AN AUDIENCE WITH…

Luciano Rossetti

Head of Global Scientific Strategy, Merck Research Laboratories, USA. Luciano Rossetti, M.D., oversees all of Merck Research Laboratory's franchise leaderships and determines how to leverage Merck's science for the benefit of patients in each of the company's current therapeutic areas of interest: cardiovascular disease, diabetes and obesity, infectious disease, oncology, neurosciences and ophthalmology, respiratory and immunology, and women's health and endocrinology. He joined Merck in 2006 as Senior Vice President and Franchise Head of Diabetes and Obesity after 15 years at the Albert Einstein College of Medicine, New York, USA.

How has the merger with Schering–Plough (SP) influenced the areas of research and development that Merck is focusing on, and which areas are you most excited about?
The merger with SP was based on the congruence of general scientific interests but with specific complementary projects. For example, both companies were interested and highly present in cardiovascular disease. We, legacy Merck, were very interested in the area of thrombosis. We had started to make strides in that direction with our licensing agreement in 2009 with Portola Pharmaceuticals to develop their investigational anticoagulant betrixaban [an oral factor Xa inhibitor]. In the area of antiplatelet therapies, the most interesting science was completed at legacy SP for vorapaxar, their protease-activated receptor 1 (PAR1) antagonist. Also, legacy Merck was heavily invested in atherosclerosis; in particular, developing innovative approaches to raising high-density lipoprotein cholesterol with anacetrapib [an investigational oral inhibitor of cholesteryl ester transfer protein]. So, through the merger we were getting stronger in some areas and maintaining our strength in others.

Two areas of particular excitement to me are hepatitis C virus (HCV) and thrombosis. Both legacy companies were heavily invested in HCV research. Merck had an early-stage pipeline candidate (vaniprevir) and SP had a late-stage pipeline candidate boceprevir [an HCV protease inhibitor] and commercial products (PEG–Intron [polyethylene glycol–interferon] and ribavirin). In the area of thrombosis, there is the real potential to develop other drug classes that will displace the standard of care. Warfarin, the current standard-of-care therapy for the prevention of cardiovascular events and strokes, is likely to be entirely displaced by more effective, safer and more convenient treatments based on targets in the coagulation cascade that do not increase the risk of bleeding.

Have any lessons been learnt from large-scale mergers of other companies that will help Merck to avoid the dangers of long-term loss of productivity and innovation that has been associated with these types of mergers?
One lesson learnt from previous large-scale mergers was the need to ensure that prioritization decisions took place quickly. So, well before the merger was completed, we prepared detailed information about each project. We were not allowed to see each other's data until the deal closed in November, but then we were ready to go through an effective process of prioritization across the new pipeline from discovery through to life-cycle management. Within ~3 months, we had done the bulk of the work and made important decisions about what should remain in the pipeline. Approximately 45% of programmes came from legacy SP and 55% from legacy Merck, so it was a pretty good balance.

Another important lesson learnt was that we studied the governance, structure and culture of each company deeply. I was part of the leadership team that made decisions about drug discovery, and I thought that our ability to accept where one company had some deficiencies and the other had strengths was impressive. This process ensured that the new governance and structure was not biased but a true integration of the two cultures.

What are the reasons behind Merck's continued commitment to cardiovascular research?
We think that the opportunity in cardiovascular disease is enormous, particularly if you consider the rapid increase in incidence of cardiovascular diseases, such as ischaemia and stroke, in emerging markets. This creates a moral obligation for us to contribute to the cure and treatment of these diseases. However, the bar for these treatments — to have commercial success as well as a big impact on cardiovascular disease — is frankly quite high and our strategies must delineate areas of need to make sure that we do not expend substantial resources in areas that already have good treatments.

We think that thrombosis and anticoagulation are areas of unmet medical need that, from a scientific point of view, have made less progress than other areas. Many products that are currently used to treat thrombosis expose patients to an increased risk of bleeding. Our PAR1 antagonist data support differentiation from these current therapies and so we think we can change the treatment paradigm. Similarly, there is an opportunity in anticoagulants as new therapies replace warfarin and heparin as standards of care. Although Merck will not be the first to market with a factor Xa inhibitor or a direct thrombin inhibitor, we do think that there are opportunities to identify best-in-class molecules.

How is molecular profiling affecting Merck's drug development strategies?
Molecular profiling pervades the overall scientific strategy of the company. In 2006, we started a campaign to increase our ability to make early predictions on the downstream success of our projects. We developed tools for early decision-making and are investing heavily in molecular profiling, in RNA interference and in other tools, such as imaging, that will allow us to interrogate specific pathways and targets at an early stage. This investment in new technology allows us to put more filters and screens in to the process of early drug discovery and development. They allow us to judge at a preclinical stage whether a project is really promising before investing in the chemistry. The technology also enables us to identify a group of patients that may benefit from a certain therapy. While the benefit is particularly obvious in oncology, we should not underestimate the impact that it is also having on other disease areas.

Interview by Bethan Hughes