PRESS RELEASE

Launch of the IMPACT project to develop the first antibody-based countermeasure for orthopoxviruses

Starting on 1 June, the **IMPACT project** aims to develop the first antibody-based countermeasure for orthopoxviruses. The project targets both variola major virus (VARV) and monkeypox virus (MPXV) with a single antibody. With the contribution of the European Union under the Horizon Europe programme, IMPACT will strengthen Europe's biodefence preparedness and responsiveness to epidemic and deliberate threats.

The eradication of smallpox in 1980 remains a major milestone in global health. However, the discontinuation of vaccination campaigns has led to a gradual decline in immunity to orthopoxviruses worldwide. Today, an estimated 75–90% of the global population lacks immunity to variola virus and therefore is vulnerable.

Recent outbreaks of monkeypox virus (MPXV), including the global spread of Clade IIb in 2022 and recurrent Clade Ib epidemics in Central Africa in 2024, demonstrate the virus's increasing ability to adapt and sustain human-to-human transmission. In addition, the threat of accidental release, deliberate misuse, or re-emergence of related zoonotic orthopoxviruses has been repeatedly highlighted in international health security assessments.

Orthopoxviruses are one of the most complex viral families characterised by diverse structures and immune evasion strategies. The high heterogeneity, understudied protein landscape and diversity of envelope-associated proteins pose significant challenges to development of therapeutic and vaccines using conventional approaches.

IMPACT is a public-private consortium made up of **11 institutions from 5 European countries and the Democratic Republic of Congo**. The project brings together leading European organizations, many belonging to the European Vaccines Hub (EVH) network, including the Fondazione Biotecnopolo di Siena where the monoclonal antibody (mAb) was discovered. The entire network has proven expertise in structural biology, computational modelling, immunology, virology, pre-clinical models, GMP manufacturing, regulatory science, and clinical trial execution. The project is coordinated by the Sclavo Vaccines Association, a non-profit organization based in Siena dedicated to advancing vaccine research and development.

The IMPACT project focuses on **broadly neutralising monoclonal antibodies (mAbs)** targeting OPG153, a conserved antigen recently discovered thanks to the use of the Reverse Vaccinology 3.0, a novel approach that combines human immunology, structural biology and artificial intelligence. These mAbs combine high potency, dual neutralisation of mature and extracellular virions, and cross-neutralisation across MPXV clades and related orthopoxviruses in a single molecule.

IMPACT will integrate **AI-driven optimisation of monoclonal antibodies mAbs** and **protein engineering** to enhance antibody efficacy. Selected candidates will be tested in **preclinical models**, followed by **GMP manufacturing and evaluation in a Phase I clinical trial**. In parallel, under the project more than 1,800 human sera samples from infected and vaccinated individuals will be analysed to **characterise the immune responses** to OPG153 and identify correlates of protection, supporting future regulatory approval.

“This project has the unique opportunity to develop a new tool to prevent and cure infections from Mpox, and other poxviruses thus providing a safety net able to protect against natural or deliberate exposures to these dangerous viruses” said Dr. **Emanuele Andreano**, Head of Serology and Immunology of Fondazione Biotecnopolo di Siena and co-leader of the IMPACT project.

“IMPACT represents a strategic effort to strengthen Europe’s preparedness against emerging infectious diseases and biodefence threats. By leveraging the integrated infrastructure and expertise of the European Vaccines Hub, the project will reinforce Europe’s capability to rapidly develop and deploy innovative countermeasures against future epidemic and pandemic threats” said Prof. **Rino Rappuoli**, Scientific Director of Fondazione Biotecnopolo di Siena and Coordinator of the IMPACT project.

“The IMPACT project brings together a collaborative network of partners committed to advancing innovative solutions against orthopoxviruses. By combining complementary expertise across Europe and beyond, the project fosters scientific advancement and contributes to strengthening global health preparedness,” said Prof. **Donata Medaglini**, Deputy Rector of the University of Siena, Chief Scientific Officer at the Sclavo Vaccines Association, and Scientific Coordinator of the IMPACT project.

“The University of Oslo is delighted to contribute to the IMPACT project by combining our expertise in antibody biology with cutting-edge engineering approaches to develop a tailored countermeasure against orthopoxviruses. This strategic European cross-sector partnership will play an important role in strengthening global health preparedness,” said Prof. **Jan Terje Andersen**, University of Oslo and in-coming Co-Director of the Centre of Excellence PRIMA.

“CEA is thrilled to participate in this high-impact project by evaluating the efficacy in vivo of the antibodies developed by IMPACT project in our state-of-the-art facility,” said Dr **Jean-Nicolas Tournier**, Deputy Director of IDMIT Department], highlighting CEA’s specific contribution in pre-clinical models as part of the IMPACT framework.

“The University of Kinshasa (through its Department of Tropical Medicine) is delighted to be part of this tremendous and timely IMPACT project that will provide relevant solutions against the monkeypox (mpox) that is endemic in the Democratic Republic of Congo. Our strong experience in clinical research will contribute to the project success,” said Prof. **Jean-Marie Kayembe**, Rector of the UNIKIN.

“Philogen is delighted to contribute to the IMPACT Project by implementing GMP production activities, aimed at the generation of clinical-grade material for clinical trials, in our authorized manufacturing facilitites” said Prof. Dr. **Dario Neri**, CEO of Philogen.

IMPACT project will provide a scalable and globally relevant antibody-based countermeasure against orthopoxviruses, integrating discovery, preclinical validation, GMP manufacturing, and first-in-human clinical evaluation. By combining world-class science with European strategic infrastructures, IMPACT will deliver not only a deployable first-in-class therapeutic but also a decisive biodefence tool, reinforcing Europe’s leadership and resilience against epidemic and biothreat pathogens.

Facts about IMPACT:

Title: Innovative Monoclonal Antibody Against Poxviruses for Advanced Countermeasures
Acronym: IMPACT
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Participants:

- *Sclavo Vaccines Association (Italy)*
- *Fondazione Biotecnopolo di Siena (Italy)*
- *Universitetet i Oslo (Norway)*
- *Stiftung Tieraerztliche Hochschule Hannover (Germany)*
- *Commissariat À L'Énergie Atomique Et Aux Énergies Alternatives (France)*
- *Universiteit Antwerpen (Belgium)*
- *Università degli Studi di Siena (Italy)*
- *Instituut Voor Tropische Geneeskunde (Belgium)*
- *Universite de Kinshasa (Democratic Republic of Congo)*
- *Université Libre de Bruxelles (Belgium)*
- *Philogen S.p.A. (Italy)*

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