Coordinated Press Release

Tackling Antimicrobial Resistance: ENABLE Selects First Clinical Candidate

Apramycin has been selected as clinical candidate for the treatment of critical systemic infections caused by Gram-negative bacteria

The IMI ENABLE consortium has achieved a key objective and taken a big step forward in its mission to develop new antibiotics capable of treating Gram-negative infections. Today, the consortium announced that it has selected one of its lead molecules, the aminoglycoside apramycin, as clinical candidate for the treatment of systemic bacterial infections caused by Gram-negative pathogens. These include carbapenem-resistant Enterobacteriaceae and *Acinetobacter baumannii* – both listed as Priority 1 on the WHO priority pathogens list. Researchers at the University of Zurich (UZH) discovered the clinical potential of apramycin as a next-generation aminoglycoside antibiotic that evades all critical mechanisms of antimicrobial resistance, and have since founded the Swiss start-up company Juvabis AG that will oversee the clinical development. Apramycin is the first drug candidate to be nominated by ENABLE, a collaborative effort by IMI, a public private partnership jointly funded by the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA).

In collaboration with the ENABLE consortium, the programme owners have demonstrated the safety and efficacy of apramycin in animal models for various indications of Gram-negative systemic infections. “We are pleased that our collaboration with ENABLE has further highlighted the potential of apramycin in the treatment of complicated systemic infections in humans”, says Sven Hobbie, who leads the apramycin programme at UZH, ”Researchers at the University of Zurich and at Juvabis feel honoured to help tackling the public health threat of antimicrobial resistance. The nomination by ENABLE of apramycin as a drug candidate will accelerate the preclinical and clinical development of our product into a life-saving medicine.” As a key feature, apramycin has proven to be efficacious in animals in the treatment of systemic infections with carbapenem-resistant Enterobacteriaceae and *A. baumannii*, including clinical isolates resistant to marketed aminoglycoside benchmark drugs such as gentamicin, amikacin, and plazomicin. The programme will soon conclude GLP toxicology studies and prepare for a Phase I clinical trial application by the end of 2018.

This candidate selection comes at a time where new approaches and new molecules to combat drug-resistant bacteria are urgently needed. Each year, an estimated 700,000 patients die from drug-resistant infections. As highlighted by a report by the Wellcome Trust and the UK Government, this number is expected to multiply by 2050. “Antimicrobial resistance is a major threat to human and animal health worldwide. The success of the ENABLE project shows that by bringing together top scientists from diverse sectors, it is possible to make progress in this challenging area”, says Pierre Meulien, Executive Director of the Innovative Medicines Initiative. “Big Pharma has to a large extent left antibiotic research. Therefore SMEs such as Juvabis are important for the development of novel antibiotics and tackling antimicrobial resistance globally”, highlights Anders Karlén, leader of the managing entity at ENABLE, and professor at Uppsala University, Sweden, “and initiatives such as ENABLE, CARB-

X, GARDP or the REPAIR Impact Fund have already demonstrated their support for SME innovation and reviving the antibiotic pipeline."

About University of Zurich and Juvabis

The University of Zurich and its start-up company Juvabis AG joined forces with ENABLE in 2016. Juvabis strives to design next-generation aminoglycoside antibiotics that evade mechanisms of bacterial drug-resistance and at the same time display a superior safety profile when compared to benchmark drugs. Its proprietary technology platform of engineered ribosomes has led to the identification of apramycin's favourable antimicrobial profile and facilitated the rational design of additional lead scaffolds that hold promise for addressing various infectious disease indications.

About ENABLE

In ENABLE, over 40 European partners from academia and industry, co-led by GlaxoSmithKline and Uppsala University, joined forces in a 6-year project funded by the Innovative Medicines Initiative (IMI) to develop novel antibiotics against key Gram-negative bacteria such as *E. coli, K. pneumoniae, P. aeruginosa* and *A. baumannii*. ENABLE has rapidly succeeded in building a bottom-up drug development engine with an engaged group of highly competent scientists all working towards new drugs. ENABLE keeps the pipeline open for new Expressions of Interest. Contact Dr Katja Bölcker (opencall@nd4bb-enable.eu) for any open question on submission. Contact Laura Griestop for any communication related question (info@nd4bb-enable.eu). If you want to stay updated on our progress – register for our newsletter by sending an e-mail to info@nd4bb-enable.eu. ENABLE is part of the ND4BB programme.

The research leading to these results has received funding from the Innovative Medicines Initiative Joint Undertaking under grant agreement n°115583, resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA companies' in kind contribution. The ENABLE project is also financially supported by contributions from Academic and SME partners. www.imi.europa.eu.

About IMI

The Innovative Medicines Initiative (IMI) is working to improve health by speeding up the development of, and patient access to, innovative medicines, particularly in areas where there is an unmet medical or social need. It does this by facilitating collaboration between the key players involved in healthcare research, including universities, the pharmaceutical and other industries, small and medium-sized enterprises (SMEs), patient organizations and medicines regulators. IMI is a partnership between the European Union (represented by the European Commission) and the European pharmaceutical industry (represented by EFPIA, the European Federation of Pharmaceutical Industries and Associations).
http://www.imi.europa.eu/