BREAKING NEW GROUND IN MEDICINE: COVEND WELCOMES THE FIRST PATIENTS IN THE PIONEERING ARDS CLINICAL TRIAL IXION 2.0

From vision to reality – a rocky path

The EU-funded COVend consortium announces the enrolment of first patients in the IXION 2.0 clinical trial at the Goethe University Hospital Frankfurt. Originally targeting the progression of mild to severe COVID-19 in high-risk patients, the trial entailed a precision medicine approach with the innovative therapeutic agent FX06. However, given the evolving dynamics of COVID-19, a strategic change has been made to instead investigate potential benefits of the drug for acute respiratory distress syndrome (ARDS) patients. Critical cases of COVID-19 and ARDS have a common molecular cause: an unbalanced immune response of the human body against pathogens or severe tissue damage leads to systemic endothelial dysfunction and subsequent failure of the lungs and other organs.

Prof. Kai Zacharowski, MD PhD ML FRCA FESAIC, the scientific coordinator of COVend, heads the Department of Anaesthesiology, Intensive Care Medicine and Pain Therapy at Goethe University Hospital Frankfurt. Prof. Zacharowski and Dr. Petra Wuelfroth, the co-founder of F4 Pharma in Vienna, have spearheaded this new scientific direction of IXION 2.0. The consortium and clinical trial were restructured in record time, underlining the unwavering joint commitment to innovative medical research in critical health conditions.

The burden of ARDS and the innovative therapeutic agent named FX06

ARDS is a critical medical challenge without drug-based treatment options and often develops as a result of an unbalanced immune response caused by viral or bacterial infections, severe trauma, major surgery, or blood transfusions. In ARDS patients, the gas exchange is impaired due to dysfunctional capillaries, damaged alveoli, and fluid accumulation in the lungs. Studies report 7-23 cases of ARDS per 100,000 inhabitants in Europe each year. ARDS accounts for around 10% of all ICU admissions and around 20% of mechanically ventilated patients, with in-hospital mortality rates of up to 45%. Despite decades of research, no effective drug treatment has yet been developed, which emphasises the urgent need for innovative therapeutic approaches.

FX06, a naturally occurring fibrin fragment in the human body, introduces a novel mechanism of action targeting the molecular origin of ARDS. It binds to vascular endothelial cadherin, a molecule at the surface of the endothelial cells lining the inside of capillaries. FX06 has an anti-inflammatory and capillary-protecting effect and can thus counteract the vicious spiral that progressively worsens the patient's condition.

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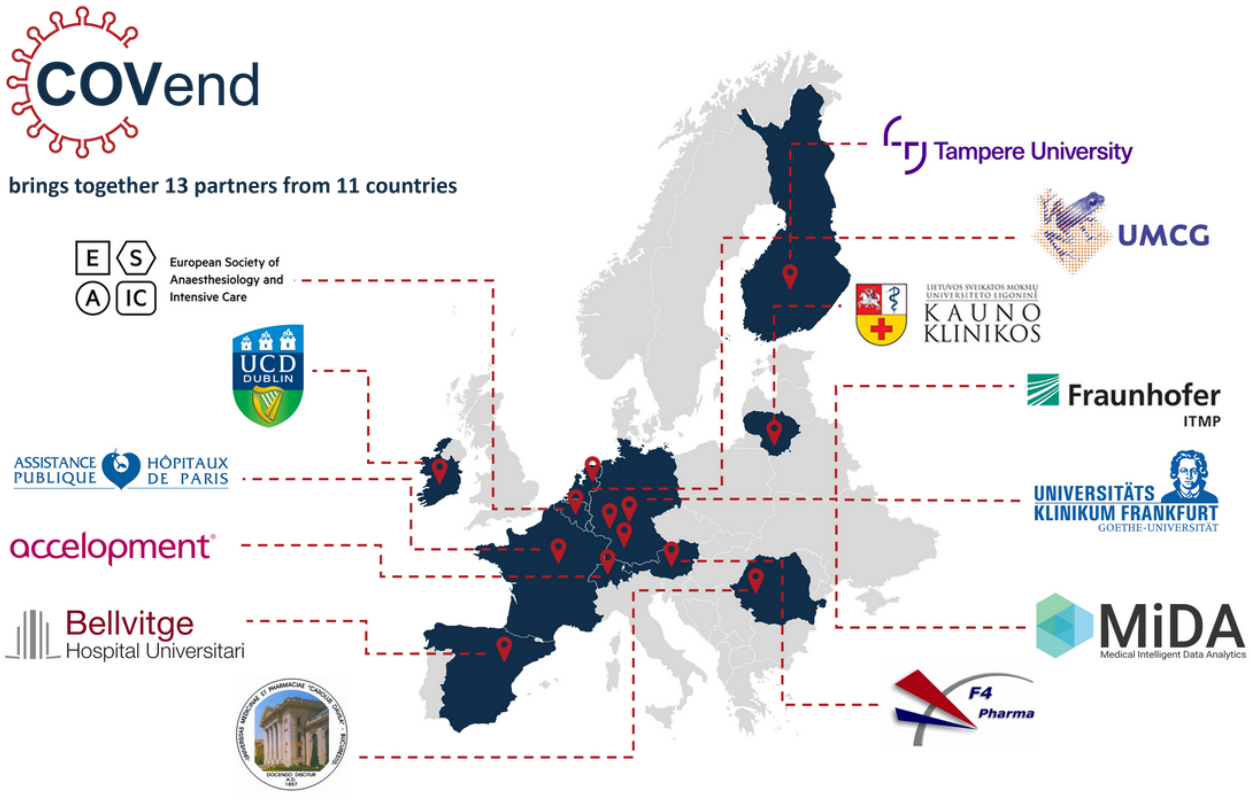
Harmonising research across borders – for patients and healthcare professionals

The IXION 2.0 study is an exploratory, randomised, placebo-controlled, double-blind, parallel phase II clinical trial. IXION 2.0 is being conducted in five European countries (France, Germany, Lithuania, Romania and Spain) and is open to patients of both sexes and all ethnicities, ensuring a diverse study population representative for all European citizens. It is embedded in the EU-funded COVend project – a multidisciplinary initiative that brings together clinicians, biochemists, data scientists, and economists to gain a comprehensive understanding of ARDS and identify effective treatment strategies for real-world scenarios.

Clinical studies in ARDS have been notoriously unsuccessful. The results of the IXION 2.0 study will therefore include patient-relevant outcomes and use an exploratory molecular analysis of the proteins, lipids, and metabolites in the blood of the study participants (known as 'multi-omic analysis') to identify subtle pathophysiological differences between patient groups. AI tools complement the data and enable an individualised clinical practice to select patients who will benefit from the therapy and monitor its efficacy based on unique biomarkers. Advanced cell biology methods using endothelial cell lines will uncover the molecular mechanism of FX06, contributing to knowledge-based trust and transparency in medicine and potentially paving the way for further life-saving applications. In addition to scientific research, the COVend consortium is also dedicated to the evaluation of FX06 from a health economic perspective. By developing a dynamic model, the socio-economic benefits and cost-effectiveness of FX06 will be assessed to ensure its practical feasibility in healthcare.



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Advancing a resilient healthcare future: Innovative focus on host response offers new hope in current and future critical clinical needs

Healthcare systems across Europe and around the world are struggling with challenges such as staff shortages, high workloads, mental health issues among medical workers, and the constant threat of emerging pathogens. The adaptation of the IXION 2.0 study to focus on ARDS provides a proactive and strategic response to these issues.

Numerous clinical events induce the immune pathways that ultimately lead to systemic endothelial dysfunction and ARDS; thus, it remains a major burden for intensive care units. In the field of infectious diseases, ARDS is not limited to COVID-19, but is also caused by other viruses of concern such as Dengue, Lassa fever, and Ebola. The focus on ARDS patients of different aetiologies addresses the immediate need for effective therapies while improving the resilience and preparedness of the healthcare system for future pandemics. This approach acknowledges the common pathophysiological mechanisms of systemic endothelial inflammation and damage that are causative for the past and likely critical for future outbreaks and clinical needs. The development of the FX06 precision therapy is particularly important given the innovative mechanism of FX06. By targeting the host response, the action of FX06 remains independent of viral mutations and strains. The COVend consortium aims to create an immediately available, precisely defined, and cost-effective treatment option that strengthens the healthcare system against a wide variety of future threats related to systemic endothelial inflammation and multiple organ dysfunction.

It is always difficult to have a vaccine or therapeutic against a disease, which we don't know. Fortunately, nature has equipped us with a defence system that is working against known and unknown pathogens. FX06 improves the response of the body and arms us against future threats.

Dr. Petra Wuelfroth
COVend Innovation Manager

Amidst the complex challenges of modern healthcare, the multidisciplinary and innovative approach of the COVend consortium is a testament to the power of scientific collaboration, diversity, and collective resilience in pushing new frontiers in medicine. For a deeper insight into our groundbreaking work, we invite you to explore further on the **COVend website** and join our community on social media (**LinkedIn**, **X**).

Questions to be directed to:

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