
CASE STUDY

“Case Studies” presents a case pertinent to contemporary issues and events in investment management. Insightful and provocative questions are posed at the end of each case to challenge the reader. Each case is an invitation to the critical thinking and pragmatic problem solving that are so fundamental to the practice of investment management.

PRICING FOR SURVIVAL IN THE BIOPHARMA INDUSTRY: A CASE STUDY OF ACTHAR GEL AND QUESTCOR PHARMACEUTICALS

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Recent cases of aggressive pricing behavior in the biopharmaceutical industry have raised serious concerns among payers and policymakers about industry ethics. However, these cases should not be confused with price increases motivated by challenging business conditions that ultimately lead to greater investment in R&D and improved patient access to therapeutics. We study the example of Questcor Pharmaceuticals, which was forced to choose between increasing the price of an effective drug in 2007 and ceasing production and shutting down. We consider Questcor’s journey from inception to its acquisition in 2014, analyze the factors leading up to the price hike of its main revenue generator, Acthar Gel, and discuss its resulting impact on patients after 2007. A counterfactual financial simulation of the company’s prospects in the case where prices were not increased shows that Questcor would have become insolvent between 2008 and 2010.



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1 Introduction

The overall cost of drug development has more than tripled in the last 15 years due to growing R&D costs and rising failure rates. Since 1950, the number of approvals for new medicines per \$1 billion of R&D investment has roughly halved every nine years (Scannell *et al.*, 2012). In 2003, developing one new drug required about \$800 million, including opportunity costs and failures (DiMasi, Hansen & Grabowski, 2003); it now

typically takes more than 10 years and \$2.6 billion for a drug to reach the market (DiMasi, Grabowski & Hansen, 2016; Mullard, 2014). Due to these high costs, drug prices are commensurately high to meet the required rate of return for shareholders. The two most expensive drugs in the world—Soliris and Spinraza—both breakthrough therapies for rare diseases, each cost over \$600,000 per patient per year (Palmer, 2015; Weintraub, 2017). Though financial rewards are necessary to create incentives for innovation and risk-taking behavior in any industry, rising U.S. healthcare costs have drawn intense scrutiny to the pharmaceutical industry's business models and practices (Gillespie, 2016).

In particular, Big Pharma has been heavily criticized for its reliance on large annual price increases to drive revenue growth (Crow, 2016). An analysis by Credit Suisse of 20 leading global pharmaceutical companies concluded that 80% of 2014 profit growth in the United States was driven by increases in price rather than sales volume (de Felice, 2017). This pervasive price-based business model has spread as R&D efficiency has plummeted, and as the frequency of new product launches has declined (Deloitte, 2016). Critics of this practice have pressured the biopharma industry to rein in prices. In response, pharmaceutical companies such as Allergan (Saunders, 2016), Novo Nordisk (Roland, 2016), and Abbvie (Stanton, 2017) have taken the lead in self-regulation, promising voluntary annual price-increase limits (Beasley, 2017).

Given that companies actively engaged in discovering new therapies face such pressure when pricing drugs, it is not surprising that even greater controversy surrounds companies and CEOs that significantly increase the prices of products they did not develop themselves. Two infamous cases of such practices, Turing Pharmaceuticals and Valeant Pharmaceuticals, have recently added to

the political and public outrage on pricing. Martin Shkreli, the CEO of Turing, acquired the 60-year-old antiparasitic drug, Daraprim, increasing the price over 5,000% from \$13.50 to \$750 per pill, while Valeant's business model seemed to be centered on routinely increasing the prices of acquired drugs (Pollack, 2015; David, 2016).

Such extreme price hikes drew considerable attention from politicians, as presidential candidates Hillary Clinton (Egan, 2016a; Kaplan, 2016) and Donald Trump (Egan, 2016b) condemned price-gouging behavior and pledged pricing reform, sending biopharma indices tumbling several times in 2016. An August 2016 Gallup poll of U.S. citizens found that pharma had the worst reputation among the 24 industries listed, its lowest standing in 16 years (Saad, 2016).

In light of these events, it is especially important to distinguish between price-gouging behavior—which is unacceptable in any industry—and business decisions that impact the wellbeing of patients. Because businesses are ultimately profit-seeking entities, the contrast may be a fine line. We hope to sharpen this line by describing the case of Questcor Pharmaceuticals, which was forced to choose between increasing the price of a life-saving drug to stay in business, or stopping its manufacture and going out of business.

Questcor Pharmaceuticals faced criticism for increasing the price of its primary drug, Acthar, over 45,000% from 2001 to 2007, and particularly in August 2007, when the price increased from \$1,650 to \$23,269 per vial (Pollack, 2012; Smith, 2016; Tirrell, 2015; Plieth, 2012; Mitchell, 2008). While this increase may have generated controversy, we argue that the basis for this decision was distinct from the price-gouging behavior that seems to have characterized other pharmaceutical products. We relate Questcor's journey from inception to its acquisition in 2014, analyzing the factors leading up to the price hike and its

resulting impact on patients after 2007. Finally, we conduct a counterfactual financial simulation of the company's prospects if prices had remained the same in 2007.

Apart from providing earlier historical information for context, we shall confine our attention in this case study to the period from 2007—when Questcor installed new leadership and changed its corporate strategy, including (but not limited to) its pricing of Acthar—to 2014 when it was acquired by the specialty pharmaceutical company Mallinckrodt and control changed hands.

2 Acthar background

Acthar Gel was developed over 60 years ago by a subsidiary of the meatpacking giant Armour & Company, and approved by the FDA in 1952 for about 50 inflammatory diseases prior to the Kefauver Harris Amendment of 1962, which required drug manufacturers to provide proof of efficacy as well as safety (Pollack, 2012; Mechcatie, 2010a; Silverman, 2014; Krantz, 1978). It was subsequently FDA-approved for acute exacerbations of multiple sclerosis (MS) in 1978 based on efficacy and safety data, though it still was not subjected to the robust efficacy standards of today (ThinkEquity Partners LLC, 2006). The French chemical and pharmaceutical company Rhone-Poulenc Rorer acquired the rights to Acthar from Armour, merged with Hoechst AG to form Aventis in 1999, and then sold Acthar to Questcor in 2001 (Pollack, 2012). In 2014, the global specialty pharmaceutical company Mallinckrodt acquired Questcor to obtain the drug, and currently manufactures it (Pollack and Bray, 2014). To this day, Acthar's production process, which consists of purifying pituitary glands from pigs, remains a trade secret rather than a patent-protected process.

Acthar is a complex formulation containing naturally occurring adrenocorticotrophic hormone (ACTH), a peptide that binds to melanocortin

receptors throughout the body (Mechcatie, 2010a). The drug provides an extended release after intramuscular or subcutaneous injection, and induces the adrenal gland to produce endogenous corticosteroids. However, evidence shows that stimulation of melanocortin receptors elsewhere may also be clinically meaningful, suggesting that Acthar's overall mechanism is more complex than a synthetic steroid such as prednisone (Seeking Alpha, 2011). Because steroids were often a good substitute for Acthar, however, the drug largely fell out of use in the 1980s when steroids became cheap to manufacture. Prior to that, Acthar was commonly used in patients with arthritis, lupus, ulcerative colitis, and a variety of other inflammatory diseases (Pollack, 2012).

Replaced by prednisone for many diseases, Acthar was then primarily used to treat acute exacerbations in MS and an off-label condition (not FDA-approved for treating the condition), infantile spasms (IS), a severe form of epilepsy that affects roughly 2,300 infants per year. If left untreated, the disease causes mental retardation and physical impairment (Mechcatie, 2010a; Oppenheimer Equity Research, 2008). An average Acthar treatment course for IS is about six weeks, requires four to five vials, and features beneficial responses in around 80% of IS cases (Stanford Group Company, 2008). Rapid therapy can achieve complete resolution of IS in 50% of patients by two years of age and in 72–99% of patients by five years (ThinkEquity Partners LLC, 2006). For example, a 1983 study published in *Neurology*, the official journal of the American Academy of Neurology, reported the following results (Snead III, Benton & Myers, 1983):

We treated 116 children with ACTH or prednisone. Fifty-two had infantile spasms with hypsarhythmia, and 64 had other types of intractable seizures. ACTH completely controlled seizures in all patients with infantile spasms and hypsarhythmia and 74% of those with other types

of seizures. Prednisone controlled 51% of patients with infantile spasms and none with other seizures.

For decades, Acthar was an important first-line therapy for IS, and was recommended as the most effective treatment for the disease by the American Academy of Neurology (Kossoff *et al.*, 2009).

Consequently, in 1995 when physicians experienced a severe Acthar supply shortage due to its difficult manufacturing process, a public health crisis ensued. Although its manufacturer at the time, Rhone-Poulenc Rorer, initially chose to discontinue the product, protests by patient groups and physicians demanded that the firm continue to make a limited supply (Leary, 1996). From 1997 to 2001, Acthar was rationed to 1,600 patients per year, compared to a demand estimated at 6,500 patients per year (ThinkEquity Partners LLC, 2006). Rhone-Poulenc Rorer, which became Aventis in 1999, suffered annual losses in the millions on the drug (Pollack, 2012). Acthar's complex, expensive manufacturing process was unsustainable at the price of \$50 per vial in a low-volume market. By 2001, its production was in the process of being discontinued; afterwards, its availability to patients would have been lost (Pollack, 2012).

3 Questcor background

Questcor Pharmaceuticals, formerly named Cypros Pharmaceutical Corporation, was headquartered in Anaheim, California, and founded in 1990. Cypros merged with RiboGene in 1999, and named the fully integrated company Questcor Pharmaceuticals (Pharmaceutical Online, 1999). The new firm sold three products with numerous clinical-stage development programs focusing on acute- and critical-care specialty hospital pharmaceutical products. Questcor's initial strategy was to build strong hospital-focused sales, marketing, and distribution capabilities, and to acquire

and develop synergistic late-stage drug candidates (Questcor Pharmaceuticals, 2001). In 2001, the company bought the struggling Acthar asset from Aventis for \$100,000 and a 1% royalty on annual sales greater than \$10 million (Pollack, 2012; Questcor Pharmaceuticals, 2001).

Acthar's previous 50-year existence had two main implications for Questcor. First, although Acthar was not patent-protected, Questcor could rely on its secret, complex manufacturing process as a key barrier to entry for competition from a generic version of Acthar (Questcor Pharmaceuticals, 2006). Second, due to different standards of approval in the 1950s, Acthar had on-label indications that were not subjected to the level of evidence demanded by more recent FDA standards (Silverman, 2014). As a result, Questcor maintained full-pricing power as the sole manufacturer of Acthar, with the option to market the drug for a variety of indications without running extensive clinical trials. After acquiring the drug, Questcor increased the price from \$50 to \$700 per vial in an attempt to make it financially viable (Pollack, 2012). However, the company continued to struggle, in part due to an expensive manufacturing transfer process and a variety of operational challenges.

4 Questcor's challenges, 2001–2007

4.1 Manufacturing

Acthar's production process consists of three main parts: extraction of the active pharmaceutical ingredient (API), production of finished Acthar vials, and quality control using three assays. Unlike a purely synthetic product, Acthar's API is a complex biologic preparation, extracted from the pituitary glands of pigs, and this preparation potentially includes as yet uncharacterized active components in its formulation. In 2003, Questcor successfully started operations at the contract manufacturer (CMO)

Chesapeake Biological Laboratories to produce vials from the API still provided by Aventis (Questcor Pharmaceuticals, 2003). A year later, Questcor enlisted CMO BioVectra to perform the API extraction. In 2005, the firm gained FDA approval for two quality control bioassays transferred from Aventis to a contract laboratory. Due to cost and time difficulties in transferring the third assay for potency, Aventis continued to perform it for Questcor (Questcor Pharmaceuticals, 2005). Because producing Acthar was complicated, transfer of the know-how incurred costs of over \$1.2 million from 2003 to 2004. The transfer of manufacturing from Aventis to new CMOs also resulted in higher unit costs and lower gross margins of 78% (Questcor Pharmaceuticals, 2004). However, manufacturing, while important, was a relatively small part of Questcor's financial struggles.

4.2 Operational challenges

Questcor's operations were consistently underperforming because its products—which spanned neurology, nephrology, and gastroenterology—did not generate adequate revenues. Until 2007, selling, general, and administrative (SG&A) expenses were consistently greater than 60% of revenues (Figure 1). In comparison to a median

34% SG&A/Revenue ratio for small- and mid-cap drug companies in the NASDAQ Biotechnology index (David, Robey & Matthews, 2017), Questcor's operating losses from inception in 1999 until 2007 were not surprising.

Acthar had such a small patient population that the sales volume was too low to be profitable, even at the 2006 price of \$1,650 per vial. Moreover, Questcor's sales representatives were prohibited by U.S. law from marketing the drug to neurologists for the treatment of IS, despite its status as *standard of care* in the United States, because the use of Acthar for IS was off-label. If a physician did happen to initiate a discussion, the sales representative had to refer the doctor to Questcor's medical science liaisons (MSLs), who were part of the firm's R&D group. By law, MSLs are only permitted to respond to inquiries and provide unannotated, published scientific literature. This was particularly problematic because physicians are often unaware of the standard-of-care treatment options for rare diseases (Shire, 2013). It is estimated that Acthar's penetration into the IS market was, at best, 50% in 2006 (ThinkEquity Partners LLC, 2006).

Questcor faced an ethical dilemma: despite Acthar's status as standard of care, the firm

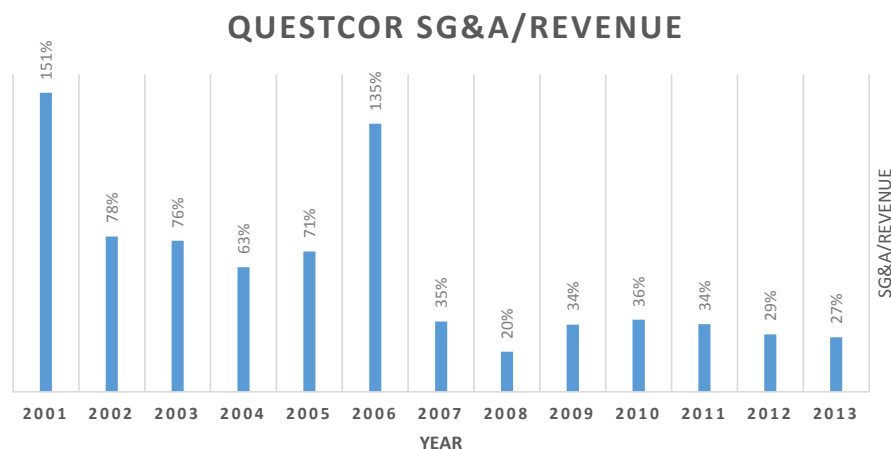


Figure 1 Questcor SG&A expenses as a percentage of revenue, 2001–2013.

Table 1 History of Acthar pricing, 2000–2012.

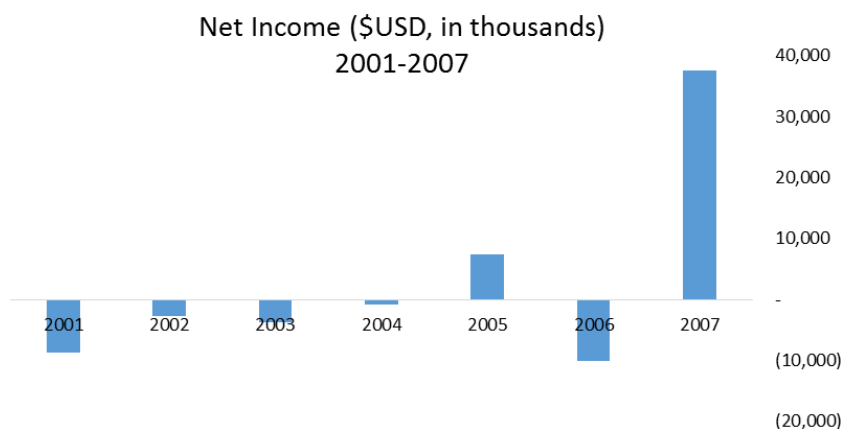
Acthar price over time			
Year	Price increase	Acthar price (\$USD)	Source
2000	N/A	50	Pollack (2012)
2001	1,300%	700	Pollack (2012)
2002	26%	879	Approximated
2003	26%	1,104	Approximated
2004	17%	1,292	(10-K 2004)
2005	14%	1,473	(10-K 2005)
2006	12%	1,650	(10-K 2006)
2007	1,310%	23,269	(10-K 2007)
2008	4%	24,153	Approximated
2009	4%	25,071	Approximated
2010	4%	26,024	Approximated
2011	4%	27,013	Approximated
2012	4%	28,000	Pollack (2012)

could not proactively educate neurologists on the drug's ability to treat IS. Consequently, Questcor invested in R&D to prepare a supplemental new drug application (sNDA) to include IS on Acthar's label (Marrone, Bass & Klinger, 2007; Stafford, 2008). Although Questcor raised Acthar's price to fund its unique situation (Table 1), the firm still endured annual net income losses between 2001 and 2006 (Figure 2), excluding 2005, when CEO James L. Fares was hired. Under his leadership, Questcor divested its non-neurology drugs for

\$22.5 million to stay in business, paid down \$6.2 million in debt, and adopted a new business strategy (Questcor Pharmaceuticals, 2005).

The firm shifted its focus to central nervous system (CNS) diseases to streamline its marketing efforts towards neurologists. In 2006, in addition to acquiring and marketing Doral, a neurology drug for insomnia, Questcor ramped up marketing efforts for Acthar in MS to build a sustainable business and fund Acthar's sNDA for IS. Questcor invested about \$7 million to expand its sales division from 15 sales representatives and managers to 40 (Questcor Pharmaceuticals, 2006). However, the larger sales team did not generate enough demand for Doral and Acthar to compensate for the company's increased SG&A expenses and the revenue lost from its 2005 divestiture. That year, revenue decrease by about \$1.4 million and the FDA rejected Questcor's sNDA for IS (Questcor Pharmaceuticals, 2006).

The expensive sales team had a significant negative impact on Questcor's bottom line, as SG&A exceeded revenue by 35% (Figure 1), leading to operating losses of \$10 million (Questcor Pharmaceuticals, 2007). This highlighted key barriers for a successful Acthar-based business model not present in previous decades when the drug was profitable at a lower price. Although Acthar was originally a first-line drug used for

**Figure 2** Questcor's net income leading up to 2007 when the price of Acthar was increased.

numerous diseases, just as the steroids that replaced it are today, its situation in the early 21st century was unusual. Though it was an approved therapy for acute exacerbations of MS since 1978, rationing of the drug due to the 1997–2001 manufacturing issues reserved the drug for patients with IS, causing it to largely fall out of use in the MS indication (ThinkEquity Partners LLC, 2006). Significant sales efforts over time were needed to drive adoption of the drug for this indication again. In IS, the drug could not be marketed to doctors under any circumstance as it had never been formally approved for this indication.

Questcor's strategic gamble had failed.

5 Questcor's performance, 2007–2014

Heading towards bankruptcy, Questcor replaced James L. Fares with Don M. Bailey—an engineer with little prior biopharma experience who was the former chairman and CEO of Comarco, a successful wireless technology company—and implemented a new strategy for Acthar (Questcor Pharmaceuticals, 2007). Questcor raised the price of Acthar from \$1,650 to \$23,269 per vial (Table 1) while simultaneously expanding

its sponsorship and co-pay assistance programs to facilitate access for uninsured and underinsured patients (Questcor Pharmaceuticals, 2007). Questcor was finally profitable in 2007, generating pre-tax income of about \$23 million (Figure 2).

With a financially viable drug, Questcor now had resources that allowed it to grow its sales and marketing capabilities, as well as to conduct new clinical trials to expand Acthar's labeled set of indications. In addition to improving adoption in MS, the company successfully marketed the drug for nephrotic syndrome (NS) and many rheumatic diseases. And in 2010, the FDA's approval of Acthar as a monotherapy for treating IS finally allowed Questcor's sales force to market the drug for the indication to which Acthar was the de facto standard of care (see Section 6.2 below for a discussion of Acthar's efficacy).

As a result of this expanded label and a concurrently growing patient population, Questcor experienced massive growth over the next seven years. The share price increased more than 200-fold, from less than 50 cents on August 7, 2007, when the new pricing level was

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*
Among Questcor Pharmaceuticals, Inc., the NYSE MKT Composite Index, and the
NASDAQ Pharmaceuticals Index

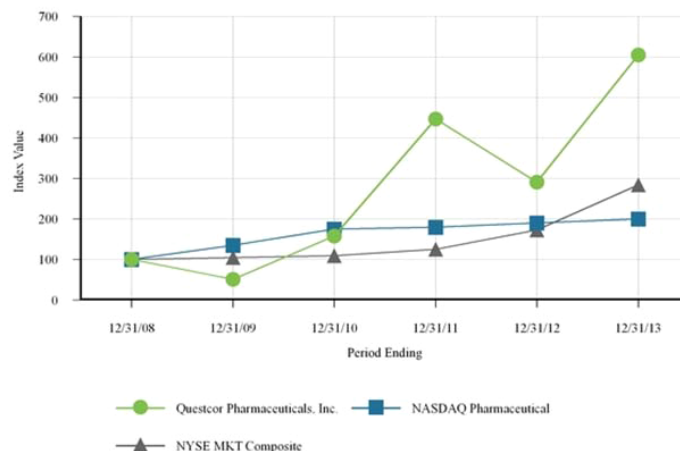


Figure 3 Questcor's historical stock returns in comparison to the NYSE MKT Composite Index and the NASDAQ Pharmaceuticals Index, 2009–2013.

implemented, to \$93.60 on August 14, 2014, when the firm completed its sale to Mallinckrodt for \$5.6 billion (Figure 3).

Throughout Questcor's rapid growth, the company consistently beat earnings forecasts while enduring significant volatility. Shares were up 13% after its Q3 2011 earnings were announced, as revenue beat analysts' expectations by over \$6 million (Reeves, 2011). The firm's Q2 2012 and Q3 2013 revenue also beat expectations, by \$2 million and \$16 million, respectively (Reeves, 2012; Investor's Business Daily, 2013). However, Questcor traded down 7% when February 2012 prescription data indicated a decline of about 20 scripts for MS. Questcor management assured investors that low-volume, single-month prescription data was highly volatile and that one month was not necessarily predictive of future trends (Investor's Business Daily, 2012a). On September 19, 2012, the health insurer Aetna announced that it would cut back reimbursements for Acthar, causing Questcor's stock to decline 56% to \$25.00 (Nathan & Siddiqui, 2012). Five days later, Questcor shares fell another 37% to \$18.00 on September 24, 2012, when Questcor announced that an undisclosed U.S. agency was investigating the firm's promotional practices (Lopatto, 2012). Questcor's stock price recovered over 2013 as the firm delivered annual revenue of \$798.9 million, a 57% increase over 2012 (Questcor Pharmaceuticals, 2013a). Though a controversial report written in February 2014 by short-selling firm Citron Research questioned Acthar's ACTH content and sent Questcor shares down 10% (Chen & Larkin, 2014), Mallinckrodt agreed to buy Questcor two weeks later for \$5.6 billion (Alpert, 2014).

6 Criticisms and controversies

6.1 Pricing

Acthar's price increase from \$1,650 to \$23,269 triggered a significant backlash. Questcor was

criticized for raising the price of an old drug it acquired and did not develop, in apparent similarity to the stories years later of Valeant and Turing (Pollack, 2012). As biotechnology reporter Andrew Pollack wrote in the *New York Times*, "How the price of this drug rose so far, so fast is a story for these troubled times in American health care—a tale of aggressive marketing, questionable medicine, and not least, out-of-control costs" (Pollack, 2012). Medicare costs associated with Acthar increased 20-fold to \$141.5 million from 2008 to 2012, despite its low single-digit price increases in this period (Table 1), due to its rapidly expanding sales volume, making it the 139th most expensive drug out of 3,000 (Silverman, 2014). Acthar also incurred large costs to private insurers, resulting in the decision by Aetna that it would no longer reimburse the drug for most diseases (Nathan & Siddiqui, 2012). Express Scripts, the firm's exclusive distributor, had its ethics questioned due to a potential conflict of interest between its mission to help negotiate lower drug prices and its reward from larger rebates on the more highly priced Acthar (Freudenheim, 2008). The price hike drew direct rebukes from critics of corporate greed, and also attracted broader scrutiny of the company and the drug.

6.2 Clinical efficacy

Because Acthar was approved by the FDA in 1952, Questcor did not need to run clinical trials for Acthar before extensively marketing it for a variety of diseases. Given the expectation that a high-priced specialty drug should be therapeutically transformative, its price hike in 2007 drew attention to its medical value and its efficacy has been questioned.

In the case of IS, Acthar is currently the first-line treatment and, as discussed in Section 2, is able to completely resolve IS in a significant fraction of the patient population. Nevertheless, the literature

contains a variety of studies indicating superiority, equality, and inferiority of Acthar relative to other options (Reuters, 2010; Metersky, 2016; Mechcatie, 2010a, Mechcatie, 2010b; Questcor Pharmaceuticals, 2010a; Snead III, Benton & Myers, 1983). A 2009 Johns Hopkins Hospital retrospective study found equivalence between Acthar and high-dose prednisone for IS, but recommended that doctors choose the latter, based on an analysis of its patients and the 250-fold price difference between Acthar and prednisone (Kossoff *et al.*, 2009). In Europe, a synthetic, truncated form of ACTH, Synacthen Depot, is used for IS instead of Acthar, also at a substantially lower cost. However, the FDA has not yet approved Synacthen Depot for any clinical use in the United States.¹

Acthar's efficacy in MS and NS has also been studied. Questions were raised when a 2009 study sponsored by Questcor to analyze data—that remains undisclosed—was terminated after a year (Neurologique Foundation Inc., 2010). The trial aimed to assess the efficacy of Acthar versus another round of steroids for non-responders to first-line treatment (Pollack, 2012). Though the majority of doctors treating MS do not prescribe it, some have found the drug useful as a rescue therapy when steroids fail. Others called prescribing a \$23,000 drug to treat an MS relapse “absurd” (Pollack, 2012; see also Hartung, 2017, for a recent criticism of Acthar efficacy and pricing). According to Questcor CEO Bailey, Acthar's particular niche in MS treatment comprised “serious, difficult-to-treat” cases (Questcor Pharmaceuticals, 2010b).

To assess the drug's value in treating NS, Questcor sponsored and collaborated with Columbia University on three clinical studies published in 2011, 2012, and 2013. While the data lacked the robustness of an independently sponsored, randomized, double blind, placebo-controlled efficacy study, about 25–50% of initially treatment-resistant

patients responded to Acthar (Bomback *et al.*, 2012; Bomback & Radhakrishnan, 2011; Hogan *et al.*, 2013). On the other hand, a nephrologist in Phoenix stopped a small study testing the drug's efficacy because of poor results (Pollack, 2012). In general, Acthar's efficacy in relation to other available treatments is inconclusive, although its niche as a rescue therapy for some difficult to treat diseases has clinical support.

6.3 Side effects

Before 2012, infants and MS patients were the predominant users of Acthar. They typically have a low number of concomitant medications and comorbidities. However, Acthar use for nephrology and rheumatology patients—who tend to have a high number of other medications and conditions—significantly increased in 2012. Since that year, Questcor has reported 20 deaths and six disabilities to the FDA that were “suspected” to be associated with the treatment, although the FDA stressed that reports of adverse events are observational and not verified as causal. In contrast, the 12 years preceding 2012 had only 13 deaths recorded (Morgenson, 2014).

In 2014, Questcor was accused of downplaying Acthar's side effects when the firm did not report a significant uptick in serious adverse events in its filings for the Securities and Exchange Commission (SEC) (Silverman, 2014). In response, Questcor filed an 8-K with the SEC disclosing that the number of adverse events reported in 2011, 2012, and 2013 as a percentage of prescriptions was 9.1%, 15.8%, and 13.7%, respectively (Questcor Pharmaceuticals, 2014). Questcor emphasized that Acthar's safety profile was well established, and that a significant change in patient population after 2011 could explain the increase in 2012. Questcor cited a disproportionate risk of severe adverse events in this new patient population to explain the poor outcomes

(Questcor Pharmaceuticals, 2014). FDA intervention has not occurred.

6.4 Government investigations

In September 2012, Questcor disclosed that the Department of Justice and the SEC were investigating the company's marketing and promotional practices. The firm drew suspicion from regulators because of its financial ties with top Medicare prescribers. In 2012, only 18 physicians wrote 15 or more Acthar scripts covered by Medicare, while at least nine of these doctors were speakers, researchers, or consultants for Questcor (Ornstein, 2014). However, the marketing investigation did not reveal any illegal practices.

Two years later, in 2014, Questcor received a subpoena from the Federal Trade Commission (FTC) for potentially violating antitrust laws when the firm acquired rights to Synacthen Depot from Novartis in 2013 for \$135 million. Here, the FTC probe did not reach a conclusion under Questcor's management, but in early 2017, its successor Mallinckrodt agreed to pay \$100 million to settle these charges, and divested its U.S. rights to Synacthen Depot because of its anticompetitive practices (Federal Trade Commission, 2017).

Government investigations are not unusual in the pharmaceutical industry. Questcor's rapid growth and price hike made the firm a target for government probes (Pollack, 2012), fueled in part by agents who stood to profit, such as potential competitors, including Martin Shkreli's company Retrophin, which had tendered a \$16 million offer to Novartis for the rights to Synacthen Depot prior to Questcor's offer (Pollack, 2013). In 2014 Retrophin filed an antitrust complaint in U.S. District Court over Questcor's asset purchase, which was settled by Mallinckrodt for \$15.5 million in 2015 (Retrophin, 2015). Shkreli now alleges to have tipped off the FTC to the antitrust implications of the Questcor deal, although the possibility

of an FTC investigation was discussed in the media at the time of the original acquisition (Pollack, 2013; Kosman, 2017).

6.5 Short selling

The controversy over Questcor was not limited to the pharmaceutical industry or the general public. The financial media and the mainstream press reported that activist short-sellers had targeted Questcor for attack, attributing several large daily downward swings in the stock's price to the release of negative research reports by these firms (Pollack, 2012; Chen & Larkin, 2014; Investor's Business Daily, 2012b). Questcor's rapid rise and Acthar's relative obscurity in an atmosphere of controversy fit a short-selling narrative template of an overvalued, possibly corrupt company.

Despite these negative reports, however, most investors continued to believe in Questcor's prospects. Although Questcor experienced significant volatility during its rise, investor confidence in the firm was ultimately rewarded. Only weeks after a two-day 16% decline attributed to short-seller activity (Chen & Larkin, 2014), Mallinckrodt purchased the firm at a 27% premium per share (Pollack and Bray, 2014).

7 Patient impact

The new price of Acthar had numerous implications for patients, the healthcare system, and Questcor's business. Without its additional assistance, uninsured patients would have directly suffered from Acthar's high price, while the government, private insurers, and insured patients still endured higher costs. However, the new price allowed Questcor to avoid bankruptcy, ensuring the continued availability of Acthar to the patients who used it. Because of Questcor's post-2007 profitability, the company re-invested in R&D and sales to better understand Acthar's efficacy and widen its patient access. By 2009, the firm

Table 2 Examples of trials and studies run by Questcor as part of their R&D activities. Source: Questcor 10-K filings, 2011 and 2013.

Research & development		
Class	Disease	Study type or purpose
On-label development	Nephrotic syndrome	Phase IV clinical trial
	Infantile spasms	Clinical study establishing quality of care indicators
	Systemic lupus erythematosus	Phase IV clinical trial
Off-label development	Diabetic nephropathy	Phase II clinical trial
	Pulse therapy for multiple sclerosis	Phase II clinical trial
	Cognitive protection/autism	Preclinical
	Traumatic brain injury	Preclinical
	Amyotrophic lateral sclerosis	Preclinical, Phase II clinical trial
	Acute respiratory distress syndrome	Phase II clinical trial
Pharmacology	N/A	Improve understanding of Acthar's mechanism
	Multiple sclerosis	Study immune modulating effects of Acthar applied to serum from MS patients Study neuroprotective properties of ACTH relevant to MS
Other	Infantile spasms	Review of evidence for sNDA submission
	N/A	Updating Acthar's product label

was funding over two dozen pre-clinical and clinical studies (Questcor Pharmaceuticals, 2009), and by 2013, over 70 studies and clinical trials were ongoing (Questcor Pharmaceuticals, 2013a) (Table 2). R&D expenses were almost 20-fold higher than in 2006 (Figure 4).

Questcor's initial focus was on patients with IS, its primary market. In late 2007, the firm launched an Acthar patient assistance program administered by the National Organization for Rare Disorders, providing over \$20 million of Acthar without charge to uninsured and underinsured patients. As a result, the company was "not aware of a single patient" in need of Acthar without access, which was not the case prior to the strategy change (Questcor Pharmaceuticals, 2008). From

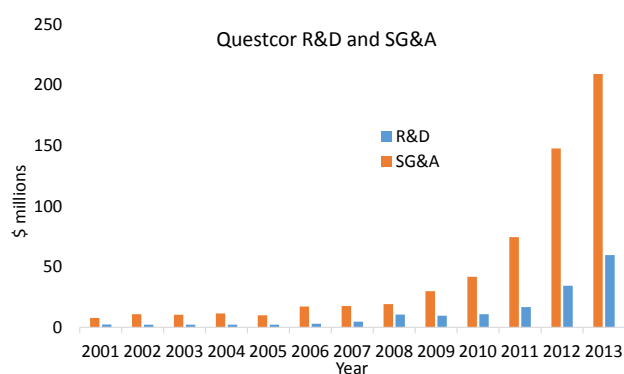


Figure 4 Questcor R&D and SG&A expenses, 2001–2013.

2007 to the end of 2011, Questcor provided \$124 million of the drug through this program, most of which has been used to treat IS (Questcor Pharmaceuticals, 2011).

The use of the drug in IS was still off-label at this point, even though physicians had been treating IS with Acthar for decades. This remarkable fact was acknowledged by the FDA in its evaluation of Questcor's application: "Though not approved for the treatment of IS (Acthar Gel was approved in 1952 and has been approved subsequently for numerous indications), Acthar Gel has been the treatment of choice for IS for many years" (CDER, 2010). Questcor's goal to complete the FDA approval process would standardize the recommended dosing regimens and administration procedures for IS, and would also replace the circuitous referral process involving MSLs with more conventional sales and marketing operations for Acthar.

The FDA rejected Questcor's initial request for approval in 2006, requiring the company to provide more evidence. However, Questcor and the FDA agreed that the firm could reanalyze data from the breadth of existing studies rather than conduct a new clinical trial (Questcor Pharmaceuticals, 2007). In particular, the FDA requested detailed records on individual patients (Stanford Group Company, 2008). With cash generated from its new business strategy, Questcor invested close to \$10 million to resubmit the sNDA with more data (Questcor Pharmaceuticals, 2009, 2008).

In 2010, the FDA found Questcor's submission of three studies supporting Acthar's efficacy, and four evaluating its safety, sufficient for its approval (Mechcatie, 2010b; CDER, 2010). In conjunction with the review of the sNDA for IS, the FDA updated Acthar's product label to include 18 other indications with evidence or rationale for efficacy, including acute exacerbations of MS and inducing remission of proteinuria in NS (CDER, 2010). In the FDA's summary of its evaluation, the regulator noted the unusual nature of the submission (CDER, 2010):

The data that the sponsor has provided differ considerably from that typically submitted in an NDA. As noted earlier, none of the studies were commissioned or conducted by the sponsor, and detailed protocols, and, in particular, detailed statistical plans for the analyses of these studies, did not exist.

However, the summary went on to confirm that the combined results did demonstrate significant efficacy (CDER, 2010):

As described above, the PCNS AC [Peripheral and Central Nervous System Advisory Committee] clearly concluded that the sponsor had provided substantial evidence of effectiveness. The review team agrees, as do I. I believe that the sponsor has met the statutory standard of substantial evidence of effectiveness based on having submitted a single adequate and well-controlled trial and confirmatory evidence. Study 01, though small, produced clear and convincing evidence of effectiveness on an outcome widely considered by the community of experts to be a clinically important measure of the utility of a treatment of IS (indeed, one could consider such a strong finding of effectiveness from such a small study as further evidence of the robustness of the result).

While improving IS patients' access to Acthar, Questcor concurrently ramped up SG&A expenses, eventually reaching over 10 times its 2006 levels by 2013 (Figure 4). The firm extensively marketed Acthar for MS, NS, and rheumatic diseases. In most cases, the drug was prescribed

Table 3 Number of paid prescriptions of Acthar for MS, NS, and IS indications, and total number of vials shipped. Source: Questcor 10-K filings.

Disease	Paid prescriptions		
	Year		
	2009	2010	2011
MS	556	1,212	3,090
NS	20	30	269
IS	349	367	427
Vials shipped	5,973	6,696	10,710

Table 4 Number of vials of Acthar shipped, 2007–2013. Source: Questcor 10-K filings.

Vials shipped	
Year	Number of vials
2007	5,100–5,700
2008	5,830
2009	5,973
2010	6,696
2011	10,710
2012	20,741
2013	28,112

by physicians for use as a second-, third-, or fourth-line treatment. Paid prescriptions of Acthar greatly increased from 2010 to 2011, largely by growth in MS and NS (Table 3). This trend, supplemented by a newly launched sales force to market Acthar to rheumatologists, continued into 2012, as vials sold almost doubled to 20,741 (Table 4).

Though Questcor initially deployed 12 sales representatives to focus on two rare neuromuscular disorders—dermatomyositis and polymyositis—positive physician response led the firm to expand the team to 50 people in order to sell Acthar for other rheumatic diseases. In 2013, Questcor's final full year as an independent company, 7,400 patients with serious diseases were treated with about 28,000 vials of Acthar prescribed by 3,000 physicians (Questcor Pharmaceuticals, 2013a, b) (Table 4). Given that 2–10 vials may be needed per Acthar prescription, over 10,000 patients have likely benefited from Acthar since 2007 (Questcor Pharmaceuticals, 2010b).

8 Counterfactual simulation

We now turn to the question of what would have happened to Questcor without the 2007 price increase. In 2006, the struggling company projected that it only had enough cash to fund

operations for a little more than a year, and disclosed that traditional debt and equity financing had not been available on acceptable terms (Questcor Pharmaceuticals, 2006). To explore the counterfactual cases where Questcor does not raise Acthar's price by 1,300%, we construct a financial model of Questcor and project its performance forward from 2006 according to three cases encompassing two alternative business strategies. The financial model consists of simulations of Questcor's balance sheet, income statement, and cash flow statement tied to a set of assumptions for Acthar revenues in IS and MS. Case 1 and Case 2 capture the best and worse-case scenarios, respectively, of an MS-focused growth strategy that maintains the prior year's sales-force expansion. Case 3 is a cost-cutting strategy that neglects potential MS sales growth. Key assumptions can be found in Table 5, and a full list of assumptions can be found in the Appendix. Key drivers of our models are the assumptions of Acthar's penetration into the MS market, Acthar's price, and SG&A and R&D expenses. The impact of investing and financing assumptions is minimal.

Our models project that Questcor would have become insolvent between 2008 and 2010 (Figure 5). In the optimistic Case 1, Questcor raises Acthar's price by 12% per year, achieves a 10% MS market penetration by Q2 2008 with a 5% increase in penetration every year. Despite such an aggressive market penetration forecast—fivefold more optimistic than Wall Street expectations at the time (ThinkEquity Partners LLC, 2006; Stanford Group Company, 2008)—the firm still becomes insolvent by Q2 2009. In Case 2, Acthar penetrates the MS market in line with Wall Street estimates and becomes insolvent by Q2 2008. In Case 3, despite an ambitious 45% cut in SG&A and R&D expenses, Questcor's IS annuity business cannot sustain the company and the firm becomes insolvent by Q2 2010.

Table 5 Key assumptions used in counterfactual simulation where Questcor does not raise the price of Acthar for three cases: Case 1: Best case MS-focused growth strategy; Case 2: Worst case MS-focused growth strategy; and Case 3: Cost-cutting strategy.

	Case 1	Case 2	Case 3
Key revenue drivers			
Acthar price/vial (\$USD)	1,650	1,650	1,650
Annual price increase	12%	12%	12%
Acthar rebate %	0%	0%	0%
Infantile spasms			
Patient population	2,300	2,300	2,300
Penetration	50%	50%	50%
Vials/patient	4.5	4.5	4.5
Multiple sclerosis			
Patient population	250,000	250,000	250,000
% r/r MS intolerant to corticosteroids	9.6%	9.6%	9.6%
Average flares/year	1	1	1
Penetration	10%	5%	1%
Penetration growth	5%	1%	0%
Vials/patient	2	2	2
Key expenses (as % of revenue)			
COGS	23%	23%	23%
R&D expense	0%	0%	-45%
SG&A expense	0%	0%	-45%

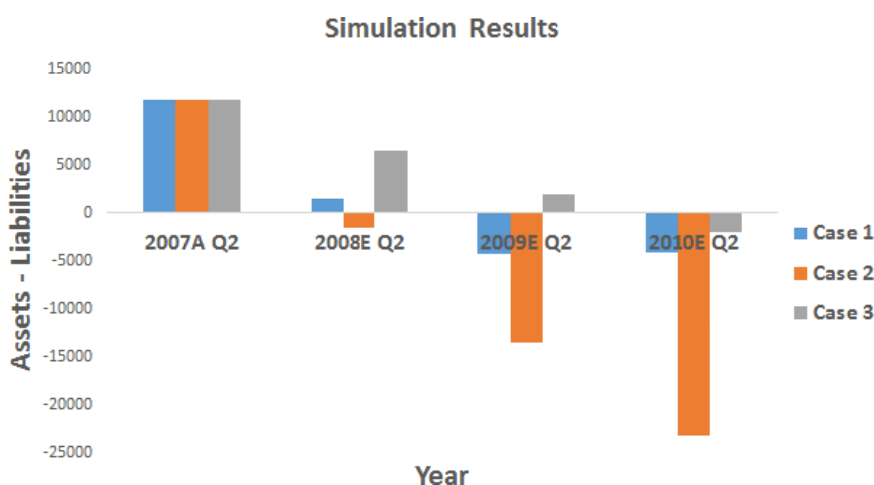


Figure 5 Results of a counterfactual simulation where Questcor adopts alternative business strategies.

In all cases, Questcor becomes insolvent and production of Acthar would have ceased unless another firm acquired Questcor's operations, although attracting buyers would have been difficult. Given the drug's poor financial performance, finding a for-profit acquirer that would not subsequently raise prices as Questcor did seem implausible. Perhaps a large pharmaceutical company with an existing sales infrastructure targeting neurologists could have integrated Acthar into its network, although its \$15 million in revenue would have been unlikely to draw interest.

9 Discussion

Pharmaceuticals have a unique combination of four characteristics. Much of the popular discussion has focused on the two best known of these: patient impact and monopoly power. However, the case of Questcor and Acthar highlights the importance of the two lesser-known characteristics of pharmaceuticals: their potential for underpricing and their capital market imperfections. This combination may require a different conceptual framework than the standard supply/demand analysis used to study other consumer product markets. We consider all four of these characteristics in turn.

First, pharmaceuticals can often dramatically alter the quality and quantity of life of its customers. This feature alone separates them from other consumer products, raising a host of moral and ethical dilemmas. For example, some wealthy individuals have paid up to \$20 million for a space flight. This may be a once-in-a-lifetime experience for them, but it causes no long-term changes in their life outcome, nor has there been any outcry over price gouging or unfair access in such cases.

Second, pharmaceuticals have elements of monopoly power. Moreover, government policy plays a central role in such monopolies, creating

and encouraging them through the patent system. The standard economic framework for analyzing monopolies suggests that price controls improve social welfare in the absence of other considerations. The government regulates electricity prices, and by the same logic, it could be argued that drug prices should be regulated as well. As a consequence of this logic, an emerging narrative is that, in exercising monopoly pricing power over compounds that literally can have life-and-death consequences, biopharma companies are setting prices that are "too high," both for the patients who take these drugs, and the healthcare economists who study price impact and value.

However, the quid pro quo of a patent is precisely the prospect of outsized monopoly profits for a finite period of time, in exchange for full disclosure of and free access to novel and unobvious ideas for posterity after patent expiration.

The case of Questcor and Acthar underscores the two other important features of the pharma industry: prices can be too low for a given product, and market imperfections can have an impact on the cost of capital.

No one benefits if an effective drug is priced so low as to cause the producer to go out of business or for the drug to be discontinued. Precisely because of the regulatory barriers that allow a pharmaceutical firm to maintain its pricing power, it is often not possible for competitors to fill a product void. However, even in the absence of patent protection, the high fixed costs associated with drug manufacturing are often a sufficient barrier to entry that can cause severe drug shortages when a manufacturer ceases operations.

A well-known case in point is the drug shortages for certain generic cancer drugs. In a 2013 survey of 214 oncologists, "82.7% were unable to prescribe the preferred chemotherapy agent because of shortages at least once during the previous

six months” and more than 75% indicated that these shortages led to major changes in the course of treatment (Gogineni, Shuman & Emanuel, 2013). An economic analysis conducted by the U.S. Department of Health and Human Services found that, among a sample of sterile injectable oncology drugs, the ones experiencing shortages since 2008 exhibited a median price decline of 49.1% between Q1 2006 and Q1 2011, whereas the ones with no shortages exhibited a median price increase of 0.3% during the same period (Haninger, Jessup & Koehler, 2011). Apparently, drug manufacturers respond to basic economic incentives, as their shareholders demand.

More recently, the U.S. Government Accountability Office (U.S. Government Accountability Office, 2016) issued a report of the price trends of generic drugs covered under Medicare Part D, and found that between 2010 and 2015, a changing basket of 2,378 generic drugs decreased in price by 59%, but a subset of 315 generics experienced a price increase of more than 100% during this period. Such diverse price dynamics are the consequence of a complex economic landscape (Reiffen & Ward, 2005) in which supply and demand factors, financial incentives, and new legislation such as the Hatch-Waxman Act of 1984 (Boehm, Yao, Han & Zheng, 2013) contribute to extraordinary price volatility.

In the case of Questcor, had the firm gone out of business, it is not clear that any competitor could have started production of Acthar over any reasonable time frame, while even today, its potential synthetic competitor, Synacthen Depot, is still only in phase 1 trials for its first indication in the U.S. (for Duchenne muscular dystrophy) (Mallinckrodt, 2016).

Moreover, there is a well-developed corporate-finance literature showing that the cost of external capital is higher than the cost of internal capital because of capital market imperfections (Froot &

Stein, 1991; Hubbard, 1998). As a result, cash-constrained firms may invest less than the optimal amount in promising new projects, and some firms may not be able to invest anything at all. This effect appears to be at work in the case of Questcor. Some of the funds made available by the higher price of Acthar led to the development of novel indications for the treatment. Acthar was finally approved by the FDA for IS, and thousands of patients now use it for NS and MS. As noted, there is debate in the literature and medical community about the relative value of Acthar versus other treatments for these conditions. In the clinic, however, we observe that many doctors and patients have chosen Acthar, and the economic theory of revealed preference suggests that they are now strictly better off.

Questcor’s journey from a small, struggling firm that acquired the unprofitable Acthar therapy to a billion-dollar single-drug company stirred tremendous controversy by its 14-fold price increase in 2007. However, the firm was also able to invest the resources to greatly expand access to the therapy, which would have been impossible otherwise. Acthar use has evolved through multiple stages since the 1990s, when only a fraction of infants in need had access to the transformative therapy. After 2001, Questcor stabilized its supply, yet in 2006 the drug almost disappeared from the market as the firm approached insolvency. Meanwhile, only a few hundred infants benefited from Acthar every year during the 2001–2006 period. The company’s 2007 actions ensured availability of the drug not just for infants with IS, but eventually for thousands of patients with severe, difficult-to-treat diseases every year.

A comparison with Valeant Pharmaceuticals and its price-hiking behavior is useful to illustrate the difference between the two strategies. From 2009 to 2013, Questcor’s financial metrics differed sharply from those of Valeant Pharmaceuticals.

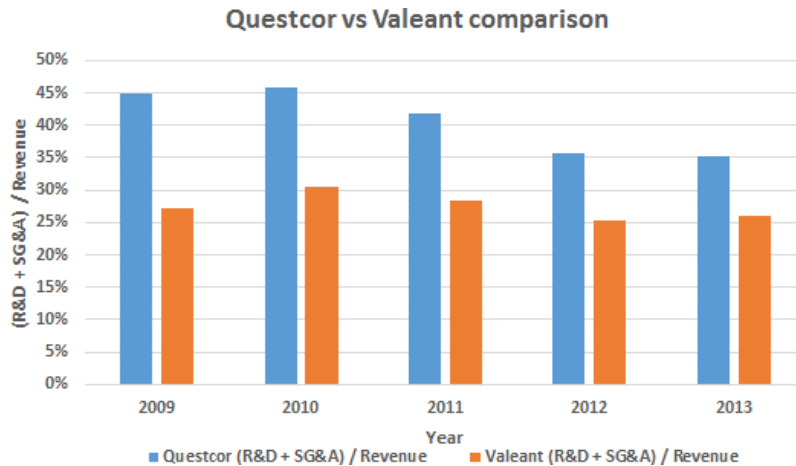


Figure 6 Comparison between Questcor and Valeant in terms of R&D and SG&A as a percentage of sales.

Questcor's R&D/Revenue ratio ranged from 7% to 11%, while Valeant's dropped to less than 3%. Comparing the sum of R&D and SG&A as a fraction of revenue further differentiates the two companies because of Acthar's large SG&A requirements. Questcor consistently exceeded Valeant in this metric by 10–15 percentage points (Figure 6), indicating the firm's greater commitment to reinvesting cash in product R&D, selling, and marketing over distributing it to shareholders and management.

As a for-profit entity, Questcor was clearly not motivated solely by altruism. Management and shareholders were rewarded financially throughout Questcor's rapid growth, and Questcor's acquisition of the rights to Synacthen Depot in 2013 demonstrated to the FTC a willingness to engage in anticompetitive—but entirely legal and commonly used—practices to maintain Acthar's high price. Nevertheless, corporations are, by construction and mandate, profit-seeking entities, and management is expected to carry out its legal fiduciary responsibilities to company shareholders. In the case of Questcor's 2007 pricing decision, this profit motive and risk-taking capacity were aligned with customer benefit, a principle that is at the core of the pharmaceutical, and all other, industries in the private sector.

It is possible to simulate a non-profit version of Questcor in which a “caretaker CEO” in 2007 might raise prices just enough to prevent the insolvency of the company, yet not enough to proceed with the Acthar sNDA, expand its sales force, provide sponsorship and co-pay assistance to the uninsured and underinsured, or fund R&D in Acthar's use for other indications, let alone the 20-fold expansion of R&D spending that occurred under Questcor's historical price increase. In such a hypothetical scenario, Questcor would only continue the manufacture and marketing of Acthar for a market limited to the small number of patients with IS, where it would remain an off-label treatment (although still the standard of care in the United States), and have no use in the treatment of the much larger group of patients with MS, NS, and rheumatic diseases. However, the viability of a nonprofit version depends critically on the availability of philanthropic support—both funding and human resources—to maintain the organization as a going concern. In this case, the number of patients treated would likely be considerably smaller than in the for-profit scenario.

More generally, there is broad consensus among economists that market prices play a critical role in the efficient allocation of scarce resources. In the wake of Hurricanes Harvey and Irma, the

prices of many consumer staples such as drinking water, food, and gasoline have skyrocketed in the affected areas, in many cases violating anti-price-gouging state laws. Although many consider such price hikes reprehensible—especially in the aftermath of a natural disaster—economists have a different view. According to Michael Giberson (Sorkin, 2017) of Texas Tech University, “Price caps discourage extraordinary supply efforts that would help bring goods in high demand into the affected area...You discourage conservation of needed goods at exactly the time they are in high demand...In a classic case of unintended consequences, the [anti-price-gouging] law harms the very people whom lawmakers intend to help.”

This logic lies at the core of many widely used pricing policies in other industries such as peak-load pricing of electricity and other regulated utilities; higher airfares during holidays; higher hourly wages for working overtime shifts; and the “surge-pricing” policies used by Uber and other ride-hailing companies. However, the fact that “price gouging” is leveled against certain parties like Uber (Lowrey, 2014), but not others, suggests that there is more to these issues than just economics. Moral and ethical dimensions can overshadow business considerations in certain markets under certain circumstances, and in these cases, a more inclusive and humanistic process for determining prices and quantities may be required.

10 Conclusion

In the business of extending life, the biopharma industry routinely faces decisions deeply mired in ethical questions that directly affect human health and welfare. An increase in profitability is too often assumed to be always at the cost of patients’ wellbeing. The case of Questcor provides a useful counterpoint to the popular narrative that drug price increases are unnecessarily high.

However, our simulations do not address the broader and vastly more complex question of what the “appropriate” price should be. From a purely economic perspective, a for-profit company charging what the market will bear is in the best interests of its shareholders and common practice in all other private-sector industries. From an ethical perspective, especially when patient lives are at stake, charging what the market will bear seems unjust and morally offensive.

Resolving this conflict is beyond the scope of our study, but the growing concerns among patients, payers, and policymakers suggest that we need to strike a better balance between private-sector therapeutic efforts and the public interest. Reaching this new balance may be facilitated by new metrics for patient impact, value-based pricing and reimbursement policies, public/private partnerships for drug development and—in extreme cases—the nationalization of key therapies that have sufficient societal benefits and insufficient private-sector support such as vaccines, antibiotics, and the repurposing of off-patent drugs.

The mixed reputation of the pharmaceutical industry—fueled by ethical violations like price-gouging behavior, which should be outlawed in all industries, including healthcare—is counterproductive, and threatens the industry’s ability to attract the best talent and earn premium prices for new, breakthrough drugs. It is in the interest of all stakeholders to distinguish between unconscionable pricing policies and the legitimate use of market forces to allocate resources where they provide the greatest good for the greatest number.

Acknowledgments

We thank Ernie Berndt, Michael Henderson, Debbie Lucas, Ilan Oren, Tomas Philipson, Cameron Turtle, Heidi Williams, and Mandy Yeung for their helpful comments and suggestions, and Jayna Cummings and Allison McDonough for

their editorial assistance and helpful comments. Research support from the MIT Laboratory for Financial Engineering is gratefully acknowledged. The views and opinions expressed in this article are those of the authors only, and do not necessarily represent the views and opinions of any institution or agency, any of their affiliates or employees, or any of the individuals acknowledged above.

Funding and Conflicts Statement: No funding bodies had any role in study design, data collection and analysis, decision to publish, or preparation of this manuscript. No direct funding was received for this study. The authors were personally salaried by their institutions during the period of writing (though no specific salary was set aside or given for the writing of this manuscript), nor did the authors have any financial stake in Questcor or Mallinckrodt, except possibly through their ownership in index mutual funds and ETFs with holdings in these two companies, where the size and timing of such holdings are beyond the control of the authors. TB reports no conflicts; SH reports personal investments in private and public biotech companies, and is undergraduate president of the MIT Biotech Group; AL reports personal investments in private biotech companies, is an advisor to BridgeBio Pharma, a director of Roivant Sciences and the MIT Whitehead Institute for Biomedical Research, and an Overseer of Beth Israel Deaconess Medical Center.

Appendix

Table 6 Detailed assumptions for all three cases used in counterfactual simulations.

	All cases
Investing and financing activities (\$thousands)	2008Q2
PPE	–

Table 6 (Continued)

	All cases
Purchase of short-term investments	–
Sale of short-term investments	10,142
Other (sale of benzodiazepines)	75
Issuance/(repayment) of debt	–
Issuance/(buyback) of stock	–
Other assumptions	2008Q2–2012Q2
Capex (% of revenue)	0%
D&A (% of revenue)	1%
Tax rate	40%
NOL balance (thousands)	103,400
Interest rates	
Interest rate (2007)	4.87%
Interest rate (2008)	2.43%
Interest rate (2009)	1.00%
Balance sheet ratios	2008Q2–2012Q2
Accounts receivable	11%
Inventory	66%
Prepaid expenses	5%
Accounts payable	50%
Accrued expenses	6%
Sales reserves	16%
Other accrued liabilities	11%
Other items (\$ thousands)	2007Q2
Cash	3,931
Common stock	106,551
Retained earnings (accumulated deficit)	–94,732
Total shareholder's equity	11,827

Note

¹ This drug has experienced controversies of its own—in January 2015, Mallinckrodt raised the Canadian price of this generic by 2000%. The reason? According to Mallinckrodt, in 2014 its European manufacturer announced it would cease production of Synacthen Depot by 2016, requiring the drug company to identify and initiate production with a new manufacturer. In a 2015 press release, Mallinckrodt explained that:

“Mallinckrodt is committed to supporting continued and broader availability of Synacthen and Synacthen Depot, and committed to investing the more than \$US50 million required to support continued manufacturing, regulatory, research and market access for the products. Importantly, though adjusting the price of the products will contribute to long-term sustainability, the company does not expect the Synacthen products to be profitable in the near-term, even with the new pricing model.”

See also the discussion in Section 6.4 regarding anti-trust issues surrounding Synacthen Depot.

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Keywords: drug pricing; biotech; price gouging; infantile spasms; Questcor Pharmaceuticals