

PRESS RELEASE

8 June 2022

NOSOPHARM AND GNA NOW ANNOUNCE POSITIVE RESULTS FOR THE LATE PRECLINICAL DEVELOPMENT OF THE FIRST-IN-CLASS ANTIBIOTIC NOSO-502

An important milestone has been reached for the GNA NOW Consortium with the completion of the GLP toxicology studies for the NOSO-502 program. The results allow for the further development of the program to Phase 1.

Utrecht, The Netherlands, and Lyon, France, 8 June 2022

Nosopharm, a biotechnology company specialized in exploring unconventional sources of antibiotics to discover new drugs to fight antimicrobial resistance, has announced the completion and positive results of toxicology studies for NOSO-502, a first-in-class antibiotic for the treatment of multidrug-resistant hospital-acquired infections. NOSO-502 is being developed by Nosopharm in partnership with GNA NOW, a European Consortium funded by the Innovative Medicines Initiative 2 (IMI2).

NOSO-502 is the first clinical candidate in the new class of antibiotics called Odilorhabdins and was discovered by Nosopharm from a *Xenorhabdus* bacteria. NOSO-502 is intended for the treatment of the main hospital-acquired infections caused by the multidrug-resistant *Enterobacterales*: *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter* spp. NOSO-502 inhibits the bacterial ribosome with a new mechanism of action. It is active against the Carbapenem-Resistant *Enterobacterales* (CRE), whatever their profile of carbapenemase production, including polymyxin-resistant isolates. These pathogens are responsible for severe and life-threatening hospital-acquired infections and the World Health Organization (WHO) classifies them as critical priority pathogens for which new antibiotics are urgently needed. The results of the GLP toxicology studies combined with other results in clinical microbiology, efficacy, and pharmacokinetics/pharmacodynamics studies enable the launch of the preparation of a Clinical Trial Authorization application, and, if granted, the entry of NOSO-502 in First-in-Human clinical studies.

“The results of these GLP toxicology studies are very encouraging. Combined with the other results acquired with the GNA NOW Consortium, they allow us to carry on the further development of the program to phase 1, provided we receive regulatory authorization. This is an important milestone. The results demonstrate the quality and the innovativeness of NOSO-502, which has the potential to treat life-threatening multidrug-resistant infections,” said Philippe Villain-Guillot, co-founder and CEO of Nosopharm.

Antimicrobial resistance (AMR) is a growing global concern, costing an estimated 1.27 million lives in 2019, with multidrug-resistant Gram-negative pathogens accounting for 59% of these deaths¹. It's the silent pandemic – the tsunami you don't see coming – declared by the WHO as one of the top 10 global public health threats facing humanity. Gram-negative bacteria are widely regarded as the main culprit representing the gravest danger to patients. There is currently a lack of new agents able to address AMR in Gram-negative bacteria, especially compounds with novel modes of action. Finding and developing such compounds represents a huge scientific challenge, one that requires the collaboration of stakeholders with different kinds of expertise.

¹ The Lancet, February 2022: Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis.
DOI: [https://doi.org/10.1016/S0140-6736\(21\)02724-0](https://doi.org/10.1016/S0140-6736(21)02724-0)



Established in 2019, the GNA NOW Consortium (Gram-Negative Antibacterials NOW), led by Evotec as a European Federation of Pharmaceutical Industries and Associations (EFPIA) representative, is focused on addressing this gap in the AMR space by progressing new classes of Gram-negative antibiotics from lead optimization to the completion of Phase I clinical trials.

Commenting on this milestone, Lynn Silver, an expert in antibacterial drug discovery and preclinical development, and a member of the general project review group for IMI said: “The positive results of the NOSO-502 program demonstrate the importance of discovery and development partnerships like the GNA NOW Consortium. It proves that this kind of work can be done collaboratively by partners from academia, industry, and big pharma. Together, it is possible to achieve positive results during the notoriously challenging early stages of antibiotic development.”

The NOSO-502 program received a unanimous recommendation from the internal and external experts of the GNA NOW Consortium to start preparing for clinical trials. This is of particular importance as novel classes of antibiotics with efficacy against the WHO critical priority Gram-negative pathogens are very rare. No novel class of antibiotics with efficacy against these pathogens has been introduced into clinical use for more than 40 years. Furthermore, according to a very recent and comprehensive analysis of the antibacterial drug pipeline², there is no first-in-class Gram-negative antibiotic with a novel target or a novel mode of action in clinical development. If successful, the introduction into the clinical use of NOSO-502 will give a new option to the physician for the treatment of patients suffering from life-threatening bacterial infections, avoiding a therapeutic dead-end. This way, NOSO-502 will strengthen the therapeutic arsenal against Gram-negative infections.

-Ends-

² Antimicrobial Agents and Chemotherapy, March 2022: Analysis of the Clinical Pipeline of Treatments for Drug-Resistant Bacterial Infections: Despite Progress, More Action Is Needed. DOI: <https://doi.org/10.1128/aac.01991-21>



FOR THE MEDIA

For more information and interview requests, please contact Daniela Bonora, Project Communications Manager at Lygature at daniela.bonora@lygature.org or gnanow@lygature.org

ABOUT ANTIMICROBIAL RESISTANCE AND GNA NOW

Antimicrobial resistance (AMR) is estimated to have cost 1.27 million lives in 2019, with multidrug-resistant Gram-negative pathogens accounting for 59% of these deaths. From a global perspective, antimicrobial resistance could kill up to ten million people every year by 2050, which could cost up to €94 trillion (\$100 tn). In February 2017, the WHO published a list of priority pathogens for the development of new antibiotics. Carbapenem-resistant gram-negative bacteria (Enterobacteriaceae, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*) were at the top of that list, with critical priority.

GNA NOW is a joint initiative of 11 partners from industry and academia, coordinated by Lygature, with the goal of developing novel antibacterial agents. The Consortium hopes to bring one of the three simultaneously developed compounds through completion of Phase I studies, with the aim of one compound reaching Investigational New Drug (IND) stage and/or up to two compounds reaching clinical development candidate stage, by 2024.

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 853979. The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

For more information, see the GNA NOW page on the AMR Accelerator website:
www.amr-accelerator.eu/project/gna-now/

ABOUT THE INNOVATIVE MEDICINES INITIATIVE

The Innovative Medicines Initiative (IMI) IMI is a partnership between the European Union and the European pharmaceutical industry, represented by the European Federation of Pharmaceutical Industries and Associations (EFPIA). It was set up to improve health by speeding up the development of, and patient access to, the next generation of medicines, particularly in areas where there is an unmet medical or social need. It works by facilitating collaboration between the key players involved in healthcare research, including universities, pharmaceutical companies, other companies active in healthcare research, small and medium-sized enterprises (SMEs), patient organisations, and medicines regulators. This approach has proven highly successful, and IMI projects are delivering exciting results that are helping to advance the development of urgently-needed new treatments in diverse areas. IMI projects are now managed by the Innovative Health Initiative (IHI), which builds on the successes of IMI and is a cross-sectoral public-private partnership involving a wider range of health industries.

ABOUT GNA NOW PARTNERS

Nosopharm

Nosopharm is an innovative biotechnology company specialized in anti-infective drug discovery. The company discovers and develops new anti-infective drugs to combat antimicrobial resistance and infectious diseases. Nosopharm developed a unique drug discovery platform based on the exploitation of the bacteria *Phototribadus* and *Xenotribadus*. Nosopharm is the only biotech company to explore these two high-potential bacteria for anti-infective applications. Founded in 2009, Nosopharm is headquartered in Lyon, France, and employs a highly-skilled team of eight. To date, the company has raised a total of €5.9M (\$6.4M) in private equity and €8.7M (\$9.4M) in non-dilutive funding from France Relance, Bpifrance, IMI and IMI2, the French Ministry of Defense, Region Languedoc-Roussillon and FEDER. www.nosopharm.com



Lygature

Lygature, a not-for-profit foundation, acts as the independent coordinator of the GNA NOW consortium, providing governance in terms of progress, finance, collaboration and communication. Since 2006, Lygature has supported over a hundred public-private partnerships in the field of life sciences & health with a combined budget of over 1 billion euros. www.lygature.org

BIOASTER

BIOASTER is a Technology Research Institute, an independent non-for-profit research organization created in 2012. It conducts innovative technological research projects in applied microbiology: Composed of high-level scientists and engineers, BIOASTER teams use state-of-the-art technological equipment within their integrated 8 technology units located in their labs (BLS2-BLS3) in Lyon and Paris. www.bioaster.org

Helmholtz Centre for Infection Research

Scientists at the Helmholtz Centre for Infection Research (HZI) in Braunschweig and its other sites in Germany, are engaged in the study of bacterial and viral infections and the body's defence mechanisms. They have a profound expertise in natural compound research and its exploitation as a valuable source for novel anti-infectives. As member of the Helmholtz Association and the German Center for Infection Research (DZIF) HZI performs translational research laying the ground for the development of effective new treatments and vaccines against infectious diseases.

www.helmholtz-hzi.de/en

North Bristol National Health Service Trust

The Microbiology Research Department at North Bristol National Health Services Trust (NBT) has over 25 years of experience in performing PK/PD in vitro experiments to aid drug development programmes. In GNA now, these PK/PD evaluations will be central to the programme success. NBT has experience in performing previous Quality Management studies in PK/PD programmes.

NBT will use their expertise to develop a Quality Management Template (QMT) to ensure all PK/PD experiments across the GNA Now drug programmes are completed to this same QMT. This will safeguard the output from these studies, give strength to the data and therefore give confidence to regulators that the pre-clinical dose determination is robust.

NBT has an established Patient and Public Involvement (PPI) group who have collaborated on a number of microbiology research projects. The group has contributed to the development of a Toolkit and Practical Guide to PPI in antimicrobial drug development and is looking forward to explore the potential for PPI in pre-clinical aspects of the antimicrobial medicines development cycle. www.nbt.nhs.uk

University of Liverpool

The Centre for Antimicrobial Pharmacodynamics (CAP) is based in the Department of Clinical and Molecular Pharmacology, Institute of Translational Medicine at the University of Liverpool. The CAP is one of relatively few academic laboratories in the world that can develop pharmacodynamic packages for new antimicrobial agents. CAP has extensive experience in providing preclinical pharmacokinetic-pharmacodynamic (PK/PD) evaluation of compounds and early phase clinical support to ensure new drugs are developed in a streamlined manner. www.liverpool.ac.uk

Inserm

Inserm U1070 "Pharmacology of Antimicrobial Agents", is a Research Unit affiliated to the University of Poitiers and Inserm. It has been created in 2012 and comprises 20 permanent staff members (clinicians, pharmacist, scientific) and 13 students (PhD and master students). It is located on the University Campus of Poitiers (France). The objective of Inserm U1070 is to develop innovative PK/PD modelling approaches to select the best dosing regimen of antibiotics administered alone or in combination as well as the best route of administration and best formulation, in order to increase antimicrobial efficacy and limit bacterial resistance. Inserm U1070 conducts translational research, from cells culture models to patients, and integrating microbiology, analytical chemistry, drug formulation, and in vivo preclinical experiments. To date, Inserm U1070 received grants from Region Nouvelle Aquitaine, ANR, PHRC, JPIAMR, IMI, and CPER-FEDER and has established collaborations with ANSES and several Universities in France (Paris Sud, Paris Diderot) and abroad (Dublin, Erasmus MC, Uppsala, Hamburg, Catholic University of Louvain), as well as leading pharmaceutical companies. www.inserm.fr

Erasmus MC University Medical Center Rotterdam

The Erasmus MC is one of the largest academic hospitals in Western Europe, employing more than 14,000 people, with researchers being involved in more than 221 EU-financed projects. With expertise in pharmacology and innovative PK/PD approaches, the department of Medical Microbiology and Infectious Diseases extensively researches the mechanisms of antimicrobial resistance, their detection and characterization. The department has more than 40 years of experience in animal models of infection, coupled to antimicrobial resistance and drug efficacy studies. www.erasmusmc.nl/nl-nl

The Medical University of Vienna

The Medical University of Vienna (MUW) is located in one of the largest hospitals in Europe. Within the university, the Department of Clinical Pharmacology is specialized on clinical studies with antimicrobial agents. They performed almost 1000 drug studies in the last 25 years and their spectrum includes the full range of Phase 1 studies from First-in-Man studies to special PK studies. Thereby the MUW will link the knowledge of the consortium to patients in the fastest possible way while being fully compliant with regulations for studies involving humans. The obtained data provide the basis to optimize dosing by PK/PD means to enhance efficacy while preventing side effects and development of bacterial resistance. www.meduniwien.ac.at/web

Fraunhofer

Fraunhofer-Gesellschaft zur Foerderung der angewandten Forschung e.V. (Fraunhofer), is the leading organization for applied research in Europe. Its research activities are conducted by 72 institutes and it employs a staff of 26,600, with an annual research budget of 2.6 billion euros. The Fraunhofer Institute for Molecular Biology and Applied Ecology IME, with over 520 employees at its six sites in Schmallenberg, Aachen, Gießen, Münster, Frankfurt/Main and Hamburg conducts research in the field of applied life sciences from a molecular level to entire ecosystems. Fraunhofer IME ScreeningPort in Hamburg contributes with its expertise in drug discovery and life science informatics. Within GNA NOW it will be providing support to the project in three main areas: Firstly, a data management plan will be formulated, including regular monitoring of the status of project data sets and annual audits of compliance to quality standards across the project team. Key to the data NEWS RELEASE 6 management plan will be systematic implementation of the IMI FAIRplus toolbox (where Fraunhofer IME is a work package leader) to FAIRify all data from the moment of generation all the way to archiving and eventual re-use of appropriate data sets. Secondly, a project wide cloud based ELN as recommended by Pillar A (IMI-Combine), where Fraunhofer IME is in the lead for platform infrastructure, which will be used to support day-to-day experimental data generation within the projects. Thirdly, provision of software tools to support aggregated discovery and handling of preclinical data sets, which will be based on the GRIT42 suite that was developed as part of the ND4BB InfoCentre in cooperation with Fraunhofer IME. www.fraunhofer.de

Evotec

Evotec is a life science company with a unique business model that delivers on its mission to discover and develop highly effective therapeutics and make them available to the patients. The Company's multimodality platform comprises a unique combination of innovative technologies, data and science for the discovery, development, and production of first-in-class and best-in-class pharmaceutical products. Evotec leverages this "Data-driven R&D Autobahn to Cures" for proprietary projects and within a network of partners including all Top 20 Pharma and over 800 biotechnology companies, academic institutions, as well as other healthcare stakeholders. Evotec has strategic activities in a broad range of currently underserved therapeutic areas, including e.g. neurology, oncology, as well as metabolic and infectious diseases. Within these areas of expertise, Evotec aims to create the world-leading co-owned pipeline for innovative therapeutics and has to-date established a portfolio of more than 200 proprietary and co-owned R&D projects from early discovery to clinical development. Evotec operates globally with more than 4,200 highly qualified people. The Company's 15 sites offer highly synergistic technologies and services and operate as complementary clusters of excellence. www.evotec.com