

GUNSTEIN PHARMACEUTICALS, INC.

A CASE STUDY in LIFE SCIENCES ENTREPRENEURSHIP

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Gunstein Pharmaceuticals, Inc.¹

Drs. George Gunderson & Michael Epstein

Case A: The Decision to Pursue a New Venture Entity

At the University of California, Napa Valley School of Medicine, George Gunderson and Michael Epstein were anything but birds of a feather. While Epstein was a spectacled, reserved professor of physiology, Gunderson was the outspoken, power-brokering director of neurological research. Despite these outward differences, their common interests would provide an intriguing story commencing at the start of a new millennium.

At the age of 46, Gunderson arrived at UCNV in 1995 with two decades of neurophysiology research experience including his Ph.D. from Yale University and subsequent post-doctoral appointments he considered to be “dead-end roads.” Gunderson’s original master plan was to involve himself in the academic hotbed of prominent scientific research and then to make a timely and profitable jump into the corporate world through the leveraging of a valuable skill set. Although that plan hadn’t exactly panned out, Gunderson had distinguished himself through nationally recognized neuropharmacology research while also collecting valuable business experience through leadership roles at several universities and through Scientific Advisory Board positions with three separate biopharmaceutical firms. This had resulted in a global network of expert scientific contacts. In his spare time Gunderson was an amateur race car driver which, like all of his other life endeavors, was a skill he acquired quite easily. Surveying these successes, he began thinking that he could start his own company. In comparison to his scientific work and analogous to his hobby as a race driver, he regarded the process of running a

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The names of the companies and the people involved in the case have been changed to protect confidentiality. The case was prepared as a basis for class discussion rather than to illustrate effective or ineffective management of specific situations or issues.

business as a simple task that could be mastered as an add-on to his concomitant university faculty and administrative duties.

Michael Epstein arrived at UCNV in 1984 having earned a highly desired position as a physiology professor. Epstein was 36 years old at the time and was transitioning from the University of Iowa where he had earned his Ph.D. and spent 10 more years performing post-doctoral research. Growing up on a farm in rural Oklahoma, he was indoctrinated with the values of trust, honesty, hard work and clean living. His fascination with wildlife on the family farm and the related process of observing nature had led him into a career in bioscience, which was his sole vocational interest. As an academic scientific type, Epstein had little interest, and even less experience, in business endeavors. As an overachiever, he had become a world authority on mammalian reproductive physiology, his academic interest and specialty. Above all else, Dr. Epstein valued his position at UCNV, and he fully intended to remain there for the duration of his career.

When Gunderson approached Epstein in 1998 to discuss a “business proposition,” Epstein was not overly enthusiastic. Gunderson opened the conversation stating that he had read some of Epstein’s recent publications and was impressed with the potential commercial applications that could arise from Epstein’s Sertoli cell research involving the creation of immune-privileged sites. With the line having been cast, Gunderson thought he saw the bobber move when Epstein responded, “Yeah, someone will probably make a million on it some day.” But when Gunderson noted, “That someone could be you,” Epstein retorted that he wanted no part of any operation that might threaten his position at UCNV. With this statement, Epstein was referring to the risk of incurring a conflict of interest situation in which university-financed time, services, or goods might be utilized in the pursuit of private enterprise. Nonetheless, Gunderson felt that he had drawn first blood in a potential business partnership and that Epstein would be back to talk. He was correct.

Gunderson’s vision was to license faculty-generated, UCNV-patented intellectual property (IP) to create products in the biotechnology sector. Since such licensing of IP generally requires prior consent by the university, and possibly the inventing professor, Gunderson realized that a partnership of faculty-inventors would be the most rapid route to a large IP portfolio. Further, he

could influence future relevant UCNV IP to pass through his control by leveraging his academic directorship and by manipulating material contacts so that he would always have the right of first refusal on new developments in his specialty area. Finally, he surmised that he could finance most of the firm's early research and development by mixing university targeted research funds with state and federal matching funds for small business start-ups.

Soon after Gunderson and Epstein's initial meeting, University of Washington professor William Villeneuve released news of his success in extracting and replicating human embryonic stem cells while Johns Hopkins professor John Gearhart followed soon after with an announcement of a similar success with embryonic germ cell lines. Suddenly a new scientific era had arrived with all eyes being focused on stem cell applications for human disease. At the time of Villeneuve's and Gearhart's announcements, Gunderson was completing studies utilizing stem cells derived from human umbilical cord blood to improve neurological outcomes in acute stroke syndromes in a rat model. Gunderson felt he was well positioned to become a "player" in this area—both in the academic and business realms. On the basis of the experimental success in a rat model, Gunderson filed, and was granted, a U.S. Patent for treating acute strokes in humans through the use of human umbilical cord blood-derived stem cells. **(Exhibit 1)**

With these turns of events, and in his role as a university medical research director, Gunderson soon found himself a sought after speaker at UCNV and elsewhere. At one such engagement in the fall of 1998, he found himself in front of a group of UCNV researchers and professors that included Epstein. It was apparent, as Epstein listened to Gunderson's fascinating research presentation, that Epstein was interested in the potential ramifications of immuno-tolerance from Sertoli cells with cellular transplantation of umbilical cord blood-derived stem cells. At the end of the presentation, Gunderson answered one-on-one questions with various members of the audience while managing to steer clear of Epstein until the last person's questions had been answered. Soon afterwards, the two were talking – first in the lecture hall and subsequently over lunch – with Epstein outwardly excited and Gunderson characteristically calm about the once taboo commercial applications of their university research. Gunderson agreed with Epstein that the Sertoli cell work had promising synergistic therapeutic applications to the neurological research presented that day, and Gunderson slowly sold the potential partnership as a "win-win"

and “no-lose” entity. Basically the project would be “win-win,” Gunderson explained, in that both professors would be stockholders and could potentially become multi-millionaires, if all went right. The “no-lose” aspect held, Gunderson reasoned, because the financing would be done all through third-party money while their corporate work time would be taken from their standard university-allotted weekly free time. Epstein began dreaming of applications of his lifelong work with the Sertoli cell, and he was quickly sold on the idea. Because Gunderson would act as the managing partner, and because he “wasn’t in it for the money,” Epstein was happy to accept a 20% minority equity stake in the potential partnership. Now that Gunderson had things initiated, all that remained was a feasibility study to assess the potential market for the products that might emerge from the potential firm’s assembled collection of IP.

In the spring academic semester of 1999, Gunderson identified an opportunity for a free market assessment to be performed by a group of UCNV business students taking a course in entrepreneurial strategic market assessment. For the professors’ potential biotechnology partnership, the students assessed all relevant IP, the business applications that Gunderson and Epstein suggested, the current and future projected markets, the projected competitors, timelines for product development, the required human resources, and the available financing methods. The major result of this study was the students’ strong recommendation that such a project was not only feasible, but had a significant possibility of success. The group also made supporting recommendations, including one caveat that the professors should procure at least one outside vehicle of finance, in addition to the state and federal grants targeted. This additional funding would more easily ensure that a dedicated staff and management team consistent with industry standards could be put in place during the start-up period and developed in a timely and appropriate manner as the firm grew, that a strong, experienced legal team could be retained immediately, and that a clear separation would exist between the university and the business.

Gunderson was happy to hear an outside group, even if “only a group of MBA students”, echo his overall thoughts that the idea was a winner. Despite the latter recommendations, which made Epstein “nervous” but were interpreted by Gunderson as mere “suggestions”, which he could, and would, easily choose to ignore, Gunderson was able to maintain a cohesive partnership by focusing on the sweet while pushing back the sour. Even though there always remained the

unanswered “What Ifs” in the back of Epstein’s mind, Epstein was led closer to the dream of a new venture with Gunderson’s reminders of “win-win” and “no-lose”, in addition to Epstein’s visions of newfound career visibility.

Case B: Valuing and Financing a Start-Up

It was November 1999, and six months had passed since Gunderson had forged the verbal agreement of partnership between himself and Epstein. With the biotech industry ripe with investors looking to enter the market of stem cell therapies—considered by many to be “the next Microsoft” financial investment opportunity—Gunderson was losing time due to inertia. The fledgling company needed a name, a business plan, and a sound method of long-term financing to be considered a legitimate contender in such an industry. Further, Epstein had again gotten cold feet after Gunderson had asked him to put up \$3,000 of paid-in capital to secure funds for the legal processes required—to write contracts, file for incorporation, license IP from the university, and apply for patents on IP not affiliated with UCNV. Although Gunderson was simultaneously paying \$12,000 in capital, Epstein was upset that a cash investment was being requested as this flew in the face of Gunderson’s initial “no-lose” assurance with funding from outside sources.

Gunderson chose this time to refresh the dream when he said to Epstein, “Michael, I’ve been thinking about our company and how we need to choose a name. Do you think that *Epderson Pharmaceuticals* or *Gunstein Pharmaceuticals, Inc.* is better?” Once again catching Epstein off-guard, Gunderson had to wait a few moments before Epstein chose the latter as the better of the two. Gunderson then nodded his head in agreement and said, “Yes, it’s a little smoother sounding. But I really wanted your name to be the headliner since your partnership means so much to me. Are you sure that ‘*Gunstein Pharmaceuticals, Inc.*’ is okay?” When Epstein nodded in affirmation, Gunderson smiled and finished, “Then ‘*Gunstein Pharmaceuticals, Inc.*’ it is. And Michael...don’t worry about the \$3,000. I’ll return it to you as soon as we get our seed money from the first investor.” Flustered from arguing his case, Epstein nodded and Gunderson cemented his role as *Gunstein Pharmaceuticals, Inc.*’s managing partner.

With a portion of the \$15,000 of paid-in capital, Gunderson retained a patent attorney to review the relevant IP and to make recommendations. Primarily, *Gunstein Pharmaceuticals, Inc.* would focus on an IP portfolio of two major technologies: UCoCe, human umbilical cord blood-derived stem cells for treatment of acute neurologic disorders (stroke, spinal cord injury, and traumatic

brain injury) and SeCe, mammalian Sertoli cells for immune-modulation in cellular and organ transplantation. While the UCoCe product would attract a defined annual market of approximately 500,000 Americans suffering from acute neurologic disorders, the SeCe market was only characterized as having potential synergistic applications with UCoCe and other types of cellular and organ transplant therapies (e.g., pancreatic cells in diabetics). The firm's retained patent attorney, referred to Gunderson by one of his fiscally-conscious business contacts, offered to review the Patent Office claims, broaden their substance in order to reduce the likelihood of legal competition from knockoff producers, and finalize long-term licensing agreements with UCNV. Although Gunderson admitted that he was no expert in this area, the attorney's work seemed adequate and quite inexpensive in comparison to other quotes Gunderson had received.

With the IP issues better defined, Gunstein Pharmaceuticals, Inc. was ready to become a reality. Retaining a competitively priced corporate attorney recommended by UCNV's Department of Licensing, Gunderson and Epstein hammered out the articles of incorporation with attorneys from the UCNV, which had a 5% equity stake in the venture per the long-term IP licensing agreement. Characteristics of the new firm included:

- 2,000,000 shares of privately held, authorized stock (valued at \$1 each)
 - 760,000 to Gunderson; 190,000 to Epstein; 50,000 to UCNV
 - 1,000,000 held in reserve
- Right to issue stock options – equity value based on most recent valuation
- Board control of option vesting schedules and strike valuations
- No stock option dilution limits (except that UCNV must retain 5% equity)
- Corporate right of first refusal in event of equity resale to outside parties
- Limit of 5% equity ownership to any non-partnered holder
- Equity resale lock-up periods of 30-days prior and 180-days after IPO
- No guaranteed equity value upon corporate merger or buy-out

Essentially, Gunderson wanted to: 1) ensure that no outsider could gain control of the firm, 2) allow the firm to conserve cash by paying for future services with non-cash assets (i.e., stock

options), and 3) minimize the firm's future liability in the event of decaying equity valuations. The most difficult time the group had with the incorporation process was during the valuation procedure, which ultimately was performed by summing a net present value calculation of projected UCoCe cash flows with an arbitrary value for SeCe. Specifically, the value of the UCoCe, Gunderson's primary contribution to the firm's IP, was calculated based on a perpetuity incorporating the probability of market success, potential sales and expected profit margins. The SeCe, Epstein's contribution, was simply calculated as 25% of the value of UCoCe. Because this final formula was consistent with Gunderson's and Epstein's prior pact, it drew no major objections from those involved and resulted in a round figure very close to the founders' overall target valuation of \$2 million, it was accepted by the group despite its marginal financial foundation. When this consensus was reached, the deal was brokered with the resultant birth of Gunstein Pharmaceuticals, Inc. on January 6, 2000. **(Exhibit 2)**

Following this success, Gunderson and Epstein were left with the largest of all tasks to date: raising cash for initial investment. Although Epstein maintained the status of being "officially out" of all such endeavors, Gunderson remained confident of success given that he had been a *scientific advisor* in a number of biotechnology firms and "understood the games" of finding investors. Armed with the "business plan" that had been prepared for him by the UCNV strategic market assessment class in the spring of 1999, Gunderson hit the road to expound to potential investors the virtues of Gunstein Pharmaceuticals, Inc. While Gunderson had told Epstein, "We'll be looking for \$10 million initially, but we'll settle for five," reality illustrated this road to be much rougher than anticipated. About 15 trips and 9 months later, Gunderson had identified no interested investors. Off the traditional finance route, the firm had found some success in securing Small Business Innovation Research (SBIR) Grants, Small Business Technology Transfer (STTR) Grants and California Napa Valley Hi-Tech Corridor Matching Grants totaling \$2.5 million, but this money was restricted from use in business operations. **(Exhibit 3)** Therefore, Gunstein Pharmaceuticals, Inc. – without office, equipment or employees and with its only available funding ineligible for use in securing these critical corporate building blocks – was a company in name only. Further, the investment market, slowed by an evolving recession and awaiting the disputed Bush-Gore presidential election outcome, promised little assistance to companies caught short of funding, especially cash.

About this time Epstein, unable to enjoy his drink after being led to water, began to see Gunderson's dream become Epstein's personal nightmare. First, Gunderson was injured while learning to race motorcycles in December 2000 and was unable to participate in the firm's activities for six months. During this time Epstein was repeatedly pestered by UCNV licensing officials with financial questions he could not answer. Additionally, rumors through the medical school grapevine suggested that Epstein and Gunderson were under investigation for a conflict of interest with respect to their simultaneous roles as officers and employees of Gunstein Pharmaceuticals, Inc. and employees of the university. Further, a former colleague from the University of Iowa was suing Epstein and Gunstein Pharmaceuticals, Inc. for patent infringement with respect to the firm's use of the Sertoli cell IP. Finally, Gunderson had not paid Epstein back his \$3,000, which reminded Epstein that he should have followed his initial instinct to stay out of private enterprise while focusing all of his energy on his true missions, research and teaching.

When Gunderson was finally able to return to his duties, Epstein, his hair now a touch more silver, had reached the end of his proverbial rope. Having received no social, financial or legal support from the firm during Gunderson's absence, the out-of-place physiology professor had given legal statements and made partial resolution with his former colleague regarding Sertoli cell patents while simultaneously managing to fend off a plethora of anxiety-provoking questions from the Dean's office regarding his daily use of time. Now out of patience, he informed Gunderson that Gunderson had two options: buy out Epstein's 160,000 shares of private Gunstein Pharmaceuticals, Inc. stock or secure a financing package consistent with prior promises that would allow the firm to develop its enterprise while paying him back his \$3,000. Epstein gave Gunderson 120 days to make a decision.

For one split second Gunderson felt out of control of "his" company, and it was uncharacteristically unnerving. He realized that he would need to secure investment capital immediately, or else he would need to find \$160,000 to prevent Epstein from selling a significant portion of the firm's stock to an outsider in early September 2001. Fortunately, at this time, President George W. Bush placed a moratorium on the research of new lines of fetal derived stem cells. This potentially strengthened the competitive advantage of Gunstein Pharmaceuticals, Inc.'s UCoCe stem cell product, which did not fall under the same sanctions.

Gunderson was introduced to North Coast Biotechnology, Inc., a publicly held, Greater Napa Valley-based umbilical cord blood storage firm that also had a Research division interested in performing research similar to that of Gunstein Pharmaceuticals, Inc. In a move of near-desperation, Gunderson made a pitch to North Coast Biotechnology, Inc. for a merger between firms. With a strong sales pitch, the timely concomitant publication of his best neurological stem cell research in *Scientific American*, and a significant dose of luck, Gunderson closed the deal.

(Exhibit 4) While North Coast Biotechnology, Inc. received 43% of Gunstein Cell Pharmaceuticals, Inc.'s private stock and one of the firm's three board positions, Gunstein Cell Pharmaceuticals, Inc. received 40% of North Coast Biotechnology, Inc.'s public stock and \$250,000 in cash. With the transaction, Gunstein Pharmaceuticals, Inc.'s equity value had jumped from \$2 million to \$3 million – based on North Coast Biotechnology, Inc.'s \$1.50 a share valuation – and it had acquired an amount of capital, additional potentially liquid assets (i.e., publicly held North Coast Biotechnology, Inc. stock), a recognized partner and a new name (Gunstein Therapeutics, Inc.). Further, North Coast Biotechnology, Inc.'s CEO Wayne Brown assured Gunderson that when the time was ripe, the Gunstein Therapeutics, Inc. entity could go public through the North Coast Biotechnology, Inc. parent company in the form of an Equity Carve-Out IPO, a process in which Brown had participated “on numerous other occasions.”

The apparent success of the sudden merger seemed to heal all of the wounds between Gunderson and Epstein. While Gunderson had regained his confidence and swagger, Epstein had begun once again to dream outside of his professorship. From time to time, an occasional rumor within the medical center would unnerve him, but Gunderson would quickly squelch such noise with the voice of reason. Everything did seem better to Epstein when the September 2001 deadline finally arrived. And even though Gunderson hadn't returned the \$3,000 in time, Epstein had a promise that it would come the following month when targeted funds had been procured upon the SEC's endorsement of the pending transaction.

Case C: Enterprise Building

Gunderson sat in his medical center office with his feet propped on his desk early one morning and relaxed. “Don’t I deserve a moment of peace in hell?”, he reasoned after having run the new venture finance gauntlet for the last year. Today he felt so calm with respect to the prior year’s roller coaster of emotions that he likened himself to being in a plane’s cockpit after surviving a terribly rocky takeoff with now only smooth skies on the foreseeable horizon. The office phone rang abruptly breaking his serenity, and he picked up the receiver while staring at his calendar. The date September 11, 2001 glared at him as he recognized Epstein’s voice imploring him to “turn on the television to CNN....terrorists have knocked down the World Trade Center and bombed the Pentagon with hijacked airplanes!” What minutes earlier would have seemed a joke was now a reality that would further tighten investment financing, hinder pending deals from reaching fruition, and plunge the country into even more uncertainty. Gunderson’s mind raced and all he could imagine was a blocked merger deal with North Coast Biotechnology, Inc. and the resumption of hell’s fires. Even though he was set to surrender absolute individual control of the firm through the pending merger, he and Epstein would retain majority control on the basis of their combined equity shares and Board of Directors’ votes. Additionally, the associated cash infusion in the deal would provide the resources needed to fund initial operations. Not only was it a good deal for Gunstein Pharmaceuticals, Inc., it was the only deal in town and it was imperative that the deal come to fruition. Would it now all go up in smoke?

Gunderson quickly hung up with Epstein and phoned North Coast Biotechnology, Inc. CEO Dan Brown, who informed him, “We’ll really have to wait and see how this affects the SEC’s process. It might slow things down a bit, but I don’t see it changing things in the long run. Hang in there, George....we still want the deal, too.” Brown’s reassurances were a sort of double-edged sword for Gunstein Pharmaceuticals, Inc. Although the firm could still count on the merger, the time frame was now uncertain. Gunderson had recently rented office space at the university-affiliated incubator and had hired an M.B.A. (Mary Worthmoore), who was married to a medical student at the UCNV College of Medicine, to commence business operations.

Although the firm initially was paying Worthmoore solely in stock options, it would need cash soon to augment her contract as well as to pay operational overhead. Further down this one-way

street, Gunderson would need more cash for business development and the hiring of additional staff. Nothing of practical importance could proceed before the merger was finalized. Once started, however, further development could not be halted without forcing a bankruptcy, merger or sell-off due to non-reversible cash flow considerations. Therefore, Gunderson had little other choice but to stick to the current plan and hope that the SEC's decision would not be circumstantially and prohibitively delayed. Glancing again at the September 11th marked on his calendar, he found it ironic that perceptions could change in such a short time. Now his smooth skies had been invaded by wind shear and uncertainty again ruled the day.

For the next month Worthmoore killed time by pouring over the firm's prior records and legal documents while attempting to organize them into sensible order. Gunstein Pharmaceuticals, Inc. previously didn't have the money to employ an administrative assistant, so everything had been thrown into a pile in Gunderson's office "for future review." Over the subsequent month Worthmoore identified a number of problems with the firm's IP claims; however, Gunderson told her to develop a working problem list that could be analyzed following the pending merger's finalization. Among the issues on Worthmoore's list were the following:

- The fact that Epstein had signed over all rights for SeCe diabetes applications to his former Iowa colleague;
- The existence of loopholes in the UCoCe IP claims limiting Gunstein Pharmaceuticals, Inc.'s protected use only to that employing intravenous application;
- The oversight of Gunstein Pharmaceuticals, Inc. by UCNV IP Trustee Michael Polatino, a Board Member of a competing firm
- The need for Gunstein Pharmaceuticals, Inc. to cede 100% ownership of the firm to North Coast Biotechnology, Inc. before becoming eligible for an Equity Carve-Out IPO

When the SEC finally allowed the North Coast Biotechnology, Inc. merger in late October 2001, Worthmoore dropped her list of findings on Gunderson's desk. He was somewhat expectant of the first two issues, surprised by Polatino's hidden role and angry regarding the IPO limitations

in the last finding. “Find a new patent attorney that will take stock options as reimbursement so that we can re-file our IP; inform the university that Michael Polatino is no longer involved with Gunstein Pharmaceuticals, Inc. in any way; and don’t tell anyone else – including Michael – about the Carve-Out IPO situation,” he snapped at Worthmoore. When she asked what she should do with the outstanding bill of \$50,000 from the initial patent attorney, he answered, “Hold it back. They deserve no more compensation for that work.” Walking back to her work area, Worthmoore began to seriously reconsider her entry into the tumult of a startup enterprise.

Now that Gunderson had most of the initial start-up factors covered, at least the ones he considered relevant and material, he realized that the next tier of growth was beckoning. Following the stem cell industry valuation models developed by Worthmoore through research of competitor trends, he knew that his immediate focus should be on coordinating product research efforts, building a management team, identifying additional investors and forging strategic alliances in addition to that with North Coast Biotechnology, Inc. Gunderson still wasn’t sure which approach was the better fit for the firm’s product development: *The Gold Rush Method*, in which all focus would be placed on rapidly moving a product to market with an expected target date ranging from 6 to 8 years and an expected annual cash burn rate ranging from \$10 to \$40 million, or *The Explorer Style*, in which difficult-to-copy IP would be developed and utilized with an indefinite product target date and an expected annual cash burn rate ranging from \$200,000 to \$2 million. Despite this uncertainty, he felt that he could work on the other strategic areas and select the product development method in 6 to 9 months when the picture had become clearer.

At this particular time Gunderson found it most urgent to work on the research coordination and team building needs. He accomplished both simultaneously by hiring a science-oriented person to develop a research schedule, and he found a thrifty lead through the university’s Kauffman Internship program. For the low four-month price of \$2,000, Gunderson was able to retain a graduating M.B.A. student, who coincidentally was a practicing medical professional with several advanced degrees. Gunderson’s success at finding a general manager, however, did not fare as well, as multiple experienced candidates rejected the firm’s “non-negotiable” offer – a salary in the 40th percentile of the market range, no benefits, and 50% of pay in stock options. By this

time Gunderson, who had been quite busy with his own university directorship duties and had noted further problems getting Gunstein Pharmaceuticals, Inc.'s directed research started, decided that he'd stick with Worthmoore to oversee all operations and management while assigning the Kauffman student "to pick up the extra slack" in place of the not-ready-to-start research coordination project that had fallen through the cracks.

Over the next four months, Gunderson, with the aid of his value-priced team and an occasional appearance by Epstein, attempted to put things in order while attending to his busy university administrative schedule, initiating road meetings with potential investors, commencing Scientific Advisory Board meetings, and catching a few hours of sleep here and there. Although Gunderson maintained a will of iron and felt that he was making great progress, all of his staff, business partners, acquaintances, and informal advisors seemed to ask the same questions over and over:

- What will be the firm's exact product(s) and what is the introduction timetable?
- Who is on the management team? What experience do they have?
- When will you hire a CEO to take over your current role in the company?
- Where and when will you obtain the next rounds of financing to drive product research?
- Are any pharmaceutical or other biotechnology firms interested in partnering with Gunstein Pharmaceuticals, Inc.?
- What is your exit strategy?

Gunderson wasn't sure of the answers to any of the above questions, but he felt that he still had plenty of time to decipher the puzzle. He knew, without question, that he was in no rush to find a management team that might do things in opposition to his wishes. He also felt that upcoming research would better define product strategy, would provide increased interest from potential investors, and would lead to a reasonable exit strategy. Life's experiences had shown him that time and patience cure all ills, so why would Gunstein Pharmaceuticals, Inc.'s growing pains be any different?

When the Kauffman student's 4-month term had concluded, Gunderson noted the potential thinning of an already shallow management team. Despite what Gunderson considered to be a very generous offer – a Vice President's position and a starting salary consistent with the median reported for the prior year's class of students graduating from American business schools – the student turned him down and left the firm citing the failure of the “non-negotiable” offer to meet his opportunity cost, to offer provisions for benefits, or to compensate him in a form other than that of 100% illiquid stock options. Although Worthmoore was alarmed, Gunderson reassured her, “No big deal, Mary. We can get another deal on a Kauffman student next fall and conserve our cash for a rainy day. Cash is king – don't forget that.”

Part D: Products and Finance

It was December 15th, 2003 and Mary Worthmoore was busy trying to complete a “draft” term sheet for a potential “angel” investor for Gunstein Therapeutics, Inc. She had to get done for two reasons: the anticipated closure date of the investment would be January 31, 2004 and she had to go to a wedding tomorrow. During a short break, she reflected on an interesting prior eighteen months.

Doni Carr, PhD, a neuroscientist had been hired as Director of Research in July 2002 to coordinate and structure the research program, to assist in product development, and to be sure the R&D program supported the anticipated product development. Dr. Carr had just completed her PhD in Neuroscience. However, the focus during her training had been behavior and learning; she had no experience or training whatsoever in cellular biology, cellular transplantation, or cellular research design.

Shortly after this, Dr. Gunderson had hired a CEO for Gunstein Therapeutics, Inc.—Darren Hernandez, MD, PhD—a non-practicing physician with significant biotechnology industry experience. But this decision was an unmitigated disaster. As had been easily predicted, significant conflicts rapidly arose between Gunderson and Hernandez over the direction and management of the company. This caused difficulties for Worthmoore and Carr with regards to whom they really answered, and made the weakness and lack of depth in the corporate management team readily apparent. Gunderson fired Hernandez within four months and resumed the title of *interim* CEO—a mechanism to deflect and minimize any potential conflicts with UCNV and his academic/administrative positions.

The underlying structural problems for Gunstein Therapeutics, Inc. had remained during the eighteen month period—lack of a strong, experienced management team, lack of adequate financing, and no strategic alliances with the exception of the merger with North Coast Biotechnology, which itself had developed potentially serious drawbacks. There was no product development underway and no real direction or decisions made regarding product focus. The R&D had slowed almost to a complete halt due to a lack of adequate quantity and quality of

umbilical cord blood-derived stem cells. The source of the stem cells was supposed to be overflow cord blood from North Coast Biotechnology, Inc. But North Coast Biotechnology, Inc. had significant problems of its own.

After 9/11, the North Coast Biotechnology stock price had dropped from a price of \$6 to \$3 immediately and continued to fall to less than \$1 fifteen months later. **(Exhibit 5)** During this same period, the anticipated European expansion for cord blood storage had failed and resulted in an expense of \$1,000,000 to North Coast. A significant management restructuring occurred with Dan Brown moving to Chairman of the Board and a new CEO being hired. The SEC required significant restatement of North Coast Biotechnology financials after rigorous accounting audits, precipitated by the Enron scandal and the resultant federal legislation. The corporate accounting firm quit/was discharged (depending on whose version one chose to believe) and the restatement resulted in de-listing by the NASDAQ because of inadequate capitalization. There were charges of harassment and corporate malfeasance by one of the displaced executives, lawsuits regarding the attempted European expansion, and more lawsuits from stockholders over corporate governance, possible accounting shenanigans, and stock performance related to all of the above. Because of all of this, and a concomitant turndown in the cord blood storage business, North Coast Biotechnology was not terribly concerned about a lack of cord blood for Gunstein Therapeutics, Inc. and the new management would have preferred to eliminate the support to Gunstein Therapeutics, Inc. entirely, but contractual obligations prevented this action.

The difficulties at North Coast caused multiple problems for Gunstein Therapeutics, Inc. Operationally, it was impossible to re-invigorate the R&D program without an adequate source of high-quality umbilical cord blood stem cells. And North Coast had never supplied an adequate amount of high quality stem cells (1-3 samples per week versus the anticipated, and required 10-15 samples per week)—whether due to lack of donors, processing problems, or to a lack of commitment was unclear. An issue that was even more important was financial in nature. The 90% decline in value of the North Coast stock had a major impact on Gunstein Therapeutics' balance sheet. The restriction period on sale of North Coast Biotechnology stock had expired, to little benefit. Early after the merger, the plan had been to sell a portion of the 250,000 shares of

North Coast stock (when the price had been \$5-10 per share) to generate funding to expand operations and the management team, but selling the stock at \$0.75 per share (or less) was not a viable option. Further, Worthmoore had concerns regarding the fallout of the North Coast governance and credibility issues relative to Gunstein Therapeutics and its efforts to raise external financing.

A second Kauffman intern (another physician with 20 years clinical experience in cardiac surgery, now completing an MBA) had joined the company in January 2003 and had developed and pushed the ideas of developing an in-house cord blood processing facility and a network of hospitals to donate cord blood, and then selling research grade stem cell products as an interim revenue source. The reasoning was that these products would not require U.S. Food and Drug Administration (FDA) approval and could generate revenues (annual revenues predicted at approximately \$1M) during the 6-10 year development period for a human therapeutic and an established network of donor hospitals would be a valuable asset for Gunstein. Further, a successful subsidiary would diversify the product offerings of the company, lessen the risk for potential investors, and generate credibility within the biotechnology industry and the investment community. Worthmoore had been instrumental in these projects. She had developed the expense structure and the required capital estimates for funding of the projects. Dr. Carr did not demonstrate any particular interest in the projects—and it was unclear whether this was due to a lack of expertise and experience or some other reason. When the research products project was presented to Dr. Gunderson, he had proceeded to raise issue after issue, but all complaints basically focused on the breakeven sales point and the initial capital requirements of approximately \$500,000, particularly the investment required. **(Exhibit 6)** Worthmoore had raised the possibility of a capital infusion by the principals and had been resoundingly dismissed out of hand by Gunderson. It was obvious that the lack of a personal financial commitment by Gunderson and Epstein was hindering the performance of the company and this fact had also been raised as a major concern by many of the venture capitalists approached for potential investment.

The research products project was untenable without financial resources, but also required a significant source of umbilical cord blood; and the company still needed a source of cord blood

in addition to the occasional sample from North Coast, just for the research to continue. The attempted development of a network of 5 local and regional hospitals (Sonoma Regional Medical Center, Napa Valley Community Hospital, and San Andreas General Hospital being the three major institutions) to provide umbilical cord blood source material initially proceeded without significant difficulty. Development of the network would require cash to pay transport costs, infectious disease testing, technicians to process the blood, storage equipment, personnel to recruit donors, and donations to the hospitals and OB-GYN departments for the blood collection. After completion of all the preparatory work and agreements, Gunderson quashed this also, with complaints regarding the costs and time frame, but in reality, due to lack of corporate financial resources and a refusal to invest personal assets to establish the project. **(Exhibit 7)**

By June, it was apparent that the prior six months work had been for naught, and the company had made little, if any, progress. But a possible source of stem cells had unexpectedly appeared at that point. Cell-Stor, Inc. was a cord blood storage company, located in San Francisco, focused on non-directed storage for allogeneic stem cell transplants—primarily for treatment of hematological malignancy (i.e., leukemia, lymphoma, etc). Cell-Stor, Inc. had a significant donor network and more cord blood than it could process. Cell-Stor was interested in a university relationship with access to scientific protocols and credibility to assist Cell-Stor in development of potential umbilical cord blood-based therapeutics. The majority stockholder of Cell-Stor, Susan Tsen, was a strikingly beautiful 43 year-old Taiwanese-American millionaire businesswoman with numerous global businesses and investments. She had graduated from Stanford University with a degree in molecular biology and a Masters degree in Business. She had inherited significant holdings in Southeast Asia from her father, but had made other lucrative investments on her own. She had significant expertise and experience in the biotechnology industry and had participated in and supported multiple spin-outs from the University of California San Francisco, the University of California Berkeley, and Stanford University. Her usual mode of operation with new companies or new investments was to become the CEO, build the appropriate management team, and then move on to the next project. She was very attuned to an appropriate exit strategy and the timing of the exit at the appropriate valuation to recoup her investment. She was a pleasant lady, but a hard-nosed, take-no-prisoners businesswoman.

Gunderson felt this was the answer to his prayers (albeit prayer was not necessarily a priority in his life). In one fell-swoop, if he could pull this off, he would solve the cord blood source material problem and convince this “angel” to make a substantial investment in Gunstein Therapeutics. He figured \$5-10 million would be just what he needed, or rather, what the company needed. Gunderson sought out meetings with this individual and a significant rapport began to develop between the two—a lot of it based on a mutual interest in race cars, or so the story went...but who knew for sure?

In the fall of 2003, an opportunity arose to participate in an FDA-sponsored, “compassionate-use” clinical trial of the use of umbilical cord blood-derived stem cells in the treatment of amyotrophic lateral sclerosis (ALS)—Lou Gehrig’s disease. This opportunity had been proposed and recommended by the Susan Tsen, since she was aware of a physician in Moscow and another in Mexico City using whole human cord blood (as opposed to just the stem cells) to treat ALS—albeit with indeterminate results. Gunderson immediately recognized that the “compassionate use” process could result in moving the umbilical cord blood-derived stem cell technology into clinical use much more rapidly. This would also result in a major increase in profile for Gunstein Therapeutics, provide the opportunity to develop a significant revenue source by providing the processed stem cells (even to Moscow and Mexico City possibly—where the treatments were going for \$25,000 per bi-weekly course—that could result in a real “mark-up” and “margins”, if the FDA and Department of Commerce would just keep their noses out of it), and provide credibility of the technology and the company. However, the lack of standardized processing protocols and FDA-approved processing facilities, which would have been a direct result of the research products project rejected in the spring, limited the likelihood that this opportunity could be acted on by Gunstein Therapeutics.

Further, entry into this project would carry the potential of significant liability if there were any side-effects to the therapy—a question impossible to answer up-front. Gunstein Therapeutics had never carried liability insurance of any kind—general, product, or even director’s and officer’s (D&O). Gunderson was less than enamored with the minimum cost of \$25,000 for just D&O and general liability—the product liability would be at least an additional \$200,000, if it could be obtained at all. Gunderson was sure that this was all an unnecessary and excessive

expense and was totally opposed. But Epstein, Worthmoore, and Carr realized the potential risk and were not willing to proceed without insurance coverage.

Undaunted, Gunderson had proceeded with another meeting with Ms. Tsen to try to entice a \$5 million investment to underwrite the ALS project, in addition to another \$5 million for expansion of research and operations and development and completion of the management team of Gunstein. Gunderson instructed Worthmoore to develop a term sheet for the potential investment. She was not really comfortable doing this, feeling this should be handled by experienced corporate legal counsel. But Gunderson, in typical style, refused to pay for the legal advice and services and assured Worthmoore that she was more than capable.

Worthmoore had little hope that an experienced, wealthy, global businesswoman/investor would accept the terms outlined by Gunderson which allowed Gunderson to maintain operational and decision-making control despite the fact that a \$10M investment would be equivalent to a purchase of 90% of the company's equity. **(Exhibit 8)** Worthmoore also had significant doubt that Gunderson would cede control of the company for an investment of “only” \$10M—particularly when the investment would be targeted toward specific company projects and operations and would provide no true exit opportunity—with significant financial benefit—to Gunderson.

The term sheet **(Exhibit 9)** needed to be completed today since Gunderson was leaving tomorrow after his marriage to Doni Carr, and would not return until New Year's, after spending their honeymoon in Hawaii where he was also supposed to meet with Susan Tsen. Worthmoore had significant trepidation regarding what 2004 would hold—if Ms. Tsen refused the deal it was unclear whether the company could remain a going concern; and if Ms Tsen agreed to invest, what would the final terms of the deal be and what would the company look like then? Would Tsen keep the current management team, including Gunderson? Where would the next year take Worthmoore since her husband didn't graduate from UCNV College of Medicine for two more years, UCNV was not a hotbed of biotechnology, and San Francisco was too far to commute? “Well, like Scarlett O'hara, ‘I'll think about that tomorrow’”, she mused as she went to complete the term sheet for Gunderson.

Exhibit 1. Short Summary of Stem Cell Biology and Potential Therapeutic Uses

NATIONAL INSTITUTES OF HEALTH
May 2000

Stem Cells: A Primer

This primer presents background information on stem cells. It includes an explanation of what stem cells are; what pluripotent stem cells are; how pluripotent stem cells are derived; why pluripotent stem cells are important to science; why they hold such great promise for advances in health care; and what adult stem cells are.

Recent published reports on the isolation and successful culturing of the first human pluripotent stem cell lines have generated great excitement and have brought biomedical research to the edge of a new frontier. The development of these human pluripotent stem cell lines deserves close scientific examination, evaluation of the promise for new therapies, and prevention strategies, and open discussion of the ethical issues.

In order to understand the importance of this discovery as well as the related scientific, medical, and ethical issues, it is absolutely essential to first clarify the terms and definitions.

Definitions

DNA - abbreviation for deoxyribonucleic acid which makes up genes.

Gene - a functional unit of heredity which is a segment of DNA located in a specific site on a chromosome. A gene directs the formation of an enzyme or other protein.

Somatic cell - cell of the body other than egg or sperm.

Somatic cell nuclear transfer - the transfer of a cell nucleus from a somatic cell into an egg from which the nucleus has been removed.

Stem cells - cells that have the ability to divide for indefinite periods in culture and to give rise to specialized cells.

Pluripotent -capable of giving rise to most tissues of an organism.

Totipotent - having unlimited capability. Totipotent cells have the capacity to specialize into extraembryonic membranes and tissues, the embryo, and all postembryonic tissues and organs.

What is a stem cell?

Stem cells have the ability to divide for indefinite periods in culture and to give rise to specialized cells. They are best described in the context of normal human development. Human development begins when a sperm fertilizes an egg and creates a single cell that has the potential to form an entire organism. This fertilized egg is **totipotent**, meaning that its potential is total. In the first hours after fertilization, this cell divides into identical totipotent cells. This means that either one of these cells, if placed into a woman's uterus, has the potential to develop into a fetus. In fact, identical twins develop when two totipotent cells separate and develop into two individual, genetically identical human beings. Approximately four days after fertilization and after several cycles of cell division, these totipotent cells begin to specialize, forming a hollow

sphere of cells, called a blastocyst. The blastocyst has an outer layer of cells and inside the hollow sphere, there is a cluster of cells called the inner cell mass.

The outer layer of cells will go on to form the placenta and other supporting tissues needed for fetal development in the uterus. The inner cell mass cells will go on to form virtually all of the tissues of the human body. Although the inner cell mass cells can form virtually every type of cell found in the human body, they cannot form an organism because they are unable to give rise to the placenta and supporting tissues necessary for development in the human uterus. These inner cell mass cells are **pluripotent** — they can give rise to many types of cells but not all types of cells necessary for fetal development. Because their potential is not total, they are not totipotent and they are not embryos. In fact, if an inner cell mass cell were placed into a woman's uterus, it would not develop into a fetus.

The pluripotent stem cells undergo further specialization into stem cells that are committed to give rise to cells that have a particular function. Examples of this include blood stem cells which give rise to red blood cells, white blood cells and platelets; and skin stem cells that give rise to the various types of skin cells. These more specialized stem cells are called **multipotent**.

While stem cells are extraordinarily important in early human development, multipotent stem cells are also found in children and adults. For example, consider one of the best understood stem cells, the blood stem cell. Blood stem cells reside in the bone marrow of every child and adult, and in fact, they can be found in very small numbers circulating in the blood stream. Blood stem cells perform the critical role of continually replenishing our supply of blood cells — red blood cells, white blood cells, and platelets — throughout life. A person cannot survive without blood stem cells.

How are pluripotent stem cells derived?

At present, human pluripotent cell lines have been developed from two sources¹ with methods previously developed in work with animal models.

(1) In the work done by Dr. Thomson, pluripotent stem cells were isolated directly from the inner cell mass of human embryos at the blastocyst stage. Dr. Thomson received embryos from IVF (In Vitro Fertilization) clinics—these embryos were in excess of the clinical need for infertility treatment. The embryos were made for purposes of reproduction, not research. Informed consent was obtained from the donor couples. Dr. Thomson isolated the inner cell mass and cultured these cells producing a pluripotent stem cell line.

(2) In contrast, Dr. Gearhart isolated pluripotent stem cells from fetal tissue obtained from terminated pregnancies. Informed consent was obtained from the donors after they had independently made the decision to terminate their pregnancy. Dr. Gearhart took cells from the region of the fetus that was destined to develop into the testes or the ovaries. Although the cells developed in Dr. Gearhart's lab and Dr. Thomson's lab were derived from different sources, they appear to be very similar.

The use of somatic cell nuclear transfer (SCNT) may be another way that pluripotent stem cells could be isolated. In studies with animals using SCNT, researchers take a normal animal egg cell and remove the nucleus (cell structure containing the chromosomes). The material left behind in

the egg cell contains nutrients and other energy-producing materials that are essential for embryo development. Then, using carefully worked out laboratory conditions, a somatic cell - any cell other than an egg or a sperm cell - is placed next to the egg from which the nucleus had been removed, and the two are fused. The resulting fused cell, and its immediate descendants, are believed to have the full potential to develop into an entire animal, and hence are totipotent. As described in Figure I, these totipotent cells will soon form a blastocyst. Cells from the inner cell mass of this blastocyst could, in theory, be used to develop pluripotent stem cell lines. Indeed, any method by which a human blastocyst is formed could potentially serve as a source of human pluripotent stem cells.

Potential Applications of Pluripotent Stem Cells

There are several important reasons why the isolation of human pluripotent stem cells is important to science and to advances in health care. At the most fundamental level, pluripotent stem cells could help us to understand the complex events that occur during human development. A primary goal of this work would be the identification of the factors involved in the cellular decision-making process that results in cell specialization. We know that turning genes on and off is central to this process, but we do not know much about these "decision-making" genes or what turns them on or off. Some of our most serious medical conditions, such as cancer and birth defects, are due to abnormal cell specialization and cell division. A better understanding of normal cell processes will allow us to further delineate the fundamental errors that cause these often deadly illnesses.

Human pluripotent stem cell research could also dramatically change the way we develop drugs and test them for safety. For example, new medications could be initially tested using human cell lines. Cell lines are currently used in this way (for example cancer cells). Pluripotent stem cells would allow testing in more cell types. This would not replace testing in whole animals and testing in human beings, but it would streamline the process of drug development. Only the drugs that are both safe and appear to have a beneficial effect in cell line testing would graduate to further testing in laboratory animals and human subjects.

Perhaps the most far-reaching potential application of human pluripotent stem cells is the generation of cells and tissue that could be used for so-called "cell therapies." Many diseases and disorders result from disruption of cellular function or destruction of tissues of the body. Today, donated organs and tissues are often used to replace ailing or destroyed tissue. Unfortunately, the number of people suffering from these disorders far outstrips the number of organs available for transplantation. Pluripotent stem cells, stimulated to develop into specialized cells, offer the possibility of a renewable source of replacement cells and tissue to treat a myriad of diseases, conditions, and disabilities including Parkinson's and Alzheimer's diseases, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis and rheumatoid arthritis. There is almost no realm of medicine that might not be touched by this innovation. Some details of two of these examples follow.

- Transplant of healthy heart muscle cells could provide new hope for patients with chronic heart disease whose hearts can no longer pump adequately. The hope is to develop heart muscle cells from human pluripotent stem cells and transplant them into the failing heart muscle in order to augment the function of the failing heart. Preliminary work in mice and other animals has demonstrated that healthy heart muscle cells transplanted into the heart successfully repopulate the heart tissue and work together with the host cells. These experiments show that this type of transplantation is feasible.
- In the many individuals who suffer from Type I diabetes, the production of insulin by specialized pancreatic cells, called islet cells, is disrupted. There is evidence that transplantation of either the entire pancreas or isolated islet cells could mitigate the need for insulin injections. Islet cell lines derived from human pluripotent stem cells could be used for diabetes research and, ultimately, for transplantation.

While this research shows extraordinary promise, there is much to be done before we can realize these innovations. Technological challenges remain before these discoveries can be incorporated into clinical practice. These challenges, though significant, are not insurmountable.

First, we must do the basic research to understand the cellular events that lead to cell specialization in the human, so that we can direct these pluripotent stem cells to become the type(s) of tissue needed for transplantation.

Second, before we can use these cells for transplantation, we must overcome the well-known problem of immune rejection. Because human pluripotent stem cells derived from embryos or fetal tissue would be genetically different from the recipient, future research would need to focus on modifying human pluripotent stem cells to minimize tissue incompatibility or to create tissue banks with the most common tissue-type profiles.

The use of somatic cell nuclear transfer (SCNT) would be another way to overcome the problem of tissue incompatibility for some patients. For example, consider a person with progressive heart failure. Using SCNT, the nucleus of virtually any somatic cell from that patient could be fused with a donor egg cell from which the nucleus had been removed. With proper stimulation the cell would develop into a blastocyst: cells from the inner cell mass could be taken to create a culture of pluripotent cells. These cells could then be stimulated to develop into heart muscle cells. Because the vast majority of genetic information is contained in the nucleus, these cells would be essentially identical genetically to the person with the failing heart. When these heart muscle cells were transplanted back into the patient, there would likely be no rejection and no need to expose the patient to immune-suppressing drugs, which can have toxic effects.

Adult Stem Cells

As noted earlier, multipotent stem cells can be found in some types of adult tissue. In fact, stem cells are needed to replenish the supply cells in our body that normally wear out. An example, which was mentioned previously, is the blood stem cell.

Multipotent stem cells have not been found for all types of adult tissue, but discoveries in this area of research are increasing. For example, until recently, it was thought that stem cells were

not present in the adult nervous system, but, in recent years, neuronal stem cells have been isolated from the rat and mouse nervous systems. The experience in humans is more limited. In humans, neuronal stem cells have been isolated from fetal tissue and a kind of cell that may be a neuronal stem cell has been isolated from adult brain tissue that was surgically removed for the treatment of epilepsy.

Do adult stem cells have the same potential as pluripotent stem cells?

Until recently, there was little evidence in mammals that multipotent cells such as blood stem cells could change course and produce skin cells, liver cells or any cell other than a blood stem cell or a specific type of blood cell; however, research in animals is leading scientists to question this view.

In animals, it has been shown that some adult stem cells previously thought to be committed to the development of one line of specialized cells are able to develop into other types of specialized cells. For example, recent experiments in mice suggest that when neural stem cells were placed into the bone marrow, they appeared to produce a variety of blood cell types. In addition, studies with rats have indicated that stem cells found in the bone marrow were able to produce liver cells. These exciting findings suggest that even after a stem cell has begun to specialize, the stem cell may, under certain conditions, be more flexible than first thought. At this time, demonstration of the flexibility of adult stem cells has been only observed in animals and limited to a few tissue types.

Why not just pursue research with adult stem cells?

Research on human adult stem cells suggests that these multipotent cells have great potential for use in both research and in the development of cell therapies. For example, there would be many advantages to using adult stem cells for transplantation. If we could isolate the adult stem cells from a patient, coax them to divide and direct their specialization and then transplant them back into the patient, it is unlikely that such cells would be rejected. The use of adult stem cells for such cell therapies would certainly reduce or even avoid the practice of using stem cells that were derived from human embryos or human fetal tissue, sources that trouble many people on ethical grounds.

While adult stem cells hold real promise, there are some significant limitations to what we may or may not be able to accomplish with them. First of all, stem cells from adults have not been isolated for all tissues of the body. Although many different kinds of multipotent stem cells have been identified, adult stem cells for all cell and tissue types have not yet been found in the adult human. For example, we have not located adult cardiac stem cells or adult pancreatic islet stem cells in humans.

Secondly, adult stem cells are often present in only minute quantities, are difficult to isolate and purify, and their numbers may decrease with age. For example, brain cells from adults that may be neuronal stem cells have only been obtained by removing a portion of the brain of epileptics, not a trivial procedure.

Any attempt to use stem cells from a patient's own body for treatment would require that stem cells would first have to be isolated from the patient and then grown in culture in sufficient numbers to obtain adequate quantities for treatment. For some acute disorders, there may not be enough time to grow enough cells to use for treatment. In other disorders, caused by a genetic defect, the genetic error would likely be present in the patient's stem cells. Cells from such a patient may not be appropriate for transplantation. There is evidence that stem cells from adults may not have the same capacity to proliferate as younger cells do. In addition, adult stem cells may contain more DNA abnormalities, caused by exposure to daily living, including sunlight, toxins, and by expected errors made in DNA replication during the course of a lifetime. These potential weaknesses could limit the usefulness of adult stem cells.

Research on the early stages of cell specialization may not be possible with adult stem cells since they appear to be farther along the specialization pathway than pluripotent stem cells. In addition, one adult stem cell line may be able to form several, perhaps 3 or 4, tissue types, but there is no clear evidence that stem cells from adults, human or animal, are pluripotent. In fact, there is no evidence that adult stem cells have the broad potential characteristic of pluripotent stem cells. In order to determine the very best source of many of the specialized cells and tissues of the body for new treatments and even cures, it will be vitally important to study the developmental potential of adult stem cells and compare it to that of pluripotent stem cells.

Summary

Given the enormous promise of stem cells to the development of new therapies for the most devastating diseases, it is important to simultaneously pursue all lines of research. Science and scientists need to search for the very best sources of these cells. When they are identified, regardless of their sources, researchers will use them to pursue the development of new cell therapies.

The development of stem cell lines, both pluripotent and multipotent, that may produce many tissues of the human body is an important scientific breakthrough. It is not too unrealistic to say that this research has the potential to revolutionize the practice of medicine and improve the quality and length of life.

¹ Michael Shamblott, *et al*, Derivation of pluripotent stem cells from cultured human primordial germ cells. *PNAS*, 95: 13726-13731, Nov. 1998.

James Thomson, *et al*, Embryonic stem cell lines derived from human blastocysts. *Science*, 282: 1145-1147, Nov. 6, 1998.

Exhibit 2. NPV Valuation of Gunstein Pharmaceuticals, Inc.—January 2000

GUNSTEIN PHARMACEUTICALS, INC. PRO-FORMA VALUATION (JANUARY 2000)

| | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|-----------------------------|---------|----------|----------|----------|----------|-----------|------------|------------|------------|------------|
| Revenues ¹ | 0 | 0 | 100,000 | 125,000 | 0 | 750,000 | | 750,000 | 30,000,000 | 50,000,000 |
| Expenses | 25,000 | 150,000 | 325,000 | 300,000 | 325,000 | 350,000 | 350,000 | 350,000 | 2,000,000 | 3,000,000 |
| Net Income | -25,000 | -150,000 | -225,000 | -175,000 | -325,000 | 400,000 | -350,000 | 400,000 | 28,000,000 | 47,000,000 |
| Investment ² | | | | 200,000 | 200,000 | 1,200,000 | 900,000 | 2,150,000 | | |
| Free Cash Flow ³ | -25,000 | -150,000 | -225,000 | -375,000 | -525,000 | -800,000 | -1,250,000 | -1,750,000 | 28,000,000 | 47,000,000 |

¹Revenues thru 2006 are non-taxable SBIR/STTR grants unavailable for general corporate operations

²Investment assumed to be venture capital

³Assume Sales begin 2007—6,000 units @ \$5,000 per unit
2008—10,000 units @ \$5,000 per unit

Assumptions: All Cash Flows from UCoCe

Valuation of UCoCe = \$1.6M

Valuation of SeCe IP: Valuation of UCoCe x 0.25 = \$1.6M x 0.25 = \$0.4M

**Total Valuation of Gunstein Pharmaceuticals, Inc.: \$1.6M + \$0.4M = \$2.0M
(January 6, 2000)**

Exhibit 3. Summary of SBIR/STTR Grants

Small Business Innovation Research (SBIR)

The SBIR Program is a Congressionally-mandated program, established in 1982 to increase the participation of small businesses in federal research and development (R&D). Ten (10) federal agencies, including: the Departments of Agriculture, Commerce, Defense, Energy, Education, Health and Human Services, Transportation, and the EPA, NASA and National Science Foundation, are required to reserve 2.5% of its external R&D budget for competitively selected SBIR awards to small businesses.

Annually, these agencies identify various R&D topics for pursuit by small businesses. The topics represent scientific and technical problems requiring innovative solutions and are bundled together into individual agency "solicitations" which are distributed to interested small businesses.

The goal of the SBIR Program is to tap into the innovativeness and creativity of the small business community to help meet government R&D objectives. At the same time, these small companies develop technologies, products, and services, which they can then commercialize through sales in the private sector or back to the government." However, strategically important provisions in the law allow products and services that have been developed under the SBIR* and STTR* programs to be procured on a sole source basis by US government agencies.

The program is offered to small companies:

- With less than 500 employees
- That employs the principle investigator (PI)."Primary employment with a small business precludes full-time employment at any other organization."
- At least 51% ownership by a US citizen.
- Performs 40% of Phase I and Phase II research with in the US. At least one person in Management who primary employment is with the applying firm.

"The small business may subcontract a portion of its work, so long as the small business "prime" performs at least two-thirds of the Phase I work and 50% of the Phase II work. For the purposes of determining compliance, percent of work is usually measured by both direct and indirect costs; however, the actual method of measurement will be verified during contract negotiations

The advantages to the small businesses: the SBIR provide funding or "seed money" for early stage innovative high-risk projects; allowing the inventor to maintain full equity ownership, ownership of the technology and intellectual property and no cash payback even if the innovation is unsuccessful.

Phase I is the entry point to this program. The inquiring company submits a proposal in response to a topic. The proposal should be no more than 25 pages and must comply with explicit, easy-to-follow instructions spelled out in the solicitation. Then it is competitively selected from solicitation submitted annually for a ward of 70,000 with an option for up to 50,000. The company must prove feasibility within 6 months. Winning SBIR proposals and grant requests have to provide answers to two primary questions:

What is so special about what is being proposed?

Why should the reviewer believe that the technology would actually be commercialized if you get the money?

The company then can submit an additional proposal for **Phase II** with would provide a SBIR for a grant of up to \$730,000 over a two-year period. 40% of Phase II proposals are selected from the successful Phase I companies/innovations. “In **Phase II Plus**, the Army provides matching SBIR funds (up to \$100,000) and allows for an existing Phase II effort to be extended for up to one year to perform additional research and development.” SBIR funding is terminated at Phase II; there is no funding for Phase III. The company is encouraged to seek investments from the private sector to expand economic growth.

Small Business Technology TRansfer (STTR)

The STTR program is funded separately goals and the goal is slightly different: to spur economic growth and strengthen industrial competitiveness. Contracts are competitively awarded to small businesses for research and development projects conducted in cooperation with research institutions. Obviously this provides a strong incentive for small businesses and technical experts at research institutions to join forces.

The STTR program has the same criteria as the SBIR with two additional components:

A written agreement must be negotiated with the research institution apportioning intellectual property

Phase I and Phase II research work must be performed by the small business and the research institution in the United States. (Joint ventures and limited partnerships are permitted for the small business provided the entity so created qualifies as a small business.)

The research institution qualifies as follows:

- A nonprofit university or college
- A nonprofit institution owned and operated exclusively for scientific or educational purposes;
- A contractor operated, federally funded, R&D center (FFRDC).

| | SBIR | STTR |
|-----------------|---|---|
| Phase I | Max 100,000 (vary by agency) | Max 100,000 |
| Phase II | Based on phase I results Max 750,00 (vary by agency) | Based on Phase I Max 500,000 |

Army SBIR

“The Army participates with the Navy, Air Force, and six other defense agencies under the overall DoD SBIR Program; however, the Army program is independent in that it seeks to support Army-specific goals within the framework of the Department of Defense (DoD) SBIR Program. The Army’s FY01 SBIR budget of \$135M will fund approximately 250 Phase I and 150 Phase II new starts. The Army makes about 200 Phase I and 100 Phase II contract awards

each year. About one in ten Phase I proposals, and one in three Phase II proposals, are selected for negotiation and award.”

The Army conducts a two level review of Phase I proposals received in response to a solicitation topic.

1. The Laboratories and Centers who "own" the topics perform a thorough technical evaluation and select the proposals to move to the next level.
2. A panel of senior Army scientists and technologists reviews the best proposals then selects the proposals that satisfy Army needs.

The Army SBIR schedule for Phase I is follows:

| | |
|---------------------|-------------------|
| Topic Pre-Release | May - July |
| Solicitation Open | July - August |
| Phase I Evaluations | August - November |
| Phase I Selections | November |
| Phase I Awards | December |

Army STTR

The biggest difference between an Army SBIR and a STTR is that proposals must be submitted by a strategic partnership between a small business and a research institute. (I think that Freeman has proposed this with USF, UM) SBIR proposals must be submitted by any U.S.-based small business, and can include other (nongovernmental) “organizations as long as the small business does at least two-thirds of the Phase I work and one-half of the Phase II work.”

| | SBIR | STTR |
|----------------------|---|--|
| Phase I | 6 months, \$70,000 max | One year, \$100,000 max |
| | 4-month option (at Gov’t discretion), \$50k max, to fund interim Phase II efforts. | No options |
| Phase II | 2 years, \$730,000 max | 2 years, \$500,000 max |
| Phase II PLUS | 1 year, \$100,000 max (subject to third-party matching funds) | |
| Phase III | No time limit No SBIR funds | No time limit No STTR funds |

Source: Army Research Office

Exhibit 4. Press Release—North Coast Biotechnology Inc. and Gunstein Pharmaceuticals Inc.

For Immediate Release

North Coast Biotechnology, Inc. Finalizes Merger Agreement with Gunstein Pharmaceuticals, Inc.

San Francisco, CA—December 1, 2001—Daniel Brown, Chairman and Chief Executive Officer of North Coast Biotechnology, Inc. and Dr. George Gunderson, Chairman of Gunstein Pharmaceuticals, Inc. jointly announced that a merger had been completed between the research subsidiary of North Coast Biotechnology, Inc. and Gunstein Pharmaceuticals, Inc. North Coast Biotechnology will own approximately 40% of the merged company Gunstein Therapeutics, Inc.

The focus of the new company will be to develop therapeutics for the treatment of stroke, spinal cord injury, and traumatic brain injury using umbilical cord blood-derived stem cells.

Pursuant to the terms of the merger agreement, North Coast Biotechnology, Inc. cannot be called for any further capital investment either in cash or stock.

North Coast Biotechnology, Inc. is a publicly traded company (symbol...NCBT).

Exhibit 5. North Coast Biotechnology, Inc. Stock Chart (NCBT)



Exhibit 6. Gunstein Therapeutics, Inc. Research Products Division

| Item | Initial Capital Required (\$) |
|-----------------------------|--------------------------------------|
| | |
| Personnel | 165,000 |
| Facility Rent | 70,000 |
| Laboratory Equipment | 140,000 |
| Laboratory Furniture | 10,000 |
| Information Systems | 25,000 |
| Laboratory Supplies | 25,000 |
| Operations | 25,000 |
| | |
| Total Investment | 460,000 |

Exhibit 7. Gunstein Therapeutics, Inc. Umbilical Cord Blood Donor Network Project

| Item | Annual Expense (\$) |
|---------------------------------|----------------------------|
| | |
| Courier Service | 25,000 |
| Infectious Disease Tests | 75,000 |
| Personnel | 150,000 |
| Equipment | 50,000 |
| Donations | 50,000 |
| | |
| Total | 350,000 |

Exhibit 8. Gunstein Therapeutics, Inc. Balance Sheet—December 2003

ASSETS

| | |
|----------------------|-----------|
| Current Assets | |
| Cash | 110,000 |
| Grants | 400,000 |
| Total Current Assets | 510,000 |
| Fixed Assets | |
| Computer Equipment | 5,000 |
| Total Fixed Assets | 5,000 |
| Other Assets | |
| Investment Portfolio | 555,000 |
| TOTAL ASSETS | 1,070,000 |

LIABILITIES AND EQUITY

| | |
|---------------------------------------|-----------|
| Liabilities | |
| Current Liabilities | |
| N/P – North Coast Biotechnology, Inc. | 100,000 |
| Total Current Liabilities | 100,000 |
| Long-term Liabilities | 0 |
| Total Liabilities | 100,000 |
| Equity | |
| Capital Stock (4 million shares) | 1,000,000 |
| Paid in Capital | 20,000 |
| Retained Earnings | (50,000) |
| Net Income | 0 |
| Total Equity | 970,000 |
| TOTAL LIABILITIES and EQUITY | 1,070,000 |

GUNSTEIN THERAPEUTICS, INC.

INVESTMENT AGREEMENT

This Investment Agreement ("Agreement") is made effective ___ day of ____, 200X ("Effective Date"), by and between Gunstein Therapeutics, Inc. a Delaware corporation, having its principal place of business at UCNV, Center for Entrepreneurship, 101 Springs Boulevard, Suite 10, Napa Valley, CA 92636. ("GUNSTEIN"), _____, a ___ corporation, with offices at _____ ("INVESTOR"); (collectively the "PARTIES").

WHEREAS, GUNSTEIN is engaged in the business of designing and developing systems and products in the nature of cellular therapies and has, over the years, acquired and developed substantial and valuable technical knowledge, know-how, and experience in the design and development of such systems and products described in detail in Schedule A attached hereto (the "GUNSTEIN Technology"); and

WHEREAS, INVESTOR is engaged in acquiring and storing raw material related to GUNSTEIN Technology, has excess material and desires to allow GUNSTEIN to utilize the umbilical cord blood ("Raw Material") in the design, development and sale of the types of products listed in the attached Schedule A (the "Clinical Products"); and

WHEREAS, GUNSTEIN and LICENSEE believe it is in their mutual interest and desire to enter into an agreement whereby PARTIES would manufacture and sell Clinical Products pursuant to the terms and conditions hereinafter provided.

NOW, THEREFORE, in consideration of the premises and the mutual covenants of this Agreement, the parties hereto agree as follows:

1. INVESTMENT OVERVIEW AND GOVERNANCE.

- 1.1. **THE INVESTMENT.** INVESTOR and GUNSTEIN hereby agree to undertake the Investment during the Term under the terms and conditions set forth in this Agreement. The Investment shall include the ALS Treatment Program.
- 1.2. **ALS TREATMENT PROGRAM ("ALS-TP").** The goal of the ALS-TP is to develop therapeutic treatments using Raw Material and GUNSTEIN Technology for clinical applications ("ALS-Therapy").
- 1.3. **GOVERNANCE –** The strategic direction and day-to-day management responsibilities of the Investment shall be the responsibility of GUNSTEIN. GUNSTEIN shall have the following responsibilities:

- 1.3.1. to review the Research Plan from a strategic, scientific, operational, and marketing perspective, including consideration of expanding or contracting the Therapeutic Areas;
- 1.3.2. to make changes to the portions of the Research Plan relating to the ALS-TP as it deems necessary to accomplish the purpose of the Investment;
- 1.3.3. to propose other changes to the Research Plan to the Board of Directors (“BOD”) of each Party as it deems necessary to accomplish the purpose of the Investment;
- 1.3.4. to prioritize and monitor progress of new Clinical Products;
- 1.3.5. to review the progress and results of the Investment to ensure, to the extent reasonably practical, that the Parties are meeting their commitments for both human and financial support and are each fulfilling all of their respective contractual obligations;
- 1.3.6. to approve changes to the allocation of Investment Funds set forth in the Research Plan, so long as such changes do not cause the Investment to exceed the budget established;
- 1.3.7. to provide guidance as to the data package required in considering a Clinical Product for further development and commercialization efforts;
- 1.3.8. to review and monitor all results of the work performed under Investment, including scientific efforts of both Parties, and providing prioritization, oversight and direction regarding such work in accordance with the Research Plan;
- 1.3.9. to review and approve the use of any Third Party, including review and approval of any related Third Party contract; and
- 1.3.10. to establish and oversee an intellectual property program to optimize the value of the intellectual property arising from the Investment;

2. ALS TREATMENT PROGRAM (“ALS-TP”)

- 2.1. DESCRIPTION AND TERM. The ALS-TP shall be conducted by GUNSTEIN in accordance with the Research Plan. The ALS-TP Term shall become effective on the Effective Date and shall continue in effect for five (5) years, the Parties otherwise mutually agree to extend or terminate the ALS-TP, or the Investment is terminated in accordance with Section 12. Both Parties shall use commercially reasonable efforts to develop clinical treatments for ALS in accordance with the Investment Plan.
- 2.2. RESTRICTION ON INVESTOR’S RIGHT TO USE ALS-THERAPY. Except as otherwise expressly permitted by this Agreement, INVESTOR shall not (i) conduct any research on any ALS-Therapy directed thereto, outside the course of the Investment

either on its own or for a Third Party or (ii) grant or assign any rights to a Third Party with respect to any ALS-Therapy directed thereto.

2.3. DISCLOSURE. Know-How generated outside the course of the Investment by GUNSTEIN, including through use of ALS-Therapy, shall not be INVESTOR Know-How, and any resulting Patent Rights shall not be INVESTOR Patent Rights.

3. DEVELOPMENT, COMMERCIALIZATION, MANUFACTURING AND SUPPLY

3.1. RAW MATERIAL. INVESTOR shall supply Raw Material to GUNSTEIN. In the event that GUNSTEIN elects to obtain additional quantities of Raw Material for use outside of the Investment, GUNSTEIN shall so inform INVESTOR in writing specifying the additional quantity desired by GUNSTEIN. If INVESTOR is not able to supply Raw Material to GUNSTEIN or if GUNSTEIN determines to obtain supply of any such Raw Material from a Third Party, then INVESTOR will, at GUNSTEIN's request and expense, promptly transfer all necessary technology and technical assistance and grant all necessary rights and licenses to permit GUNSTEIN, a GUNSTEIN Sublicensee, or Third Parties on behalf of GUNSTEIN or a GUNSTEIN Sublicensee, to supply such Raw Material.

3.2. ALS-THERAPY. Upon request by INVESTOR, GUNSTEIN will supply all of INVESTOR's requirements of any ALS-Therapy required by INVESTOR through the completion of Phase II Clinical Trials on such ALS-Therapy.

3.3. DEVELOPMENT AND COMMERCIALIZATION. GUNSTEIN shall be solely responsible for all development and commercialization of ALS-Therapy, including toxicology, clinical development, regulatory, manufacturing and commercialization efforts, except as agreed otherwise by the Parties. GUNSTEIN and its Sublicensees shall have the sole right and responsibility for the preparation of any regulatory filings required in order to conduct clinical trials on ALS-Therapy in the Territory, together with the preparation of suitable applications for marketing approval in the Territory and shall be the owner and party of record of all such regulatory filings. INVESTOR shall cooperate with GUNSTEIN as reasonably required in preparing such regulatory filings including, without limitation, any and all data contained therein.

4. GRANT OF RIGHTS

4.1. LICENSES TO INVESTOR.

4.1.1. RESEARCH LICENSES. Subject to the terms and conditions of this Agreement, GUNSTEIN hereby grants to INVESTOR a non-exclusive, non-sublicensable, royalty free license, under the GUNSTEIN Technology solely to the extent necessary or appropriate to carry out INVESTOR's responsibilities under the Research Plan.

4.2. LICENSES TO GUNSTEIN.

4.2.1. RESEARCH LICENSES. Subject to the terms and conditions of this Agreement, INVESTOR hereby grants to GUNSTEIN:

4.2.1.1. an exclusive, sublicensable, royalty free license during the Investment Term under the INVESTOR Technology and INVESTOR'S rights to any JOINT INVESTMENT IP RIGHTS, as further described in Section 9, solely to the extent necessary or appropriate to carry out GUNSTEIN' responsibilities under the Research Plan;

4.2.1.2. an exclusive, sublicensable, royalty-bearing license under the INVESTOR Technology and INVESTOR'S rights to any JOINT INVESTMENT IP RIGHTS, as further described in Section 9, to conduct research outside the course of the Investment.

4.2.2. PRODUCT LICENSES. Subject to the terms and conditions of this Agreement, INVESTOR hereby grants to GUNSTEIN an exclusive, sublicensable, royalty-bearing license, including the right to sublicense, under INVESTOR Technology and INVESTOR'S rights to any JOINT INVESTMENT IP RIGHTS, as further described in Section 9, to develop, make, have made, use, import, offer for sale and sell ALS-Therapy in the Territory. GUNSTEIN shall provide INVESTOR with annual written reports that include a description of the research, development and commercialization activities by GUNSTEIN on any ALS-Therapy.

4.3. NO IMPLIED LICENSES. Except as expressly provided otherwise herein, neither Party hereto will be deemed by this Agreement to have been granted any license or other rights to the other Party's intellectual property rights.

4.4. TECHNOLOGY TRANSFER. Upon expiration or termination (other than for breach by INVESTOR) of the Investment Term, GUNSTEIN shall have the option to obtain a non-exclusive license, including the right to sublicense solely in connection with the grant of a license to develop, make, use, import, offer for sale and sell ALS-Therapy, to use the INVESTOR Technology and INVESTOR'S rights to any JOINT INVESTMENT IP RIGHTS, as further described in Section 9.

IN WITNESS WHEREOF, the Parties hereto, intending to be legally bound hereby, have each caused to be affixed hereto its or his/her hand and seal the day indicated.

Gunstein Therapeutics, Inc.

INVESTOR

By: _____

By: _____

Name:

Name: _____

Title:

Title: _____

Date: _____

Date: _____

Gunstein Pharmaceuticals, Inc.

Instructor's Notes

Objectives

This case was designed to evaluate the unique issues and challenges face by a start-up life sciences company, the founders, and the employees. The critical objectives for the students of this case include:

- Identify and understand the critical requirements and first steps in formation of a life sciences start-up venture;
- Understand the crucial differences in life sciences new ventures relative to most other start-ups;
- Assess the critical leadership issues seen with many new life sciences ventures, and the effects on the management teams;
- Discuss the valuation techniques, and the limitations thereof, for life sciences new ventures;
- Understand the financing options at different points in the life cycle of new ventures, the appropriate indications for each investment source, and the critical differences faced by life sciences firms;
- Discuss how inadequate financing limits the flexibility of all start-ups and the specific issues for life sciences companies;
- Discuss the potential liabilities of multi-national corporations with regards to global product sales;
- Review the intellectual property concerns and regulatory control issues in the global marketplace.

Appropriate Audiences

This case is designed for advanced MBA students with interest in new venture formation and the financing and valuation of early phase companies. It would also be useful in executive and doctoral business programs, in doctoral scientific programs, and in continuing education programs.

It will be most beneficial if students should have background in:

- Organizational Structure and Team-building
- Managerial Leadership
- Issues in New Venture Formation
- Valuation Models of firms and their strategic assets
- Appropriate Sources, Amounts, and Timing of investment capital for new ventures
- International Business
- Intellectual Property and Regulatory Compliance

Case Summary

Life Sciences companies, especially those focused on the development of therapeutics, have to deal with multiple complex issues often not seen in other industries including:

- the expense and uncertainty of Research and Development;
- Intellectual Property development and protection—domestic and international;
- Regulatory Compliance—domestic and international;
- the long time-frames for product development and approval;
- the requirements for large amounts of investment capital over long periods of time;
- global markets and business considerations.

Many life sciences companies are started by scientists and physicians—often extraordinarily intelligent and successful individuals in their chosen fields. However, these individuals have little, if any, business experience, in addition to usually being used to working independently without being questioned. This can cause its own unique set of issues for start-up life sciences ventures and their founders, which exacerbate the complex issues already present.

The valuation of early-stage life sciences ventures has its own set of difficulties. These companies usually have few tangible assets, with the only assets of value being intellectual property, the developers of the IP, and any technology or products based on the IP. The long time-frames of product development and approval are also a major concern. Use of Net Present Value / Discounted Cash Flow models are difficult when costs, pricing, and demand are difficult to predict, not including being able to define start and stop points for the various cash flows. The risks engendered by unpredictable clinical results and the required regulatory approval can be almost impossible to measure—making the appropriate discount rate more difficult to determine—and even more difficult to hedge.

Financing is a struggle for most new ventures, but the uncertainties and risks inherent in life sciences companies compound the problems—especially the long time-frames, expensive equipment and personnel, and the expenses of regulatory testing. Strategic partnerships, joint ventures, and licensing agreements are necessities for most successful life sciences firms; but this is another layer of complexity that must be navigated successfully by often inexperienced founders.

Gunstein Pharmaceuticals Inc. and Gunstein Therapeutics Inc. experienced the entire spectrum of most all these issues and challenges. Basic problems with the approach of the founders resulted in many of the issues, but the managing partner also demonstrated some of the positive characteristics of successful entrepreneurs. Considerations of being prepared when opportunities present themselves by having appropriate infrastructure in place, with appropriate standards, protocols, and scalability are often overlooked. Windows of opportunity, be they financial, R&D, or product competitiveness, can rapidly close. The difficulties of competing in a global marketplace and dealing with intellectual property and regulatory differences in various countries can be intimidating—the U.S. can be difficult enough in its own right. It is anticipated that students will be stimulated and challenged by this case, the players, and their decisions.

Key Issues

- Founders' Issues
 - Business Expertise and Experience
 - Inter-personal Relationships
 - Technology Development
 - Research and Development
 - Intellectual Property Control

- Venture Formation and Structure
 - Legal Structure
 - Management
 - “Key-Person” Issues
 - Intellectual Property Development and Identification, Control, Protection
 - Investment Capital and Financing Issues
 - Debt
 - Convertibles
 - Equity
 - Principals
 - “Angels”
 - Venture Capitalists
 - Strategic Partners
 - Internal Cash Flows
 - Government Grants

- Product Development
 - R&D
 - Intellectual Property (Domestic and International)
 - Time Frame
 - Regulatory Issues (Domestic and International)

- International Business Issues

- External Events
 - Economic
 - Financial Markets
 - Governmental
 - Catastrophic
 - “Act-of-God”
 - Terrorist

Theoretical Linkages

- Organizational Structure and Team Building
- Corporate Formation and Structure
- Executive and Managerial Leadership—Effects on Corporate Success
- Intellectual Property Development, Identification, Control, and Protection
- Product Development and Market Assessment
- Regulatory Compliance
- Investment Valuation Techniques and Limitations
- Investment Sources and Timing
- International Business

Discussion Questions

The following questions can be provided to the students to assist them in reaching the case objectives:

- What competitive advantages might Dr. Gunderson see that would support a company?
- What does Dr. Epstein bring to the firm?
- What must Gunstein Pharmaceuticals, Inc. have to survive as a “going concern”?
- Describe Dr. Gunderson’s leadership characteristics and style. Is it appropriate for what he wants to accomplish?
- What initial financing options do Drs. Gunderson and Epstein have? Do they use them appropriately—how and/or how not?
- Discuss the initial valuation of Gunstein Pharmaceuticals, Inc. Is it appropriate? Why and/or Why not?
- Discuss the corporate strategic options in 2003. Which would you choose and why?
- Discuss the corporate financing options in 2003. Which would you choose and why?
- Is moving into international product sales appropriate? Can Gunstein Therapeutics support this decision?

Teaching Suggestions

This case has been developed in segments that are temporal in nature. The case segments demonstrate a number of critical issues that are experienced by almost all new ventures at one time or another. Certain issues may have more significant impact in life sciences new ventures.

The case is designed to be taught either in its entirety at one time, to be taught one segment at a time, or only a specific segment, as appropriate for the course/instructor. Specific timing of each segment is left to the discretion of the instructor as these discussions may be quite variable depending on the backgrounds and interests of the students and the instructor(s).

Teaching Outline

Case A

1. Case Overview
 - a. Review industry and specific technology
 - b. Pros and cons of entry into this industry at this time with this technology
2. Discussion of the two principals—backgrounds, apparent psychological make-up, likelihood of a successful partnership
 - a. Poll students: Would they go into partnership with either or both principals?
3. Discuss the outcome of the MBA students' strategic market assessment and recommendations.
 - a. Discuss Dr. Gunderson's response to the strategic recommendations—appropriate or inappropriate?
4. Discussion Questions
5. Epilogue (Case B)—if Case A used as stand-alone
6. Learning Points
 - a. Articulation of important insights and lessons
7. Final Discussion

Case B

1. Case Overview
 - a. Review Valuation Models
 - b. What is the calculated discount rate for the pro-forma valuation January 2000 (Exhibit 2)—is it appropriate? (The discount rate is 50%—given the risk of the company, etc. this is probably the minimum it could be.)

- c. Analyze the pro-forma's given in Exhibit 2. Are these estimates appropriate? Why/Why not? (The time frame is too short for R&D, product development, regulatory approval, etc.; and the expenses are much too low—This type of estimate is what would be expected from inexperienced, industry-naïve, entrepreneurs.
2. Discuss division of equity between partners—appropriate or in appropriate?
 - a. Discuss the use of equity in this firm in the future? Are there protections for current and future stockholders to protect their investment?
3. Is this company adequately capitalized? What is the likely result?
 - a. Why is it so difficult for Gunderson to raise capital for Gunstein Pharmaceuticals?
4. Discuss the terms of the merger with North Coast Biotechnology, Inc.—good, bad, or indifferent?
5. Discussion Questions
6. Epilogue (Case C)—if Case A & B used or Case B used as stand-alone
7. Learning Points
 - a. Articulation of important insights and lessons
8. Final Discussion

Case C

1. Case Overview
 - a. Discuss the effects of the general economy on corporate fund-raising.
 - b. Discuss the effects of the financial markets on corporate fund-raising.
2. Has Gunderson done anything to improve the likelihood of raising investment capital? What else should he do?
3. How are Gunderson's business expertise and experience affecting his approach to the corporate issues and challenges?
4. How is Gunderson's psyche affecting his approach to the corporate difficulties?
5. Discussion Questions
6. Epilogue (Case D)—if Case A, B, & C used, or Case C used as stand-alone
7. Learning Points
 - a. Articulation of important insights and lessons

8. Final Discussion

Case D

1. Case Overview
 - a. Discussion of managerial changes during the period.
2. What are Gunderson’s primary focus and goals at this point?
 - a. What are the limiting factors for accomplishment of the goals?
3. Discuss the effects of a 2nd round of investment funding on the earlier investors.
 - a. What protections are needed for the early investors and whose responsibility is it to see that the protections, if appropriate, are in place?
4. Discuss the issues of intellectual property and regulatory compliance from both domestic and global standpoints. Is it ethical to take unproven therapies into under-developed, less regulation-restrictive countries for initial clinical trials? Is it financially beneficial for the company?
5. What potential impacts does the marriage of Gunderson and Carr have with respect to Gunstein Therapeutics, Inc. and its future? What have the effects already been?
6. Discussion Questions
7. Epilogue
8. Learning Points
 - a. Articulation of important insights and lessons
9. Final Discussion

Board Plan

Case A

Industry

| Enter | Not Enter |
|--------------|------------------|
| | |
| | |
| | |
| | |

Partnership

| Partner | No Partner |
|----------------|-------------------|
| | |
| | |
| | |
| | |

Case B

Division of Equity

| Fair | Unfair |
|------|--------|
| | |
| | |

Case C—None

Case D—None

Detailed Discussion and Analysis

Case A: The Decision to Pursue a New Venture Entity

Synopsis

When the story commences in 1998, the principals – Gunderson and Epstein – are 49 and 50 years old, respectively. Gunderson, a jack-of-all-trades, is clearly the chief architect while Epstein, committed to his university role, participates as an afterthought. Gunderson is one who defines his environment while Epstein is much less aggressive and more reactive than proactive. Overall, Gunderson is determined to start a biotech firm, appreciates the industry’s window of opportunity, and maintains the patience needed to pursue the dream on his own terms.

Questions:

1. What are the rationale and functions of taking a partner in a new venture?
 - a. Why does Gunderson want Epstein as his partner?
 - b. Could Gunderson manage the start-up without a partner using only his once-a-week free day?
 - c. Is there such thing as a “no-lose” proposition in a new venture?
 - d. Is an 80:20 equity distribution reasonable and/or appropriate?
2. What are some of Gunderson’s entrepreneurial strengths? Weaknesses? Which of these factors are more important? Does the relative importance of such factors change during the evolution of most start-ups?

3. Is it ethical to utilize the *pro bono* work of college students as a source of labor in private enterprise? To use academic “free time” to run one’s company? To use an academic position to enhance the profitability of one’s firm?
4. How does a market/opportunity assessment differ from a business plan? Is there a problem in espousing some aspects of the market assessment as fact while relegating other aspects into the category of unimportant suggestions?
5. Why is the students’ market assessment recommendation for the early retention of a strong legal team important for a start-up firm in the biotech industry? What would one look for in developing such a team? Which partner seems to give the most consideration towards this caveat?
6. Is starting a new venture as easy, and simple to learn, as Gunderson seems to think? What are some of the major pitfalls?
7. Is Gunderson’s attitude about new venture formation unusual in scientists, physicians, academicians? What are some of the reasons this is the case? Will this attitude affect the development of a strong management team?

Responses:

1. The acquisition of an additional partner for a new venture serves to share risk, reduce one’s workload, and create synergy between primaries.
 - a. Gunderson desires Epstein’s partnership because he has the capability to create additional value for the firm. The elements of such value to Gunderson would include Epstein’s original IP, Epstein’s work ethic and integrity, and Epstein’s willingness to let Gunderson dictate policy.
 - b. It is unlikely that Gunderson could manage the firm by himself on limited time. Further, it would be difficult for Gunderson to realistically refute any conflict of interest charges if he had no other partners to whom he could credit completed work.
 - c. Minimally, a person will always risk sweat equity – time, emotion, reputation etc. – on a business start-up even if he has no capital investment requirement. Further, the hidden financial costs of a business start-up will often minimally convert a “no risk” proposition to a “low risk” one, and potentially to a moderate risk situation.

- d. The fair equity distribution in any partnered business is dependent on a variety of factors including tangible goods supplied by each party, intangible factors unique to each party, and the expectations held by each party.
2. Gunderson's strengths include his persistence, patience, knowledge base, experience, and ability to sell his ideas. His weaknesses include his overconfidence, his assumed knowledge and expertise in areas in which he has none, and his shortsightedness in policy review. The most important of these factors for the start-up at this time include persistence and patience, fundamentals inherent in successful start-ups. Over time, the relative importance of such factors usually changes as a firm's inner processes move through evolutionary adjustments.
3. Using students to perform work would seem ethical if all parties benefited and agreed to the terms of the relationship. Academic free time should be eligible for any use a professor deems appropriate as long as it conforms to university policy. However, using one's academic position to promote a private business would seem inappropriate and perhaps, if that position were funded through governmental sources, unethical and/or illegal.
4. A market assessment, although containing many similarities to a business plan, differs in that its focus is on the relative feasibility of a potential start-up while the business plan focuses on the aspects fundamental in the successful opening and growth of a firm. Stratifying market/business assessment recommendations into categories of intended acceptance is generally a mistake as it introduces bias into a process that was originally conducted to consider and discuss all factors evenly.
5. A strong legal team is important initially to ensure that one's IP is protected and that associated patents are properly aligned with projected product development. To develop such a legal team, one would look for industry experience, networking capability, reasonable pricing, overall professionalism, and commitment to one's company. Neither Gunderson nor Epstein seem particularly worried about these factors. Gunderson illustrates concern with minimizing costs but generally ignores the quality, experience, networking, or commitment of those retained for legal purposes.
6. Starting any new venture is demanding, difficult, and carries unexpected problems and risks. The best way to learn is to develop first-hand direct experience while being mentored by an experienced expert who can shorten and flatten the learning curve.

Major pitfalls include arrogance, lack of experience, legal and accounting misadventures due to lack of and acceptance of appropriate advice, poor management due to lack of understanding and expertise, and inadequate financing.

7. This is a very common attitude among this type of individuals. These individuals tend to be driven, successful, and often over-impressed with their abilities. They seldom have failed at anything attempted and feel that anything is possible given their intelligence and commitment. These traits and attitudes tend to make it difficult, if not impossible, to develop a strong management team due to an inability to share control and decision-making.

Case B: Valuing and Financing a Start-Up

Synopsis

The story continues in late 1999 as Gunderson tries to finance the start-up while Epstein finds that there is no such thing as a free lunch. Hiring a series of unrelated attorneys in piecemeal fashion, Gunderson manages to inexpensively get the firm off the ground while also developing incorporation guidelines that minimize the risk of a future hostile takeover. The partnership runs into trouble when Epstein – contrary to prior promises – is asked to contribute to the firm’s initial capital requirement and when unexpected events leave the “hands off” Epstein as the *de facto* man in charge for six months. Finally, Gunderson’s attempts to bankroll the firm run into considerable difficulty; however, this is ultimately rectified through the North Coast Biotechnology, Inc. merger which lessens the original partners’ combined ownership to only 52% of the distributed equity while bringing them hope of an IPO at some future point.

Questions:

1. Although Gunderson seems to have a knack for maintaining the entrepreneurial dream, some of his and Epstein’s business shortcomings become constraints during this focal period of firm incorporation and start-up financing. In light of this, discuss the following:
 - a. How might Gunstein Cell Pharmaceuticals, Inc.’s “business plan” hinder investor interest?

- b. How might the “hire the lowest bidder” approach to professional services backfire in the long run? Is Epstein’s pending lawsuit over Sertoli cell patents such an example?
 - c. Have Epstein and Gunderson adequately considered the “hit-by-car”/”key man” scenarios in advance?
 - d. Do Epstein and Gunderson seem to have a well-formed exit strategy? What examples illustrate this point?
 - e. How well does Gunderson weigh the presence of an evolving national recession into his chances of success in finding investors?
2. With respect to the firm’s rules of incorporation as related to the handling of equity, what seem to be the overall themes with respect to Gunderson and Epstein’s control of the firm?
What future problems might these rules present to the firm when it is trying to attract executive talent with the use of stock and/or stock options?
3. In general, is the process of valuation of a firm’s assets a well-defined process, a poorly defined process, or a process dependent on factors that vary from firm to firm?
Where does Gunstein Pharmaceuticals, Inc.’s experience fall in this respect?
4. How realistic is the NPV/DCF valuation of Gunstein Pharmaceuticals, Inc.? What other methods of valuation could be used? Which would give the most accurate value?
Is there really any way to accurately value Gunstein Pharmaceuticals Inc.?
5. Gunderson thinks of Gunstein Pharmaceuticals, Inc. as “his” company. In what respects is this correct? In what manner is this inaccurate?
How do these answers change upon the firm’s merger with North Coast Biotechnology, Inc., and how might this change the relationship between Gunderson and Epstein?
6. Is an Equity Carve-Out IPO as simple as Brown suggests? What conditions must hold to allow this process? How might Gunstein Pharmaceuticals, Inc. make adjustments to allow these conditions to exist, and what might go wrong? How does the Equity Carve-Out (aka, partial spin-off) differ from a “Split-Off” (aka, full spin-off)?

Responses:

1. With respect to the partners’ business oversights:
 - a. Gunstein Cell Pharmaceuticals, Inc.’s “business plan” is actually a strategic market assessment plan. Although the components of these two types of plans are similar, they are not the same. The presentation of the latter as a representation of the former would suggest to a sophisticated prospective investor that the management team is inexperienced.

- b. The overly frugal approach can backfire through poor legal work in patent applications and corporate by-law construction, through the lack of qualified staffing, and through the unwillingness of investors to support a firm without a solid management team. The Sertoli cell patent problems probably are an example of frugality gone awry – these patents were reviewed initially by the least expensive attorney, who failed to note the potential for problems with another firm claiming similar IP.
 - c. Obviously the partners never considered that one of the two could become incapacitated or unavailable. This oversight, a major blunder in the process of a business start-up, markedly illustrates the partners’ need for an outside advisor(s).
 - d. Epstein and Gunderson have no exit strategy as exhibited by these examples:
 - The “win-win” and “no-lose” strategies do not include end-points;
 - At no point prior to the merger with North Coast Biotechnology, Inc., or after, did Gunderson have a defined, structured plan for the firm’s future;
 - Although the firm finally negotiates a merger, and passively discusses a future IPO opportunity, there are no defined long term plans to show potential investors the return that might be expected.
 - e. Gunderson’s assessment of the recession during 2001 is essentially non-existent. He feels certain that there are numerous investors waiting to jump on the biotech bandwagon. He goes out on the road to find these investors without analysis of the national economy, and is sorely disappointed, and mystified, at his subsequent failures.
2. As noted in the text, Gunderson was primarily interested in long-term control of the firm. This is exhibited in his ownership of 76% of the issued stock, the firm’s first right of first refusal in potential equity re-sales, and the 5% limit on equity ownership by any non-partner. Additionally, Gunderson wanted a broad equity pool as a non-cash source from which to compensate future associates. Thus, the by-laws were arranged so that stock options could be issued freely in place of currency with minimal concern for dilution of equity held by prior investors. Gunderson could maintain his share by the award of options or stock to himself for “consulting fees.” Finally, Gunderson wanted to minimize liability

from these actions. Therefore, a disclaimer was added to distance the firm from future claims should the equity values plummet due to the policies noted. The problems these rules pose with respect to recruiting a management team include:

- Talented management might aspire to own more than 5% of firm's equity;
- Most experienced professionals won't work for options, in place of cash, for an unproven start-up;
- Those who will work for options will want a guarantee of a minimum "cash-in value";
- Those who wish to stay with the firm for a long period usually will be concerned about dilution and reputation issues.

3. The process of valuation is dependent on factors that vary from firm to firm and from industry to industry. With respect to Gunstein Pharmaceuticals, Inc., a firm that won't have a product for at least 6 to 8 years, only shows value through unproven IP, and still needs management and financing; it is quite difficult to set a present corporate value. For a company like Microsoft, this process is much more defined because the firm is actively producing products for sale, is operating in a well-defined industry, has publicly available financial records, and has publicly traded stock.

4. The NPV/DCF valuation of Gunstein Pharmaceuticals, Inc. is basically "blue-sky". Revenue estimates regarding unknown products based on an ill-defined, unproven technology at some unknown future time are ludicrous and would be recognized as such by any experienced investor and/or analyst. The desired valuation can be "back-filled" by adjusting any assumption.

Other methods of valuation include use of comparable firms with comparable risk profiles, valuation of similar IP portfolios (since the only real value in the company is the IP), and option pricing methods.

The most reasonable method would probably be use of comparables, but it is doubtful that there is any way to truly accurately value a company like Gunstein Pharmaceuticals, Inc. at this early stage—any valuation would be primarily a "blue-sky" valuation.

5. Gunstein Pharmaceuticals, Inc. is Gunderson's company because he originally owned 76% of the stock, maintained control over the Board of Directors, functioned as the *de facto* (or

actual, despite university rules to the contrary) CEO, developed a large portion of the IP and is irreplaceable to the firm. Gunstein Pharmaceuticals, Inc. is not Gunderson's company because his absolute Board control is only 1 of 3 votes, his available time and prior business experience are inadequate, and his IP is unproven except in a rat model. Further, the merger with North Coast Biotechnology, Inc. has left him with only 41.6% ownership of the firm's equity – North Coast Biotechnology, Inc. has 43%, Epstein has 10.4%, and UCNV has 5%. Gunderson will now, and subsequently, need Epstein's full support to pass any issues in votes of both stockholders and the Board of Directors.

6. An Equity-Carve Out IPO is not as simple as Brown hints. A parent company may carve out and arrange an IPO for up to 20% of the voting stock and up to 50% of the economic value of the stock of a wholly owned subsidiary. This means that North Coast Biotechnology, Inc. must demonstrate to the SEC that it owns 100% of Gunstein Therapeutics, Inc. before the Gunstein becomes eligible for this partial spin-off. Therefore, Gunstein Pharmaceuticals, Inc. can only manage this process by arranging a deal in which all equity is temporarily signed over to North Coast Biotechnology, Inc. Of course, signing over all equity also entails the temporary transfer of all corporate power, and this could allow North Coast Biotechnology, Inc. management to make unwanted changes during this interlude. The Equity Split-Off differs from the Carve-Out in that the ownership and the voting power of the subsidiary are both completely transferred to other parties in a tax-free process that requires one of the companies to be at least 5 years of age. The major practical difference between the carve-out and the split-off involves their typical uses: carve-outs are generally utilized to raise cash for the parent firm while split-offs are generally utilized for passing dividends to stockholders of the parent firm.

Case C: Enterprise Building

Synopsis

In this segment, Gunstein Pharmaceuticals, Inc. has become a firm with a pending merger partner, which promises to supply much needed early capital. Unfortunately, the road remains rocky with the September 11th tragedies and subsequent uncertainty in the economy and financial markets. Although the merger finally goes through, Gunderson loses momentum. As

a result of past, present and future tendencies towards strict cash conservation and lack of capital investment by the principals, Gunstein Pharmaceuticals, Inc. suffers from repetitive and persistent growth restrictions relating to inadequate legal representation, a shallow management team, and flexibility restricted by inadequate capital resources. Ultimately, Gunderson waits for another day to answer key questions while hoping to find bargain responses in an expensive industry.

Questions:

1. Does Gunstein Pharmaceuticals, Inc.'s vulnerability to market forces following the September 11th tragedies signal a further example of poor corporate planning or is it simply a characteristic of the overall national experience at that time?
2. How does merger partner Wayne Brown function as an asset to Gunstein Pharmaceuticals, Inc.'s well being? How does he function as a liability? In retrospect, does the net sum of these factors create value for the firm?
3. Which factors should weigh most heavily in selecting Gunstein Pharmaceuticals, Inc.'s product development strategy: Market conditions? IP characteristics? Available finance? Management's preference?

Which style, *The Gold Rush Method* or *The Explorer Style*, is the better fit for the firm?

4. Is the lack of an exit strategy reasonable for a firm that is circulating a working business plan and is actively pursuing outside investors? What exit strategy do you think Gunstein Pharmaceuticals, Inc. should adopt?
5. The Kauffman Foundation lists the entrepreneurial principles that it considers to be critical success factors as:
 - The determination to pursue an opportunity
 - The ability to secure key knowledge and resources
 - The willingness to give back to the community

How well does Gunderson demonstrate each of these principles? Is it possible to be a successful entrepreneur while completely ignoring the Kauffman principles?

6. Gunderson offers the "cash is king" philosophy as the final word in new venture management. Is this a correct philosophy and approach?

Responses:

1. Gunstein Pharmaceuticals, Inc.'s vulnerability on September 11th was a characteristic attributable to most firms on that day. In October 2001, *The Wall Street Journal* estimated

that 5% of the nation's firms would ultimately go out of business as a result of September 11, while the total equity in global stock markets saw losses averaging 5% to 10% over the following few weeks. Nonetheless, the more balanced and better-prepared companies fared better during this period.

2. Wayne Brown and North Coast Biotechnology, Inc. are assets to Gunstein Pharmaceuticals, Inc. by supplying sorely needed capital, by becoming corporate affiliates, and by supporting Gunderson during the stressful period of September 11th. Brown is a liability in that he passed off the Equity Carve-Out IPO process as a simple measure when, in fact, it requires Gunstein Pharmaceuticals, Inc. to sign the company over to North Coast Biotechnology, Inc. as a prerequisite. In summing these facts, however, most would probably agree that Gunstein Pharmaceuticals, Inc. is better off with the deal when considering the alternatives at the time.
3. In weighing product development strategy factors, Gunstein Pharmaceuticals, Inc. management should probably weigh IP characteristics first, market conditions second, available finances third and their preferences last. The rationale for this is that there can be no value in a biotechnology firm without IP, there can be no profitable use of IP without demand, and there can be no exploitation of demand without appropriate corporate financing. Management's preferences are essentially irrelevant and come a distant last to these factors in a market economy. Because Gunstein Pharmaceuticals, Inc. has the majority of its patents' lifetimes remaining, strong proprietary IP that is difficult to duplicate, and a gross inability to finance a \$10 to \$40 million annual cash burn rate, *The Explorer Style* is a better development approach for it at this time, even though it will be impossible to fund this either without external investment.
4. Most experienced investors will not consider funding a firm that cannot enunciate its exit strategy. Since Gunstein Pharmaceuticals, Inc. is aggressively searching for investor financing, it is unreasonable for it to lack a defined exit strategy in its written and oral presentations. At this time Gunstein Pharmaceuticals, Inc., which lacks management, financing, and essentially, any strategic partners, might fare best by pursuing a merger with, or sell-off to, a competing firm that has solid management and adequate financing but lacks the IP that Gunstein Pharmaceuticals, Inc. can provide.

5. Gunderson shows great determination in pursuing his business dream despite multiple barriers as he survives a motorcycle crash, a lack of funding, constant pressure from university officials, and an unanticipated national disaster. Gunderson slips somewhat with respect to his ability to secure key knowledge and resources as he is overly confident with his own business abilities and subsequently makes a number of related mistakes. Gunderson is an uncertain quantity with respect to his philanthropy to the community. On the positive side, he diligently pursues a cure for tragic diseases and participates in the national Kauffman Entrepreneur Internship Program (KEIP). On the negative side, he puts his own corporate power and financial status ahead of the success of the firm and appears to use the KEIP intern more as a vehicle for inexpensive labor than as an opportunity for mentoring. With respect to the Kauffman principles, there certainly are well-documented cases of people who have fared well without supporting the principles. For instance, some entrepreneurs in strict government-regulated industries lack incentive and/or determination to maximize a business opportunity and yet still do fine due to their monopoly power; some entrepreneurs start businesses in which they initially know little and ultimately do well by learning from their own mistakes rather than through the advice of others; some entrepreneurs are successful despite completely ignoring stewardship towards their communities. However, it is virtually impossible to ignore all of these time tested critical success factors while remaining a successful entrepreneur as these factors outline a type of new venture Darwinism that ultimately functions to separate those firms that survive from those that succumb.
6. The proper management of cash is certainly within the top echelon of importance for critical new venture factors – Worthmoore’s note to Gunderson ranks cash concerns among the top four factors along with the management team, strategic partnerships and product/IP portfolio. Placing one of these four biotechnology industry success factors in front of the others at this time, however, is probably a mistake in that it hinders the development of the corporate balance that has typically been required for new venture survival. By micro-managing cash concerns, Gunderson has limited the proper growth of the management team, stifled product research and development, and limited the firm’s attractiveness to potential partners and/or investors. Of course, when cash and investors are scarce due to situational conditions, conservative cash management and appropriate corporate

adjustments become necessary. All things considered, Gunderson's low-ball approach to contract negotiations, attempts to use overvalued and risky stock options as a major source of reimbursement to colleagues and advisors, and unannounced withholdings of payments to business associates have all undoubtedly tarnished or will tarnish the firm's goodwill in the business community and the biotech industry.

Case D: Products and Finance

Synopsis

Gunstein Therapeutics, Inc. has continued to progress—but more laterally than forward. Additional management team members have been hired, but have subsequently left or been fired. There are obvious issues with corporate control and corporate focus that are recognized by potential investors, outside observers, and by some of the management team, albeit not accepted by Dr. Gunderson. He finally begins to realize the need for a product line and interim revenue streams during the period that will be required for the desired development and approval of a human therapeutic. The potential for a corporate alliance/partnership and/or an investment by a wealthy “angel” (the major stockholder in the potential corporate partner) may resolve the capital issues and provide a long-term source of donated cord blood to allow accelerated R&D and processing of stem cells for research purposes and for clinical use. The investor may also be able to assist the movement of the company into clinical trials—in the U.S. and internationally—although it is unclear that the company can hurdle the regulatory barriers or manage its potential risk exposure. Additional unknowns are Dr. Gunderson's willingness to trade control of Gunstein Therapeutics for a capital infusion into his company and the willingness of North Coast Biotechnology to go along with the deal.

Questions:

1. How are the persistent weaknesses in the management team of Gunstein Therapeutics, Inc. being manifested?
2. What specific effects are prior decisions now having on corporate policy and decision-making? Is Gunstein Therapeutics, Inc. limited in its ability to seek and develop profitable projects?

3. Discuss the pros and cons of the potential investment by Susan Tsen from the standpoints of Gunstein Therapeutics, Inc., Dr. Gunderson, and Susan Tsen.
4. How does North Coast Biotechnology, Inc. impact the potential new investment and how will might the investment impact North Coast Biotechnology, Inc.?
5. As CEO (*interim* or otherwise), what are Dr. Gunderson's responsibilities to Gunstein Therapeutics, Inc. and to its current investors?
6. Should Gunstein Therapeutics, Inc. proceed with the investment? Why/Why not? Under what terms?
7. Is Gunstein Therapeutics ready and able to begin stem-cell processing with a resultant standardized product for clinical use—in the U.S. or internationally?

Responses:

1. The major weakness is that all decisions are made by one person who has his own personal agenda—which may or may not coincide with what is best for the company. This has resulted in the maintenance of a skeleton staff and an inability to hire additional expertise due to a lack of capitalization and a desire to have no one who might challenge the status quo.
2. The lack of adequate capitalization of the company prevents the progress of projects to begin product development at a crucial point in time. The lack of production impedes progress with a subsequent project that could have enormous benefits from revenue, credibility, and visibility standpoints. Despite strong recommendations by the staff at the prior points, Gunderson's refusals have a serious negative effect on the company. Gunstein Therapeutics is unquestionably limited in its flexibility and ability to respond because of the inadequate capitalization.
3. From the corporate standpoint, the investor may well bring enough funding to allow the company to make major strides in R&D and in product development. She may also demand appropriate strengthening of the management team, or even take personal control of the management team, which would probably also benefit the company. Potential negative effects could include disruption of the team already present or the desire of the new investor to sell off the IP or the company itself.

From Gunderson's standpoint, the investor may require that Gunderson step aside as CEO and significantly change or minimize Gunderson's role in the company—if not initially, then in the intermediate term. Gunderson's ownership stake will be minimized and his exit strategy is then out of his control entirely. It is likely that Gunderson will be very reluctant to accept an investment except under very strict terms which will leave Gunderson in control; a situation to which a sophisticated investor is unlikely to agree.

4. North Coast Biotechnology, Inc. has an approximate 40% stake in Gunstein Therapeutics, Inc. It is obvious that the new investment will decrease that stake substantially. Whether this will be agreeable to North Coast is unclear. With the issues that North Coast has, changing their investment to a minority passive status may be a good idea, but if this is not what North Coast desires, they could impact the situation by attempting to influence other investors (e.g., Dr. Epstein and/or UCNV) to oppose it or they could seek legal recourse which would undoubtedly hinder, if not totally prevent, the investment.
5. Dr. Gunderson, as CEO, has ethical, legal, and fiduciary responsibilities to all stockholders. He should, at the very least, discuss the potential investment with all stockholders, especially large stockholders such as North Coast Biotechnology, Inc. However, his ultimate responsibility is to maximize the return for his stockholders and if this potential investment will be beneficial to the majority of his stockholders, he should recommend it and proceed accordingly, once he has a majority of stockholders in agreement.
6. Gunstein Therapeutics, Inc. must assess the terms of any investment agreement to be sure it is in its, and its stockholders, best interest. A significant capital infusion that would allow aggressive R&D and product development must be looked on favorably. The ultimate effects on the founders, management, and employees must also be taken into consideration.
7. Gunstein does not have the appropriate standards, protocols, or quality controls in place for any product development, much less products for clinical human use, at least in the U.S. However, international standards are often much lower and much less stringent. This often creates significant ethical and moral issues—particularly where life-threatening diseases, with extraordinarily expensive therapies, are involved. Resolution of

these types of problems can become quite complicated and complex depending on one's position, point of reference, and inherent values.

Epilogue

Gunstein Therapeutics, Inc. continues to be funded with SBIR/STTR Grants. Attempts to obtain “angel” or institutional funding continue, but the same issues remain:

- 1) lack of significant financial investment by the principals;
- 2) lack of organizational focus;
- 3) lack of adequate capitalization;
- 4) stunted product development;
- 5) limited operational options and flexibility due to inadequate capitalization;
- 6) management team limitations—breadth, depth, and experience.

Some progress in the R&D for neurological disease continues, and the company is attempting to move into the field of cardiac cellular transplantation for acute myocardial infarction and congestive heart failure. This is a significantly larger market (both U.S. and worldwide) with anecdotal clinical evidence of success in humans using a number of different types of stem cells. These reports have come primarily from South America and Europe. It was hoped that this might lighten the FDA requirements in the U.S., but that does not seem to be the case.

The company is also focused on development of a standard cellular processing protocol and development of an semi-automated closed Good Laboratory Practices / Good Tissue Practices process for production of a standardized stem-cell product.

Recent Kauffman interns have been instrumental in the diversification into cardiac cellular transplantation and in the engineering design of the semi-automated closed processes and facility layout.

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