

Three lead structures from SMEs identified for novel antibiotics

ENABLE nominates compounds from Juvabis, Mutabilis and Nosopharm for candidate development / Novel compounds address WHO-listed pathogens

Berlin/Brussels, 19 December 2017: To fuel the global pipeline with novel antimicrobials against antibiotic-resistant pathogens, three European small- and medium-sized enterprises (SMEs) have been selected for continued funding from the Innovative Medicines Initiative (IMI) project ENABLE: Juvabis (Switzerland), Nosopharm and Mutabilis (both from France). The companies will be supported to bring innovative lead compounds with promising antimicrobial activity against Gram-negative bacteria through pre-clinical development. In total, the European Gram-negative Antibacterial Engine (ENABLE) is providing 85 million Euro of funding from 2014 – 2020.

In the past three years, ENABLE has received more than 70 Expressions of Interest – two third from small and medium-sized enterprises and one third from academia. “The number and quality of programmes attracted as well as their diverse nature show that ENABLE is a huge contribution to antibiotic research,” highlights Anders Karlén, Leader of the managing entity at ENABLE, and professor at Uppsala University, Sweden. With its integrative approach the consortium has enabled the development of programmes for new antibiotics that might not otherwise have been supported.

Within ENABLE, SMEs and research organisations with Gram-negative antibacterial compounds (hit or lead stage) can apply to benefit from a drug discovery platform that resembles big pharma approaches. Expertise and resources involved in the platforms on medicinal chemistry, microbiology, liability and PK studies, *in vivo* pharmacology or preclinical safety allow for the parallel development of several promising compounds from hit to lead to candidate. Using the collective knowledge of the ENABLE team members and external scientific expertise, each programme is reviewed and evaluated on a quarterly basis. In the mid-term review of the project it was stated that “ENABLE is on its way of evolving into a consortium model for drug development that itself could prove to be unique”.

The three nominated companies develop novel lead structures targeting Gram-negative carbapenem-resistant pathogens such as *P. aeruginosa*, *A. baumannii* and *Enterobacteriaceae*, among others. “According to the WHO these pathogens belong to the most pressing antibiotic-resistant strains. With ENABLE, we pave the way to find effective new drugs to fight multi-drug resistance”, says Neil Pearson, project coordinator of ENABLE and senior director medicinal chemistry at GSK.

- Mutabilis (Romainville, France) was founded in 2001 and is specialized in the discovery of new therapeutic approaches for the treatment of bacterial infections. Within ENABLE, Mutabilis is working on a family of innovative compounds that specifically target PBPs (Penicillin-Binding Proteins). “These new antibiotics have a crucial advantage over the beta-lactams in that they are unaffected by beta-lactamase-induced resistances: They are effective against Gram-negative bacteria such as Carbapenem-Resistant *Enterobacteriaceae* (CRE) and potentially, *P. aeruginosa*” emphasizes programme leader François Moreau.

- Juvabis (Zurich, Switzerland) is a start-up company founded in 2016. It strives to design next-generation aminoglycoside antibiotics that withstand mechanisms of bacterial drug-resistance and at the same time display superior tolerability due to increased target selectivity by rational design. Currently, Juvabis is preparing for GLP toxicology studies to commence clinical phase I trials by the end of 2018. “It has been truly impressive to witness the highly collaborative spirit and the synergistic expertise within ENABLE that allowed us to drive the preclinical development at a very competitive pace” stresses programme leader Sven Hobbie.
- Nosopharm (Lyon, France) is a biotechnology company founded in 2009. It is specialized in the research and development of new antibacterial molecules from natural resources. It brings a promising first-in-class compound with a novel mechanism of action for the treatment of multidrug-resistant hospital-acquired infections (NOSO-95179) to ENABLE. “NOSO-95179 belongs to the antibiotic class of the Odilorhabdins, a new family we discovered from the bacterial genus *Xenorhabdus*. Odilorhabdins have shown promising efficacy in *in vivo* infection models with multidrug-resistant *Enterobacteriaceae*. With the support of ENABLE, we are currently characterizing the pharmacology of our lead compound comprehensively”, says Philippe Villain-Guillot, CEO of Nosopharm.

The ENABLE consortium aims at further enlarging its project portfolio with new antibiotics. “The selection of two antibacterial clinical candidate programmes for preclinical testing will be considered in the next few months. Despite these big steps forward, ENABLE keeps the pipeline open for new Expressions of Interest,” says Frederik Deroose, chair of the programme management committee (PMC) of ENABLE and founder of Asclepia.

Furthermore, ENABLE members regularly attend science and business conferences. One of the next opportunities to meet will be at the Berlin Conference “Novel Antimicrobials and AMR Diagnostics”, which will take place on 2 March 2018 in the German capital. Together with other stakeholders from industry, policy and science, the challenges for SME-driven innovation in the AMR field will be discussed.

About ENABLE

In ENABLE, over 40 European partners from academia and industry, co-led by GlaxoSmithKline and the University of Uppsala, 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. By 2019, ENABLE aims to select three lead compounds and two candidate drugs and to progress at least one novel anti-bacterial for systemic Gram-negative infections into phase I clinical trial. Aside from the three lead compounds, ENABLE currently has three more promising early stage compounds in the pipeline. ENABLE keeps the pipeline open for new Expressions of Interest. Contact Dr Katja Bölcker (opencall@nd4bb-enable.eu) for any open question on submission. If you want to stay updated on our progress – register for our newsletter by sending an e-mail to info@nd4bb-enable.eu.

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About ND4BB

IMI's New Drugs 4 Bad Bugs (ND4BB) programme represents an unprecedented partnership between industry, academia and biotech organizations to combat antibiotic resistance in Europe by tackling the scientific, regulatory and business challenges that are hampering the development of new antibiotics. It is made up of seven projects, including ENABLE.

<http://www.nd4bb.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/>