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Financing the Biotech Industry: Can the Risks Be Reduced?

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Stanley C. Erck, Jonathan R. Beckwith,
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Dean Ronald Cass:

1. The biotechnology field is challenging notions of what life is, where it begins, and how it develops.[1] We are going to talk more about the life of the companies represented here today than we are going to discuss real life. But the corporate lives we will discuss are very real to all the people on today's panel. Our first speaker will be Professor Joshua Lerner of the Harvard Business School. He will be followed by Farah Champsi, Managing Director and head of the Life Sciences Investment Banking Group at Robertson, Stevens & Company.[2] Our third panelist will be Stanley Erck, President and Chief Executive Officer of Procept, Inc.,[3] a company which is working on biotechnology drugs for human immune system deficiencies.[4] Following Stanley Erck will be Dr. Jonathan Beckwith, the

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1 *See generally* Gina A. Kuhlman, *Alliances for the Future: Cultivating a Cooperative Environment for Biotech Success*, 11 BERKELEY TECH. L.J. 311, 312-13 (1996) (explaining how biotechnology breakthroughs enhance the quality of life).

2 Robertson, Stephens & Co. is a multi-million dollar investment firm, founded in 1978 and based in San Francisco, California. *See* DUN & BRADSTREET, D&B MILLION DOLLAR DIRECTORY 4436 (1997) [hereinafter D&B MILLION DOLLAR DIRECTORY].

3 Procept, Inc. is a biotechnical research firm, founded in 1985 and based in Cambridge, Massachusetts. *See id*. at 4244.

4 *See* John R. Wilke, *Two Foreign Firms Plan Investments in Biotech Concerns*, WALL ST. J., Sept. 16, 1993, at B10 (announcing that Sandoz Pharma Ltd. will invest $29 million in Procept, Inc. to "fund research into drugs to treat immune system disorders and organ transplant rejection").

American Cancer Society Research Professor at Harvard Medical School, and then Leslie Davis, a partner at Testa, Hurwitz & Thibeault, LLP. Our final speaker is Henri Termeer, President, Chairman, and Chief Executive Officer of Genzyme, Inc.,[5] one of the larger players in the industry.[6] After each panelist makes an opening statement, we will have a discussion among the panelists and the audience.

Joshua Lerner:

2. I am going to start by focusing on the venture side of biotechnology financing and then continue with public market and alliance sources of financing. Before we begin discussing venture financing in the United States biotechnology industry, I will discuss some of the patterns in venture capital as a whole. In particular, it is worth underscoring that venture capital in the United States has undergone a dramatic change in the past three decades.[7] After the Department of Labor permitted pension funds to invest in venture capital in the late 1970s,[8] there was a tremendous influx of money, which led to a ten-fold increase in the venture capital pool.[9] This period of growth was not totally harmonious. During the 1970s when there was relatively little money coming into venture capital, returns were quite high.[10] Once there was this substantial influx into venture capital, the returns throughout fell dramatically; in some cases, private equity subclasses experienced negative returns in the mid-1980s.[11] Only in the last few years have we seen spectacularly high returns and substantial influxes into venture capital.[12]

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5 Genzyme, Inc. is a biological laboratory that specializes in enzyme and isoenzyme diagnostic agents and in pharmaceutical preparations. *See* D&B MILLION DOLLAR DIRECTORY, *supra* note 2, at 2060. Genzyme was founded in 1981 and is located in Cambridge, Massachusetts. *See id.*

6 *See* STANDARD & POOR'S, INDUSTRY SURVEYS: BIOTECHNOLOGY 7 (Aug. 28, 1997) [hereinafter STANDARD & POOR'S] (ranking Genzyme fourth among publicly owned biotechnology companies by 1996 revenues).

7 *See generally* Paul Gompers & Josh Lerner, *The Use of Covenants: An Empirical Analysis of Venture Partnership Agreements*, 39 J.L. & ECON. 463, 465-69 (1996) (presenting a history of the venture capital industry).

8 *See id*. at 466 (citing 44 F.R. 50367) (stating that the Department of Labor's clarifying ruling "explicitly allowed pension managers to invest in high-risk assets, including venture capital").

9 JOSH LERNER & PAUL GOMPERS, WHAT DRIVES VENTURE CAPITAL FUNDRAISING? (unpublished working paper, Harvard University, 1998) (on file with Joshua Lerner).

10 *See generally* VENTURE ECONOMICS, INVESTMENTS BENCHMARK REPORTS: VENTURE CAPITAL (1997).

11 *See generally id.*

12 *See generally id;* VENTURE ONE CORP., VENTURE ONE ANNUAL REPORT (1997).

3. There are significant challenges associated with financing biotechnology companies. The challenges to biotechnology investors are extreme, and perhaps unique. If we think in general about small high technology companies, it is easy to see why they find it difficult to go to banks or other traditional financing firms.[13] The bank loan officer will look at their balance sheet and is likely to ask where are the assets. Because high technology company assets are likely to be intellectual property—patents and know-how which does not show up on the balance sheet - it is very difficult to finance these firms through traditional mechanisms.[14] It is often difficult to figure out the value of the patents and know-how. There are also problems of information asymmetries: the nature of patent protection is often incomplete, and known best by the inventor.[15] Finally, the amount of money which high technology firms must raise is enormous, often in the hundreds of millions of dollars.[16]

4. The single most important form of financing, it can be argued, has been venture capital. One way of showing this is through an examination of the success of firms that have been backed by venture capitalists. Of the 1300 biotechnology companies established over the last twenty years,[17] approximately one-third have been backed by venture capitalists.[18] But, when one looks at the success of biotechnology firms, the venture-based firms represent the lion's share, whether measured by patents and other intermediate outputs, or in terms of their ultimate output of drugs and other successful products.[19] Venture capital, however, represents a small slice of the total financing raised by biotechnology companies.[20]

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13 *See* Josh Lerner, *Angel Financing and Public Policy: An Overview,* J. BANKING & FIN. (forthcoming).

14 *See id.*

15 *See id.*

16 *See* STANDARD & POOR'S, *supra* note 6, at 16-17 ("[M]ost new products cost between $200 million and $350 million to fully develop."); J. Casey McGlynn & Grant Heidrich, *Biotech Financing Remains a Tough Row to Hoe*, 13 BIO/TECH. 638, 639 (1995) (estimating that biotechnology research and product development often require over $200 million for one product).

17 *See generally* Josh Lerner & Robert P. Merges, *The Control of Technology Alliances: An Empirical Analysis of the Biotechnology Industry,* J. Indus. Econ. 46 (June 1998). *[Editor's Note*: The author's unpublished additional analysis was shown in slides at the Symposium.]

18 *See id.*

19 *See id.*

20 *See id.*

The venture financing has been, however, the foundation on which much of the financing has been raised over the years.[21]

5. We could talk at considerable length about why venture capitalists have been so successful in financing biotechnology companies.[22] I will highlight a few of the key mechanisms venture capitalists employ. Much of the process involves sorting through the many competing technologies, using various formal and informal mechanisms to cull out the most promising technologies.[23] In addition to providing funds, venture capitalists add value to companies by providing intensive oversight and certifying the quality of the firms to investment bankers, corporations, and others.[24]

6. Venture financing has changed dramatically in recent years. The amount of venture financing dollars for biotechnology has not changed substantially, but there has been a substantial drop in the number of firms receiving financing.[25] Rather than funding smaller companies with relatively modest sizes of money, the funds have been increasingly concentrated in companies trying to develop broader platform concepts.[26]

7. In conclusion, biotechnology companies are difficult to finance for a variety of reasons. Venture financing, which bundles money with control mechanisms, is a key form of the financing that is linked with the success of biotechnology companies. At the same time, there have been some changes in terms of the way that financing is dispersed, leading to relatively fewer companies getting initial financing.

Farah Champsi:

8. The public market has been very supportive of the biotechnology industry over the last several years. In fact, 1996 was a record year for public market capital

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21 *See id.*

22 *See id.*

23 *See* Paul A. Gompers, *Optimal Investment, Monitoring and the Stage of Venture Capital,* 50 J. FIN.1461, 1461-1489 (1995); Josh Lerner, *The Syndication of Venture Capital Investments,* 23 FIN. MGMT., 16, 16-27 (1994) [hereinafter *Syndication of Venture Capital Investments*]; Josh Lerner, *Venture Capital and the Oversight of Private Held Firms,* 50 J. FIN. 301, 301-318 [hereinafter *Venture Capital and the Oversight of Private Held Firms*]; W. A. Sahlman, *The Structure and Governance of Venture Capital Organization,* 27 J. FIN. ECON. 473, 473-521.

24 *See* Gompers, *supra* note 23; *Syndication of Venture Capital Investments, supra* note 23; *Venture Capital and the Oversight of Private Held Firms, supra* note 23; Sahlman, *supra* note 23.

25 This is based on the speaker's unpublished analysis.

26 This is based on the speaker's unpublished analysis.

going into the biotechnology sector.[27] Biotechnology companies raised approximately $4 billion.[28] Biotechnology is a very high risk business in which you have an enormous amount of lead time associated with generating real revenues and earnings.[29] Moreover, there are very few profitable companies.[30] In fact, among the 1300 biotechnology companies Joshua Lerner talked about, I can count on my hands the number that have managed to break into actual product revenues and profitability.[31] For that reason, the way the public market looks at the biotechnology industry today changes as it begins to experience the trials and tribulations of some of the younger companies. An enormous amount of capital has gone into these companies, and many of the biotechnology companies could not survive without accessing the public market for capital.[32] The Chiron Corporation is a prominent, successful biotechnology company in this sphere.[33] It came to the market approximately six times and it has raised over $600 million of public capital

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27 According to Ernst & Young, dollars raised in initial public offerings from July 1995 to June 1996 increased 537% from amounts raised in the previous twelve months, and dollars raised in follow-on offerings for the same period increased 1195%. *See* ERNST & YOUNG LLP, BIOTECH 97: ALIGNMENT 21 fig. 9 (1996) [hereinafter ERNST & YOUNG BIOTECH 97]; *see also* Marjorie Shaffer, *1996 Banner Year for Biotech Drug OKs; Some Say Industry's Best Ever*, BIOTECH. NEWSWATCH, Jan. 20, 1997, at 1, *available in* 1997 WL 8790304 (stating that in 1996, the biotechnology industry raised a record amount of money through initial public offerings and secondary offerings).

28 *See* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 22 (reporting that companies raised almost $4.4 billion in 357 financings for the period July 1995 to June 1996); *see also Europe Poised for Biotech Boom, as U.S. Pros Seek New Opportunities*, BIOTECHNOLOGY NEWSWATCH, June 16, 1997, at 1, *available in* 1997 WL 8790920 (reporting that U. S. biotechnology companies raised nearly $4 billion in public financings in 1996).

29 *See* STANDARD & POOR'S, *supra* note 6, at 16-17 (estimating that biopharmaceutical products take eight to twelve years to go from preclinical development to marketing approval).

30 *See* Tim Stevens, *The Gene Machine*, INDUSTRY WK., Aug. 18, 1997, at 168, 169 ("In the [United States] alone, there are about 1,300 biotech companies, yet only a handful are profitable.").

31 *See id.* (stating that Amgen, Genzyme, and Biogen are the only companies that have been able to remain independent and take a product to market under the company's own label; other major biotechnology companies offer "branded" products but they are either wholly or partially owned by pharmaceutical companies).

32 *See* Joan Hamilton, *Biotech Stocks: So Sexy—and So Scary*, BUS. WK., Sept. 11, 1995, at 44 (stating that recent initial public offerings by start-up firms will impede the ability of existing companies to obtain the critical capital needed for long-term survival)**)**; *see also Biotech on a Roll*, 271 SCIENCE 151, 151 (1996) ("[W]hile the venture capital providers have become more picky, the pharmaceutical industry has become a major financier of biotech.").

33 *See* STANDARD & POOR'S, *supra* note 6, at 7 (ranking Chiron Corporation second among publicly owned biotechnology companies by 1996 revenues); Lisa Piercey, *Chiron Goes for Gold*, SIGNALS (Aug. 1997) <http://www.recap.com/signals.nsf>.

to get where it is today.[34] That is a huge sum compared to just about any other industry.[35]

9. One of the things that we are seeing that increasingly helps the public market investor is the contribution of the pharmaceutical industry to the biotechnology sector. The pharmaceutical industry is well-equipped to make the decisions as to which companies to finance.[36] In 1996, biotechnology companies raised close to $3.5 billion using the pharmaceutical industry.[37] There was also a record number of collaborations between biotechnology companies and pharmaceutical companies, approximately 180.[38]

10. The initial public offering ("IPO") market cannot adequately gauge which companies are going to make it and which are not. Many companies do not have revenues, earnings, or market share.[39] It is impossible to think of other parameters

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34 *See* MOODY'S INVESTORS SERVICE, MOODY'S OTC INDUSTRIAL MANUAL 1242 (1997) [hereinafter MOODY'S INVESTOR SERVICE] (reporting offerings of common stock as follows: 1.5 million shares at $12 per share in 1983; 1.75 million shares at $13.75 per share in 1986; 1.9 million shares at $24 per share in 1986; and 2 million shares at $57.50 per share in 1991). As of December 31, 1996, Chiron had outstanding $225,215,000 in 1.9% convertible subordinated debentures, due in 2000. *See id.*; *Chiron Offers $75 Million in Debt*, BIOTECH. NEWSWATCH, May 21, 1990, at 8, *available in* 1990 WL 2177321 (reporting that Chiron has filed a registration statement with the Securities and Exchange Commission to offer $75 million of convertible subordinated debentures, due 2015); *see also* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 71 fig. 33 (stating that Chiron had a market capitalization of $4.258 billion in 1995).

35 Compare Chiron's offerings with Microsoft Corporation's one-time offer of 2.795 million shares of common stock at $21.00 per share. *See*, *e.g.*, MOODY'S INVESTORS SERVICE, *supra* note 34, at 2132 (reporting Microsoft's offering).

36 *See* STANDARD & POOR'S, *supra* note 6, at 13 (stating that alliances with pharmaceutical companies "are perceived as vindication of a firm's prospects, and they also tend to put a valuation on its products and technology"); *see also* Stevens, *supra* note 30, at 168, 170 (stating that alliances with pharmaceutical companies "help take some of the Fund-raising pressure off the biotech organizations and give the pharmaceutical companies access to technology that is best stimulated in small, entrepreneurial settings").

37 *See* Alan Walton & Kimm Walton, *Biotechnology Investing 1995 to 1996: It's All a Matter of Perspective*, BIOVENTURE VIEW, Jan. 1, 1997, available in 1997 WL 8685977 (reporting that biotechnology alliances with corporate partners brought in approximately $4 billion to the biotechnology industry in 1996, and deals between biotechnology firms and pharmaceutical companies reached $2 billion for the first three quarters of 1996); *see also* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 27-30 (describing recent alliances between biotechnology companies and pharmaceutical companies).

38 *See* Alice Naude, *Partnering Up at the Discovery Stage*, CHEMICAL MARKET REP., Apr. 14, 1997.

39 Through June 1996, 206 of the 365 companies that went public had no reported earnings. *See* Ida Picker, *IPO ka-boom*, INSTITUTIONAL INVESTOR, July 1996, at 93, 96. Companies that have no revenues or business but decide to go public are may be referred to as "blank-check companies." *Id.*

by which one can gauge success. In any given year or two during the last decade, it is easy to find a public biotechnology company that seems to be doing very well on the stock market. Although the company may have reported very good Phase II clinical data, a year or two later the company might have a huge disappointment in Phase III when it tests the product in a broader population.[40] Synergen[41] is one example. The stock price can go from $60 or $70 per share all the way down to $6 per share. [42] The public market has been burned enough to know that it probably ought to throw most of the rules out the window and start over again.

11. One of the reasons we have these issues with the IPO market is because we are dealing with institutional investors who are much more sophisticated than the average retail investor.[43] However, most of the institutional investors are money managers who run small-cap growth funds. They are not biotechnology specialists. There are certainly a few biotechnology-specific funds;[44] but for the most part, you are dealing with individuals who are relying on research analysts on Wall Street and are looking at whatever benchmarks they can to predict whether the company will be successful and whether they ought to invest in it. Biotechnology stock prices are driven by the momentum of the overall equity

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40 "To win FDA approval, products must pass extensive Phase I (safety), II (efficacy) and III (confirmation) clinical trials. In the past, once a drug entered Phase III trials, approval seemed virtually guaranteed and raising funds became easier." Gail Dutton, *Biotech: Risky Business?*, MGMT. REV., Jan. 1995, at 36, 38. Recently, however, companies such as Centocor and Synergen have failed in Phase III; their stocks quickly declined nearly 50%. *See id.*

41 In the early 1990s, Synergen was a high-profile biotech company intent on curing sepsis. *See* Stephen Taub, *Strike Three*, FIN. WORLD, Sept. 27, 1994, at 56. That profile quickly changed when the company's drug, Antril, failed. *See id.* Synergen was later acquired by Amgen, Inc. *See Amgen's Net Income Fell 95% in 4th Period; Write-Off Is Cited*, WALL ST. J., Feb. 2, 1995, at B4.

42 In 1994, Synergen's stock fell after it "zoomed to the low 70s, only to crash twice before collapsing yet a third time." Taub, *supra* note 41, at 56.

43 *See*, *e.g.*, In re Kmart Corp. Sec. Litig., Fed. Sec. L. Rep. (CCH) ¶ 99,511 (E.D. Mich. Dec. 16, 1996) (permitting "individual retail investors" to represent a class that includes almost 200 institutional investors, even though "institutional investors, unlike individual investors, have access to sophisticated research and analyst information that was not used by individual investors in making their portfolio decisions")

44 As of December 1996, Fidelity Select Biotechnology was the only mutual fund to focus exclusively on the biotechnology sector. *See* Eric J. Savitz, *Unappreciated: A Money Manager Sees Lots of Bargains Among the Beaten-Down Biotechs*, BARRON'S, Dec. 2, 1996, at 22. One money manager has recommended a split of 60% investment in biotechnology and 40% investment in technology generally. *See id*.

market; thus, when there are big corrections in the Dow Jones Industrial Average or S&P 500, these vibrations are felt by the biotechnology sector.[45]

12. There are essentially four factors that the market can use to attempt to assess IPOs. First, there is the technical risk and the difficulty of the science. This is very difficult for an investor to figure out on the basis of a short presentation. Second, there is the development risk, or the length of time that the clinical trials are going to take.[46] Third, there is the marketing risk. This involves evaluating how good the drug must be to capture a significant amount of the market[47]—precisely, who are the company's competitors, and is the company going to be able to address the market segments it is pursuing.

13. Finally, there is the financial risk.[48] Wall Street today does not want to be the last resort of capital for a company. If a company has a large amount of cash on its balance sheet, it has as much security as the company needs to weather the ups and downs of clinical trials and drug development.[49] One of the key aspects of making an investment decision in a young company is to determine how strong it is financially. You will often find that there are a lot of public market investors who will not invest in companies that have less than two years of cash burn on their

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45 *Cf.* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 22 (noting that the downturn in high technology stocks in the third quarter of 1996 "took biotechnology with it," and stating that "[b]iotech remains vulnerable to financial market trends beyond its control").

46 *See, e.g.*, *Interview with Alan Walton,* BIOVENTURE VIEW, Jan. 1, 1998, *available in* 1998 WL 9219211 ("On average, it takes a new drug 6.1 years in discovery, 6.9 years in clinical development, and 2.3 years waiting for FDA review before approval."); Andrew Lawler & Richard Stone, *Congress Mixes Harsh Medicine*, 269 SCIENCE 1038, 1038 (1995) (reporting Biotechnology Industry Organization's estimate "that it now takes an average of 6 years of animal and clinical testing before a company files for a [New Drug Application], up from 4 years a decade ago"); Shawn Tully, *You'll Never Guess Who Really Makes*, FORTUNE, Oct. 3, 1994, at 124, 128 ("Bringing a drug to market takes about 12 years, and biotech companies typically develop only one or two products at a time.").

47 *See generally* DALLAS MURPHY, THE FAST FORWARD MBA IN MARKETING 41-48 (1997) (discussing strategies for capturing market share).

48 *See* Cynthia Robbins-Roth, *What Makes a Great Idea Fundable?*, BIOVENTURE VIEW, Dec. 1, 1996, *available in* 1996 WL 13633873 (noting that biotechnology firms need more than 18 months of cash in the bank so that they can free management resources from constant fundraising and "have a chance to fund their product development regardless of market behavior"); *cf.* Walton & Walton, *supra* note 37 (stating that with respect to venture investments, "[e]arly-stage investors have to wait five or more years for a return on their investment").

49 *See* STANDARD & POOR'S, *supra* note 6, at 21 ("[F]or development-stage biotech companies with no earnings, we like to see at least two years of cash on hand to fund operations at the current 'burn rate,' or the consumption of cash to fund [research and development]."); Alan Walton, *Biotechnology Investing 1994-1995: Halcion or Valium Days?*, BIOVENTURE VIEW, Jan. 1, 1996, *available in* 1996 WL 8331529 ("The public and private investors have focused in recent years on the cash survival index (liquid assets vs. cash burn rate) as an indicator of the health and prospects for the sector.").

balance sheets. These investors recognize that management can make the wrong business decisions when it is very concerned about the availability of funds to finish product development.[50]

14. The model of biotechnology today is quite different from the model that Wall Street has financed over the last ten years. The old model consisted of pursuing what I would call "maximizing profits," where the company would target a single product to develop and pursue in the hope that it would be the first to address a large market.[51] The model did not encourage the company to pursue the product as long as possible by itself, but rather the model induced it to enter a partnership with a pharmaceutical company when it was ready to market and manufacture the product.[52] Pharmaceutical companies had deep pockets, and companies did not have to give up a huge amount of the upside of the product.

15. There were many failures with the old model strategy.[53] Consequently, we have become much more astute as to what it takes to be successful in drug development and have built companies around that concept. The model today is not based on maximizing profits but is focused on risk reduction. The venture industry is forming many companies that the public market is embracing.[54] The parties are pursuing a platform approach to technical development. They are developing tools

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50 "Cash burn" is the rate at which "a fledgling biotech company 'burns' cash provided by venture capitalists or early-stage investors as it strives to push new products through research and development, clinical testing and the Food and Drug Administration approval process. This strenuous obstacle course can take as long as 15 years and cost $500 million or more, during which time there are few sources of revenue, intense competition and no guarantees of success." Ida Picker, *Staying Alive: How Sepracor Inc. Managed to Raise Money to Finance Its Biotechnology Ventures*, INSTITUTIONAL INVESTOR, May 1, 1997, *available in* 1997 WL 9673564; *see also* STANDARD & POOR'S, *supra* note 6, at 20 (stating that without sufficient cash on the balance sheet, a biotechnology company "may be forced to under-invest in its [research and development] efforts").

51 *See Investors Backing Preclinical Biotech Firms*, MARKETLETTER, Dec. 8, 1997, *available in* 1997 WL 14510669 (reporting that the biotechnology industry and investors have categorized biotechnology firms into two groups: traditional "old" model companies that are geared toward drug discovery and marketing products, and second-generation "platform" firms that focus on drug platforms and for developing broad product lines); STANDARD & POOR'S, *supra* note 6, at 10 ("As the industry took shape in the 1980s, most biotechnology companies planned to transform themselves into fully integrated pharmaceutical companies with the ability to develop, manufacture, and market their own therapeutics."). Synergen is a company that followed the "old model." It invested much of its assets into the development of a single drug for the treatment of sepsis. *See* Taub, *supra* note 41, at 56-57.

52 *See Investors Backing Preclinical Biotech Firms, supra* note 51 (stating that such "old model" companies utilized licensing agreements to market their products to pharmaceutical companies).

53 For example, five other companies, in addition to Synergen, put many (if not all) their eggs in one basket to come up with a sepsis treatment, and all failed. *See* Taub, *supra* note 41, at 57. Those companies were Cortech, Xoma, Chiron, Immunex, and Centocor. *See id.*

54 *See Investors Backing Preclinical Biotech Firms, supra* note 51.

that accelerate drug discovery and are not necessarily focused on a single product in the hopes that it will eventually be a multibillion dollar product.[55] This approach enables companies to pursue multiple corporate collaborations because they are not giving away their sole crown jewel. [56] They can slice it many different ways and use it to raise a lot of capital and thereby reduce their burn rate and their financial risk to public market investors and the company.

16. Biotechnology is really the wrong word for this industry today; it is a biopharmaceutical industry. Our new understanding of the science means that we are certainly going to see a lot of major new diseases addressed that we have not seen addressed thus far.[57] Perhaps in the end, the public market investor must rely on the intellectual capital that is devoted to the particular problem that the company has been formed around. That means assessing the management, the venture capitalists involved, and the academic and scientific minds behind the technology. At the end of the day, that intellectual capital is probably the single most important reason why biotechnology companies get financed by the institutional market.[58] Institutional investors recognize that they are not much smarter than anybody else; they bet on the people and adopt a risk reduction approach. Institutional investors base their investment decisions in part on the fact that very credible pharmaceutical partners are willing to support the company through difficult times.

17. Looking forward, the rules are changing, and it is a very promising time for the biotechnology industry. There is an enormous amount of public capital

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55 The synergistic alliance between biotechnology and pharmaceutical companies is realized in the use of platform technology. *See Platform-Technology Deals Increasingly Will Drive Genomics and Gene Therapy Alliances*, GENETIC ENGINEERING NEWS, Mar. 15, 1997, *available in* 1997 WL 8970479. Such platforms are divided into either "tool" technologies or "target" technologies. *See id.* The tool technologies embrace the generation of libraries with novel information regarding combinational chemistry or DNA. *See id.* The target technologies involve genomics. *See id.* In short, biotechnology companies provide biotechnical information for the pharmaceutical company's drug manufacturing. *See id.*

56 "Since the development of each of the technologies gives almost infinite numbers of candidate compounds and targets [pharmaceutical companies] can use, a platform technology company can make multiple nonexclusive corporate deals based on one early-stage technology." *Id.*

57 *See* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 25 ("[P]harmaceutical companies are using their alliances with biotech companies to bundle their products for specific disease indications and market niches.").

58 *See*, *e.g.*, STANDARD & POOR'S, *supra* note 6, at 18-20 (identifying factors for evaluating investment decisions in biotechnology companies, including product portfolio and pipeline, effectiveness of research and development efforts, quality and experience of management, and collaborations or partnerships).

available.[59] It remains to be seen whether all biotechnology companies are going to succeed. However, many companies will be successful by presenting a new model and reducing their risk profile, because history has proven that the old model does not work for every company.

Stanley Erck:

18. I am the Chief Executive Officer of Procept, Inc.,[60] a biotechnology company, one of two biotechnology companies represented here. On my left is Henri Termeer of Genzyme, a company that is in a very successful position and one of the top five most profitable biotechnology companies in the world.[61] He can talk about the tactics that he used to get there. I will tell you about a developing company that is midway between start-up status and being one of the most successful companies. Procept was founded seven or eight years ago by a technology and core scientific group from Harvard University. We formed a company, were venture-backed, and the process started.[62]

19. I marvel at the number of people who will start biotechnology companies. It is a unique industry, in my view, because you have to be willing to start a company that will not produce sales from real products for a minimum of ten, and often fifteen, years.[63] You have to have a business plan without product sales for ten to fifteen years. In that business plan, you must project how you are going to develop the product, which always requires a scientific breakthrough. You must tell your board of directors which month and year you are going to make the scientific breakthrough that will lead to a marketable product. For the first eight to ten

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59 From July 1995 through June 1996, the biotechnology industry raised more than $8 billion through venture capital, private placements, initial public offerings, and follow-on offerings. *See* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 21 fig. 9; *see also* G. Steven Burrill, *The European Biotech Industry: Gathering Momentum*, BIOPHARM, May 1, 1995, *available in* 1995 WL 13882566 (reporting that start-up biotechnology firms in Europe, like U.S. firms, recently have been able to raise substantial capital through public equity markets).

60 "Procept, Inc. is a biopharmaceutical company engaged in the discovery and development of novel drugs for the treatment and prevention of: (i) auto-immune diseases and organ transplant rejection and (ii) infectious diseases." Procept, Inc., *Welcome to Procept* (visited Jan. 21, 1998) <http://www.procept.com>.

61 *See* STANDARD & POOR'S, *supra* note 6, at 7 (ranking Genzyme fourth out of the top ten publicly owned biotechnology companies in 1996 revenues).

62 The process in which Procept participated is a common one in biotechnology. *See, e.g.,* Edward Penhoet, *Science & Technology Policy: A CEO's View*, 33 CAL. W. L. REV. 15, 22 (1996) (describing venture capital investments in start-up biotechnology companies).

63 *See, e.g.*, Milt Freudenheim, *Drug Companies Feeling Pressure of Clinton's Plan to Keep Their Prices Down*, N.Y. TIMES, Sept. 30, 1993, at A22 (reporting that a new drug by Genzyme for the treatment of Gaucher's disease took 10 years to develop).

years, you will have to hire eighty to ninety percent scientists—often Ph.D. level scientists who may not work together on project teams for over ten years.[64] The company will also face regulatory hurdles from the Food and Drug Administration ("FDA")—that is part of the ten to fifteen year process.[65] It requires a minimum of $100 million dollars to bring a product to market, and over its lifetime, the company will have to be able to raise hundreds of millions of dollars.[66]

20. Part of the solution is the unique financing climate that we have enjoyed in the United States; it is fairly unique in the world.[67] Venture capital has been willing to supply money to firms with these sorts of business plans.[68] This is followed by a combination of public equity—public stockholders who are willing to invest in small companies—with large pharmaceutical companies who seek biotechnology as part of their research arms to help finance drugs.[69] That is a unique framework.

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64 *See* Nicholas Veronis, *Exotic Enzyme is Stuff of Biotech Co.'s Dreams*, BOSTON BUS. J., Dec. 4, 1989, at 1 ("Most biotech companies spend their time and money on research and development, hoping to uncover valuable new products. The business of R&D is time-consuming, risky and expensive—Ph.D.'s don't come cheap.")

65 *See generally* STANDARD & POOR'S, *supra* note 6, at 16-17 (providing an overview of the drug approval process in the United States and estimating that it takes eight to 12 years to go from preclinical development to market approval); *Interview with Alan Walton*, *supra* note 46 ("On average, it takes a new drug 6.1 years in discovery, 6.9 years in clinical development, and 2.3 years waiting for FDA review before approval.").

66 *See*, *e.g.*, Freudenheim, *supra* note 63 (reporting that Genentech has spent more than $100 million seeking an AIDS vaccine and Genzyme spent $170 million developing a treatment for Gaucher's disease); STANDARD & POOR'S, *supra* note 6, at 6 (stating that research and development expenditures in the biotechnology industry still outweigh the industry's revenues, resulting in continued industry losses).

67 *See* Dan L. Burk, *Biotechnology and Patent Law: Fitting Innovation to the Procrustean Bed*, 17 RUTGERS COMPUTER & TECH. L.J. 1, 18-21 (1991) (briefly describing the numerous financing options available to U.S. biotechnology companies, including venture capital, public stock offerings, mergers, and alliances with domestic and foreign companies).

68 *See, e.g.*, Michael Selz, *Financing Is Increasing for Genetic-Information Firms*, WALL ST. J., June 11, 1996, at B2 (reporting that "total investments by venture capital funds soared to $2.14 billion in the first quarter [of 1996,] nearly double the $1.17 billion" invested in the first quarter of 1995).

69 *See Bio-pharma Alliances Hit New High in 1996*, BBI NEWSL., Feb. 1, 1997, *available in* 1997 WL 10160059 ("As biotech firms continue to create and evolve new drug discovery tools from combinatorial chemistry to genomics, from high-speed screening methods to data bases of DNA sequences so do pharmaceutical companies seek access to those leading-edge technologies. In fact, big pharma is even willing to help finance the basic research that goes into creating ever more sophisticated ways to search for new drug leads."); STANDARD & POOR'S, *supra* note 6, at 10-11 ("For large companies, collaborations provide limited-risk access to cutting-edge research expertise in

21. On a global basis, it is the availability of venture capital, combined with the willingness of Wall Street to support companies with initial public offerings, that has put the United States as much as five to ten years ahead of Europe and Japan in developing a biotechnology industry.[70] Either venture capital was not available in those areas, or the ability to cash out as a venture capitalist into a public market was much more difficult.[71] These factors have allowed the United States to develop its biotechnology industry to the point where it is today.

22. My job as a biotechnology CEO has been to think about financing one hundred percent of my time and to actively do something about it for greater than fifty percent of my time. Procept has raised approximately $80 million over the last seven or eight years: half from public markets and half from pharmaceutical partners. [72] We are always thinking about raising more money. Our first product has just entered the first phase of clinical trials.[73] Procept must raise many more dollars in the years ahead before it has a product for sale. These are daunting issues. Although overwhelming at times, the challenges are often fun.

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areas where they're weak; this is preferable to developing their own in-house research capabilities in those fields.").

70 The primary reason for the United States advantage is access to financial markets and sources of capital, and the formation of dedicated biotechnology companies which focus exclusively on biotechnology product development. *See* OFFICE OF TECHNOLOGY ASSESSMENT, U.S. DEPARTMENT OF COMMERCE, PUB. NO. 88-246939, NEW DEVELOPMENTS IN BIOTECHNOLOGY: U.S. INVESTMENT IN BIOTECHNOLOGY 82-85 (1988). *See generally* John Ashworth, *Development of the European Biotechnology Industry*, 33 CAL. W. L. REV. 83, 83-99 (1996) (discussing the biotechnology advantages held by the United States, Europe, and Japan). *But cf.* Burrill, *supra* note 59 (stating that the European biotechnology industry "has made major strides in recent years and is closing the competitive gap with U.S. companies"); ERNST & YOUNG BIOTECH 97, *supra* note 27, at 42-45 (stating that Europe's biotechnology industry has begun to grow due to changes in the European Union's financial structures and increased access to capital from European financial markets).

71 "Historically, European venture capitalists were cautious about funding European companies. Much of their capital went to U.S. companies, which had the option of going public and providing investors with an out." Burrill, *supra* note 59. In recent years, however, the European financial markets have become more accommodating to start-up biotechnology companies. *See id.* For example, the London Stock Exchange has eliminated the requirement that biotechnology companies in the healthcare sector demonstrate profitability before being publicly listed. *See id.* In addition, the European Venture Capital Association has proposed a centralized public financial market for all of Europe's entrepreneurial growth-oriented companies. *See id*.

72 *See Procept Raises $9.25 Million from VCs*, BIOTECH. NEWSWATCH, Sept. 3, 1990, *available in* 1990 WL 2177140 (reporting that Procept completed venture financing totaling $9.25 million; investors included Montgomery Medical Ventures, Bristol-Myers Squibb, and Venture Founders).

73 Procept, Inc. "has developed PRO 2000, a topical microbicide [that acts as] a chemical barrier to prevent HIV infection and other sexually transmitted diseases." *Procept Develops Topical Microbicide to Prevent HIV*, BIOTECH BUS., Apr. 1, 1997, *available in* 1997 WL 2025711. The British Medical Research Council will give Procept over one million dollars to co-fund Phase I of the study. *Id*.

23. The availability of capital will allow us to reach the ultimate goal of becoming profitable on a sales or a product basis. For the few companies that make it to drug-approval status, the investors are often the ones that are rewarded generously for their risk-taking.[74]

Jonathan Beckwith:

24. I do basic research in genetics at Harvard Medical School. While my own research focuses on the fundamental biological processes in bacteria, I have been involved in evaluating the social consequences of genetic research for over twenty-five years. I was recently a member of the Working Group on Ethical, Legal, and Social Implications of the Human Genome Project ("ELSI"),[75] a National Institutes of Health-Department of Energy ("NIH-DOE")[76] sponsored group.

25. I would like to point out what I consider to be serious social and ethical issues regarding one of the biotechnology industry's largest efforts: the development of genetic tests.[77] I want to discuss scientists, academics, and others' roles in the development of this industry. Genetic tests are tests that detect hereditary variations in a person's or fetus's DNA that either (i) predispose them to some disease or to some deviance from what is considered the norm,[78] or (ii) raise the

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74 *See generally* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 16-18 (describing biotechnology products receiving recent FDA approval).

75 The Working Group on Ethical, Legal, and Social Implications of the Human Genome Project was formed in 1989 "to provide a new approach to scientific research by identifying, analyzing and addressing the ethical, legal and social implications of human genetics research at the same time that the basic scientific issues are being studied." The National Human Genome Research Institute, *About the Ethical, Legal and Social Implications Program* (visited Jan. 23, 1998) <http://www.nhgri.nih.gov/ELSI/aboutels.html>.

76 The National Institutes of Health ("NIH") is one of eight health agencies of the Public Health Service, which is a part of the U.S. Department of Health and Human Services. *See* National Institutes of Health, <http://www.nih.gov/welcome/nihnew.html>. The NIH conducts research in its own laboratories and supports the research of universities, medical schools, hospitals, and research institutions. *See id.* The U.S. Department of Energy ("DOE") Office of Energy Research is a co-partner with the NIH's National Human Genome Research Institute in the U.S. Human Genome Project. *See* National Human Genome Research Institute, *supra* note 75. The DOE reserves a portion of its funding for ELSI research and education. *See id.*

77 For a longer discussion of these tests, see Symposium, *Gene Therapy: Legal, Financial and Ethical Issues*, 4 B.U. J. SCI. & TECH. L. 2 (1998).

78 *See generally* INSTITUTE OF MEDICINE, ASSESSING GENETIC RISKS: IMPLICATIONS FOR HEALTH AND SOCIAL POLICY (L.B. Andrews et al. eds., 1994) [hereinafter ASSESSING GENETIC RISKS].

possibility that their children may be so predisposed.[79] I want to make clear from the outset that I do not oppose the development or marketing of such tests.

26. The pace of discovery of these DNA variances and the resultant development of such tests has been extraordinary. I would guess that one reads of a new mutant gene of this sort more than once a month in the newspapers and even more frequently in the scientific literature.[80] When one reads about the discoveries in the media, the article always includes a suggestion that the finding will lead to a cure for the condition.[81] It is very important to realize that, so far, none of these tests have led to cures, and for the overwhelming majority of such conditions, no cure is available.[82]

27. Nonetheless, people have already reaped important benefits from genetic tests. In some cases there are already treatments for genetic conditions, and the tests allow for early detection.[83] For others, simply knowing may provide peace of mind. For prospective parents, the knowledge that they are carriers of a genetic condition allows them to make reproductive decisions ranging from adoption to amniocentesis and abortion.[84] In some cases, people will make lifestyle changes to lessen their chances of developing a particular disease because of the results of a test.[85]

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79 *See, e.g.,* Leslie Roberts, *To Test or Not to Test?*, 247 SCIENCE 17, 17-19 (1990) (reporting that scientists have developed a genetic screening test for couples carrying the cystic fibrosis gene).

80 *See, e.g.*, *Life in Isolation Yields Clue to Fatal Disease*, WASH. POST, Apr. 9, 1993, at A4 (reporting that discovery of the gene that causes severe combined immune deficiency disease may lead to a treatment in the future); Jeff Lyon & Peter Gorner, *Detective Saga Unfolds in Genetic Discoveries on M.D., Cancer*, CHI. TRIB., Oct. 19, 1986, § 6, at 1 (reporting that scientists have identified the genes that cause Deuchenne muscular dystorphy and retinoblastoma and stating that the discoveries "are major steps toward cures for M.D. and cancer").

81 *See Life in Isolation Yields Clue to Fatal Disease*, *supra* note 80.

82 Shannon Brownlee & Joanne Silberner, *The Assurances of Genes: Is Disease Prediction a Boon or Nightmare?*, U.S. NEWS & WORLD REP., July 23, 1990, at 57, 59 (noting that genetic tests for diseases without cures may only give people "little more than a glimpse of a bleak medical future").

83 *See generally* Bruce Ponder, *Genetic Testing for Cancer Risk*, 278 SCIENCE 1050, 1051 (1997) (stating that genetic testing may be useful for early detection and prophylactic intervention for medullary thyroid carcinoma, hereditary nonpolyposis colorectal cancer, and even breast and ovarian cancer).

84 *See* ASSESSING GENETIC RISKS, *supra* note 78, at 146-84; Roberts, *supra* note 79, at 17-18 (discussing reproductive decisions in the context of genetic screening for cystic fibrosis).

85 *See* Rick Weiss, *Discovery of Genetic Defect Will Aid Colon Cancer Detection Testing*, L.A. TIMES, Oct. 20, 1997, at S9.

28. There is a long history of problems associated with genetic test information.[86] There have been reported cases of serious psychological trauma and family disruption because of genetic test information. [87] This is partly the result of a lack of understanding of genetics among the general public and a paucity of health professionals with expertise in genetics. For example, there are only 1200 certified genetic counselors in the country.[88] That means that most people who are deciding whether or not to have a genetic test, or who take the test and receive genetic information, are unlikely to receive proper support and information. This becomes particularly problematic because most genetic tests only give the probabilities of whether an individual will suffer from a condition.[89]

29. For instance, consider the test for heredity breast cancer in those families that have a history of breast cancer. If a particular BRCA1 mutation[90] is found, one cannot predict whether the individual will contract breast or ovarian cancer or at what age it will occur.[91] Furthermore, it is unclear whether mutations known to cause breast cancer in one family background will have the same probability of causing it in another.[92] The more we learn about the genetics of human health conditions, the more complexities are revealed. This is not to say that the information cannot be obtained and presented in a useful way, but rather that a well thought and tried approach is necessary.

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86 *See* NEIL A. HOLTZMAN, PROCEED WITH CAUTION: PREDICTING GENETIC RISKS IN THE RECOMBINANT DNA ERA 242-43 (1989).

87 *See* ASSESSING GENETIC RISKS, *supra* note 78, at 146-84, 247-289.

88 *See* Weiss, *supra* note 85 (stating that the approximately 1200 genetic counselors in the United States may not be able to provide sufficient genetic testing services and noting that other health professionals such as doctors do not have the training to provide adequate genetic counseling); *cf.* Bonnie Benwick, *The Facts About Genetic Counseling*, WASH. POST, Mar. 9, 1997, at C4 (reporting that there are 1500 genetic counselors in the United States, up from 1200 in 1994).

89 *See, e.g.*, Gina Kolata, *Breaking Ranks, Lab Officers Test to Assess Risk of Breast Cancer*, N.Y. TIMES, Apr. 1, 1996, at A1 (reporting that the test for a mutation of a normal gene called BRCA1 can predict the probabilities that women will develop breast and ovarian cancer); Ponder, *supra* note 83, at 1052 (stating that although genetic testing can provide an estimate of probability of cancer over a lifetime, current testing cannot ascertain the probability for a shorter duration of time).

90 *See* D. Shattuck-Eidens et al., *BRCA1 Sequence Analysis in Women at High Risk for Susceptibility Mutations: Risk Factor Analysis and Implications for Genetic Testing*, 278 JAMA 1242 (1997).

91 *See* Kolata, *supra* note 89 (reporting that researchers have indicated that they cannot say for certain that all the women with the BRCA1 mutated gene are at risk for cancer).

92 *See id.*

30. In addition to personal and family trauma, there are numerous reports of people being stigmatized and discriminated against on the basis of genetic test information.[93] I am part of a group that conducted two surveys of people who described instances of stigmatization and discrimination. The survey findings are reported in two published articles in the *American Journal of Human Genetics*[94] and *Science and Engineering Ethics*.[95] Those studies found numerous cases where people had lost or been denied health insurance or employment and had been discriminated against by other social institutions, including adoption agencies, armies, and schools.[96] Other groups have reported numerous similar incidents.[97]

31. All of the problems associated with the dissemination of genetic tests have led segments of the scientific and medical communities to call for restraint in the marketing and use of the tests.[98] In many cases, they have advocated using the tests only for research purposes; for instance, ELSI has supported research groups that would evaluate the interest in and consequences of testing for cystic fibrosis and for breast cancer susceptibility.[99] Despite these warnings, and despite some

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93 *See* E. Virginia Lapham et al., *Genetic Discrimination: Perspectives of Consumers*, 274 SCIENCE 621, 621-23 (1996) (reporting significant levels of perceived discrimination for members of genetic support groups with one or more genetic disorders in the family); Gail Geller et al., *Genetic Testing for Susceptibility to Adult-Onset Cancer: The Process and Content of Informed Consent*, 277 JAMA 1467, 1471-72 (1997) (reporting on the Task Force on Informed Consent of the Cancer Genetics Studies Consortium's recommendation for disclosure of the risk of insurance and employment discrimination based on genetic test results).

94 Paul R. Billings et al., *Discrimination as a Consequence of Genetic Testing*, 50 AM. J. HUM. GENETICS 476 (1992).

95 *See* L.N. Geller, *Individual, Family, and Societal Dimensions of Genetic Discrimination: A Case Study Analysis*, 2 SCI. & ENGINEERING ETHICS 71 (1996).

96 *See* Billings et al., *supra* note 94, at 478-79.

97 *See, e.g.*, Philip J. Hilts, *Panel Reports Genetic Screening has Cost Some Their Health Plans*, N.Y. TIMES, Nov. 5, 1993, at A20 (describing National Academy of Science's panel statements concerning American workers who have lost their jobs and health insurance on the basis of information obtained through genetic screening).

98 *See* Roberts, *supra* note 79, at 17 (reporting that the American Society for Human Genetics called for a voluntary moratorium on widespread population screening for the cystic fibrosis gene); Kolata *supra* note 100 (reporting geneticists' concern for dissemination of genetic screening tests for breast cancer); *see also* Billings et al., *supra* note 94, at 481-82 (recommending "carefully considered legislation" about the use of testing information).

99 *See* Eliot Marshall, *The Genome Program's Conscience*, 274 SCIENCE 488, 490 (1996) (reporting that ELSI sponsored a study, conducted by seven investigators, to examine the risks, benefits, and demands for the cystic fibrosis genetic test); Roberts *supra* note 79, at 18 (stating that Integrated Genetics is promoting the cystic fibrosis test "only to academic genetic centers and private genetic practices—'the only ones who can understand the test and provide support services'"); Kolata, *supra* note 89 (describing a statement by Neil A. Holtzman, a geneticist at Johns Hopkins

degree of restraint in the commercial sector, there is enormous economic and public pressure on the companies to make these tests widely available.[100] It seems inevitable that the fierce competition between biotechnology companies, as well as the limited number of profitable products that can be conceived, is leading to the widespread marketing of tests, with potentially severe consequences. Recently, Myriad Genetics, Inc.[101] announced the availability of a chance susceptibility test for the BRCA1 gene.[102] Some individuals reacted to the announcement by raising serious ethical concerns.[103] Myriad withdrew a public stock offering shortly after offering the test. [104] Perhaps this was influenced by the negative publicity associated with the test, although the company stated that it was due to unfavorable market conditions.[105]

32. Marketing these tests too rapidly or extensively could lead to many problems. These problems are discussed in an article published in *Barron's* by Dr. Neil A. Holtzman, a pediatrician and geneticist at Johns Hopkins University.[106] He observes that biotechnology companies do not mention the pitfalls of marketing genetic tests when they promote their stock to investors.[107]

Medical Institutions, that test for risk of breast cancer should only be used in research until it is "scientifically and clinically evaluated").

100 *See*, *e.g.*, Brownlee & Silberner, *supra* note 82, at 57-59 (noting that insurers may require genetic screening to exclude those at risk of incurring high-cost medical treatment and stating that the genetic test for cystic fibrosis represents a multibillion dollar industry to biotechnology companies); *cf.* Marshall, *supra* note 99 (noting that although the cystic fibrosis test is available, few people want the information).

101 Myriad Genetics, Inc. is a commercial biotechnical research firm founded in 1991 and located in Salt Lake City, Utah. *See* D&B MILLION DOLLAR DIRECTORY, *supra* note 2, at 3282.

102 *See*, *e.g.*, *Gene Testing to Be Big Business*, APPLIED GENETICS NEWS, Dec. 1, 1996, *available in* 1996 WL 8541893 (reporting that Myriad Genetics has established a genetic analysis and information business for its BRCA1 and BRCA2 tests).

103 *See* Michael Waldholz, *Predictive Use of Breast-Cancer Genetic Test is Disputed*, WALL ST. J., May 15, 1997, at B1; Karen Wright, *Patent Medicine*, DISCOVER, Jan. 1991, at 78.

104 *See*, *e.g.*, *Myriad Pulls IPO from Inhospitable Market*, NATURE BIOTECH., Jan. 1, 1997, *available in* 1997 WL 8913460 (reporting that Myriad Genetics cited market conditions when it withdrew its public offering of equity, but one analyst linked the withdrawal to lower than expected sales figures for BRCA1 and BRCA2 tests); *cf. infra* p. 29 ("I was involved in this situation while working on the Myriad offering. I can assure you that Myriad did not withdraw the offer for any reasons other than the company's stated reasons.").

105 *See id.*

106 Neil A. Holtzman, *Come to the Fair: But Investors Should Be Wary at the Biotech Booth*, BARRON'S, July 10, 1995, at 40.

107 *See id.*

33. In the interest of complete disclosure, I would like to conclude with a little personal history and relate it to the role scientific researchers play in this process. As I mentioned, I have been concerned about the misuse of science, genetics in particular, for over twenty-five years. In 1970, I received the Eli Lilly and Company Research Award for outstanding research in microbiology.[108] At the award ceremonies, I criticized drug companies' practices and announced that I was donating the award money to the Black Panther Free Health Clinic in Boston and to a defense fund for the Panther 13 of New York City.[109] Over the following years, I maintained my ability to speak out freely on these kinds of issues by avoiding connections with biotechnology companies. I was an advisor for many years to New England BioLabs,[110] which I consider to be one of the most progressively run of such companies.

34. A few years ago, however, I began to develop a close scientific relationship with researchers at Genentech[111] in San Francisco. Eventually, they asked me to be a consultant, and after some thought, I agreed. The week that I signed the contract, an article appeared on the front page of the *New York Times*[112] discussing serious ethical problems in the way Genentech had been marketing the human growth hormone Protropin.[113] Through its subsidiaries, the company had been marketing the human growth hormone, which is very important for the treatment of some forms of dwarfism, to families with children who were shorter than average. The marketing tactics were clearly offensive to many people. For example, in some cases, doctors were allowed to measure the kids' heights in

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108 The Eli Lilly and Company Research Award is given each year by the American Society for Microbiology "[t]o recognize fundamental research in microbiology and immunology of unusual merit by an individual on the threshold of his or her career." American Society for Microbiology, *The Eli Lilly and Company Research Award* (visited Feb. 28, 1998) <http://www.asmusa.org/acasrc/aca15.html>.

109 *See* Jonathan Beckwith, *Gene Expression in Bacteria and Some Concerns About the Misuse of Science*, 34 BACTERIOL REVS. 222, 222-27 (1970).

110 New England BioLabs is a private cooperative laboratory engaged in the production of restriction endonucleases and other products for molecular biology research. *See* New England Biolabs, Inc. (visited Feb. 28, 1998) <http://www.neb.com/neb/company/company.html>.

111 Genentech, Inc. is a biomedical research firm located in San Francisco. It manufactures pharmaceuticals for the treatment of cystic fibrosis, heart attacks and blood clots in the lungs, growth hormone inadequacy, and chronic granulomatous disease. Genentech has approximately 3,000 employees and its 1996 sales totaled $904.6 million. *See* HOOVER'S MASTERLIST OF MAJOR U.S. COMPANIES 1997-1998 310 (1997).

112 Gina Kolata, *Selling Growth Drug for Children: The Legal and Ethical Questions*, N.Y. TIMES, Aug. 15, 1994, at A1.

113 "'Protropin' [is a] genetically engineered version of human growth hormone . . . that can make some short children grow taller than they otherwise would." Kolata, *supra* note 112.

classrooms and then approach the shorter kids' parents.[114] One parent reported being pressured by remarks such as, "How is your kid going to feel if he grows up to be quite short and knows that you could have prevented it?" Clearly, the market for growth hormone was small, and Genetech and its subsidiaries were trying to expand that market. The public furor, among other factors, led to the resignation of the president of Genentech.[115] This particular issue illustrates two problems. First, as I have indicated, there is pressure to market test drugs for inappropriate purposes. Second, in the case of drug hormones, companies treat non-medical conditions as though they were medical conditions.

35. I was faced with a dilemma that week. I had actually signed the contract, sent it off, and then saw this article a few days later. Should I sever my relationship or use my position to express my disgust with this practice? What I did—and I did not do as much as I had planned—was to contact officials and my scientific colleagues at Genentech, express my concern, and suggest that they have a strong ethical staff at the company to warn them of problems of this sort. I intended to try to contact other consultants to suggest that they take similar action, but I never did. This is just one example of where the need for profit can cause a company to market a product in a manner that breaks ethical boundaries, at least from my perspective. The increasing development of genetic tests makes me fearful of similar practices.[116]

36. Perhaps naïvely, I have always thought that academic scientists' strong role in the biotechnology industry had the potential to introduce more ethical concerns into the industry. I do not think that has happened, but I believe that the potential is there.

Leslie E. Davis:

37. In assessing the topic of this seminar, one must first evaluate: risks of what, risks to whom, can the risks be reduced, and ought they be reduced? All of us are very familiar with certain risks faced by the biotechnology industry. Risks may be a synonym in this case for problems. I would like to discuss several of these risks.

38. Jonathan Beckwith discussed some of the concerns with Myriad Genetics. I was involved in this situation while working on the Myriad offering. I

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114 *See* Kolata, *supra* note 112.

115 At least one new article implies that the marketing of protropin was a factor in the ouster of the Genentech president. *See* C.T. Hall, *Genentech Executive Forced Out, Questions About Leadership, Ethics,* S.F. CHRON., July 11, 1995, at 1. *Cf.* Lawrence M. Fisher, *Genentech President Ousted*, N.Y. TIMES, July 11, 1995, at D1 (reporting that Genentech's president and chief executive, G. Kirk Raab, was ousted for seeking a personal loan guarantee from the company's majority stockholder while the companies were in merger negotiations).

116 *Cf.* Roberts, *supra* note 79, at 18-19.

can assure you that, so far as I know, Myriad did not withdraw the offering for any reasons other than the company's stated reasons. I also remember meeting Robert Carpenter when I worked on an offering for Integrated Genetics.[117] I remember Bob discussing a group that he belonged to that met regularly to assess the ethical elements, problems, issues, and considerations involved in genetic research. At that point, we were early enough in the biotechnology revolution to be talking about genetic engineering to produce any protein or modify any gene. I cannot remember very many "all-hands meetings"[118] in which ethical considerations were not discussed. It was and is always a concern. I think one of the things that we have learned is that they are very difficult issues, and, as I believe Jonathan Beckwith has very clearly stated, there are not any easy answers.

39. But does that excuse us from the basic task or the basic notion before our panel: "Can you reduce the risks of biotechnology financing?" My answer is clearly yes. But in order to do that you have to define the risk. You have to decide who bears the risk, whether it is going to be shifted or relieved, and how you can go about doing it. In a typically lawyer-like fashion, you start taking it apart. Some problems are intractable, others are not. You have to figure them out and do the best you can.

40. When I was an undergraduate, I worked in the pediatric oncology unit of the University of Missouri Teaching Hospital. That was in the early 1960s, and it seemed that virtually all of the patients in that unit died. I do not believe that virtually all the patients in pediatric oncology units die today.[119] That is primarily the result of the financial community, businesses, and universities working together.

41. I would like to examine a couple of the problems I encounter in my legal practice. A primary issue in financing biotechnology stems from the fact that one individual, group, or the public market cannot easily absorb the length of time or the high cost of bringing a new pharmaceutical product to the market. The two risks that cannot be minimized are whether the technology will work and whether the company will be able to develop an effective pharmaceutical product. Some of the smartest people in the world work as hard as they can on these issues. Every time they solve a problem, there is another one. Competition is another issue, because no one knows what their competitors are doing. The competition among

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117 Robert J. Carpenter was the president of Integrated Genetics. *See Integrated Genetics Financial Results,* BUS. WIRE, Jan. 28, 1988, *available in* LEXIS, Market Library, PROMT File.

118 An all hands meeting occurs when the parties in an IPO transaction get together to draft the documents. *See Counselors to Rising Start-Ups,* NAT. L.J., Feb. 17, 1995, at B9.

119 *Guidelines for the Pediatric Cancer Center and Role of Such Centers in Diagnosis and Treatment*, 99 PEDIATRICS 139, 140 (1997) ("Dramatic progress has been made in he development of successful treatment programs for children and adolescents with cancer.").

academics and research labs has produced many of the drugs and discoveries that we have today.[120] Thus, I would encourage competition rather than discourage it.

42. Farah Champsi discussed a number of the things that companies have already done to reduce risk, and she has pointed out what investors are looking for. There are other ways to reduce risk and the cost of failure. For example, there are far fewer "mini-Mercks" now in existence. Mini-Mercks are companies that announce on the day of their formation that they expect to be a fully integrated pharmaceutical company with manufacturing and marketing capabilities. Some companies have achieved this, but it is very difficult and expensive.[121] Instead, there are companies today that will help to purify proteins,[122] and other companies, called contract research organizations ("CROs"),[123] that will help to design and carry out clinical trials. In addition, there are contract manufacturers to reduce investment in manufacturing facilities.[124] This is one way to reduce risk. I am sure there are other ways to reduce risk; I think it requires looking at the problem with an open mind.

43. Biotechnology investors and venture capitalists are always ready to go public. The best guarantee of making money for the biotechnology venture

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120 *See, e.g.,* Bradford Cornell, *Why Droves of Foreign Profs Toil in U.S. Groves*, WALL ST. J., Mar. 29, 1990, at A12 ("Scientists working on problems in molecular biology and immunology move constantly between leading private research labs and major universities."); Rick Weiss, *Reports Warn Against Dependence on Corporate Funds for Scientific Research*, WASH. POST, Feb. 8, 1996, at A6 (quoting Jerome Groopman, professor of medicine at Harvard Medical School, "'It is essential to the future of the research enterprise in the United States and our competitive position in the world that there be a healthy symbiosis between private companies and the academic labs'").

121 "As the [biotechnology] industry took shape in the 1980s, most biotechnology companies planned to transform themselves into fully integrated pharmaceutical companies with the ability to develop, manufacture, and market their own therapeutics. Only a handful of companies have attained that goal: Amgen Inc., Chiron Corp., and Genentech Inc. are among the favored few. This goal has proven unrealistic for the vast majority of companies. This is mainly due to the exceptionally high entry barriers in the pharmaceutical industry—including the high cost of building manufacturing facilities and a commercial infrastructure—along with the risks associated with drug discovery and development. When financing through the capital markets dried up in the early 1990s, most small biotechs began to alter their business strategies." STANDARD & POOR'S, *supra* note 6, at 10.

122 *See* INSTITUTE FOR BIOTECHNOLOGY INFORMATION, PHARMACEUTICAL INDUSTRY GUIDE: DRUG COMPANIES, BIOTECH FIRMS & CROS 29-73 (1995).

123 *See* INSTITUTE FOR BIOTECHNOLOGY INFORMATION, *supra* note 122, at 75-82; ERNST & YOUNG, BIOTECH 95: REFORM, RESTRUCTURE, RENEWAL 27 (1994) (describing the role CROS can play in biotechnology development).

124 *See* INSTITUTE FOR BIOTECHNOLOGY INFORMATION, *supra* note 122, at 7-28. "Contract biologics manufacturing is ideal for smaller biotech start-ups and virtual companies, which often have intellectual property but limited capital." Matthew Lerner, *Contract Biotech Manufacturing on the Move,* CHEMICAL MARKET REP., Apr. 14, 1997, *available in* LEXIS, News Library, Chmmkt File.

capitalist is to get the company organized with the best scientists it can and then get a corporate partner. Venture capitalists must also carefully evaluate the market and keep in close contact with one of the good underwriters, such as Farah Champsi's company, Robertson, Stephens & Co. As soon as Farah says we can enter the public market, we do it. That is how you do it if you are working with a company or if you are investing. I do not think many biotechnology companies decide to wait when a good underwriter says they can do a public offering. The biotechnology market is far too volatile.[125]

44. In terms of more systemic things, I, like Jonathan Beckwith, have issues with our system and the way it works. My own question has to do with the FDA. I remind you that the FDA is not soliciting my opinion on this subject. Having said that, there are many proposals to reform the FDA.[126] Most of the proposals have to do with tinkering—hiring more investigators and statisticians and proceeding faster after the New Drug Application ("NDA") is filed.[127]

45. A company must complete several steps before getting FDA approval of a drug.[128] First, a company must perform pre-clinical in vitro work. The company identifies a substance that appears to have an effect, in theory and in the test tube, on the problem or the disease that it is attacking.[129] Next, the company tries it on animals; if it still looks good, then the company sees if it can test the substance on humans.

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125 *See* STANDARD & POOR'S, *supra* note 6, at 14 (stating that biotechnology firms have difficulty raising capital in part due to the "enormous cyclicality" of the public equity markets, and thus biotechnology companies try to raise capital in anticipation of future needs).

126 *See generally* 142 CONG. REC. H5631-33 (daily ed. May 29, 1996) (statements of Rep. Greenwood and Rep. Barton) (proposing reformation and modernization of the FDA to accelerate the drug review and approval process); *see also* Henry I. Miller, *FDA Loves Kids So Much, It'll Make You Sick,* WALL ST. J., Aug. 18, 1997, at A14 (arguing that FDA regulatory requirements increase costs to consumers and put consumers at risk because of delays in drug approval).

127 One example is the Food and Drug Administration Modernization and Accountability Act of 1997. The Food and Drug Administration Modernization and Accountability Act of 1997, S. 830, 105th Cong. §§ 406-10 (1997); *see also* 143 CONG. REC. S5342-02 (daily ed. June 5, 1997) (statement of Sen. Jeffords); *see also* Barbara Kanegsberg, *Shortening Biopharmaceutical Approval Times,* CHEMICAL MARKET REP., Apr. 14, 1997, *available in* LEXIS, News Library, Chmmkt File (reporting that the biotechnology industry "is evaluating the role of FDA-sponsored research in biopharmaceutical review and is looking for FDA involvement earlier in drug development").

128 *See generally* STANDARD & POOR'S, *supra* note 6, at 15-16 (providing an overview of the drug development process).

129 *See id.*

46. At each stage of the process, the first thing the company tests for is toxicity.[130] The question is whether the substance is going to be more trouble than it is worth. In any case, I propose that the long series of clinical trials focus more on safety and less, after a threshold is met, on efficacy. I think medical practitioners are more likely to be able to determine efficacy.

Henri Termeer:

47. This is a remarkable industry. We have been spending money at a remarkable rate. In 1996, the biotechnology industry spent close to $8 billion on research and development.[131] The industry spent $7.7 billion in 1995[132] and $7.1 billion in 1994.[133] The 1300 biotechnology companies in the United States also managed to lose $4.5 billion in 1996[134] and $4.6 billion in 1995.[135] Total industry revenues, including collaborative research payments and product sales, were $14.6 billion in 1996.[136] These losses are not funded through tax money, but by individuals, corporations, mutual funds, public organizations, and venture capitalists.[137]

48. Venture capital clearly is the most important funding in a company's early stages, though it becomes insignificant the moment the company's products begin to flower. Consider the case of Genzyme. Genzyme has raised close to a billion dollars over the years, of which only $10 million was venture capital.[138] Genzyme used any financing vehicle that we could understand and invented some

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130 *See id*. at 16 (stating that during Phase I testing small doses of the drug are given to a small number of healthy people to determine its safety).

131 *See* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 6 fig. 1.

132 *See* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 6 fig. 1.

133 *See* ERNST & YOUNG LLP, BIOTECH 96: PURSUING SUSTAINABILITY (1995) [hereinafter ERNST & YOUNG BIOTECH 96] ("Current Biotech Highlights").

134 *See* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 6 fig. 1.

135 *See id.*

136 *See id.*

137 *See generally* STANDARD & POOR'S, *supra* note 6, at 4-5, 10-14 (describing the various sources of capital for biotechnology companies); Pete Barlas, *Biotech Companies Raising Record Funds*, BUS. J.—SAN JOSE, Apr. 15, 1996, *available in* 1996 WL 10046911 (stating that "the capital flow into biotechnology has been fueled by mutual fund managers"); Udayan Gupta, *Experience Pays*, WALL ST. J., May 20, 1994, at R15 (noting that "[w]ealthy individuals, corporations and investment banks have stepped up as new sources of biotech funds").

138 In its initial public offering, Genzyme sold 2,862,000 shares of common stock for $10 each. *See* WALL ST. J., June 6, 1986, at A43.

along the way. It did things for which there was no precedent. There is no precedent for an industry that society permits to spend exorbitant amounts of money on research and development over a period of twenty years. NIH's biotechnology budget is a little over $4 billion,[139] and research and development expenditures of large corporations are similar.[140] The remaining NIH money is dedicated to more traditional research.[141]

49. Large corporations are clearly funding more research and development than they did in the past. Very large amounts of money are being spent to bring solutions and opportunities to the marketplace. We are spending one trillion dollars on healthcare,[142] yet we are not happy with the results. I know someone who died of cancer; I know at least one person who has cystic fibrosis, multiple sclerosis, or Parkinson's disease. How can we afford to pay a trillion dollars and have such bad results? We are not advancing at all despite having spent all of this money. We spend approximately 14% to 15% of the gross national product ("GNP") on healthcare, and we complain.[143] England spends 6% of the GNP on healthcare, and they are complaining too.[144] In Holland[145] and Germany,[146] both spend about 10%, and they are complaining bitterly as well.

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139 *See* U.S. Congress, Office of Technology Assessment, *New Developments in Biotechnology: U.S. Investment in Biotechnology - Special Report*, OTA-BA-360, 38 (July 1988) (visited October 4, 1998) <http://www.ota.nap.edu/pdf/data/1988/8840.PDF> (showing that the NIH spent $2.276 billion on biotechnology research in 1987).

140 Public biotechnology companies spent $4.7 billion on research and development in 1996. *See* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 6 fig. 1. Large pharmaceutical companies, such as Johnson & Johnson and Pfizer, spent $1.634 billion and $1.442 billion, respectively, on research and development in 1995. *See id*. at 71 fig. 33.

141 *See* Office of Mgmt. & Budget, Executive Office of the President of the United States, Budget of the United States Government, Fiscal Year 1998, at app. 505 (1997) (showing that the overall NIH budget estimate for 1998 was $13.497 trillion).

142 *See* National Institutes of Health, *Estimates of National Expenditures for Total Health Costs, Total R&D, and Health R&D, 1985-1995* (last modified Nov. 22, 1996) <http://www.nih.gov/grants/award/trends95/PDFDOCS/FEDTABL2.PDF> (stating that in 1995 the United States spent approximately $1.02 trillion on health care).

143 In 1994, 13.7% of the U.S. gross domestic product ("GDP") consisted of health care expenditures. *See* BUREAU OF THE CENSUS, U.S. DEPT. OF COMMERCE, STATISTICAL ABSTRACT OF THE U.S. 1996 111 tbl. 154 (1996).

144 In 1990, England spent 6.6% of its GDP on health. *See* WORLD RESOURCES INSTITUTE, ET AL., WORLD RESOURCES 1996-97 194 tbl. 8.3 (1996).

145 In 1990, the Netherlands spent 8.7% of its GDP on health. *See id.*

146 In 1990, Germany spent 9.1% of its GDP on health. *See id.*

50. Every day, this industry gets recognized for chipping away a little bit of the mystery of creating and improving health and life. The goal is not to extend life beyond a 100 years, but to help people live a healthy life. The solution is not more hospitals, doctors, nurses, or waiting rooms. It is a matter of devising effective solutions to cure people or guiding them to a healthy life.

51. Joshua Lerner talked about the market. We will see over the next twenty-five to fifty years the fruits of this investment. The money has come from investors taking clear-cut risks as part of their portfolios. I think people are drawn to investing in this area if there is a glimmer of hope that a company can come up with a solution. The biotechnology industry now has 276 products in late stages of clinical development.[147] It also has the ability to conduct more genetic testing to provide people with information about their genetic risks. Over the next five years, we can do many of these things and start to push genetic tests into the marketplace. Health maintenance organizations ("HMOs"), however, consider anything that comes out of the biotechnology industry as experimental at this stage.[148] They have not planned to fund this changeover or to re-deploy resources from where they are spent today.[149]

52. I heard bitter complaints from economists at the Kennedy School of Government about the fact that a product that treats multiple sclerosis exists, but it costs $9000 per year.[150] This is a lot of money, but we may be able to decrease the

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147 *See* Roberta Gerry, *Charting Biotechnology Investment,* CHEMICAL MARKET REP., Apr. 14, 1997, *available in* LEXIS, News Library, Chmmkt File (reporting that there are "272 drugs in human clinical trials, and hundreds more in early development").

148 *Cf.* Sally Lehrman, *H&Q Pundits See 1997 as "Year of the Investor,"* BIOTECHNOLOGY NEWSWATCH, Jan. 20, 1997, *available in* LEXIS, Market Library, Biotech File (reporting that according to one analyst, managed care companies are "moderating their emphasis on cost and demonstrating a greater interest in quality . . . [which] has helped new drugs and devices, particularly those which had cost-benefit analyses built into their clinical trials"). *But see* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 40 (stating that although many are concerned that managed care could preclude use of new biotechnology products, there has actually been an increased selection of biotechnology products for use in the healthcare industry).

149 *Cf.* ERNST & YOUNG BIOTECH 96, *supra* note 133, at 21 ("The impact of managed care and the drive to control costs is putting increasing pressure on biotechnology companies to come to grips with the evolving and often 'fuzzy' disciplines of pharmacoeconomics and outcomes research."). *But see* STANDARD & POOR'S, *supra* note 6, at 8 (noting that HMO spending reductions will come from healthcare services, not "cost-effective drug therapy"); *Biotechnology Partners with HMO's to Boost Bottom Line,* BIOTECH BUS., Jan. 1, 1996, *available in* LEXIS, Market Library, Biotech File (reporting that according to a KPMG Peat Marwick Industry Guidebook, "[b]iotechnology companies are increasingly teaming up with managed care organizations to help them finance growth, leverage technology, and market products").

150 *Cf.* Laurie Paine Stoneham, *Keeping MS at Bay,* REAL LIVING WITH MULTIPLE SCLEROSIS, Feb. 1997, *available in* 1997 WL 9438564 (giving information about and approximate annual costs of

cost of healthcare if such technologies are brought into the marketplace. The question is not to ask where can we stop spending, but rather, to redeploy that spending for a greater payback.[151] Society will insist on this. If knowing more about our genetic buildup means that we can take more control over ourselves and create a healthier life, we will live less fatalistically. Even if it takes twenty-five years to get there, we will want to have that information as consumers because we like to be healthy.[152]

53. In 1989, Genzyme acquired a company called Integrated Genetics.[153] At that time, Genzyme was about six years old and had become profitable.[154] At the outset, Genzyme wanted to be able to continue in business even if the businesses were relatively straightforward and not very technologically advanced. Genzyme wanted to learn to compete and innovate the markets in which it was participating. It had profits in 1988 of approximately $600,000.[155] Integrated Genetics, one of the foremost companies in the field of recombinant technology, was losing one million dollars per month. Genzyme stock at that time was eight or nine dollars per share.[156] Integrated Genetics stock was about three dollars per share.[157] Genzyme had gone public a few years earlier, and the stock dropped from thirteen dollars at the IPO to nine dollars per share at the time of the merger.[158] We thought we were

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three drugs for the treatment of multiple sclerosis: Copaxone ($7,350 per year), Avonex ($9,230 per year wholesale), and Betaseron ($10,000 per year retail)).

151 STANDARD & POOR'S, *supra* note 6, at 8 (noting that improved drugs may reduce the number of surgeries and the amount of long-term care that would otherwise be required).

152 *See generally* AUBREY MILUNSKY, CHOICES, NOT CHANCES: AN ESSENTIAL GUIDE TO YOUR HEREDITY AND HEALTH 3 (1989) ("Only by understanding your genetic endowment will you best be able to care for yourself and your children.").

153 *See Genzyme Completes Purchase,* WALL ST. J., Aug. 15, 1989, at C17 (reporting that Genzyme completed its acquisition of Integrated Genetics, Inc. in a stock swap valued at approximately $31.5 million).

154 *See, e.g., Genzyme Says Profit More Than Tripled in Fourth Quarter,* WALL ST. J., Mar. 7, 1989, at A19 (reporting that Genzyme expects to report earnings of $450,000, the gain stemming from sales of Genzyme's first major product).

155 Genzyme reported net income of $671,000 for the year 1988. *See Genzyme Reports Financial Results*, BUS. WIRE, Nov. 10, 1989, *available in* LEXIS, News Library, Bwire File.

156 *See* WALL ST. J., July 19, 1989, at C7 (Genzyme stock closed at 9 3/8 on July 18, 1989); WALL ST. J., Aug. 15, 1989, at C7 (Genzyme stock closed at 10 on August 14, 1989).

157 *See* WALL ST. J., July 19, 1989, at C8 (Integrated Genetics stock closed at 2 11/16 on July 18, 1989); WALL ST. J., Aug. 15, 1989, at C8 (Integrated Genetics stock closed at 2 13/16 on August 14, 1989).

158 At the time of the 1989 merger with Integrated Genetics, Genzyme's stock price was $10. *See* Wall St. J., July, 19, 1989, at C7. Genzyme's stock price during the quarter of its public offering

doing quite well. But the company did not get much recognition. Integrated Genetics got a little stuck—still at $20 million in cash. I could not refinance Genzyme in the public market because the stock was selling at approximately 40% below what its selling price when it went public some years earlier.[159] To manage the risk, we merged Integrated Genetics with Genzyme. We merged a profit stream of $600,000 from Genzyme and a loss of twelve million dollars from Integrated Genetics, and the stock rose immediately.[160]

54. Within four months thereafter we engaged in three transactions. One was a research and development limited partnership that placed the risk of financing a clinical trial onto a private group of investors.[161] There was one piece of Integrated Genetics that was in the genetic testing business. It did DNA testing; single gene carrier testing for cystic fibrosis, Huntington's chorea, and hemophilia. Many had hoped that it would become a very large market. Indeed, cystic fibrosis is manageable if everyone is tested. Society was not ready to absorb that kind of technology. It could not be marketed, and people did not buy it.[162] In particular, people did not buy genetic counseling. The market still does not pay for genetic counseling.[163]

55. We were beginning to create the largest DNA laboratory in the country. The next largest lab was at Baylor University in Texas. We had to consider whether we should compete and lose money, or figure out a way to develop the business and the technology. How could we manage the risks associated with doing

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in 1986 reached a high of 13. *See* GENZYME CORP., 1986 ANNUAL REPORT 14, 16 (1987) [hereinafter GENZYME 1986 ANNUAL REPORT]. In 1990, Genzyme's stock rebounded, posting quarterly highs from 17 1/8 in the first quarter to 28 5/8 in the fourth quarter. *See* GENZYME CORP., 1991 ANNUAL REPORT 31 (1992) [hereinafter GENZYME 1991 ANNUAL REPORT].

159 *See supra* notes 156. 158 (Genzyme stock went public at approximately 13 and closed at 9 3/8 on July 18, 1989).

160 *See Genzyme Reports Financial Results, supra* note 155 (Genzyme assumed more than $11 million in IG liabilitities). Genzyme's stock increased after the merger in 1989, from a high of 10 in the second quarter to 15 in the fourth quarter. *See* GENZYME CORP., 1989 ANNUAL REPORT 21 (1990) [hereinafter GENZYME 1989 ANNUAL REPORT].

161 *See*, *e.g.*, Nicholas Veronis, *supra* note 64 (reporting that Genzyme has completed a research and development partnership "in which it raised $36.8 million to fund the development of surgical products based on hyaluronic acid").

162 *See Genetic Diseases: Many Small Markets But Not One Big One*, GENESIS REP., Jan. 1, 1993, *available in* 1993 WL 2815603 (reporting that the market for each disease-specific genetic test remains small because of the small number of sufferers); *see also Genzyme Introduces Cystic Fibrosis Test*, BIOTECHNOLOGY NEWSWATCH, Nov. 20, 1989, *available in* 1989 WL 2176492 (Integrated Genetics' general manager, Peter Lanciano, predicted that the market for a cystic fibrosis test would be "modest" because only high-risk people would be tested).

163 *See Genetic Diseases: Many Small Markets But Not One Big One, supra* note 162 (reporting that "[w]idespread genetic counseling is still many years in the future").

that? I considered whether we should go to a venture capitalist. Venture capitalists trust us because historically we have made them money.[164] If they bought 40% of the business, we could give the employees 20%, and we could keep 40%. We could raise five million dollars, have two years of cash and have laid off some of the losses to outside people. We would have a shot at a marketplace that might have some promise. Unfortunately, the venture capitalist had absolutely no interest in us at that moment. Venture capitalists who had worked with the company for years refused to finance us.

56. Then I found Oppenheimer & Co., which had an analyst who examined the biotechnology industry and started to believe in it.[165] We worked together. We had also started to enter discussions from a business point of view. This approach is actually very critical because it is a way to become a quicker business and to reduce the risks of the business. We entered the pre-natal genetic testing business.[166] It has been around for a long time, and is being performed all around the country.[167] The technology was relatively fixed, but there was an opportunity to get away from amniocentesis if the fetal cells could be extracted from maternal blood.[168] We thought we really had a chance to innovate the market as well as to learn the business and develop an entry point to DNA testing. So we took the company public six months later,[169] in part because the brokers knew a lot about the risks associated with birth and pregnancies in women over thirty-five years old.

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164 *Cf.* Michael Valenti, *Biotech Turns a Corner; Amgen Expects Product Sales to Reach $140 Million for Fiscal Year Ending 3/91*, CHEMICAL BUS., Dec. 1990, LEXIS, News Library, ASAPII file (reporting that Genzyme is one of only "about a dozen of the larger biotech companies" that can raise money easily in face of risky investments).

165 *See Genzyme's IG Laboratories Sets IPO*, BIOTECHNOLOGY NEWSWATCH, May 21, 1990, *available in* 1990 WL 2177340 (reporting that Oppenheimer & Co. is underwriting IG Laboratories' $14 million initial public offering).

166 *See* GENZYME 1989 ANNUAL REPORT, *supra* note 160, at 10.

167 *See* Rick Weiss, *Geneticists Hope to Put a Simple Fetal Test Into Circulation*, WASH. POST, Nov. 11, 1996, at A3 ("The idea of conducting prenatal tests on mother's blood dates to 1969."); Beverly Merz, *New Maternal Blood Test May End Fetal Risk in Prenatal Screening*, AM. MED. NEWS, Oct. 21, 1991, at 6, *available in* 1991 WL 4846348 (reporting that University of Tennessee, University of California, Harvard Medical School, and Genzyme researchers are all developing prenatal blood tests).

168 *See* Merz, *supra* note 167; Weiss, *supra* note 167.

169 IG Laboratories completed a public offering of its stock in May 1990. *See* GENZYME 1991 ANNUAL REPORT, *supra* note 158, at 48.

57. Instead of selling 40% of the company for $5 million, we sold 10% of the company for $15 million.[170] It became an independent company called Integrated Genetics.[171] Since that time, we bought it back, and it is now a $60 million business, by far the largest genetic testing operation in the country. [172] It employs approximately 10% of all genetic counselors in the country.

58. Public discussion concerning what we do with the knowledge from genetic tests is critical. The way we manage the privacy questions and other issues will make the difference between having a market and having no market. The risk is not that the company will choose to market the product too early. The projections that were mentioned by Jonathan Beckwith in the breast cancer field are very exaggerated and will not be met. The market is infinitesimally small. Very few pioneering individuals are prepared to do that kind of testing or to pay $2500 for a test.

59. For genetic testing to succeed, we need public support. We need to set up social systems that stimulate ongoing public discussion so that we can agree and disagree. We cannot deny that the technology exists or leave the discussion to only a few people. It needs to be put out in the open, but in a very responsible way. Businesses, including Genzyme, will not start marketing these tests. For example, we are at the clinical trial stage in a collaboration on colon cancer with Kaiser Permanente[173] that we will not start marketing. The market for a product of this nature is incredibly risky, and you can lose tremendous amounts of money. The financial risk to the company is incredible because only a few people in the market will buy the product. The greater risk, however, is that we as a society will fail to make the changes and adaptations necessary to allow this field to develop in a

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170 In May 1990, IG Laboratories sold 2,075,000 shares of common stock to the public for $7.50 per share, resulting in net proceeds (after expenses) of $14 million. *See id*. Genzyme accepted 133,334 shares of IG Laboratories common stock in settlement of approximately $1 million debt. *See id*. "At the conclusion of this transaction, [Genzyme] owned approximately 2,883,334 shares or 54% of the outstanding shares of [IG Laboratories] ([Genzyme] had owned 88% before the offering, the remaining shares being held by various employees, officers and directors of [IG Laboratories])." *Id*.

171 *See IG Laboratories Announces Consolidation of Company Names*, BUS. WIRE, Sept. 20, 1993, *available in* LEXIS, Market Library, Promt File (reporting that IG Laboratories and Vivigen Inc., which IG Laboratories manages for Genzyme, will begin using the name, "Integrated Genetics").

172 *See Genzyme Negotiating Buyout of Minority Interest in IG Labs*, BUS. WIRE, Feb. 15, 1995, *available in* LEXIS, Market Library, Promt File (reporting that Genzyme, currently owner of approximately 69% of the outstanding shares of Integrated Genetics, announced a proposal to acquire the remaining outstanding shares of the company); *Developments in Biotechnology—Feature: A Profile of Genzyme Corporation*, BIOACCESS, June 1, 1997, *available in* 1997 WL 12803153 (stating that revenues for IG, now called Genzyme Genetics, increased 31% in 1996 to $61.6 million).

173 *See Genzyme to Start Colon Cancer Study*, BIOTECHNOLOGY NEWSWATCH, Oct. 7, 1996, *available in* 1996 WL 8453899.

responsible way so that people can benefit by it. Society must allow other areas in the market to develop so that participants can generate financial returns.

Question and Answer Session

Dean Ronald Cass:

60. Farah Champsi stated that the game had changed; the old model had been profit maximization, and the new model is risk reduction. For Stanley Erck and Henri Termeer, who are in the business part of the industry, is that the way you look at it? Is the game from your standpoint one of reducing risk or of maximizing profit, or do you not think about the industry in those terms?

Stanley Erck:

61. Maximizing profit is really just taking the amount of potential return and weighing it by the potential outcome, i.e., the risk. What we are trying to do is discern ways to develop a wider base, either by using bigger platform technology that can be spread across a number of different product opportunities, or by having the ability to develop five drugs in parallel instead of one. This is the goal of minimizing risk, and spreading it over many pieces. Risk always has to be gauged by how much money you have in the bank.[174]

Henri Termeer:

62. It is always a matter of minimizing risk. You always choose the least risk. There are numerous hedging possibilities available, which are much more effectively used today than they used to be. We have a very different atmosphere in virtual companies; people are prepared to work together and form true strategic alliances—not just an exchange of technology for money. I find great encouragement in the industry's currently developing general trend.

Dean Ronald Cass:

63. Henri Termeer discussed Integrated Genetics, how Genzyme tried to get the venture capital market involved and then sold a smaller stake in the business for a larger amount in a public offering. Joshua Lerner, how does that scenario fit with your findings with respect to the role that venture capitalists play?

Joshua Lerner:

64. I think that is a challenging question, because certainly one of the patterns you see is that companies take very distinct trajectories. Venture

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174 *See, e.g.,* STANDARD & POOR'S, *supra* note 6, at 20-21 (providing an overview of biotechnology company financial statement analysis, and recommending to investors that companies have at least two years of cash on the balance sheet to sustain research and development efforts and to insulate the company from downturns in the capital markets).

capitalists, as they look over the range of companies to finance, will, in many cases, have a profile in mind of a kind of the type of technology, or a way a company should be organized.[175] As I alluded to earlier, a venture capitalist often has 200 business plans to sort through before it selects one to fund.[176] As a result, businesses which do not fit into the standard template, because of a troubled situation or a restructuring, will in some cases be shunned solely on the ground that the costs of understanding the company are too high to invest the time and effort. Instead, the venture capitalist turns to a company that is more understandable and is closer to the template that he is most comfortable with. That is not to say that venture capitalists are heedless or careless, but simply that in the sorting process, companies with troubled financing histories or checkered pasts are not always given the attention they deserve.[177]

Dean Ronald Cass:

65. Let me ask Jonathan Beckwith one question before I turn the discussion over to the audience. Not to argue with Henri Termeer about the characterization of the industry, but Leslie Champsi made an argument for a reduction in the amount of regulation, specifically with respect to efficacy. What reaction do you, as someone who has been very concerned about the way the industry develops and the rules by which it operates, have to that comment?

Jonathan Beckwith:

66. Certainly genetic tests are barely regulated, and the regulations themselves are in terms of efficacy.[178] For instance, if the FDA were to consider it, the question really is whether the test works and if it actually measures what it says it is measuring. Thus, the whole range of issues I talked about are well beyond what that level of regulation would deal with. It is complicated because in the case

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175 *See* GEORGE W. FENN, ET AL., BOARD OF GOVERNORS OF THE FEDERAL RESERVE SYSTEM, THE ECONOMICS OF THE PRIVATE EQUITY MARKET (1995).

176 *See id.*

177 *See id.*

178 *See* Proposed Recommendations of the Task Force on Genetic Testing; Notice of Meeting and Request for Comment, 62 Fed. Reg. 4539, 4540-41 (1997) [hereinafter Task Force on Genetic Testing] (recognizing that the public is not being protected adequately because "organizations have on occasion developed and offered genetic tests without always collecting data on test validity and utility and without external review"). A Stanford University task force has urged that the FDA develop rules requiring evidence of medical, psychological, and social safety and efficacy before genetic tests enter the market. *See Stanford Says Most Women Should Not Request Breast Cancer Gene Tests*, BIOTECHNOLOGY NEWSWATCH, Dec. 16, 1996, *available in* 1996 WL 8454166. The task force has also recommended that the FDA regulate the advertising and marketing of genetic tests in the same manner as they regulate prescription drugs. *See id.*

of human genetics you are dealing with a sensitive and dangerous area.[179] There is a lack of public understanding about genetics.[180] You will find groups that consider it beneficial to have a certain test, yet oppose the test because they are worried about discrimination.[181] People are struggling with whether one can regulate the tests, and the regulation seems to be more by consensus and by discussion than through the work of any governmental agency. I have met a number of people from the biotechnology industry at conferences and meetings who discuss ethical issues. Although there already is great concern and awareness—probably more than in most other industries—I think there still needs to be more discussion.

Audience Member:

67. How do you ethically arrive at a fair price for a product or service for what may be a life threatening disease, and at the same time command a premium price in the marketplace?

Henri Termeer:

68. That is an excellent question because in almost every case, there is a monopoly situation occurring for quite a while.[182] It is a matter of studying with great care all the different dynamics that come together around your product. Of course, the simplest part is that you have to know your own economics. But that is the simple part, and the more important part is the outside world. One part of that pricing scheme is long-term collaboration. A year or two before you get to the point that something reaches the market, you begin working with the health

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179 The Task Force on Genetic Testing has identified several concerns that exist or are certain to arise in the genetic testing industry as genetic test procedures rapidly expand. *See* Task Force on Genetic Testing, 62 Fed. Reg. at 4540. These concerns include: (i) the rapid expansion of genetic testing leading to inexperienced providers making genetic testing decisions; (ii) informing healthy people about risks of future disease will creating uncertainty and psychological distress in many individuals; (iii) providers may "unduly influence[]" patients facing personal reproductive decisions; (iv) providers have little guidance on how to communicate genetic risks to relatives and maintain confidentiality; and (v) confirmation of genetic test predictions often cannot be made. *See id.*

180 *See, e.g.,* Sandra Anderson Garcia, *Sociocultural and Legal Implications of Creating and Sustaining Life Through Biomedical Technology*, 17 J. LEGAL MED. 469, 499 (1996) (claiming that the idea of manipulating genes is unfamiliar to most Americans, but that knowledge will increase with the rise of genetic testing and counseling).

181 *See* Task Force on Genetic Testing, 62 Fed. Reg. at 4541.

182 *See* Orphan Drug Act, 21 U.S.C.A. § 360cc (West 1998) (granting seven year monopoly to companies producing drugs that affect relatively few people). *See*, *e.g.*, Dorothy Nelkin, *Covering Gene Therapy: Beware of the Hype*, QUILL, Sept. 1, 1996, *available in* 1996 WL 9282202 (discussing the seven-year monopoly granted by the government under the Orphan Drug Act to companies producing drugs that affect relatively few people).

organizations. In the end, the Health Care Financing Administration ("HCFA")[183] may become involved through Medicare and Medicaid to work through pricing issues.[184]

69. You have to make sure that you provide a fair return to the investors and the risk takers involved, as well as a fair return for the company so it can grow into the next phase of development. But, you must have a price that you can defend. Moreover, you can turn to Congress.[185] We asked the Office of Technology Assessment,[186] which no longer exists, to come in and work with us on what we had done. You need to price the product in a way that accounts for the possibilities and advances that the product creates and the possibility for the market to absorb the product. You should work with the market early on to help the HMO integrate the costs associated with the product into future expenditures.

Leslie Davis:

70. Henri Termeer has talked about how you price a product. One question that has to be factored in is, who ought to bear the cost? First, companies and their investors assume the risks, at least the financial risks.[187] Second, there is the balancing concern of how much you should charge for the product.[188] Finally, there

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183 The Health Care Financing Administration is a federal agency within the Department of Health and Human Services. *See* Health Care Financing Administration, *About the Health Care Financing Administration* (visited Feb. 27, 1998) <http://www.hcfa.gov/about.htm>. HCFA was created in 1977 to administer the Medicare and Medicaid programs. *See id.*

184 HCFA's duties include working with pharmaceutical manufacturers to ensure that pricing for pharmaceutical products is fair and reimbursable under Medicare and Medicaid. *See id. See generally* Baruch Brody, *Public Goods and Fair Prices: Balancing Technological Innovation With Social Well-Being*, HASTINGS CENTER REP., Mar. 13, 1996, *available in* 1996 WL 10189233 (discussing issues concerning the pricing of drugs funded by public dollars).

185 *See, e.g.*, 138 CONG. REC. D5-01 (daily ed. Jan. 21, 1992) (testimony regarding the pricing of certain orphan drugs, presented to the Subcomm. on Antitrust, Monopolies and Business Rights by, among others, Henri Termeer, of Genzyme Corp).

186 The Office of Technology Assessment ("OTA") existed from 1972 to 1995 and was intended to provide Congress with an impartial source of scientific and technical advice. *See* 143 CONG. REC. S7593 (daily ed. July 16, 1997) (statement of Mr. Bingaman). It was disbanded in 1995 due to government downsizing. *See id.* For more information about the role of the OTA, see *Technology Assessment and the Work of Congress* (visited Oct. 12, 1998) <http://www.wws.princeton.edu/~ota/ns20/proces_f.html>.

187 *See* David Lumsden, *Investor Relations for Emerging Companies*, BIOPHARM, June 1, 1995, *available in* 1995 WL 13882572 (describing the nature of the risks that biotechnology companies and their investors face).

188 *See* OFFICE OF TECH. ASSESSMENT, U.S. CONG., PHARMACEUTICAL R&D: COSTS, RISKS & REWARDS, OTA-H-52 (1993) (study finding that profit rates in the pharmaceutical industry run two or three percent higher than in other industries and predicting increased congressional pressure for

is the issue of who ought to pay for the product. I do not think there is an easy answer to this, and I do not think it necessarily should be either the individual who receives the drug or that person's insurance company. In some cases, I think the product or drug addresses a social risk or problem and that a larger group should bear the cost of it.

Audience Member:

71. My question concerns the special nature of intellectual property ventures when companies collaborate to develop patents from governmental funding. Is it possible to obtain reasonable price terms based upon the Bayh-Dole Act?[189]

Farah Champsi:

72. One of the key issues for investors is the proprietary position of companies and the extent to which the companies rely on technology from academia or from the government. Companies do have to demonstrate that they are going to have an exclusive position in the technology. Collaborators often construct relationships with biotechnology companies in which they get access to a product for its eventual marketing and manufacturing.[190] They are not necessarily going to have rights to the technology itself, and there are always issues in the case of joint development.[191] How that technology ultimately gets shared between the two parties and the strength of the patents are important factors for investors. At the end of the day, however, it will not be the sole investment criteria for the public market.

Dean Ronald Cass:

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drug price controls). *See also* Gregory N. Racz, *Drug Companies' Profit Margins Top Most Industries, Study Says*, WALL ST. J., Feb. 26, 1993, at B6 (citing Office of Technology Assessment study finding that profit rates in the pharmaceutical industry run two to three percent higher than in other industries and predicting increased congressional pressure for drug price controls).

189 The Bayh-Dole Act covers "patent rights in inventions made with federal assistance." Bayh-Dole Act, Pub. L. No. 96-517, § 6(a), 94 Stat. 3019, 3019-28 (1980) (codified as amended at 35 U.S.C. §§ 200-211 (1994)). For an overview of the pricing issues and the Bayh-Dole Act, see Brody, *supra* note 184.

190 *See* 35 U.S.C. § 200 (1994) (stating that one of the primary goals of the Bayh-Dole Act is "to promote collaboration between commercial concerns and nonprofit organizations, including universities"); *see also* Rebecca S. Eisenberg, *Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research*, 82 VA. L. REV. 1663, 1670-71 (1996) ("In biomedical research fields researchers in government, university and commercial laboratories are often working simultaneously on the same problems, whether collaboratively or competitively.")

191 *See* Eisenberg, *supra* note 190, at 1671, 1715-18 (stating that investment recoupment problems and commercial and academic institutional differences are some of the conflicts of interest that may develop between joint researchers).

73. Consider the issue of federal budgets and how federal money impacts industry. How does the decline of federal funding affect the biotechnology industry?

Henri Termeer:

74. There is no doubt that this industry exists because the NIH has spent its money wisely for many years.[192] If the money dries up or becomes more difficult to obtain, there is no doubt that progress in this field will be hampered. The rate of new company creation will decline—and it has already declined—if there is a reduction in federal funding.[193]

Dean Ronald Cass:

75. Another funding issue arises when external funding comes into the universities. I am sure that this is something Jonathan Beckwith faces occasionally. To what degree should pharmaceuticals and other companies be allowed to invest in universities and then ask the universities to return the results of the research?

Jonathan Beckwith:

76. It certainly is an issue, but where I work I do not see it as a huge problem. On the other hand, I think our administration, and I would suspect other institutions, are seeing this as the wave of the future. I agree that the basic research that goes on in universities and medical schools has been fundamental and will continue to generate new approaches, ideas, and techniques for the industry.[194]

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192 *See* National Institutes of Health, *Annotations to the Table & Graphs for NIH Extramural Data and Trends, Fiscal Years 1986-1995* (last modified Nov. 26, 1996) <http://www.nih.gov/grants/award/trends95/ANNOTATE.HTM> [*hereinafter NIH Extramural Data Trends*] (stating that NIH Small Business Innovative Research (SBIR) grants were "designed to enhance private sector commercialization of technology through research"); *see also* National Institutes of Health, *Average Size of NIH Awards by Mechanism, FY 1986-1995* (last visited Jan. 26, 1998) <http://www.nih.gov/grants/award/trends95/PDFDOCS/TAB3.PDF> (providing total award amounts made for SBIR grants from 1986 to 1995); *see also* Beth Baker, *Young Investigators Have Lost Financial Edge*, 44 BIOSCIENCE 591, *available in* 1994 WL 13106220 (1994) (reporting that in the early 1980s, the NIH funded many young scientists to help them set up their own labs).

193 Michael Selz, *Finance Firms Targeting Small Business Are on the Rise*, WALL ST. J., Aug. 6, 1996, at B2 (reporting that decreases in NIH Small Business Innovation Research grants will threaten many small businesses engaged in tomorrow's innovative research); *cf.* George Anders, *The Benefactors: Brushes With Death Turn the Very Wealthy Into Medical Medicis*, WALL ST. J., Jan. 6, 1998, at A1 (reporting that private donations to medical research have grown to nearly $13.9 billion in 1996, exceeding the NIH's overall budget).

194 *See* David E. Korn, Note, *Patent and Trade Secret Protection in University-Industry Research Relationships in Biotechnology*, HARV. J. ON LEGIS., 191, 197 (1987) (stating that biotechnology firms are dependent on universities for basic research because that is where much of the original research began and is still where much of the "talent" is located).

Dean Ronald Cass:

77. What changes will occur if pharmaceutical companies invest in university-based research?

Jonathan Beckwith:

78. It depends on how the investment is made. What I have seen so far has been mixed—some of it is very directed research, but most is not directed.[195] There was a company that supported a lot of research at Massachusetts General Hospital, but has slowly withdrawn most of its money.[196] I am not sure whether the company withdrew because the research was too basic and not benefiting them enough or for some other reason. Even when people are not receiving funds from industry, there is more of an orientation toward applied research.[197] There needs to be a balance between applied and basic research in the university. So far we have achieved this.[198] Actually, the money from NIH has not been reduced, but the rate of increase has slowed down enormously.[199] I have worked in other countries, such as Italy, where the government has been supportive of funding only applied research.[200] People often managed to find ways around the policy, however.[201]

Dean Ronald Cass:

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195 *Cf.* Peter G. Gosselin, *Pact Between MGH and a Japanese Cosmetics Firm Fuels Debate Over Academic, Corporate Alliances*, BOSTON GLOBE, Sept. 10, 1989, at A1 ("Although companies may sometimes pay for research in new areas, they are as likely to encourage work on subjects that will produce products, rather than new knowledge.").

196 *See generally*, Anthony Flint, *Researchers Say Aid from Japan Falling*, BOSTON GLOBE, Dec. 27, 1993, at 27 (detailing decline of relationships).

197 *See Integration Replacing Invention As Key to Success in R&D?*, NEW TECH. WEEK, June 30, 1997.

198 *See* Thomas A. Massaro, M.D., *Innovation, Technology Transfer, and Patent Policy: The University Contribution*, 82 VA. L. REV. 1729, n.15 (1996); *cf.* Gosselin, *supra* note 195, at A1 (reporting that in contrast to Europe and Japan, universities in the United States have generally distanced themselves from business, "focusing on basic scientific questions and leaving to others the task of turning their answers into products").

199 *See NIH Extramural Data and Trends, supra* note 192 (stating that although the average NIH grant has increased over the last ten years, much of the increase is due to inflation).

200 *Cf.* Paul Bompard, *Revising the Campuses,* TIMES (London), July 14, 1994 (discussing Italian university reform movement calling for increased concentration on applied research and discussing the dissension which has followed from the movement).

201 *See id.*

79. That is the government's policy in Italy, but it is always a question of how long that policy will last.

Jonathan Beckwith:

80. Right.

Audience Member:

81. How do the panelists manage financing risk in their companies?

Henri Termeer:

82. We have used two alternatives. One is a private research and development partnership.[202] They are quite expensive, and the company must issue stock warrants.[203] You have to be a public company. The partnerships can be extremely beneficial, particularly when the stock goes up as a result of a successful clinical trial. The second alternative is a public research and development vehicle called stock-and-warrant offerings for research and development ("SWORDs"), which trade on the National Association of Securities Dealers Automated Quotations system ("NASDAQ").[204] In both alternatives, the company maintains control over the result and puts the risk into the hands of the investor.[205]

Audience Member:

83. That is not an option for a privately held company.

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202 *See* Veronis, *supra* note 64 (reporting that Genzyme established research and development partnerships in 1987 to fund the development of Ceredase and in 1989 for the development of surgical products based on hyaluronic acid); *cf.* Richard P. Shanley, *Pumping Up Your Research Arm*, FIN. EXECUTIVE, Nov./Dec. 1994, at 54, 54-55 (describing research limited partnerships as a private placement that the investor "must hold until the fruition of the deal," thus eliminating any potential for liquidity).

203 *See* ALAN GILPIN, DICTIONARY OF ECONOMIC TERMS 242 (2d ed. 1970) (defining stock warrant purchase as "[a] certificate giving the holder the right to purchase a specified number of stocks or shares at some future time at a fixed price.").

204 "SWORDs are Stock Warrant, Off-balance-sheet Research and Development financings, a way to raise money in a risky research and development project by creating a publicly owned shell company that has a contract with a biotech firm. If the project is successful and leads to a product, the biotech firm uses its contract to acquire the project from the shell company at a nice profit to the shell company's investors. If the research fails, the biotech company has minimized its risk and the losers are the shell company investors." Ronald Rosenberg, *Biotech Alliances Replacing Early '90s Creative Financings*, BOSTON GLOBE, Mar. 22, 1995, at 80; *see also* ERNST & YOUNG BIOTECH 95, *supra* note 123, at 55 fig. 30 (including SWORDS among the variety of stock options). For potential tax and accounting problems with SWORDS, see notes 240-42 and accompanying text.

205 *See* Rosenberg, *supra* note 204.

Henri Termeer:

84. The choices are few for privately held companies. You really need a partner.

Leslie Davis:

85. If you have a partner, then you have some choices. If you look at most of the agreements in the industry, there is a fairly direct correlation between how much risk a company takes and its share of the profits.[206] One of the possibilities is to get the pharmaceutical company to fund the clinical trials.[207] The pharmaceutical company is then deemed to have contributed to the clinical trials and therefore, gets a larger piece of the profits through pre-paid royalties.

86. Another way, if your company wants to participate in clinical trials, is to partner during or after Phase I trials because they cost less., and the biotechnology company may be willing and able to bear their risks and costs.[208] Or, there are a number of instances in which the biotechnology firm and a big pharmaceutical company cooperate in the clinical trials, with the biotechnology company taking over certain functions that it can do better or as well as the pharmaceutical company.[209]

Farah Champsi:

87. There is a tax or an accounting problem with SWORDs now. Companies used SWORDs because the company did not have to account for the expenses on its balance sheet, and thus, the losses did not show up.[210] You cannot do that anymore,

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206 *See* ERNST & YOUNG BIOTECH 95, *supra* note 123, at 33-34 (stating that biotechnology companies retain greater rights to the product when pharmaceutical companies ally with the biotechnology company in the later, and hence less risky stages of development, such as in clinical phases).

207 *See, e.g., Big Pharmaceutical Firms and Small Gene Therapy Companies: Should We Develop Internally or Search For a Good Partnership?*, GENETIC ENGINEERING NEWS, Oct. 1, 1997, at 4, available in 1997 WL 8970583 (reporting that Amgen and Guilord Pharmaceutical entered into a deal in which Amgen signed away future royalties in exchange for additional funding for clinical trials); *see also* ERNST & YOUNG BIOTECH 95, *supra* note 123, at 33-34 (noting that Asian companies have been more interested in funding clinical trials and less interested in funding research and development).

208 *See, e.g., CEO Interview: XOMA Corporation*, WALL ST. TRANSCRIPT, May 2, 1994, *available in* 1994 WL 3568116 (comparing Phase I trials, costing less than $100,000, with Phases II and III trials which cost from $100,000 to $1 million and $1 million to $20 million, respectively).

209 *See* STANDARD & POOR'S, *supra* note 6, at 11 (stating that biotechnology and pharmaceutical company alliances allow "each company to stick to its strengths" in pre-clinical development and clinical development and product marketing).

210 A SWORDS arrangement allows a company to spend millions of dollars in research and development without showing any costs on its books for several years. *See* Shanley, *supra* note 202,

but companies still manage to find groups to fund specific projects that are not accounting-driven projects.

88. Chiron Corporation[211] did a joint venture in the vaccine business with a corporate partner, and both contributed technology.[212] It was important for Chiron to maintain fifty percent ownership in the joint venture, but they did not have any money to put into it. Basically, they negotiated with the corporate partner to pay for their portion of the capital in the joint venture and Chiron maintained the right downstream to buy back their equity ownership by paying off that amount.[213] This is an interesting structure because it gives flexibility to young companies that have very little money.

Leslie Davis:

89. There is another way to obtain ideas for managing financing risk without spending very much money. There are professionals that can help you, but you might want to use your own resources before you talk to them. You can get several biotechnology prospectuses and read them. In each case, the details, or at least the broader strokes, of how all of these agreements work are laid out in the prospectuses. The prospectuses themselves are available on the Internet. You can get the contract, which generally includes all information except the pricing, from the Securities and Exchange Commission.[214] Nevertheless, you may need help from professionals in the industry to figure out the details of the transaction.

Audience Member:

90. Over the last few years, venture capitalists have learned from some of their past mistakes. Venture capitalists now demand that technology be more developed than they perhaps would have required five or ten years ago.[215] Federal

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at 54. The SWORDS arrangement also enables the company to comply with the accounting requirement of writing off its research and development costs instead of capitalizing them as assets. *See id.* at 56.

211 Chiron Corporation ranked second, behind Amgen Inc., in 1996 annual revenues among publicly owned biotechnology companies. *See* STANDARD & POOR'S, *supra* note 6, at 7

212 *See generally* Susan Pulliam, *Chiron's Pact to Sell Large Stake to Ciba-Geigy Looks Like Good Time to Pocket Some Profits*, WALL ST. J., Nov. 22, 1994, at C2 (detailing Chiron's partnership agreement with Ciba-Geigy in which Chiron will receive a 50% interest in the vaccine joint venture as well as Ciba-Geigy's diagnostic business).

213 *See generally, Ciba-Geigy to pay $26M for Access to Chiron's Combinatorial Chemistry*, BIOWORLD TODAY, Nov. 29, 1995, *available in* 1995 WL 14406878.

214 The Securities and Exchange Commission maintains a database ("EDGAR") of various down-loadable form templates at <http://www.sec.gov/edgarhp.html>.

215 *See* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 24 (stating that "[i]n 1994 and 1995 venture investors shifted capital from startups to later-stage portfolio companies to sustain

funding is really for basic research, although funding may be available for AIDS and cancer research.[216] Thus, it seems that a gap is developing between products coming out of the basic federal funding of academic research and into the corporate world. I wonder whether the panel agrees with this point of view and what mechanisms they see emerging to bridge this gap.

Henri Termeer:

91. My impression is actually quite different. I find that a company runs into major struggles once it gets into the development cycle because at that stage the company needs large sums of money. The company wants to take something into manufacturing and development, but it cannot turn to the public markets. Thus, the company will have to enter into a partnership, which is a horrible position to be in if you negotiate. Where I see the biggest problem is in the current phase of development. Fortunately, the larger operations and the medium-sized biotechnology companies have been able to enter into arrangements.[217] The number of programs in this stage are numerous at the moment.[218]

Stanley Erck:

92. At Procept, we are doing early-stage deals that involve basic technology. There are more and more companies with the capability of developing from very basic research to more applied research companies. I agree with Henri Termeer that the problem Procept and many businesses face is the huge development costs in the clinic.[219] We have done a couple of new academic deals in the last year, and I see them happen frequently.[220]

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expensive clinical trials," and that "[b]iotechnology funding in early 1996 reflects a tendency to fund companies with multiple novel products in the pipeline").

216 *See generally*, 144 CONG. REC. H7476-01, 1998 WL 575438, at *H7478 (daily ed. Sept. 9, 1998)(statement of Rep. Cunningham) (containing statistics on NIH research allocations for AIDS and various forms of cancer).

217 *See* STANDARD & POOR'S, *supra* note 6, at 10-11, 13-14.

218 *See* generally ERNST & YOUNG BIOTECH 97, *supra* note 27, at 25-30 (summarizing current alliances between biotechnology companies and pharmaceutical companies).

219 *See* STANDARD & POOR'S, *supra* note 6, at 16-17 ("Studies of the development process indicate that most new products cost between $200 million and $350 million to fully develop.").

220 *See 1995-1994 Press Releases* (visited Oct. 17, 1998) <www.procept.com/htmls/pressreleases/03-11-94.txt> (announcing that Procept, Dana-Farber Cancer Institute, and Harvard University received a grant from the National Cooperative Drug Discovery Group (NCDDG) of the National Institutes of Health (NIH) to conduct AIDS research). *See generally ICOS Collaborations Represent Biotech Trend*, BIOTECHNOLOGY NEWSWATCH, July 6, 1992, at 2, *available in* 1992 WL 2513689 (announcing ICOS research agreement with USC and University of Utah); Sally Lehrman, *Ties that Bind Industry to Academe Growing Tighter, More Complex*,

Leslie Davis:

93. I agree with you. I think Henri Termeer is right in that there are some interesting initiatives happening. For example, some of the established companies are incubating start-up companies in-house.[221] Frequently, I see people who have located interesting technology that is licensable from a university and want to start a biotechnology company. Finding the seed money can be extremely difficult. If they want to do it on their own, there are still some venture capitalists who are interested. Many venture capitalists, however, want to see a product in late animal stage testing[222] or a company that is ready to submit an Investigational New Drug Application ("IND")[223] before they invest. While there are some new ways emerging to deal with this problem, people trying to start biotechnology companies that need a few hundred thousand or one million dollars face great difficulty.

Audience Member:

94. When is the biotechnology industry itself willing to address the issues that Jonathan Beckwith has raised? The market has to be prepared for the products. Yet, as Jonathan mentioned, there are some inappropriate uses of biotechnology. Does the biotechnology industry see itself as sufficiently mature industry to begin engaging these issues with the public? I know the chemical industry has tried to do this over the last twenty years—for example, taking pledges that they will not sell dangerous chemical products to companies that do not know how to use them safely.[224] Are similar self-regulatory initiatives being taken by the biotechnology industry?

BIOTECHNOLOGY NEWSWATCH, July 7, 1997, at 1, *available in* 1997 WL 8790958 (discussing interdependence of universities and biotech companies).

221 *See, e.g.,* Johnson, *supra* note 29 ("Companies like Alza, Amgen, Biogen, Chiron, Collagen, Genentech and Genzyme are now generating sufficient product sales to meet most if not all of their capital needs. These companies in turn are using their improved cash flow to help finance new product development at younger biotech companies.").

222 In recent years venture capitalists have invested more dollars in later-stage companies with products in clinical trials. *See* ERNST & YOUNG BIOTECH 96, *supra* note 133, at 13; *see also* ERNST & YOUNG BIOTECH 95, *supra* note 123, at 31 (stating that venture capital investments are likely to shift to companies with drugs in Phase I clinical trials).

223 A company must submit an IND application to the FDA before it begins human product testing. *See* STANDARD & POOR'S, *supra* note 6, at 16. The IND application notifies the FDA that unless it objects, the company's human studies will start in 30 days. *See id.*

224 *Cf. New Controls on Export of Dangerous Chemicals are Implemented on 1/22/95*, SPECIALTY CHEMICALS, Mar. 1, 1995, *available in* 1995 WL 14143699 (discussing EC regulation and concern over exports of pesticides to developing countries which lack the resources or expertise to use them safely).

Henri Termeer:

95. Yes. I am Chairman of the Biotechnology Industry Organization ("BIO"),[225] which has close to 700 biotechnology company members throughout the country.[226] BIO formed a bioethics committee, and when we asked for volunteers to participate in this effort, the response was enormous. We also have approximately thirty-six board members, all of whom are CEOs of large companies, major pharmaceutical firms, or smaller firms.[227] We have people such as Phillip Reilly[228] lecture about the ethics concerns. I find it extremely interesting trying to moderate these discussions, because the opinions among the leadership in the companies are very different. The opinions concerning the extent of debate necessary for market development also differ. Thus, there is a lot of learning going on, and we are learning how to effectively in manage this process. I am personally convinced that unless we manage it well, the industry will be hurt badly in the future.

Dean Ronald Cass:

96. Are the panel members comfortable with the notion, set forth earlier, that you want the companies selling the inventions to monitor who is using them—as opposed to limiting the companies' responsibility to developing new products and making them available, and then having the market and the government make determinations as to how to use those products? Is it the role of your company to see how the product is used or just to produce it?

Stanley Erck:

97. That is an interesting question. I do not think that it is the biotechnology company's role to monitor the users of the technology. What we are

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225 BIO is a trade association that was officially formed in 1993 with the merger of the Association of Biotechnology Companies and the Industrial Biotechnology Association. *See Newsbriefs*, BT CATALYST, Sept. 1, 1993, *available in* 1993 WL 12282258. The Applied Biotreatment Association, a trade association representing bioremediation manufacturers, also merged into BIO. *See id.* BIO represents "biotechnology companies of all sizes, academic institutions and state biotechnology centers engaged in the development of products and services in the areas of biomedicine, diagnostics, agriculture food [sic], energy, environmental, and industrial applications." *Biotechnology Industry Organization* (visited Oct. 17, 1998) <http://www.bio.org/aboutbio/main.dgw>.

226 BIO also represents state biotechnology centers, industry suppliers, educational institutions, and has local chapters and affiliates in 27 countries. *See* BT CATALYST, *supra* note 225.

227 For a complete list of the BIO board members, see Biotechnology Industry Organization, *BIO Board of Directors 1997-98* (visited Jan. 26, 1998) <http://www.bio.org/aboutbio/board.dgw>.

228 Philip Reilly is the Executive Director of the Shriver Mental Retardation Research Center in Waltham, Massachusetts. *See* Frances Bishopp, *11th International BIO Conference: Ethical Issues in Genetics Create Challenges for Biotech Industry*, BIOWORLD TODAY, June 11, 1997, *available in* 1997 WL 11130296. Reilly recently spoke to a BIO conference group concerning bioethics and genetic disclosure. *See id.*

learning about ourselves and our ability to manage the way we take care of our health is going to continue. It is going to become more complex as we focus on the details of how diseases can be prevented or stopped and at what stage. I think it is part of our industry's responsibility to educate the public as best we can. We have a lot of knowledge about the potential for tests and drugs.[229] It is up to society to determine whether they are to be consumed.

Leslie Davis:

98. I think that the companies that participate in developing the products have an obligation to make clear how products can be used and what the consequences are, similar to that of the companies that developed seat belts and air bags. I do not think that there is any one group who should hold itself out as the arbiter of whether society should engage in genetic therapy or genetic testing. It is society's decision, which ought to be made with extensive input from specialists. There is no one group, company, or person that knows enough about what we all want or need to decide the issue for us. I think that it is a legislative undertaking at some point.[230]

Jonathan Beckwith:

99. I absolutely agree, but I am going to speak from the perspective of a scientist. I have felt for many years that scientists should take responsibility for contributing to the public debate about these issues. However, I am in an extremely small minority among scientists. For whatever reasons, most scientists avoid public debate.[231] For instance, I think people working in genetics should have something to say about the use of genetics and racial differences, specifically with the publication of *The Bell Curve*.[232] In that book, the authors use genetics to argue

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229 *See generally* Michael J. Malinowski, *Coming into Being: Law, Ethics, and the Practice of Prenatal Genetic Screening*, 45 HASTINGS L.J. 1435 (1994) (Questioning whether current ethical principles are sufficient to protect the public in a world with ever-expanding genetic testing and information available).

230 *See id*. at 1451 ("Without public policy foresight and resulting regulation, there is some danger that society will not discover violations of its ethical principles until the technology and practices responsible for these violations have already been introduced and widely applied.").

231 One commentator has suggested that scientists do not involve themselves in public debates and congressional hearings because of "[t]he apparent inability of many people—including lawyers, judges, legislators, and journalists—to appreciate the inherent uncertainty in science." Reed F. Noss, *Some Principles of Conservation Biology, as They Apply to Environmental Law*, 69 CHI.-KENT L. REV. 893, 907-08 (1994).

232 RICHARD J. HERRNSTEIN & CHARLES MURRAY, THE BELL CURVE: INTELLIGENCE AND CLASS STRUCTURE IN AMERICAN LIFE (1994).

about racial differences in intelligence.[233] Very few geneticists had much to say about it. The point is that the use of genetics is a very sensitive issue because the use of genetics has real social consequences. People involved in genetics should contribute their knowledge to public discussions of the issues.

Audience Member:

100. I would like to ask a question concerning the responsibility of the biotechnology companies to develop human growth hormone products. What if a certain group of doctors promoted the product for short children, rather than the company producing the drug? Do you think that the company has an obligation to stop that practice, or counsel others from doing it? Or, should we let the market decide the best uses for the product?

Jonathan Beckwith:

101. It depends on what you think about the use of the product for that purpose. Maybe some people think it is fine. But, I think scientists, geneticists, and people in the field who know something about it have a responsibility to speak out. If there is an egregious misuse, the company probably would be as concerned as anyone else because in the long run it could be harmful to the company's own prospects.

Henri Termeer:

102. I think that is the correct answer. Companies are very concerned with situations that they cannot represent comfortably. The gain from a misrepresentation is extremely temporary, if there is a gain at all. You cannot develop a significant market on the basis of misuse. The one potential exception is cancer, where physicians experiment greatly with off-label uses, but no one knows if it helps the patient or not.[234] That situation is very well understood by everyone, including the FDA.[235] But in the example that you used, I think companies would ask themselves some tough questions. Is this appropriate? What do we know about it? If a company feels uncomfortable, they have a responsibility to speak out, rather

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233 For critical analysis of the arguments set forth in *The Bell Curve*, see THE BELL CURVE DEBATE: HISTORY, DOCUMENTS, OPINIONS (Russell Jacoby & Naomi Glauberman eds., 1995).

234 A General Accounting Office study found that about one-third of all drug treatments for cancer involved off-label drug uses. *See* U.S. GEN. ACCOUNTING OFFICE, PUB. NO. GAO/PEMD-91-14, OFF-LABEL DRUGS: REIMBURSEMENT POLICIES CONSTRAIN PHYSICIANS IN THEIR CHOICE OF CANCER THERAPIES 19 (1991).

235 *See generally* Mike Pezzella, *BIO Expects Industry Boost from FDA Overhaul,* BIOTECHNOLOGY NEWSWATCH, Dec. 1, 1997, at 1, *available in* 1997 WL 8791511 (reporting new FDA guidelines for off-label use of drugs, and quoting BIO President Carl Feldbaum that "inherent in the [new] regulations is the requirement that the FDA work with companies to set a more definite as well as a more reliable type of trial.").

than leaving the decision to the physicians. The most appropriate entity to speak to is the FDA.[236] Nevertheless, every situation has its own very complex set of issues.

Dean Ronald Cass:

103. Are those questions going to differ among companies? Are large companies that are long-term players with a large portfolio of drugs and development going to ask different questions than a smaller company that essentially has one or two potential products?

Henri Termeer:

104. No. In the last twenty-five years, large companies made enormous blunders in this area.[237] People do make mistakes of judgment. In a large company, usually two or three people make judgment errors, and they are usually removed from the company. Of course, policies are put in place in the large companies to protect against mistakes,[238] but I am always surprised, year after year, that both large and small companies make very strange judgments. Sometimes the judgments are pragmatic and very short-term. There is no way you would ever make a decision that would put the corporation's integrity into question, which is the most important thing in the healthcare industry.

Audience Member:

105. First, how much has the marketplace changed since the first biotechnology companies were formed? Second, concerning the issue of discrimination, how do we determine who gets care and how do we redeploy healthcare resources? Finally, how do we deal with the HMO environment?

Henri Termeer:

106. These are very difficult questions emerging from within the biotechnology community. At a recent BIO conference, biotechnology

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236 *See Off-label Use of Drugs an Issue*, CHAIN DRUG REV., Jan 20, 1997, *available in* 1997 WL 10433409 ("Nevertheless, the FDA restricts pharmaceutical companies on information they can distribute concerning off-label uses . . . .").

237 *See*, *e.g.,* Love v. Wolf, 38 Cal. Rptr. 183, 195 (Cal. Ct. App. 1964) (holding Parke-Davis liable when it knew that physicians were prescribing its product chloromycetin for off-label uses and did not tell its salesmen to remedy the problem, even when it knew of potentially severe ill effects of such uses); *see also* William M. Sage, Note, *Drug Product Liability and Health Care Delivery Systems*, 40 STAN. L. REV. 989, 1017 n.113 (1988) ("Because companies must recover their investment quickly, the incentives for a company, once a drug has been released, are to suppress adverse information, conduct blitzkrieg advertising campaigns, and delay FDA regulatory actions.").

238 *See How a Biotech Drug is Developed* (visited Oct. 14, 1998) <http://www.bio.org./whatis/guide1.dgw#develop> (detailing strict reports drug companies must make to the FDA).

representatives started a discussion which assumed that if all BIO-member companies were successful, will they revolutionize healthcare?[239] The hundreds of companies represented addressed all major medical needs. Of course, not all companies will be successful, but quite a few will succeed. We have started an initiative to set up a permanent organization within BIO to start communication on these points.[240] The organization will deal with everyone, including the patent office, the FDA, and payer and healthcare systems.[241]

107. In Europe, healthcare budgets are smaller.[242] This begs the question, how much is appropriate to spend? Should we spend more? Is the advancement worth enlarging the budget? Approximately 8% of the total healthcare dollar is spent on pharmaceuticals.[243] If you calculate the return required to pay back the investments that are being made, and have been made historically, you need to double the size of that share over time.[244] You can imagine the political reaction if that is the only piece of healthcare that grows as other areas are tightened. Nevertheless, it may be a worthwhile thing to do.

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239 *See* Henri Termeer, Address at the Forum of the Task Force on Science, Health Care, and the Economy (June 23, 1998).

240 *See Economic Importance of Biotechnology, Medical Research, and Improved Health Care* (visited Oct. 14, 1998) <http://www.bio.org/laws/economic_impact.dgw> (report prepared by the Forum of the Task Force on Science, Health Care, and the Economy).

241 *See id*.

242 *See generally* BUREAU OF THE CENSUS, U.S. DEPT OF COMMERCE, STATISTICAL ABSTRACT OF THE U.S. 1996, *supra* note 143, at 834 tbl. 1332 (providing table of world healthcare expenditures by country for the years 1980 to 1994); ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT, 1 OECD HEALTH SYSTEMS: FACTS AND TRENDS 1960-1991, 18 tbl. 1 (1993) (providing table of healthcare expenditure growth in the OECD area for the years 1960 to 1991).

243 *See* James Heenan, *Prescription Drug Benefits in a Managed Care Plan: Balancing Quality and Costs*, 7 MED. INTERFACE, Jan. 1994, at 84, 85; Michael A. Weber, *Impact on the Pharmaceutical Industry of Changes in the American Health Care System: A Physician's Perspective*, 24 SETON HALL L. REV. 1290, 1322 fig. 4 (1994); *see also Chain Drug Stocks Reach Record High of 1,042.9 in April*, CHAIN DRUG REV., May 26, 1997, *available in* 1997 WL 10433634 (estimating that "pharmaceutical products represent just 8% to 10% of United States healthcare outlays").

244 *See Prescription Drug Price Increases, 1985: Hearings Before the Subcomm. on Energy and Commerce*, 99th Cong. 88 (1985) (statement of Gerald J. Mossinghoff, President of Pharm. Mfrs. Ass'n). As research and development costs have risen, drug companies have increased the proportion of sales revenue to finance research and development. *See id.* "In the healthcare industry as a whole, [research and development] spending as a percentage of sales is typically around 11%, still considered high compared with other industries." STANDARD & POOR'S, *supra* note 6, at 6. "Major U.S. pharmaceutical drug companies spent some 17.1% of their sales on [research and development] in 1996." *Id*. at 18. Regulatory compliance and regulatory time constraints also affect the likelihood that a drug will recoup its research and development costs. *See* Barry S. Roberts & Sara M. Biggers, *Regulatory Update: The FDA Speeds Up Hope for the Desperately Ill and Dying*, 27 AM. BUS. L.J. 403, 409-10 (1989).

Farah Champsi:

108. By putting pressure on pharmaceutical companies to develop novel drugs and justify the premium prices have enjoyed for many years, managed care has had a positive effect on the entire biopharmaceutical industry.[245] Eventually, when we have new drugs on the market that are biopharmaceutical agents, cost efficacy will be a critical issue. Companies are going to have to develop their marketing strategies with the managed care payer in mind and be able to justify why a particular therapy—be it from Genzyme, or any other company—is an important addition to addressing a particular disease. Ultimately, there is an enormously positive effect on the whole healthcare system by reducing the healthcare service dollars that are spent on managing a particular patient. I think the forces are headed in the right direction by putting the burden on the biotechnology companies—with funding from their pharmaceutical partners—collectively to rationalize their research efforts and come up with new and better products than those currently produced by the industry.

Audience Member:

109. Some of the most interesting technologies that we have been working on, such as electric batteries for cars, come from Eastern Europe and the former Soviet Union.[246] I was wondering whether there is strong competition in the U.S. biotechnology industry from Eastern European or Russian companies. If so, do you engage in joint ventures with these countries in the United States?

Stanley Erck:

110. My experience is that not only have we found some of our best scientists from Eastern European companies and countries, but we have also heard of a

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245 *See* Henry Grabowski, *Health Reform and Pharmaceutical Innovation*, 24 SETON HALL L. REV. 1221, 1259 (1994); *see also* Richard M. Cooper, *Some Effects of the Clinton Health Care Reform Proposals on Regulated Aspects of the Pharmaceutical Industry*, 24 SETON HALL L. REV. 1260, 1265-69 (1994) (arguing that centrally managed healthcare plans would decrease pharmaceutical prices and promote competition among drugs on the basis of safety and effectiveness). *But see* STANDARD & POOR'S, *supra* note 6, at 8 ("Despite its emphasis on cost control, the growth of managed care isn't expected to reduce overall drug spending, especially for novel treatments that represent significant therapeutic breakthroughs. A biotech-derived drug that cures, prevents, or significantly reduces the morbidity of a disease can save many times its cost by reducing medical expenses.").

246 *See, e.g.,* Alan C. Miller & Hugo Martin, *Group Seeks a Place to Park Electric Car Industry*, L.A. TIMES, Jan. 20, 1992, at B3 (reporting that Ashurst Technology Corp. is working with Ukrainian scientists to acquire electric car battery technology originally developed in the former Soviet Union); *Industry News: Selected Battery-Related Stock Performance,* BATTERY & EV TECH., Dec. 1, 1993, *available in* 1993 WL 2575557 (reporting that Intex Corporation and TEI, Inc. of Moscow have formed a joint venture to develop energy storage technology from the former Soviet Union).

number of drugs licensed from compounds actually discovered in Russia or Eastern Europe.[247] These drugs are licensed and developed in collaboration with a U.S. biotechnology or pharmaceutical company.[248] In Eastern Europe and Russia, the financial infrastructure probably is not in place to start a biotechnology industry.[249] Nevertheless, I do see the technology coming out of these countries and being developed in exchange for royalties.[250]

Joshua Lerner:

111. Another aspect of internationalization is the relationship between the United States biotechnology industry and Western Europe. The British and many of the continental universities have been the original sources of the intellectual property that were ultimately developed into biotechnology drugs.[251] But when you look at the patterns of alliance financing coming from large companies, the role of

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247 In November 1993, Russian and American scientists held the first "Russian Biotech" conference in Virginia to discuss Russian innovations in biotechnology and medical devices. *See* Daniel Southerland, *Virginia Offers Helping Hand to Russian Scientists*, WASH. POST, Nov. 22, 1993, at F5. As a result of the exposition, Virginia Commonwealth University entered into an agreement with Russia's Ministry of Atomic Energy to promote exchanges of technology and use of Russian technology to develop consumer products. *See id.* In 1990, E.I. Du Pont de Nemours & Co. obtained FDA approval to market "Ethmozine," making it "the first Soviet drug licensed and clinically developed by an American pharmaceutical company." *Du Pont Gets Okay to Sell Soviet Drug*, CHEMICAL MARKETING REP., July 2, 1990, *available in* 1990 WL 2675009.

248 *See Du Pont Gets Okay to Sell Soviet Drug, supra* note 247 (reporting that Du Pont will pay the Soviet government a 4% royalty to manufacture and market the drug "Ethmozine"); *see also Slovakofarma: A Credible Investment Opportunity*, MARKETLETTER, June 2, 1997, *available in* 1997 WL 10362317 (reporting that Slovakofarma, a Slovakian pharmaceutical company, has established a joint venture with the U.S. firm Eli Lilly to manufacture cephalosporin antibiotics).

249 *See, e.g., Russians Show Their Biotech Goods*, BIOTECH. BUS. NEWS, Dec. 3, 1993, *available in* 1993 WL 11411906 ("The Russians are looking to western investors for help with funding, marketing and management. The present economic situation in Russia precludes domestic investment.").

250 *See DuPont Gets Okay to Sell Soviet Drug*, *supra* note 247 (licensing of "Ethmozine"); Southerland, *supra* note 247 (reporting that during the Russian biotechnology exposition in 1993, two venture capital firms entered into discussions with Russian Academy of Sciences officials concerning a purchase of the Academy's technology); *Russian Drugs Finding a Cure: Imports Dominate Russian Market, With $998 Million of Pharmaceutical Products Imported in 1995*, CHEMICAL MARKET REP., Feb. 24, 1997, *available in* 1997 WL 8496291 (reporting that in 1996 and in 1997, Bayer and Searle (Monsanto) signed joint venture agreements with Russian enterprises for the manufacture and development of medical products and organic compounds).

251 *See* Mark Edwards, *The New Europeans: Biotech's Biggest Spenders*, SIGNALS (1996) (visited Oct. 22, 1998) <http://www.signalsmag.com/signals.nsf/>.

Europe—in particular, Germany, France, and some others recently—has increased in importance.[252]

Leslie Davis:

112. I think most of the invention, however, goes on in American universities. There is plenty of anecdotal evidence, but I think that it is conceded that in the pharmaceutical industry, the United States maintains an impressive lead in the number of inventions.[253] The foreign pharmaceutical companies finance United States biotechnology companies because they do not find opportunities closer to home.[254]

Audience Member:

113. What are the panelists' viewpoints concerning the issues of capital, reinvestment, and profit?

Henri Termeer:

114. The way that my company looked at it was not to invest and create opportunities for payback along the way, but rather to make the investment payback somewhat independent of the speed with which the progress was made in research. The money that the company raised for eight or nine projects in the partnerships allowed that to be done. In the early days when we were working on the venture capital side, we raised enough money for one year, and then looked for more financing. In those early days, two million dollars was a year's financing.[255]

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[252] See STANDARD & POOR'S, *supra* note 6, at 5 ("Recognizing the leadership position that U.S. companies command in biotechnology, European pharmaceutical companies are increasing their investments in U.S. biotech firms."); Daniel Green, *The Cloning of U.S. Biotech Success*, FIN. POST, May 20, 1997 (stating that Germany and France plan to invest $123 million and $365 million, respectively, in their biotechnology industries); *see also Biotechnology: Drug Companies' Target Practice*, ECONOMIST, Dec. 6, 1997, at 66 (reporting that Abbott Laboratories announced a $20 million investment in the French biotechnology company Genset, and that Britain's SmithKline Beecham unveiled a joint venture with Incyte Pharmaceuticals from California).

[253] *See* Gerald J. Mossinghoff & Thomas Bombelles, *The Importance of Intellectual Property Protection to the American Research-Intensive Pharmaceutical Industry*, COLUM. J. WORLD BUS., Mar. 1, 1996; *cf.* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 42 (stating that Europe's biotechnology industry has begun to grow significantly, due primarily to changes in the European Union's financial structures).

[254] For example, in February 1997, the Switzerland-based pharmaceutical company Novartis completed its acquisition of SyStemix Inc. *See* STANDARD & POOR'S *supra* note 6, at 5. Novartis also holds a 49.9% ownership interest in Chiron Corporation. *See id.* However, recent European financial market reforms have encouraged European venture capitalists to move their money from the U.S. biotechnology sector to European companies. *See* Green, *supra* note 252.

[255] In contrast, Genzyme's expenditures for research and development in 1996 were $80.8 million, or 15.8% of the company's revenues. *See* STANDARD & POOR'S, *supra* note 6, at 7.

We took it for granted that we had to reinvest. But, we had to reinvest in an environment where the first investor has to feel good; you cannot reinvest unless they feel good because investors talk to each other. It is not a scientific gain or a mathematical formula, but rather, how you look at the amount of patience that you require the investor to have for payback. You cannot expect the investor to be there for ten years.

Audience Member:

115. My question concerns the future of the pharmaceutical industry, specifically small pharmaceutical companies. Venture capitalists and investment bankers have been infatuated with biotechnology. There are approximately 1300 pharmaceutical companies under $250 million in value.[256] Do you foresee continued investment in small biotechnology companies? If it does not continue, what will be the effect of a lack of financing from both venture capital and IPOs? Is there too much reliance on the market right now?

Farah Champsi:

116. My guess is that we are not going to see a let up of company formation because our understanding of the science is increasing dramatically, and every day there are new opportunities to be funded.[257] Having said that, the venture capital community is reducing the number of new start-ups that they want to pursue, primarily because they are so capital intensive.[258] It is not just raising the venture money, but making sure that these companies then have access to public markets

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256 *See* STANDARD & POOR'S, *supra* note 6, at 6 (stating that although there are more than 1300 public and private biotechnology firms in the United States, "the five largest players accounted for approximately one-third of the industry wide revenues in 1996"). Amgen Inc., the largest publicly owned biotechnology company, has a market capitalization of $14.75 billion, while the seventh largest, Immunex Corp., has a market capitalization of only $545 million. *See* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 71 fig. 33.

257 *See* Roger Longman, *Biotech Sidesteps Consolidation*, IN VIVO, Dec. 1997, at 41, 41 ("[N]ew companies—most based on discovery technologies, not clinical-stage products—continue to be formed."); *see also* STANDARD & POOR'S, *supra* note 6, at 8-10 (explaining that new drug-discovery technologies, such as combinatorial chemistry, high throughput screening, and genomics, will stimulate industry-wide growth).

258 According to an Ernst & Young survey, "[f]unding for early-stage companies during calendar 1994 and 1995 fell by more than half of the 1992 and 1993 funding level. In 1994 and 1995, venture investors shifted capital from startups to later-stage portfolio companies." ERNST & YOUNG BIOTECH 97, *supra* note 27, at 24. The Ernst & Young survey also notes that recent biotechnology funding "reflects a tendency to fund companies with multiple novel products in the pipeline rather than companies focused on becoming a full-scale drug manufacturer." *Id.*

and other resources where they can obtain capital to realize a business eventually. My guess is that we will ultimately see some consolidation.[259]

117. For example, ChemGenics Pharmaceuticals, Inc. just merged with Millennium Pharmaceuticals, Inc.[260] I would expect other companies to realize that perhaps the best way to prosper is to form an alliance, a merger, or an acquisition. Although we will see more of that occurring than we have historically,[261] it has not been the case thus far in the biotechnology industry. [262] Genzyme has probably done a better job of trying to encourage people to consolidate than others.[263] I would expect that we will continue to see new companies, albeit at a slower rate from the venture side of the business. At the same time, we will see some consolidation take place among the companies that are creating platform approaches to fit with companies that have complementary technologies.[264] This will accelerate drug discovery. We cannot always rely on the public market being there because it is cyclical. When equity markets are bleak, it does not matter what you are doing; it is very difficult to raise money.[265]

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259 "Biotech companies have also stepped up their research and development ("R&D") efforts in recent years, resulting in an expanded stream of new products expected to be launched before the decade's end. Merger and acquisition activity in this group is also likely to continue as firms combine their assets to finance R&D programs and commercialize their products. ERNST & YOUNG BIOTECH 97, *supra* note 27, at 1. *But see* Longman, *supra* note 257, at 41-42 (arguing that significant consolidation in the biotechnology industry is not likely to occur because of corporate structural and managerial concerns).

260 *See* Eric Convey, *Millennium to Buy ChemGenics in Stock Deal*, BOSTON HERALD, Jan. 21, 1997, at 25 (reporting that the deal will create a company with the ability to engage in the "entire drug-development process").

261 *See*, *e.g.*, *Pharmacia & Upjohn, Amersham in Biotech Megamerger*, CHEMICAL WK., June 18, 1997, at 8, 8 (reporting that Pharmacia & Upjohn merged its Pharma Biotech business with the Amersham Life Science biotechnology unit of British health care company Amersham International, creating "the world's largest biotechnology supplier"); Daniel Green, *US Biotech Groups to Merge*, FIN. TIMES, Nov. 4, 1997, at 26 (reporting that Arris Pharmaceuticals of San Francisco is buying Sequana Therapeutics, combining drug development with genetic analysis technologies).

262 *See* Longman, *supra* note 257, at 41 (noting the lack of consolidation and acquisition in the biotechnology industry).

263 *See* Deborah Erickson, *Keeping Track of Genzyme,* IN VIVO, Oct. 1997, at 11, 11 (stating that Genzyme has engaged in innovative methods of financing to make acquisitions and diversify its business).

264 *See* Longman, *supra* note 257, at 41 (stating that these platform approaches will protect the companies from clinical failures and induce investment).

265 *See* STANDARD & POOR'S, *supra* note 6, at 14 (stating that in 1993 and 1994, the public equity market "dried up" for biotechnology companies so that even the top companies had difficulty raising capital); Scott Reeves, *Mature Babies: New Stock Offerings Set a Surprisingly Calm Pace in the Second Quarter*, BARRON'S, July 7, 1997, at 17, 18 (noting that initial public offerings slowed "to a

Audience Member:

118. What drives the cycle in the public market? Is there a correlation between companies in trial phases, stability, and IPOs?

Farah Champsi:

119. There is no correlation today. People are tempted to have some rules. In the early 1980s and 1990s, you needed a product in clinical trials that was a pretty good benchmark—in addition to perhaps having a corporate partner—to try to raise public funds.[266] We have seen too many disappointments in clinical trials to know that that is not the right benchmark any more. [267] The rules have changed today. It really is an issue of how strong the equity markets are overall. Perhaps the number one driving factor of interest in the biotechnology IPO market is the funds flowing into the mutual fund industry today.[268] That is driving stock prices higher overall.[269]

120. The number of biotechnology companies that have been financed in the IPO market in 1996, and the amount of dollars that were raised is much lower than

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near-halt" in early 1997 when stocks in the overall market experienced a downturn); *Analysts Expect an Avalanche of Biotechnology Offerings for the New Year*, GENETIC ENGINEERING NEWS, Jan. 1, 1997, *available in* 1997 WL 8970411 ("The fact that numerous [biotechnology companies] are competing for funds in a lackluster market may force some to consider other financial strategies, such as mergers to create larger, stronger companies that will be more attractive to investors.").

266 *See Headlines Proclaim Calamity for the Industry: "Biotech: Why It Hasn't Paid Off,"* BT CATALYST, Dec. 1, 1994, *available in* 1994 WL 2562647 (hereinafter *Headlines Proclaim Calamity for Industry*) ("In the early 1980s, eager investors, hoping to find the next Chiron, provided millions of dollars to companies founded on a single technology concept with minimal concern for development hurdles."); *see also* STANDARD & POOR'S, *supra* note 6, at 14 (noting that biotechnology companies usually attempt initial public offerings with a least one corporate partner).

267 *See Headlines Proclaim Calamity For the Industry*, *supra* note 266 (stating that public investors retreated "in 1992 as Centocor and others were smashed by FDA decisions and disappointing clinical results"); Peter K. Wirth, *Biotech ROI: New Paradigms in Search of the King*, CA03 A.L.I.-A.B.A. 57 (1995) ("Starting with the failure of clinical trials for Centocor's leading drug, Centoxin, in January 1993, a series of high-profile disappointments in late stage clinical trials in 1993 and 1994 sent the stock of public biotech companies into a tailspin."); *see also* ERNST & YOUNG BIOTECH 96, *supra* note 133, at 26 fig. 8 ("Product Disappointments Create Continued Stock Vulnerability").

268 *See also* Pete Barlas, *Bulging Product Pipeline Cures Biotech's Financial Ills*, SAN FRANCISCO BUS. TIMES, Apr. 19, 1996, *available in* 1996 WL 10041896 ("[T]he capital flow into biotechnology has been fueled by mutual fund managers seeking undervalued opportunities.").

269 *See id.* at 306 (stating that the increased capital flow by mutual funds into biotechnology has increased the value of the top 200 biotechnology companies, sending stock prices higher and prompting further investment in biotechnology).

the price performance of public companies in 1995. [270] In 1995, the biotechnology index that measures the top 100 stocks went up 88.5%.[271] That opened the doors of all of the young companies with investors wanting to realize those huge returns; they were willing to buy high-risk young companies that had proven very little.[272] If you look at that same index in 1996, it was essentially flat.[273] Thus, if you bought biotechnology IPOs in 1996 you barely made any money at all.

121. That is the way the financing cycle works: it is always looking in the rear view mirror. Going forward, the best way to get biotechnology financing is not to focus on one specific benchmark, such as clinical trial results or having a specific partner, but rather, to focus on risk diversification, pursuing multiple approaches, and having a very strong team in place.[274] Hopefully, by having multiple partners and by not needing to go public to raise money, you have enough cash in the bank to support yourself. Then, you can think about pursuing an IPO.

Joshua Lerner:

122. When one looks at the alliances that firms are able to make with big pharmaceutical companies, the firms which have the most resources obtain the most favorable agreements in terms of maintaining contractual controls over clinical development rights, manufacturing rights, and so forth.[275] Having the

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270 *See*, *e.g.*, Deborah Lohse, *Biotech Shares Look Tempting to Some Analysts*, WALL ST. J., Apr. 15, 1996, at C1 (stating that in 1995, large pharmaceutical companies and several small biotechnology companies earned large profits due to a favorable outlook for FDA approvals and successful clinical trials at certain companies).

271 *See id*. (stating that the Nasdaq Biotechnology Index rose 88.5% in 1995).

272 *See id.* at C1 (stating that although biotechnology companies are highly risky investments, small biotechnology companies with multiple products in the pipeline and established partnerships with larger pharmaceuticals may be good investments in early 1996); ERNST & YOUNG BIOTECH 97, *supra* note 27, at 24 ("In the second half of 1995 and the first half of 1996, biotech IPOs raised more money at higher valuations than in the prior two years."). *But see* E.S. Browning, *Biotech Issues Offer Opportunity, Danger*, WALL ST. J., Nov. 24, 1997, at C1 (stating that investment banks and analysts sometimes "generate overly ambitious profit estimates" for young companies raising research money).

273 *See Nasdaq Data Download: 1996 Market Statistics - Daily* (visited Oct. 22, 1998) <http://www.nasd.com/mr4b.html#1996>; *see* ERNST & YOUNG BIOTECH 97, *supra* note 27, at 22 (stating that the biotechnology sector took a downturn in the third quarter of 1996 and capital raised through initial public offerings dropped from almost $300 million in June to $52 million in July).

274 *See*, *e.g.*, Erickson, *supra* note 263, at 11 (noting that Genzyme has pursued an approach of diversifying research programs, separating divisions, and creating incentives for employees and management with stock in their particular division).

275 *See generally* Lerner & Merges, *supra* note 17.

financial resources at the bargaining table strengthens a small firm's ability to negotiate an agreement.

Audience Member:

123. Please distinguish between contract research and strategic alliances.

Joshua Lerner:

124. A strategic alliance is when you share the risk, when both companies have a true incentive to share the information.[276] You do not mind the people from either company working on your premises and you recognize the investments that both companies make. By contrast, in the case of contract research, you deliver something that the other party can develop further.

276 *See id.*