MANAGING DISCOVERY IN THE LIFE SCIENCES

In this book, distinguished scholars Philip A. Rea, Mark V. Pauly, and Lawton R. Burns explore the science and management behind marketable biomedical innovations. They look at how the science actually played out through the interplay of personalities, the cultures within and between academic and corporate entities, and the significance of serendipity not as a mysterious phenomenon, but one intrinsic to the successes and failures of the experimental approach. With new aggregated data and case studies, they consider the fundamental economic underpinnings of investor-driven discovery management, not as an obstacle or deficiency as its critics would contend or as something beyond reproach as some of its proponents might claim, but as the means by which scientists and managers can navigate the unknowable to discover new products and decide how to sell them so as to maximize the likelihood of establishing a sustainable pipeline for still more marketable biomedical innovations.

Philip A. Rea, Professor of Biology in the School of Arts & Sciences of the University of Pennsylvania, and Rebecka and Arie Belldegrun Distinguished Director, co-founded the Roy and Diana Vagelos Program in Life Sciences & Management at the University of Pennsylvania. A Fellow of the American Association for the Advancement of Science, he has received several prestigious prizes and awards for his pioneering research on membrane transporters and his creative science teaching, including the President's Medal of the Society for Experimental Biology and a Lindback Foundation Award for Distinguished Teaching.

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Harnessing Creativity to Drive Biomedical Innovation

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Preface

This book seeks to contribute to the public's understanding of how and why biomedical discoveries and products arise. We focus on discoveries, made primarily but not exclusively in the United States, that have had or promise to have an impact on health outcomes. As is implicit in the book's main title, "Managing Discovery," our goal is to better understand how investigators manage to make discoveries (as in, "manage to pull them off, especially against heavy odds") and how managers (as in, "those who manage or administer the investigators") encourage and sometimes discourage this process. The book examines the interplay of scientists, managers, investors, regulators, and others involved in the process of discovering new drugs and medical devices and bringing them to the marketplace. Their efforts rely on a combination of public support – often but not always for the more fundamental, "academic" aspects of the research effort – and private support from profit-seeking firms who can count on patent protection and FDA-sanctioned market exclusivity, but still face buyers who must be willing and able to buy what is offered.

This juxtaposition of the biomedical sciences and management has been uppermost in the minds of the three faculty authors for the last decade because of their involvement with a unique cross-disciplinary program, the Roy and Diana Vagelos Program in Life Sciences & Management (LSM) at the University of Pennsylvania (Penn), since its inception. It is through this program that the three of us – a biochemist, an economist, and a sociologist by training – have found our research and pedagogical activities converging on the management of life sciences as it applies to the interface between discoveries made in the research laboratory and their realization in the marketplace. The program's introductory core course labels this interface the "twin towers of innovation."

LSM is a dual-degree undergraduate program that operates jointly between Penn's College of Arts & Sciences and the Wharton School. Each

year approximately 25 students are admitted who pursue two bachelors' degrees – a BA in one of the life sciences and a BS in Economics. The program's origins stem from an appreciation that anyone interested in science implementation must not only have a rigorous understanding of the science itself but also an understanding of product development, mechanisms of funding, regulatory policy, organizational infrastructure, and marketing. In short, they must have the facility to think, write, and speak in the languages of both science and business. Therein is the core of this book: a set of case studies built out of the life science discovery process that integrate considerations of the basic science and the managerial choices that accompanied each line of investigation. The case studies in question, many of which started their lives as first drafts researched and written by students and teaching assistants in the program, were framed with an eye to bringing the languages and systems of thought of science and business into one place.

Some of the cases are empirical and concerned with how scientific and managerial factors have played their part in the flow (or its absence) of new products targeted at significant medical needs. Others are conceptual and concerned with the raw economics of biomedical research and development (R&D) in terms of the decisions and forces behind market entry and pricing strategies. In all of these cases there was extensive collaboration among faculty, students, and outside experts with the objective of clearly explaining and illuminating the science and history behind the discoveries, while at the same time assembling the information in as unbiased a way as possible with regard to how and why the scientists made the discoveries they did, how the discoveries were or were not incentivized and/or financed, and how the marketable products that were to issue from the programs (in the cases in which marketable products have issued) were priced.

The overall framework for the book is one that starts with three questions about discovery: (1) what was the incentive or reward; (2) where did the resources for the discovery and the discoverer come from; and (3) how was the discovery translated into a marketable product? Each of the case studies addresses these questions, together with the sometimes tortuous and almost always intriguing twists and turns of scientific investigation and commercialization. Two chapters on the economics of discovery explain recent patterns of volume of new products, their R&D costs, and the factors underlying the decisions made by firms to find something of value that meets an unmet medical need. Then a series of 11 case studies provides examples of the many ways this process has been pursued and the varying degrees of success. Each case study is followed by a "Managerial Note" that summarizes both the managerial process and the

links to the three questions. The penultimate chapter examines the part played by organizational structure in encouraging marketable discoveries in the biomedical sciences through incentives, resource allocation, and the establishment of innovative cultures, hand in hand with consideration of the subtle but significant difference between managerial infrastructures that promote creativity and those that promote productivity within and between projects and companies. The last chapter examines the question of whether public policy could change the managerial process in ways likely to do more good than harm. In so doing, we find ourselves stating and making reference to our final conclusions on what we know and need to know about discovery.

Along the way, we do our fair share of myth busting: that only a single genius is needed for discovery or, its contrary, that it is enough if enough smart people sit around a conference table long enough; that any restriction of profits for biomedical firms is going to do more harm than good or, its contrary, that prices and returns can be slashed without adverse consequences for the supply of discoveries for new products; and – the big myth – that as long as those working on a problem are smart enough discovery will be a linear, rational process with an upward trajectory from beginning to end or, its contrary, that blind luck alone is sufficient for discovery. The other thing we do, or more correctly what the stories we relate force us to do, is lay emphasis on the important roles played by (a) uncertainty and failure and (b) their nemesis, serendipity – whether it be at the level of making a discovery in the first place, demonstrating clinical efficacy, or developing and manufacturing a marketable product that actually meets an unmet medical need (or its surrogate). Uncertainty before the fact is ever-present but when it is overcome, more often than not, it is born of dogged determination, insight, imagination, and serendipity – apprehension about a way forward based on the answer to a question that was not even asked. And the same goes for failure. High probabilities of failure and high failure rates dominate but, again, when they are overcome it is through dogged determination, insight, imagination, and, as is so often the case, serendipity. Given that these are recurrent themes in the cases examined, we argue that one should be careful not to evaluate managerial acumen based only on a small number of wins or losses, but on the extent to which management increases the percentage or likelihood of success by staying the course and being receptive to the unanticipatable in an often hostile or at least inertial environment.

This book would not have been possible without the participation not just of those credited with authorship of particular chapters but many

others, including industry experts associated with the LSM Program and the students who gave so freely of their time with good humor and a sense of responsibility. Special thanks go to those who performed often thankless tasks – to Dr. Peter Stokes for editorial assistance in helping us achieve a consistent and correct English style, to Allison Hedges in the early stages of this enterprise and Tina Horowitz in the many months that were to follow for formatting the manuscript, assisting with the preparation of publication-quality graphs, charts and tables, and for helping coordinate the efforts of the team of authors who were often heading in different directions, and to Sara Jarret, the medical illustrator who deftly crafted the high-end illustrations. Others who played their part in the early days were Dr. John V. Martin, formerly of the University of Leicester, England, for translating some of the early German pharmacological literature and Irtiqa Fazili who helped with the first drafts of some of the illustrative material. Finally, in taking what started out just as an idea first voiced over lunch at Penne Restaurant, Philadelphia on December 19, 2012, about three years before it was pitched to Cambridge University Press, to completion, the faculty authors wish to take this opportunity to thank each other for reading, rereading, editing, and reading again each of the chapters of what is now a book created in a spirit of cooperation and determination. If nothing else this book is a testament to the fact that scientists and management school faculty really can get on rather well with each other on a joint project of this type. Perhaps in the final analysis, it is our differences that are our strength and make it such an enriching experience.

Mark Pauly would like to dedicate his work on this book to the memory of his late brother Philip J. Pauly, a distinguished historian of science at Rutgers University. Phil's work was the inspiration to start this project; his informed counsel has been much missed.

It goes without saying, and usually it does go unsaid, there are those who through their inestimable patience and understanding gave selflessly of their time in supporting us morally and emotionally in this project. They are those most near and dear to us – Jenny, Ames and Ems (Rea), Kitty (Pauly), and Alexandra (Burns).