first of two APVACs applied to the patient.

BioNTech uses its next-generation sequencing (NGS) expertise to identify immunogenic tumor mutations and to generate a blueprint for the personalized vaccine that will include patient-specific tumor mutated peptides to be confirmed with regard to their natural presentation by *immatics* through mass spectrometry. Previously, BioNTech has demonstrated that the integrated use of NGS for genome-wide mutation identification (the "mutanome") followed by mutation-targeting vaccination is feasible and led to tumor control in pre-clinical models.

The APVAC "on-demand" manufacturing will be performed by the GMP unit at the Department of Immunology (led by Prof. Dr. Hans-Georg Rammensee and Dr. Stefan Stevanovic), University of Tuebingen. The peptide warehouse was manufactured by BCN Peptides in Spain, an enterprise focused on peptide synthesis for clinical use. In addition, ten academic partners from Europe and the US are part of the consortium to apply the APVACs to their patients as well as contributing to the project with their own research. These are: Eberhard Karls University Tuebingen (Germany), University Hospital Geneva (Switzerland), University Hospital Heidelberg (Germany), Herlev Hospital/ Rigshospitalet (Denmark), Leiden University Medical Centre (The Netherlands), University of California San Francisco (United States), University Southampton (UK), Technion (Israel) and Vall d'Hebron University Hospital (Spain).

The clinical trial is being accompanied by an extensive biomarker program led by the Association of Cancer Immunotherapy (CIMT), a non-profit organization dedicated to the advancement of cancer vaccines, and *immatics* to confirm the mechanism-of-action and to identify biomarker signature candidates predicting which patients are most likely to benefit from treatment with APVACs. CIMT will also act as the

dissemination platform and will contribute to the biomarker program and regulatory approach through its working parties.

In 2013, the CIMT Regulatory Research Group outlined a regulatory pathway for actively personalized immunotherapies after discussions with the Innovation Task Force of the European Medicines Agency (EMA), the regulatory authority in Europe responsible for marketing approval of new drugs. The results were published by Britten et al., "The regulatory landscape for actively personalized cancer immunotherapies", Nature Biotechnology, Vol. 31 (10), October 2013.

For more information about GAPVAC, visit the consortium website www.gapvac.eu.

About CIMT

About the Association for Cancer Immunotherapy (CIMT) The Association for Cancer Immunotherapy (CIMT) is an international networking and education platform aiming to facilitate the development of new immunotherapies against cancer for the benefit of patients. CIMT was founded in 2002, and has its home office in Mainz, Germany. The association hosts the largest European expert meetings on cancer immunotherapy, publishes therapeutic guidelines and has established two topic-specific working groups: the CIMT Regulatory Research Party, focusing on the regulatory aspects of drug development, which is pioneering the regulatory framework of actively personalized vaccines for single patient use only; and the CIMT Immunoguiding Program (CIP), which focuses on the quality control and harmonization of immunomonitoring assays. To reach its goals, CIMT closely cooperates with various partners, among them the Cancer Research Institute's Cancer Immunotherapy Consortium (CRI-CIC). Visit www.cimt.eu for more information.

For additional information on CIMT please visit www.immatics.com or contact:

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