AN AUDIENCE WITH…

Jean-Jacques Garaud

Head of Roche Pharma Research and Early Development, Roche, Basel, Switzerland. Before joining Roche in 2007 as Global Head of Pharma Development and Chief Medical Officer, Jean-Jacques Garaud was at Novartis Pharma in the USA for 5 years. He started as Head of Clinical Research and Development in Global Medical Affairs, progressing to Global Head of Exploratory Development. Prior to Novartis, Garaud spent 10 years in senior positions at the Schering–Plough Research Institute in the USA.

What changes have been made to Roche's R&D organization since the acquisition of Genentech? Are there any aspects of the previous R&D structure that you have chosen to maintain, and if so, why?

We wanted to maintain the diversity of approaches that we have in research and early development at both organizations to enable and protect innovation. At Genentech the organization is called Genentech Research and Early Development (gRED), which is located in South San Francisco, USA. At Roche, the equivalent organization is called Pharma Research and Early Development (pRED), which is a global organization with three main centres: Basel, Switzerland; Nutley, New Jersey, and Penzberg, Germany. The two organizations, gRED and pRED, are also complemented by a worldwide network of partners.

One major change due to the acquisition was that Genentech's Late-Stage Development and Manufacturing operations were combined with the global operations of Roche, thereby achieving substantial scale benefits and operational synergies. However, the gRED organization has kept its structure and decision-making process as it was before the merger. At pRED, we continue to work in five disease biology areas — oncology, inflammation, neuroscience, metabolism and virology — which are now known as discovery translational areas. The discovery translational areas work side by side with all the research functions such as non-clinical safety and, following the merger, now also include translational expertise and early development under the same roof. We have been successful with both pRED and gRED and we do not want to stop what has worked well before.

Are gRED and pRED working together, and if so, how?

At the early research stages pRED and gRED do not share information on the biology — such as targets or pathways — so that we can maintain a true diversity of approaches. However, when we start to prepare for an investigational new drug dossier, we open up the books. We then determine whether we want to merge efforts on a particular project or whether we want to continue to explore two different avenues.

The independence of the two 'REDs' is crucial to ensure a good mix of therapeutic modalities and technology platforms. But this doesn't mean that we do not talk to each other: we want to benefit from the expertise of both organizations and to ensure mutual knowledge transfer and sharing of technology platforms in certain areas. So, for example, gRED has done a lot of work in the field of armed antibodies (antibody–drug conjugates) that pRED can benefit from when starting a project in that area. pRED offers the same support for stem cell research or small interfering RNAs (siRNAs), in which we have a strong integrated effort. All the platforms are to be shared and we have established a clear process to do so.

From a scientific perspective, which areas of Roche's R&D are you most excited about and why?

I am particularly excited about protein engineering, especially related to antibodies. We have a proprietary technology that allows us to generate antibodies that have multifunctionality to target therapies to tumours more effectively. For example, there are new ways of engineering proteins and antibodies to target cytotoxic and immunomodulating cytokines to inflammatory processes in the tumour stroma.

Another hot field is siRNA. The challenge here is to deliver the siRNA to the right part of the cell to silence a critical target without destroying the tissue or the organ. We are exploring the use of highly engineered antibodies to carry the siRNA to the target itself. It is perhaps a bit like science fiction right now, but within 2–5 years we should make progress in that direction.

How is Roche approaching the potential to develop more personalized/stratified medicine? For example, how are activities such as biomarker qualification integrated into R&D programmes?

The research and development of biomarkers is now completely integrated into the drug development process at Roche. When a target is validated our researchers start to identify markers of efficacy and treatment response, which, for example, will be used in early clinical development from Phase I to Phase IIa. In fact, we include a biomarker strategy for most of our clinical programmes. We have a direct connection with our Diagnostics Division that offers a broad range of technologies and tools to develop a biomarker test that accompanies clinical development. Not all tests will become a true companion diagnostic but the biomarkers will be extremely valuable during clinical research to identify the patients that are most likely to benefit from a drug. We will of course always look for potential new companion diagnostic tests.

How is Roche addressing industry-wide challenges such as high attrition rates in late-stage development, and the need for more effective predictors of drug toxicity?

We are involved with the Innovative Medicines Initiative in the European Union at a high level and are involved in many of the research collaborations. We are also part of the US National Institutes of Health's Biomarkers Consortium and the Predictive Safety Testing Consortium led by the US FDA's Critical Path Initiative. We consider that being part of these initiatives is crucial, particularly when it comes to drug safety. Overall, we need to improve the benefit–risk ratio in drug development and we think that personalized health care offers a solution. With this approach we are able to focus on the patient population that is most likely to respond to a drug. This should improve its benefit–risk ratio, and lead to a greater therapeutic benefit for the patient.

Interview by Bethan Hughes