Is Marketing the Enemy of Pharmaceutical Innovation?

BY KALMAN APPLBAUM

Clinical trials are the most credible and powerful form of marketing in the prelaunch period.

—Francoise Simon and Philip Kotler[1]

Two alarming trends have surfaced in the pharmaceutical industry these past two decades. The first is a surge in ethics violations. Despite journalists, researchers, bloggers, and lately lawmakers who have been working to shame the industry into self-reform, the pace at which new scandals are born appears, if anything, to be accelerating.[2] There is wrongdoing in every stage of drug development and promotion. The list includes campaigns to "ghost manage" the conduct of basic science, to rig clinical trials, to run trials in poor countries where ethical oversight is weak, to market medical conditions far beyond their natural incidence ("condition branding," as the marketers term it), to sway public health criteria for the threshold of disease risk, and to lure some of the nation's most respected doctors into risky off-label promotion schemes.[3] All of these problems can be traced back to marketing-inspired ruses.

The second, less apparent trend is a decline in new drug applications marking breakthrough discoveries. In the words of a 2006 Government Accountability Office report to Congress, "Innovation in the pharmaceutical industry has become stagnant."[4] Merrill Goozner, head of the Center for Science in the Public Interest, explains, "Three out of every four drug applications involve drugs that either replicated the action of medicines already on the market or were new formulations that at best added minor conveniences for patients and doctors."[5]

Some have had the intuition that these two trends are connected, but the dots have not been empirically or even notionally linked in a way that would light a path to reform. The two appear to be effects of a different order. I will argue that they are joined because they reflect the ascendancy of marketing throughout the pharmaceutical industry and in particular because they result from the integration of pharmaceutical firms' marketing efforts with their formerly semiautonomous research and development (R&D) divisions.

My goal in this essay is to connect some of the dots—to show that the decline of innovation is also linked to the rise of marketing. Discovery of medical cures relies on honestly pursued scientific outcomes and a clear separation of influence over scientific practices and goals. I specify the rise in the early 1990s of blockbuster drugs—the handful of brands that account for nearly half the industry's profit—as the catalyst for yoking R&D to marketing, a development that would have been unfamiliar and unnatural to most pharmaceutical executives of prior generations. I draw on industry sources to depict managerial principles at work in defining the relationship, the most telling of which is referred to as "precommercial planning and marketing."

Precommercial planning and marketing demonstrates how the marketing-driven outlook in pharmaceutical companies today pushes these enterprises toward an escalation in the adoption of marketing rationales at the expense of public health. What emerges is a system in which the scientific search for cures and the marketing-led pursuit of meeting unmet medical needs stand not in

Kalman Applbaum, "Is Marketing the Enemy of Pharmaceutical Innovation?" *Hastings Center Report* 39, no. 4 (2009): 13-17.

cooperative tandem, one with the other, but in direct competition. Precommercial planning and marketing, in short, is a legal but unethical practice when applied to humanly vital industries such as the pursuit of medical cures.

Marketing and R&D

What is precommercial planning and marketing? A recent podcast at Pharmavoice, "a Website for life-sciences executives and other healthcare-service related professionals," was entitled "Pharmaceutical Marketing and Planning: Securing Future Success through Meaningful Differentiation." The guest speaker was Laurie Lucas, founder of L3 Healthcare Marketing, LLC, which explains its objective this way: "The pharmaceutical market is evolving rapidly, growing in complexity, and there is less time to maximize a product's potential. Medical communications are critical to understanding the target therapeutic area, and to communicating a product's unique attributes."[6] The "less time" here refers to the length of time under patent during which a firm can sell and accrue profits for a drug. Since a patent is taken out upon the formulation of a molecule and several years elapse before the drug is developed, approved, and brought to market, companies are always seeking to shorten the time between patent registration and product launch. The clinical research phase and the approval process can hardly be made shorter than it has been already. Lucas wishes to teach her clients that by starting the marketing prior to the launch itself, the period of time before the drug can be sold can nevertheless be leveraged to improve profitability during the commercial phase of the drug. She refers to this, using the general parlance, as "precommercial planning and marketing."

Many people assume that a drug goes through a three-step pipeline:

Research → Development → Marketing

This model, if it was ever accurate, is certainly not sustainable now. If you start just with discovery and development of a product and only subsequently think about marketing it, you risk bringing to market a product that may have had only modest potential for commercial success to begin with. Logically, you would want to have a little market research mixed in with the drug R&D: you would have market researchers gather data at clinics and hospitals, and you would use this data to select among research proposals for drugs with the greatest market potential. Or, executives might go to the laboratory and solicit research into known diseases. In this case, the laboratory personnel need not be bothered with marketing considerations per se. They might take their orders from those who have the market's needs clearly in mind, but their scientific work would not otherwise be affected. A flow chart of this sequence might be:

Market Research →Research →Development→Marketing

This model was apparently accurate for many historical cures, and it remains the image the pharmaceutical industry projects to the public about how it operates. But this model has in fact ceased to apply. Given the time crunch for generating profits from a drug, this model, too, is not sustainable. Precommercial planning and marketing is the attempt to compress the sequence by involving scientists and incorporating their research capacities directly into the marketing process. This is the integration of marketing and R&D.

Beginning in the 1990s, pharmaceutical marketing executives began speaking obsessively about the integration of marketing and R&D. The first to do this may have been William Steere, Jr., who was promoted from the marketing department to CEO at Pfizer in 1991. In his book *Generation Rx*, Greg Critser describes Steere's priorities for the company upon assuming command. There were three. "The first one was get marketing and research closer together. The second one was get marketing and research closer together. And then he said the third one was get marketing and research closer together."[7]

The procedural details of this transformation—and a transformation clearly was what was entailed—would have to be worked out by field officers such as Laurie Lucas. A white paper produced by her firm, L3 Healthcare Marketing, declares that "Pre-commercial marketing requires the collaboration of multiple brand stakeholders, including clinical affairs, pre-clinical, regulatory, legal, medical affairs, and marketing. Everyone involved should have an understanding of the broad commercial issues that will or are likely to affect the product when it reaches the market, as well as the elements that create value for a product."[8] In 2002, at a roundtable entitled "When Worlds Collide: The Unleashed Power of Marketing/R&D Collaboration," one executive observed, "At Takeda we believe that the opportunity is integrating early and through target product development profiles, making sure that everyone is going in the same direction."[9] He described the drug Trovan as an ideal example of such integration.[10] Another executive said, "At AstraZeneca R&D people started to embrace more of the entrepreneurial mindset and understand customer needs better"—in other words, the institutional reorganization under the direction of marketing. "We struggled initially, but it eased once the R&D folks truly understood what we were all working toward, which is *value enhancement*. We were all trying to figure out how to have an impact on the bottom line." And an executive from Wyeth concluded, "You can't have a blockbuster without [integration]."

In these and many more comments we hear that integration of marketing and R&D is the first important step toward what marketers in many consumer goods industries call *value creation*. Since the internally created value has to mirror what external stakeholders will value also, its counterpart is *value demonstration*. Value creation and demonstration therefore mirror the distinction between internal and external stakeholders. If *creating* value is the focus of the pharmaceutical company team, with implications for how therapies are iden-

tified and researched, the complementary task is *demonstrating* that value to the world outside the company.

This distinction is more analytical than practical. The organizational approach to creating value internally in fact bears a strong resemblance to demonstrating value to external stakeholders—regulators, physicians, and insurers who must be brought "on board" in the drug marketing process. In theory and practice, value creation and demonstration work best when they are absolutely simultaneous and perceptually coincident in the minds of all stakeholders, internal and external. Lucas speaks of the "collaboration of internal team members and external experts." Since the internal team—which includes sales reps, "regulatory," "publication planners," and in-house physicians employed as marketing personnel—and the external actors—which include physicians and the public—both need to be convinced of the new product's value in order to maximize its commercial potential, the responsibility of marketing also extends across this divide.

The practical implication of this is that even from the outset the entire team, including lab researchers, is devoted to demonstrating the efficacy and safety of the product yet to be born. The new flow chart becomes:

Value Creation/Demonstration (Marketing Research)→R&D →Marketing Control

A fuller schematic that temporally juxtaposes clinical and commercial strategies is produced as a prelaunch strategy map used by the SDC Group consulting company. The map should be read not as a static set of procedures associated with each prelaunch stage, but as an emergent set of strategic considerations. Even before phase I trials, "thought leaders"—meaning influential doctors—are "developed."[11] Publications are brought out to begin the awareness campaign and to initiate a paper trail for future citations. Françoise Simon (president of the SDC Group) and Philip Kotler estimated in 2003 that thought leader development accounted for 20 percent of marketing costs and was rising.[12] By comparison, direct-to-consumer advertising in 2004 accounted for only 14 percent of pharmaceutical spending.[13] In the preclinical stage, thought leaders can "communicate unmet medical needs and shape the design and endpoints of Phase I and II clinical trials." Thus, depending on what thought leaders learn from doctors and patients—and what selling points they are able to "communicate" to them regarding the promise of a drug still in development—clinical trials can be altered accordingly. Thought leader participation in successive trial phases is itself part of the procedure aimed to ensure awareness and adoption at the time of launch. "Opinion leaders drive the second-most crucial premarketing component, that is, publications. There is a close correlation between successful launches and aggressive publication programs."[14] Laurie Lucas calls this "value through data."

Simon and Kotler are not speaking the language of cooperation between marketing and science but of the strategic integration of the two at every step *under the direction of marketing*. Marketing must *own* the pipeline, not just react to its outcomes. As one of the executives from the "When Worlds Collide" roundtable said, "The companies that do it right don't talk about R&D and marketing. If you can get the key people to all be brand managers—to look for brands rather than just compounds . . . Branding is about the ownership of ideas. The Cox-2 inhibitors are the most recent examples of owning the science from day one." The Cox-2 inhibitors, of course, are Vioxx, Celebrex, and Bextra, a class of drugs associated with the most florid marketing malfeasance in recent history.

Given the time crunch for generating profits, drug companies try to integrate marketing and R&D by incorporating scientists' research capacities directly into the marketing process.

Contradictory Notions of Value

What is meaningful to marketers may be meaningless to science and vice versa. Medical, scientific value consists in a discovery's capacity to explain phenomena verifiably and then be applied to reduce human suffering from disease. Marketing value, by contrast, is fluid, relative, and contingent on perceived utility. Marketing value is measured in accordance with its ability to achieve product differentiation, which refers to the process of making one's product offering appear unique in the marketplace and superior to those of one's competitors. Product differentiation is in many ways the prime directive of all marketing.

In the integration of marketing and R&D across contemporary medicine, we find fewer and fewer expressions of scientific value—an outright cure for Dread Disease X, or a frank evaluation of the many-sided approaches to delaying or managing diseases we cannot yet cure. Instead, we find in increasing abundance the promotion of marketing values and the gargantuan effort to demonstrate these to the different stakeholders whose cooperation is required for the successful launching of the product. Marketing and scientific concepts of value can but need not overlap. What is valuable to mar-

keters can be meaningless, dangerous, and costly to everyone else.

For pharmaceutical marketers, as we have seen to especially great effect in the heyday of the industry's quest for blockbusters since the early 1990s, pharmaceutical value has often been a marketing proposition, not a scientific one. The number of "me too" drugs that have been proposed since then is a predictable outcome of the integration of marketing and R&D. The very expression "me too" is telling: the development of these drugs creates marketing value through the subsegmentation of existing markets.[15] The ethical violations stem from the same source as the drag on innovation—namely, the uncontrolled pursuit of marketing values and the company philosophy this reflects and produces.

When we look at pharmaceutical companies' ethical violations, we tend to conclude that greed (as reflected in excessive marketing) and individual unethical decisions are to blame. To some degree, they are, but we should not lose sight of the nonprosecutable organizational norms that lie behind these abuses and that both fuel ethical breaches and dampen the impetus to develop innovative products. By organizational norms, I mean the marketing practices that have at their back sound managerial principles, marketing's peculiar but accepted form of apprehending market needs, and the unrelenting requirement to adapt to a patent-driven competitive commercial environment.

Pharmaceutical value has increasingly become a marketing proposition, not a scientific one. What is valuable to marketers can be meaningless, dangerous, and costly to everyone else.

What should strike us most in the marketing practices that have come to light in various court trials is how routine they appear to be. The spectacle of the trials is in this sense a distraction, since it focuses our attention on violations. But the violations stem from marketing practices that are not at all covert—in fact, they are positively embraced.

As the system is now organized, patents encourage drug firms to sideline the uncertain and difficult search for pioneering cures to serious diseases in favor of what they call "meaningful product differentiation strategies." In that scheme, meaningfulness is defined relative to an image of novelty, efficacy, and safety that firms endeavor to influence through myriad forms of propaganda. The vast resources expended on defending and promoting what Alastair Matheson aptly calls "corporate science" are bleeding us of health care resources and muddying the scientific and clinical waters in which bona fide researchers must also swim.

Publicly Funded Research?

Any discussion aimed at realigning existing arrangements, much less granting oversight responsibility to government, is likely to arouse fears about meddling in the private sector. Nevertheless, the point has been reached where neither the interests of public health nor the private patient are being served by an industry that has, officially or otherwise, been entrusted to deliver a significant portion of our health products.

I propose sequestering pharmaceutical R&D as a strategic and humanitarian industry, in the same sense as one speaks of national defense-related industries such as aerospace or, formerly, telecommunications and semiconductors. No one would argue that these industries have not generated scientific breakthroughs, or that the eventual commercialization of these technologies has been unprofitable. Only the dogged faith of free-market devotees that breakthroughs spring not from paternalistic expert systems but from industrial competition stands as an obstacle to accepting this framework.

Merrill Goozner argues that there has been a huge misperception about the sources of scientific creativity in the pharmaceutical and biotech industries. He shows "that the inception of drugs which have truly made a difference in recent years and which will make a difference in the twenty-first century can almost always be found in the vast biomedical research enterprise funded by the federal government."[16] If he is correct, then an appropriation of the research function of the pharmaceutical industry to federal responsibility, with the aim of separating marketing and R&D, will disable the vast machinery of tendentious, marketing-driven science without making useful invention less likely. The corruption described at the beginning of this essay will be mitigated, and rare diseases and those suffered mainly by poor people would get the research and development attention they deserve. There would be tremendous health care savings from the dismantling of the vast marketing expenditures devoted to marketing-adjunct R&D, to the production of drugs showing no advantage over their predecessors, and to the competitive carpet bombing of doctor's offices with sales reps.

The public has much at stake in how pharmaceutical research is conducted; its participation in the industry's governance should reflect that investment. At present, the public's participation in pharmaceutical governance is restricted because pharmaceutical companies, as private enterprises, are

legally entitled to keep most of their practices, strategies, and data (market and scientific) secret. The privilege that has been afforded the private sector to determine what our health care priorities should be derives from the incongruous belief that, as Richard Henry Tawney put it nearly a century ago, "The enjoyment of property and the direction of industry are considered to require no justification, because they are regarded as rights which stand by their own virtue, not functions to be judged by the success with which they contribute to a social purpose."[17]

In an age in which treatment of the sick is increasingly dependent on pharmacological intervention, there is work also for salesmen and market researchers. Encouraging pharmaceutical industry marketers to concentrate on their expertise of commercialization and distribution can also yield many goods. We can seek their help in assessing clinicians' needs and treatment outcomes, in devising inventive schemes for treatment adherence, and for helping in the logistical management of the delivery of medicines to patients who so desperately need them, both at home and in other parts of the world.

1. F. Simon and P. Kotler, *Building Global Biobrands* (New York: Free Press, 2003), 147.

2. As I was revising this essay, the following appeared in my hometown newspaper: "The conclusions were clear: Women who took hormone therapy drugs were at increased risk for breast cancer, heart disease, stroke and blood clots. The findings were so strong that researchers stopped a clinical trial in 2002, five years early, because it would have been unethical to continue giving the drugs to women. But that same year, the University of Wisconsin-Madison's School of Medicine and Public Health began a medical education program for doctors that promoted hormone therapy, touted its benefits and downplayed its risks. For the next six years, thousands of doctors from around the country took the online course that was funded entirely by a $12 million grant from Wyeth Pharmaceuticals, which makes the hormone therapy drugs used in the study, Prempro and Premarin." J. Fauber and S. Rust, "Are Doctors' Loyalties Divided? UW Course for Doctors Pushed Risky Therapy," *Milwaukee Journal Sentinel*, January 25, 2009.

3. See D. Healy, "The Engineers of Human Souls and Academia," *Epidemiologia e Psichiatria Sociale* 16, no. 3 (2007): 205-11; S. Sismondo, "Ghost Management: How Much of the Medical Literature Is Shaped Behind the Scenes by the Pharmaceutical Industry?" *PLoS Medicine* 4, no. 9 (2007): e286; S. Sismondo, ed., "Special Issue on Intersections of Pharmaceutical Research and Marketing," *Social Studies of Science* 34, no. 2 (2004); A. Petryna, "Ethical Variability: Drug Development and Globalizing Clinical Trials," *American Ethnologist* 32, no. 2 (2005): 183-97; R. Moynihan and D. Henry, "The Fight against Disease Mongering: Generating Knowledge for Action," *PLoS Medicine* 3, no. 4 (2006): e191; K. Applbaum, "Pharmaceutical Marketing and the Invention of the Medical Consumer," *PLoS Medicine* 3, no. 4 (2006); K. Applbaum, "Getting to Yes: Corporate Power and the Creation of a Psychopharmaceutical Blockbuster," *Culture, Medicine and Psychiatry* 33, no. 2 (2009): 185-215.

4. Government Accountability Office, "New Drug Development: Science, Business, Regulatory, and Intellectual Property Issues Cited as Hampering Drug Development Efforts," 2006, http://www.gao.gov/new.items/d0749.pdf.

5. M. Goozner, "GAO: Drug Innovation Lags Despite High Drug Prices," *Gooznews on Health*, December 19, 2006; http://209.85.229.132/search?q=cache:akdAKwFemfUJ:www.gooznews.com/archives/2006_12.html, accessed June 18, 2009. Another study revises the estimate of nonbreakthrough applications to 92 percent; P. Shetty, "More Creative Thinking Needed On Drug R&D," *YaleGlobal Online*, http://yaleglobal.yale.edu/display.article?id=5678.

6. L3 Healthcare Marketing, LLC, home page, http://www.l3hm.com/index.php, accessed June 29, 2008.

7. G. Critser, *Generation Rx* (New York: Houghton Mifflin, 2005), 91.

8. L3 Healthcare Marketing, "Pharmaceutical Marketing and Planning: Securing Future Success through Meaningful Differentiation," http://www.l3hm.com/documents/L3_Pre-CommercialWhitepaper0508.pdf, p. 1, accessed June 30, 2008.

9. W. Koberstein, "When Worlds Collide: The Unleashed Power of Marketing/R&D Collaboration," *Pharmaceutical Executive,* September 1, 2002, http://pharmexec.findpharma.com/pharmexec/Current+Issue/When-Worlds-Collide/ArticleLong/Article/detail/29963.

10. Trovan later became infamous for the ethical research abuses associated with its testing practices in Nigeria.

11. Thought leaders are also known as "key opinion leaders" or KOLs. An excellent description of how KOLs are recruited and the purposes they serve can be found in A. Matheson, "Corporate Science and the Husbandry of Scientific and Medical Knowledge by the Pharmaceutical Industry," *BioSocieties* 3 (2008): 355-82.

12. Simon and Kotler, *Building Global Biobrands*, 147.

13. J.M. Donohue, M. Cavasco, and M.B. Rosenthal, "A Decade of Direct-to-Consumer Advertising of Prescription Drugs," *New England Journal of Medicine* 357 (2007): 673-81.

14. Simon and Kotler, *Building Global Biobrands*, 147.

15. Arguments have been offered in favor of the utility of "me too" drugs, the most robust of which is that drugs in the same therapeutic class might offer differential efficacy and side-effect profiles for different patients. This is true and offers some qualification to the criticism of these drugs. Factually, however, the number of "me too" drugs among a narrow range of profitable therapeutic classes is disproportionate, and the distinguishing profiles among these tend to be narrower than advertised. My argument here is that drug companies do not pursue the production of "me too" drugs with the aim of offering medically meaningful differences, but rather to win easy market share in markets where development of these drugs contributes to their absolute growth.

16. M. Goozner, *The $800 Million Pill: The Truth Behind the Cost of New Drugs* (Berkeley: University of California Press, 2004), 8.

17. R.H. Tawney, *The Acquisitive Society* (New York: Harcourt, Brace and Company, 1920), 24.