

To satisfy its investors and generate the profits to fund future development of these ultra-ultra-orphan drugs, Genzyme has sought to expand into new areas that share many characteristics with its LSD franchise. In 2003, it bought SangStat Medical Corporation, which enabled it to enter the immune-disease marketplace with a profitable antibody product used in organ transplants. In 2004, it announced two further acquisitions in the cancer field: ILEX Oncology (pending receipt of regulatory approval), whose lead product is an antibody approved for treating the most common form of chronic leukemia, and IMPATH's cancer diagnostics business "which will bring to Genzyme a leading array of solid tumor and blood-based cancer tests."<sup>11</sup> These, together with DNA tests from Genzyme Genetics, might be used to identify and develop more personalized treatments linked to particular forms of cancer and an individual's genetic profiles. These acquisitions significantly contribute to Genzyme's revenues and potential future growth. They also are expected to add more than 1000 employees and several new business leaders, all of whom will need to be socialized in Genzyme's distinctive culture while also altering it with their own ideas and experience. Despite these recent additions, Hillback stressed that the firm's commitment to putting patients first, by treating serious conditions in which the treatment can have a major impact, is as strong as ever:

We've reiterated this message more strongly lately. We could call it a decision rule, even though nothing is really a rule at Genzyme. This focus also is a central idea in the concept of a value-based, rather than a cost-based, healthcare system. Genzyme's patient-oriented approach would help the company do well in that kind of world.

As he looked toward this future, and to the more immediate task of integrating these new acquisitions, Hillback pondered some of the key challenges Genzyme would face: "Can we perpetuate the culture without formalizing it? And can we continue to depend on culture, consensus and personal self-regulation, rather than formal rules, as we diversify and grow?"

<sup>11</sup>Genzyme. 2003 Annual Report, p. 4.

# 4

## MILLENNIUM PHARMACEUTICALS, INC.: CREATING AND SUSTAINING CORPORATE VALUES<sup>1</sup>

### INTRODUCTION

Every time he tells this story, Millennium's former Chief Business Officer (CBO), Steven Holtzman, smiles and shakes his head as if he still can't believe it. The story deals with the conditions under which he was hired, in 1994, by the Cambridge, Massachusetts biotechnology company. The company was a small start-up at the time, and its founder and interim chief executive, Mark Levin, was looking for a permanent chief executive officer (CEO) from established pharmaceutical companies with research and development backgrounds. Levin's wife, Becky, a corporate recruiter, met Holtzman during this search. Holtzman had founded, built, and taken public a biotech company,<sup>2</sup> and he had other qualities that Becky thought would interest Levin. She convinced the two of them to have a glass of wine together, just to talk. As Becky predicted, Levin and Holtzman hit

<sup>1</sup>The case study was written by Margaret L. Eaton based on interviews with 10 Millennium employees on September 25, 2002 at company headquarters. Interviews were conducted with David Finegold, who also gave valuable editing assistance. Rahul Dhanda provided important insights and Emily Taylor collected and provided helpful background materials. This case study is one in a series produced under a grant funded by The Seaver Institute and Genome Canada to study models of informed ethical decision making in bioscience firms. Grateful appreciation is extended to all those who participated and assisted, especially to Millennium's Gary Cohen, without whose efforts this case study could not have been written.

<sup>2</sup>Holtzman had held several management positions at the biotech company, DNX Corp., including the presidency of its wholly owned subsidiary DNX Biotherapeutics.

it off. Levin was attracted to Holtzman's experience in bioscience-business, and to this former Rhodes Scholar's philosophy degree, his interest in ethics, and his dedication to unleashing the potential of innovative technology to do social good. For his part, Holtzman admired Levin's commitment to excellence and his beliefs about corporate integrity. Levin asked Holtzman to become Millennium's CBO. Levin's thinking was that Holtzman, the biotech entrepreneur, would have sufficient clout to negotiate alliances with large pharmaceutical companies, essentially David-and-Goliath deals. In addition, Levin was captivated by Holtzman's "non-science" side. Levin subsequently sent Holtzman an offer letter that was unique in the hiring of any corporate business officer. As Holtzman remembers it, the offer letter enumerated his various responsibilities (perform the job of CBO, execute certain deals, build specific corporate programs, etc.) and then stated that he was to spend 10 to 15% of his time dealing with company values and ethics, so as to "make Millennium a recognized leader in socially responsible deployment of genomics and genetic technologies." This is the part that makes Holtzman smile. But he was not the first, and by no means the last, employee who was hired or who sought employment at Millennium because of its two qualities of *scientific excellence* and *corporate values*.

#### MILLENNIUM PHARMACEUTICALS INC.<sup>3</sup>

Incorporated in January 1993, Millennium Pharmaceuticals was among a group of second-generation biotechnology companies whose business plan was devoted to genomics: translating the knowledge gained from the human genome-sequencing projects<sup>4</sup> to identify genes associated with human disease and, from there, discovering drug targets important in combating these diseases. This work was highly valuable to the large pharmaceutical companies that would be Millennium's first customers. Millennium's business proposition was created at a time when the large pharmaceutical companies were having new drugs approved at a dwindling rate and when a significant number of big money-making drugs were losing patent protection. Therefore, large pharmaceutical companies were seeking new avenues

<sup>3</sup>Unless otherwise specified, company information was obtained from financial reports and interviews with the company employees listed above. Further information about Millennium's business plans and strategies can be obtained from: Champion D. Mastering the value chain: an interview with Mark Levin of Millennium Pharmaceuticals. *Harvard Business Review*. 2001 June;109-115. See also Harvard Business School case study. Millennium Pharmaceuticals, Inc. (A) (9-600-038).

<sup>4</sup>The human genome is the entire genetic information contained in a human being. The sequencing projects were primarily the US government-sponsored Human Genome Project in collaboration with the International Human Genome Sequencing Consortium begun in 1990, and a similar rival sequencing program run by the private biotechnology company Celera Genomics, Inc. The goal of these two projects was to determine the sequences of the 3 billion chemical base pairs that make up human DNA. Substantial completion of both projects was announced in February 2001. With this sequencing information, scientists could identify the approximately 30,000 human genes, work on discovering their function, and translate that knowledge into important discoveries about human physiology and disease.

and sources of drug development to fill their product pipelines, and to replace income from the generic competition they would face when their drug patents expired. The promise of gene-based drugs lay in their potential to exploit the genetic component of most diseases, which could result in thousands of new drug candidates.<sup>5</sup> The second major commercial promise of genomics came from the likelihood that drugs could be developed that could alter the effects of disease genes. Because such drugs would operate by altering the physiologic causes of diseases, they were expected to be much more effective and less toxic than drugs that ameliorated only the symptoms of disease. A third expected benefit of genomics-based discovery of drug targets was that the technologies would speed up the process, and reduce the cost of their identification and, hence, development of the drug. Anything that could speed up drug development would be a tremendous boon to any pharmaceutical company.<sup>6</sup> Lacking in-house genomics expertise, many large pharmaceutical companies naturally looked to smaller genomics firms like Millennium to provide new drug targets and their associated benefits.

Millennium started by associating with key scientists<sup>7</sup> such as Massachusetts Institute of Technology's (MIT) Eric Lander, the head of the largest genome center in the United States. The company continued to be very successful in hiring or consulting with top-level scientists and acquiring or licensing state-of-the-art technologies, all of which facilitated the process of gene discovery, gene-function analysis, and identification of drug targets. In addition to venture capital, Millennium raised money by forging technology transfer, research and development (R&D), and commercialization partnerships with a series of biotechnology

<sup>5</sup>Scientists calculated that human genome sequencing information would yield an estimated 3000 to 10,000 gene-based therapy targets. This number comes from an estimate of about 100 important diseases that are caused by 5 to 10 genes each (most common diseases are associated with a number of genes), yielding perhaps 500 to 1000 disease-related genes, each of which probably interacts with 3 to 10 proteins associated with a disease process. Cohen J. Drug Companies, Biotechs, and Wall Street Investors are Putting Their Money Down on Efforts to Unlock the Secrets of Human DNA. *Science*. 1997;275:767-772.

<sup>6</sup>According to the Tufts University Center for the Study of Drug Development, in 2001 it was taking 12 years and costing up to \$800 million for a pharmaceutical company to develop and market a new drug. These figures included the cost of failure. For every 5000 chemical entities tested, only 5 made it to human trials and, of these, only 1 was eventually approved by the FDA for marketing. Any company that could deliver viable drug targets would allow pharmaceutical companies to improve on these numbers. See <http://csdd.tufts.edu/>.

<sup>7</sup>In addition to Mark Levin, the founding scientific advisors included Daniel Cohen, MD, PhD, a Director of the Jean Dausset Foundation/Centre d'Etude du Polymorphisme Humain (CEPH) in Paris; Eric Lander, PhD, a member of the Whitehead Institute for Biomedical Research and Director of the Massachusetts Institute of Technology Center for Genomic Research; and Raju Kucherlapati, PhD, of the Albert Einstein College of Medicine. Other original scientific advisors included David Baltimore, PhD, a Nobel Prize winner and professor at Rockefeller University; Patrick Brown, MD, PhD, of Stanford University and the Howard Hughes Medical Institute; Neal Copeland, PhD, of the ABL-Basic Research Program, National Cancer Institute; Frederick; Nancy Jenkins, PhD, of the ABL-Basic Research Program, National Cancer Institute, Frederick; and Richard Wilson, PhD, of the Washington University School of Medicine.

and large pharmaceutical companies. The R&D and commercialization partners were firms with no genomics expertise, and they paid to acquire access to Millennium's technology and/or to have Millennium produce a series of high-quality, gene-based drug targets. With these targets, the pharmaceutical companies could then do what they did best: complete the process of drug development by taking drug candidates through the costly, prolonged, and arduous animal and human research process, seek and obtain Food and Drug Administration (FDA) marketing approval, and then manufacture, market, and sell the new drug. Included in the value proposition for Millennium was that, at least at first, the company would avoid all these downstream costs and uncertainties, but would share in the revenues when a Millennium-enabled drug was eventually marketed. Mark Levin put it this way: "We don't have to risk the company on clinical costs, which are an order of magnitude more expensive than what we do... Our approach is, instead of risking the company on a single drug or two drugs, to take the 5% to 15% cut of dozens, if not hundreds of [drug] leads."<sup>8</sup> Eventually, however, Millennium wanted to set itself up to become a fully fledged biopharmaceutical (drug) company—to discover, develop, and market its own drugs. Recognizing that it could take 10 years to market its first drug, partnering with large pharmaceutical companies was a way to obtain interim revenues that would allow it to grow into a drug company.<sup>9</sup> To achieve this goal, the company would first need to become successful in the discovery of drug targets and then structure its deals, enhance its infrastructure, and purchase or license expertise so as to position itself for a transition into a drug company. Keys to success in this endeavor included the ability to maximize large pharmaceutical company revenues while retaining significant assets: scientists, knowledge, and product rights.

Starting with publicly available information from the Human Genome Project, Millennium developed and acquired methods, automated equipment, and powerful computer programs to analyze gene sequences to identify genes involved in the biochemical pathways of certain diseases.<sup>10</sup> To produce a useful "deliverable" to a pharmaceutical company partner, Millennium identified disease genes in a specific category. Other corporate competitors were doing the same thing, so Millennium distinguished itself by also identifying the function of the genes and the specific proteins expressed by the genes that were implicated in particular disease processes.

<sup>8</sup>Prewitt, E. What You Can Learn from Managers in Biotech. *Harvard Management Update*, 1 May 1997.

<sup>9</sup>Drug discovery and development required contributions from bench scientists (such as chemists, biologists, and pharmacologists) to work on understanding the structure and function of new drugs in laboratory assays and animals. Clinical scientists (physicians and clinical pharmacists) were needed to conduct studies in humans to test for safety and efficacy. In addition, regulatory affairs, manufacturing, marketing, and sales groups were needed to get a drug approved by the FDA and on to the market.

<sup>10</sup>Millennium used a technique, called *positional cloning*, to identify disease genes. Positional cloning involves the study of the genomes of large families, many of whom are afflicted with a particular disease. Comparisons are made within the family between those with and without the disease to identify genetically linked molecular markers that allow scientists to discover the position of the sought-for gene on a particular chromosome.

EXHIBIT 4.1 Millennium Pharmaceuticals, Inc. (Major Pharmaceutical Partnership Deals)

| Company                                       | Date        | Value  | Purpose                                                                                                        |
|-----------------------------------------------|-------------|--------|----------------------------------------------------------------------------------------------------------------|
| Hoffmann-La Roche                             | 3/94        | \$70M  | Obesity, type II diabetes                                                                                      |
| Eli Lilly                                     | 10/95, 4/96 | \$90M  | Atherosclerosis and cancer                                                                                     |
| Astra                                         | 12/95       | \$60M  | Respiratory disease                                                                                            |
| Wyeth-Ayerst division, American Home Products | 7/96        | \$100M | Central nervous system disorders (Alzheimer's, stroke, epilepsy, substance abuse, etc.)                        |
| Eli Lilly                                     | 5/97        | \$47M  | Secreted proteins                                                                                              |
| Pfizer                                        |             |        |                                                                                                                |
| Beckton, Dickinson                            |             |        |                                                                                                                |
| Monsanto                                      | 10/97       | \$343M | Agricultural                                                                                                   |
| Bayer AG                                      | 9/98        | \$465M | 225 new drug targets, including cancer, cardiac disease, pain, osteoporosis, and infectious and blood diseases |
| Bristol-Meyers Squibb                         | 11/99       | \$32M  | Cancer drug pharmacogenomics                                                                                   |
| Aventis                                       | 6/00        | \$450M | Inflammatory, allergy, and arthritis diseases                                                                  |
| Abbott Laboratories                           | 3/01        | \$250M | Metabolic diseases                                                                                             |

These extra steps made it more likely that a useful drug could then be developed, and these drug targets were thus called *validated* or *druggable* in the industry jargon.<sup>11</sup>

Beginning in 1994, Millennium started on a path of creating more than 20 strategic alliances with leading technology, biotechnology, and pharmaceutical companies (see Exhibits). By the end of 2002, these alliances provided Millennium with close to \$2 billion of committed funding used to conduct its work in discovering drug targets. The large pharmaceutical company deals were often combinations of equity investments, upfront and milestone payments for R&D that led to the identification of drug targets, license fees, and combinations of profit sharing and royalties when the pharma collaborators were successful in developing and commercializing products using Millennium's technologies and discoveries. In many later deals, Millennium also retained rights to co-develop and jointly commercialize products and/or rights to claw back those drug targets not developed by its partner. Millennium also entered into technology development and transfer arrangements with other companies to enhance its technology platform and to license its technology, in exchange for fees or royalties if products using the company's technology platform were commercialized.

During most of its history, Millennium was known for having the greatest amount of pharma alliance revenue of any genomics-based company. Millennium's first big hit occurred in Spring 1994, when it signed a \$70 million, 5-year research collaboration with the large pharmaceutical company Hoffmann-La Roche, Inc.,

<sup>11</sup>Gura T. After the Gold Rush: Gene firms reinvent themselves. *Science*. 2002;297:1982-1984.

a deal typical of many for Millennium. Hoffmann-La Roche took a small equity position in Millennium, and the majority of the \$70 million was devoted to milestone payments to support Millennium's research, which would focus on drug targets for obesity and type II diabetes. Both are thought to have genetic bases and, with more than 100 million clinically obese people in the world and 12.5 million Americans with type II diabetes, cures could prove quite profitable. The companies split the marketing rights to the drugs that would be developed through this collaboration. As with most of Millennium's large pharmaceutical company deals, the companies had to acknowledge the uncertainty about the possibility of identifying disease genes whose expressed proteins were amenable to drug treatment and, if it were possible, whether Roche could develop and get marketing approval for these drugs. Despite the fact that a gene can play a crucial role in the development of a disease, a drug that interacts in this pathway can still fail because of unacceptable side effects, or because other genes may override its effects. In any case, it would take years before it was known if Roche could capitalize on any targets identified by Millennium. This double-sided uncertainty was a feature of each of Millennium's large pharmaceutical company deals.

Over the next 2 years, Millennium added several deals with large pharmaceutical companies (see Exhibits). Considered very promising income-generating ventures, they gave Millennium sufficient credibility to proceed with a successful initial product offering (IPO) in May, 1996.<sup>12</sup> A string of subsequent such deals added revenue and employees to the company rolls and allowed Millennium to begin shopping for companies that would initiate expansion efforts into drug development. In 1997, Millennium merged with ChemGenics, a local biotech company that gave Millennium new abilities to validate drug targets and the ability to begin to discover drugs that would interact with Millennium's drugs targets. In 1998, after losing money in most preceding years, Millennium reported \$10.3 million in net income from its large company deals, and was spending \$200 million a year on research. By June 1999, Millennium's payroll had reached 800 employees and its research collaboration commitments totaled \$1.25 billion.

The year 2000 was different from any other. Renewed interest in the biotechnology industry coincided with the imminent completion of the human genome-sequencing projects. Investors were betting that genomics offered unprecedented ability to discover the causes of disease and to shorten the time it took to produce vastly more effective and less toxic drugs. Despite the fact that many biotech companies were years away from market approval of any drug and were losing more money than ever, their stock prices were at all-time highs, and investors poured a record-breaking \$31 billion of capital into the biotech industry. A huge run-up in Millennium's stock price that year gave it a September capitalization of \$12 billion.<sup>13</sup> Millennium was able to complete a public offering that year that resulted in net

<sup>12</sup>4,500,000 common shares were offered for initial public sale at \$12 each.

<sup>13</sup>See Exhibits.

## EXHIBIT 4.2 Financial Information

### Income Statement (in millions)

|      | Sales              | EBIT    | NA    | Total Net Income    | EPS    |
|------|--------------------|---------|-------|---------------------|--------|
| 1996 | 31.8               | (8.0)   | 3.9   | (8.8)               | (0.10) |
| 1997 | 89.9               | (83.2)  | 12.2  | (81.2) <sup>1</sup> | (0.72) |
| 1998 | 133.7              | (1.4)   | 16.3  | 10.3                | 0.09   |
| 1999 | 183.7              | (351.0) | 21.0  | (352.0)             | (2.62) |
| 2000 | 196.3              | (182.1) | 79.3  | (309.6)             | (1.84) |
| 2001 | 246.2              | (182.7) | 100.1 | (192.0)             | (0.88) |
| 2002 | 353.0 <sup>1</sup> | n/a     | n/a   | (590.2)             | (2.13) |

<sup>1</sup> Revenue in 2002 included \$193 million of strategic alliance revenue and \$160 million of copromotion revenue from worldwide sales of INTEGRILIN<sup>®</sup> (eptifibatide) Injection.

### Balance Sheet (in millions)

|      | Current Assets | Current Liabilities | Long-Term Debt | Shares Outstanding |
|------|----------------|---------------------|----------------|--------------------|
| 1996 | 72.1           | 11.8                | 9.3            | 95.7               |
| 1997 | 101.9          | 16.4                | 19.8           | 116.7              |
| 1998 | 202.7          | 24.3                | 24.8           | 139.7              |
| 1999 | 286.5          | 59.2                | 27.5           | 178.6              |
| 2000 | 1485.6         | 136.2               | 125.3          | 214.0              |
| 2001 | 1514.6         | 203.2               | 118.4          | 224.3              |
| 2002 | n/a            | n/a                 | n/a            | 287.0              |

Source: Financial reports.

proceeds of \$767.4 million. This positive financial climate helped Millennium take big steps toward the goal of becoming a drug development company.<sup>14</sup> By the end of the year, the company had 1300 employees, had spent close to \$270 million in R&D, and the company had 6 drugs in human clinical trials. It had also developed a fully functional medical diagnostics and pharmacogenomics unit, MPMx, that would produce tests to predict which patients would respond to specific drugs. By then, the value of Millennium's partnership deals totaled \$1.8 billion, and the company was still leading the biotech industry in earned alliance revenues.<sup>15</sup>

By 2002, Millennium had succeeded in becoming a biopharmaceutical company. At the end of 2001, it had announced its intent to acquire COR Therapeutics,<sup>16</sup> which not only added to its ability to work in the area of cardiovascular research,

<sup>14</sup>LeukoSite was purchased in December 1999 for \$550.4 million in a stock deal. Cambridge Discovery Chemistry was purchased in July 2000 for \$51.8 million in cash. Millennium was also actively engaged in licensing rights for many technologies.

<sup>15</sup>Licking E. A Pharma Star is Born? *Business Week*, 2000 September 25:100.

<sup>16</sup>Millennium acquired this company through the issuance of about 55 million shares of common stock. The deal was valued at \$2.2 billion.

but also gave Millennium its first drug, INTEGRILIN® for injection, an intravenous cardiovascular drug with annual sales, at the time, of approximately \$230 million.<sup>17</sup> COR also brought with it a sales and marketing organization. In addition, Millennium had co-developed a leukemia drug, Campath®, with a subsidiary of ILEX Oncology, Inc.<sup>18</sup> The commercialization of a third product was pending. This was the diagnostic Melastatin™, a test used to determine the aggressiveness of melanoma tumors. Eleven other products were in various stages of human research. Millennium had close to 1900 employees, almost \$2 billion in committed funding from its pharmaceutical and biotechnology alliances, and had begun to earn royalties on drugs. It planned to increase its drug pipeline and, even though it needed to spend heavily in clinical research, expected to turn profitable in the next several years. Millennium's future depended on being able to: manage its growth; maximize income from its alliances (both from the initial deals and from downstream royalties from marketed Millennium-enabled drugs) while diluting the company as little as possible; navigate the expensive and uncertain process of clinical research; and retain rights to sufficient technology, intellectual property, and markets so as to preserve the ability to grow into a company that, on its own, could discover, develop, and take new drugs to market. These were daunting tasks, but the company was highly optimistic about its chances for success.

#### INSTITUTIONALIZING CORE VALUES AND ETHICS

Millennium's focus on values and ethics was instilled in the company by its founder, Mark Levin, and then institutionalized in several ways:—by hiring a CBO who also focused on ethics; through educational programs; hiring ethics-minded employees; setting standards of best practice for internal and external relationships, learning from the mistakes of others; monitoring, assessment and feedback programs, corporate vision projects, corporate social responsibility programs, and repetition and reinforcement with the aid of artifacts.

#### FOUNDER'S ROLE

As part of its commitment to its core business, Millennium has been dedicated to the ideals of corporate values and ethics. This vision began with Mark Levin, who started his career as a chemical and biomedical engineer at Eli Lilly. Then, with some detours into unrelated fields (beer brewing and computer systems),

<sup>17</sup>Millennium copromotes this drug with Schering-Plough, Ltd. and Schering Corporation.

<sup>18</sup>At the end of 2001, ILEX acquired Millennium's equity interest in the partnership in exchange for which Millennium will receive a series of payments and obtain royalty payments on sales of the drug.

#### EXHIBIT 4.3 Core values

**PATIENTS** — We make a difference for our patients, their families, and healthcare providers.

**PEOPLE** — We hire, motivate, and develop outstanding people.

**EXCELLENCE** — We cultivate an environment where each of us can excel.

**INNOVATION** — We encourage innovation in the discovery, development, and commercialization of breakthrough products.

**COLLABORATION** — We seek results through collaboration — with each other, and with our customers.

**RESPECT** — We listen, understand, and learn from each other.

**INTEGRITY** — We insist on absolute integrity in everything we do.

**RESPONSIBILITY** — We are a socially and ethically responsible corporation.

**VALUE** — We are committed to creating sustainable value for our shareholders.

**POSSIBILITIES** — We believe that nothing is impossible!

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**MILLENNIUM**

Levin went on to work for the biotechnology company Genentech. Having distinguished himself at Genentech as a consummate deal-maker, Levin then joined the San Francisco Bay area venture capital firm, the Mayfield Fund, where he founded 10 bioscience companies and served on their boards.<sup>19</sup> At each company, he collected perspectives that contributed to his vision for the corporate culture he brought to Millennium. According to Levin, Eli Lilly had a “tremendous sense of their place in the community”<sup>20</sup> and were highly cognizant of their history and what people meant to the organization. Lilly’s culture included recognizing the value of employees and treating them well. Genentech believed in hiring the best, and tolerated and even encouraged eccentricities in employees so long as they were

<sup>19</sup>Rifkin G. (2003, January 12). The Boss: Always Avoid Boredom. *The New York Times*, p. 13.

<sup>20</sup>Quotes attributed to Mark Levin and not cited were obtained in an interview with Mr. Levin in March 2003 by Gary Cohen based on questions posed by the author.

passionate about their work, intelligent, and committed to excellence. "Passion, not fashion" was how Levin described it. Genentech also built a values-based company and, as a result, Levin saw employees respond positively to the company and adopt its values. Company values became part of employee consciousness, and Levin understood that this situation did not come about by accident. Later, when Levin operated as a venture capitalist and interim CEO of the start-ups he funded, he stressed the importance of values and vision, right from the beginning. He told Gary Cohen, Millennium's in-house ethics leader, "It's more than just vision, actually; it's about what each of these companies was going to be, about who the people at each of these companies were, and what they wanted to do with their lives."

According to those who have commented about him publicly, Levin has great energy and commitment to his work that attracts people to him. He has a different and sometimes offbeat way of thinking through problems that also allows him to spot opportunities faster than others. Levin was quick to recognize and respond to the commercial potential of the Human Genome Project, meaning that he understood that the genome sequencing would lead to the discovery of human disease genes that, in turn, would lead to the development of gene-based medical products of unprecedented value. At Mayfield, he became intrigued by the prospect of funding and founding a company with this as its business strategy. He enlisted his wife Becky to use her recruiter talents to find a CEO to run such a company. After a fruitless 9-month search, Becky became convinced that the company concept was so unusual, and the vision and understanding needed to run it so unique, that only her husband could do the job. So, in January 1993, Levin founded Millennium Pharmaceuticals, Inc. with \$8.5 million in initial venture funds.<sup>21</sup> Although, in the past, Levin had served only as interim CEO for the companies he founded at Mayfield, in January 1995 he agreed to become Millennium's permanent CEO and has stayed on at Millennium full-time ever since.

Millennium was going to be about something very important, Levin decided. Dedicated to the discovery of genetically based drug targets, the company would be "transcending the limits of medicine" by revolutionizing the process of drug development. The disease genes the company would seek would be for complex and widespread diseases, for which the current treatments were inadequate or non-existent. Its founders recognized early that this business plan would raise ethical issues, primarily because of misunderstandings about the link between genetics and disease: for instance, the prevalent belief that there is one clear genetic cause for a disease that is discovered to have a genetic connection, rather than that the disease may have multiple causes. Such a misconception could lead to stigmatizing individuals found to have a particular disease gene.<sup>22</sup> Any social misuse of genetic and genomic technology could create a public backlash that could

<sup>21</sup>Blanton K. (1999, June 13). Biotech's Pied Piper: Relentless in Recruiting, Generous in Research Budget. Levin Draws Experts, Money. *The Boston Globe*, Section F1.

<sup>22</sup>People found to have genes that predisposed them to certain diseases could be denied health insurance or employment, for instance.

threaten the firm. The human genome sequencing projects had already caused some public concern over the harm that could result from manipulating genetic knowledge. Millennium's founders viewed social and ethical issues such as this as an important force in the new genomics industry. Devoting attention to these issues was seen as essential to the success of the firm. With Levin's philosophy of corporate values as a guiding force, this view easily generalized into the determination that Millennium would operate with integrity in all fields of endeavor; the scientists would strive for excellence, and corporate practices would be socially and ethically responsible. According to Steven Holtzman, for all companies that produce medical products, the two goals are linked: being innovative and socially responsible both contribute to making a company competitive.

To implement this vision, Levin met with the top executives of the fledgling company to discuss his ideas about key corporate values—those he would abide by personally and expected everyone else in the company to follow. From this, a set of core values was developed that ended up on every employee's mouse pad:

Millennium Core Values.<sup>23</sup>

We hire only the best people.

We are creating an environment where our people can excel.

We listen to and learn from everyone.

We encourage innovation in the search for breakthrough products.

We insist on the absolute integrity of all our interactions.

We believe that both outstanding individuals and focused teams are critical for our success.

We have created and continue to build a socially and ethically responsible corporation.

When asked what prompted him to institute Millennium's core values, Levin said:

At Millennium, we were determined to think about, and talk about, and act on a set of core values, right from the beginning. So, I suppose my experiences at Lilly, and Genentech, and the start-ups influenced my thinking. We hired people who were interested in a values-based employer, people who would share our vision on Day One about the kind of place they wanted to build. We talked about our values a lot, at major company meetings and in smaller groups. We took actions based on our values, and there were real consequences for the few people over the years who weren't acting according to those values... It's not just about having a statement of core values, it's about executing those values.

<sup>23</sup>In November 2003, based on the company's year-long discussion of its values, Millennium adopted and reaffirmed the Core Values included in Exhibit 4.3.

By all accounts, Levin both talks the talk and walks the walk. Below is an example of what employees said about Levin's leadership:

*Linda Pine, Senior Vice President of Human Resources and one of Levin's earliest nonscience hires:*

It is just the type of person Mark is. Passionately committed to being open, inclusive, listening to and learning from anyone. Someone who works in the mailroom can walk into Mark's office and share his ideas. There are not a lot of CEOs who start from the perspective of creating a great workplace. [He has a] grand vision of entrepreneurship, great science, creating great products that save lives. [He understood] early on that the area of mapping the human genome and doing genetic studies meant we should be on the front end of understanding ethical issues. He connects ethics to bottom-line business issues. [His mantra is still] 'We believe that nothing is impossible.'

*Steven Holtzman, original (and former) CBO, and also responsible for ethics:*

Holtzman knows that Levin did not give him the ethics assignment to make the company ethical. "All people in business want to deal with people of integrity. I was on a panel [with someone] where he said that if you need to hire a [corporate] bioethicist, it must be because you were in trouble. I agree and disagree. If you lack integrity, hiring someone to make you have integrity, I can tell you, it ain't going to happen." Holtzman added that Levin's sense of integrity was what made him believe that the CBO should also focus on maintaining corporate integrity. However, Holtzman maintains that employees will not behave in an ethical manner just because they are told to do so by the company ethicist. Rather, the company leadership creates an environment that supports ethical decisions, and provides avenues for participation and education about ethics, so that each employee is engaged and will then incorporate ethics as an aspect of his or her work. As a result, the corporate community as a whole will then function in an ethical manner.

*Jack Douglas, Corporate Secretary, and former Senior Vice President and General Counsel:*

Jack Douglas believes that Levin's leadership is critical to the company's core values.

Early on [Levin] created a set of core values and he made commitments to integrity and corporate and social responsibility. When I interviewed with Levin for the position of general counsel, I asked him about an exit package given that this was a vulnerable position. He turned around and asked me what about my secretary, what would she get? I got so excited about this general approach, I gave up what I was asking for and came to work here, where no executive has more benefits than anyone else has.

*Gary Cohen, Vice President, Ethics and Corporate Responsibility:*

In the business ethics arena, it is particularly important, notwithstanding any programs you do, to have an identifiable leader with charisma and a deep sense of commitment to the institution, and who models ethical behavior for his or her employees. Most stuff I've read suggests that a good business ethics program needs as its anchor an ethical and deeply committed CEO. We're fortunate to have a business ethics 'rock-star' in Mark Levin. He's a remarkable guy.

Throughout Millennium, any employee who talks with him or reads his periodic e-mails will see that he brings a deep respect for core values and connecting to them in meaningful ways. Our CEO sets a beautiful ethical standard.

*Fabio Benedetti, Vice President of Medical Affairs, responsible for investigator-initiated studies and medical affairs activities:*

Dr. Benedetti came to Millennium from a large pharmaceutical company, already imbued with a set of values that drives his work of implementing and supervising late-stage human research trials. He said:

My boss at Roche used to say, 'Good medicine is good business.' I'm a big believer in it. If I make decisions that help patients, this will ultimately translate into good medical outcomes. I think the opposite is also true. Short-sighted decisions will catch up to you in the long run. This seems obvious, but many don't do it. [What attracted him to Millennium is that] everything in this firm seems to reinforce behaving ethically. The patient-first emphasis comes from Mark [Levin]. It is part of the reason I joined. And I had a lot of other offers. When I was done with the one-on-one interview with Mark, that was when I knew I wanted to join. In my position, I can assure ethical reporting of outcomes for this firm in clinical trials. I can assure we won't put out anything that isn't appropriate since I head Medical Affairs. While I can't stop individual rogue behavior, it appeals to me that I can make these assurances.

*Joanne Meyer, Director of Human Genetics:*

Dr. Meyer believes that "genetics has always been a hot-button issue for ethics because of implications of profiting from DNA." When she was hired at Millennium, she was attracted to the company's ability to make a difference with the technology, which was greater than the impact that could be made in academia. In addition, she liked the corporate leadership. "When upper management displays an interest in ethics, it trickles back down to employees."

*Chuck Gray, Director of Scientific Development:*

Dr. Gray was hired to negotiate and monitor important academic research and technology agreements and budgets. He said that he was initially attracted by the financial package, but soon also became impressed by the senior people he met and their passion and excitement for the place. He especially liked Levin's style of leadership, which was "unusual, off beat, and he had integrity. He created this environment and, early on, it was evident that the Company was very entrepreneurial." The core values "start with the CEO and go all the way down the line. For instance, Levin flies coach, he doesn't go for expensive meals. He doesn't have the perks. He has a small office, and doesn't have an entourage. He's an honest guy. He meets with lots of employees throughout the year and answers e-mails and takes suggestions seriously. Other CEOs can be very different, they take what they can get."

*Rob Kloppenburg, former Senior Director, Corporate Communications:*

Kloppenburg said that Millennium has shown him that the ethics focus at a company starts at the top. He sees the management teams approach issues with "eyes wide open, keeping an ethics perspective, and this influences the culture of the company." He believes that the idiosyncratic effect of corporate leadership has



more influence on how the company behaves than is often realized. And because of the leadership at Millennium, people feel empowered to make ethical decisions. He is especially impressed by the fact that Levin has committed to fund a full-time ethics position (Gary Cohen's) in such a young company.

*Sue Nemetz, former Vice President, International Commercial Operations:*

When the Company was filing new drug applications for a cancer product, discussions took place about which countries would be suitable to seek marketing approval. Obviously, there were various business and regulatory factors that needed to be considered. However, the business decision not to file in any particular country meant that citizens would not have access to the new drug, and some managers wanted that factor to be included in the decision making process. They wanted a discussion about whether the company considered all the ethical implications of this launch. According to Sue Nemetz, "Mark made it okay to look at such a question."

### IN-HOUSE ETHICS LEADER

In the beginning, CBO Steven Holtzman was directed by CEO Levin to spend 10 to 15% of his time on corporate ethics issues. From the time he was hired in 1994, Holtzman implemented or advised on most of the programs described below. He was also available to advise anyone in the company on any ethical questions regarding company activities. Holtzman, therefore, played a vital early role in implementing and sustaining Millennium's values and ethics culture. In 2002, however, Holtzman decided to leave Millennium to start his own company. His challenge at that point, he said, was to "clone himself" to ensure that the ethics and values focus of the company would not leave with him. Eventually, Levin, Holtzman, Pine, and Douglas decided that Gary Cohen, the company's first corporate lawyer, would take on full-time responsibility for ethics. Cohen was chosen because of his interest in public policy and ethics, which he'd first cultivated at Genetics Institute, Inc., and later as a Vice President and General Counsel to Genzyme Transgenics (now GTC Biotherapeutics).

Cohen accepted the offer to become responsible for Millennium's ethics and corporate responsibility. He interviewed its top managers and learned that they were interested in seeing if he could expand on the bioethics endeavors. Cohen then set about expanding and enlarging on Holtzman's ethics work. According to Cohen, his program was "modest" in the first year, costing the company his salary and half of an assistant's, plus overhead and limited outside spending for consultant fees and conferences. Since then, Cohen, at Levin's request, has broadened the ethics programs to regularize business ethics practices firm-wide. Spending on ethics and values programs has remained stable, culminating in a year-long "Living Our Core Values" program to celebrate the Company's 10<sup>th</sup> anniversary (see below for a full description). Cohen has future plans to reissue an updated statement of the corporate core values and to conduct training to help employees connect the core values to business practice standards.

## ETHICS EDUCATION PROGRAMS

### IN-HOUSE ETHICS INSTRUCTION

Early on, Linda Pine identified, and Steven Holtzman hired, Dr. Phil Reilly to create an ethics education program for Millennium employees. Dr. Reilly is a physician specializing in medical genetics and a recognized expert in issues of public policy raised by advances in genetics.<sup>24</sup> Holtzman's goal with this eminently qualified teacher was to give employees an opportunity to become knowledgeable about biomedical and research ethics, and how they applied to company activity. In addition, ethical reasoning was taught so that employees would feel empowered to incorporate an ethical aspect into business decision making. According to Joanne Meyer, these seminars were started in 1994-95 when the whole company could fit in the conference room. She described the seminars as very interactive, with plenty of give-and-take discussion. Over the years, Dr. Reilly's sessions were well attended and popular, especially in the later years, by mid- to lower-level employees from the medical and science departments. Sue Nemetz found Dr. Reilly's class to be "fascinating; my brain would hurt with the challenges he posed."

### FILM SERIES

Later, in September 2002, the in-house ethics education program was expanded to include a film series open to all employees. Employees who sign up for the program leave work at 4:00 PM and, with pizza and soft drinks provided, view and then discuss films that have an ethics subtext. These events last up to 3 hours and originally were moderated by Rahul Dhanda, an executive of Interleukin Genetics, Inc., who has training and an interest in biotech business ethics.<sup>25</sup> In advance, Dr. Dhanda provides employees with film reviews, background articles, and a list of possible questions for ethics discussions, and then moderates the group discussion after the film. The films presented to date include *Gattaca* (about a future where personal and professional destiny is determined by one's genes); *Jurassic Park* (about the wisdom of cloning dinosaurs); and *Inherit the Wind* (a fictionalized version of the Scopes "Monkey Trial" of 1925, in which a schoolteacher is prosecuted for teaching evolutionary theory). According to Dr. Dhanda, the post-film discussions are always wide-ranging, but someone always swings the discussion around to address the applicability of the issues to work at Millennium. Plans are underway to continue the film series in 2003.

<sup>24</sup>Dr. Reilly is also a lawyer who is past president of the American Society of Law, Medicine, and Ethics and was the executive director for 10 years of the non-profit Eunice Kennedy Shriver Center for Mental Retardation, Inc. He has also held numerous teaching positions at Tufts University School of Medicine, Harvard Medical School, and Brandeis University. Later in 1999, Dr. Reilly became the CEO of Interleukin Genetics in Concord, MA.

<sup>25</sup>Dr. Dhanda has written a book on the subject: *Guiding Icarus*. New York: John Wiley & Sons, Inc.: 2002.



### DISCUSSION GROUPS

Additional ethics education occurs with in-house discussion groups focused on a particular topic. Gary Cohen has briefed upper management and various management teams (Safety Review, Marketing and Sales Committees, etc.) on ethical issues relevant to current corporate activity. He also initiated a series of management discussions about the book *Dispensing with the Truth* by Alicia Mundy. The book was about the corporate misbehavior behind the Fen-Phen debacle.<sup>26</sup> For these discussion meetings, Cohen purchased close to 100 copies of the book for managers to read, and he prepared the same number of detailed briefing books and discussion materials. The purpose of the discussions was to present the Fen-Phen case as a cautionary tale and to prepare the corporate managers to think about drug safety and how to manage a drug recall, should it ever be needed. Rob Kloppenburg, public-relations senior director, endorsed these discussion sessions, because "companies can potentially collapse over ethical issues, plus, as an individual you have to be able to sleep at night. Doing the wrong thing to get out of a short-term jam is ruinous."

### CORPORATE GOVERNANCE PRACTICES

Governance issues were addressed early in the firm's history. Jack Douglas came to Millennium as General Counsel with an interest in reinforcing good corporate governance practices, not only because he and the chief financial officer (CFO) "were on the hook for it," but also because he wanted to have the company run according to the highest standards of integrity. Douglas saw the adoption of ethical corporate governance practices as one way that the legal department could participate in value creation for the company. He put into place a set of best practices for corporate governance dealing with auditing, conflicts of interest, compensation practices, disclosure policies that focused on clarity and transparency, and provisions for objective input from outside directors. In 2001-2002, when the corporate governance scandals involving energy-trading companies such as Enron were uncovered, Douglas took the opportunity to review and compare Millennium's practices with those companies that had come under fire. Douglas found that the company was already doing what auditors and the regulators were asking for, and he felt good about its position. Another aspect of the post-Enron review, according to Gary Cohen, involved asking the question of "why firms with impeccable codes of ethics, like Enron, didn't drive it into the behavior of employees." Cohen came to believe that, for Enron and other companies, developing a corporate code of ethics was an exercise that lacked carry-through; the ethics codes ended up "sitting on shelves collecting dust bunnies." Cohen understood that having an ethics-guidance manual is only the first step in

<sup>26</sup>Fen-Phen was a drug combination for weight loss that was withdrawn from the market after the regimen had been shown to cause life-threatening heart valve problems. The book highlighted various corporate failures in the drug recall process.

a process to motivate behavior change. Enron was not the first company that had struggled and failed to make that connection but, at Millennium, this was an ongoing effort.

### PARTNERSHIP RELATION

Partnering with pharmaceutical companies was fundamental to Millennium's early success, and the approach to partnering included aspects of its core values. Steven Holtzman, who negotiated the company's earliest agreements with large pharmaceutical companies, believed that the company's focus on values and ethics was one reason for Millennium's attractiveness to these companies. He listed several values that contributed to this, among them being that Millennium hired the best people and then created an environment where "great people can do great things, both as individuals and as members of a team." He told one interviewer: "Partnering would not have happened but for the fact that there was an incredible group of scientists and business people working together to build something very special. The partners recognized this and therefore realized the need and desire to tap into it." In addition, Holtzman believed that Millennium's partners appreciated the integrity with which business relationships were maintained:

Once you have established relationships, it is a small world, and people essentially reference you with your own existing partners. The most important things then are whether you have a reputation for integrity and that, when you enter into a relationship or partnership, you really strive to have open dialogue and live up to your commitments in so far as you can. The fact is that the nature of drug discovery is that you are going to fail more often than you succeed, so all one can expect from each other is your best effort and acknowledgment when things are working and when they are not.<sup>27</sup>

### EMPHASIZING VALUES IN EXTERNAL RELATIONS

Steven Holtzman took Millennium's vision of corporate ethics outside the company: he served as a galvanizing force in organizing BIO's<sup>28</sup> Bioethics Committee in 1994; he was the only member from industry appointed to President Clinton's National Bioethics Advisory Committee; he also coauthored a paper published in a scientific journal about gene tests and patient privacy.<sup>29</sup> The paper was a collaboration with the Chief Patent Counsel and the company ethics-educator, Phil Reilly, and addressed the ethical aspects of genetic testing. The authors stressed the need to broaden the disclosures made to research subjects that would allow them to fully understand the risks of genetic research, including genetic discrimination and emotional distress flowing from detecting a gene predisposing to a disease.

<sup>27</sup>Lawrence RN. Holtzman Discusses Partnering. *Drug Discovery Today*. 2001;6:1042-1045.

<sup>28</sup>BIO is the Biotechnology Industry Organization, the main industry trade group.

<sup>29</sup>Reilly PR, Boshart MF, Holtzman SH. Ethical Issues in Genetic Research: Disclosure and Informed Consent. *Nature Genetics* 1997;15:16-20.

Millennium also commented on drafts of the new PhRMA<sup>30</sup> code of ethics regarding corporate interactions with healthcare professionals.

### MILLENNIUM ORGANIZATIONAL SURVEY

Initially done twice, now once, a year, the employee survey is used as a way for employees to comment on such things as how satisfied they are with their work and whether their work aligns with their goals, how committed employees feel, etc. In 2002, Millennium was pleased to see that 81% of the employees responded to the survey, giving management a good sense of the workforce. A section of the survey is devoted to how effectively the company is living up to its core values. Following is the percentage of employees who "strongly agreed" or "agreed" that:

- Millennium is a socially and ethically responsible organization (85%)
- My manager provides a good example of how to live the Millennium core values (82%)
- My manager treats me with respect (87%)

Because the company uses a professional consultant to perform the survey, Millennium can also obtain comparisons with other companies who use the same consultant. Millennium found that their ratings were "off the chart," according to Linda Pine. The lowest-scoring statements (those questions about which employees were either "neutral" or "disagreed or "strongly disagreed") included:

- Millennium hires only the best people (50%)
- Employees listen to and learn from everyone (50%)

Senior and line managers are encouraged to use the results of the survey to improve on the lower-scoring items. Given the importance attached to treating employees well, even neutral ratings on some items are addressed as areas of concern by human resources. One such rating involved the core values of listening to and learning from people. The rating had slipped from the prior year and prompted the company to initiate a management communication and training program run by its Internal Communications Director, Mike Houldin.

### EMPLOYEE PERFORMANCE REVIEW PROCESS

Ethics and the core values are also explicitly included in a rigorous employee performance-review process. The wording in this survey includes language that allows the appraiser to relate behaviors linked to core values. In the forms for "Self/Manager Assessment" and "360 Feedback Form" (which allows employees to evaluate all their peers), how colleagues are "living up to the core values" is included in the rating of an employee's effectiveness, and "teamwork, cooperation, information sharing, respect, and listening" are included in the rating for collaborating.

<sup>30</sup>PhRMA is the Pharmaceutical Research and Manufacturers of America, the industry trade group.

In the "Self/Manager Assessment," employees are also rated on how well they empower staff to "own part of Millennium and take action" and foster the company culture by asking, "Does this person set an example and take responsibility for building local culture?" and "Does this person model the Core Values?" Another section of the same form asks whether the person is recognized as an external ambassador for the company: does the person "transcend turf-orientation and hidden agendas?" "We're strongly committed to having people who live up to, and adhere to, core values," said Human Resources executive Linda Pine. "Even senior employees who are competent and smart will derail at Millennium if they do not treat people fairly and consistently or do not communicate honestly."

Chuck Gray, in Scientific Development, described his impressions of how the employee evaluation program works to reinforce the core values, such as creating an environment where all can excel.

We have a 360 feedback program here that can show you how you may not have lived up to the core values... At my performance review with my boss, [the way I complained about employee performance] came back to bite me. I learned a lesson from it. All of an employee's good points and warts are exposed in the 360 process. They are the most complete reviews I've ever had—and not just from close buddies. The process is really designed to make you better—for instance, that I have to work on not being impatient. You get told that you need to work on some things. It is tough to change some things that are 'hard wired,' for instance, to go from being an introvert to an extrovert. But you may be able to change on the edges. You end up knowing what you need to work on. The 360-degree review process takes a lot of time and effort. They can cripple work for a couple of weeks. But the company cares that much about it, that they devote the time. The focus in the reviews is on how we are all behaving with the other people... If I'm not treating people with respect, I would get nailed on it. So everyone takes the core values seriously.

### ETHICS HELPLINE

In 2002, Gary Cohen proposed to Linda Pine that the company set up an internal ethics helpline for employees. Pine agreed, seeing in this program a significant link with what Human Resources was trying to achieve for the employees by way of an existing Employee Assistance Program. Cohen also saw the helpline as an early warning system for ethics violations or employee problems. The system would allow employees to speak candidly and confidentially with a trained ethics advisor, without fear of reprisal. The company manager would then receive advance notice so that problems can be dealt with proactively when they are more amenable to resolution. In addition, while it was not the driving motive for the program, a helpline would meet the federal sentencing guidelines for a system that allows employees to report corporate misbehavior. Other options under consideration for the ethics helpline include a mechanism to advise employees on how to have conversations with other employees about ethical problems, with advanced training for all employees on how to respond to others who seek such conversations.

### CORPORATE VISION PROJECT

Sue Nemetz believed that she was handed the "dream job" of proposing a commercial vision for Millennium. Nemetz, who had a long-term career in the pharmaceutical industry and had started a business unit within Dupont Pharmaceuticals, could not believe that Millennium would pay her for this work, something she loved to do. The reason for her enthusiasm was that not only was the company's appetite for innovation very high, but that she was also asked to design the "Nirvana view" of how a commercial organization would operate and interact with customers. "A key theme in this project was to consider trust and integrity," she said. She worked with key cross-functional groups at Millennium, including Gary Cohen, and she initiated a program of interviews with customers and intermediaries, clinical research organizations, government agencies, industry lobbyists, public relations firms, medical educators, and industry consultants. With each group, she asked what they would consider an ideal working relationship with a company like Millennium. How would they design an ideal commercial organization? At the end of the first series of interviews, Nemetz had six primary components, some of which were overlapping. People told her that the company should:

1. Be truly customer-centric—and achieving this would be novel in the pharmaceutical industry
2. Improve commercial productivity
3. Have a strong clinical-commercial interface
4. Develop a new economic model
5. Redefine the talent profile
6. Be committed to trust and integrity

Nemetz's next step is to use this feedback to design the specifics of a business plan. She remains amazed that Millennium cares enough about its business integrity to seek this feedback and input. Nemetz described her impressions from this project:

What we learned from the interviews of the intermediaries is that few customers or constituents really trust corporations, particularly in the pharmaceutical industry. A lot of what people said about corporations is very concerning. It was clear that there was a lot of mistrust of corporations, that a corporation could not be trusted to do the right things, and it pretty much confirmed what we saw in the studies and surveys about public trust of corporations. Trust level is low. Biotech companies are viewed more favorably because it's perceived that they put science first. We talked a lot about how a story gets spun. For instance, data is usually not black and white, there are nuances. Depending on company philosophy, they can emphasize information differently. If the data was not all positive, if you were up-front about the negatives, people could trust you. Trust is lost when you only talk about the good results. We learned from these interviews that it was OK to sell your product and make a profit, but people want full disclosure.

### CORPORATE SOCIAL RESPONSIBILITY PROGRAMS

According to Gary Cohen, corporate social responsibility addresses the following questions for Millennium:

1. What are the unique responsibilities of biotech or pharma firms in this world—for instance, in the areas of clinical trials, and the pricing and other decisions made that impact access to products by developing countries?
2. How does a company "think globally, but act locally"—for instance, how should the company engage with the local community where Millennium is one of the largest tenants besides MIT and Harvard?

Gary Cohen's group mission addresses the questions of how the company acts responsibly as a member of the global corporate community. One of the decisions made under the umbrella of the legal department concerns the sharing of materials discovered or made by Millennium scientists. A common gripe about biotech companies is the degree to which they obtain proprietary rights and do not share basic science materials, thus limiting the research of others who wish to advance the science. Mindful of this problem, Millennium has had an active practice of sharing those genes or other materials discovered by Millennium scientists, especially ones that do not fit within the company's commercial plans. The vehicle used to share such materials is called a material transfer agreement (MTA),<sup>31</sup> which is issued to outside academic scientists for their research. Even the simplest MTA costs Millennium several hundred dollars to complete. According to Cohen, there is no expectation of any subsequent benefit from these MTAs, except for the accompanying goodwill and satisfaction of knowing that the MTA will help to move the science forward. As he said, "There is only a slight chance that the academic will be able to make a commercially valuable discovery with Millennium's material, to which we have the right to negotiate a license, but the sole expectation of profit is not the reason we do this."

An older aspect of the company's corporate social responsibility program is a grass-roots community outreach program called Millennium Makes a Difference (MMAD). This program was initiated by Peter McLoughlin, a long-time Human Resources employee, in response to employees' requests for help in organizing community service programs. McLoughlin refrained from making this an executive-driven effort, and he maintained the low-key and employee-centric nature of MMAD. Consequently, MMAD reflects the company culture as defined by the employees; they choose which initiatives to undertake according to the connections

<sup>31</sup>A Material Transfer Agreement (MTA) is a contract that governs the transfer of materials from one organization to another and allows the recipient to use the material for research purposes. The MTA defines the rights and obligations of the provider and the recipient with respect to how the materials and any derivatives can be used, and usually specifies that no further transfer of the materials can be made to any third entity. MTAs also usually specify what intellectual property and licensing rights are retained by the materials provider for any discoveries resulting from the recipient's research.

they want to make with the community. MMAD programs, which are run by employee volunteers, include donation drives, environmental programs, blood drives, and tutoring in community schools. They also make suggestions about the manner in which other company programs are run: one MMAD suggestion involved the Biomedical Science Careers Program, where local bioscience firms sponsor scholarships for minority students pursuing an education in biology and related sciences. One Millennium employee noticed that the awards ceremony, a fancy black-tie event, typically consisted of Anglo, or Asian, male business executives presenting awards to African American or Latino students, a situation often reflective of the racial mix in the executive ranks of the local biotech companies. The next year, the MMAD initiative addressed the imbalance by having Millennium's award presented by the young African American woman who had been Millennium's past award recipient, and who had since become a Millennium employee. Gary Cohen, who attended this event, said that the difference of all white-male presenters followed by the young African American female was startling to see. Cohen believed that the corporate and community audience immediately understood that Millennium's employees were trying to make a difference, and that this gesture was "emblematic of the ethos, if not the ethics of place."<sup>32</sup>

#### ARTIFACTS: MOUSE PAD AND THE ETHICS QUICK TEST

In keeping with its ethics mandate, Millennium has deployed several tools for self-reflection and reinforcement, which have often led to a dialogue about how decisions should be made. The first was a computer mousepad on which was printed the list of core values. The mousepad is distributed to each employee during orientation, for placement on the employee's desk. Another such tool, developed and launched by Cohen in 2002, is an Ethics Quick Test, which encourages employees to ask the following questions before making important business decisions:

- How do I FEEL about this action?
- Is this action the RIGHT THING TO DO—does it align with our Core Values?
- How would I feel if my MOST RESPECTED PERSON knew of my action?
- Would I behave differently if I knew my action would be REPORTED in the newspaper?

These questions were made into posters displayed throughout the company as, one interviewee observed, "a reminder to every employee that they were encouraged and empowered to make decisions consistent with whether it feels right, is the right thing to do, and would not bring disrepute."

<sup>32</sup>Philanthropy is also part of Millennium's social responsibility effort: a "modest" program devoted to provide support to institutions and agencies that meet important healthcare needs of society.

#### IMPACT OF INSTITUTIONALIZATION OF VALUES AND ETHICS

To assess the impact of the values and ethics programs implemented by Millennium, information about the following was obtained: whether the core values influenced the hiring and retention of employees; whether employees integrated the company values and ethics in their work; how the company's values and ethics influenced company-sponsored human research. Various employees also gave examples of how they were motivated to make certain decisions based on the company's core values.

#### HIRING

One of the company's core values is the dedication to hire only the best people. In addition, according to Linda Pine, one way to maintain a focus on the other core values is to start during the hiring process. Pine admits that it can sound trite to say that Millennium "is all about our people [but] our assets are our intellectual capital devoted to pursuing the goals of the firm. [Our hiring is] all about attracting world-class people and creating an environment for them to be innovative and entrepreneurial." Millennium decided that it not only wanted its scientists and other employees to be excellent, it wanted those who could fit the corporate culture. Most employees tell tales of the series of interviews they experienced to determine how they would fit in. Ethics and values are explicitly included in the employee-selection criteria, and behavior-based interviews are used to learn about this aspect of a candidate. According to Pine:

One of our core values is building an ethically and socially responsible firm. We want to recruit people who sign up and are passionate, not just about the work, but about being part of our core values. People who want to make a difference. We select for culture-fit as well as skills, education, and experience. We use extensive interviewing and multiple visits with many people. We make clear in the interview process what life at Millennium is all about. The flip side to the 'Nothing is Impossible' attitude is a fast-paced and demanding work climate where the bar is raised all the time. New people have to know what they are getting into.

This approach to hiring was evident from the time of Levin's earliest employment choices. Early on, for instance, he hired the veteran Linda Pine to run Human Resources, and gave her a senior position in the company. This was an unusual move, as most other start-up biotech companies tended to hire junior managers to provide only basic Human Resources support. Knowing this, Pine had to be convinced to take the position. She had had 20 years of corporate Human Resources experience and had left in-house work to concentrate on high-level consulting. She had worked for 25 to 30 CEOs as a consultant and had no intention of going back inside a firm, especially for mundane work. However, Levin convinced her that his company would be "all about the way you treat people" and his commitment to

this value convinced her to reverse her career path. "There is no one else I'd have done it for," she said.

According to Linda Pine, "Steven [Holtzman] came with a philosopher's bent and an interest in ethical issues. He's a brilliant, very engaging person with a broad range of skills. He understands science and business. He had founded another biotech firm, so had business experience, but I'm sure commitment to people and ethical issues was one thing that attracted Mark to Steven." Holtzman readily admits his interests in public policy and bioethics, a trait that sets him apart from most corporate business officers. He told one interviewer that, by the end of his career, he wants to have "contributed to the creation of a bioscience industry that takes seriously our social responsibility to ensure that our technologies are used broadly for the benefit of as many people as possible."<sup>33</sup> Steven Holtzman later hired Gary Cohen as a corporate lawyer. Holtzman liked the fact that Cohen was thoughtful (something Holtzman attributed to Cohen's having studied literature) and because Cohen had interest and experience in corporate ethical issues. Cohen had been at Genetics Institute, an early biotech pioneer, and later at Genzyme Transgenics (now GTC Biotherapeutics), a company in the forefront of making human proteins in animal milk. Because of the nature of its products, GTC had been aware of ethical concerns surrounding the use of animals to produce human therapeutics, and then became immersed in the ethics of cloning after the birth of Dolly, the first cloned sheep. For these reasons, Cohen's Genetics Institute and GTC work had involved components of public policy and ethics. Cohen was prompted to join Millennium, inspired, he said, because Holtzman's "company work on bioethics really engaged me and my attention."

Holtzman also helped to hire Millennium's General Counsel, Jack Douglas, a highly experienced business lawyer. According to Holtzman, Millennium hired Douglas because we "wanted someone who was good as well as wanted him to be values-based, a person who fit the culture." Douglas fit the bill since he had had experience of, and an interest in, corporate social responsibility when, as General Counsel at Reebok, he started a human rights program that dealt with the ethical responsibilities of American manufacturers operating in developing countries. Fabio Benedetti had a similar affinity to the Millennium's focus on values. Dr. Benedetti was an oncologist at Sloan Kettering who had worked at large pharmaceutical companies before coming to Millennium. He accepted the job as Millennium's Vice President of Medical Affairs because Levin "told me about his vision and concept of putting the patient first. The company platform focused on finding the right drug for the right patient, which is a great underlying ethos. This was one of the things that inspired me. This fits with the ethics oath that all doctors take." Another prominent hire that came about because of a mutual interest in ethics was Rob Kloppenburg, to public relations. He had previously worked for Bayer Canada and had been responsible for the development of what was, at the time, the first corporate-financed, independent advisory bioethics council in

<sup>33</sup>Lawrence RN. Steven Holtzman Discusses Partnering. *Drug Discovery Today*. 2001;6:1042-1045.

the world.<sup>34</sup> Of all his work, he said that he is proudest of this, and he wanted to continue to find similar purpose and meaning when he accepted employment at Millennium.

In the hiring and interview process, prospective employees are introduced to the company's core values and learn about such things as the policy not to grant one employee more benefits than another. During employee orientation, the core values are explicitly covered and ethical issues are discussed, applying the core values to expected employee behavior. The sexual harassment policy is reviewed as well as the general expectation that employees will treat each other with dignity and respect. When Millennium grew to the point where it needed sales representatives, a separate policy was developed to govern interactions with health professionals. Future hiring initiatives include addressing the question of diversity in the workforce, especially in upper management where, typical of most biotechnology companies, most executives are male.

### EMPLOYEE BUY-IN

In addition to the views of employees documented above, and the responses from the organizational survey, there is other evidence that the employees of Millennium have integrated company values and ethics into their work. The manner in which this is done seems to be a mixture of pragmatism, business necessity, and idealism. Steven Holtzman's approach typified this triad of influences. As he told one interviewer in 1999, "Many companies have become savvy enough to understand that the single greatest obstacle to utilizing new technologies is the potential for a public backlash. In 1995, it was more difficult to get companies involved in these issues, because they didn't see the relevance of them. That changed for the most part when Dolly came along."<sup>35</sup> According to Holtzman, a growing number of executives began to recognize that ethical issues could impact the companies that were commercializing biotechnologies. However, from what he has seen, the biotech companies that pay attention to bioethics tend to treat the issues as part of public relations or government relations, with responsibility assigned to a lower-level employee. These people, for instance, would be assigned to lobby against the anti-stem-cell legislation, part of which included addressing the moral and religious objections to stem-cell derivation. At Millennium, in contrast, ethics has its own standing, and those responsible for ethics leadership are in senior management. Holtzman verified that the CEO often displays the core values at company meetings, and that they are discussed repeatedly to emphasize what

<sup>34</sup>The Bayer Advisory Council on Bioethics was initially set up to address the ethical issues associated with the provision of blood-collection and transfusion services in Canada. At the time of Kloppenburg's involvement, Bayer was bidding on these services after the Red Cross had lost the business due to a failure to introduce screening and withdrawal procedures quickly enough to prevent infections and deaths from hepatitis C and AIDS.

<sup>35</sup>Brower V. Biotech Embrace Bioethics. *BioSpace.com*, June 14, 1999. Available from [http://www.biospace.com/articles/061499\\_ethics.cfm](http://www.biospace.com/articles/061499_ethics.cfm).

the company stands for. Holtzman endorses this approach and believes that if the message is good and right, people will "absorb it and believe."

When asked for examples of how he sees the core values and ethics being integrated into employee decision making, Holtzman listed a series of questions that would be asked about an issue and then addressed the same questions from an ethical perspective. Examples of key questions about whether to develop a research project would include, he said, "Why am I doing the research? How am I doing it? What will we do with the results?" The related ethics inquiries would go something like this: "Why am I doing the research? Is the goal of the research ethical? How am I doing it? Does the research method include obtaining informed consent or including people who can't afford the product, etc. What do I do with the research results? Are there social justice issues?" According to Holtzman, asking such questions is fundamental to making ethics operational. "What is important to ethics is the inquiry." From what he has seen, this inquiry approach is applied to all major company decisions.

Another Millennium executive, Chuck Gray, the Director of Scientific Development, also spoke about how the company's core values had influenced the way he worked and made decisions. He said that he was initially surprised about the impact that Millennium's core values had:

A lot of firms have core values but not much is done about them. But here, they are. I've gone to 15 or 16 all-firm meetings and each time the CEO goes through the core values. I realize that the core values keep coming at you. The people here kind of live by them. For instance, that nothing is impossible—so you are encouraged to go out and try new things. I've generated lots of new initiatives, and they support it. Another value is that you don't discriminate—I'm an Orthodox Jew, and was surprised at how they go out of their way to accommodate me. The general counsel called me, for instance, and wanted a list of all Jewish holidays to avoid conflicts with board meetings. Another core value is to hire the best and brightest—and there are a lot of smart people here. So, the core values are taken very seriously here. They begin to influence how you behave and how you treat other people.

Gray, who is responsible for research collaborations with academia, listed some examples of how the core values were implemented in his case. Early on, he would attempt to obtain the "killer agreement." Now, instead of looking for maximal advantage in contracts with academic researchers, he views these relationships as:

... a mix of practicality and ethics. If both sides can share views on what they need, we can end up with good decisions. There have been cases where I could squeeze the professors who need our funding, but what would I gain? We're in the center of an academic universe here and we have to worry about our reputation. We need the academics and they need us. I have to deal with partners with integrity and honesty. If I say I will share data with them but then I tell them they have to wait a year or more, then I have shot one of our core values with holes. My word is key to my reputation.

Irving Fox, a Millennium Scientific Fellow, also described how the company focus on core values had influenced him. Prior to Millennium, he'd had a successful

career at Biogen, had done some teaching, and was consulting part-time for biotech companies. He was financially secure enough to pick and choose what companies to work for. His criteria for consulting with a company were: technology that could improve medical care; people and resources to make it happen; colleagues who would listen. He started at Millennium part-time, and quickly became an 80% employee.

I learned about Millennium's core values at the employee orientation—I got the mouse—and it is what keeps me here. I got more excited as I learned more and believed it was possible. I decided that this is how I want to spend the rest of my career as an older person, because time is my most valuable commodity.

For Fox, living the core values was reinforcing and he wanted to be associated with a company that was making products that mattered.

For Rob Kloppenburg, there is a definite connection between the core values and his public relations work. "An ethics approach is encouraged here from the top down and there tends to be a consistent approach." Kloppenburg sees public relations and ethics as closely aligned. "If the company screws up, I'm the person who has to face the public and the press." His main philosophy is that "good corporate policy equals good PR. Defending the reputation of the company is a lot easier if the company behaves responsibly."

## CLINICAL RESEARCH PROGRAM

Clinical research (meaning research in humans) is the most heavily regulated aspect of a bioscience business; it is also the activity most closely linked to ethical concerns. Modern concepts of ethics in human research arose from the medical research atrocities of Nazi Germany, have been promulgated through the Nuremberg Code and the Declaration of Helsinki, and incorporated into the United States regulations intended to protect the interests of human subjects.<sup>36</sup> Medical products companies must follow these regulations to obtain FDA permission to conduct human research, on which data the FDA bases its decisions to approve marketing. Thus, ethical practices in clinical research are essential, and any bioscience company dedicated to ethical practices would naturally focus on its clinical research activities.

Early on, Millennium made commitments not only to adhere to the regulations, but also to consider the broader ethical consequences of its research activities. For instance, academic scientists conducting Millennium-sponsored genetic research

<sup>36</sup>FDA regulations regarding human subjects rights are found generally at 21 CFR Part 50. Research ethics guidelines generally include the following provisions: a subject's well-being takes precedence over the interests of science; the voluntary and fully informed consent of the human subject is absolutely essential; the researcher should avoid all unnecessary physical, mental suffering, and injury; medical information about the subject should remain confidential; the degree of risk should never exceed that determined by the humanitarian importance of the problem to be solved; research should be justified by its benefit to society; and research should be conducted only by qualified persons using scientifically sound methods.

knew they were not obliged to disclose to subjects who provide tissue samples that the tissue will be used by a for-profit company. However, Holtzman decided that the research consent document would contain the disclosure, because this fact would matter to some people. This decision, though not legally required, is representative of Millennium's approach to consider the wider consequences of its research. Following Holtzman's lead, other research managers at the company routinely made decisions consistent with this approach.

Joanne Meyer, Millennium's Director of Human Genetics, described how Millennium's business and legal groups were early promoters of ensuring that human subjects recruited for Millennium-sponsored studies gave full informed consent so that they understood the consequences of deciding to donate tissue samples for genetic research. Also, responsible systems were put into place to protect the privacy interests of those who volunteer to be human subjects. Even though the DNA samples could reveal limited information at the time collected, in the future, advances in genetic testing were likely to reveal extensive amounts of medical information about the tissue donors, some of which would be unwelcome news to them. For instance, studies to identify disease genes often involve collection of tissue samples from families. According to Meyer, in any given genetic study of families, 10% of the samples will reveal genetic evidence of non-paternity. Anticipating this problem in advance, Steven Holtzman and Phil Reilly helped the group decide how they would handle this information and address questions such as whether to reveal the information to the tissue donor, and what to do if the tissue donor or the donor's spouse or child asked about paternity. Ultimately, Meyer's group decided that under no circumstance would they reveal paternity information to anyone: it was not the subject of their research and there were other means available for family members to obtain the information in ways that protected the interests of all involved. In addition, Millennium's informed consent document would warn subjects that paternity problems could be revealed to Millennium scientists, but that this information would be disclosed to no one, including the tissue donor.

This heads-up approach influenced the entire process of deciding what constituted acceptable informed consent practices for Millennium's initial genetic research. Rather than rely on the existing practices of its research partners, which could vary from site to site, Millennium was proactive in drafting informed consent templates for the company and its research partners. In this process, Meyer's group talked with 30 to 40 different academic groups to obtain input before the consent and protection practices were implemented. As a result, in Meyer's experience, Millennium was significantly in front of the existing standards to ensure informed consent for disease gene studies—that all subjects fully understood in advance the consequences of providing tissue samples for genetic study. Other systems were put into place to ensure that tissue samples and data were protected. Practices to ensure the privacy of subjects also included mechanisms to limit both access to DNA information and disconnects to protect against the discovery of the identity of the tissue donor. Meyer was dedicated to ensuring that “every step along the way, we implement policies that protect the patient.”

Although it was not a common practice in the industry, Mark Levin decided that the company needed an internal board to monitor the safety of its clinical trials. Dr. Fox was chosen to run this clinical trials Safety Review Board and, according to him, with clinical trials, “ethical issues arrive everywhere.” The Safety Review Board makes decisions about the human trials sponsored by the company, such as when it is appropriate to test a new chemical entity in humans, and when it is safe to increase the dose of an investigational drug. In addition, the Board addresses the emergencies or unanticipated events that occur during clinical trials, such as when a production glitch causes doubts about the safety of research materials, or whether the appearance of abnormal blood tests in human subjects presages an unacceptable risk of side effects such that the trial should be stopped.

In making calls such as this, Dr. Fox's motto is “safety first, no shortcuts.” The Board evaluates the impact of the decision on the human subjects: how significant is the potential harm; do patients have other options for treatment; how sick or close to death are the human subjects; and what does the therapy contribute to subjects' health and longevity? Many of these clinical trial decisions must be reported to shareholders and can have significant financial impact on the company, such as when the company announces that it has abandoned the trial of an important drug. However, Dr. Fox views these decisions as ones that need to be made with “blinders on for business issues. We leave [the business ramifications of our decisions] to someone else. We make rulings that might not be in the best interests of firm, but are for the patient,” he said. Many of the decisions the Board must make are of the “nail-biting” type, as neither the company scientists, nor the external research review boards, nor the FDA can reliably predict how a compound will behave when studied in humans. Unexpected toxicity is always a possibility. The board's job is to ensure as much as possible that everything has been done to minimize this possibility in clinical trials. Dr. Fox views this work as a trust that is given to him that he cannot fail to uphold.

Dr. Fox is assisted in his work on the Safety Review Board by some very senior managers. The Board is composed of the Vice Presidents of Regulatory Affairs, Preclinical Research, Medical Affairs, and Quality, and the Director of Drug Safety. Gary Cohen was a non-voting member of the board when he worked as the company lawyer. However, when Cohen's position in the legal office changed into being the “company ethicist,” the Board invited him to be a voting member. Prior to that change, the Board considered itself as having a technical function (to analyze the preclinical data and decide if it was safe enough to put into humans, etc.). Even though the technical function in the hands of experienced and knowledgeable, professionals could have been enough, in Fox's opinion, to ensure that the board “did the right things” to protect subjects, with Cohen's presence and focus, an ethical dimension to such issues was made explicit. According to Dr. Fox, even though Cohen is still learning about the process of drug development, he raises questions that “make people think... He has an influence... I was skeptical initially when he came as a lawyer. But I am comfortable with Gary's role as an ethicist.”



Dr. Benedetti, who is responsible for investigator-initiated studies (usually, later stage or post-marketing studies), took a similar approach and developed a research protocol review team for the studies that he supervises. He was motivated to do so because of his belief that not all questions about conducting clinical trials were answered by consulting the regulations. "We won't accept deviations from them," he said. "But they are not always super-detailed, so there is room for flexibility and differences in interpretation." For these reasons, research review boards need to work out the specifics of what constitutes a medically sound and ethical study. Dr. Benedetti described an example of such a dilemma. Should a clinical trial be stopped early when a data-monitoring board discovers that an anti-cancer drug has shown a potential clinical benefit (i.e., has reduced the rate of occurrence of a cancer) over a placebo, before the study has matured enough to reach its most important clinical endpoint? Stopping the trial early and offering the drug to the placebo group possibly benefits the subjects in the placebo group and future patients who receive the drug. But the early stop also prevents the researchers from studying whether the drug can actually prolong survival, or just delays the onset of cancer. Such a question had arisen in the famous Tamoxifen breast-cancer trial,<sup>37</sup> and no consensus had been reached about whether the decision to stop the trial early had been correct. In addition, the precedent created by the Tamoxifen trial decisions will make it difficult to conduct future survivability studies in similar circumstances. According to Dr. Benedetti, there is no clearly right decision in such a case, and reasonable people can disagree on what is the ethical choice. Do you focus mainly on the subjects at hand, or do you continue the research hoping to benefit the many other cancer patients? When asked how he would make such a decision, Dr. Benedetti said he would engage in careful reasoning about the dilemma, consider all consequences, and make a decision with the right intentions. Part of the careful analysis in a corporate setting, he said, is the necessity to distinguish between the commercial needs of the company and the medical needs of the subjects and future patients. Dr. Benedetti believes that it is his responsibility to know when these two interests are (or are not) aligned, and to ensure that the medical needs of patients always come first.

Another clinical trials question being explored at Millennium, by Rob Kloppenburg, involves the manner in which human trials are conducted overseas: can studies be done in other countries that cannot be done in the United States? Do the same values prevail, or should the company proceed under the rubric of cultural relativism, operating under the standards of the foreign country? The active discussion of these questions was triggered by an incident in 2000 that had occurred in a Chinese study. At the time, Millennium was one of few genomics

<sup>37</sup>The Breast Cancer Prevention Trial began in 1992 and was largely funded by the National Cancer Institute, a branch of the National Institutes of Health. The study enrolled more than 13,000 women at high risk for breast cancer, half of whom received tamoxifen and the other half placebo. The study was intended to last 5 years but was stopped early when data showed a 45% reduction in the incidence of breast cancer in the tamoxifen-treated group compared with the women on placebo.

companies to sponsor genetic studies involving the collection of tissues from people in remote regions of the world, where genetic diversity was expected to be at a minimum. As is in the nature of pioneering research, some unanticipated questions arose about Millennium's partial sponsorship of a Harvard researcher in China who was conducting population studies looking for disease-linked genes. Millennium's interest was in an obesity gene in a group of people who were obese despite low caloric intake. The study was being conducted in a remote province where there was a high degree of poverty, low educational levels, and a correspondingly low ability to comprehend the nature of the study. As detailed in a lengthy front page *Washington Post* article,<sup>38</sup> the Harvard researcher was accused of inadequate disclosure about the nature of the study and of duping the local people to enter the study by promising, but not delivering, free or low-cost medical treatments. In addition, the Harvard researcher unexpectedly encountered genes linked to schizophrenia in the same population of people and failed to consider the stigma attached to mental illness when disclosing this information. Once the *Washington Post* article was published, the study came under wide criticism, some of it quite vitriolic.<sup>39</sup> Each time an article was written about the study, Millennium was listed as one of the study's sponsors. This criticism was painful for a company that had prided itself on being a leader in ethics; managers worked hard to brief employees on what had occurred before the article appeared and to assist them in explaining Millennium's role to inquiring outsiders. With Phil Reilly's help, Millennium's management reviewed what had happened, and the company's obligations as a sponsor of an academic researcher who used Harvard University's research review board to approve the study, and whose field work Millennium could not fully control. As part of the review, Reilly and others consulted with many different research review boards and analyzed the newly emerging national rules about the research treatment of genomic material. As a result of this project, Millennium now structures its genomic studies differently to reflect the different requirements, sensibilities, and needs in each research site, and takes more care to consider in advance the impact of the gene hunting research it sponsors.

## INVESTOR RELATIONS

Employees were asked to give an example of an investor relations decision that was influenced by the core values. Rob Kloppenburg recalled such an instance. A suggestion had come up at a high-level meeting that Levin attended that Millennium should disclose some positive interim data from a company clinical trial.

<sup>38</sup>Pomfret J. Nelson D. (2000, December 20). An Isolated Region's Genetic Mother Lode—Harvard-Led Study Mined DNA Riches; Some Doctors Say Promises were Broken. *The Washington Post*, Section A1.

<sup>39</sup>One UK group accused the researchers of being "gene vampires." See "Gene Vampires Strike in Rural China," published by the Institute of Science in Society. Available at <http://www.i-sis.org.uk/isisnews/i-sisnews7-24.php>.

Someone else at the meeting objected that Millennium did not have a practice of releasing interim study data. Further, in fairness to shareholders, if the company adopted a practice of disclosing interim data, it should be comprehensive, meaning that both good and bad data should be included. According to Gary Cohen, Levin then asked for more information ("he's a data hound"). Levin wanted to be consistent and follow the industry standard. A 2-month study commenced, headed by Gina Brazier (Investor Relations) and Ruju Srivastava (Business Development), to research industry practice about releasing interim study data. Scores of press releases were studied and information was compiled, leading to a recommendation that the company not engage in this practice. Employees who conducted this study explicitly invoked Millennium's core values. And when the press reported the problems with the timing of ImClone Systems Inc.'s announcements about an FDA filing for a drug approval, when ImClone was quick to announce the filing and slow to announce when the FDA rejected the filing, Millennium made this an opportunity to study FDA filing announcements, to guide the company in adopting responsible practices.

#### PERSONALIZED MEDICINE AND STAKEHOLDER EDUCATION

New business endeavors have also been developed, taking into consideration whether the business plan is consistent with core values. Many of Millennium's future drugs will be developed based on "pharmacogenomics"—drugs tailored to an individual patient's genetic predisposition to respond to the compound. As an example, if a gene is discovered that is responsible for causing drug toxicity, the drug would not be prescribed to those patients who test positive for the gene. This personalized medicine approach offers great promise to both enhance the efficacy and reduce the toxicity of future drugs. However, Millennium's molecular medicine group has recognized that personalized medicine (gene testing prior to drug prescribing) poses medical, business, and ethical dilemmas that need consideration prior to commercialization. Joanne Meyer has engaged in active discussions and debates, both within and outside her group, to develop personalized medicine strategies that will benefit patients, physicians, and the company. The strategy group meets weekly and deals with these broad questions as well as many more tactical issues.

#### PRESERVING A FOCUS ON CORE VALUES

##### 10<sup>TH</sup> ANNIVERSARY—LIVING OUR CORE VALUES

To keep the vision of the company's core values alive, Millennium decided to celebrate its 10<sup>th</sup> anniversary by making the year 2003 dedicated to one theme, "Living Our Core Values." Over the course of the year, numerous discussions among employees across the company took place, guided by Gary Cohen and

a discussion book containing questions to address, worksheets, and feedback forms. The discussions were intended to re-evaluate, renew, and reinforce the company's core values and seek input for enhancing their impact.<sup>40</sup> At the end of the year, Millennium wanted to know how to enhance and integrate their mission and value statements into all aspects of corporate life. It also wanted to fill in the gaps to reflect changes in the company business plans that have occurred over last decade. For instance, Gary Cohen predicts that the reaffirmed core values will address the company's responsibility to patients who receive its drugs. Gary Cohen views the anniversary exercise as an attempt to mirror and recreate with the current employees what Mark Levin did with the first 15 to 30 employees: a new corporate Constitutional Convention, as it were. The idea, Cohen said, is to "try to bond people to the values in the same way as the founders were bonded to our original core values and mission."

#### THE FUTURE

By the early winter of 2002, there was good news and bad news for Millennium. The company had continued to pursue joint development and merger and acquisition opportunities to provide itself with products on the market, products in later-stage development, and additional capabilities necessary to accelerate its own downstream efforts in drug discovery. It was succeeding in making the leap from genomics to being a fully integrated biopharmaceutical company. In addition to COR, it had purchased other companies with drug-making capabilities and ramped up infrastructure and in-house expertise. R&D growth was continuing, and the company expected to spend from \$525 to \$540 million on R&D in 2003. As a result, the company was steadily filling its product pipeline. Ten drugs had progressed into human clinical trial testing. Millennium was about to file a new drug application to market Velcade®, a treatment for relapsed and refractory multiple myeloma, a life-threatening condition for which there were few treatment options.<sup>41</sup> In addition, Millennium was receiving co-promotion revenues from sales on Integrilin®.

However, the year 2000 industry boom was over and the financial community was looking more skeptically at genomics companies that were attempting to

<sup>40</sup>The planned discussions were February: "Why do values make a difference?" March: "What does it mean to 'hire only the best people?'" April: "How can I help create an 'environment where our people can excel?'" May: "Do I really 'listen to and learn from everyone?'" June: "What does it take to 'encourage innovation' in a growing company?" July: "What does 'absolute integrity' mean to me and my colleagues?" August: "How are 'outstanding individuals and focused teams' critical for our success?" September: "What's required to build a socially and ethically responsible corporation?" October: "Walking the talk." November: "10th Anniversary Statement of Core Values."

<sup>41</sup>On May 13, 2003, Millennium received approval from the FDA to market Velcade® for the treatment of multiple myeloma patients who have received at least two prior therapies and have demonstrated disease progression on the last therapy.

move into the pharmaceutical industry sector with gene-based drugs.<sup>42</sup> Because it was moving into this industry sector, Millennium would be facing much more formidable competition against other genomics-to-drugs companies (such as Human Genome Sciences and Celera) and against pharmaceutical companies with their greater resources and experience in drug development, manufacturing, and marketing. Millennium was also caught in an industry downswing that had started in late 2000 and had not recovered. From its high in November 2000 of \$89, Millennium's stock price was bumping along in the \$13 area. The company was still reporting losses that were expected to reach, in 2003, between \$295 and \$310 million on revenues that had been expected to be in the \$450- to \$475-million range. New, marketed drugs were also years away, and the company had to maintain its ability to weather the financial dry spell. However, the expected cash balance of more than \$1 billion by the end of 2003 meant that Millennium's prospects were better than most.

Gary Cohen knows that Millennium will face other challenges as well; principally, it will be difficult, as Millennium grows, to keep employees focused on the set of core values that were fundamental to the founding employees. Once products are on the market and the employees are held accountable for sales results and growth, marketplace pressures could both divert attention from, and tend to undermine, the ethical aspects of business decision making. He uses this analogy: "People in large apartment buildings don't behave the same way to each other as those in a three-unit building. It is the same issue in firms as they grow. There is a danger of losing the sense of shared commitment that we had as a start up." In addition, employees were reporting in the annual survey that they felt increasingly under pressure, so Cohen knew that he could not "drop huge ethics training programs on the workforce at this stage. We have a preposterously overworked group of people. We want to infuse an awareness of ethics into the workforce without creating more [of a] burden on them."

Cohen was focusing on managing corporate values for his growing company at a time when business ethics was part of the national discourse. Egregious corporate ethics violations, involving venerable companies such as Enron, WorldCom, Adelphia, Tyco, and Global Crossing, and some of their accounting firms, including Arthur Andersen, had been widely reported throughout 2001 and 2002. While these companies were being prosecuted for self-dealing and fraud and were filing for bankruptcy, newspapers and websites printed the companies' values and ethics statements and detailed how each had been ignored and violated. These publications were devoted to highlighting the hypocrisy of, and disconnect between, corporate values and corporate behavior. Business values and ethics were definitely taking a beating in the public press and in Congressional investigation committees. Business consultants were also publishing articles about how companies could

<sup>42</sup>Carey J. Nice Job on the Genome. Now, Let's See Some Profits. *Business Week*. 2001 February 26:34.

both benefit from adhering to values and be harmed when they were ignored. According to one business consultant, not related to Millennium:

Enron—although an extreme case—is hardly the only company with a hollow set of values. I've spent the last 10 years helping companies develop and refine their corporate values, and what I've seen isn't pretty. Most values statements are bland, toothless, or just plain dishonest. And far from being harmless, as some executives assume, they're often highly destructive. Values statements that are empty create cynical and dispirited employees, alienate customers, and undermine managerial credibility.

The consultant went on to say that strong commitments to core values can make a company stronger, both competitively and culturally. But the commitment is not pain-free:

Indeed, an organization considering a values initiative must first come to terms with the fact that, when properly practiced, values inflict pain. They make some employees feel like outcasts. They limit an organization's strategic and operational freedom and constrain the behavior of its people. They leave executives open to heavy criticism for even minor violations. And they demand constant vigilance.<sup>43</sup>

Steven Holtzman and Gary Cohen believed that Millennium's core values had been successfully woven into most aspects of the company business. But it was not a time for complacency. Cognizant of the prevailing cynicism and the challenges for Millennium, Cohen is working on devising programs that fit the needs of his growing company. Steven Holtzman and he knew that many of the ethics programs had been so strongly identified with Holtzman that corporate ethics could easily have dissipated on Holtzman's departure. Therefore, Cohen and Holtzman worked closely together, over a transition period, to ensure that Holtzman's legacy would carry on after he left. Cohen was successful in increasing the number of employees engaged in ethics programs and initiatives. The ethics and business law activities were solidified within the legal department, and other programs expanded. So far, with respect to filling Holtzman's shoes, Cohen felt pretty good. "It's not possible to replace someone as unique as Steve, but with support from Mark [Levin] and Linda [Pine], the ethics program has grown, and is deeper and richer," he said. Cohen's next step is to determine for himself what differences and similarities exist between biomedical and business ethics so that he could build on the first to inform the second, to create complementary in-house programs and system approaches. He found this to be a difficult task, as the two disciplines did not coexist often enough in the same setting for him to learn from the experiences of others. While working on the question of how to integrate biomedical and business ethics within the company, Cohen was also addressing some management issues that were strictly of business ethics. His first step was to learn from the business ethics failures of other companies, such as Enron. Cohen was meeting with other corporate ethics officers at large companies in an attempt to

<sup>43</sup>Lencioni PM. Make Your Values Mean Something. *Harvard Business Review*. 2002 July:5-9.

learn why the company's statements of core values and ethics had become so disconnected from the way employees spent their work day. With these insights, Cohen hopes to raise the ethics perspective for such issues as corporate transparency, audit procedures, tax practices, and executive compensation, loan, and stock option plans.

Another challenge for Cohen was to address those who were skeptical of any large company that described itself as ethical or dedicated to set of core values. He had spoken to one such sometime skeptic, George Annas, Professor of Health Law, Bioethics, and Human Rights at Boston University School of Public Health.<sup>44</sup> According to Cohen, Professor Annas sometimes has seen corporate bioethics as an oxymoron, a view, Cohen knows, that is not uncommon. The suspicion is that companies use bioethics programs to enhance public relations and shareholder value, and that in-house ethics officers such as Cohen are simply mouthpieces to serve that effort. Rather than being discouraged by these views, Cohen finds it worth knowing they exist. "This is something I ask myself each day, and I conclude that it isn't just that," he says. "I can't concede the bioethics field to academia."

Other Millennium employees voiced concerns about the fate of company values and ethics similar to Gary Cohen's. Rob Kloppenburg's experience told him that "just having ethics statements doesn't matter if employees are continually asked to step over the line." Dr. Fox is interested to see if the new marketing groups blend with Millennium's values. Dr. Benedetti, having come from a large pharmaceutical company, has a perspective on the differences between large and adolescent bioscience companies and is counting on Millennium's flexibility and past history to prevent it from becoming a company that, for instance, decides what studies to fund based primarily on commercial needs. Sue Nemetz had also done quite a bit of thinking about how the core values would fare in Millennium's future. She wondered whether, as Millennium grew, it would be able to balance the competing demands of "making our numbers, ethics, and organization survival." She had seen and heard about managers at larger businesses bowing under the need to "make the numbers" by doing such things as "booking sales" by overloading the supply chain and then failing to inform the CEO for fear of losing bonuses tied to the sales figures. Another industry practice, driven by similar motives that she hoped Millennium would avoid, involved paying physicians to conduct small "studies" of product use in order to garner product loyalty. The practice was viewed by some as "buying new business," and it raised ethical questions in her mind. Having a strong ethical foundation would help to keep Millennium from falling into the same traps. In addition, the lessons from the energy trading industry scandals were on everyone's mind. Several managers who were committed to the company's values noted that Levin's strong moral leadership would have to be reflected throughout the company for Millennium to continue to pursue financial imperatives ethically.

<sup>44</sup>Beginning in 2003, Cohen began a Masters in Public Health (bioethics) course of study at Boston University. He asked Professor Annas to be his academic advisor.

Some employees worried that the values and ethics focus might slip if Levin's influence diminished, despite Cohen's involvement. Although most in-house ethics education classes dealt with biomedical ethical issues and not business ethics, some employees were discouraged that very few business managers attended. There were also reports of some employees voicing opinions contrary to the core values that, according to one interviewee, would trouble Levin if he learned of them. The merger with COR Therapeutics also had prompted introspection at the combined company about the "right" way to maintain sales growth for their one marketed product, according to Nemetz. As Millennium grew into a company that marketed products, the decisions that had ethical dimensions would be addressed not by one group, but by many, which would add complexity. For instance, in exercises to define the long-range products plan, some senior managers appeared more focused on business imperatives; less thought was given to questions such as constrained healthcare resources and affordability when deciding which products to develop. Issues that also might be difficult to manage because they were not specific to one group were product pricing and factoring in physicians' off-label prescribing practices,<sup>45</sup> both of which had ethical dimensions that might affect financial goals. As such pressures begin to accumulate, employees at Millennium are confident that their CEO will continue to focus on doing what is right. However, with strong external pressures and potential distance from Levin's vision and influence as the company grows, one interviewee wondered about whether "doing the right thing" would always prevail.

It was encouraging, nonetheless, that, as Millennium was revving up to fulfill its expanded business plans, many of the senior managers were cognizant of the challenges, asking the right questions, and dedicated to keeping Millennium grounded in its core values. All the managers interviewed for this case study were optimistic, as was Levin himself. As he wrote in his message to the company about the "Living Our Core Values" anniversary program:

When I reflect on my experience over the last ten years, it's often the way our accomplishments have been achieved, rather than the accomplishments themselves, that have provided me the most joy... We have a bright future ahead. We'll achieve our goals, and be proud of how we get there, if we continue to act with integrity.<sup>46</sup>

<sup>45</sup>Off-label drug prescribing occurred often in one of Millennium's main target businesses, oncology, where a drug is prescribed by physicians for diseases other than those approved by the FDA. The term comes from the fact that the FDA regulates what is contained in a drug's labeling (indications, side effects, etc.) and does not regulate the practice of medicine. This allows physicians to prescribe approved drugs for any indication deemed medically appropriate without fear of FDA sanction. Millennium does not engage in off-label drug promotion and trains its sales force to comply with laws and regulations.

<sup>46</sup>Living Our Core Values. Discussion Guide, Millennium Pharmaceuticals, Inc., 2003.