

Case vertex

Business



GARY PISANO LEE FLEMING ELI PETER STRICK I've never made a bad decision. I've just had bad data.

— Joshua Boger, CEO and Founder of Vertex Pharmaceuticals Like many New Englanders on this bright October morning in 2003, Josh Boger, CEO of Vertex Pharmaceuticals, had been up until 2:00 a.m. the previous evening watching the Boston Red Sox playoff game. The game, predictably, ended in a heartbreaking loss for the Red Sox, but Boger's lingering disappointment (and regret over staying up so late) quickly faded as he strode down the halls of the Cambridge, Massachusetts company he had founded 15 years earlier.

Vertex had four promising drugs in various stages of clinical development, and Boger was excited by the possibilities: "The portfolio is playing out exactly as we hoped. We've got a stream of revenues from our partnered project that will help fund our development costs.

There are multiple paths for us to become profitable. We're in a position to choose." While the company had revenue from various corporate partnerships and roughly \$600 million in cash and short-term investments on its balance sheet, it was unlikely that the company could fund more than two of its four primary development projects. Therefore, Boger and Vicki Sato, Vertex's president, had to decide which two projects should be funded. This was not an easy question, as each project had strong proponents in various parts of the organization. A second decision for the company was what to do with the two projects that did not receive funding.

Again, opinions differed within Vertex, with some favoring licensing out the projects while others believed Vertex should hold the two projects as backups in case something happened to the others.

The implications of these decisions were enormous, as the chosen candidates would be the first products Vertex attempted to bring through development, and hopefully onto the market, on its own. Do 1 According to its third-quarter 2003 10-Q statement, Vertex had \$77. 5 million and \$518. 2 million in cash and marketable securities on its balance sheet, respectively.

Professors Gary Pisano and Lee Fleming and Research Associate Eli Peter Strick prepared this case.

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harvard. edu or 617-783-7860. No tC op yo Vertex Pharmaceuticals: R&D Portfolio Management (A) rP os t 9-604-101 REV: JUNE 20, 2006 604-101 Vertex Pharmaceuticals: R&D Portfolio Management (A) The Pharmaceutical Industry2

Vertex Pharmaceuticals Founded in 1989, Vertex's age and size caused many to categorize it as a biotechnology firm. 7 However, because the company focused on chemically synthesized molecules rather than biologics, Vertex generally viewed itself as a classical pharmaceutical company. In fact, many of the company's 2 For a more extensive overview of the pharmaceutical industry, see Stephen Bradley and James Weber, " The Pharmaceutical Industry: Challenges in the New Century," HBS Case No.

703-489 (Boston: Harvard Business School Publishing, 2003). Do Herman Saftlas, " Healthcare: Pharmaceuticals," Standard & Poor's Industry Surveys, December 11, 2003. 4 L. J. Sellers, " Fourth Annual Pharm Exec 50," Pharmaceutical Executive, May 2003.

5 Pharmaceutical Researchers and Manufacturers of America (PhRMA) Web site, www. phrma. org, accessed January 9, 2004. 6 Pharmaceutical Industry Profile 2003 (Washington, D. C.

: PhRMA, 2003). 7 At fiscal-year-end 2002, Vertex reported 980 employees, \$816 million in assets, and \$161 million in revenue. 2 Copying or posting is an infringement of copyright.harvard. edu or 617-783-7860.

No tC

Before a company could apply to have a new drug approved by the FDA (file a new-drug application, or NDA), it first had to pass tests concerning its safety in patients (Phase I trials), efficacy as a treatment (Phase II trials), and relative performance to existing treatments (Phase III trials). Animal toxicology testing preceded each more advanced and lengthy human-testing stage. Producing a new drug, from initial concept to commercialization, took companies anywhere from 10 to 15 years and was estimated to cost, on average, more than \$800 million. Only one of every 250 drugs in preclinical testing (i. . . , prior to Phase I) ever reached FDA approval, and only 30% of approved drugs ever produced enough revenue to break even with their R costs.

6 Based on the extensive investment, in both time and money, and extreme risk inherent in drug development, pharmaceutical companies were forced to carefully select which projects they pursued. (Exhibit 1 shows statistics on average cost and success rates for the different stages of clinical development.) op Between 1993 and 2003, pharmaceutical research companies in America invested over \$200 billion in R, spending \$34 billion in 2002 alone.

During the same decade, the U. S. Food and Drug Administration (FDA) approved more than 363 new medicines, biologics, and vaccines for the prevention and treatment of more than 150 diseases and conditions.

5 yo Global pharmaceutical sales for the 12 months ending June 2003 totaled \$433 billion. The U. S. pharmaceutical market alone totaled \$219 billion in 2002. Revenue in 2002 for the top 10 companies in the industry, including names such as Pfizer, GlaxoSmithKline, and Merck, was over \$184 billion. 3 <https://assignbuster.com/case-vertex/>

Lipitor, Pfizer's cholesterol reducer, brought in nearly \$8 billion by itself in 2002. Typical research and development (R&D) budgets for major pharmaceuticals were in the range of \$1 billion to \$5 billion per year. rP During the beginning of the twenty-first century, the pharmaceutical industry was changing in every aspect. Headlines abounded concerning the rising costs of health care, declining research productivity, and the potential to be reached from decoding the genome. New standards concerning patent protection, clinical testing, and government subsidies for drugs were being introduced.

Scientific discoveries and new technologies were revolutionizing the way drugs were discovered.

Along with new discoveries came new entrants into the industry. While the large pharmaceutical powerhouses turned to mergers and strategic partnerships to maintain their competitive positions, smaller companies were constantly forming, specializing in the latest research techniques. os t Vertex Pharmaceuticals: R&D Portfolio Management (A) 604-101 Vertex's Research Strategy The Vertex Culture Vertex's scientific culture was not isolated to inside the laboratory but spread throughout the company. " Decisions are made from the top down at Vertex .

. . he ' top' consisting primarily but not exclusively of scientists," mentioned Phil Tinmouth, director of business development. Even in an industry known for its strong emphasis on science, the scientific credentials of Vertex's senior management stood out. Boger was a Harvard Ph. D.

in chemistry and was one of Merck's top scientists until he founded Vertex. Before joining Vertex in 1992, Sato had been vice president of research at Biogen and, before that, a professor in Harvard's biology department.

(Exhibit 4 gives brief biographies for some of Vertex' s senior management.)

Do The scientific culture at Vertex pervaded the decision-making process. As described by Sato, “ Choosing between analysis-paralysis versus shoot-from-the-hip decision making, Vertex errs on the side of analysis.

” While Boger and Sato retained the final say, they were careful to keep communication open throughout the company, enabling any employee to influence their decision, even at the last minute. Boger explained: No tC Vertex used an interdisciplinary research approach, incorporating advanced biology, biophysics, chemistry, and automation and information technologies.

While it had an impressive spread of capabilities, what separated Vertex from its industry peers was its focus on “ rational drug design. ” Traditionally, many drug companies relied heavily on random testing of compounds to generate drug candidates. Modern technologies had benefited this traditional approach, allowing scientists to industrialize the early testing stage. High-throughput screening (HTS), for instance, provided companies with the capability to simultaneously test hundreds of thousands of chemical compounds against disease targets to identify drug-like reactions.

While Vertex also used advanced screening technology to speed up testing, it focused on increasing productivity by starting with detailed knowledge of the underlying biology of a disease and the molecular structure of relevant

drug “ targets. ” A drug target for Vertex was a protein molecule, produced by a gene, which had a biological function involved in some stage of a disease. A drug molecule interacted with or affected a target’s “ active site,” changing the target’s structure and altering its function.

A common “ lock and key” analogy was often used when describing drug-target interactions, targets being similar to locks and drugs to keys. If a key fit correctly in a lock, it had an effect. However, if a key were the wrong shape to fit the lock, it would be unable to act.

(Exhibit 3 shows a diagram of a small-molecule drug interacting with a target molecule [enzyme].) Starting with knowledge of the shape and other attributes of a disease target, Vertex scientists tried to search for and design the best drug that fit.

Ideally, using the underlying science of a disease to direct its research efforts more carefully, Vertex hoped to remove some of the randomness from the discovery process. op yo rP initial recruits came from the ranks of established pharmaceutical companies, including Boger himself, who had been a senior scientist at Merck. Furthermore, while Vertex was younger and smaller than most pharmaceutical companies, that had not subdued the company’s ambitions.

Vertex management believed that a small firm could compete head-to-head with the larger breed of pharmaceutical firms, being just as productive but with greater efficiency due to its size.

By staying trim and nimble, avoiding large-company bureaucracy, and investing heavily in the right people and technologies, Vertex looked to <https://assignbuster.com/case-vertex/>

create a better model for producing novel and important drugs. (Exhibits 2a and 2b show Vertex's financial statements for 2002.) Copying or posting is an infringement of copyright.harvard.

edu or 617-783-7860. os t 3 604-101 Vertex Pharmaceuticals: R Portfolio Management (A) A lot of biotechs are founded on the German academic model, with a couple PIs [principal investigators] and their closest troops.

As the firm expands, later employees are considered less important. In contrast, we believe that the last person in the door is just as important as the first. We consciously reject the German model for the Silicon Valley model. We want the guy on the loading dock to be thinking about clinical programs.

Vertex has a long history of ignoring my opinions. For example, our original charter specifically states we will work on chronic infectious diseases—except HIV. So, what happened? People began working on HIV during the 12 a. m. to 6 a. m.

shift.

Once they demonstrated an advantage in concept, I was convinced and we decided to pursue it. Our first product to get to market was an HIV drug which we licensed to Glaxo. While Vertex was sometimes divided by different initiatives and scientific beliefs, one common conviction existed throughout the company: Vertex was a “ serious” drug company. “ We go after serious drugs for serious diseases, not wrinkle creams,” said Timmouth.

John Thomson, vice president of research and one of Vertex's first employees, agreed: " I started out to make an important drug company, not just one that makes me financially comfortable. Vertex's Evolution Do we want to be a drug discovery factory, creating new drug candidates, or a fully integrated pharma company, commercializing the drugs we create in our own research labs? Vertex is creating a model that will be supported by both partners and independently commercializing innovative drugs; in eight to 10 years, the goal is to be a research-driven company which picks priority clinical candidates to move forward into development and can be successfully commercialized by Vertex. We will retain rights, U. S. first and later Europe, for drug candidates that fit with our strategy and capabilities and use a partner strategy for others.

— Ian Smith, Senior Vice President and CFO of Vertex Pharmaceuticals For much of its history, Vertex was a company focused on early-stage research and drug discovery. The company's broad discovery approach produced drug candidates in over six different therapeutic categories, including infectious diseases, autoimmune/inflammation diseases, genetic disorders, cancer, neurological diseases, and pain. However, rather than focusing on certain disease classes (e. . , obesity, cancer, etc.

), Vertex worked on entire families of targets (e. g. , kinases, caspases, etc.).

John Randle, the program executive in charge of Vertex's ICE/caspase inhibitor development projects, explained: " Vertex has often used the model in which the attractive drug target is selected first, then the best therapeutic area is selected as the drug is developed and knowledge of the target accumulates.

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Most large pharmaceutical companies start by focusing on certain therapeutic areas and then look for targets implicated in the selected disease indications. Vertex's R budget for fiscal-year 2002 was reported as roughly \$200 million, research spending contributing significantly to that number. Its largest program was its kinase program, followed by its ion channel and caspase program, among others. Its kinase and caspase programs were partnered with Novartis and Serono, Do 4 Copying or posting is an infringement of copyright.

harvard. edu or 617-783-7860. No tC op yo Boger tried not to make premature decisions. If there was more data arriving, or there were more opinions to be weighed, he was willing to postpone a choice until its deadline.

At times, this extensive amount of analysis and discussion left Vertex employees in the dark as to which direction the company would take.

" I have an incredible tolerance for ambiguity . . . not indecision, but openness to contradictory points of view," mentioned Boger. " As a result, it takes longer for Vertex to make a decision.

" Different points of view were not only allowed at Vertex but also encouraged. Boger believed such variance in opinion was good for the company: " Success in drug development is usually tied to two or three people who are passionate about their opinion beyond explanation. He offered this example: rP os t Vertex Pharmaceuticals: R Portfolio Management (A) 604-101 By licensing out some of its compounds (often just regionally), collecting milestone payments from partners, and retaining a

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percentage of its drugs' sales, Vertex's "research boutique" business model provided the company a steady flow of cash. However, partnering caused other difficulties for the company. Kenneth Boger, senior vice president and general counsel at Vertex, described the obstacles involved with codeveloping drugs: "It's more difficult for a two-headed snake to crawl through the grass. .

. You don't control the process with partners, which can be frustrating. For example, we synthesized the first HIV protease inhibitor but were the fifth to market. " Not only did entering alliances limit Vertex's ability to control the momentum of its projects, it also meant Vertex was dependent on the industry's demand for in-licensing deals. While Vertex had been successful 8 In 1993, Vertex entered into an alliance with GlaxoSmithKline (GSK) covering the research, development, and commercialization of HIV protease inhibitors.

GSK has paid Vertex \$47 million in research, development, and commercialization payments for Agenerase and Lexiva, as well as royalty payments based on the sales of each drug.

In addition, Vertex will receive milestone payments based on the development of VX-385, another HIV protease candidate. GSK has exclusive rights to commercialize Vertex's HIV protease inhibitors worldwide, except in the Far East. Kissei Pharmaceutical Co. holds commercial rights for Agenerase (amprenavir) in the Far East and pays Vertex a royalty on sales. (Source: "Collaborations," Vertex Pharmaceuticals, company Web site, <http://www.>

vertex.com/collaborations.html, accessed June 10, 2004.)⁹ Royalties could range dramatically (roughly between 8% and 30%) depending on the stage of development at which the deal was signed as well as other factors. Do Not TC With a business plan that contemplated multiple drug candidates in multiple indications, broadbased research funding would be required and, if successful, the number of drug candidates would exceed the resources necessary to fund and carry out late-stage clinical testing (Phase II and beyond). Vertex's strategy was to choose corporate partners with complementary strengths to assist with the development of its lead compounds.

By forming alliances with larger pharmaceutical firms, Vertex gained financial support for its broad discovery efforts and access to the clinical testing, manufacturing, marketing, and sales expertise necessary for bringing a drug to market. Of course, sharing the cost, risk, and work of developing a drug also meant sharing any potential rewards from commercializing the drug. In many cases, entering an alliance forced Vertex to give up much of its ownership over a drug, leaving it with royalties from the drug's sales.⁹ op yo

In the 14 years Vertex had been in business, it had succeeded in getting two of its drug candidates approved by the FDA and into the marketplace (impressive given the average time for research and development of a drug was in the 12- to 15-year range, if not longer). Both of these products, Agenerase® and Lexiva™, were HIV protease inhibitors developed through a collaboration with GlaxoSmithKline (GSK).⁸ Even after acknowledging the time investment and risk inherent in placing a new drug on the market, <https://assignbuster.com/case-vertex/>

many onlookers questioned why Vertex had not sent more candidates into later stages of development.

As put by Tinmouth, “ Wall Street analysts are telling us they’d like to see more compounds in later-stage development. ” Tinmouth offered some possible explanations for why Vertex had not produced more late-stage molecules in 14 years: “ Vertex has chosen to go after difficult, pioneering projects: HCV protease, ICE inhibitors, etc. —these are highly difficult compounds to develop. ” And unlike the case with many other companies, all of Vertex’s compounds had been developed internally. rP respectively.

Vertex’s ability to stay broad and “ follow any lead” was partially enabled by its not having more infrastructure to support.

Larger, fully integrated pharmaceutical companies were pressured to produce drugs in certain disease areas in order to support their existing brands and large sales forces (which specialized in certain therapeutic domains). According to Sato, “ I never want to get too stuck protecting a franchise in a specific therapeutic area. Larger companies factor in their franchise when making a decision, which often leads to picking the best ‘ franchise idea,’ which can be the 12th-best idea overall. ” Copying or posting is an infringement of copyright.

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Pharmaceuticals: R Portfolio Management (A) Vertex started building its internal development organization in 1997 by hiring John Alam to be its vice president of clinical development. Alam had spent the previous six years at Biogen directing the development of Avonex.

Serious about adding capabilities, Alam's development group grew from 25 members in 1997 to 110 members in 2002. Meanwhile, Vertex made some initial investment in its commercial operations by hiring a small group of sales and marketing professionals.

The company's commercial initiative grew in March of 2002 with the hiring of Tony Coles as the senior vice president of commercial operations. Coles came over to Vertex from Bristol-Myers Squibb, where he had served as the senior vice president of marketing and medical affairs for its neuroscience, infectious diseases, and dermatology units. Commercial ops was charged with increasing the level of commercial strategy in Vertex's analysis and decision making. Additionally, Vertex planned to ramp up its marketing and sales force in preparation for launching any proprietary products.

In January 2003, at the 21st J. P Morgan H Annual Healthcare Conference, Josh Boger announced that Vertex would commit to developing and commercializing two of its drug candidates on its own. The investment required to build new development and commercial capabilities meant Vertex would have to scale back its research spending. In June 2003, Vertex laid off roughly 20% of its research department. However, while it was committed to commercializing drugs, Vertex was trying to be careful to preserve its strength in discovery research.

According to Sato, " Technology is changing too fast to say we'll take a holiday from discovery and get back to it later—too many Do 10 These notes were convertible, at the option of the holder, into Vertex common stock at a price of \$92. 26 per share. 6 Copying or posting is an infringement of copyright.harvard. edu or 617-783-7860.

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No top Vertex carried a large research investment as a critical part of its strategic plan, which for a long time was supported by successful partnering of the majority of this investment.

Big Pharma, through early-stage deals, was a key source of funding for Vertex. As Big Pharma pipelines started drying up, they began to dedicate their investment towards late-stage product acquisitions. . . .

Additionally, we could always raise money in the past from the capital markets to fund research, but that source of funding is more expensive right now. The capital markets have moved away from “ story stocks. ” Research companies are cash burners and, at the moment, the capital markets are less receptive to cash burners.

Hence we are more and more reliant on Pharma collaborations to support our broad investment into the business. At the same time that Vertex was observing less interest from Big Pharma in forming research partnerships, it was also facing a new climate in the capital markets.

Investors had come down from being infatuated with the potential revenues of the many start-ups focused on biomedical research and returned to looking for companies that had more than just promise but also revenue and profits. (Exhibit 5 shows a diagram of Vertex’s stock performance relative to Nasdaq’s Biotech Index. Since Vertex had \$315 million of convertible debt maturing in 2007, the capital market’s perception of Vertex was of critical and timely concern. Smith, Vertex’s CFO, explained how the market for partnerships, along with the capital markets, influenced Vertex’s situation: rP inking early-stage deals during the early 1990s, current market conditions

had shifted demand to products in later stages of development (with a higher probability of success). Mark Murcko, Vertex's chief technology officer, explained: " We recognize that it's very hard to do research deals now.

Big Pharma wants to see clinical data and clear IP [intellectual property] positions before doing a deal.

We have had projects we chose not to start because, in part, we believed we would need to go it alone for a very long time before we could generate enough data to excite a potential partner. " Vertex quickly realized it needed the ability to control its own destiny. Said Ken Boger, " Drug development is a hugely risky business; the optimal position is to have all the assets: research, development, and commercial. " os t Vertex Pharmaceuticals: R Portfolio Management (A) 604-101 ompanies have paid the price for that in terms of maintaining sustainable, product-driven businesses. " 11 Entering Phase IIb trials without a partner represents a big jump in commitment for Vertex. Electing to prioritize its Vertex-controlled portfolio around two candidates, Vertex will narrow its focus, giving itself a specific identity.

— Lynne Brum, Vice President of Corporate Communications and Financial Planning & Analysis at Vertex By the middle of 2003, apart from its discovery research, preclinical studies, and HIV protease inhibitors already on the market, Vertex had several drug candidates in clinical testing. Exhibit 6 shows Vertex's development pipeline.) Two of these candidates, VX-385 and pralnacasan, were covered under existing alliances with GSK and Aventis, respectively. Of the remaining programs that had not yet been partnered,

four candidates were thought to be the most promising: VX-148, VX702, VX-765, and VX-950. The company had decided that it held sufficient resources to develop only two candidates on its own but, according to Murcko, “ A large pharmaceutical company would take all of these molecules forward . . . but we can’t afford this right now.

We have no choice but to swallow hard, picking some to move forward ourselves, and partner the others. ” VX-148: Psoriasis Do In October 2003, VX-148 was nearing the end of its Phase II study in patients with moderate-to-severe psoriasis, a three-month study designed to evaluate the drug’s safety and efficacy. Psoriasis was a chronic disease characterized by scaling of the skin and inflammation.

These scaly patches often itch, burn, and crack, causing pain. Psoriasis was originally believed to be a skin disease; however, later research had indicated that the cause of psoriasis was related to overactivity of the immune system.

Psoriasis was a very competitive market for pharmaceutical companies with multiple lines of treatment already existing as well as new biologic agents nearing FDA approval. ¹² According to the National Institutes of Health (NIH), roughly 1% of people in the U. S.

(approximately 2. 7 million individuals) were affected by psoriasis. Of these, 30% suffered from ¹¹ Jeffrey Dvorin, “ Vertex: Sticking To Its Story,” In Vivo: The Business And Development Report, October 2002, p. 66. ¹² Standard treatments for psoriasis at the time included topical treatments, phototherapy, and different types of systemic drugs (e.

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g. methotrexate and cyclosporine, etc.). Recent drugs, such as Amevive® and Raptiva™, worked by modulating the human immune processes involved in psoriasis. No tC VX-148 was a molecule that inhibited an enzyme in the body known as inosine 5'-monophosphate dehydrogenase (IMPDH).

IMPDH was believed to play an important role in the regulation of immune system activity. As a result, VX-148 had the potential to treat a number of important diseases with unmet medical needs, such as psoriasis, multiple sclerosis, and even cancer. IMPDH was also a “ validated target,” meaning there were already drugs on the market known to affect IMPDH.

Other medicines targeting the enzyme were used in helping to prevent against organ transplant (kidney, heart, liver, etc.) rejection. Vertex had other IMPDH inhibitors in development besides VX-148.

Merimepodib (VX-497), the company's first IMPDH inhibitor, was in Phase II trials for treating hepatitis C viral infections. VX-944 was a second-generation IMPDH inhibitor in Phase I trials similar to VX-148. However, VX-148 was considered by many in the company to be the most promising candidate in the IMPDH program. op yo rP The Portfolio Candidates Copying or posting is an infringement of copyright.

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edu or 617-783-7860. os t 7 604-101 Vertex Pharmaceuticals: R Portfolio Management (A) moderate-to-severe symptoms. Steven Lyons, the IMPDH program executive, described some of the characteristics of VX-148: The IMPDH mechanism was established 20 years ago, so there is low target risk, only molecule risk. . .

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. It also has a large market with unmet medical needs. Merimepodib, an earlier IMPDH inhibitor, was initially tested in psoriasis and produced encouraging data but was less attractive than VX-148 for other reasons.

VX-148 may be more potent than Merimepodib, and we already have a formulation and manufacturing process. However, Brum was very hesitant to abandon VX-148 simply because it lacked novelty: “ In the drug industry, viable drugs are so rare that you don’t kill them.

Maybe it’s not exciting, but it’s a drug. ” VX-702: Acute Coronary Syndrome ACS was the term used to describe a wide range of conditions resulting from insufficient blood supply to the heart muscle, including chest pain and heart attacks. ACS afflicted roughly 1.9 million people each year in the U. S. alone.

Inhibition of the p38 enzyme represented a novel approach to treating acute cardiovascular events through their underlying inflammatory responses. 13 MAP kinases were key enzymes believed to be involved in signal transduction and amplification of cellular responses to stimuli. The p38 MAP kinases, specifically, regulated the production of proinflammatory cytokines, which had been shown to play a significant role in numerous acute and chronic diseases, such as rheumatoid arthritis (RA), osteoarthritis (OA), osteoporosis, Crohn’s disease, and cardiovascular diseases. 4 Pharmacodynamic studies looked at how drugs produced their effects. Pharmacokinetic studies examined how well a drug was absorbed, distributed, and metabolized in the body. Do 15 In September 1997, Vertex and Kissei Pharmaceuticals formed a strategic alliance to develop and

commercialize p38 MAP kinase inhibitors for the treatment of inflammatory and neurological diseases.

In return for commercial rights in the Far East, Kissei paid Vertex up to \$22 million in up-front fees, milestone payments, and research funding.

Kissei also agreed to pay a proportional share of any development costs. While VX-702 was one of the drug candidates covered under the Kissei alliance, Vertex retained exclusive commercial rights for the drug, excluding in the Far East, unless further licensing occurred. (Source: " Collaborations," Vertex Pharmaceuticals, company Web site, <http://www.vrtx.com/collaborations.html>, accessed June 10, 2004.) 8 Copying or posting is an infringement of copyright.harvard.edu or 617-783-7860.

html, accessed June 10, 2004.) 8 Copying or posting is an infringement of copyright.harvard.edu or 617-783-7860.

No tC VX-702 was an inhibitor of an enzyme called p38. The p38 enzyme was a specific member of the MAP kinase family, believed to be associated with the onset and progression of inflammation. 13 In June of 2002, Vertex began Phase I clinical testing of VX-702. Testing showed that the drug was well tolerated in patients and had an excellent pharmacokinetic and pharmacodynamic profile. 14 Vertex was testing VX-702 in a Phase IIa pilot study designed to evaluate the safety and tolerability of VX702 in patients with acute coronary syndrome (ACS).

Vertex also had a second-generation p38 MAP kinase inhibitor, VX-850, in preclinical development. 5 op yo VX-148 had plenty of other proponents at Vertex, especially since it was the candidate that, if successful, would get Vertex to the market the quickest. According to Coles, " It's the most <https://assignbuster.com/case-vertex/>

advanced—we would be remiss if we didn't fully explore 148 as an option. " However, Brum, who was also a supporter of the program, pointed out that VX-148 was not an obvious choice for some at Vertex: " Earlier in the year, VX-148 was not an obvious choice for the company given some of its characteristics. It has the least scientific sizzle of all the candidates.

VX-148 doesn't have a novel mechanism; some view it as a ' me too' drug. The market is established—psoriasis drugs already exist. " rP os t Vertex Pharmaceuticals: R Portfolio Management (A) 604-101 VX-702 had some strong supporters within Vertex, including Ken Boger: " It's a beautiful drug, cheap and easy to make. Seventy-five percent of the drug stays in your system for therapeutically attractive periods. There are manageable side effects. " Since inflammation was responsible for a wide range of diseases, VX-702 had the potential to be tested in multiple indications.

Coles also expressed his excitement over VX-702 from a commercial standpoint: VX-702 has lots of promise. It's an oral drug in a field of injectables, such as Enbrel. Right now, very few oral meds are covered by Medicare but, if the prescription drug benefit bill passes, oral drugs could be covered under this legislation. There are multiple possible indications for VX-702—ACS, rheumatoid arthritis, and others—which could be considered. Inflammation is a hot topic in cardiology right now. We are currently in Phase II, doing safety studies but also looking for efficacy signals.

We still need to demonstrate proof of mechanism for this compound. One concern was that p38 MAP kinase drugs seemed prone to toxicity issues. Several companies had tried developing p38 drugs, and most had failed. VX-765: Rheumatoid Arthritis and Osteoarthritis OA was a degenerative joint
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disease and the most common form of arthritis, afflicting more than 21 million people in the U. S. alone.

OA generally occurred after people reached middle age and, over time, caused loss of cartilage, bone damage, and inflammation of soft tissue. Patients with OA suffered from pain, swelling, and loss of mobility.

Mild-to-moderate cases of OA were usually treated using over-the-counter (OTC) medicines, while patients with more severe cases benefited from a range of prescription drugs. Many older treatments for arthritis—such as analgesics and nonsteroidal anti-inflammatories— treated the symptoms rather than the causes of arthritis. Recently, a new class of drugs that attacked the underlying biological causes of arthritis was introduced to the market. Known as diseasemodifying anti-rheumatic drugs (DMARDs), this class included such products as Enbrel, Remicade, and Kineret.

7 While these drugs were effective in many patients, as larger protein molecules they required injection, making them inconvenient and painful to administer. As a small molecule, VX-765 could be taken orally and was thus thought to have excellent market potential. Do 16 ICE was shown to drive the activation and release of IL-1? as well as IL-18, which regulated the release of interferon- gamma, another proinflammatory cytokine. IL-1 was identified in the mid-1970s, while IL-18 was later discovered by Vertex. 17 SG Cowen Securities Corp.

estimated 2003 sales for Enbrel, Remicade, and Kineret at \$1, 280 million, \$1, 500 million, and \$75 million, respectively. “ Perspectives: Pharmaceutical Therapeutic Category Outlook,” SG Cowen Securities Corp. , October 2003,

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Thompson Research, <http://research.thomsonib.com>, accessed March 1, 2004.

No tC RA was a progressive systemic autoimmune disease characterized by inflammation of the membrane lining in joints. Inflammation in the membrane caused a loss of joint shape and alignment, resulting in pain, stiffness, and swelling.

Severe RA, in its later stages, invaded bone and cartilage, typically causing loss of movement and disability. Treatment for RA usually involved a multidisciplinary approach using one or more drugs, exercise, rest, physical therapy, and surgery. op VX-765 was a drug that inhibited the Interleukin-1 β converting enzyme (ICE).

ICE belonged to a structurally related class of enzymes called caspases, believed to play an important role in a number of chronic inflammatory diseases, including rheumatoid arthritis (RA) and osteoarthritis (OA). 6 yo rP Copying or posting is an infringement of copyright.harvard.edu or 617-783-7860. os t 9 604-101 Vertex Pharmaceuticals: R Portfolio Management (A) VX-950 was being investigated by Vertex as a novel small-molecule inhibitor of the hepatitis C virus (HCV) protease.

18 The molecule, which entered preclinical tests in 2002, had shown potent properties as an inhibitor of a protease enzyme believed to be essential for HCV viral replication. HCV was a serious disease that caused inflammation in the liver.

This inflammation could lead to a number of other dangerous conditions, such as fibrosis, cirrhosis, and liver cancer, and could ultimately lead to liver failure. 19 Chronic HCV afflicted roughly 2. 7 million people in the U. S.

and 185 million people worldwide. Each year, an estimated 8, 000 to 10, 000 people died from HCV-related complications. Furthermore, current treatments for the disease were only effective in roughly 40% to 60% of chronically ill HCV patients. Most of these treatments were associated with significant side effects, and none was a direct antiviral therapy.

In October 2003, VX-950 was still in preclinical studies, with expectations to begin Phase I trials in early 2004.

While this made VX-950 the least developed of all the portfolio candidates, Lyons, the program executive in charge of VX-950, described the attractiveness of the candidate: Do VX-950 is potentially a billion-dollar drug. There exist large unmet medical needs in this area—current medicines are suboptimal. Vertex has a leadership position in HCV protease, 18 Vertex scientists solved the three-dimensional atomic structure of HCV protease, which they reported in the journal Cell n 1996. 19 HCV could go undetected for many years while causing progressively worse liver inflammation. 10 Copying or posting is an infringement of copyright.

harvard. edu or 617-783-7860. No tC VX-950: Hepatitis C op Even as a “ fast follower” of pralnacasan, VX-765, Randle believed, was a good contestant for further development: “ There are two reasons to develop follow-up compounds: one, if the first compound fails, and two, if the first

compound succeeds. ” While VX-765 had strong support, there were concerns about the impact on the Aventis partnership.

In addition, the in vivo potency of the drug was yet to be determined, and there was some question regarding the proper dose needed for adequate results.

VX-765’s relatively high manufacturing costs (at this stage of development) were another point to consider. By August of 1999, VX-765 had started Phase II testing after successfully meeting the safety objectives for the compound in Phase I. While VX-765 was fully owned by Vertex, it was also a “ second-generation” compound to another Vertex-originated drug, pralnacasan (VX-740), an earlier ICE inhibitor being developed through a partnership with Aventis.

By October, pralnacasan was nearing completion of Phase II trials in both RA and OA. VX-765 was chemically distinct from pralnacasan, giving Vertex full rights over the compound.

However, under a licensing agreement with Aventis, if Vertex decided to go ahead with the development of another ICE inhibitor, it would have reduced influence on certain committees governing the development of pralnacasan, lose rights to a subsidized sales force in U. S. /Europe, and sacrifice certain financial benefits of copromotion. P Coles ranked VX-765 as one of his favorites: “ It has the largest possible financial return of all the candidates and has multiple indications to drive its value. It’s doable. Success with VX-765 could provide a breakout opportunity for the company.

“ Thomson agreed: “ VX-765 is everyone’s sweetheart. Success with 765 on our own could launch Vertex out of low orbit. ” John Randle, the program executive in charge of Vertex’s ICE inhibitors, also expressed his excitement: “ VX-765 uses proprietary chemistry.

We have a strong patent position in ICE inhibitor chemistry—there are no other ICE inhibitor candidates on the market right now. If ICE inhibitors work, it could be a blockbuster opportunity. ” os t Vertex Pharmaceuticals: R Portfolio Management (A) 604-101 potentially best in class, and also benefits from its experience with HIV protease inhibition.

Vertex has antiviral drug development experience and in-depth knowledge about the structure of the HCV protease molecule. . . . There is a focused audience for the drug; doctors treating Hep C [hepatologists] are specialized physicians.

Also, there is a lot of overlap between HIV and HCV patients, which allows Vertex to leverage existing relationships with doctors. VX-950 was a premier example of Vertex’s ability to do rational drug design and caused plenty of excitement within the company. “ VX-950 has the right concept—we believe it will work,” said Sato. Thomson agreed: “ HCV is a profoundly important medical area where Vertex can make a difference. We have a locked-down target with low biological risk.

” Another advantage, from a commercial standpoint, was that Vertex could sell the drug to doctors using a specialty sales force.

On the other hand, VX-950 was complex and costly to make. In addition, because alpha-interferon (? -IFN) was the existing standard for treating HCV, <https://assignbuster.com/case-vertex/>

it was unclear whether Vertex could test VX-950 as a “ monotherapy” in extended studies. For regulatory and medical ethical reasons, the company would be required to test VX-950 in combination with ? -IFN. Acquiring adequate supplies of ? -IFN significantly increased the cost of testing VX-950. Some people in the company thought it better to find a partner with deeper pockets to help with the compound’s development.

Also, a decreasing number of new infections made HCV a time-sensitive market, and even optimistic expectations put VX-950 reaching the market in 2010. Vertex management knew it could not wait long on this opportunity. The Portfolio Decision Process The portfolio problem is completely underestimated by almost every company in terms of complexity. — Peter Mueller, Chief Scientific Officer, Vertex Pharmaceuticals Given its strategy of developing two candidates internally and its current financial situation, Vertex expected to partner the majority of its other research and drug candidates.

The decision to limit growth of discovery research to allow buildup of a balanced development capacity would also mean that Vertex might see a reduced rate of new “ VX” drug candidates being generated outside its partnered programs from 2004 to 2006.

The decision to choose two candidates for internal development caused some stir among Vertex employees. Even beyond the program executives, some employees were nervous about narrowing the company’s options prematurely. According to Coles: Right now the mantra is: “ We will do two. I think we should be thoughtful about narrowing our choices because of the

attrition in this process. There is high risk with any candidates we choose, and we would ideally want to hedge our risk.

We should choose the best two candidates to focus our resources on and hold two in reserve as backups, not necessarily for partnering. We may need to look at partnering one, but not two. Smith agreed with Coles's philosophy: Do I wouldn't necessarily pick two—I would pick all four but prioritize two. We have a twofold decision: Which two primary candidates do we put the bulk of our resources on?

Of the two that are secondary, do we partner them or hold on to them? Secondary projects can be given limited funding and moved to primary status if additional funding can be found . . .

otherwise they are partnered. There will always be attrition in development and narrowing the pipeline to two drugs is risky, hence I believe prioritization based on the data in hand is more appropriate. No tC op yo rP Copying or posting is an infringement of copyright.harvard.

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However, Josh Boger emphasized that partnering two candidates was not a losing proposition: " By choosing two, we aren't shooting the other portfolio candidates in the head. " Some also believed that Vertex would benefit from narrowing its focus. Wilson, whose group was responsible for chemical-process development, discussed how Vertex would be better off

concentrating its development efforts on fewer candidates: We can handle two candidates, not three. We have 12 process chemists, six with Ph. D.

s and six with master's degrees. It's a learned lesson; if you spread too thin, you can't do it.

Take VX-765, for example; 12 months ago we couldn't make a kilo of the drug using a 10-step process. Now we'll have 200 kg from a four-step process. We were able to do this because of focus.

Real-option valuation is one of the more speculative components in the portfolio decision. You have to be aware and have wisdom. A simple top-down decision using gut feeling might be better. — John Thomson, Vice President of Research, Vertex Pharmaceuticals
Vertex senior management began to grapple with the portfolio issue in May 2003 at an off-site meeting to discuss the company's overall strategy.

In July 2003, management followed up with a second meeting, this time including the program executives and other top managers in the discussion, to review the details of the specific programs and to try and rank the candidates. The challenge was to compare drug candidates at different stages of development, with different technical properties and different potential therapeutic applications.

Just like its approach to drug discovery, Vertex preferred to look at the problem from several angles. Vertex used “real-option valuation” as part of its analysis of each candidate's potential.

ROV took into consideration the expected cost and risk of each drug's clinical development as well as the estimated commercial value of the drug upon being approved and reaching the market. As a result, management was able to produce a rough measure of the value of each candidate, as an investment opportunity, in present-dollar terms. Based on its calculations, VX-765 generated the greatest ROV of the four candidates.

(Exhibit 7 shows some of the inputs and assumptions used in the ROV analysis of the four Vertex candidates. Exhibit 8 shows the average pattern of sales after launching a new drug. ROV was appropriately named for its similarity to models used for valuing options on financial assets (e. g. , stock options). As its name suggested, ROV was used for valuing options on " real" assets, such as real estate or physical equipment.

ROV analysis had become a common method for estimating the value of investment projects with payoffs conditional on events that had high degrees of uncertainty. Net present value (NPV), another standard measurement, took the present-day value of a fixed stream of cash flows stemming from an investment and subtracted the present value of the associated fixed costs.

While ROV utilized the same concepts as NPV, such as discounting future payoffs, it also allowed cash flows to be valued that were not fixed but, rather, were conditional on future decisions. By applying probabilities to different paths an investment might take, ROV took into account the variability of investment outcomes. Also, by incorporating an investor's future alternatives, especially the option to terminate a project, ROV was

especially well suited for opportunities that called for progressive investment. Do 12 Copying or posting is an infringement of copyright.

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No tC Financial Value and Commercial Potential op yo Portfolio Choice Criteria rP os t Vertex Pharmaceuticals: R Portfolio Management (A) 604-101 While ROV and other valuation techniques provided the ability to compare different drug candidates as investments, Vertex management knew such methods were far from exact measurements and questioned how much they could be relied upon. Smith described the challenges involved with using ROV analysis: Portfolio Risk Do Vertex divided the risk of developing a candidate into four broad categories: target risk, mechanism risk, molecule risk, and market risk.

Target risk pertained to how much was known about the molecular target a drug worked on.

Were there other drugs on the market that validated this target, connecting the target with a therapeutic cause? Mechanism risk, similar to target risk, considered how much was understood about the “ mechanism of action” of a particular drug, essentially, how much was known about the underlying biology of how a drug worked and the series of effects it had inside the body. Molecule risk took into account a drug’s ability to reach its intended target and any adverse effects it might have along the way.

While a drug might interact well with a particular target, plenty of risk remained in getting the drug to reach the target, having it remain in the

body for a long enough period of time, and avoiding additional complications (i. e. , side effects).

Finally, market risk took into consideration a drug's therapeutic area, the amount of competition surrounding a drug, the manufacturing, sales, and marketing costs associated with selling the drug, and so on. What would peak sales for the drug be 10 years from now, and how many years of peak sales could be assumed?

Josh Boger believed that the key principle in managing a portfolio of R projects was to diversify the types of risk the company would encounter: 13 Copying or posting is an infringement of copyright.harvard.edu or 617-783-7860. No tC NPV and ROV models are more valid for late-stage development compounds, when you have a pretty good feeling of the potential market ahead in one or two years.

Everything else is pure speculation. For us to predict ROI [return on investment] 10 years out gives us a nice number, but it's not terribly meaningful.

The research and development process is extremely complex, dynamic, and sensitive to a wide range of internal and external factors as is a proper risk assessment. I'm not aware of any prediction for early-stage compounds even close to market outcomes. .

. . Businesspeople will depend more on models because they are further from the details of the R process and can't easily distinguish between research programs and the specific inherent risk linked to them. Compounds

in research and early development stages are by nature very high risk and therefore always less attractive in models.

Unfortunately, if portfolio decisions are made purely on financial modeling considerations, pipelines will dry up as potentially innovative projects get killed.

. . . For me, the importance of the models is in facilitating the conversation, getting the questions out, and helping interdisciplinary conversation. op yo Even as a relative measure, some Vertex personnel questioned how much the company should rely on ROV as a criterion for deciding the portfolio. With candidates in early stages of development, the number of unknowns made ROV very sensitive to the company's assumptions.

Peter Mueller, Vertex's chief scientific officer, questioned whether any company could make these assumptions with enough accuracy to make ROV useful: rP We perform ROV on each indication. ROV is an important, sophisticated tool, but it's not the only tool. It gives you a relative measure, not an absolute value. You need to scrutinize the inputs, which are the main drivers of value; what are your assumptions? Time to market? Total future costs of development? An HCV drug, for example, would have huge Phase II/Phase III development costs but a significant return. However, do we prioritize that drug if it does not get to the market until 2009?

The inputs are important.

os t 604-101 Vertex Pharmaceuticals: R Portfolio Management (A) Sato talked about the risk attributes of the different candidates and the trade-offs involved with choosing two: The IMPDH mechanism is already selling

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product. Therefore, VX-148 has low mechanism risk but average molecule risk. On the other hand, VX-702 and VX-765 have new mechanisms with more unknowns. VX-765 and VX-950 both have novel targets. Choosing a follow-on drug, such as VX-765 or VX-148, you may know the molecule works, but you are facing a possible land war once the drug is approved.

Alternatively, choosing a new drug is more risky in the beginning, but you have less competition in the marketplace. Choosing candidates in the same therapeutic area causes correlated risks and returns. However, different therapeutic areas require multiple sales forces. VX-702 [in ACS] and VX-765 [in RA] have overlapping therapeutic areas. Together, VX-950 and VX-765 have similar risks and put a lot of pressure on new infrastructure.

Also, it could take the longest to get to market. Some people at Vertex thought the company should work on minimizing certain kinds of risk.

These being the first two drugs Vertex would develop by itself, they would have a large impact on the company's growth and organizational learning. According to Murcko, " First and foremost, which drug is most likely to make it onto the market? We should favor drug candidates with lower biologic risk, even if their sales potential is lower. " John Alam, senior vice president of drug evaluation and approval, agreed: " We don't want to choose a compound that fails and has to be pulled from the clinic in the next six months .

. . it would have a serious impact on the organization's psychology. " Medical and Scientific Merit

While maximizing the commercial value of the portfolio was a concern, management knew it took more than financial incentive to get a drug on the market. Vertex employees were driven by the opportunity to solve important medical problems, and they were also excited by new scientific challenges. The scientific reputation of a drug and the disease it treated had a strong influence on Vertex scientists' preferences for candidates. Since getting a drug to market would require a great deal of effort throughout the organization, it was in Vertex's best interest to pick candidates its scientists were motivated to work on.

Alam explained: " There must be compelling scientific and medical rationale to develop a drug. Josh and Vicki must be really excited about it. When a company brings its first drug to market, there is hell to pay along the way. Things will go wrong; it will be incredibly difficult. You will only follow through for something that is really worthwhile, not just money. " Do Sato discussed how the scientific novelty of a drug program and the medical need it targeted influenced the portfolio decision: When choosing between going after the fifth beta blocker or the first or second something else, what do you really want to do?

Are you going to be more excited about making a drug for disease X or disease Y, X and Y being otherwise equal? Having medical impact is important when picking a candidate. " Dollars-in" is a legitimate proxy for medical need as well as an

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Companies tend to have biases in how they evaluate risks and which risks they are comfortable with. Some companies systematically underestimate

target risk, some underestimate molecule risk, and some underestimate market risk.

And, the interesting thing is that when you're inside the company, you are probably not even aware what your biases are. So, to protect ourselves against these hidden biases, we deliberately want to make sure we're taking different kinds of risks in our portfolio. By balancing our risks, we can avoid being blindsided 10 years later. os t Vertex Pharmaceuticals: R Portfolio Management (A) 604-101 independent marker in its own right. However, you need to be careful when assessing medical need using commercial success.

Did Lipitor, the fifth statin to reach the market, address significant medical need? Maybe, but maybe not as much as its sales suggest. Do No tC op Josh Boger reflected on the status of the programs and knew that a final decision would have to be made soon. He was well aware that Wall Street analysts, as well as company insiders, were closely following the company's actions: " Vicki and I have talked about this a lot since July and have pretty much made up our minds. However, we want to keep the channels of information open and to keep the discussion going.

Discussion, however, doesn't mean consensus. I expect there to be disagreement. I could change my mind tomorrow if someone came to me with new information. " Josh Boger now wondered what new information he might need to make a final commitment. yo The internal incentives were not the only reason Vertex considered the novelty of a disease area. The portfolio chosen by Vertex would also affect the company's external image. With a large amount of resources tied up in a two-candidate portfolio,

Vertex's corporate identity was sure to become intertwined with the diseases it focused on.

Tinmouth pointed out, " Marquee value considerations should not be ignored. For example, imagine the headline: ' Vertex cures muscular dystrophy,' or Parkinson's, or HCV—curing such diseases would be a substantial accomplishment for Vertex, or anyone for that matter. " Brum added as an example, " If we did both VX-765 and VX-702, Vertex could be viewed as ' the inflammation company. "' rP Although making scientific discoveries was a large incentive for Vertex scientists, working with new mechanisms of action and new therapeutic targets only increased the risk of developing a drug.

Sato was cautious about betting everything on extraordinary science: " It shouldn't be so cutting edge that, if the mechanism goes away, you lose all your options. " Copying or posting is an infringement of copyright. harvard. edu or 617-783-7860. os t 15 604-101 Vertex Pharmaceuticals: R Portfolio Management (A) Exhibit 1 Average Costs and Success Rates of Drug Development Discovery Preclinical Testing File IND w/FDA Phase I Phase II Phase III File NDA w/FDA FDA Review In vitro analysis Laboratory animalsd 2 to 10 years 3. 5 years \$121. 0e 100 to 300 patient volunteers 1, 000 to 3, 000 patient volunteers years 3 Years Source: Adapted from " Convergence: The Biotechnology Industry Report," Ernst & Young, Millennium Edition, and Joseph DiMasi, Ronald Hansen, and Henry Grabowski, " The price of innovation: new estimates of drug development costs," Journal of Health Economics 22 (2003). aDiscovery and preclinical testing stages overlap. study listed the " total capitalized cost per approved drug" to be

\$802 million, which accounts for a firm's opportunity cost (cost of capital) and failed research projects. cThe 2002 DiMasi et al. study also estimated an overall clinical success rate (Phase I to FDA approval) of 21. %. dLong-term animal toxicology testing also occurs throughout the clinical testing cycle and averages \$5. 2 million per drug. eThe average cost of preclinical testing per approved new drug is estimated at \$121 million. This amount includes the cost of preclinical testing that cannot be attributed to one drug candidate.

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harvard. edu or 617-783-7860. No tC b" Out-of-pocket"

costs in 2000 dollars, as estimated by J. A. DiMasi et al. in their 2002 study of

Tufts CSDD data. The same op 1. 5 Years yo \$23. 5 \$86. 3 0 to 80 healthy

volunteers 1 year \$15. 2 rP Stage of Development Test Population Average

Durationa Mean Cost (MM)b Success Ratec 5, 000 to 10, 000 compounds

screened 250 lead candidates enter preclinical testing Five candidates enter

Phase I testing 80% pass Phase I testing 30% pass Phase II testing 80% pass

Phase III testing One drug receives FDA approval os t Vertex

Pharmaceuticals: R Portfolio Management (A) 604-101 Exhibit 2a Vertex

Pharmaceuticals Balance Sheet (five-year history) Cash Marketable

Securities Receivables Other Current Assets Total Current Assets Total Long-

Term Assets Total Assets 08, 098 526, 886 13, 200 8, 388 656, 572 159, 148

815, 720 189, 205 553, 997 20, 265 12, 625 776, 092 149, 039 925, 131

346, 659 467, 402 33, 906 9, 464 857, 431 83, 705 yo 941, 136 12/31/2001

91, 553 315, 000 43, 227 449, 780 12/31/2000 69, 856 345, 000 12, 269

427, 125 751 778, 018 (314, 532) 11, 114 475, 351 925, 131 735 757, 522

(248, 299) 4, 053 514, 011 941, 136 Annual Liabilities (000s) Fiscal Year

Ending Total Current Liabilities Convertible Debt Other Long-Term Liabilities

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Total Liabilities Net Common Stock Capital Surplus Retained Earnings Other
Equities Shareholder Equity 12/31/2002 64, 597 315, 000 57, 542 437, 139
op 64 794, 206 (423, 153) 6, 764 378, 581 815, 720 Total Liabilities and Net
Worth No tC Source: Vertex Pharmaceuticals 10-Ks, Thomson Research. Do
rP 31, 548 84, 080 5, 956 1, 439 123, 023 109, 422 232, 445 12/31/1999 18,
518 NA 4, 693 23, 211 514 400, 631 (190, 827) (1, 084) 209, 234 232, 445
Annual Assets (000s) Fiscal Year Ending 12/31/2002 12/31/2001 12/31/2000
12/31/1999 Copying or posting is an infringement of copyright.
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221, 483 1, 462 1, 594 248, 708 17, 638 266, 346 12/31/1998 13, 102 NA 7,
032 20, 134 254 395, 332 (149, 861) 487 246, 212 266, 346 17 04-101
Vertex Pharmaceuticals: R Portfolio Management (A) Exhibit 2b Vertex
Pharmaceuticals Income Statement (five-year history) Source: Vertex
Pharmaceuticals 10-Ks, Thomson Research. Do 18 Copying or posting is an
infringement of copyright.harvard. edu or 617-783-7860.
No tC op Outstanding Shares 76, 357 yo 75, 055 59, 613 Net Sales Cost of
Goods Sold Gross Profit R Expenditures Selling, General, and Admin. Exp.
Income Before Deprec. and Amort. Depreciation and Amortization
Nonoperating Income Interest Expense Income Before