In conversation with GNA NOW Project Lead Eric Bacqué of Evotec

Antimicrobial Resistance (AMR) is a global and serious threat to human health and today, Gram-negative bacteria are widely regarded as the main culprit representing the gravest danger for patients. Established in mid-2019, the GNA NOW Consortium (Gram-Negative Antibacterials NOW) is focused on progressing new classes of Gram-Negative antibiotics from lead optimization to the completion of Phase I clinical trials. To find out more, we spoke with Project Lead, Eric Bacqué from Evotec.

Can you introduce yourself and tell us a bit about your background?

My name is Eric Bacqué, I'm a chemist by training and have been working on anti-infectives for more than 20 years in various companies like Aventis and Sanofi. I joined Evotec ID Lyon in mid-2018 as Head of Chemistry to work on antibacterials, but also antivirals and antimycobacterials. I've seen a lot of changes in the AMR field over the course of my career. When I started off in this field in the late 1980s it was a very different world. The focus then was on Gram-positive bacteria as there were no major concerns of resistance with Gram-negative bacteria. In the years to follow, I saw the progressive de-investment of Big Pharma in this field because of the low returns on investment and the lengthy and costly clinical trials. Since then, the spread of AMR among Gram-negatives has made it an even more challenging area to work in, but I'm pleased to be able to contribute to positive changes through projects like GNA NOW, which is helping to curb the major threats posed by AMR.

Can you tell us more about your role as Project Lead?

I took over the role of Project Lead of the GNA NOW Consortium in 2020. The Consortium is a European collaboration of 11 partners, and it is my privilege to serve as Project Lead for this partnership of expert scientists. My main responsibility is to align all aspects of the project and make sure everyone is kept informed of developments and key milestones. I also help with solving any problems that may arise with the help of the coordinating partner Lygature. For each program of the Consortium's portfolio, we gather together all the key players and define an action plan in terms of timelines and check points to agree upon in order to meet deliverables. As Project Lead, it is important to accommodate the different views of the various partners and project teams – helping everyone get what they need, whilst keeping in mind the constraints and capacity of the partners in the Consortium.

"Due to the complexities of finding new antibacterials, especially Gram-negatives, you cannot expect to succeed alone. You have to find partners with different expertise and experiences to maximize your chances of success."

How did you get involved in GNA NOW?

I am the EFPIA coordinator of the IMI ENABLE Consortium, which is coming to a close this year. In 2018, at Evotec, we were looking for a similar successor project and were ready to embark on a new challenge. We wanted to continue working within a European public-private partnership to secure co-financing to continue our work on Gram-negatives with high caliber partners. One of the main reasons to get involved in the GNA NOW Consortium and continue with these kinds of partnerships is because I strongly believe that due to the complexities of finding new antibacterials, especially acting against Gram-negatives, you cannot expect to succeed alone. You have to find partners with different expertise and experiences to maximize your chances of success.

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

What interests you most about the project?

For me, there are two sources of interest. Of course, there is the scientific interest to progress work in this very critical area of AMR. We have a chance to make a difference – developing compounds that have the potential to be first-in-class antibacterials, which is very exciting and valuable work. In addition to this, the daily operational processes are also of interest to me – this is science in the making and it is really something I am invested in. As part of this project, I have the pleasure to partner and work with some of the key opinion leaders in this field, which is incredibly valuable to me. It's fascinating to work with this mix of different mindsets from academic and industry.

"We need new antibacterials – they are the cornerstone of modern medicine. Without them, we essentially go back in time to the middle ages. Today, AMR may not seem like a major issue, but we have to be prepared. It's like watching a storm approach: once the storm has arrived it will be too late."

What have been the biggest changes in the AMR field over the past few years and how do you see things progressing going forwards?

As already alluded to, there has been a fundamental shift from focusing on Gram-positive pathogens to Gram-negative pathogens with the progressive surge of Gram-negative resistant bacteria over the last 20 or so years. Over the same period, the number of new approved antibacterials has considerably fallen, especially those with a new mechanism of action. In parallel, the players in the field have dramatically changed from the traditional large pharmaceuticals to academics and small biotech companies, with more limited means and expertise in the field. Overall, finding, optimizing, developing, and commercializing antibacterials has become a major challenge. In recent years, we have even seen a new concept: bankruptcy by success. Registration of new antibacterials has been followed by the immediate bankruptcy of the corresponding companies because the expected sales couldn't compensate for the post approval costs (e.g., pediatric clinical trials, pharmacovigilance, supply chain maintenance). On a positive note, there has been growing awareness of the AMR threat among the public and politicians. We have seen the creation of so-called "push incentives" to fund early drug discovery projects, which has been a tremendous help in the search for finding and optimizing new antibacterials. But even so, even if you can progress your favorite project to Phase I trials, you have to then progress to Phase II and III trials, which are very expensive. And finally, you have to reach the market where returns on investment can currently take more than 10 years. Things are slowly changing and there has been progress with the emergence of the first so-called "pull incentives", but this is a devastated field. Something has to dramatically change in the AMR business model to attract new players and investors to ensure that we will have new antibacterials for current and future patients so that we can cope with the spread of resistant bacteria.

Has there been more buy-in from governments to raise awareness and stimulate funding?

Yes, we have seen some new initiatives. The AMR problem has been on the G7 and G20 agendas for a few years. It's progressing, but slowly. Even Big Pharma has made a comeback with the creation of the AMR Action Fund in July 2020 that aims to bring two to four new antibiotics to the market by 2030, relying on a one-billion-dollar fund gathered by more than 20 pharma companies. This is a key initiative that should help biotech stakeholders to cross the late stage of clinical development (Phase II and III), the so-called "valley of death" for AMR programs.

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What do you consider the biggest challenges of the GNA NOW project?

Probably the fact that for obvious reasons, we haven't been able to meet face-to-face over the last year. As mentioned, there are a lot of partners involved in GNA NOW: 11 spread all over Europe. It's unfortunate that we have to resort to videoconferences, as meetings in person can go a long way in creating the necessary links, especially for young projects like this.

Lastly, what do you think has been the biggest achievement to date?

No official milestones have been reached as yet, but one of the biggest achievements has been the progress of the NOSO-502 project, for which we have managed to answer some key questions that were outstanding at the beginning of the project. NOSO-502 is the first clinical candidate from the novel antibiotic class called *Odilhorhabdins*, discovered by the project partner Nosopharm. It inhibits the bacterial ribosome with a new mechanism of action and is intended for the treatment of complicated urinary tract infections and intra-abdominal infections. We have completed the synthesis of large-scale batches of the clinical candidate that will be the key material needed to progress through preclinical development. We are on track and have made good progress so far.

About GNA NOW

Established in July 2019, the GNA NOW Consortium is a European collaboration of 11 partners focused on progressing Gram-Negative antibiotics from lead optimization to the completion of Phase I trials. Working under the AMR Accelerator umbrella, the project is funded by the Innovative Medicines Initiative (IMI) with in-kind contributions from industry partner, Evotec.

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