NATIONAL ACADEMIES Sciences Engineering Medicine

A Conversation with Dr. Jack Scannell, CEO of Etheros Pharmaceuticals Corp.

Dr. Jack Scannell is best known for his work on the causes of the decline in R&D productivity in the drug and biotechnology industry. He coined the term “Eroom’s Law” (from computer science’s “Moore’s Law” spelled backwards) to describe the fall in biopharma R&D output efficiency since 1950 in the face of spectacular gains in basic science and in the brute force efficiency of the activities on which drug discovery is generally believed to depend. His work considered the contributions of scientific, economic, regulatory, and organizational factors. Recently, he has focused on the predictive validity of screening and disease models in drug R&D, which constitute perhaps the major productivity bottleneck. Dr Scannell is the CEO of Etheros Pharmaceuticals Corp. Etheros is developing small molecule enzyme mimetics, based on fullerene chemistry, for neurodegenerative diseases. He is an Associate of the Department of Science, Technology, and Innovation Studies at Edinburgh University. Previously, he led Discovery Biology at e-Therapeutics PLC, an Oxford-based biotech firm. He has experience in drug and biotech investment at UBS and at Sanford Bernstein where he ran the European Healthcare teams. He holds a Ph.D. in neuroscience from Oxford University and a degree in medical sciences from Cambridge University.

Dr. Scannell participated as the keynote speaker during GUIRR’s June Workshop titled "GUIRR at 40: Reimagining the Triple Helix of Innovation, Investments, and Partnerships." Following his presentation, he engaged in a Q&A session with GUIRR Director, Michael Nestor, revisiting some of his main points from the session to share with the larger GUIRR community.

Are there lessons from your work on biotechnology and pharmaceutical R&D that you think may have wider relevance to innovation in other domains?

I’ll give you a methodological answer first. I think it has proven helpful to model the innovation process in formal quantitative terms. I accept that this may be easier for pharmaceutical R&D than in some other domains. But by doing this, it can become clear that the factors to which innovative efficiency is sensitive are not the “common sense” factors that you would have guessed before you did the quantitative work.

Another thing that strikes me is that the pharmaceutical innovation process looks, in retrospect, much more predictable than it really is on a prospective basis.

We tend to overestimate the importance of bottom-up design and underestimate the importance of experimentation and serendipity. This is then reflected in the way we fund science and organize industry. The error here is analogous to the error that creationists make when they look at biological systems; they overestimate the degree of intelligent design and they underestimate the effect of selection on underlying variation.

Your work highlights the paradox between improved R&D technology and declining productivity in the pharmaceutical industry. What do you see as the primary factors contributing to this decline, and how can the US research innovation ecosystem address these issues to avoid similar outcomes in other sectors?

The first factor probably applies in other sectors. Drug R&D in the 1950s was like the wild west; remarkably unregulated and often dangerous for patients who found themselves as the subjects of medical experiments. But it was, at the same time, remarkably productive. I suspect this is because cycle times were short, and because humans are very good models of humans. There are many reasons to prefer today's regulatory environment, but it does bring huge financial and time penalties that almost certainly slow the rate of innovation.

The second factor is probably less generalizable, and mainly relates to industries where intellectual property is key, but where consumers don't get bored of the old intellectual property and, instead, demand novelty. Drugs are invented, launched, and generally get a decade or two of patent protection before patents expire and they face very cheap competition from "generic" copies. Around 90% of US prescriptions are for generally cheap generic drugs. This is great for consumers, but it means that the disease areas where the drug industry has been most successful face progressive commercial exhaustion. It becomes uneconomic to launch drugs to compete with the generics, so R&D gets pushed towards the disease that lack plentiful generics. Those are the diseases where, over the last 100 years or so, the drug industry has been relatively unsuccessful; diseases that are, one way or another, likely to be "difficult."

Incentivization was a leading topic during the workshop, can you identify any incentives that have driven the decline in R&D productivity in the pharmaceutical industry?

I'll qualify my answer by saying that stable and predictable incentives are very important if you want private-sector R&D investment. But with that proviso, I think the drug pricing and reimbursement mechanisms and the patent system currently under-incentivize investment in new drug discovery technologies – let's call them "disease models" - that are better at distinguishing between drug candidates that are more or less likely to work in patients. Lots of disease models are pretty good (infection models for example) but when we have good models, we soon discover good drugs, which then go generic, and so exhaust the economic potential of the good disease models. We are left with diseases where the disease models rarely identify good drugs (e.g., Alzheimer's, advanced solid cancers). In those diseases, the private sector generally sees better financial returns in testing yet more new compounds, with good patent protection, by using the same old lousy models than it does in investing to design and evaluate better models.

We incentivize low-probability chemical roulette, when we should be incentivizing the creation of tools that improve the odds of the game.

You have shown how "resource depletion" (e.g., exhausting the suite of useful disease models) can reduce overall innovative efficiency despite huge improvements in the efficiency of R&D inputs. Can science policy help identify research areas likely to face resource depletion and prevent this scenario? If so, what specific role could science policy play in this context?

Very interesting question. I have not really thought about this much before. I have two tentative answers. First, I come back to the point about trying to produce formal quantitative models of the innovation process in question. The way innovative efficiency declines over time as resources are depleted is very sensitive to the nature of the search process and the way the "prizes" are distributed in the search space, The 19th century whaling industry had very different resource depletion dynamics to the 20th century oil industry, for example.

Second, I would try to ask how each new discovery influences the value of things that are as-yet-undiscovered. Each new drug to treat high blood pressure, for example, tends to reduce the value of as-yet-undiscovered high blood pressure drugs. Once we have a few kinds of high blood pressure drugs, and once their patents expire, the value of as-yet-undiscovered high blood pressure drugs drops to near zero. I suspect there are domains where the economics is very different. If you look at oil extraction through the 20th Century, each extracted barrel of oil was burned, so it did not reduce the value of as-yet-unextracted oil. And then there are some domains where new discoveries make as-yet-undiscovered or un-invented things much more valuable; electricity in general is a great example, or the more recent development of battery technology. So, one answer would be for science policy to try to identify, and push investment towards, domains where new discoveries will tend to increase, rather than decrease, the value of future innovation.