CASE 52

Purinex, Inc.

To lead the world in discovering, developing & commercializing novel therapeutic compounds acting on the purine receptors in order to save and improve patients' lives.

Company mission statement

In June 2004, Purinex, Inc., a pharmaceutical company with several clinically and commercially promising drugs in development, had reached a turning point. Sometime in the next four to twelve months, the company stood an excellent chance of securing a partnership with a major pharmaceutical company. That partnership, if secured, would enable Purinex to develop one of its leading compounds into a drug for the treatment of one of the world's deadliest and most widespread diseases. The company had no sales or earnings, however, and there was only enough cash on hand to last 11 months.

Gilad Harpaz, Purinex's chief financial officer, believed that if a partnership deal came through, the company would be in an excellent position to carry out its mission. Moreover, securing a deal was practically a prerequisite for any eventual initial public offering,[1] which was an attractive exit strategy for many of the company's investors. But, as things stood, it was unclear whether the firm could stay afloat until such a partnership could be consummated.

Harpaz believed that the company could either attempt to secure financing now or wait until it struck a partnership deal. "But if we wait," Harpaz thought, "the terms of a deal would get a lot worse." Harpaz, a former officer in the Israeli special forces who had earned a graduate degree in business, considered how to structure this decision. What were the probabilities that a collaboration with a pharmaceutical company would actually happen? How would the company stay above water until that occurred? Besides insolvency, what were the other risks to the company under these circumstances?

[1]An initial public offering (IPO) was the first sale of stock to the public by a private company. IPOs were often issued by smaller, younger companies seeking capital to expand, but could also be done by large privately owned companies looking to become publicly traded.

This case was prepared by Sean D. Carr under the supervision of Robert F. Bruner. "Purinex, Inc." and the individuals in the case are fictitious, but the circumstances portrayed reflect issues facing actual firms and managers. It was written as a basis for class discussion rather than to illustrate effective or ineffective handling of an administrative situation.

Purinex, Inc.

Purinex was a drug-discovery and -development company based in Syracuse, New York, that sought to commercialize therapeutic compounds based on its purine drug-development platform. Purine was a naturally occurring molecule that played an important role in numerous biochemical processes. Purinex had developed a process for creating small molecules that acted as selective agonists (activators) or antagonists (blockers) for specific purine receptors in the cell membrane.[2] These molecules could initiate physiological responses or block the activation of receptors by endogenously produced signaling molecules. Purinex's goal was to develop products that evoked a receptor-specific pharmacodynamic effect without producing undesirable outcomes that could result from interactions with other receptors.

The company had 14 employees and maintained a chemistry laboratory a few miles from its main office. Purinex's intellectual-property portfolio consisted of more than 35 patents pending or issued in the purine field. The company planned to take its new receptor-selective drugs into clinical trials to address a broad range of potential indications. In June 2004, the most promising indications for its compounds were for the treatment of diabetes and sepsis.

Diabetes

Diabetes was a long-term condition that affected the body's ability to process glucose and hampered its use of other nutrients, such as protein and fat. Glucose, a common product of digestion, circulated in the blood to the body's cells, where it served as one of the chief sources of energy. Diabetes disrupted the body's mechanisms for moving glucose out of the bloodstream and using it in cells. As a result, levels of blood glucose (blood sugar) stayed excessively high, leading to serious health complications over time.

High levels of blood glucose affected the eyes, kidneys, and the nervous system. In addition, diabetes increased the risk of atherosclerosis, which narrowed arteries, especially those carrying blood to the heart, brain, and legs. Diabetes affected more than 100-million people worldwide, and was among the most common causes of death and disability in North America and Europe. Purinex had a patent on the use of any purine antagonist for the treatment of diabetes and its related conditions within the United States. The company had also developed a series of proprietary antagonist molecules that showed great promise in preclinical studies of diabetes. Potential annual sales for this drug were believed to be $4 billion.

Sepsis

Sepsis was a serious medical condition caused by a severe infection leading to a systemic inflammatory response. The more critical subsets of sepsis included severe sepsis (sepsis with acute organ dysfunction) and septic shock (sepsis with refractory arterial

[2]An *agonist* promoted certain kinds of cellular activity by binding to a cell's receptor. An *antagonist* prevented certain types of cellular reactions by blocking other substances from binding to a cell's receptor.

hypotension). Septicemia was sepsis of the bloodstream (blood poisoning) and was caused by bacteremia, which was the presence of bacteria in the bloodstream. The systemic inflammatory response syndrome led to widespread activation of inflammation and coagulation pathways. This could progress to dysfunction of the circulatory system and, even under optimal treatment, into multiple-organ dysfunction syndrome and, eventually, death.

Sepsis was more common and more dangerous in the elderly, immunocompromised, and critically ill patients. It occurred in 2% of all hospitalizations, and accounted for as much as 25% of intensive care unit (ICU) bed utilization. It was a major cause of death in ICUs worldwide, with mortality rates that ranged from 20% for sepsis to 40% for severe sepsis to more than 60% for septic shock. In the United States, sepsis was the leading cause of death in noncoronary ICU patients, and the tenth leading cause of death overall. One problem in the management of septic patients was the delay in administering the right treatment after the sepsis had been diagnosed.

One of Purinex's agonists for the treatment of sepsis had been shown (in animals) to have limited side effects and to be fast acting and effective at treating sepsis, even if treatment were significantly delayed after onset of the disease. Further, it had been proved safe in humans in a phase I clinical trial. Harpaz estimated that annual sales for this product could be around $500 million.

Development of Pharmaceutical Drugs

In 2005, the pharmaceutical industry remained one of the world's most dynamic economic sectors, with more than $530 billion in global sales. Although pharmaceuticals continued to grow faster than most other segments of the economy, some analysts predicted a softening in its growth over the next five years. As part of an effort to remain competitive, many large pharmaceutical firms had moved aggressively to partner with smaller firms in the biotechnology sector[3] in order to identify the next generation of drug candidates. In recent years, the U.S. biotechnology industry had mushroomed, as sector revenues grew from $8 billion, in 1992, to nearly $40 billion, at the end of 2003.

Collectively, the biotechnology industry devoted a higher percentage of its sales to research and development (R&D) than did any other major U.S. industry. According to Standard & Poor's, R&D spending by biotechnology firms was close to 40% of the industry's revenues. This high percentage was largely because many biotechnology companies did not generate revenues. R&D spending by public biotechnology companies was $17 billion in 2003 and $12.5 billion in 2002. Among the reasons for the high R&D costs was that the drug development and approval process was lengthy and risky. According to a June 2001 study by the Boston Consulting Group (BCG), the total cost to develop a new human-therapeutic compound was $880 million; a 2003 report by Tufts University placed that cost at $897 million (in 2000 dollars).

[3]In its broadest sense, *biotechnology* referred to the use of biological processes to solve problems or to make useful products, agribusiness, biology-based environmental remediation, biodefense, and drug research and development by small pharmaceutical firms.

The BCG report estimated that drug-development failures accounted for 75% of the total R&D cost.

While the total development time for a drug was highly variable, it took 10 to 15 years, on average, to move a drug from preclinical development to marketing approval. The process for discovering, developing, and gaining approval for new therapeutics consisted of several distinct steps: early discovery, preclinical development, clinical trials, and regulatory filing and review. **Exhibit 1** illustrates schematically the phases of development for a new compound.

According to a number of studies, the preclinical phase accounted for about 40% of the time and resources required to bring a new compound to market. The preclinical stage included target identification, target validation, assay development,[4] primary and secondary screening, lead optimization, and preclinical studies. The significant challenges of the preclinical phase were exemplified by a rule of thumb adopted by Pfizer, Inc. On average, it took about 7 million primary screen candidates to produce one new chemical entity.

In the United States, the drug-approval process was overseen by the Food and Drug Administration (FDA), which required extensive testing to ensure drug safety and efficacy. The drug manufacturer had to undertake three sequential sets of clinical tests before applying for regulatory approval. The FDA estimated that, out of every 20 drugs that entered clinical testing, on average, 13 or 14 would successfully complete phase I. Of those, about 9 would complete phase II; only 2 would likely survive phase III. On average, only 5% to 10% of drugs entering clinical trials were ultimately approved for marketing, often after several attempts.

Access to Capital

Given the magnitude of R&D requirements, early-stage biotechnology firms needed sufficient access to capital. Typically, biotechnology entities were funded through seed money from individual angel investors[5] or venture-capital[6] (VC) firms. According to Burrill & Company, a private merchant bank specializing in life sciences, funding from such sources for North American biotechnology firms was $2.6 billion in 2002 and more than $2.8 billion in 2003. A recent report by Standard & Poor's indicated that funding for most biotechnology firms would remain attractive, but "…we see deal terms remaining clearly less attractive than the valuation premiums that were commanded in 2000, when the market was in a euphoric state."

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[4]An assay was a test that measured a biological response or assessed physical attributes, or, as here, referred to a screening process for new drug candidates.

[5]Angel investors were individuals who provided financing to small start-ups or entrepreneurs. Angel investors were often friends or relatives of the firm's principals, but they could also be sophisticated and experienced investors. Angel investors were rarely involved in the firm's management, but they could add value through their contacts and expertise.

[6]Venture capital was a broad term that referred to the financing provided by professional/institutional investors to start-up firms and small businesses with perceived growth potential. Venture capital was often a very important source of funding for new firms that might not have access to capital markets and that usually entailed high risk for investors, but that had the potential for above-average returns.

If a firm had a promising investigational drug candidate, it could also seek an alliance with a larger pharmaceutical or biotechnology company. The larger company could provide up-front fees, R&D funding, milestone payments,[7] royalties,[8] and, possibly, copromotion rights. In addition, the company could supply production facilities or sales organizations, often in return for marketing rights under licensing arrangements. **Exhibit 2** describes the terms of recent partnership deals between biotechnology and pharmaceutical firms. **Exhibit 3** provides the median and mean values of a broad sample of those deals at each stage of the drug development process.

The number of collaborative agreements between "Big Pharma" (large-capitalization pharmaceutical firms) and biotechnology entities had increased steadily in recent years. According to Burrill & Company, such partnering arrangements had reached $8.9 billion in 2003, up from $7.5 billion in 2002. These partnering deals were expected to surpass $10 billion in 2004. **Exhibit 4** depicts the relative proportion of funding sources for North American biotechnology firms in 2003.

Investment and Financing Decisions

In June 2004, Purinex had a broad range of technologies under development, two of which had applications appropriate for partnership deals with a larger pharmaceutical company: a preclinical stage antagonist program for the treatment of diabetes and an agonist program for the treatment of sepsis that had completed a phase I clinical trial.

Over the past several months, Purinex had initiated discussions with several, large, well-capitalized pharmaceutical companies regarding a possible collaboration for both compounds. Two companies had come forward with preliminary term sheets: one sought a deal for the treatment of sepsis, and the other wanted a deal for diabetes. Each proposed deal would entitle Purinex to receive a combination of up-front fees, milestone payments, and royalties, as described in **Table 1:**

TABLE 1 | Combinations of monies to be received for each deal.

	Sepsis	Diabetes
Up-front	$5 million	$8 million
Milestones (total, undiscounted[9])	$108 million	$80 million
Royalty	10.0%	12.0%

[7]Milestone payments were a series of payments made upon the successful completion of certain triggering events in the drug development process.

[8]A royalty was a payment to an owner for the use of property, especially patents, copyrighted works, or franchises. Royalties were usually calculated as a percentage of the revenues obtained through the use of the property.

[9]Harpaz's initial practice was to assess partnership deal terms on an undiscounted basis; but where time allowed and forecast assumptions were available, he would do further analysis.

Harpaz believed there was about a 75% chance that Purinex would secure a partnership with a pharmaceutical company for either sepsis or diabetes sometime during the next four to twelve months. If that partnership occurred, he estimated a 60% probability that it would be a deal for sepsis. If a partnership did not occur during the next four to twelve months, Harpaz believed there was a very strong chance—perhaps a 95% probability—that a different partnership with a third company for the diabetes application would occur about a year later. This later deal would likely have half the value of the one he was currently considering.

Harpaz thought it unlikely that Purinex would form partnership deals for both sepsis and diabetes. The company's management believed it was important for Purinex to retain at least one of those programs in order to maintain the firm's viability as a strategic acquisition target or as a possible IPO candidate ("so as not to sell off all of the crown jewels," he thought). Therefore, he believed the two deals were mutually exclusive.

Harpaz remained very concerned that Purinex had only $700,000 in cash on hand. The firm's burn rate[10] was about $60,000 a month (Purinex had no sales or earnings other than income from federal research grants, which offset about $100,000 of the company's $160,000 in monthly expenses). Because the sepsis and diabetes partnerships were so uncertain in the short term, Harpaz was considering three options for his firm. Each option came with its own risks:

- **Venture-capital round:** Purinex could seek to raise a one-time round of financing from a VC firm. VC firms had expressed serious interest in biotechnology investments lately, and Purinex showed great promise. Harpaz believed it would take about three months to secure $10 million from a VC firm, and that VC firms would likely give the company a premoney valuation[11] of $15 million. The VC financing would come with a significant number of restrictions, including preferences for board appointments, antidilution rights, liquidity, participation, and positive and negative covenants.
- **Wait six months:** Purinex could simply wait in the expectation that either the sepsis deal or the diabetes deal would come through. Purinex's current owners would then retain complete control of the company, which Harpaz believed could be valued at $25 million. While Purinex had about twelve months of cash available, the company could only wait about six months before securing additional financing. If either the sepsis or the diabetes deal failed to happen during the next six months, Purinex would be forced into a down-round[12] scenario with potential investors.

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[10]The burn rate was the rate at which a new company depleted its capital to finance operations before it began to generate a positive cash flow. The burn rate was usually quoted in terms of cash spent per month.

[11]Premoney valuation was the value of a company before external financing alternatives were added to its balance sheet.

[12]A down round was a round of financing in which investors purchased stock from a company at a lower valuation than the one placed on the company by earlier investors. Down rounds caused the dilution of economic value for existing investors, which often meant that the company founders' stock or options were worth much less or possibly nothing at all. For start-up firms in a down round, VC firms would typically impose more onerous covenants, dictate a lower premoney valuation, and even remove current management.

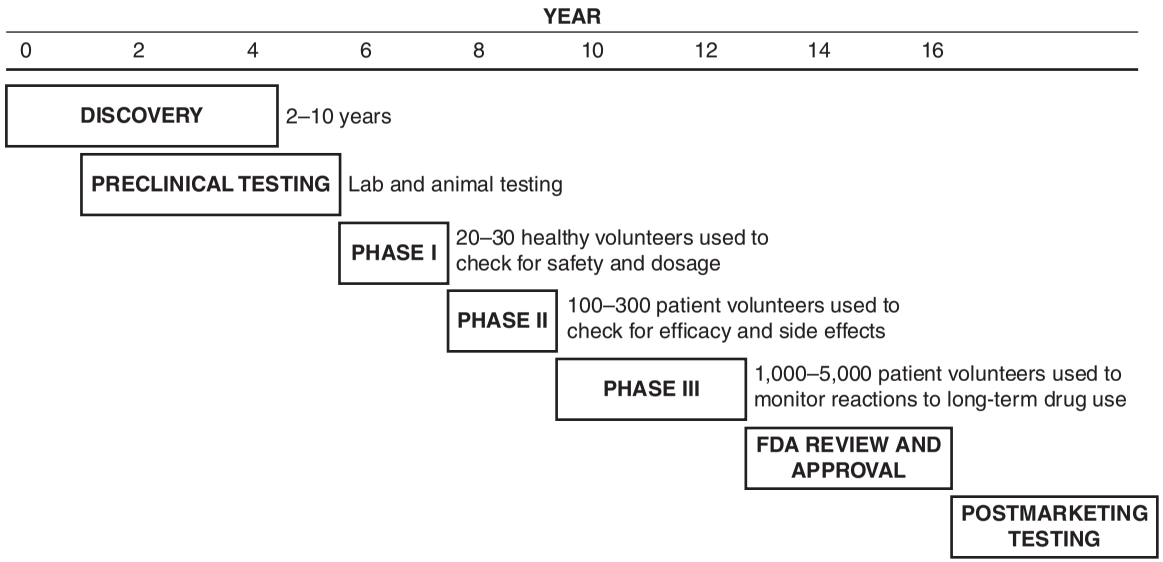
Under those dire circumstances, Harpaz believed that the premoney valuation for Purinex would drop to $8 million or possibly as low as $5 million.

- **Angel round:** A third option for the company would be to undertake another one-time round of financing from a number of angel investors. Harpaz did not think Purinex could raise as much from angel investors as it could from VC firms—probably only $2 million. But with angel investors, Harpaz could probably ensure a higher firm valuation—about $17.5 million—and a diverse group of angels would not demand many preferences. It would take about six months to complete an angel round of financing.

In the back of his mind, Harpaz knew that if the firm were well capitalized, it would have a better chance of securing a collaboration with a major pharmaceutical firm and getting a better deal;[13] there was a "credibility value" in being adequately funded. How could the firm survive until that happened? What was the best way to finance the firm, yet also maximize the value of the firm today? Certainly, there was value in having the founders and current principals maintain control of the company, but what was that worth? "There are certain risks we're willing to take, and certain ones we're not," Harpaz thought to himself. "We are in the technology risk business, not the finance risk business." How could he evaluate all those risk-and-return scenarios?

[13]Harpaz believed that a round of VC funding could possibly increase the value of a pharma deal by 10%.

EXHIBIT 1 | The Drug-Development Process



Source of data: Ernst & Young, LLP, *Biotechnology Industry Report: Convergence 2000* (cited in the *Guide to Biotechnology*, The Biotechnology Industry Organization [BIO]).

EXHIBIT 2 | Recent Biotechnology/Pharmaceutical Partnering Deals

Companies	Date	Details of the Deals
Curagen/TopoTarget	Jun–04	Histone deacetylase inhibitor: $5 million (m) in equity, $5m in license fees, plus $41m in milestones and royalties; deal includes rights to follow-up compounds at $1m license fee and $30m in milestones per product
Serono/4SC	May–04	Licenses worldwide rights to small-molecule dihydroorotate dehydrogenase inhibitors for autoimmune disorders—up-front, R&D funding and milestones, plus undisclosed royalties
Arqule/Roche	Apr–04	E2F pathway: $15m up-front, $276m in milestones, plus undisclosed royalties
Lundbeck/Merck	Feb–04	Gaboxadol, sleep deprivation: $70m up-front plus $200m in milestones plus royalties plus copromotion rights to undisclosed Merck product
Biostratum/NovoNordisk	Jan–04	Cancer project focused on Anti-laminin 5 antibodies: $80m milestones per antibody plus royalties and undisclosed royalties
Array Biopharma/AZ	Dec–03	Oncology: $10m up-front, $85m milestones, R&D funding plus milestones
Neurogean/Merck	Dec–03	Neurology/pain: $42m up-front, $118m in milestones, plus R&D funding plus milestones
MorphoSys/Pfizer	Dec–03	Five-year license, $50m in potential milestones plus royalties
Actelion/Merck	Dec–03	Renin inhibitor: $10m up-front, $262m in milestones
Neurosearch/GSK	Dec–03	Central nervous system area: $82m in guaranteed payments plus $200m in “bioworld payments”

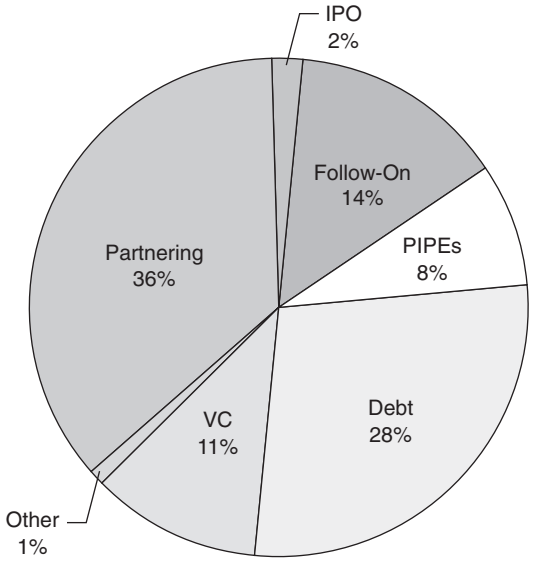
Source of data: Credit Suisse First Boston.

EXHIBIT 3 | Mean and Median Terms of Partnership-Deal Licensing (in millions of dollars)

	Preclinical Stage	Phase I	Phase II	Phase III
Total Value				
Mean	$82.7	$268.0	$212.3	$227.0
Median	$57.0	$200.4	$179.5	$247.5
Up-front				
Mean	$30.2	$32.6	$44.6	$42.7
Median	$19.0	$11.7	$25.0	$32.0
Milestones				
Mean	$72.9	$213.0	$196.6	$241.7
Median	$62.0	$184.6	$120.0	$200.0

Source of data: Credit Suisse First Boston, citing *Biocentury* (2003–February 2004).

EXHIBIT 4 | Financings in the North American Biotechnology Industry, 2003



Source of data: Burrill & Company.

Note: PIPEs were private investments in public entities.