AN AUDIENCE WITH…

Joseph Bolen

Chief Scientific Officer, Millennium: The Takeda Oncology Company, Cambridge, Massachusetts, USA. Prior to joining Millennium, Joseph Bolen, Ph.D., held positions including Vice President and Global Head of Oncologic Diseases at Hoechst Marion Roussel, and Executive Director of Oncology Drug Discovery at the Bristol–Myers Squibb Pharmaceutical Research Institute. In addition to other senior academic positions, he was Section Chief of the Biochemical Oncology Department at the National Cancer Institute in Maryland, USA, and a founding member of their Laboratory of Tumor Virus Biology.

What has Millennium gained from last year's acquisition by Takeda, and vice versa?

Millennium became a subsidiary of Takeda responsible for the clinical development and global marketing of all oncology products. Before the acquisition, Millennium focused primarily on the US market but, as we did with bortezomib (Velcade), the plan was to partner with other firms to do the sales and marketing outside of the United States. The biggest change is that we now have to think about the global oncology market, with multiple regulatory submissions worldwide. To do this, we have had to increase our clinical development and regulatory staff to scale everything up and move our and Takeda's compounds into the clinic (increased from ~4 to14 compounds).

By acquiring Millennium, Takeda gained an organization that had a lot of experience in oncology product development, marketing and sales. Despite being small, it could be proportionally built up depending on what the expectations and needs of the company might be at any one time.

In addition, even though we only had four or five molecules in the clinic, the vast majority were novel molecules. It takes a certain kind of development organization to have the courage to develop novel drugs for novel targets and be really out on the edge doing things for the first time. I think that entrepreneurial spirit appealed to the folks in Japan. From the science standpoint, they also gained our expertise in small-molecule drug discovery in the area of protein homeostasis, which was an area of science that they were interested in but they had no local expertise.

Which anticancer strategies that Millennium is pursuing are you most excited about and why?

From my standpoint, the area of protein homeostasis — learning the rules of how protein synthesis is balanced with protein degradation — is one of the most exciting oncology areas to be in. If you look back to the early to mid 1980s, when I was at the National Cancer Institute, the oncology research that was most exciting was the area of protein kinases, and that is how I see protein homeostasis today. The area is rich in targets, and we are going to see many different drugs come out of this area, not only for cancer but many types of diseases (such as neurodegenerative diseases). With advances in proteomics, particularly in the mass spectrometry area, we are starting to get the kind of perspective that in the late 1990s we could only get for genomics. Now we have the scientific expertise at Millennium to be at the forefront of that research and to rapidly translate it into novel medicines, so it is quite exciting.

Our job at Millennium is not to simply make medicines for people who have cancer, but to make medicines that can change how medicine is practised. This is what happened with bortezomib. Cancer is an extraordinarily complex genetic disease and we have to take several approaches to come up with therapeutics that might be not just useful, but hopefully transforming. It takes a large, multi-modal, multi-disciplined approach to get a critical mass of scientific and clinical understanding to develop something significant.

Could you provide your perspective on the lessons that were learnt from the development of bortezomib?

One of the most important lessons that we learnt from the development of bortezomib was the need to hire experienced sales, marketing and regulatory staff who could translate the complex science into forms that all of the different stakeholders (patients, physicians, insurance companies and the regulatory agencies) could understand. I think most scientists would expect that a compound that works should just sell itself, but nothing could be further from the truth. When we hired experienced staff, the first thing they said was that the scientific explanation of bortezomib was too complicated. I never thought it would be that hard to get the explanation across, so that it could be understood and judged appropriately. The commercial people we hired helped us. They sat down and listened and ensured that the relevant information was used to explain the potential utility of a proteasome inhibitor to the appropriate constituencies.

How is Millennium adapting to the need for increased stratification of patients in anticancer drug development?

In oncology, this idea of personalized medicine, or patient stratification, is something that we have tried to build into our development processes over the past 10 years to analyse the potential outcomes in certain types of disease states. We all work very hard to tease out who would receive most benefit from a compound that we are putting into the clinic. For all of our products, our intent is to try to define as best as possible which patients will benefit most from a potential drug and in what combination it would be most useful. With a single compound, the most practical stratification is going to be to find out how compounds work on different genetic backgrounds and if the evidence points to a parallel pathway that will allow the cancer cell to survive when the first pathway is inhibited. A recent example is the agreement between Merck and AstraZeneca to combine two experimental drugs to target two pathways at the same time, in a Phase I clinical trial. I expect we will be seeing more development like that because it is important to try to understand the whole picture of the disease that you are treating.

Bethan Hughes