Foreword

I am delighted to contribute this Introduction to *Pharmacology for Chemists,* in which experienced authors cover the drug discovery and development process from laboratory to clinic. I am sure this book will become essential reading for newcomers and experienced scientists across the drug-discovery continuum, as well as medicinal chemists. I have always believed that drug-discovery scientists should have an integrated understanding of the range of challenges involved in translating new ideas into clinical candidates and that they should appreciate the strengths and limitations of all the disciplines involved. *Pharmacology for Chemists* is a major step forward in meeting these ambitions.

Before speculating on the future it is worth analysing our past achievements and then laying out the future challenges before us. Dramatic progress has been achieved in overall healthcare quality over the past fifty years with life expectancy increasing significantly in both developed and developing nations, and major medical threats such as hypertension, elevated cholesterol and HIV AIDS have been brought under better control, for example. However, we cannot rest on our laurels as the World's population increases and ages, and serious conditions such as cardiovascular disease (CVD), cancer, diabetes and obesity are increasing on a global scale. Forty percent of Europeans will be affected by some sort of brain disorder and anti-microbial resistance continues unabated with the WHO predicting impending disasters, but only four new classes of antibiotics have been introduced over the past forty years. In the face of these formidable challenges, the relentless demand for new medicines will continue unabated, and new paradigms for research focus, collaboration and funding will be required.

Pharmacology for Chemists: Drug Discovery in Context
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The past decade has seen tremendous consolidation in the pharmaceutical sector where the negative impact of mergers and acquisitions on productivity has finally sunk in. Innovative research cannot be properly nurtured in massive organisations with multi-billion budgets spread over numerous locations and with ever-changing leadership. Technology can be expanded in a modular and global manner, but innovation simply does not scale. For the future, such large groups should be broken down into nimble multi-disciplinary teams, which should be largely autonomous but accountable, with a move away from consensus management and upward decision making. Drug discovery should become a personal and shared experience not a metrics-driven mechanical event, and organisation should be driven by critical mass not absolute scale.

Decentralisation will continue apace as Pharma strives to control fixed costs by externalising routine activities to CROs while working more closely with academic communities. Some disease areas will become virtual with Pharma scientists located in academic and biotech laboratories in order to provide early access to new biology, but translation to successful drug discovery projects still has to be realised and inevitable tensions between publications and IP resolved. However, such interactions may address the serious concern that over fifty percent of academic publications cannot be repeated as proper quality control will be demanded before committing significant industry resource. It will also be important to safeguard core expertise in Pharma as successful collaborations require complementary intellectual contributions from both partners, with coherence on objectives. A development-only industry would lose unique and valuable synergies.

Pre-competitive collaborations will become more important as cost constraints force reductions in budgets, risk and duplication. It seems reasonable to assume that most Pharma portfolios share high similarity with multiple parallel approaches to the same targets, often with similar scaffolds. For example, various companies took neurokinin and endothelin antagonists to the clinic with little to show for it, while the cumulative costs of parallel renin programmes was absolutely staggering. Such duplicative failures might be avoided through pre-competitive collaborations between industry and academia for target validation and identifying patient populations who would respond to new mechanisms of action. Such concerted efforts should have significant impact on candidate attrition, which is currently unsustainable and continually erodes the very foundations of drug discovery and development. If validated targets and patient subsets do enter the public domain, then robust IP will depend largely

on innovative medicinal chemistry, which will become too valuable to contract out.

Some twelve years ago, I suggested to a sceptical audience that the future pharmaceutical industry would be located largely in the US with outposts in Europe and Japan, which appears to have come to pass. Household names have been consigned to the past, thousands of jobs have been lost, state-of-the-art research facilities closed and Pharma's capacity to meet the medical needs of the 21st century compromised. Taking refuge in the record number of FDA approvals in 2016 may be short sighted as half target rare diseases, and not the chronic conditions that afflict the majority of the population. Given the vagaries of VC funding, it seems unlikely that Biotech will make up all the shortfall, or that pharmaceutical R&D would make a major shift Eastwards in the foreseeable future.

In order to regain capacity, now would be an opportune time to strengthen drug discovery in the public sector by co-localising industry-experienced medicinal chemists alongside world-class biologists and clinicians with a real commitment to the discovery of new medicines. In many cases, a fundamental change in mind set will be required for medicinal chemists to be accepted as equal partners, rather than a service function, and critical mass will be required not just one or two chemists here or there. Of course, there are research institutes and academic groups focused on drug discovery, but not on the scale required and often focused on cancer or neglected disease. Integration of Pharma veterans within the wider community would take some time as there is little appreciation of the skills base required for medicinal chemistry but at steady state, barriers between ''academic'' and ''industry'' researchers may soften with increased permeability across previously defined disciplines and sectors without compromising quality control. Long-term investment in the most challenging disease areas such as antibacterials and neuroscience would be encouraged and there would also be important roles for Public–Private Partnerships. Overall, there is a strategic and pressing need to strengthen drug discovery initiatives outside of Pharma and Biotech and concerted efforts from interested parties will be required to ensure that research capabilities are commensurate with future medical needs.

Sir Simon Campbell