AN AUDIENCE WITH…

Francis Collins

When Francis Collins was appointed as Director of the US National Institutes of Health (NIH) last year, he listed translational medicine as one of his top five priorities. Although some elements of this push were already in place, others remain to be implemented. Taken together, he hopes these efforts will both 'de-risk' drug development and empower academic researchers to become better partners for industry. **Asher Mullard** caught up with Collins to discuss the industry's woes and how the NIH can help.

Why did you prioritize translational medicine?

We have seen a deluge of new discoveries in the last few years on the molecular basis of disease. This is true for rare diseases, common diseases and neglected diseases, and allows us to feed new ideas into the therapeutic pipeline. That's the good news. But there is bad news too. Despite increasing investments by the private sector, there has been a downturn in the number of approved new molecular entities over the last few years. Also, drug development research remains very expensive and the failure rate is extremely high.

Perhaps in part responding to these factors, and to the downturn in the economy, pharmaceutical companies have cut back their investments in research and development. We can't count on the biotech community to step in and fill that void either, because they are hurting from an absence of long-term venture capital support. So, we have this paradox: we have a great opportunity to develop truly new therapeutic approaches, but are undergoing a real constriction of the pipeline. One solution is to come up with a non-traditional way of fostering drug development — through increased NIH involvement.

How do you plan to do this?

I like to think of this in a broad sense of "what kind of paradigm can we initiate and expand between academic researchers and the private sector to move the therapeutic agenda forward?" Academic investigators have always played some role in drug development, but usually in the earliest stages of target identification. If we want to see those targets exploited — recognizing that many of them are not initially attractive economically because of their uncertain druggability or perhaps relevance for only a rare disease — then academic investigators need to have the tools to push discovery efforts forward themselves.

By having the NIH more engaged in the pipeline, we can also ask whether we can improve the success rates of drug development. Pharmaceutical companies have been making drugs for a long time, and have created some great products, but there's been less consideration of the whole drug development pipeline itself as a scientific problem. We need to re-engineer the process, with a lot more focus on the front end.

What programmes do you have in place?

We have several different programmes that we are working to fit together. We have four NIH-funded facilities that collectively have the capacity of a midsized pharmaceutical company to do high-throughput screening, assay development and medicinal chemistry. In the preclinical space — moving promising compounds through the expensive and risky 'valley of death' — Therapeutics for Rare and Neglected Diseases (TRND) supports projects that would not be of interest to commercial players because of modest market sizes. The Cures Acceleration Network (CAN), the newest arrival on the scene, will also support preclinical 'high need' research, defined pretty much as any area where therapeutics are lacking and in need of development: it is not limited to rare and neglected diseases, and could also support neglected targets. CAN was created as part of the Healthcare Reform Act, though we are still awaiting funding approval for the 2011 financial year. The Clinical and Translational Science Awards (CTSA) and the NIH Clinical Center then provide broad support by empowering academics to run Phase I and II trials.

Another opportunity we are talking about is to pay particular attention to compounds that have been extensively studied by pharmaceutical firms but have for some reason been abandoned. Companies have been reluctant to open their freezers to us in the past, but are now much more interested in doing so.

There are a lot of moving parts to this set of resources that ultimately need to be synthesized into a smooth process. One of my goals over the next year is to try to identify ways to put these together into a more seamless enterprise.

How is the NIH's relationship with the US Food and Drug Administration (FDA) evolving as you pursue drug development?

Peggy Hamburg and I started talking about the need for tighter collaboration between the NIH and the FDA even before I was formally appointed. And we've now set up an NIH–FDA Leadership Council to focus on improving the prospects for getting effective and safe drugs to market as quickly as possible. A lot of the NIH investigators who are being empowered to conduct drug development work aren't that familiar with how the FDA does business — I hope that by working more closely together researchers will have greater understanding of what they need to do so that they don't stub their toes and then have to backtrack to meet FDA standards.

Drug discovery is a risky, expensive activity. How will the NIH be compensated for its efforts?

Our approach will be to 'de-risk' projects that might otherwise be seen as economically unattractive. As soon as the risks are reduced sufficiently to attract commercial attention, we plan to hand over projects to companies to carry out the next step. There is absolutely no intention of turning the NIH and its grantees into competitors with the private sector. We are aware of just how risky this approach is: most projects will fail and we will not reap rewards overnight. But in projects where the NIH has invested a lot of the upfront effort, there will be a model — which pharmaceutical companies seem pretty comfortable with — for sharing intellectual property rights in a way that royalties will flow back into public research. I think that's only fair.