Yale University Department of Economics

# The Effect of Acquisitions on Pharmaceutical Drug Prices

Senior Essay

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# I. Abstract

The high, and rapidly rising, cost of pharmaceutical drugs has been criticized by policy makers, patients, prescribers and payers.<sup>1</sup> Spending on prescription medications has increased at unprecedented rates in the past five years, outpacing the growth of aggregate health care expenditure in the United States.<sup>2</sup> While researchers and lobbyists have focused most of their attention on the prices of novel brand-name prescription drugs, the rising prices of generic drugs has become an increasingly pertinent issue that merits further analysis.

In recent years, the prices of old, off-patent therapeutics with limited competition have become the target of a profit-boosting tactic among pharmaceutical companies: acquiring potentially underpriced drugs and subsequently increasing the prices. Strong candidates for this practice include therapeutics with few, or no, bioequivalent alternatives serving niche markets. Despite having long lost patent protection and exclusivity, many of these medications treat smaller populations and thus promise insufficient profits to potential generic competitors.<sup>3</sup>

In this paper, I explore the impact of these acquisitions on pharmaceutical drug prices. Specifically, I compare pricing trends among therapeutics that have been acquired and those that have not. The implications of this study provide further urgency for policy surrounding not only enhanced generic availability, but also drug acquisition practices in the United States, in order to protect consumers' affordable access to essential care, as well as to control the growth of health care spending in the United States.

<sup>&</sup>lt;sup>1</sup> Aaron S. Kesselheim, Jerry Avorn, and Ameet Sarpatwari, "The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform," *JAMA* 316 (2016): 858–71, doi:10.1001/jama.2016.11237.pref <sup>2</sup> Ibid.

<sup>&</sup>lt;sup>3</sup> Ravi Gupta et al., "Generic Drug Approvals Since the 1984 Hatch-Waxman Act," July 18, 2016, http://archinte.jamanetwork.com/.

# **II. Background**

### Health care expenditure trends

Historically, aggregate health care expenditure in the United States has increased at high rates, and per capita health care expenditure has consistently outpaced overall economic growth.<sup>4</sup> From 2000 to 2010, national health spending per capita grew by 5.7%, exceeding the annual GDP growth rate of 2.9%.<sup>5</sup> While this gap has begun to decrease in recent years, health care expenditure growth continues to exceed that of GDP: from 2010-2015, health spending per capita grew at a rate of 3.6% while GDP continued to grow at 2.9%.<sup>6</sup>

Kaiser Family Foundation's 2015 "Health Spending Trends Slideshow," which tracks health care spending trends over the past five decades, reveals shocking statistics surrounding national health spending. Kaiser reports that, from 1970 to 2015, total national health expenditures increased from \$365.8 billion (in constant 2015 dollars) to \$3.2 trillion,<sup>7</sup> representing a 775% increase over the period. In 2015, health care expenditure increased by 5.8% from the previous year and accounted for almost 18% of Gross Domestic Product (GDP).<sup>8</sup> In addition, per capita expenditures increased from \$1,742 (in 2015 dollars) to \$9,990 per capita over the same period,<sup>9</sup> representing a 480% increase. Furthermore, out-of-pocket spending per capita was \$1,054, compared to \$583 in 1970 (in constant 2015 dollars).<sup>10</sup> There are various drivers of health spending increases, but—especially in recent years—the high cost of

<sup>&</sup>lt;sup>4</sup> Peterson-Kaiser Health System Tracker, "Health Spending Trends Slideshow," 2016, http://kff.org/slideshow/health-spending-trends-slideshow/.

<sup>&</sup>lt;sup>5</sup> Ibid.

<sup>&</sup>lt;sup>6</sup> Ibid.

<sup>&</sup>lt;sup>7</sup> Ibid.

<sup>&</sup>lt;sup>8</sup> "National Health Expenditures 2015 Highlights" (Centers for Medicare & Medicaid Services, 2015), https://www.cms.gov/research-statistics-data-and-systems/statistics-trends-and-reports/nationalhealthexpenddata/nationalhealthaccountshistorical.html.

<sup>&</sup>lt;sup>9</sup> Peterson-Kaiser Health System Tracker, "Health Spending Trends Slideshow." <sup>10</sup> Ibid.

prescription drugs has been heavily scrutinized as a key contributor to historical, and recent, increases in health care expenditure.

# Prescription drug spending

In 2015, prescription drug spending reached \$342.6 billion, representing 10% of aggregate health expenditure (\$3.2 trillion) and a 9% increase from the previous year.<sup>11</sup> Despite slowing from its 12.4% growth in 2014, prescription drug spending growth outpaced that of all other health services in 2015.<sup>12</sup> This exorbitant spending is unique to the United States; expenditure on pharmaceuticals in the United States has long exceeded that of other countries.<sup>13</sup> In fact, the United States' per capita spending on prescription medications was \$858 in 2015, more than double the average of \$400 among 19 advanced industrialized nations.<sup>14</sup>





<sup>&</sup>lt;sup>11</sup> "National Health Expenditures 2015 Highlights."

<sup>&</sup>lt;sup>12</sup> Ibid.

<sup>&</sup>lt;sup>13</sup> Aaron S. Kesselheim, Jerry Avorn, and Ameet Sarpatwari, "The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform."

<sup>14</sup> Ibid.

<sup>&</sup>lt;sup>15</sup> Ibid.

This gap is largely driven by comparatively higher prices in the United States. A recent study published by Health Affairs found that, among the 15 drug companies that manufactured the 20 top-selling drugs globally in 2015, United States list prices represent an "outsized premium" to those in other developed countries. Specifically, list prices abroad were, on average, 59% lower than US net drug prices.<sup>16</sup> Even though prices now comprise a smaller share of total health care expenditure than the historical average—outpaced by increased health services consumption (1.0% growth compared to 5.0% growth)<sup>17</sup>—the high cost of many therapeutics remains a key issue threatening patients' ability to access affordable life-saving medications.<sup>18</sup>

As a result, high drug prices have garnered much attention—and criticism—in recent years. In fact, based on a recent Office of the Assistant Secretary for Planning and Evaluation (ASPE) issue brief, "Observations in Prescription Drug Spending," published on March 8, 2016, 77 percent of adults believe that "making sure that high-cost drugs for chronic conditions, such as HIV, hepatitis, mental illness and cancer are affordable to those who need them" should be prioritized.<sup>19</sup> Making these treatments more affordable is a crucial step towards enhancing patients' access to critical care and driving down overall health care expenditure. Similarly, in the report, "Kaiser Health Tracking Poll: Health Care Priorities for 2017," Kaiser finds that American citizens prioritize lowering the share of health care costs that fall on individuals, lowering the cost of prescription drugs and addressing the prescription painkiller addiction

<sup>&</sup>lt;sup>16</sup> Nancy Yu, Zachary Helms, and Peter Bach, "R&D Costs For Pharmaceutical Companies Do Not Explain Elevated US Drug Prices," March 7, 2017, http://healthaffairs.org/blog/2017/03/07/rd-costs-for-pharmaceutical-companies-do-not-explain-elevated-us-drug-prices/.

<sup>&</sup>lt;sup>17</sup> Peterson-Kaiser Health System Tracker, "Health Spending Trends Slideshow."

 <sup>&</sup>lt;sup>18</sup> "Observations on Trends in Prescription Drug Spending" (Assistant Secretary for Planning and Evaluation (ASPE), March 8, 2016), https://aspe.hhs.gov/system/files/pdf/187586/Drugspending.pdf.
 <sup>19</sup> Ibid.

epidemic above all other issues.<sup>20</sup> In another study, Kaiser reports that prescription drugs landed

at the top of the list of forms of care that patients delayed or sacrificed due to cost in 2015.<sup>21</sup>

# Historical perspective

From 2008-2012, expenditure on pharmaceutical drugs slowed to approximately 2% per

year, largely due to increased generic competition and a decline in blockbuster (drugs with over

\$1 billion in revenue<sup>22</sup>) development.<sup>23</sup>

	Personal Health Care (PHC)	Retail Prescription Drugs	Percent of all PHC	Non-Retail Prescription Drugs <sup>1</sup>	Percent of all PHC	Total Prescription Drugs	Percent of all PHC
	. ,		%		%		%
2009	2,118	255	12.0	99	4.7	354	16.7
2010	2,196	256	11.7	100	4.5	356	16.2
2011	2,282	263	11.5	103	4.5	366	16.0
2012	2,379	264	11.1	103	4.3	367	15.4
2013	2,469	271	11.0	106	4.3	377	15.3
2014*	2,596	305	11.8	119	4.6	424	16.3
2015*	2,729	328	12.0	128	4.7	457	16.7
2016*	2,862	343	12.0	134	4.7	477	16.7
2017*	3,016	364	12.1	142	4.7	506	16.8
2018*	3,184	385	12.1	150	4.7	535	16.8

# Table 1: Expenditures on Personal Health Care Services and Prescription Drugs, 2009 to 2018, in Billions of Nominal Dollars<sup>24</sup>

2018 \* Projected.

Projected Growth

2013-

5.2%

Source: CMS, National Health Expenditure (NHE) Amounts by Type of Expenditure and Source of Funds: Calendar Years 1960-2024. The projections are based on the 2013 version of the NHE released in December 2014.

<sup>1</sup> Estimated based on the assumption that non-retail drugs are 28 percent of all drug expenditures.

7.3%

<sup>&</sup>lt;sup>20</sup> Ashley Kirzinger, Bryan Wu, and Mollyann Brodie, "Kaiser Health Tracking Poll: Health Care Priorities for 2017," Polling (The Henry J. Kaiser Family Foundation, January 6, 2017), http://kff.org/report-section/kaiser-health-tracking-poll-health-care-priorities-for-2017-methodology/.

<sup>&</sup>lt;sup>21</sup> Bradley Sawyer and Cynthia Cox, "Despite Lower Rates of Access Barriers for Some Groups, Health Costs Remain a Concern for Many Americans," *Peterson-Kaiser Health System Tracker.*,

http://www.healthsystemtracker.org/2016/11/despite-lower-rates-of-access-barriers-for-some-groups-health-costs-remain-a-concern-for-many-americans/.

<sup>&</sup>lt;sup>22</sup> Stefanos Zeinos, Robert Chess, and Lyn Denend, "Abbott Laboratories and Huira: Launching a Blockbuster Drug" (Stanford Graduate School of Business, June 20, 2005), https://cb.hbsp.harvard.edu/cbmp/content/61775275.

<sup>&</sup>lt;sup>23</sup> "Observations on Trends in Prescription Drug Spending."

<sup>&</sup>lt;sup>24</sup> Ibid.

However, since 2012, spending on pharmaceuticals has been increasing at rates exceeding projected overall growth in total health care expenditure in the United States (20% compared to 11%).<sup>25</sup> Approximately 30% of this increase can be attributed to a shift towards higher price products and drug price increases, which together drove mean price increases that exceeded general inflation from 2010-2014.<sup>26</sup> Between May 2015 and May 2016, pharmaceutical prices in the United States increased by 9.8%, representing the second sharpest increase among the 20 "largest products and services" listed on the Bureau of Labor Statistics' Producer Price index.<sup>27</sup>

# Figure 2: Pharmaceuticals ranked second in price increases among Labor Statistics' Producer Price Index products from 2015-2016<sup>28</sup>



<sup>&</sup>lt;sup>25</sup> Aaron S. Kesselheim, Jerry Avorn, and Ameet Sarpatwari, "The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform."

<sup>&</sup>lt;sup>26</sup> "Observations on Trends in Prescription Drug Spending."

 <sup>&</sup>lt;sup>27</sup> Joseph Walker, "Drugmakers' Pricing Power Remains Strong," *The Wall Street Journal*, July 14, 2016, https://www.wsj.com/articles/drugmakers-pricing-power-remains-strong-1468488601.
 <sup>28</sup> Ibid.

In his *Wall Street Journal* article, "Drugmakers' Pricing Power Remains Strong," biotechnology reporter Joseph Walker calls special attention to this trend due to the necessity of these critical medications. Demand for pharmaceuticals is substantially more inelastic than demand for discretionary consumer products. As a result, pharmaceutical companies have a unique ability to adjust prices without losing demand for their products. Leerink Partners biotechnology analysts provides a clear example: "You can't take the price of the iPhone…up 10% a year."<sup>29</sup> Pharmaceutical manufacturers take advantage of their pricing power by raising prices for their drugs unexpectedly and without justification. Walker highlights various examples of companies whose revenues have benefitted from high prices—in addition to increased consumption in certain cases—as reported in SEC filings for first quarter of 2016, summarized in the table below.<sup>30</sup>

Company	Price- and volume- driven revenue increases
Pfizer Inc.	- \$2 billion in U.S. revenue driven largely by price increases and in some cases higher prescription volume
Biogen Inc.	<ul> <li>U.S. sales of Tecfidera (multiple sclerosis) increased by 15%, reaching \$744.3 million</li> <li>Higher U.S. revenues for Avonex and Tysabr driven by price increases</li> </ul>
Gilead Sciences Inc.	- Combined sales for four HIV drugs reached \$2.43 billion

 Table 2: Examples of recent price- and volume- driven revenue increases among large pharmaceutical companies<sup>31</sup>

<sup>31</sup> Ibid.

<sup>&</sup>lt;sup>29</sup> Joseph Walker, "Drugmakers' Pricing Power Remains Strong."

<sup>&</sup>lt;sup>30</sup> Ibid.

Company	Price- and volume- driven revenue increases
	- Truvada revenues increased by 16%, reaching \$898 million, due to higher prices and increased consumption
Amgen Inc.	<ul> <li>Global revenues for Enbrel (anti- inflammatory drug) increased by 24%, reaching \$1.39 billion in the first three months of 2016, primarily driven by a higher "net selling price"</li> <li>Amgen increased Enbrel's U.S. list price by 28% in 2015 and an incremental 9.9% in July 2016</li> </ul>
AbbVie. Inc.	- U.S. revenues for Humira (anti-inflammatroy drug) increased by 32%, reaching \$2.2 billion, due to price hikes and higher prescription volume

# Justification for high prices

The high costs of some medications can be justified by their clinical importance and uniqueness, and potentially even cost-effectiveness. However, prices of many other drugs remain inexplicably high.<sup>32</sup> Sudden price hikes—which are not associated with any improvements in the drug's clinical safety or efficacy—of old, off-patent drugs, certainly fall into the latter category. Pharmaceutical companies often cite R&D costs as justification for high prices. However, the Health Affairs study referenced above found that, in 2015, price premiums drove excess

<sup>&</sup>lt;sup>32</sup> Aaron S. Kesselheim, Jerry Avorn, and Ameet Sarpatwari, "The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform."

revenues of \$116 billion for pharmaceutical companies manufacturing top-selling drugs. The same companies spent only \$76 billion, on average, on global R&D.<sup>33</sup>





# Drug development: Prescription drug approval process (NDA)

Manufacturers engaging in research and development (R&D) for a novel therapeutic drug or biologic (large molecule drug) typically carry out these evaluations in three phases: preclinical, clinical and FDA review.<sup>35</sup> Upon completion of preclinical and clinical testing, the manufacturer submits a New Drug Application (NDA) to the FDA. After assessing the safety,

<sup>&</sup>lt;sup>33</sup> Nancy Yu, Zachary Helms, and Peter Bach, "R&D Costs For Pharmaceutical Companies Do Not Explain Elevated US Drug Prices."

<sup>&</sup>lt;sup>34</sup> Tufts Center for the Study, of Drug Development, and Tufts Center for the Study, "Cost of Developing a New Drug," November 18, 2014, http://csdd.tufts.edu/files/uploads/Tufts CSDD briefing on RD cost study -\_Nov\_18,\_2014..pdf. <sup>35</sup> Joseph S. Ross, MD, MHS and Aaron S. Kesselheim, MD, JD, MPH, "FDA Policy and Cardiovascular

Medicine," American Heart Association, Inc., doi:10.1161/CIRCULATIONAHA.114.010295.

efficacy and labeling of the drug, along with determining whether or not the benefits of the product outweigh the risks, the FDA either approves the NDA or requests additional data.<sup>36</sup>

This process is time-consuming and costly. In a recent study, the Tufts University Center for the Study of Drug Development found that developing a novel therapeutic takes 12-14 years and costs, on average, \$2.6 billion.<sup>37</sup> Although this estimate has been disputed, there has long been consensus among experts in the field that the R&D process is expensive—and risky. The odds of successful commercialization are unattractive: the probability that a new molecular or biologic entity that enters Phase I clinical testing will eventually be granted regulatory approval is less than 12%.<sup>38</sup>

As a means to incentivize innovation in this risky and costly context, manufacturers of novel therapeutics can apply for both patent and market exclusivity, granted by the US Patent and Trademark Office (USPTO) and the FDA, respectively. Officially, patents "exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States" for roughly 20 years.<sup>39</sup> These patents must be submitted to the FDA, the governing body that subsequently grants new drugs approved via NDA five to seven years of market exclusivity, which determines when a competitor can enter the market.<sup>40</sup>

<sup>&</sup>lt;sup>36</sup> Joseph S. Ross, MD, MHS and Aaron S. Kesselheim, MD, JD, MPH, "FDA Policy and Cardiovascular Medicine."

<sup>&</sup>lt;sup>37</sup> Tufts Center for the Study, of Drug Development, and Tufts Center for the Study, "Cost of Developing a New Drug."

<sup>&</sup>lt;sup>38</sup> Ibid.

 <sup>&</sup>lt;sup>39</sup> "Patents and Exclusivity," FDA/CDER Small Business and Industry Assistance (SBIA) Chronicles, May 19, 2015, https://www.fda.gov/downloads/drugs/developmentapprovalprocess/smallbusinessassistance/ucm447307.pdf.
 <sup>40</sup> Joseph S. Ross, MD, MHS and Aaron S. Kesselheim, MD, JD, MPH, "FDA Policy and Cardiovascular Medicine."

In addition, manufacturers often acquire exclusivity extensions through various avenues—such as testing in children<sup>41</sup>—which typically last for at least seven years.<sup>42</sup> As a result, in reality, brand-name manufacturers often maintain market exclusivity for approximately 12 to 14 years before generic alternatives begin to compete in the market.<sup>43</sup> Market exclusivity is even more pronounced for orphan drugs—drugs that treat rare diseases affecting less than 200,000 patients per year in the United States—as a result of the 1983 Orphan Drug Act.<sup>44</sup> In order to incentivize development in this market, which has historically been characterized by low projected revenues, orphan designation grants market exclusivity for seven years from approval date, tax cuts and a waiving of various FDA fees.<sup>45</sup> While these various measures are crucial to provide incentive for development, they can also have negative implications by enabling high drug prices; brand-name manufacturers often take advantage of lack of competition by raising prices unexpectedly and unjustifiably.

### Drug development: Generic approval process

Defined as bioequivalent versions of brand-name small-molecule drugs, generics follow the same dose form, route of administration and intended use as their brand-name counterparts.<sup>46</sup> Once approved by the FDA via an Abbreviated New Drug Application (ANDA), generics can legally enter the market upon the expiration of regulatory and patent exclusivity periods for brand-name drugs.<sup>47</sup> Generics are manufactured by one or more companies and can be

<sup>&</sup>lt;sup>41</sup> Aaron S. Kesselheim, Jerry Avorn, and Ameet Sarpatwari, "The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform."

<sup>&</sup>lt;sup>42</sup> Joseph S. Ross, MD, MHS and Aaron S. Kesselheim, MD, JD, MPH, "FDA Policy and Cardiovascular Medicine."

<sup>&</sup>lt;sup>43</sup> Ibid.

<sup>&</sup>lt;sup>44</sup> Ibid.

<sup>&</sup>lt;sup>45</sup> Ibid.

<sup>&</sup>lt;sup>46</sup> Ibid. <sup>47</sup> Ibid.

exchanged for brand-name drugs by pharmacists, since they are equally effective.<sup>48</sup> Historically, the generic approval process mirrored the extensive and costly new drug approval process, requiring thorough proof of safety and efficacy. As a result, among the 150 off-patent brand-name drugs approved after 1962, only 15 faced competition from generic alternatives before 1984.<sup>49</sup>

# Drug development: 1984 Hatch-Waxman Act and growth of the generics market

In order to incentivize generic development, Congress passed the Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act in 1984, officially enabling the FDA to approve generic alternatives based on bioequivalence.<sup>50</sup> This legislation began to transform the pharmaceutical industry by lowering R&D timelines and costs in order to encourage generic competition.<sup>51</sup> In addition, loss of patent protection among various blockbuster drugs—known as the "patent cliff"<sup>52</sup>—has been a key driver of growth in the generics market.<sup>53</sup>

In fact, over the past six years, brand-name drugs have been decreasing as a share of overall pharmaceutical drug spending and total prescriptions,<sup>54</sup> and today, generic drugs comprise over 85% of prescriptions in the United States.<sup>55</sup> However, while branded medications make up only 10% of total filled prescriptions in the United States, they constitute 72% of total pharmaceutical expenditure.<sup>56</sup> Due to the lower R&D costs associated with generic development,

<sup>&</sup>lt;sup>48</sup> "Facts about Generic Drugs" (U.S. Food & Drug Administration.),

https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/ucm167991.htm.

<sup>&</sup>lt;sup>49</sup> Joseph S. Ross, MD, MHS and Aaron S. Kesselheim, MD, JD, MPH, "FDA Policy and Cardiovascular Medicine."

<sup>&</sup>lt;sup>50</sup> Ibid.

<sup>&</sup>lt;sup>51</sup> Ravi Gupta et al., "Generic Drug Approvals Since the 1984 Hatch-Waxman Act."

<sup>&</sup>lt;sup>52</sup> "Observations on Trends in Prescription Drug Spending."

<sup>&</sup>lt;sup>53</sup> Ibid.

<sup>&</sup>lt;sup>54</sup> Ibid.

<sup>&</sup>lt;sup>55</sup> Ravi Gupta et al., "Generic Drug Approvals Since the 1984 Hatch-Waxman Act."

<sup>&</sup>lt;sup>56</sup> Aaron S. Kesselheim, Jerry Avorn, and Ameet Sarpatwari, "The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform."

in addition to increased competition among manufacturers, generic prices are substantially lower than prices of brand-name drugs.<sup>57</sup> Generic entry also helps to drive down prices of the original branded drugs. In their study, "FDA Policy and Cardiovascular Medicine," Ross et al. find that the introduction of at least four generic drives brand-name prices down by approximately 60%.<sup>58</sup> Furthermore, the FDA reports that the sharpest price reduction results from entry of a second generic competitor.<sup>59</sup>



Figure 4: Inverse relationship between number of generic competitors and drug prices<sup>60</sup>

Largely due to its impact on prices, the shift towards generic drug use following the passage of the Hatch-Waxman Act was accompanied by savings of \$254 billion in 2014 and accumulated savings of \$1.68 trillion over the past decade.<sup>61</sup>

<sup>&</sup>lt;sup>57</sup> "Facts about Generic Drugs."

<sup>&</sup>lt;sup>58</sup> Joseph S. Ross, MD, MHS and Aaron S. Kesselheim, MD, JD, MPH, "FDA Policy and Cardiovascular Medicine."

<sup>&</sup>lt;sup>59</sup> "Generic Competition and Drug Prices," U.S. Food and Drug Administration, (.),

https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm. <sup>60</sup> Ibid.

<sup>&</sup>lt;sup>61</sup> "Observations on Trends in Prescription Drug Spending."

# Drug development: Limitations of generic competition

Despite the positive impact of the Hatch-Waxman Act, which helped to promote generic competition and drive down drug prices, there are several limitations that still exist in the generics market. For example, in her 2011 AARP Bulletin article, "Drugmakers Hike Prices of Meds Facing Generic Competition," Patricia Barry reports that manufacturers often increase prices of top-selling brand-name drugs about a year before they lose market exclusivity rights.<sup>62</sup> She goes on to paint a hopeful picture for the future, asserting that certain blockbuster drugs that were set to lose patent protection in 2011—including Lipitor and Lexapro—would face generic competition and help to drive down overall pharmaceutical drug prices.<sup>63</sup> Unfortunately, however, prices rose at even higher rates from 2012-2015,<sup>64</sup> perhaps due to limitations in the generics industry.

First, manufacturers employ various strategies to extend market and patent exclusivity for their brand-name drugs, engaging in a process called "life cycle management."<sup>65</sup> For example, pharmaceutical companies often utilize patents for peripheral components of their approved therapeutics—such as metabolites and the coating of the pill—to block generic competition, even after expiration of the original patent.<sup>66</sup> Some of the other tactics employed by brand-name manufacturers to "evergreen" their products—and their monopolies—include licensing the same product for a new condition, changing the dosage, and modifying the drug—developing a

<sup>&</sup>lt;sup>62</sup> Patricia Barry, "Drugmakers Hike Prices of Meds Facing Generic Competition," *AARP Bulletin*, March 28, 2011, http://www.aarp.org/health/drugs-supplements/info-03-2011/drugmakers-raise-prices-on-drugs-facing-generic-competition.html.

<sup>&</sup>lt;sup>63</sup> Ibid.

<sup>&</sup>lt;sup>64</sup> Aaron S. Kesselheim, Jerry Avorn, and Ameet Sarpatwari, "The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform."

<sup>&</sup>lt;sup>65</sup> Joseph S. Ross, MD, MHS and Aaron S. Kesselheim, MD, JD, MPH, "FDA Policy and Cardiovascular Medicine."

<sup>66</sup> Ibid.

"follow-on"—to extend the patent.<sup>67</sup> For example, in their paper "Avoidance of generic competition by Abbott Laboratories' fenofibrate franchise," Downing et al. chronicle Abbott's "product-hopping" or "switching" strategy. Abbott was able to block generic competition by launching reformulations—or newer branded formulations—without proving clinical superiority.<sup>68</sup>

Lack of incentive is another significant limitation in the generics market. In particular, in certain niche markets—even when patents expire—generic manufacturers lack sufficient incentive to enter the market with a bioequivalent version of an existing branded drug. This is the case for brand-name drugs that target small patient populations and thus promise insufficient revenue to generic manufacturers, as is the case for many of the off-patent drugs explored in this paper.

# III. Literature Review: Rising Prices Of Older Drugs

There is a plethora of literature and media coverage surrounding increases in health care expenditure and highlighting specific cases of drug price hikes. However, most of these studies focus on novel branded therapeutics and, to date, there exists no systematic evaluation of how acquisitions impact pricing trends among old, off-patent drugs.

In their *JAMA* article, "The High Cost of Prescription Drugs: Origins and Prospects for Reform," Kesselheim et al. attribute increasing pharmaceutical expenditure mainly to branded

<sup>&</sup>lt;sup>67</sup> Andrew Hitchings, Emma Baker, and Teck Khong, "Making Medicines Evergreen," *BMJ* 345, no. e7941 (November 29, 2012), doi:10.1136/bmj.e7941.

<sup>&</sup>lt;sup>68</sup> Downing, Ross, Jackevicius, Krumholz, "Avoidance of generic competition by Abbott Laboratories' fenofibrate franchise" https://www.ncbi.nlm.nih.gov/pubmed/22493409

drugs that enjoy market exclusivity granted by the USPTO and the FDA.<sup>69</sup> Historically, exorbitant prices for novel therapeutics were reserved for life-saving treatments that targeted rare and oncology diseases. For example, the Gaucher disease treatment, alglucerase, cost \$150,00 per patient per year at the time of its launch in 1991 and now costs \$300,000.<sup>70</sup> However, in the past few years, these pricing schemes have expanded into treatment markets that serve millions of patients in the United States. Kesselheim et al. provide the example of insulin, a hormone used for diabetes treatment, which experienced an increase in average price of 300% from 2002-2013.<sup>71</sup>

Kesselheim et al. also recognize the role generics have played in the recent increases of drug prices and health care spending: "…another area that has captured the attention of the public and of policy makers has been the sharp increase in the costs of some older generic drugs."<sup>72</sup> The authors cite the widely covered 5500% increase in Turing Pharmaceutical's pyrimethamine (Daraprim), from \$13.50 a pill to \$750 a pill, in 2015, along with the almost 400 other generic drugs that saw a greater than 1000% increase in price between 2008 and 2015. The authors attribute these price hikes to lack of competition and negotiation power, while calling into question the justification provided by pharmaceutical companies that high prices "reflect the research and development costs a company incurred to develop the drug, and are necessary to pay for future research costs to develop new drugs, or both."<sup>73</sup> However, the article does not address the potential impact of acquisitions on the price hikes of these generic drugs.

Similarly, in their letter to The Journal of the American Medical Association (JAMA),

<sup>&</sup>lt;sup>69</sup> Aaron S. Kesselheim, Jerry Avorn, and Ameet Sarpatwari, "The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform."

<sup>&</sup>lt;sup>70</sup> Ibid.

<sup>&</sup>lt;sup>71</sup> Aaron S. Kesselheim, Jerry Avorn, and Ameet Sarpatwari, "The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform."

<sup>72</sup> Ibid.

<sup>&</sup>lt;sup>73</sup> Ibid.

"The Rising Price of Cancer Drugs-A New Old Problem?" Prasad et al. raise awareness of price increases among older drugs and the subsequent impacts on health care expenditure. The authors analyze the Average Sales Price (ASP) for a sample of 86 Part B drugs in 2010 compared with 2015, in order to evaluate trends over the past five years. After dichotomizing the sample into old and new drugs based on median approval date (December 29, 1992), Prasad et al. found that prices of older drugs (those approved before December 29, 1992) increased more than prices of newer drugs. Prasad et al. report a median increase of 22.7% among older drugs, compared to 6.2% among new drugs (P=0.001). In addition, the most dramatic price increase among older drugs was 89.9% compared to 17.3% among newer drugs.<sup>74</sup> This letter exposes the harsh reality that "new drug pricing seems to bear no relationship to novelty or efficacy."<sup>75</sup> It follows that prices and clinical benefits of drugs are fundamentally disconnected.<sup>76</sup> However, the authors acknowledge, "Whether and to what degree examples like pyrimethamine (Daraprim) represent a common problem or exceptional cases remains unknown."77

In their New England Journal of Medicine article, "Essential Medicines in the United States-Why Access Is Diminishing," Alpern, Song and Stauffer review a few important case studies to show that the Turing case was not, in fact, unique. The authors provide a list of ten offpatent drugs on the World Health Organization (WHO) List of Essential Medicines that have only one manufacturer and whose prices have increased anywhere from 212% to 5433% in the past decade.<sup>78</sup> They also cite acquisitions as a key factor driving price hikes and recognize that orphan-designated drugs with few or no bioequivalent alternatives are the best acquisition

<sup>&</sup>lt;sup>74</sup> Vinay Prasad, MD, MPH et al., "The Rising Price of Cancer Drugs – A New Old Problem?," JAMA Oncology 3, no. 2 (February 2017), http://jamanetwork.com/pdfaccess.ashx?url=/data/journals/oncology/936042/. <sup>75</sup> Ibid.

<sup>&</sup>lt;sup>76</sup> Ibid. 77 Ibid.

<sup>&</sup>lt;sup>78</sup> Jonathan D. Alpern, M.D., John Song, M.D., M.P.H., and William M. Stauffer, M.D., M.S.P.H., "Essential Medicines in the United States - Why Access Is Diminishing," The New England Journal of Medicine 374, no. 20 (May 19, 2016).

candidates.<sup>79</sup> Alpern at al. discuss CorePharma's acquisition of Albendazole from GlaxoSmithKline, and its subsequent sale to Amedra Pharmaceuticals—a private equity firm which then bought the only potential competitor, mebendazole, from Teva Pharmaceuticals. On average, its price has increased by 3299% (from \$5.92 per typical daily dose in 2010 to \$207.27 in 2015).<sup>80</sup> The authors also cite Valeant's openness surrounding its goals to minimize R&D costs and to maximize profits in order to benefit their shareholders: Valeant spends only 3% of revenue on R&D, while charging extremely high prices for its drugs.<sup>81</sup>

In a similar vein, Jonathan D. Rockoff and Ed Silverman critique some high profile cases of recent price hikes in their *Wall Street Journal* article, "Pharmaceutical Companies Buy Rivals' Drugs, Then Jack Up the Prices," focusing on Valeant's recently popularized strategy. In particular, Rockoff and Silverman highlight Valeant's acquisition of Nitropress and Isuprel and the subsequent price hikes, which were not accompanied by clinical improvements nor more costly manufacturing: "the big change [...] the drugs' ownership."<sup>82</sup>

These price hikes are adversely affecting health care providers across the country. Ascension health system, operator of 131 hospitals in the United States, predicts that these two price increases will triple its expenditure on medications in 2016.<sup>83</sup> Similarly, the Cleveland Clinic has reported an unexpected \$8.6 million (7.0%) increase to its 2016 budget of approximately \$122 million for medicines administered in its facilities.<sup>84</sup> The authors acknowledge that other pharmaceutical companies are adopting similar tactics, purchasing

<sup>&</sup>lt;sup>79</sup> Jonathan D. Alpern, M.D., John Song, M.D., M.P.H., and William M. Stauffer, M.D., M.S.P.H., "Essential Medicines in the United States — Why Access Is Diminishing."

<sup>&</sup>lt;sup>80</sup> Ibid.

<sup>&</sup>lt;sup>81</sup> Ibid.

<sup>&</sup>lt;sup>82</sup> Jonathan D. Rockoff and Ed Silverman, "Pharmaceutical Companies Buy Rivals' Drugs, Then Jack Up the Prices," *The Wall Street Journal*, April 16, 2015, https://www.wsj.com/articles/pharmaceutical-companies-buy-rivals-drugs-then-jack-up-the-prices-1430096431.

<sup>&</sup>lt;sup>83</sup> Ibid.

<sup>&</sup>lt;sup>84</sup> Ibid.

undervalued, older drugs, and then jacking up the prices. Rockoff and Silverman highlight Mallinckrodt's and Horizon Pharma's price hikes of their pain medications Orfimev and Truven, respectively.<sup>85</sup>



Figure 5: Price spikes following acquisitions (average wholesale prices)<sup>86</sup>

# More on Valeant: the highest profile price hiker

Rockoff and Silverman are not alone in their crusade against Valeant. In recent months,

Valeant's pricing tactics have been widely criticized by various media outlets. Some of the key recent stories, including Rockoff's and Silverman's, are outlined in the table below.

Media Source	Headline	Key Findings
THE WALL STREET JOURNAL.	4/26/2015 – "Pharmaceutical Companeis Buy Rivals' Drugs, Then Jack Up the Prices" <sup>87</sup>	- On the same day that it acquired the drugs, Valeant hiked the prices of Nitropress and Isuprel by 525% and 212%, respectively <sup>88</sup>

Table 3: Recent headlines depicting Valeant's price-hiking strategies

87 Ibid.

<sup>&</sup>lt;sup>85</sup> Jonathan D. Rockoff and Ed Silverman, "Pharmaceutical Companies Buy Rivals' Drugs, Then Jack Up the Prices."

<sup>&</sup>lt;sup>86</sup> Ibid.

Media Source Headline		Key Findings
The New York Times	10/4/2015 – "Valeant's Drug Price Strategy Enriches It, but Infuriates Patients and Lawmakers" <sup>89</sup>	- Overnight, Valeant more than quadrupled the price of Cuprimine (Wilson disease), forcing consumers to pay \$1,800 per month out-of-pocket, compared to \$366 <sup>90</sup>
	1/28/2016 – "Clinton targets Valeant price hikes in campaign appearance" <sup>91</sup>	- Clinton criticizes Valeant's price increase of migraine drug D.H.E. 45 (dihydroergotamine), a generic injectable analgesic, from \$3,000 in June 2014 to over \$14,000 in December 2015 <sup>92</sup>
Bloomberg	2/2/2016 – "Shkreli Was Right: Everyone's Hiking Drug Prices" <sup>93</sup>	<ul> <li>Prices more than doubled for 60 drugs in the past year</li> <li>Valeant was the most aggressive price hiker; 13 of its drugs at least doubled in price since December 2014<sup>94</sup></li> </ul>
BUSINESS Insider	2/2/2016 – "A government document dump just confirmed the ugliest things Wall Street didn't	- Email from then-Chief Financial Officer Howard Schiller to then-CEO Michael Person published in memo: "Excluding marathon, price represented about 60% of our growth. If you include marathon, price represents 80%" (Valeant acquired two

<sup>&</sup>lt;sup>88</sup> Jonathan D. Rockoff and Ed Silverman, "Pharmaceutical Companies Buy Rivals' Drugs, Then Jack Up the Prices."

<sup>94</sup> Ibid.

<sup>&</sup>lt;sup>89</sup> Andrew Pollak and Sabrina Tavernise, "Valeant's Drug Price Strategy Enriches It, but Infuriates Patients and Lawmakers," The New York Times, October 4, 2015, https://www.nytimes.com/2015/10/05/business/valeants-drugprice-strategy-enriches-it-but-infuriates-patients-and-lawmakers.html.

<sup>&</sup>lt;sup>91</sup> Deena Beasley, "Clinton Targets Valeant Price Hikes in Campaign Appearance," January 28, 2016,

http://www.reuters.com/article/us-usa-election-clinton-valeant-pharms-idUSMTZSAPEC1SOMIOHM.

<sup>&</sup>lt;sup>92</sup> İbid.

<sup>&</sup>lt;sup>93</sup> Robert Langreth and Rebecca Spalding, "Shkreli Was Right: Everyone's Hiking Drug Prices," Bloomberg, February 2, 2016, https://www.bloomberg.com/news/articles/2016-02-02/shkreli-not-alone-in-drug-price-spikes-asskin-gel-soars-1-860.

Media Source	Headline	Key Findings
	want to believe about Valeant <sup>**95</sup>	drugs from Marathon in 2015) <sup>96</sup>
FORTUNE	10/17/2016 – "How Valeant Is Justifying Its New Kinder, Gentler Drug Price Hikes" <sup>97</sup>	- Valeant announces its single-digit increases (2.0% to 9.0%) in the prices of various neurology, gut and urology treatment products <sup>98</sup>
CBC <b>NEWS</b>	3/14/2017 – "Valeant shares plunge another 10% to all-time low after Ackman sells stake" <sup>99</sup>	<ul> <li>Following activist investor Bill Ackman's sale of his entire stake in Valeant (writing off close to \$4 billion), Valeant's stock dropped 10%<sup>100</sup></li> <li>In the past two years, Valeant has lost 95% of its value<sup>101</sup></li> </ul>

The media have succeeded in decimating Valeant's reputation through relentless

coverage and criticism of its price manipulations. However, there are similar tactics being

employed by countless other pharmaceutical companies that deserve further evaluation.

<sup>100</sup> Ibid.

<sup>&</sup>lt;sup>95</sup> Linette Lopez, "A Government Document Dump Just Confirmed the Ugliest Things Wall Street Didn't Want to Believe about Valeant," *Business Insider*, February 2, 2016, http://www.businessinsider.com/valeant-house-documents-show-pricing-strategy-2016-2.

<sup>96</sup> Ibid.

<sup>&</sup>lt;sup>97</sup> Sy Mukherjee, "How Valeant Is Justifying Its New Kinder, Gentler Drug Price Hikes," *Fortune*, October 17, 2016, http://fortune.com/2016/10/17/valeant-new-drug-price-hikes/.

<sup>98</sup> Ibid.

<sup>&</sup>lt;sup>99</sup> Pete Evans, "Valeant Shares Plunge Another 10% to All-Time Low after Ackman Sells Stake," *CBC News*, March 14, 2017, http://www.cbc.ca/news/business/valeant-bill-ackman-1.4023891.

<sup>101</sup> Ibid.

# **IV. Hypothesis**

In this study, I conduct a systematic analysis of the effects of drug acquisitions on prices of currently marketed pharmaceuticals in capsule or tablet formulation that have zero or one bioequivalent alternative. I hypothesize that there will be a statistically significant difference in price levels—and changes—among drugs with zero or one generic equivalents that have been acquired versus those that have not.

For my regression analysis, I expect to observe an association between the most recent available price and the main independent variable: acquisition (yes/no). I also control for generic competition (yes/no), orphan drug (yes/no) and therapeutic area (categorized), since these variables also likely affect last available price. In particular, I predict to see higher last available prices among drugs that have been acquired, since this tactic has been accompanied by substantial price increases. For the control variables, I predict that higher prices will be associated with orphan drugs, since these drugs treat smaller populations and thus attract less competition and also warrant higher prices to justify R&D costs. I do not predict to see a strong association between last available prices and generic availability; although generic competition generally drives prices down, the drugs in our sample either face zero or one generic competitors, which is not enough to drastically affect price. Finally, I predict to see an association between last available price and therapeutic area (categorized), depending on the size of the treatment market and clinical necessity of treatments associated with each therapeutic category; smaller treatment markets and higher clinical necessity of treatments (for deadly diseases with few therapeutic options) will likely be associated with higher prices. The regression will treat therapeutic category as a fixed effect variable.

# V. Data / Methods

The sample I analyze includes all currently marketed pharmaceutical drugs in tablet or capsule formulation that have zero or one bioequivalent alternatives. The Drugs@FDA database was used to identify this sample of drugs approved under NDA in either tablet or capsule formulation.<sup>102</sup> Combinations with non-novel therapeutics, along with drugs ineligible for generic competition, were excluded, as were all other drug formulations available, including infusions, injections, intra-nasal, transdermal and so-on.<sup>103</sup>

I determined the following characteristics for each currently marketed brand-name, offpatent drug: number of FDA-approved (via ANDA) therapeutic equivalent products (0 or 1); NDA application number; approval date; National Drug Code (NDC) code; formulation (tablet or capsule); therapeutic area; orphan designation (yes/no); and strength (in milligrams). The Drugs@FDA database was used to determine generic equivalent availability, application numbers, FDA approval dates, orphan designation and formulation. The FDA's NDC database was used to determine NDC codes, and the WHO Collaborating Centre for Drug Statistics Methodology website was used to determine therapeutic areas, which were then categorized into ID (infectious disease), CANCER, AUTOIMM/MUSK (autoimmune/musculoskeletal) and CV/DM/LIPIDS (cardiovascular/diabetes/lipids) or OTHER.<sup>104</sup> When a drug was not listed on the WHO website, data from the Bloomberg terminal and scholarly articles were used to determine therapeutic area, and these drugs were categorized using the same criteria.

<sup>&</sup>lt;sup>102</sup> Ravi Gupta et al., "Generic Drug Approvals Since the 1984 Hatch-Waxman Act."

<sup>&</sup>lt;sup>103</sup> Ibid.

<sup>&</sup>lt;sup>104</sup> "ATC/DDD Index 2017" (WHO Collaborating Centre for Drug Statistics Methodology.).

# **VI. Acquisition Information**

The following table details—for each pharmaceutical drug that was acquired—the most recent post-2000 merger and acquisition date, along with information regarding companies involved, deal terms and acquisition price, when available. I utilized the Bloomberg terminal at the Yale School of Management to identify corporation and manufacturer; merger and acquisition activity; and pricing data for each drug in the sample. I searched each drug in the Drug Explorer tab via the {BI BIOT} tool, which sources data from Symphony Health Solutions. Company press releases, SEC filings and news sources were also used to research merger and acquisition activity in order to determine dates and specific terms of each deal. In some cases, pharmaceutical companies acquired the rights to an NDA, while in other transactions an entire company was acquired or merged with another. For the sake of this analysis, these M&A activities are treated the same.

Table 4: List of all currently marketed pharmaceutical drugs in tablet or capsuleformulation that have zero or one bioequivalent alternatives that have been acquired since2000

Drug Name	Acquisition Year	Acquisition Details
ALBENZA	2015	- Impax acquires Tower Holdings, including operating subsidiaries CorePharma and Amedra Pharmaceuticals LLC <sup>105</sup>
HEXALEN	2007	- Eisai acquires MGI Pharma <sup>106</sup>

<sup>&</sup>lt;sup>105</sup> "Impax To Acquire Tower Holdings, Inc. And Lineage Therapeutics Inc." (Press Release, October 9, 2014), http://investors.impaxlabs.com/Media-Center/Press-Releases/Press-Release-Details/2014/Impax-To-Acquire-Tower-Holdings-Inc-And-Lineage-Therapeutics-Inc/default.aspx.

<sup>&</sup>lt;sup>106</sup> "Eisai to Acquire MGI Pharma for \$41 per Share in All Cash Transaction" (News Release, December 10, 2007), http://www.eisai.com/news/news200743.html.

Drug Name	Acquisition Year	Acquisition Details
RIDAURA	2011	<ul> <li>Prometheus Laboratories acquires rights from Connetics Corporation for \$9 million plus royalties<sup>107</sup></li> <li>Nestle subsidiary acquires Prometheus Laboratories<sup>108</sup></li> </ul>
ANZEMET	2015	- Validus Pharma acquires U.S. rights from Sanofi <sup>109</sup>
CESAMET	2000	- Valeant acquires rights from Eli Lilly <sup>110</sup>
VIRACEPT	2000	- Pfizer acquires Warner-Lambert <sup>111</sup>
NILANDRON	2015	- Concorida acquires Covis for \$1.2 billion <sup>112</sup>
ORFADIN	2007	- Synosia acquires rights from Syngenta <sup>113</sup>
DIPENTUM	2016	- Mylan acquires MEDA <sup>114</sup>

<sup>&</sup>lt;sup>107</sup> "Prometheus Laboratories Raises \$95 Million to Complete Acquisition of Four Pharmaceutical Products," *PR Newswire*, May 10, 2011, http://www.prnewswire.com/news-releases/prometheus-laboratories-raises-95-million-to-complete-acquisition-of-four-pharmaceutical-products-71742902.html.

<sup>&</sup>lt;sup>108</sup> "Nestlé Health Science Acquires Leading US Gastrointestinal Diagnostics Company" (Press Release, Nestle, May 24, 2011), http://www.nestle.com/media/pressreleases/AllPressReleases/Nestle-Health-Science-acquires-leading-US-gastrointestinal-diagnostics-company.

<sup>&</sup>lt;sup>109</sup> "Validus Pharmaceuticals Further Expands Marketed U.S. Portfolio with Product Lines Purchased from Leading Healthcare Company," *PR Newswire*, December 14, 2015, http://www.prnewswire.com/news-releases/validus-pharmaceuticals-further-expands-marketed-us-portfolio-with-product-lines-purchased-from-leading-healthcare-company-300192162.html.

<sup>&</sup>lt;sup>110</sup> "Valeant Pharmaceuticals Acquires Rights to Nabilone in United Kingdom and Europe," *Business Wire*, February 15, 2007, http://www.businesswire.com/news/home/20070215005880/en/Valeant-Pharmaceuticals-Acquires-Rights-Nabilone-United-Kingdom.

<sup>&</sup>lt;sup>111</sup> "2000: Pfizer Joins Forces with Warner-Lambert" (Company History.),

http://www.pfizer.com/about/history/pfizer\_warner\_lambert.

<sup>&</sup>lt;sup>112</sup> "Concordia Healthcare Corp. Announces Completion of Acquisition of Covis Pharma Commercial Assets for US\$1.2 Billion," *PR Newswire*, April 21, 2015, http://www.prnewswire.com/news-releases/concordia-healthcare-corp-announces-completion-of-acquisition-of-covis-pharma-commercial-assets-for-us12-billion-500798171.html. <sup>113</sup> "Synosia Acquires HPPD Inhibitor from Syngenta," *The Pharma Letter*, May 28, 2017,

https://www.thepharmaletter.com/article/synosia-acquires-hppd-inhibitor-from-syngenta.

Drug Name	Acquisition Year	Acquisition Details
ELMIRON	2001	- Johnson & Johnson merges with ALZA Corporation <sup>115</sup>
CHEMET	2012	- Recordati acquires from Lundbeck <sup>116</sup>
THIOLA	2014	- Retrophin acquires US licensing rights from Mission Pharmaceutical Company <sup>117</sup>
FARESTON	2012	- ProStrakan Group acquires rights and related assets from GTx for \$21.7 million <sup>118</sup>
SYPRINE	2010	- Valeant acquires rights <sup>119</sup>
ZYFLO	2004	- Critical Therapeutics (now Chiesi USA) acquires rights from Abbott Laboratories (now AbbVie) <sup>120</sup>
TARGRETIN	2013	- Valeant acquires rights from Eisai Inc. <sup>121</sup>
TEVETEN	2005	- Kos Pharmaceuticals (now AbbVie) acquires from Biovail Corporation <sup>122</sup>

<sup>&</sup>lt;sup>114</sup> "Mylan to Acquire Meda," *PR Newswire*, February 10, 2016, http://www.prnewswire.com/news-releases/mylan-to-acquire-meda-300218394.html.

<sup>&</sup>lt;sup>115</sup> "Johnson & Johnson to Merge With ALZA Corporation In \$10.5 Billion Stock-for-Stock Transaction," *Johnson & Jonson*, March 27, 2001, http://www.investor.jnj.com/releasedetail.cfm?releaseid=63833.

<sup>&</sup>lt;sup>116</sup> "Lundbeck to Divest a Portfolio of Non-Core Products as Part of Its Strategy to Focus on Newer, Strategic CNS-Products" (Press Release, December 14, 2012), http://investor.lundbeck.com/releasedetail.cfm?releaseid=727029.

<sup>&</sup>lt;sup>117</sup> "Retrophin Enters Into U.S. License Agreement for Thiola® (Tiopronin)," Mission Pharmacal, May 29, 2014,

https://www.missionpharmacal.com/press-release/retrophin-enters-us-license-agreement-thiola%C2%AE-tiopronin. <sup>118</sup> "ProStrakan Acquires Breast Cancer Product for the US," *PR Newswire*, October 1, 2012,

http://www.prnewswire.com/news-releases/prostrakan-acquires-breast-cancer-product-for-the-us-172064531.html. <sup>119</sup> Andrew Pollak and Sabrina Tavernise, "Valeant's Drug Price Strategy Enriches It, but Infuriates Patients and Lawmakers."

<sup>&</sup>lt;sup>120</sup> Bloomberg LP, terminal accessed at the Yale School of Management

<sup>&</sup>lt;sup>121</sup> "Valeant Pharmaceuticals Acquires U.S. Rights to Targretin® from Eisai Inc.," *Valeant Pharmaceuticals International, Inc.*, February 21, 2013, http://ir.valeant.com/news-releases/2013/21-02-2013.

<sup>&</sup>lt;sup>122</sup> "Kos Announces Strategic Commercialization and Research and Development Alliance with Biovail in Cardiovascular Arena," *Business Wire*, May 3, 2005,

Drug Name	Acquisition Year	Acquisition Details
GLYSET	2003	- Pfizer merges with Pharmacia & Upjohn <sup>123</sup>
SULAR	2008	- Shionogi acquires Sciele Pharma <sup>124</sup>
MYCOBUTIN	2003	- Pfizer merges with Pharmacia & Upjohn <sup>125</sup>
GABITRIL	2002	- Cephalon acquires rights, through its subsidiaries, from Sanofi <sup>126</sup>
TASMAR	2004	- Valeant acquires rights from F. Hoffman- Laroche (Roche) for \$13.5 million <sup>127</sup>
LEVITRA	2004	- Schering-Lough (now Merck & Co.) acquires US commercialization activities from Bayer and GSK <sup>128</sup>
MYLERAN	2009	- GSK acquires 16% stake in Aspen Pharmacare, divests 8 specialist medications to Aspen <sup>129</sup>
LEUKERAN	2009	- GSK acquires 16% stake in Aspen Pharmacare, divests 8 specialist medications to Aspen <sup>130</sup>

http://www.businesswire.com/news/home/20050503005500/en/Kos-Announces-Strategic-Commercialization-Research-Development-Alliance.

<sup>123</sup> "2003:Pfizer and Pharmacia Merger" (Company History.),

http://www.pfizer.com/about/history/pfizer\_pharmacia.

<sup>124</sup> Mark Todoruk, "Shionogi to Buy Sciele Pharma for \$1.4 Billion," FirstWord Pharma, August 29, 2008,

https://www.firstwordpharma.com/node/32478.

<sup>125</sup> "2003:Pfizer and Pharmacia Merger."

<sup>126</sup> "Cephalon Strengthens Its Global Presence By Acquiring International Rights to GABITRIL," *PR Newswire*, January 8, 2002, http://www.prnewswire.com/news-releases/cephalon-strengthens-its-global-presence-by-acquiring-international-rights-to-gabitril-75356057.html.

<sup>127</sup> "Valeant Pharmaceuticals Acquires Rights to Tasmar," PR Newswire, May 6, 2016,

http://www.prnewswire.com/news-releases/valeant-pharmaceuticals-acquires-rights-to-tasmar-73854662.html.

<sup>128</sup> Bloomberg LP, terminal accessed at the Yale School of Management

<sup>129</sup> "Aspen and GSK Agree on Strategic Deals" (Press Release, 2009),

http://www.aspenpharma.com/2009/05/12/aspen-gsk-agree-strategic-deals/.

<sup>130</sup> Ibid.

Drug Name	Acquisition Year	Acquisition Details
KEVEYIS	2016	- Stongbridge Biopharma acquires US rights from Taro <sup>131</sup>
PREMARIN	2009	- Pfizer acquires Wyeth <sup>132</sup>
TRECATOR	2009	- Pfizer acquires Wyeth <sup>133</sup>
PEGANONE	2012	- Recordati acquires from Lundbeck <sup>134</sup>
NALFON	2012	- XSPIRE acquires from Pedinol Pharmacal <sup>135</sup>
MARPLAN	2007	- Validus Pharma acquires from Oxford Pharmaceuticals <sup>136</sup>
ALKERAN	2009	- GSK acquires 16% stake in Aspen Pharmacare, divests 8 specialist medications to Aspen <sup>137</sup>
DEMSER	2010	- Valeant acquires from Aton Pharma for \$318 million <sup>138</sup>
DARAPRIM	2010	- Turing Pharmaceuticals acquires Daraprim from Impax Laboratories for approximately

<sup>&</sup>lt;sup>131</sup> "Strongbridge Biopharma Plc Announces Acquisition of U.S. Rights to KEVEYIS® From Taro" (Press Release, December 23, 2016), file:///Users/alexishenkel/Downloads/Releasee3a876a9-7042-4222-ac03-06c5e33019b2 2231581%20(1).pdf.

<sup>&</sup>lt;sup>132</sup> "Pfizer to Acquire Wyeth, Creating the World's Premier Biopharmaceutical Company" (Press Release, January 26, 2009), http://press.pfizer.com/press-release/pfizer-acquire-wyeth-creating-worlds-premier-biopharmaceutical-company.

<sup>&</sup>lt;sup>133</sup> Ibid.

<sup>&</sup>lt;sup>134</sup> "Lundbeck to Divest a Portfolio of Non-Core Products as Part of Its Strategy to Focus on Newer, Strategic CNS-Products."

<sup>&</sup>lt;sup>135</sup> "Xspire Pharma Acquires Nalfon® Oral Capsules," Evaluate Pharma, August 24, 2012,

http://www.evaluategroup.com/Universal/View.aspx?type=Story&id=351698.

 <sup>&</sup>lt;sup>136</sup> "Marplan Acquisition" (Press Release, May 14, 2007), http://validuspharma.com/blog/marplan-acquisition/.
 <sup>137</sup> "Aspen and GSK Agree on Strategic Deals."

<sup>&</sup>lt;sup>138</sup> Andrew Pollak and Sabrina Tavernise, "Valeant's Drug Price Strategy Enriches It, but Infuriates Patients and Lawmakers."

Drug Name	Acquisition Year	Acquisition Details
		\$55 million <sup>139</sup>
DYRENIUM	2001	- WellSpring Pharmaceutical acquires Shire Canadian OTC product line <sup>140</sup>
EDECRIN	2006	- Princeton Pharma Holdings acquires Aton Pharma, a subsidiary of Merck & Co <sup>141</sup>
NARDIL	2003	- Pfizer acquires manufacturing rights from Parke-Davis <sup>142</sup>
PARNATE	2011	- Covis Pharma acquires U.S. rights from GSK <sup>143</sup>

# **VI. Pricing Information**

One of the key reasons there are so few systematic evaluations surrounding drug pricing is that data are difficult and time-consuming to acquire. For this analysis, I acquired pricing data from the Bloomberg terminal at the Yale School of Management. I manually searched each of the 68 drugs in our sample of currently marketed, off-patent drugs with zero or one bioequivalent generics. I pulled all available pricing data for each manufacturer, corporation strength and

<sup>&</sup>lt;sup>139</sup> "Impax Announces Sale of Daraprim® to Turing Pharmaceuticals AG" (Press Release, August 10, 2015), http://investors.impaxlabs.com/Media-Center/Press-Releases/Press-Release-Details/2015/Impax-Announces-Saleof-Daraprim-to-Turing-Pharmaceuticals-AG/default.aspx.

<sup>&</sup>lt;sup>140</sup> "WellSpring Pharmaceutical Corporation Completes Acquisition of Shire Canadian OTC Product Line," *PR Newswire*, September 4, 2001, http://www.prnewswire.com/news-releases/wellspring-pharmaceutical-corporation-completes-acquisition-of-shire-canadian-otc-product-line-71914817.html.

<sup>&</sup>lt;sup>141</sup> "Aton Pharma, Inc Acquired by Princeton Pharma Holdings, LLC," *Evaluate Pharma*, October 12, 2006, http://www.evaluategroup.com/Universal/View.aspx?type=Story&id=214946.

<sup>&</sup>lt;sup>142</sup> "Old Nardil vs. New Nardil Comparison: Was The Old Version More Effective?," *Mental Health Daily*., http://mentalhealthdaily.com/2014/08/16/old-nardil-vs-new-nardil-comparison-was-the-old-version-more-effective/.'re alre

<sup>&</sup>lt;sup>143</sup> "Covis Pharma to Acquire U.S. Rights from GlaxoSmithKline for Fortaz®, Zinacef®, Lanoxin®, Parnate®, and Zantac® Injection," *PR Newswire*, December 22, 2011, http://www.prnewswire.com/news-releases/covis-pharma-to-acquire-us-rights-from-glaxosmithkline-for-fortaz-zinacef-lanoxin-parnate-and-zantac-injection-136058673.html.

package size. Each of these criteria—along with each set of dates—required a separate search and a separate data pull. I also verified these findings against an online database created by Sandy Balkin, with data acquired from First Data Bank's AnalySource Online drug pricing database.

I used strength and manufacturer as the key criteria for selecting which set of prices to include in the analysis for each drug (prices are consistent among different package sizes but equivalent strengths). I searched each drug by proprietary name on the NDC Directory to compare and verify that the NDC codes matched those listed in the pricing data pulled from Bloomberg. For each drug, I selected the U.S. manufacturer listed on the NDC database and the strength that was consistent with the First Data Bank data—if data were available—or for which there was the most available pricing information.

For drugs that have one bioequivalent alternative (n=28), I acquired the same pricing data for each generic version from the Bloomberg terminal. Among the 28 generic drugs, 27 had at least one price available. For the analysis, I used pricing information for the same strength as that of the brand name version in order to be consistent.

I compiled all of the data pulled from Drugs@FDA, the Bloomberg terminal, the First Data Bank pricing database, the NDC Directory, the WHO ATC/DDD Index database, company reports, SEC filings and various other online resources. I created an excel sheet detailing the following data for each drug: drug name, molecule, generic equivalents (0 or 1), product NDC, formulation (tablet or capsule), strength, package size, orphan code, therapeutic code, corporation, manufacturer, application number, merger and acquisition (M&A) activity (yes/no), M&A dates, and prices. The following table provides an example of the data acquired for one of the drugs in the sample, Daraprim (pyrimethamine). These three rows of data represent one row of my data sheet and are repeated for each of the 96 drugs (68 brand and 28 generic).

drug_nan	ne molecule	generic_0-1	product_ndc	generic_brand	formulation	strength	package_size
DARAPE	RIM PYRIMET	THAMINE 0	0179-0090	BRAND	TABLET	25MG	100
orphan _code	therapeutic_ code	corporation	manufacture	r application_ number	approval_ date	_ m& a	m&a1_date
No	ID	TURING PHARMACEUTICALS LLC.	TURING/ , AMEDRA	08578	1/23/53	Y	8/10/15
price_1	price1_date	price2 pr	ice2_date	price3 price3	3_date j	price4	price4_date
8.91	1/4/12	11.79 1/1	1/13	13.55 1/3/14	4 ,	750.00	8/11/15

 Table 5: Data acquired for Daraparim (pyrimethamine)

# VII. Results & Analysis

Among all currently marketed drugs in capsule or tablet formulation with zero or one generic bioequivalent alternatives (n=68), I dichotomized the sample into therapeutics that have been acquired at least once since 2000 (n=38 drugs) and those that have not (n=30 drugs); of these 68 drugs, 26 (27.4%) have one approved therapeutic equivalent. Among the 38 acquired drugs, the median most recent, post-2000 market acquisition date was January 1, 2009, and 22 (58%) had pricing data available before and after the acquisition date. Occasionally, the exact market acquisition date was unavailable. When only a year was listed, I used 01/01/x year as the date,

and when a month and year was listed, I used the first of that month as the market acquisition date.

# **Table 6: Sample characteristics**

# Off-patent pharmaceutical drugs in capsule or tablet formulation with zero or one bioequivalent generics

<u>Characteristic</u>	
Overall, No. (%)	68
Acquired, No. (%)	
Yes	38 (55.9)
No	30 (44.1)
Bioequivalent generic availal	oility, No. (%)
Yes	26 (38.8)
No	42 (61.2)
Orphan Status, No. (%)	
Yes	15 (22.3)
No	53 (77.6)
Therapeutic Area, No. (%)	
Infectious Disease	14 (20.6)
Cancer	13 (19.1)
Cardiovascular / Diabetes / Lipids	7 (10.3)
Autoimmune / Musculoskeletal	7 (10.3)
OTHER	27 (39.7)

# Price changes pre- and post- acquisition

I was first interested in whether there were significant changes to drug pricing for drugs with limited generic competition following a merger or acquisition event. To answer this question, I compared median pre-acquisition prices to median post-acquisition prices using the Wilcoxon matched-pairs signed-ranks test, the most appropriate test for comparing paired, non-normally distributed data. Among the 22 acquired drugs that had pricing data available before and after the acquisition date, the median most recent available price from before and after the acquisition date, the median most recent available price from before and after the acquisition date was **\$4.69** (Interquartile range [IQR], \$1.88-\$16.10) and **\$12.13** (IQR, \$3.34-\$25.88), respectively (p<0.001). This represents an average 28% increase (IQR, 15.0%-126.3%). Thus, it can be concluded that acquisition of a drug with limited generic competition is associated with significant price increases.

I also calculated average drug price compounded annual growth rates (CAGRs) over the available years for each drug in order to compare the mean CAGRs for acquired and non-acquired drugs. The average CAGR for acquired drugs (n=38) was 34% compared to 17% for non-acquired drugs (n=30), demonstrating that acquired drugs grow at twice the rate, on average, of their non-acquired counterparts.

	Median most recent available price before acquisition	Median most recent available price after acquisition	Average Increase
Acquired Drugs	\$4.69	\$12.33	28%

### Table 7: Summary of price changes pre-post acquisition

Table 8: Examples of price hikes following a merger or acquisition event; price before acquisition represents the most recent pre-acquisition price, and price after acquisition represents the most recent post-acquisition price

Drug Name	Acquisition Year	Price Before Acquisition	Price After Acquisition	Price Increase
SYPRINE	2010	\$4.35	\$212.67	4792%
TARGRETIN	2013	\$39.54	\$118.31	199%
MYLERAN	2009	\$2.37	\$23.42	889%
LEUKERAN	2009	\$2.05	\$24.33	1087%
MARPLAN	2007	\$1.17	\$3.94	236%
DEMSER	2010	\$16.1	\$327.944	1937%
CUPRIMINE	2010	\$3.89	\$261.89	6637%
DARAPRIM	2015	\$13.55	\$750	5433%
PARNATE	2011	\$1.42	\$6.38	349%
NILANDRON	2013	\$17.48	\$215.88	1135%
HEXALEN	2007	\$9.83	\$20.08	104%
RIDAURA	2011	\$5.48	\$20.80	280%



Figure 6: Examples of price hikes following a merger or acquisition event

Figure 7: Average drug price CAGR for acquired and non-acquired drugs



# Most recent prices of acquired brand drugs vs non-acquired brand drugs

Next, I compared most recent prices among brand drugs that have been acquired at least once since 2000 and those that have not. Among the 38 acquired brand drugs, 37 (97%) had at least one price available. Among the 29 non-acquired brand drugs, 26 (90%) had at least one price available. The median most recent price of acquired versus non-acquired brand drugs was **\$23.42** (IQR, \$5.20-\$95.1) and **\$7.61** (IQR, \$2.19-\$41.27), respectively (p=0.03 when analyzed using the Wilcoxon rank-sum test). The median most recent date available for acquired brand drugs was 2016 and for non-acquired brand drugs was 2015.5.

Table 9: Summary of most recent prices of acquired brand drugs vs non-acquired brand drugs

	Most Recent Price	IQR	p-value
Acquired Drugs	\$23.42	\$5.20 - \$95.1	0.03
Non-acquired Drugs	\$7.61	\$2.19 - \$41.27	

# Most recent prices of generic version of acquired brand drugs vs generic version of nonacquired brand drugs

Among the 26 brand drugs with one generic version, 12 (46%) were acquired brands. Among the generic versions of the 12 acquired brand drugs, 11 (92%) generics had at least one price available. Among the generic versions of the 14 non-acquired brand drugs, 13 (93%) generics had at least one price available. The median most recent price of generic versions of acquired (n=11) and non-acquired (n=13) brand drugs was **\$13.16** (IQR, \$2.23-\$97.87) and \$3.26 (IQR, \$1.36-\$10.33), respectively (p=0.22 when analyzed using a Wilcoxon rank-sum

test).

 Table 10: Summary of Most recent prices of generic version of acquired brand drugs vs generic version of non-acquired brand drugs

	Most Recent Price	IQR	p-value
Generic version of acquired brand drug	\$13.16	\$2.23 - \$97.87	0.22
Generic version of non- acquired brand drug	\$3.26	\$1.36 - \$10.33	

# Most recent prices of non-acquired brand drugs vs generic version of non-acquired brand drugs

The median most recent price of non-acquired brand drugs versus that of the generic

version of non-acquired brand drugs was \$7.61 (IQR, \$2.19-\$41.27) and \$3.26 (\$1.36-\$10.33),

respectively (p=0.14 when analyzed using a Wilcoxon rank-sum test).

	Most Recent Price	IQR	p-value
Non-acquired brand drug	\$7.61	\$2.19 - \$41.27	0.14
Generic version of non-acquired brand drug	\$3.26	\$1.36 - \$10.33	

# Table 11: Summary Most recent prices of non-acquired brand drugs vs generic version of non-acquired brand drugs

# Regression analysis:

In addition to comparing pre- and post- acquisition prices for drugs that have been acquired, along with most recent available prices for drugs that have been acquired versus those that have not, I performed a regression analysis using the last available price as the dependent variable and acquisition (yes/no), therapeutic alternative availability (yes/no), orphan drug (yes/no) and therapeutic area (categorized) as the independent variables. I selected last available price as the dependent variable instead of change in price since many of the non-acquired drugs did not have multiple prices available. Acquisition (yes/no) is the main independent variable, and the others are controls. Among the 68 off-patent drugs with zero or one therapeutic alternatives in our sample, 64 had at least one price available.

# Regression:

Last available Price =  $\beta_0 + \beta_1 acquisition (yes/no) + \beta_2 generic availability (yes/no) + \beta_3 orphandrug (yes/no) + \beta_4 i. therapeutic area (categorized) + <math>\varepsilon_i$ 

Linear regression	Number of observations = 64					
	<b>R-squared = 0.083</b>					
Root MSE= 135.7						
		Robust Std.			[95%	
last price	Coef.	Err.	t	P>t	Conf.	Interval]
acquisition	30.1258	38.5214	0.7800	0.4380	-47.0729	107.3244
generic_01	-31.9910	33.5771	-0.9500	0.3450	-99.2810	35.2990
orphan	18.7897	47.7488	0.3900	0.6950	-76.9011	114.4804

# **Table 12: Regression Results**

therapeutic_code_numb								
2	43.7580	55.2101	0.7900	0.4310	-66.8855	154.4014		
3	-24.8402	33.6385	-0.7400	0.4630	-92.2533	42.5729		
					-			
4	43.8177	72.7966	0.6000	0.5500	102.0699	189.7052		
5	14.2112	39.8689	0.3600	0.7230	-65.6879	94.1103		
6	-10.3261	40.6802	-0.2500	0.8010	-91.8510	71.1988		

While the p-value is not statistically significant (p=0.44), possibly due to the small sample size, the direction of the acquisition coefficient strongly points to a trend in the data. Likewise, the coefficient for the generic alternative variable is large and negative, indicating that drugs with one therapeutic alternative would have lower most recent prices (negative association); however, the p-value is not significant (p=0.35). It was hypothesized that generic availability would have the smallest effect on last available price, since one therapeutic alternative does not typically drive prices down significantly, but the results suggest that this had the largest effect of the three key independent variables (largest absolute value coefficient and smallest p-value). Finally, the regression shows a positive association between orphan designation and most recent price, but the p-value is not significant (p=0.70). The regression model accounts for the effect of the threapeutic categorizations using a fixed effect variable.

Given the small size of the sample of off-patent drugs with zero or one therapeutic alternatives that had at least one price available (n=64), it is reasonable that the p-values are not significant. However, the results of the regression demonstrate that most recent price is associated with acquisition (yes/no), while controlling for bioequivalent availability (yes/no), orphan (yes/no) and therapeutic area (categorized). Taken together with the results from the statistical analyses and comparisons above, it can be concluded that acquisitions indeed lead to higher drug prices in the sample.

# VIII. Discussion & Policy Implications

In order to analyze the effects of corporate acquisitions on pharmaceutical drug prices, this paper focuses on off-brand drugs with zero or one therapeutic equivalents, which make for strong targets for this tactic because they face little competition and thus offer strong pricing power to potential acquirers. The results from the statistical comparisons above, along with the variable associations in the regression analysis, support the conclusion that there is indeed a systematic difference in price levels—and changes—among drugs that have been acquired and those that have not. These results imply the need for regulatory and market-based reforms that target the generics market.

#### Regulatory reform: historical and proposed

The FDA's review process is already the quickest among major regulatory agencies worldwide. In their study "Regulatory Review of Novel Therapeutics – Comparison of Three Regulatory Agencies," Downing et al. find that –between 2001 and 2010—that the FDA had the shortest median review completion time, as compared to the European Medicines Agency (EMA) And Health Canada (303 days compared to 366 days and 352 days, respectively).<sup>144</sup>

In addition, the passage of various Acts in recent years has aided, and accelerated, the FDA approval process for novel drugs. For example, the Food and Drug Administration Safety Innovation Act (FDASIA), passed in July 2012, sets guidelines for Breakthrough Therapy Designation: "i) intended alone or in combination with one or more other drugs to treat a serious or life threatening disease or condition and ii) preliminary clinical evidence indicates that the

<sup>&</sup>lt;sup>144</sup> Nicholas S. Downing, A.B. et al., "Regulatory Review of Novel Therapeutics — Comparison of Three Regulatory Agencies," *The New England Journal of Medicine* 366, no. 24 (June 14, 2012).

drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development."<sup>145</sup> Once a drug has been labeled with breakthrough therapy designation, its development and review process is shortened 60 days or fewer.<sup>146</sup> Similarly, the Priority Review Voucher System, enacted in 2007, ensures that rare pediatric and tropical diseases receive "upstream incentive to work on diseases that otherwise wouldn't have enough incentive" by cutting approval time for drugs from ten months to six months.<sup>147</sup>

Furthermore, the 21<sup>st</sup> Century Cures Act, which passed the Senate in early December 2016, will provide \$4.8 billion to the NIH and \$500 million to the FDA over the next ten years, along with \$1 billion to fight opioid abuse.<sup>148</sup> The stated goal of the Act is to "speed up the time it takes new medicines to get to patients, while favoring the 'voice' of the patient more in its reviews and decisions, and allowing clinical trials to be designed with fewer patients while being less expensive, and generally easier-to-achieve goals."<sup>149</sup> In addition, the various Prescription Drug Users Free Act (PDUFA) renewals have consistently increased approval rates and decreased and median approval time.<sup>150</sup>

Clearly, recent legislation has targeted the novel brand-name pharmaceuticals market. These policies, which accelerate approval timelines for novel therapeutics, are beneficial—and necessary—but reform within the market for old, off-patent drugs should be emphasized as well.

<sup>&</sup>lt;sup>145</sup> "Fact Sheet: Breakthrough Therapies" (U.S. Food and Drug Administration.),

http://www.fda.gov/RegulatoryInformation/Legislation/SignificantAmendmentstotheFDCAct/FDASIA/ucm329491. htm.

<sup>&</sup>lt;sup>146</sup> Salim Syed, "Biotech Industry: Initiating Coverage" (Biotechnology Equity Research, Mizuho., 2016).

<sup>&</sup>lt;sup>147</sup> Devin Rosenthal, Kelly Roney, and Sheila Bello-Irizarry, *Understanding FDA's Priority Review Voucher System*, 2016, https://engage.vevent.com/production?eid=6727&code=Direct

Access&lc=en&cc=US&rand=1481760659979&seid=874&page=10000&standalone=false&nologin=false#/webcast/dynamic-template.

<sup>&</sup>lt;sup>148</sup> Ben Adams, "An Easy Pass for Cures; so Too for New Meds?," *FierceBitoech*, December 8, 2016, http://www.fiercebiotech.com/biotech/easy-pass-for-cures-so-too-for-new-meds.

<sup>&</sup>lt;sup>149</sup> Ibid.

<sup>&</sup>lt;sup>150</sup> Salim Syed, *Biotech Industry: Initiating Coverage*.

Ultimately, the generics market is the key to bringing down prices of the drugs in this sample. Prioritized review is imperative not only for novel therapeutics with breakthrough potential, but also for generic versions of old off-patent drugs that lack competition. Gupta et al. suggest prioritized review of drugs with three or fewer generic equivalents.<sup>151</sup> In addition, regulatory processes should block life cycle management strategies which brand-name manufacturers employ to extend their patent exclusivity periods. These discussions are especially relevant in the current political climate in the United States. In fact, newly appointed F.D.A. commissioner Scott Gottlieb has prioritized restructuring generic approval processes and standards in order to enhance generic competition.<sup>152</sup>

# Market solutions: promoting competition

In addition to regulatory reform, enacting market solutions that address the lack of incentives for generic entry, along with blocking exclusivity-extending strategies among brandname manufacturers, is a crucial step towards lowering drug prices. Biotechnology investor and author of LifeSciVC Bruce Booth emphasizes the importance of "encouraging and accelerating competitive generic markets [...] striking down pay-for-delay tactics, improving physician and patient understanding of value and price relations, encouraging value-based pricing based on cost-effectiveness and reducing the United States' pharmaceutical market's reliance on premium pricing."<sup>153</sup> In the context of these policy initiatives, the results of this study call for a heightened focus on drugs with limited generic competition.

<sup>&</sup>lt;sup>151</sup> Ravi Gupta et al., "Generic Drug Approvals Since the 1984 Hatch-Waxman Act."

<sup>&</sup>lt;sup>152</sup> Toni Clarke, "Trump Chooses Gottlieb to Run FDA; Pharma Breathes Sigh of Relief," *Reuters*, March 10, 2017, http://www.reuters.com/article/us-usa-health-fda-gottlieb-idUSKBN16H2AM.

<sup>&</sup>lt;sup>153</sup> Bruce Booth, "Seven Important Policy Agenda Items For BioPharma," LifeSciVC, (January 31, 2017), https://lifescivc.com/2017/01/seven-important-policy-agenda-items-biopharma/.

In addition, experts have proposed various solutions to address the adverse effects of price increases among pharmaceuticals while continuing to encourage innovation in the space.<sup>154</sup> For example, Kesselheim et al. propose improved competition, government efforts and various physician- and patient-level solutions. In order to improve competition, the authors suggest better regulation of pharmaceutical companies' market exclusivity-extending strategies, such as pay-for-delay and "product hopping," lowering industry expenses and enhancing permission of generic equivalent substitutions at the state level.<sup>155</sup> Regarding government efforts, Kesselheim et al. urge policy makers to authorize negotiation by Medicare for drugs covered by its Part D plans and to increase efforts to gather and share critical information regarding "comparative clinical and economic value of drugs."<sup>156</sup> This dissemination of information would help physicians and patients better understand the relationship between pricing and value.

#### **Discussion**

This paper calls attention to a tactic that has recently been covered by the media and health care literature—but mostly in the form of case studies of one or a few drugs—by providing results from a systematic evaluation on this topic. Pharmaceutical companies' acquisitions, and subsequent increase in prices, of old, off-patent drugs, with few or no bioequivalent generics is a profit-boosting strategy that has proven effects on the prices of drugs. Furthermore, it is possible that the acquired drugs in the sample were in fact more valuable than those that were not acquired and thus had even less price elasticity, indicating that—when a drug offers increased value—the current system punishes patients while benefiting non-inventive

<sup>&</sup>lt;sup>154</sup> Aaron S. Kesselheim, Jerry Avorn, and Ameet Sarpatwari, "The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform."

<sup>&</sup>lt;sup>155</sup> Ibid.

<sup>156</sup> Ibid.

generic manufacturers. Policy makers should shift their attention to regulation and market dynamics in the generics space, in order to speed up and incentivize generic competition and preclude unwarranted exclusivity-extensions among these off-patent drugs, such that they no longer become candidates for this type of manipulation.

Decreasing overall health care expenditure in the United States has long been a priority among patients, physicians, payers and policymakers. This study reveals a key driver of high prescription drug costs, which have been a major contributor to overall health spending over the past decade. More than exposing a revenue-boosting tactic among pharmaceutical companies, the results of this analysis reveal broader issues and limitations surrounding the generics market and regulatory processes. The first step towards preventing pharmaceutical companies like Valeant from acquiring old, off-patent drugs and subsequently increasing the prices is to enhance generic competition by improving regulatory processes, incentivizing competition and blocking exclusivity extensions. Ultimately, if the drugs analyzed in this study faced more competition, they would no longer be such strong candidates for this price-hiking acquisition strategy.

# IX. Appendix





Figure 9.1: Syprine price, 2007-2016



Figure 9.2: Targretin price, 2007-2016



Figure 9.3: Demser price, 2007-2016



Figure 9.4: Cuprimine price, 2007-2016



Figure 9.5: Myleran price, 2007-2016



Figure 9.6: Syprine price, 2007-2016



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