The Value of Acedia®
Case Study

(2008 Version)

Ethics and Industry Decision-Making:

Access to & Affordability of Breakthrough Biotechnology Products

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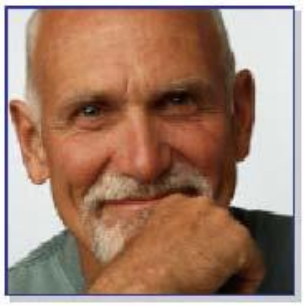
Characters

Dara Devan, MD, PhD
President and Chief Executive Officer

- Educated at the Weitzmann Institute
- Former professor of immunology-oncology at Harvard Medical School

"Dara was mindful of her obligation to patient-stakeholders; as a physician, this was easy. Shareholder-stakeholders were more difficult for her to visualize."



Owen Coyne, MBA
Chairman of the Board

- Educated at MIT and University of Pennsylvania (Wharton)
- Rich Richman's mentor at Stanford Business School; venture capitalist

"How can it be morally wrong to invent something that people desperately want, and then charge them what the market will bear?"

Kipp Konrad, MD, PhD
Chief Scientific Officer

- Educated at Cambridge and Washington University in St. Louis
- Dara's Harvard collaborator; co-inventor of the cedimab antibody
- Wife died of breast cancer before he and Dara met

"$45,000?" Kipp exhaled and sat down. "If we re-treat, it's $90,000! What are we thinking? What is *marketing* thinking?!"

Rich Richman, MBA
Chief Financial Officer

- Educated at Stanford and Stanford Business School
- Biotech financial *wunderkind*

"Isn't it ethically unacceptable for us to ask our shareholders to finance 'doing our part,' without assurances from government, the insurers and even the patients that they will do their part?"

The Value of Acedia®: Preface

Monday morning, still early, but Dara was running late. Usually at her desk before 7:00, she had been slow to clamber out of bed after a toss-and-turn night. Yesterday's headache had become today's, and her mood, pensive after a work-filled weekend, wasn't brightened by the fog and intermittent drizzle. She had lived in South San Francisco for nearly eight years since her westward move from Boston academia to Bay Area biotech. It had been a great decision, but she still missed the warmer New England summers.

This morning, yet again, was off to a gloomy start. When she left the Harvard faculty for San Francisco, her neurology department collaborator, Kipp Konrad, had warned her about the summer chill. A Londoner, Kipp understood fog. Dara, who had grown up in Tel Aviv, preferred the heat. Her last day at Harvard, Kipp sent her an oversized umbrella, with a Post-It note: "The coldest winter I ever spent was a summer in San Francisco," he scribbled, quoting Mark Twain, and added, "If this venture also turns foul, this was your idea! See you in SF, Kipp."[2]

For a few seconds, Dara managed a grin. "Let's go," she scolded herself. Her executive committee would be meeting at 9:00. Maybe tempers had cooled over the weekend? No matter, she conceded; time to make a decision. It wasn't going to be an easy day.

This case study was originally prepared for the Biotechnology Industry Organization's BIO 2004 Annual International Convention. BIO thanks the Massachusetts Biotechnology Council's bioethics advisory group (Rahul Dhanda, chairperson; George Annas, Janice Bourque, Gary Cohen, Norman Daniels, Rashi Fein, Steven Holtzman, Howard Koh and Marc Roberts, members), which first met in June 2003 to discuss ethics issues in biotechnology, including the ethical dimensions of drug pricing and accessibility. This case, which is informed by those discussions and the thoughtful comments of many individuals[1], is not meant to reflect any actual situations, individuals, companies, policies or products.

PART I: SIXTEEN WHIRLWIND YEARS

Dara and company

As president and chief executive officer of IntroSpect Pharmaceuticals, Dara Davan had gone from post-doc to professor to running a public company in sixteen whirlwind years. After earning an MD-PhD (the latter in neurology) from the Weitzmann Institute and completing a post-doctoral fellowship in neurology-systems biology at the NIH, Dara moved to Boston and an assistant professorship at Harvard. She met Kipp Conrad at the NIH. Both were intense researchers, Dara in neurology, Kipp (an MD-PhD from Washington University in St. Louis) in systems biology. Dara and Kipp immediately hit it off. Tragically, Kipp's father had died from complications related to Parkinson's Disease a year before he and Dara first met.

In contrast to Kipp, Dara appeared focused on everything, including business. A voracious reader, Dara had become equally comfortable with the *Wall Street Journal* and the journal *Science*. She was fascinated by the accelerating changes in corporate biotechnology. In addition to her academic appointment, Dara was consultant to several firms and served on the board of another. In her travels through biotech, Dara met Richard ("Rich") Richman, biotech's newest financial *wunderkind*. At 38, just a few years out of Stanford's business school (he had grown up in nearby Palo Alto), Rich already had been vice president of finance at a small, privately-held informatics company (eventually swallowed whole by a "Big Pharma" giant which had set up shop in Cambridge, where he moved after B-school) and chief financial officer of a pharmaco-genomics company (which he helped take public, at a near-record valuation). Dara and Rich became good friends. Rich knew Kipp, too; Rich's company and Kipp's NIH lab had collaborated a few years back. When Kipp was recruited to Harvard, Dara re-introduced them.

On rare occasions when in town and not at work, the three non-New Englanders would take in an evening Red Sox game at Fenway Park, or have dinner in Harvard Square. "Someday," Rich liked to say, half-kidding, "we need to start our own company."

Wait 'til next year

For each friend, the next decade's inevitable frustrations were few and widely separated by astonishing accomplishments. Rich marked each year's passage with the letter "Q" – Q1, Q2, Q3 and Q4 – and by the up-and-down-and-up-again price of her company's stock. Science remained Kipp's sole focus, which he measured by semester, grant application, and successful clinical research.

He also managed to see patients once a week. Dara also wanted to see patients in clinic, but her lab and business obligations limited her patient contact to investigator rounds at Harvard's Longwood Medical Area hospitals. Dara, her friends joked, had become half-scientist half-businessperson: a biotech chimera. She saw scientific success in her many publications, true, but also in a growing portfolio of patentable discoveries. Harvard policies required professors to assign their inventions to the university, and the technology license office made them available to companies interested in pursuing their potential.

Two of Dara's discoveries had been commercialized, but many – too many, Dara thought – had not. She grew frustrated, but not bored. Impatient by nature, Dara knew that university-based research, genteel at turns, political at others, wasn't forever for her. In April, he and Kipp co-authored a bold *Nature* article, announcing a stunning (and, Dara thought, quite possibly valuable) breakthrough in neurology and the targeted delivery of neural growth factors to treat Parkinson's Disease. Their decade-long work had been funded entirely by the government, and the Harvard patent lawyer who wrote the applications was near-certain that broad patents would result.

At an early-season Red Sox-Yankees game, Dara and Kipp nearly chanted Rich's familiar "we-need-to-start-our-own-company" refrain. OK, Rich replied, he'd call her Stanford business school mentor-*qua*-heavyweight venture capitalist, Owen Coyne. "Let's see what Owen has to say," Rich concluded, not well disguising her own excitement.

By the end of the summer, Dara and Kipp had exchanged their campus confines for even more cramped quarters in a nondescript South San Francisco biotech incubator park owned by Owen Coyne's VC firm. Rich had a wife, two young kids and truckloads more belongings than Dara and Kipp combined. It took her a few months longer to relocate.

An act of self-examination

Rich's wife Amy came up with the new company's name, but it was so good everyone had wanted to take credit: Introspect Pharmaceuticals. "INTROSPECTION," he read aloud from a dictionary, "*a view of the inside or interior; a looking inward; specifically, an act or process of self-examination.*' It fits the science. . . ." Rich suggested they capitalize Introspect's internal "S," in keeping with corporate nomenclature's pandemic trend. A makeshift sign, with the agreed-upon spelling, was taped to the company's front door before Dara arrived the next morning.

Rich was at work on capitalization, too. Before he left Boston, Rich had negotiated an exclusive license to the Harvard-owned patents that had resulted from Dara's and Kipp's work, and cobbled together IntroSpect's first business plan. On the West Coast, Dara (to her surprise) was beginning to like venture capitalist Owen Coyne; perhaps, Rich deadpanned, Coyne's willingness to fund the company had something to do with it. In return for her group's seed money – and on account of Dara's admittedly thin business résumé – Coyne became IntroSpect's chairman. ("Don't call me _*chairperson*,'" Coyne had warned everyone.) With her chairman's support and strong votes of confidence from her colleagues, Dara became IntroSpect's first (and, to date, only) president and CEO. Rich did double-duty, confidently, as chief business/financial officer; and Kipp was named chief scientific officer. Kipp's foggy funk lifted when her hand-picked crew of physician-researchers and eager East Coast post-docs settled into their new IntroSpect offices and labs. Each of them was looking to do something – too many somethings, Dara worried – really, really big.

Not a viable model

Three years and a mezzanine round later, IntroSpect was almost out of money. "There was no income at all, only huge development expenses," Rich later recalled. "If you looked at the P&L, the profit and loss statement, there was no income, no sales, just red ink – tremendous expenses, huge losses, that was it. Slowly, you know, it sort of dawned on me: this was not a viable financial model in that environment! We needed earnings, or at least a reasonable prospect of making earnings – and soon. The pipeline looked good, our lead molecule was heading toward a Phase I trial in Parkinson's Disease, but, hey, this wasn't widgets, this was pharmaceuticals. At least 10 years of development, maybe twice that unless we were smart and lucky, and hundreds of millions of dollars to get a new drug on the market. I didn't see how we could take IntroSpect public and go out at a decent valuation if that's what our P&L was going to look like."[3]

One option would have been to sell the company to Big Pharma, but Dara wasn't ready to give up control, Kipp remained vocal and passionate about the science, and in any case, Rich thought the premium from a Big Pharma buy-out would be awful. Coyne agreed. And so they stayed at it. Molecules were mothballed. New hires were not hired. Space was sparse. Attrition and trimming reduced headcount by nearly 20%.

The remaining employees were exhausted and, looking back on it, exhilarated. Dara, Rich and Kipp had filled the labs and offices with optimistic and, above all observable else, *driven* scientists and businesspeople, many of them new to corporate biotech. IntroSpect didn't – couldn't – pay them Big Pharma salaries, but it could match their optimism with options – stock options – and it did.

Big-burn to break-even

Slowly, the cost-cutting, focus and sleep deprivation turned things around. Instead of selling IntroSpect outright, Rich pursued an aggressive strategy to out-license the mothballed molecules to Big Pharma. When preclinical data from IntroSpect's lead molecule exceeded expectations, Rich was able to negotiate a surprisingly lucrative co-development deal with a pipeline-deficient European pharmaceutical powerhouse. Rich had "volunteered" a non-exclusive license to IntroSpect's cell-targeting IP for all uses outside of neurology; in exchange, IntroSpect got to keep North American marketing rights to any neurodegenerative disease therapy which emerged from the arrangement. From these out-license revenues and the development cost reimbursements, IntroSpect went from big-burn to break-even. Rich had wanted IntroSpect to look fairly good, financially, before going public, and Coyne was tenacious about establishing solid value pre-IPO. They thought the window had opened in early summer and wanted to hit the road, but Coyne's venture partners were reluctant, given the skittish market.

But with the European deal, momentum began to build, and so did the VCs' enthusiasm. Rich had been through half-a-dozen IPOs (only one, for her old pharmacogenomics company, had been in biotech). Coyne was an experienced, mostly-patient coach for Dara, explaining the road show, how the investment bankers built the book, how the IntroSpect offering would be oversubscribed – if everything went right. Rich was a natural, and Dara and Kipp inspired confidence in the science. "The road show was great," Dara remembers. "We just knocked their socks off. I don't remember how many times we were oversubscribed, fifty maybe. It was just a wild deal. Sure, there were questions: _You guys don't make any money; sales could be years off, profits even further out, how can you possibly justify this kind of valuation?' But they came around. They bought the stock. They bought us. . . ."

All meetings, all the time

The IPO (NASDAQ: INTRO) added a new dimension to Dara's days – too many hours-long meetings with stock analysts, investment fund managers and biotech business reporters left her cranky. Meetings with Parkinson's patients and their families, and even their understandably demanding advocacy groups: these were different. From her first days in medical school, Dara had been moved by her patients' courage and the faith they placed in their doctors.

Now, he was doubly moved; clearly, they saw IntroSpect's promising approach as the "next great hope," to stop the progression of this terrible disease. No amount of cautionary language or disclaimers seemed to temper their belief. Dara regularly heard from the Bay Area's indefatigable (Kipp thought he was "pushy") Parkinson's Disease crusader – and patient – Ron Brown. Generally, he was looking for information – how the clinical trial was going, that sort of thing.

Sometimes, he called for a contribution – sponsorship of a Parkinson's Disease fundraiser, perhaps. Mostly, he was just looking for hope. Hope. Dara was mindful of her obligation to patient-stakeholders; as a physician, this was easy. Shareholder-stakeholders were more difficult for her to visualize. She was often reminded – by Rich; by Coyne; and occasionally, by surprise – of her shareholders' high hopes, and her obligations to them, too. Without hype, INTRO shares had doubled in price since the offering, five years and 78 million (un-reimbursable) dollars ago. IntroSpect had no products on the market, no drug candidates yet in the clinic. To the stock analysts, bruised by biotech sector volatility, the run-up was mostly speculation. Dara preferred to see this too as hope. On her desk she kept a framed, handwritten note ("quaint," Rich had remarked, dryly) from her high school biology teacher. "I'm so proud of you," Ms. Peterson had written, in familiar, neat script. "Mr. Peterson and I put all our savings in your company. Good luck!"

The residue of design

Luck, Kipp liked to say, quoting baseball legend Branch Rickey, "is the residue of design."[4] At their university lab, and now at IntroSpect, Dara and Kipp had produced – *designed* – their own luck. IntroSpect's research, slowly at first and now with astonishing speed, was looking very promising.

The company's lead molecule, code-named "NGF-115," was a neural growth factor. Though encapsulated, it was provided to patients in a surgical procedure. It would help the body create dopamine-producing cells and improve motor function in patients. It might even stop the progression of the disease. This would be a huge breakthrough for the one million Americans with Parkinson's disease. At least, that was the way Dara and Kipp hoped it would work. There were dozens of obstacles in their way. Few if any clinical trials for Parkinson's patients were successful. Currently, physicians treat symptoms, but no one is completely sure how the disease progresses at a molecular level. And since the product is used in the brain, any missteps – scientific or otherwise – are potentially lethal. Moreover, the drug's effects almost certainly would not be permanent, meaning that younger patients would need re-treatments, perhaps every 10 or 15 years.

It took Kipp's team 12 years to feel confident in their biological calculations. Finally, with FDA go-ahead, IntroSpect started its first-ever clinical trial.

On the fast track

Six months later, the company's Boston-based clinical collaborator published the results: in a Phase I trial, NGF-115 appeared to be well-tolerated – no one among the clinical trial subjects showed detectable immunity problems. Even better: for an early-stage clinical trial, there were intriguing clues that the growth factor had shown symptomatic efficacy and caused some regeneration of dopamine producing cells in some patients.

The infusion of cash from the public offering and European partnership accelerated IntroSpect's progress. The early-stage trial was followed by even more promising data from multi-center Phase II trials. In these trials, Parkinson's patients received NGF-115 in a surgical procedure performed in the hospital. The results were compelling – "unbelievable," Kipp had gloated. NGF-115 stopped the progression of Parkinson's Disease in 40% of the patients in the study, as confirmed by SPECT imaging which showed no additional loss of dopamine producing neurons. This was a huge improvement in current standard of care. The drug was particularly effective for those with "young onset" Parkinson's. These are the approximately 10% of Parkinson's patients who are diagnosed with the disease before age 40. Of those who benefited, more than half were in this category. Since NGF-115's effects were predicted to last on 10-15 years, these patients would need to get several more treatments throughout their lifetime."

"Unbelievably unbelievable," Kipp had exclaimed. Confident of the data, IntroSpect requested (and was soon granted) "fast track designation" for NGF-115. This designation allowed IntroSpect to submit parts of its new drug application, or NDA, to the FDA when ready. Even more boldly, IntroSpect asked for and received both "accelerated approval" and "priority review" status. Accelerated approval allowed IntroSpect to file for approval based on its Phase IIa/IIb data (although the FDA insisted on an IntroSpect commitment to demonstrate more durable clinical benefit in a post-marketing study). Priority review meant that the FDA would reduce the target review period for

IntroSpect's application from ten to six months. Dara felt certain that her company's promising therapy, now named "Acedia" after a protracted and unimaginably expensive name search, was quite likely to be approved, even before year-end.

“Hospital pharmacies will have Acedia® on their shelves early next year,” Rich predicted at the next company meeting. Outside, buses waited to take most of IntroSpect’s 380 employees to nearby SBC Park for a late-August baseball game-celebration. “Our shareholders have been patient,” he continued, pausing, “and so have you, so have we…” When his voice cracked, everyone looked surprised at her uncharacteristic show of emotion – except Dara. She knew how hard her friend had worked, how little his family had seen of her, how many less-risky jobs he had passed up to stay with IntroSpect.

Rich managed to introduce Kipp, but when Kipp couldn’t finish his first sentence, *nobody* was surprised. Ever-emotional, Kipp had thought of nothing but Acedia® since leaving Harvard. Rich and Owen Coyne had been tenacious about building shareholder value; but Kipp... It had been 21 years since he first witnessed the inexorable march of Parkinson’s Disease and how it destroyed a patient’s life, and cast a shadow over an entire family. After his training, Kipp’s tenacity had been directed against the disease. “We have all been patient,” Kipp picked up where Rich trailed off, “but,” his voice quavering, “some of us have known patients...”

Dara surveyed the now-silent room: young people mostly, gazing down, tearful. They had been patient *and* they knew patients.

PART II: THE DISEQUITABILITY EFFECT

A home run

Only the marketing group stayed behind when their colleagues boarded the ballgame-bound buses. With Acedia®, the IntroSpect scientists had hit a home run; now, it was marketing's turn. Later that week, following months of analysis, they would recommend a $50,000 price for Acedia® – a record-breaking price for a breakthrough Parkinson's product. "*This is a novel drug – first-in-class*," the marketing group's pricing memorandum read (emphasis theirs). "The importance of this new drug justifies premium pricing. Given the drug's expected market position, we will optimize shareholder value by pricing Acedia® at a marginal price which maximizes revenues and profits without regard to reductions in overall production volumes."[5]

Dara read the memo's we-will-optimize-shareholder-value sentence three times – the third reading, aloud – before emailing Board chairman Owen Coyne. "What?" she had typed in the subject field. Dara read on. "As is the case with any commodity," the memo continued, "if IntroSpect charged higher and higher prices for Acedia®, fewer and fewer patients would be willing (or able) to buy the drug. For IntroSpect, the most important question is: How high can we raise the price before the difference between (i) revenue gained from higher prices and (ii) revenue lost from patients' inability/ unwillingness to pay those prices (sometimes termed "MR," for "marginal revenue") declines until MR equals our cost of production?"

The marketing group had used a powerful software program, d-Lem-Ā version 8.0, made by MarketSoft, Inc., to answer this question.

Weaving together basic economic principles, industry benchmarking, pharmacoeconomic data and actuarial predictions, and using simple rules deduced from thousands of payer decisions, the software enabled pharmaceutical companies to predict payer behavior. A company could tinker with the program's adjustable parameter-scales – for example, the "switch cost effect" and "switch end benefit effect" scales, and thus deduce the optimal pricing strategy for its product.

Dara remembered the first time MarketSoft had demo'd the software at her company. Along with "switch cost," "switch efficacy" and other parameters, the software included a scale labeled, "disequitability effect."

Dara didn't know – she still didn't know – what "disequitability" meant, but she remembered feeling uneasy when the MarketSoft representative repeatedly clicked the on-screen "+" symbol to increase "disequitability." Within the software program's presumably model marketplace, increases in "disequitability" didn't seem to have much affect on net revenue. The marketing memo concluded: "With FDA approval, IntroSpect will have met a previously-unmet medical need for patients with Parkinson's Disease.

For many of these desperately ill patients, only one thing will stand between resignation and hope: Acedia®."

The most difficult decision

Over the weekend, Owen Coyne answered Dara's email plea. Dara was grateful for the tutoring but unsure about some of his advice. Even before Dara's pre-IPO tutoring, Coyne knew that his scientist-CEO needed business guidance. Back then, he taught her all he knew about road shows; now, he was going to teach her everything she needed to know about taking care of stockholders in a free market. "Price," Coyne wrote, "may be the most difficult decision we'll have to make.

Basically, it's a balancing act – we've got an obligation to maximize shareholder value" – Dara was accustomed to this reminder from her chairman – "while managing the potential risks of our pricing strategy. If we set the price too low, we're not doing our jobs, and the shareholders have a right to send us packing; set the price too high, we're not doing our jobs, and the public and the government will be all over us."

"Thanks, Owen," Dara muttered to herself, and read on.

"For me," he continued, "maximizing market value is the primary consideration. We live in a free economy" – Coyne truly thought the rest of the world was ruled by socialists – "where price is determined by the suppliers' willingness to supply something at various prices, and the purchasers' willingness to buy that something at those prices. If there are few suppliers, or if the product somehow is _essential' to purchasers, they won't have much say over prices – basically, the supplier gets to set prices and profit margins."[6]

Coyne didn't need to remind Dara, but did so anyway, that Harvard's patent attorney – brilliant, idiosyncratic and, within a year of Dara's arrival in San Francisco, IntroSpect's first in-house lawyer – had secured broad patent protections (at considerable expense). "Patents make it easier for suppliers to set higher prices," Coyne added, obviously.

The chairman continued: "The demand for life-saving drugs is relatively inelastic," using an economic term Dara mostly understood. "Acedia® will have great product positioning. There are some drugs in development but nothing on the market that can compete with our product. Acedia® is novel, there's nothing else like it, and we think it's going to have a major impact."

"I've read through everything marketing sent me," Coyne went on, "and I think the numbers are with us. Your marketing and finance kids did a great job; I know this is their first time through pricing. I agree with their cost per dose, which rolls up to the $50,000 AWP – for one course. Not bad."

"There are other factors to consider," Coyne wrote. "I know you're all over these – shareholder and analyst expectations, the European partner's plans for ex-US pricing. Don't forget about the cost of the follow-on trials; that's the only way the FDA would have let us move this quickly. And the market for Parkinson's products is small. There are tens of millions of patients with diabetes; our market is less than one-tenth of that. Most important, we've got to keep pushing – Kipp's optimistic about improving the success rate and going after other neurodegenerative diseases. This is going to be very expensive."

Coyne wasn't finished. "Remember, you still need to balance these market and financial considerations against the risks of a $50,000 AWP strategy. The $50,000 is high but still in line with the market. The patients who need a few treatments will cost $150,000-$200,000, which is going to create a stir. But you'll be fine. It's not yet clear how many people will need a later course; in any case," Coyne teased her, I know you like the heat."

Dara, a little annoyed, read on. "Given demographics and the average age of people who get Parkinson's Disease, Medicare will be the likely primary payer for Acedia®. We're lucky: Acedia® is administered in the hospital."

Dara skipped over Coyne's paragraph on Part A reimbursements and C-Codes; she already knew that Medicare would cover all charges for the inpatient procedure. She was more worried about the patients needing multiple treatments. These patients were not likely to be on Medicare so they could have high out of pocket expenses. Moreover, a large percentage of patients with Parkinson's are agricultural workers – a typically under insured population with limited resources.

Thus, the product will be expensive – or out of reach – for some patients.

"Medicare and the Medicaid states won't announce polices about paying for Acedia® until we announce price. They'll push back, that's their role, but in the end we should see full coverage at the price we've been discussing – at least for the first course of therapy," Coyne wrote. "And the private insurers should allow coverage, too, but I've got the same uncertainty about the later course. We will be setting a price record, after all. You know I think this price is justifiable, but sooner or later we're going to run into some ceiling on what society and the private payers are willing to pay, even for diseases like Parkinson's." "But we're not at that ceiling yet," Coyne continued. "Few insured patients are going to see big out-of-pocket costs. People on Medicare will only have to pay the hospital deductible and that's not much. And many have supplemental insurance that covers it.

"Even if lots of patients end up on the second course, the noise will die down. This is first in class therapy for a devastating disease. The press doesn't hammer us when we save lives. Plus, IntroSpect is biotech, not Big Pharma; until Acedia® is approved and revenue rolls in, we get to wear our white hats. Sure, there'll be hot air in Washington, but most of their beef is with the me-too drugs which, they claim, add little incremental benefit." Coyne ended by making a plug for a single worldwide price, but Dara only scanned her diatribe. He had heard it before. For now, Dara was only thinking about IntroSpect's US pricing strategy.

The European partner had to work out pricing in the EU, and a deal for East Asia still was beyond the horizon. Eventually, IntroSpect would file in Canada – IntroSpect had North America – but Dara wasn't worried about re-importation or parallel imports right now. "The marketing geniuses got it right," Coyne concluded her email. "$50,000: the value of Acedia®."

Little use for Coyne

Kipp had little use for Coyne and less use for her economics, and so Dara kept the email to herself. Kipp had flipped when he first read the marketing department's proposal. "Patients will hate us!" Dara heard him growl through her speakerphone.

A pause.

Dara stared at the phone and waited. Is he composing herself, she wondered, or maybe he ripped the phone cord from the wall? Dara jumped when Kipp rushed in. Red-faced and out of breath, he resumed in person.

"I know this is first-in-class, but do we really want to set a new record price? I mean—", then stood up. "We're not even planning to advertise! This drug ought to sell itself! [Kipp didn't want to think about what an advertising agency would do with Acedia®.] "$50,000—?" Kipp exhaled, and sat down.

Investigating the commotion, Rich had walked in. Up again, Kipp resumed pacing. "—and its not just $50,000! If we re-treat, it's $100,000! What are we thinking?" Kipp shrugged, arms out, palms to the ceiling. "What is *marketing* thinking?!" he shouted, not listening for an answer. "They can't be thinking! There's not a word in their memo about the consequences of a $100,000 price for patients who will need re-treatment. Come on, Dara, we've talked about this," Kipp addressed her CEO.

"Think! Who's going to benefit from re-treatment the most? Yes, that's right! Young onset patients and agricultural workers, many of whom are Latinos! An extra $50,000? Brilliant idea! You work in the field all day with little chance to improve your life and now we're going to make you pay $100,000."

Now glaring at Rich, Kipp raced onward. "Brilliant! Just brilliant! We're about to tell these under-treated, under-insured families, not to worry. If you're sick, we can help. What? Symptoms returning after the first course? Still not to worry. You're in luck – young-onset Parkinson's patients, after living with an impoverishing disease for fifteen years – you'll do great with a second course. That'll be $50,000, please."

"What do you want us to do?" Rich interrupted. Dara glanced at Rich, then quickly returned her wide-eyed gaze to Kipp. "Do you want us to give it away? Just because we haven't made a profit yet doesn't make us a non-profit! You want us to be a public charity?!"

"Hey, that's unfair," Kipp defended herself. Nobody's talking about giving it away free. But $50,000? That's your proposal? Right, OK, here's mine: let's just break even. We're about to get approval, we've got a big European partner that'll pay us royalties. I say we break even – price it at the cost of production and – ." "Kipp, that's just won't work, and you know it," Rich cut her off. "If we price at the cost of production, you and your researchers are out-of-luck and out-of-work. We have other costs, you know, like the millions you keep adding back to the budget for your other research programs. Cost-of-production for Acedia® is a fraction of IntroSpect's costs; pricing Acedia® at break even means an end to your R&D."[7]

Kipp was too aggravated to concede much.

"Fine, we're not shutting down the research, but that's not the same thing as $50,000! So we price at the cost of production *plus* some amount – call it an _assessment' – to cover Acedia® R&D.[8] Maybe we price it to subsidize our other neurology programs. But we can't ask these patients to cover the costs of all of our research! $50,000? You want me to be cheery about this?" Kipp brushed past Rich, who pivoted to watch him leave. "I didn't sign up to be labeled a price pincher," Kipp muttered, and was gone. Just outside the door, Dara's assistant hopped out of her way.

The wall of access

Mid-afternoon, a note arrived for Dara. "Sorry," the note began and ended, in Kipp's bad scrawl. To the note, Kipp had clipped a photocopied page; it appeared to have been pulled from a longer document. Kipp had scribbled alongside one paragraph, presumably the most important:

"We need to be more focused than ever before on what is most on the minds of patients and their families today, namely, making the medicines we develop and supply more accessible and more affordable. For the people we help, our products can be priceless; but for those without access, our products are useless. The wall of access that divides Americans from one another is a national tragedy that we should not allow. We are talking about saving ~~and improving the quality of~~ people's lives. And nothing is more important than that. That's why today's medicines must be more than life-enhancing and life-saving; they must be accessible and affordable. . . ."[9]

Dara thought he had read (or maybe heard) this unidentified piece before; was it from an op-ed or a lecture? She couldn't remember the source, which bothered her, so she read the paragraph again.

That is Rich

Over the next few days, chief business officer/chief financial officer Rich Richman took on a third title: chief peacemaker. Shuttling between Kipp's fourth floor office, Dara's ground floor suite and the marketing department's overcrowded basement "war room," Rich tried to put together a patient assistance program which he hoped Kipp would accept and that Dara would be able to sell to Owen Coyne and the board.

Rich reviewed several Big Pharma programs, including PharmaCo's well-regarded Patient Assistance Program, which was posted on the company's website.

When patients who need access to specific prescription medications cannot afford them, they can work with their physician to find out about PharmaCo's Patient Assistance Program. The PharmaCo Patient Assistance Program is designed to provide temporary assistance to patients who have no access to any insurance coverage for prescription medications and are truly unable to afford prescription medications.

For nearly 50 years, PharmaCo has provided its medicines without charge through this program to the uninsured and those who cannot afford to pay for their medicines. The program offers PharmaCo's medicines entirely free of charge: there are no application fees, no co-pays, no age restrictions and no targeted discounting. In general, any patient of any age is eligible if he/she is without pharmaceutical coverage and has an income below $18,000 for individuals and $24,000 for a household. Those with incomes above these levels may also be eligible on a case-by-case basis. Patients can get information about the program through the company website or a toll-free number for patients.

As in the past, patients can also continue to apply through their physician's office. Physicians certify patient eligibility for the program at the time a prescription is written and the application is signed. Once eligibility has been verified by PharmaCo, the medicines are shipped directly to the patient's home or the prescribing physician's office. Each applicant may receive up to one year of medicines, and patients may reapply to the program after that period if their need continues.

Rich thought the PharmaCo program was thoughtful and well-balanced. Was it a reasonable approach for IntroSpect? Or was it only appropriate for an established company with a track-record of revenues (hardly IntroSpect's situation)? Would it satisfy Kipp? "It's not a bad starting point," Rich said to himself, and decided to bring it to Dara and the executive committee.

You have a message

Returning home late, Dara dialed into voicemail. From his message, Ron Brown, the Bay Area Parkinson's Disease activist, left no doubt that someone had leaked news of the marketing department's recommended price. Dara leaned against the counter, eyes closed, and listened.

"Hi Dara, this is Ron! Congratulations! Fast track, that's really great! We're counting on your Acedia – but you know, some of our members have been calling, they're really wondering about your pricing. Anything to announce yet? We want to work with you on this, it's so important. You know we love your company. Let's just talk about pricing in a way that [unintelligible] for our members, OK? Please, you know, we don't want to add to the cynicism out there, OK? I mean, I hope we don't need to chat about right and wrong! Do we? Listen. I know you're ethical. IntroSpect has been terrific. We like working with each other, right? So [unintelligible] ready to announce on pricing, let's check in, we'll drive down, it might really help if we understood your reasons, OK? That's it. Thanks, Dara. Call me, OK? Bye. Oh, yes. Hope to see you at our annual fundraising gala dinner."

Free-for-all

After the high-volume encounter in Dara's office, Kipp had retreated to the comparatively placid confines of her fourth floor lab. Rich continued her shuttle diplomacy. Coyne was traveling, but seemed to be reading/sending email just as if he were at home. Dara's executive committee wouldn't meet until Monday to review the marketing proposal. Until then, the debate was conducted by email. Dara just read – she didn't want to prematurely direct these discussions.

-----Original Message-----
From: Kipp Konrad
[mailto:kkonrad@introspect.com]
Sent: Wednesday, June 2, 2004 10:39 AM
To: Dara Devan, Owen Coyne
Cc: Rich Richman
Subject: Fairness

Owen, Dara – Rich stopped by to talk about a patient assistance program. I know the PharmaCo program, it's worth considering. What I want to know is: should our social responsibility go beyond traditional philanthropy (isn't that what a patient assistance program really is?), especially when we're talking about high pricing for a breakthrough drug? We've been working for years on this, our shareholders understand we're part of healthcare. Some of them may need Acedia® someday. They'll think $50,000 is unreasonable – even unethical! We do more good by covering our expenses plus enough to keep our neurology research going.

-----Original Message-----
From: Owen Coyne
[mailto:owen.coyne@biomargin.com]
Sent: Wednesday, June 2, 2004 2:15 PM
To: Kipp Konrad
Cc: Dara Devan, Rich Richman
Subject: Re: Fairness

Kipp: every business needs to earn a profit, and not just enough to cover expenses. How can we ever judge profits unreasonable, never mind unethical[10] — especially for a first-in-class drug like Acedia®? Our shareholders have an expectation for a return on investment that balances the huge risks they took in backing us. If we deliver a return that matches those paid out by, say, a public utility company, the shareholders will park their money somewhere else. So would I. How long do your think American consumers will be happy to host a home-grown biotech industry that can't out-innovate and out-perform their public water and sewer departments?

-----Original Message-----
From: Kipp Konrad
[mailto:kkonrad@introspect.com]
Sent: Thursday, June 3, 2004 7:17 AM
To: Owen Coyne
Cc: Dara Devan, Rich Richman
Subject: Re: Re: Fairness The water companies have innovated enough to get their product to nearly everyone, at least in more developed countries, right? Why shouldn't that be our industry's aim, too? You and Rich keep talking about _market forces' – the burden of social responsibility is best handled in the marketplace, etc., etc. But isn't it wrong to charge $50,000, even if the market will pay? And we know that some won't pay – can't pay. Aren't you forgetting them? Should we charge a high price at their expense? What about doing our part?

-----Original Message-----
From: Owen Coyne
[mailto:ocoyne@biomargin.com]
Sent: Wednesday, June 2, 2004 2:15 PM
To: Kipp Konrad
Cc: Dara Devan, Rich Richman
Subject: Re: Re: Re: Fairness

I'm not forgetting about anybody. Are you? What about our shareholders? They financed your research. What about our employees? They did most of the work, they have stock options. They already did their part: they're about to get this drug on the market. Are we going to forget about our commitment to them? And the patients – all of them have no problem saying, "I'd do anything to get well again!" That's a rational response to illness. How can it be morally wrong to invent something that people desperately want, and then charge them what they the market will bear? If they can't pay, that's got to be someone else's problem.

-----Original Message-----
From: Rich Richman [mailto:rrichman@introspect.com]
Sent: Friday, June 4, 2004 8:07 PM
To: Kipp Konrad
Cc: Dara Devan, Owen Coyne
Subject: Re: Re: Re: Re: Fairness

Kipp, even if we wanted to, we can't succeed as a public charity. If we charge a rock-bottom price for the drug and ask our shareholders to accept reduced (or even no) profits, we're not solving society's problems. Isn't it ethically unacceptable for us to ask our shareholders to finance _doing our part,' without assurances from government and the insurers and even the patients, that they will do their part, too?

The Gala

"Hi, Kipp! I thought I might see you here!" "Um——hello Ron." Kipp wasn't surprised to see Ron Brown at the Parkinson's Action Network dinner, although he suspected that he had planned to run into her. "This is a wonderful event," Kipp said, meaning it. "Wouldn't miss it. Great turnout, I'm sure the coalition is pleased –" The exuberant crowd made it difficult for Kipp to hear Ron's answer. Since moving to the Bay Area, Kipp had missed only a few Gala dinner's sponsored by local Parkinson's Disease groups.

As usual, IntroSpect purchased several tickets for the event and many company employees were there. Ron told Kipp about the message (as yet, unreturned) that he left on Dara's voicemail. "What's going on with the pricing plan," Ron asked nonchalantly. Kipp deflected the question by repeating publicly available information – we're pleased with the NDA's progress, our commercial plans are shaping up, etc. Kipp knew better than to discuss sensitive information outside the company; there aren't many topics as sensitive as pricing. But Ron pressed; and Kipp was in no mood for an ear-banging.

At another time, in another setting, Kipp would have expressed sympathy – even admiration – for the "DON"T CHOOSE PROFITS OVER PATIENTS" message on the oversized button which Ron wore. Kipp-the-scientist admired Ron's inventiveness: last year, after her organization acquired INTRO shares, Ron organized a shareholder's resolution in advance of the corporation's annual meeting. It was unusual for a shareholder to argue *against* profits, but Ron was unusual. Moreover, her resolution was not without support.

"Concern about the high price of prescriptions and those who are uninsured motivated this resolution," Ron had said at the annual meeting, before Dara announced the resolution's sound defeat. "You could set an affordable price, Kipp. No one expects you to lose money. You should set prices just high enough to stay in business." Tonight, though, Kipp didn't want the lecture. "Look around, Ron," Kipp spoke up, gesturing at the diverse crowd.

"Imagine that all of these people have Parkinson's," a horrible thought, Kipp realized immediately. "Many will respond to Acedia®, but plenty won't, and I want to know why. Agricultural workers are more likely to have Parkinson's Disease. I want to understand why. Some people will have no side effects, but others will, and I want to know why. These people—," he pointed at her colleagues, all of whom had no trouble hearing her, now, "—they want to know why, too, and you know what—," he again gestured toward the larger crowd, "— these people *need* us to know why. We can't muck about; we need to do the work.

"I know, I know, 'people-not-profits;' 'it-doesn't-do-much-good-to-invent-drugs-that-nobody-can-afford.' But it doesn't do anyone any good if we can't do the work. Who's going to pay for the research?

"You'd like to, of course; but there aren't enough gala dinners to finance drug development! If we price this thing just enough to _stay in business' – there's no way we're going to make enough progress. I'm all for the rules of fair play and justice, but you can't expect us to completely repeal the laws of the marketplace and still have the resources to get anything done."[11]

PART III: A MORAL DIMENSION

An act of self-examination (reprise)

Dara had requested return-on-equity projections from Rich's finance department number-crunchers. IntroSpect's financial planners had prepared a confidential memo filled with forward-looking guesses about IntroSpect's likely stock price over the next five years, under the pricing scenarios advocated by Owen Coyne, Kipp and Rich. Finance compared these projections to a prediction that the NASDAQ Biotechnology Index would average 24% over the next five years. Assuming likely Acedia® rollout and market demand, here's what the finance department reported.[12]

Using marketing's original proposal ("pricing at a marginal price which maximizes net revenues and profits without regard to reductions in overall production volumes"), IntroSpect's likely return on equity would average 34% over the next five years. Under Rich's peacemaking initiative – the addition of a patient assistance program similar to PharmaCo's – the likely return on equity would be reduced to 31.5% over the next five years. Assuming pricing per Kipp's break even-*plus* approach ("price at the marginal cost of production *plus* an assessment to cover a percentage (the finance group used 50% in its calculations) of ongoing Acedia® R&D"), IntroSpect's likely return on equity would average 13% over the next five years.

Under this scenario, profits would be attributable to fees and royalties from existing and anticipated out-licensing of the mothballed molecules, royalties from eventual Acedia® sales in Europe, and a likely deal to partner or out-license Acedia® for the East Asian territory.

When pressed, Rich acknowledged that the 13% forecast took into account investor flight from IntroSpect to other biotech companies and/or sectors, but not any possible migration to IntroSpect stock of "social responsibility" investors. Quite possibility for her edification only, Dara also asked the finance department to look at return-on-investment ("if any," Rich protested) were IntroSpect to permit Ron Brown to dictate the pricing strategy ("set prices just high enough to stay in business"), IntroSpect's likely return on equity might average 8% over the next five years, but then fall off sharply. As was the case for Kipp's break even-*plus* scenario, all profits would derive from non-Acedia®-related fees and royalties, and ex-US Acedia®-related income.

Here, too, it was hard to assess how much bottom-liners and social responsibility investors would flee from/be attracted to INTRO.

What's bioethics got to do with it?

Dara took a sip of long-cold coffee from her IntroSpect-logo mug. her head ached – all weekend, he realized. Since college, he kept a bottle of Tylenol® with her, and he'd been popping aspirin all day. He rustled around her suitcase, until he remembered that the bottle was empty – no aspirin here.[13] Slowly, he massaged her temples. Did he need advice more than Tylenol®?

At the Weitzmann Institute, Dara had taken several bioethics courses – interesting stuff, she remembered. Her textbooks, including the well-worn bioethics books from her Weitzmann days, seemed to follow Dara everywhere. From her bookshelf, Dara randomly grabbed a bioethics book, scanned the table of contents, and flipped to the chapter on healthcare. "Pricing for healthcare products," she read, "will be deemed ethical if the pricing respects the ethical values and principles that are appropriate and relevant to the situation and have been justified as taking priority over competing values or principles."[14]

She read on, pausing long enough to notice the once-familiar terms: rights and personhood; distributive justice and fairness; utility; beneficence and non-malfeasance.[15] Under non-malfeasance, he read, "To the extent that pharmaceutical companies, like doctors and other moral agents within healthcare, have an obligation to 'do no harm,' is premium pricing morally defensible, when people who desperately need a drug but cannot afford it will have to go without?"[16] She set the book down.

Her company was wrestling with more than an economics problem, Dara understood. Did she need bioethics advice to properly sort out the competing interests? Even if she consulted a bioethicist, would Kipp's break-even pricing be seen as the only ethically defensible approach? Would Owen Coyne's what-the-market-will-bear recommendation, and even the patient assistance program advocated by Rich, be perfunctorily dismissed? And what if she found a bioethicist to endorse (or at least, not instantly reject) Coyne's recommendation?[17] Industry-employed bioethicists, she knew, had been labeled mouthpieces of corporate marketing departments. "While most bioethicists are no doubt well-intentioned," she read from a *Washington Post* clipping which protruded from her textbook, "their work is sometimes being used as cover, allowing corporate conundrums to masquerade as ethical problems, often with solutions that serve corporate interests. [18]

A bad time to get sick

Dara returned the clipping to the book, the book to the bookshelf, and her attention to her computer.

She returned to her desk and composed this email to her colleagues:

"Owen, Kipp, Rich – hello – it's Sunday afternoon –I've been thinking about tomorrow morning's meeting. I wish this wasn't so hard, but it is. We need to make a decision tomorrow if we're going to get a pricing recommendation to the board on Wednesday. I'm still not sure where I come down on price, so I'd appreciate hearing from each of you again. The three of you have been terrific, thanks. What I'm still struggling with, what I think all of us are struggling with, are values. We can try, but it's pretty hard to have a values-neutral discussion about anything – including pricing. For tomorrow at least, let's just assume that everything we're going to talk about has a moral dimension.[19] Whether we're talking about pricing high because of inelasticity or pricing no more than the marginal cost of production, we need to justify our arguments. We're not ethicists, true, but we have ethics. We'll do the best we can."

Dara leaned back in her chair, re-read what she had just written, and added this: "I'm proud of the way we are getting to an answer – the right answer, I hope. Thank you. See you in the morning." She clicked send. Within minutes, Dara had replies from all three. She chuckled; they were wrestling with the dilemma, too. Rich's email was, like Rich, to the point: thanks, see you tomorrow. That was it. Kipp, it seemed, was still feeling badly about last week's outburst; her conciliatory email, also brief, quoted a leading economist: "No other area of managerial activity is more difficult to depict accurately, assess fairly, and prescribe realistically in terms of morality than the domain of price."[20]

Dara appreciated her note. Owen Coyne's email was the last to arrive, and it didn't auger well for an easy morning meeting. Quoting Oscar Wilde, he wrote: "Morality is simply the attitude we adopt towards people we personally dislike."[21] Dara's headache worsened. Was she getting a sore throat, too? She gazed out her office window, looking for, but not seeing, the fog-shrouded outlines of the Bay Bridge. The morning's periodic drizzle had crescendoed to a steady, cold rain. "This is a lousy time to get sick," Dara thought, and once again, she reviewed her options. . . .[22]

[1] BIO thanks everyone who reviewed earlier drafts, offered comments, sent materials and identified important themes for inclusion in these materials, including Richard Hoffman, Steven Coit and the students in her Boston University School of Management class, Michael Werner, Debra Aronson, Simon Best, Steven Holtzman, Rahul Dhanda, Margaret Eaton, Bruce Leicher, Scott Brown and Jason Raisner.

[2] Attributed to Samuel (Mark Twain) Clemens.

[3] This section on aspects of starting a biotechnology company draws on resources from the symposium, "Biotechnology at 25: Perspectives on hertory, Science, and Society," Stanford University, March 1999, and from the Library's collection of oral hertories of biotechnology pioneers.

[4] Branch Rickey, US baseball player, 1881-1965.

[5] Richard Hoffman provided this articulation of a basic economic principle, and contributed to development of the board chairman's business/economic arguments in the next section of the case.

[6] For an overview of pharmaceutical pricing and industry economics, see Reinhardt, "Perspectives on the Pharmaceutical Industry," *Health Affairs* 20(5) (2001).

[7] Danzon, "Making Sense of Drug Prices," *Regulation*, 23(1) (2000): 61.

[8] The suggestion for the chief science officer's cost-*plus* argument came from Professor Steven Coit's Boston University School of Management class discussion of ethics and drug pricing.

[9]This quotation is an excerpt from an address by board chairman Miles D. White, "Making a Difference in the Cause of Affordability and Access," to the Pharmaceutical Research and Manufacturers of America (April 4, 2004), posted to the PhRMA Website.

[10]For an excellent discussion of bioethics principles and pharmaceutical pricing, see Richard A. Spinello, "Ethics, Pricing and the Pharmaceutical Industry," *Journal of Business Ethics,* vol.

[11] (August 1992), reprinted in Lisa H. Newton and Maureen M. Ford, ed., *Taking Sides: Clashing Views on Controversial Issues in Business Ethics and Society* (Guilford, Connecticut: McGraw-Hill/Dushkin, 2002).

[11]Steven Holtzman framed the moral dilemma in terms of duty to patients who rely on an existing drug *versus* duty to develop new drugs for patients who have unmet medical needs.

[12]Simon Best proposed this section of the case.

[13]Rahul Dhanda proposed the idea of the company CEO having an unmet need for medication to treat a minor malady.

[14]Schrecker and Somerville, "Making Ethically Acceptable Policy Decisions: Challenges Facing the Federal Government," Canadian Biotechnology Strategy Task Force report (1998): 83.

[15]For a discussion of basic bioethics concepts, see Ronald Munson, *Intervention and Reflection: Basic Issues in Medical Ethics* (Belmont, California: Thompson Wadsworth, 2004); see also Spinello, *supra.*

[16]See Munson, supra, Ch. 8; see also Spinello, supra at 97.

[17]Rahul Dhanda's thinking and writing about bioethics within corporate biotechnology, see, *e.g.*, Dhanda, *Guiding Icarus: Merging Bioethics with Corporate Interests* (New York: Wiley & Sons, 2002), influenced this section of the case.

[18]Raymond De Vries, "Businesses Are Buying The Ethics They Want," *Washington Post* (February 8, 2004)

[19]Steven Holtzman helped clarify that business decisions, which are too often perceived to feature separate "ethics issues" and "economic issues," in fact present overarching dilemmas which have, *e.g.,* moral and economic dimensions.

[20]Walton, *Ethos and the Executive* (Englewood Cliffs, New Jersey: Prentice Hall, 1969):209, quoted in Spinello, supra at 97.

[21]Oscar Wilde, *An Ideal Husband*, act 2, paraphrased in Leisinger, "The Pharmaceutical industry and Social Responsibility: Ideals without Illusion and Realism without Resignation," *Novartis Foundation for Sustainable Development* (October 2002), citing Kapstein, "The Corporate Ethics Crusade," *Foreign Affairs*, Vol. 80 (2001).

[22]BIO thanks Emily Taylor, Katie Sawyer and other colleagues for assistance in contacting and inviting the outstanding bioethicists, economists, industry leaders and chief executive officers who are scheduled to participate in the BIO 2004 roundtable discussion of this case. BIO is especially grateful to Professor Charles Nesson for agreeing to serve as roundtable moderator.

Please send comments to Debra Aronson, Director of Bioethics at BIO, daronson@bio.org.