BOOK REVIEWS

The Entrepreneurial Twist

The Billion-Dollar Molecule. One Company's Quest for the Perfect Drug. BARRY WERTH. Simon and Schuster, New York, 1994. 445 pp. $25.

Many scientists trace their interest in a scientific career to a reading of Paul de Kruif's *Microbe Hunters*, published in 1926. In that work de Kruif described the adventure of scientific discovery in the study of infectious disease starting with Leeuwenhoek and extending through Walter Reed in the early 20th century. De Kruif drew his subjects as lone scientific pioneers and romantic societal heroes. A half-century after *Microbe Hunters*, the Alfred P. Sloan Foundation commissioned the autobiographies of a number of great scientists of the mid-20th century in an effort to promote public interest in science. The Sloan books portray their adventurers most often in the setting of academic or public research institutes, and, unlike some of de Kruif's lone heroes, the Sloan subjects have been revered in their own time. A flurry of recent books now continues to portray the scientist as adventurer and social hero. A contemporary twist is that the scientist has also become an entrepreneur.

Emblematic of the scientist/hero/entrepreneur's story is Barry Werth's *The Billion-Dollar Molecule: One Company's Quest for the Perfect Drug*. The "perfect drug" is an immunosuppressant to be used in the organ transplant setting, and the site of the quest is a start-up biotechnology company, Vertex Pharmaceuticals. Werth's hero is Josh Boger, a brash scientist who at the start of the book has recently left Merck to found Vertex. Boger promises to build a next-generation pharmaceutical company using a 1990s paradigm for drug discovery. He argues that he will do at Vertex what he couldn't do at Merck. In the manner of many new entrepreneurs, he promises that the proof of his model will be a drug that has eluded many. At the close of the narrative the company has been well established, although the drug has still not been attained.

This is a fascinating and complicated story woven together of several strands. One strand is the evolving paradigm of drug development. In the early 1900s, drug discovery was serendipitous. Werth shows how the brute-force screening of plant extracts and chemicals employed at Merck and other companies eventually gave way to more "rational" drug screening programs in which the target against which screening is performed is a purified molecule (such as a receptor or an enzyme responsible for a known phenomenon. This so-called "rational drug screening" paradigm has further evolved in the past decade into "rational drug design." Here computer-aided molecular modeling is employed to design small molecules that can be synthesized and then empirically tested for activity against the purified biological target. This latest approach is the one championed by Vertex.

Another strand of the story is the shift of fundamental research from the public to the private sector. Werth has written a well-researched (but overly lengthy) narrative that follows Boger's fortunes. As the book opens, Boger is raising money on Wall Street. The narrative traces Vertex's attempt to implement its drug-discovery approach in parallel with the building of the company. This story is juxtaposed with that of another scientific pioneer in organ transplantation, the Pittsburgh-based transplant surgeon Tom Starzl, and his efforts to use another promising immunosuppressant, FK-506. There are fascinating parallels between Boger and Starzl despite the differences in their generations, between their specialties (surgery and drug design), and between the academy and Wall Street. For this reader, this comparison is the most interesting and revealing part-of Werth's book. Both protagonists are single-minded in their determination to be first in achieving the perfect immunosuppressant. One can easily draw the conclusion that the exact same sets of skills are needed by the two men despite the differences of the public and private venues. Both men's efforts are set against professional and personal rivalries played out in international scientific forums. In Boger's case the result of the battle can be traced on a daily basis in the close of his company's stock price.

A third strand in Werth's narrative relates to the issues of building a technology-based company. Here *The Billion-Dollar Molecule* joins Stephen Hall's *Invisible Bullet*, Robert Teitelman's *Gene Dreams*, and Natalie Angier's *Natural Obsessions*. Each of these works—to a different extent—is a biotech version of Tracy Kidder's *Soul of a New Machine*, the now-classic book (and the very best of the genre) that chronicles the early days of the computer industry. Taken as a class, these books show that the attributes ascribed by Werth to Boger and Vertex are really common characteristics of the scientist/entrepreneur. In fact, the self-confidence and seemingly inexhaustible energy that fuel Boger are the same that fueled the scientist-heroes of *Microbe Hunters* and the Sloan series.

The founders of the more than 1000 start-up biotech companies are driven people who each believe they are truly special and are determined to succeed. Clearly, all can't. Biomedical research is a capital-intensive enterprise, and not all young companies will have sufficient capital to bring their efforts to closure. Thus Werth's book, read as a metaphor for the biotechnology industry, has clear lessons for both the investment community and those concerned with the future of biomedical research. Research is a high-risk, high-reward venture regardless of whether it is done in public- or private-sector settings. When the fortunes of a company's stock rest on the progress of its fundamental research the buyer had best beware. And those who are confident that basic research will be richly supported by the public markets should ask whether the markets will continue to support young biotech companies when research falters and stock prices decline.

Those who read *The Billion-Dollar Molecule* will also learn how seductive but difficult simultaneous success in research and business can be. And among young readers, I suspect that the story will nurture many an entrepreneurial-scientist dream.

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Genomic Odyssey

Travelling Around the Human Genome. An *in situ* Investigation. BERTRAND JORDAN. INSERM, Paris, and Libbey Eurotext, Montrouge, France, 1993. x, 188 pp., illus., + plates. Paper, $35 or F 180 or £22.

Voyage Autour du Génome. Le Tour du Monde en 80 Labos. BERTRAND JORDAN. INSERM, Paris, and Libbey Eurotext, Montrouge, France, 1993. x, 182 pp., illus., + plates. Paper, $35 or F 180 or £22.

Travelling Around the Human Genome: An in situ Investigation provides an excellent overview of the international collaboration