Innovation in development

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Just over 140 years ago, the world's first industrial-sized R&D laboratory opened. As someone who's devoted his working life to finding new R&D breakthroughs, I'm envious of the explosion of activity that made the lab's owner, Thomas Edison, one of history's most remarkable inventors. But it's his process of innovation that inspires me, as much as his life-changing creations.

After hitting a brick wall with one approach, he famously said: 'I have not failed. I've just found 10,000 ways that won't work.' And so it is in pharma R&D. Although we strive to find the best treatments and deliver them swiftly to patients, many of our efforts will be unsuccessful. These frustrating missteps are crucial, however, because, like Edison, they take us closer to our ultimate goal, provided we react with agility.

This begs the question: Can we discover which treatments are unlikely to be successful, earlier on? We might address this question using 'experimental medicine', a new approach to clinical development, which I'm confident will reap significant rewards for the industry, especially around decision making timelines. As opposed to relying on large-scale trials, which require significant investments over long periods of time without the guarantee of success, experimental medicine takes a more disruptive approach.

Programmes that are unlikely to deliver transformational medicines early on can simply be halted. Scarce resources can then be allocated to fewer priority assets with positive signals, and that these can be sufficiently backed.

Considering that decisions are made based on a relatively small, high density of clinical trials, these three questions should be asked:
1 Are there trends towards clinical improvement?
2 Do we hit the pathway in the right way?
3 Does this translate into changes in biomarkers associated with common final pathways known to be relevant for clinical success?

If you hit the mechanistic pathway but answer 'no' to all these questions, it's unlikely that the medicine is transformational – and the programme should be stopped. Although in some ways effective, the current model of pharmaceutical development is slow, expensive and unsustainable. What we need is to implement approaches with a greater and faster probability of success, liberating scientists to accelerate or discontinue with maximum efficiency.

I remember the first patients with rheumatoid arthritis who were treated with anti-TNF antibodies in the 1990s. Until that time, most patients were severely disabled by their disease but after treating only a few, we knew we were watching clinical effects we'd never seen before. It was a therapeutic revolution.

If we want to develop medicines that can not only be approved by regulators but are also strongly needed by patients and supported by payers and healthcare professionals because they meet relevant needs, we only need to observe a small number of patients to test the effect.

Speed, knowledge and innovation are the core of experimental medicine. In addition to early decision making, this approach provides deeper insight into the optimal dose and the effects in the target tissue. It also helps scientists identify biomarkers of response in specific subsets of patients. The results support the rationale for larger, focused studies of a limited number of medicines, examining whether the positive effects of the medicine shown in the experimental medicine study really translate into clinically meaningful improvement.

Thus, this approach helps to reduce attrition and increases the probability of success in late stage development. Other approaches to reduce attrition include better target identification and validation, *eg* by requiring genetic evidence, and a strong focus on high quality molecules.

Previously, swift decisional analysis based on observations in small numbers of patients was seen as controversial; today it's termed 'disruptive innovation'. Such innovation is the mantra of our age, and one we must embrace if we're to create a new generation of transformational treatments.

Disruption, however, is not easy. To achieve this, we need smart, empowered leadership that balances the need to listen with that for action.

Embedding unsettling disruptive techniques in a settled corporate culture, however, requires some patience. This is because the experimental medicine approach puts us in the spotlight as leaders, asks demanding questions of us. Therefore, we need more training and communication programmes to accelerate group learning, improve laboratory capabilities and enable teams to interact in a less siloed, more collaborative manner.

Everything we do in R&D has to add value, but creating value takes time and requires us to embrace disruptive philosophies with agility.

It is the nature of paradigm shifts, that what is initially controversial soon becomes the norm. Edison demonstrated this perfectly, when he viewed inevitable R&D disappointment as a step in the process to achieving success. And this is what experimental medicine is all about.

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