

# **THE PRICE OF SOVALDI AND ITS IMPACT ON THE U.S. HEALTH CARE SYSTEM**

## **Note**

This inquiry began as a Senate Committee on Finance investigation when Senator Wyden was Chairman and Senator Grassley was a member of the Committee's Minority. During the course of the investigation, leadership on the Committee changed in January 2015. Both senators instructed their staffs to continue the investigation and produce a staff report to the Finance Committee. All references to "investigative staff" or "staff" refer to the current Minority staff of the Finance Committee and the staff of Senator Grassley.

## **Introduction**

Hepatitis C (HCV) is the most common blood-borne virus in the United States, affecting as many as 5.2 million people.<sup>1</sup> The virus attacks the liver, resulting in inflammation, scarring and cirrhosis, while increasing the risk of liver cancer. Left untreated, HCV can cause serious illness; the disease is the leading cause of liver transplants in the United States. The aggressiveness of the virus makes it a potent public health issue in the United States. The virus is disproportionately concentrated among Americans who are likely to receive health coverage from public payers including Medicaid, Medicare, the Veterans Administration, and the State and Federal prison system.<sup>2</sup> The high cost of HCV drugs sold by Gilead Sciences, Inc., continues to put tremendous strain on these public payer systems, creating difficult decisions about how to provide medically necessary drugs to patients while staying within budgets. As a result of the high cost of these drugs, many public and private payers adopted access restrictions to control HCV treatment costs, which reduced the number of patients eligible for treatment.

Gilead brought two drugs to market in recent years, Sovaldi and Harvoni, which have improved therapies to cure HCV. Sofosbuvir—the drug that would ultimately reach the market as Sovaldi and used in combination with ledipasvir to create Harvoni—was largely developed by Pharmasset, Inc., a pharmaceutical company that was based in Princeton, New Jersey. Gilead acquired Pharmasset in January 2012.

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<sup>1</sup>Eric Chak et al., *Hepatitis C Virus Infection in USA: An Estimate of True Prevalence*, 31 Liver Int'l 1090, 1090–1101 (Sept. 2011), available at <http://www.ncbi.nlm.nih.gov/pubmed/21745274>.

<sup>2</sup>*Id.* at 1096, Table 6.

Sovaldi and Harvoni have reduced the time needed for treatment to a fraction of what it was five years ago. In addition, the effectiveness of treatment, that is, the probability that a patient will be cured, has increased. The new drugs have resulted in more patients being able to receive HCV therapy with limited or no use of interferon, an injectable drug that complicates treatment because it typically requires visits to a health care provider, and is often accompanied by difficult side effects.

Progress in therapeutics has come at a high cost for both the public and private sectors. Concurrent with drug price increases, greater numbers of providers and patients have been drawn to these new drugs, leading to increased outlays for HCV treatment. In the run-up to launching Sovaldi, Gilead estimated that worldwide spending on HCV treatment in 2008 totaled \$2.4 billion.<sup>3</sup> By 2014, Gilead alone reported net product sales of \$12.4 billion for its HCV drugs, primarily from sales in the United States and Europe.<sup>4</sup> A competitor drug developed by Johnson & Johnson, known as simeprevir, or Olysio, generated sales of \$2.3 billion in 2014,<sup>5</sup> primarily due to “off label”<sup>6</sup> co-prescriptions with Sovaldi.<sup>7</sup>

Gilead’s recent financial results show that the company has generated an additional \$14.3 billion in net product sales from its HCV drugs through the first nine months of 2015, bringing its 21-month total for its HCV drugs to \$26.6 billion, \$20.6 billion of which was from sales to U.S. consumers.<sup>8</sup>

An analysis by the consulting firm IMS Institute for Healthcare Informatics (IMS Institute) showed that U.S. spending on Sovaldi in 2014 was \$7.9 billion, and from 2010 to 2013 U.S. spending on all HCV drugs totaled \$7.8 billion. Sovaldi alone accounted for 64% of U.S. HCV drug spending in 2014, which totaled \$12.3 billion, and more than a third of the \$20.3 billion spent that year on new pharmaceutical treatments.<sup>9</sup> HCV treatments also caused a jump in spending for “specialty therapies,” which the IMS Institute defines in part as “mostly used by specialists and include treatment for cancer and other serious conditions.”<sup>10</sup> According to the IMS Institute, U.S. “specialty medicine spending increased by 26.5% to

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<sup>3</sup> Appendix E, Ex. 1, Gilead Sciences, Inc., *Gilead Liver Disease Therapeutics Strategy Overview: Board of Directors Review* (2011), GS-0019261, at GS-0019265—GS-0019266 (2011).

<sup>4</sup> Gilead Sciences, Inc., Annual Report (Form 10-K), at 59 (Feb. 25, 2015), available at <http://www.sec.gov/Archives/edgar/data/882095/000088209515000008/a2014form10-k.htm>.

<sup>5</sup> Johnson & Johnson, Annual Report (Form 10-K), Exhibit 13, at 5 (Feb. 23, 2015), available at <http://www.sec.gov/Archives/edgar/data/200406/000020040615000004/ex13-form10k20141228.htm>.

<sup>6</sup> The practice of a health care provider prescribing a drug or combination of drugs in a manner outside of what has been officially approved (in the U.S., by the Food and Drug Administration).

<sup>7</sup> Chris Hepp, *Drug Sales Bolster J&J’s Bottom Line*, Phila. Inquirer (Apr. 21, 2014), available at [http://articles.philly.com/2014-04-21/business/49268459\\_1\\_olysio-gilead-sciences-sovaldi](http://articles.philly.com/2014-04-21/business/49268459_1_olysio-gilead-sciences-sovaldi).

<sup>8</sup> Gilead Sciences, Inc., Third Quarter 2015 Financial Results (Form 8-K,), Exhibit 99.1 (October 28, 2015), available at <http://www.sec.gov/Archiver/data/882095/000088209515000031/exhibit991earningspressrel.htm>; Gilead Sciences, Inc., Fourth Quarter and Full Year 2014 Financial Results (Form 8-K), Exhibit 99.1 (Feb. 3, 2015), available at <http://www.sec.gov/Archiver/data/882095/000088209515000003/exhibit991earningspressrel.htm>.

<sup>9</sup> IMS Institute for Healthcare Informatics, *Medicines Use and Spending Shifts: A Review of the Use of Medicines in the U.S. in 2014*, at 8 (2015) [hereinafter IMS Institute for Healthcare Informatics, *Medicines Use and Spending Shifts*].

<sup>10</sup> *Id.* at 8.

\$124.1 billion in 2014; the increase was 16.3% excluding hepatitis C treatments.”<sup>11</sup>

After the introduction of Sovaldi at end of 2013, millions of Americans had a potentially viable path to a cure, but the price and cumulative cost on the health care system caused roadblocks for many. In response to treatment access and cost issues, Senators Ron Wyden and Charles Grassley sent a letter to Gilead on July 11, 2014, requesting documents and information about how the company determined the price for Sovaldi, the first of its two HCV drugs.

For over a year, investigative staff reviewed more than 20,000 pages of internal company documents provided by Gilead, as well as documents obtained from the Federal Trade Commission (FTC), Food and Drug Administration (FDA), state Medicaid programs, the Centers for Medicare and Medicaid Services (CMS), the Federal Bureau of Prisons (BOP), and other companies. In addition, investigative staff interviewed more than 100 people with expertise in HCV, or who had interacted with Gilead regarding Sovaldi and/or Harvoni. Lastly, investigative staff collected data from Medicaid programs in 50 states and the District of Columbia that provide important information about the breadth of HCV infection for one segment of public payers, and the cost that states faced in order to treat the disease.

Based on all of the information reviewed, it appears that in pricing its line of HCV drugs Gilead may have underestimated the warnings of patient groups, insurers, health care providers, and other organizations about the potential impact that price would have on access. Such warnings were made not only through the media, but directly to company officials, both in private correspondence and various public forums. While publicly saying it prioritized patient access, Gilead set Sovaldi’s price at a level where ultimately many patients would not receive treatment. Sovaldi was on the market for almost a year without serious competitors, allowing Gilead to maintain a high effective price despite efforts by many payers to negotiate volume or treatment discounts or rebates.

The costs incurred by Gilead to bring the drugs to market included its \$11.2 billion purchase of Pharmasset in 2011. Pharmasset performed the initial development of the drug and began the process of FDA approval, which Gilead then completed following the acquisition. Several months after Gilead agreed to buy Pharmasset, a Gilead executive described the acquisition as a “bargain.”<sup>12</sup> The company failed to provide sufficient information to determine how much additional cost it incurred to complete the development, finish the FDA approval process, and bring the drug to market.

This report describes how Gilead set the price for Sovaldi and its follow-on drug, Harvoni. In addition, this report discusses and analyzes the financial and budgetary impacts of Gilead’s pricing decisions on payers—public and private—as well as the resulting access restrictions imposed due to Sovaldi’s cost. And finally, the re-

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<sup>11</sup> *Id.*

<sup>12</sup> Appendix E, Ex. 2, Email from John McHutchison to Matthew Young, Re: Bristol-Inhibitex (Jan. 7, 2012), GS-0010634.

port describes Gilead's response to resultant market forces, including payer access restrictions and competition.

### **Appendices**

Several appendices to the report provide additional information and documents related to the investigation.

Appendix A contains data collected by investigative staff from state Medicaid programs showing the amount of money spent on Sovaldi and Harvoni in 50 states and the District of Columbia, as well as the estimated number of Medicaid clients with HCV in states where the information was available.

Appendix B presents a review of prior authorization restrictions put in place by state Medicaid programs for Sovaldi and Harvoni, as well as a sample of other payers. The study was completed by researchers at the Oregon Health and Sciences University.

Appendix C presents data provided by the Centers for Medicare & Medicaid Services (CMS) on Medicare spending on Sovaldi, Harvoni, and other HCV drugs.

Appendix D contains correspondence and other documents received by the Senators or investigative staff regarding Sovaldi or Harvoni.

Appendix E contains all Gilead documents cited in this report.

Appendix F contains all narrative answers cited in this report from Gilead in response to questions in the July 11, 2014 letter from Senators Wyden and Grassley.

## **Section 1: Hepatitis C, its Human Toll, Treatment, and the Effect of “Warehousing” on Pharmaceutical Markets**

### **Hepatitis C and Its Human Toll**

In 2013, HCV was listed as the cause of death for 19,368 people in the United States.<sup>13</sup> This number likely underestimates the number of HCV deaths. CDC researchers have found that fewer than 20% of HCV-infected decedents have HCV listed on their death certificates, even though at least 75% of HCV-infected dece-dents had pre-mortem evidence of serious liver disease.<sup>14</sup> Despite the likely undercounting, a 2012 study reported that the number of HCV-associated deaths was greater than the number of human immunodeficiency virus (HIV)-associated deaths in the United States between 1999 and 2007.<sup>15</sup> This trend has continued in recent years. The virus is a killer not just in the United States, but across the world. Globally, between 130 million and 150 million people have chronic HCV; annually, the virus and related liver disease kill 704,000 people worldwide.<sup>16</sup> In comparison, the World Health Organization (WHO) estimated that in 2010, malaria caused 660,000 deaths, and that in 2011, tuberculosis caused 1.4 million deaths and HIV caused 1.7 million deaths.<sup>17</sup>

Prior to the virus’s identification in 1989, HCV was frequently spread through unscreened blood transfusions.<sup>18</sup> The virus is disproportionately concentrated among baby boomers born from 1945 through 1965. In 2011, about 75% of HCV deaths in the United States were among forty-five to sixty-four-year-olds.<sup>19</sup> The CDC estimates that 3.2% of baby boomers are positive for HCV, five times higher than people born prior to 1945 or after 1965. Consequently, in 2012 and 2013, the CDC and the U.S. Preventative Services Task Force recommended that all people born from 1945 through 1965—more than 60 million people—be tested for the virus.<sup>20</sup> The virus is most commonly transmitted in the United States through the use of unsanitary needles, leaving intravenous drug users at

<sup>13</sup> Centers for Disease Control and Prevention (CDC), *Surveillance for Viral Hepatitis—United States, 2013*, Table 4.5, at 58, available at <http://www.cdc.gov/hepatitis/statistics/2013surveillance/commentary.htm>.

<sup>14</sup> Reena Mahajan et al., *Mortality Among Persons in Care With Hepatitis C Virus Infection: The Chronic Hepatitis Cohort Study (CHCS)*, 2006–2010, 58 Clinical Infectious Diseases 1055, 1055–61 (2014).

<sup>15</sup> Kathleen N. Ly et al., *The Increasing Burden of Mortality From Viral Hepatitis in the United States Between 1999 and 2007*, 156 Annals of Internal Medicine 271, 271–78 (2012).

<sup>16</sup> GBD 2013 Mortality and Causes of Death Collaborators, *Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013*, 385 Lancet 9963, 117–71 (2015).

<sup>17</sup> World Health Organization, *Global Policy Report on the Prevention and Control of Viral Hepatitis in WHO Member States* (2013), available at [http://apps.who.int/iris/bitstream/10665/85397/1/9789241564632\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/85397/1/9789241564632_eng.pdf?ua=1).

<sup>18</sup> Q.L. Choo et al., *Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome*, 244 Science 359, 359–62 (1989).

<sup>19</sup> CDC, Number and Rate\* of Deaths with Hepatitis C Listed as a Cause of Death, by Demographic Characteristic and Year—United States, 2007–2011, available at <http://www.cdc.gov/hepatitis/Statistics/2012Surveillance/Table4.4.htm>.

<sup>20</sup> Bryce D. Smith et al., CDC, *Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965* (2012), available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6104a1.htm>; U.S. Preventative Services Task Force, *Hepatitis C: Screening*, (June 2013), available at <http://www.uspreventiveservicestaskforce.org/Page/Topic/recommendation-summary/hepatitis-c-screening>.

high risk for contracting the disease.<sup>21</sup> With a growing number of people who inject intravenous drugs, such as heroin or other opiates, rates of HCV infection are increasing, as the recent HCV outbreak reported in Indiana illustrates.<sup>22</sup>

### **Distinct Genotypes Across the World Create Distinct Markets**

There are seven different genotypes of HCV and within each genotype, there are sub-genotypes.<sup>23</sup> Each genotype and sub-genotype reacts differently to treatment, and the FDA has approved drug regimens for specific HCV genotypes and sub-genotypes, rather than the entire spectrum of HCV. The current generation of HCV drugs, including Sovaldi and Harvoni, are not “full spectrum” drugs that can treat all genotypes, and they are not an equally effective treatment against all sub-genotypes.

The prevalence of specific genotypes and sub-genotypes varies among different regions of the world. About 70% of HCV cases in the United States are genotype 1, the majority of which are sub-genotypes 1a and 1b. Genotypes 2 and 3 are estimated to account for 16% and 12% of cases in the United States, respectively, while genotypes 4, 5 and 6, in total, account for fewer than 4% of cases in the United States.<sup>24</sup> Conversely, in many Middle Eastern and African countries, genotype 4 accounts for more than 90% of HCV infections.<sup>25</sup> Genotype 5 is almost entirely contained within South Africa and select countries in Europe and the Middle East.<sup>26</sup> Drug manufacturers have concentrated their focus on selling HCV drugs that treat genotypes with prevalence in developed countries.<sup>27</sup>

### **HCV Symptoms**

A major challenge associated with HCV is its tendency to go undiagnosed, due to its slow progression and tendency to remain asymptomatic for years. These attributes have earned HCV the moniker “the silent killer,” and have contributed to poor surveil-

<sup>21</sup> Centers for Disease Control and Prevention, *Viral Hepatitis Surveillance, United States, 2013*, at 6 (last updated Oct. 19, 2015), available at <http://www.cdc.gov/hepatitis/statistics/2013surveillance/pdfs/2013hepsurveillancert.pdf> (“HCV is transmitted primarily through percutaneous (parenteral) exposure that can result from injection drug use, needle stick injuries, and inadequate infection control in health-care settings.”); *id.* at 52 (“Of the 955 case-reports that had information about injection drug use, 61.6% (n=588) indicated use of injection drugs.”).

<sup>22</sup> Centers for Disease Control and Prevention, CDC Health Alert Network, *Outbreak of Recent HIV and HCV Infections Among Persons Who Inject Drugs* (Apr. 24, 2015), available at <http://www.bt.cdc.gov/han/han00377.asp>.

<sup>23</sup> Donald G. Murphy et al., *Hepatitis C Virus Genotype 7, a New Genotype Originating from Central Africa*, 53 J. Clinical Microbiology 967, 967–72 (2015).

<sup>24</sup> See e.g., Jane P. Messina et al., *Global Distribution and Prevalence of Hepatitis C Virus Genotypes*, 61 Hepatology 77, 77–87 (2015); M. Michele Manos et al., *Distribution of Hepatitis C Virus Genotypes in a Diverse U.S. Integrated Health Care Population*, 84 J. Med. Virology 1744, 1744–1750 (2012), available at <http://www.ncbi.nlm.nih.gov/pubmed/22997077>.

<sup>25</sup> Sanaa M. Kamal & Imad A. Nasser, *Hepatitis C Genotype 4: What We Know and What We Don't Yet Know*, 47 Hepatology 1371, 1371 (2008), available at <http://webhome.weizmann.ac.il/home/liorg/HCV.pdf>.

<sup>26</sup> N. Antaki et al., *HCV Genotype 5: An Orphan Virus*, 18 Antiviral Therapy 263, 263–69 (2012), available at <http://www.ncbi.nlm.nih.gov/pubmed/23111702>.

<sup>27</sup> Appendix E, Ex. 3, Pharmasset, Board of Directors Meeting, Princeton, NJ (July 21, 2011), GS-0004488; Appendix E, Ex. 4, Gilead Sciences, Inc., Gilead to Acquire Harry (Nov. 19, 2011), GS-0009179, at GS-0009187; Jane P. Messina et al., *Global Distribution and Prevalence of Hepatitis C Virus Genotypes*, 61 Hepatology 77, 77–87 (2014), available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4303918/>.

lance of the disease.<sup>28</sup> A recent study estimated that half of people in the U.S. with chronic HCV are aware they are infected.<sup>29</sup> When HCV symptoms do develop, they include easily bleeding or bruising, itchy skin, fluid accumulation in the abdomen (ascites), swelling in the legs, weight loss, confusion, drowsiness, slurred speech (hepatic encephalopathy), and development of spider-like blood vessels on the skin (spider angiomas).<sup>30</sup> Approximately 20% of chronic HCV patients, if untreated, will develop cirrhosis.<sup>31</sup>

Hepatitis C remains the leading primary indication for people receiving or waiting for liver transplants.<sup>32</sup> The most recent available federal data show that 1,402 patients received transplants in 2012, and 4,612 patients were on waiting lists.<sup>33</sup>

### **Advancing Treatment for Hepatitis C**

There is no vaccine for HCV, unlike for Hepatitis A and Hepatitis B. However, in recent years, significant progress has been made in improving standards of care (SOC). The effectiveness of a drug is primarily measured by the speed of viral reduction (early virologic response, or EVR, and rapid virologic response, or RVR) and the percentage of cured patients. A patient is considered cured when blood tests do not detect the virus twelve or twenty-four weeks after treatment, which is called sustained virologic response (SVR).<sup>34</sup> Each successive SOC has simplified and shortened treatment regimens, increased effectiveness, and minimized side effects.

HCV treatment relied on interferon for nearly twenty-five years. It is a naturally occurring protein that cells secrete when they are attacked by a virus and was first identified in 1957. Interferon exists in three different forms—alpha, beta, and gamma—and each is used to treat numerous diseases, including cancer, multiple sclerosis, AIDS, and genital warts.<sup>35</sup> Interferon works by boosting the immune system to effectively block new cell sites to which a virus could attach. However, interferon has drawbacks, especially when used for prolonged treatment. Interferon treatment requires injections, necessitating weekly or semi-weekly visits to a provider's office or regular access to other health care services. Additionally, interferon causes side effects, including flu-like symptoms, such as

<sup>28</sup>Patrick Strudwick, *Hepatitis C: Hunting the Silent Killer*, The Guardian (Feb. 25, 2015), available at <http://www.theguardian.com/society/2015/feb/25/hepatitis-c-hunting-the-silent-killer>.

<sup>29</sup>Balign R. Yehia et al., *The Treatment Cascade for Chronic Hepatitis C Virus Infection in the United States: A Systematic Review and Meta-Analysis*, PLoS ONE (July 2, 2014), available at <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0101554>.

<sup>30</sup>Mayo Clinic, *Diseases and Conditions: Hepatitis C* (Jan. 15, 2015), <http://www.mayoclinic.org/diseases-conditions/hepatitis-c/basics/definition/con-20030618?p=1>.

<sup>31</sup>David H. Spach, *HCV Epidemiology in the United States*, University of Washington, Hepatitis C Online (June 16, 2014), available at <http://www.hepatitis.c.uw.edu/go/screening-diagnosis/epidemiology-us/core-concept/all#hcv-incidence-prevalence>.

<sup>32</sup>United States Department of Health & Human Services, Organ Procurement & Transplantation Network, Scientific Registry of Transplant Recipients, 2012 Annual Data Report: Liver, at 69, 75 (Table 1.3) and 81 (Table 4.7), available at [http://srtr.transplant.hrsa.gov/annual\\_reports/2012/flash/03\\_liver\\_13/v2files/assets/downloads/publication.pdf](http://srtr.transplant.hrsa.gov/annual_reports/2012/flash/03_liver_13/v2files/assets/downloads/publication.pdf).

<sup>33</sup>*Id.*

<sup>34</sup>H. Nina Kim & David H. Spach, *Virologic Responses During Treatment of Hepatitis C*, University of Washington, Hepatitis Web Study, (last updated Oct. 1, 2012), available at <http://depts.washington.edu/hepstudy/hepC/mgmt/viroresponse/discussion.html> (last updated Oct. 1, 2012).

<sup>35</sup>*Interferon*, Encyclopedia Britannica Online (Aug. 7, 2009), available at <http://www.britannica.com/EBchecked/topic/290230/interferon>.

fever, fatigue, muscle aches, and myalgia.<sup>36</sup> Patients have likened the side effects to having the flu throughout treatment. Many patients cannot tolerate interferon, and thus did not have a viable treatment option.<sup>37</sup>

Researchers began testing the effectiveness of interferon-alpha (interferon) therapies for HCV in the mid-1980s before the virus was identified and was still known as non-A-non-B hepatitis.<sup>38</sup> After the virus' identification in 1989, interferon became the first SOC for those that could tolerate it. Interferon, as a standalone SOC, has a poor SVR rate. A twenty-four-week regimen has an SVR of only 6%, and a forty-eight-week regimen increases the SVR to 16%.<sup>39</sup> In 1998, the FDA approved ribavirin, an antiviral drug, for use in combination with interferon for treatment of HCV.<sup>40</sup> The combination improved the effectiveness of treatment; a twenty-four-week regimen resulted in an SVR of 34%, and a forty-eight-week regimen resulted in an SVR of 42%. Ribavirin further increased the SVR to 54% when combined with pegylated interferon, which combines polyethylene glycol (PEG) with interferon.<sup>41</sup>

The next major advance in treatment was the development of direct-acting antiviral (DAA) drugs, which work by attacking specific viral proteins encoded within the virus's RNA. These viral proteins include enzymes such as the NS5B polymerase and NS3/4A protease, as well as the NS5A protein, which is involved in the HCV replication complex. In 2011, the FDA approved two DAAs, boceprevir (Victrelis) and telaprevir (Incivek).<sup>42</sup> In 2013, the FDA approved two additional DAAs, simeprevir (Olysio) and sofosbuvir (Sovaldi).<sup>43</sup> Each successive DAA advanced HCV treatment by maintaining or improving SVR, while also reducing treatment time for most patients, thereby reducing the use of interferon.

The introduction of drugs that could treat patients without interferon critically advanced HCV treatment. Although the FDA approved Sovaldi for use without interferon for genotype 2 and genotype 3 patients, the primary cohort of genotype 1 patients still required the use of interferon and ribavirin with Sovaldi. However,

<sup>36</sup> Mary L. Filipi et al., *Nurses' Perspective on Approaches to Limit Flu-Like Symptoms During Interferon Therapy for Multiple Sclerosis*, 16 Int'l J. of MS Care 55, 59 (2014), available at <http://ijmsc.org/doi/pdf/10.7224/1537-2073.2013-006>.

<sup>37</sup> *Id.*

<sup>38</sup> Jay H. Hoofnagle et al., *Treatment of Chronic Non-A, Non-B Hepatitis with Recombinant Human Alpha Interferon: A Preliminary Report*, 315 New Eng. J. Med. 1575, 1575–1578 (1986), available at <http://www.ncbi.nlm.nih.gov/pubmed/3097544>.

<sup>39</sup> Doris B. Strader & Leonard B. Seeff, *A Brief History of the Treatment of Viral Hepatitis C*, 1 Clinical Liver Disease 6, 6 (2012), available at <http://onlinelibrary.wiley.com/doi/10.1002/cld.1/epdf> [hereinafter Strader & Seeff, *A Brief History of the Treatment of Hepatitis C*].

<sup>40</sup> Press Release, Schering-Plough Corp., Schering-Plough Announces FDA Approval of Rebetron(TM) Combination Therapy for Previously Untreated Hepatitis C Patients; Rebetron Combination Therapy Now Approved for Use in Both Previously Untreated and Relapse Hepatitis C Patients (Dec. 9, 1998). Ribavirin was discovered in 1972 and, in addition to treating HCV, treats other RNA viruses. Shane Crotty et al., *Ribavirin's Antiviral Mechanism of Action: Lethal Mutagenesis?*, 80 J. Molecular Med. 86, 86 (2001), available at <http://www.liai.org/files/Ribavirin-Crotty.pdf>. Ribavirin does not effectively treat HCV as a monotherapy because it does not reduce the production of HCV RNA, although it does significantly reduce liver damage. *Id.* at 91.

<sup>41</sup> Strader & Seeff, *A Brief History of the Treatment of Hepatitis C*, at 6.

<sup>42</sup> VICTRELIS Prescribing Information (2011), available at [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2011/202258lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/202258lbl.pdf); INCIVEK Prescribing Information (2011), available at [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2011/201917lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/201917lbl.pdf).

<sup>43</sup> OLYSIO Prescribing Information (2013), available at [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2013/205123s001lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/205123s001lbl.pdf); SOVALDI Prescribing Information (2013), available at [http://www.accessdata.fda.gov/spl/data/24e7ec0a-9f1b-4b63-8e48-53a63cd7c46f.xml](http://www.accessdata.fda.gov/spl/data/24e7ec0a-9f1b-4b63-8e48-53a63cd7c46f/24e7ec0a-9f1b-4b63-8e48-53a63cd7c46f.xml).

in January 2014, the American Association for the Study of Liver Disease (AASLD) recommended that providers combine Sovaldi with Olysio for patients who could not tolerate interferon-based therapies. This off-label combination comprised approximately one-third of all Sovaldi-based treatments by the second quarter of 2014.<sup>44</sup> The off-label drug combination further increased the cost of treatment for a portion of the patient population, primarily genotype 1 patients who could not tolerate interferon.

In October 2014, nine months after the AASLD recommendation, the FDA approved Gilead's ledipasvir-sofosbuvir (Harvoni), the first FDA-approved interferon-free HCV therapy for genotype 1 patients.<sup>45</sup> In November 2014, the FDA approved Johnson & Johnson's application for the AASLD-recommended Olysio-Sovaldi combination,<sup>46</sup> but use of these drugs and their combination has fallen due to market competition from Viekira Pak and Harvoni<sup>47</sup> (see slide below).<sup>48</sup> In December 2014, the FDA approved another interferon-free regimen, consisting of a combination of drugs—ombitasvir, paritaprevir, ritonavir, and dasabuvir (Viekira Pak).<sup>49</sup> Notably, Harvoni is a single-tablet therapy, whereas Viekira Pak is a multi-tablet therapy.

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<sup>44</sup> Appendix E, Ex. 5, Gilead Sciences, Inc., Miscellaneous powerpoint slides (2014), GS-0019034, at GS-0019036.

<sup>45</sup> HARVONI Prescribing Information (2014), available at <http://www.accessdata.fda.gov/spl/data/a3f06ce8-e0c0-4d41-9126-c43c94e4c87c/a3f06ce8-e0c0-4d41-9126-c43c94e4c87c.xml>.

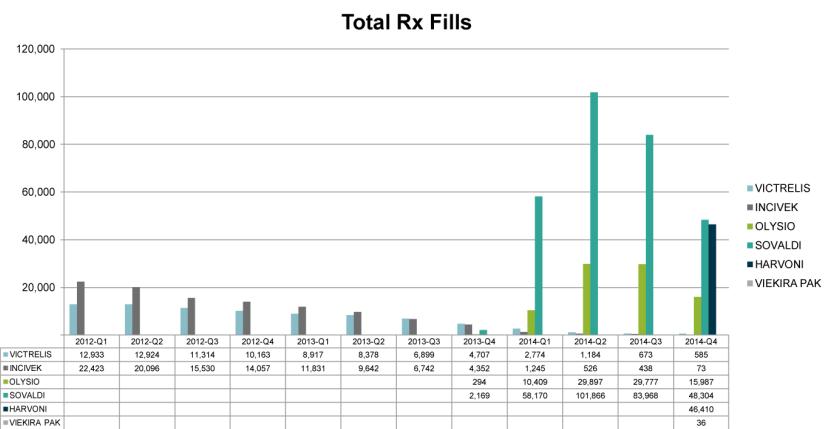
<sup>46</sup> Anna Edney, *J&J Wins U.S. Approval for Hepatitis C Combo with Gilead*, Bloomberg (Nov. 5, 2014), available at <http://www.bloomberg.com/news/articles/2014-11-05/j-j-wins-u-s-approval-for-hepatitis-c-combo-with-gilead>.

<sup>47</sup> Olysio generated revenue of \$234 million during the first three months of 2015, an annualized pace of \$936 million, compared to \$2.3 billion in sales during the full year 2014.

<sup>48</sup> Appendix D, Ex. 1, Email from Ann Walker-Jenkins, Director, Federal Government Affairs, CVS Health Corp., to Peter Gartrell (Mar. 9, 2015), attaching written response to investigative staff, at 6.

<sup>49</sup> VIEKIRA PAK Prescribing Information (2014), available at <http://www.accessdata.fda.gov/spl/data/045ddc2b-403e-7db2-b3e1-9627632ab3d7/045ddc2b-403e-7db2-b3e1-9627632ab3d7.xml>.

## Industry HCV Treatment Trend



Source: IMS data Jan 2012 to Dec 2014



Even after competition entered the genotype 1 market, Sovaldi was the only drug that the FDA had approved to treat genotypes other than genotype 1—its label included indications for the treatment of genotypes 1, 2, 3, and 4 patients. Consequently, Gilead did not face significant competition in the U.S. for genotype 2 or 3 treatments besides the interferon-ribavirin combination, which has significantly worse side effects and, in some genotypes, worse outcomes. On July 24, 2015, the FDA approved daclatasvir (Daklinza) for treatment of genotype 3; however, its label indicates that it should be used in combination with Sovaldi,<sup>50</sup> which means there remains no standalone competitor. The AASLD has added the Daklinza-Sovaldi combination to its recommended treatment regimens for genotype 1 and 2 patients. In addition, the FDA has approved a combination of ombitasvir, paritaprevir, and ritonavir (Technivie) for genotype 4 patients without cirrhosis.<sup>51</sup>

### Fibrosis and Patient “Warehousing”

The severe side effects of interferon-based regimens coupled with the anticipation of new, more tolerable treatment regimens, and the slow progression of HCV, caused many providers to advise their HCV patients to wait until more tolerable and effective therapies came to market. This practice is known as “warehousing.” Providers warehoused patients based in part on fibrosis scores, which correspond with declining liver function and range from 0 (no fibro-

<sup>50</sup> DAKLINZA Prescribing Information (2015), available at <http://www.accessdata.fda.gov/drugsatfda/docs/label/2015/206843Orig1s000lbl.pdf>.

<sup>51</sup> TECHNIVIE Prescribing Information (2015), available at <http://www.accessdata.fda.gov/drugsatfda—docs/label/2015/207931Orig1s000lbl.pdf>.

sis) to 4 (severe fibrosis or cirrhosis).<sup>52</sup> Warehousing can result in sharply increased demand when an anticipated treatment comes to market. Fibrosis scores played two key roles in the recent debate over HCV treatment in part because low fibrosis scores are an indicator of a patient's ability to forestall treatment. Patients with early stages of the disease (fibrosis scores of 0, 1 or 2) were frequently advised to wait until new drugs were released before beginning treatment. The rationale was that there would be better outcomes for patients who could medically afford to wait on new treatments with shorter durations, higher cure rates, and fewer side effects.

Warehousing had previously occurred in 2000, in anticipation of the FDA's approval of pegylated interferon, and again in 2010, leading up to the approval of DAA medications. Warehousing has been a focus of pharmaceutical makers, Wall Street analysts, and the financial press because pent up demand materially affects revenue when regulatory approvals for improved treatments are anticipated. Such warehousing with HCV medications was noted in 2000 ahead of regulatory approval of pegylated interferon:

One issue is a study released in late October showing that Schering-Plough Corp.'s experimental hepatitis drug Peg-Intron is more effective than the standard treatment for hepatitis C when the drug is combined with ICN's ribavirin. The study compared the combination to the standard therapy of ribavirin and Intron A, a combination sold by Schering-Plough as Rebetron. The study results "have led to some speculation that doctors may be warehousing their patients instead of giving them Rebetron now as they wait for approval of Peg-Intron and ribavirin," Smith said. If that's true, that could lead to a temporary weakness in ribavirin sales, Smith said.<sup>53</sup>

Again in 2010, warehousing occurred leading up to approval of the first DAA medications:

At Fred Poordad's bustling hepatitis C clinic in the heart of Los Angeles, one in every five patients receives no treatment. They are waiting for a wave of new drugs, expected in the next 18 months, that may boost their chance at a cure by as much as 10-fold. The medicines also may bolster the prospects of Merck & Co., Vertex Pharmaceuticals Inc. and Johnson & Johnson, the companies in a race to get the first new treatment to the market in a decade. About half of patients can't tolerate the side effects of existing therapies, which generate \$2 billion annually in sales. The new drugs could expand the market to \$10 billion in five years,

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<sup>52</sup>Marc G. Ghany et al., *Diagnosis, Management, and Treatment of Hepatitis C: An Update*, 49 *Hepatology* 1335 (2009), available at <http://onlinelibrary.wiley.com/doi/10.1002/hep.22759/abstract>.

<sup>53</sup>Karen Fessler, *Panic Abandons Plan to Sell 50,000 ICN Shares*, L.A. Times (Dec. 14, 2000), available at <http://articles.latimes.com/2000/dec/14/business/fi-47>.

said Geoff Porges, an analyst for Sanford C. Bernstein & Co. in New York.<sup>54</sup>

With the expected introduction of new, more effective HCV drugs, Pharmasset noted the projected effect of warehousing on the market in financial filings after Gilead announced its intention to buy the company: “Warehousing in 2012 and 2013 results in the 2011 treatment rate being halved for these years. The treatment rate then accelerates in 2014 to twice the 2011 treatment rate and remains stable through the end of the forecast period.”<sup>55</sup> In a 2013 New York Times article, Dr. Scott Friedman explained the rationale behind the patient warehousing that occurred in anticipation of Sovaldi:

Many doctors are now “warehousing” their hepatitis C patients—urging them to forgo treatment until the new drugs are approved. “There’s no way I’m going to put them on an interferon regimen when we’re a year away from having interferon-free regimens,” said Dr. Scott Friedman, the chief of liver diseases at the Icahn School of Medicine at Mount Sinai. “It’s rare you have to pull the trigger and get them on treatment in that period of time.” Gilead estimates that only 58,000 Americans with hepatitis C are now undergoing treatment, a small fraction even of those who know they are infected. Wanting to avoid interferon’s side effects, some patients without symptoms try to monitor their liver and start treatment only if it shows signs of deterioration. But with the new more tolerable treatments, some experts say, it makes sense to treat early-stage disease to prevent cirrhosis and the accompanying risk of liver cancer.<sup>56</sup>

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<sup>54</sup> Michelle Cortez & Naomi Kresge, *Warehoused Hepatitis C Patients May Boost Merck, J&J*, Bloomberg (Apr. 19, 2010), available at <http://www.bloomberg.com/news/articles/2010-04-18/warehoused-hepatitis-c-patients-may-boost-sales-for-merck-j-j-vertex>.

<sup>55</sup> Pharmasset, Inc. Amendment No. 2 to Solicitation/Recommendation Statement Under Section 14(d)(4) of the Securities Exchange Act of 1934 (Schedule 14D-9), at 9 (Dec. 20, 2011), available at <http://www.sec.gov/Archives/edgar/data/1301081/000119312511347237/d270458ds14d9a.htm>.

<sup>56</sup> Andrew Pollack, *Hepatitis C, A Silent Killer, Meets Its Match*, N.Y. Times (Nov. 4, 2013), available at [http://www.nytimes.com/2013/11/05/health/hepatitis-c-a-silent-killer-meets-its-match.html?pagewanted=all&\\_r=0](http://www.nytimes.com/2013/11/05/health/hepatitis-c-a-silent-killer-meets-its-match.html?pagewanted=all&_r=0).

## **Section 2: Gilead's Acquisition of Pharmasset and the Final Approval Phase for Sovaldi**

### **Pharmasset's Path From University Labs to Hepatitis C Front-Runner**

Pharmasset was launched by four medical researchers in 1998, with its first headquarters in a suburb of Atlanta. Soon thereafter, the company signed licensing agreements for drug candidates discovered during university-based research and signed additional agreements with several pharmaceutical companies.<sup>57</sup>

As Pharmasset prepared to become a publicly traded company in 2006, it focused on the clinical development of drugs to treat HIV, Hepatitis B, and HCV.<sup>58</sup> By 2008, Pharmasset's financial filings showed that it began spending money on pre-clinical studies for PSI-7977, which Gilead would eventually market as Sovaldi, and include as a component of Harvoni.<sup>59</sup> Between 2008 and 2011, Pharmasset spent \$62.4 million researching and developing PSI-7977.<sup>60</sup> Those research funds included a federal grant of \$244,479.25 awarded under the Qualifying Therapeutic Discovery Program for development of PSI-7977.<sup>61</sup>

Pharmasset executives understood PSI-7977's potential as a drug candidate. More than a year before acquisition talks began with Gilead, Pharmasset executives informed their board of directors that the drug's safety and efficacy profile proved promising in clinical trials, and that PSI-7977 "is less risky than other drugs at this stage of development."<sup>62</sup> Pharmasset received unsolicited buyout offers from other pharmaceutical companies, prompting the company to engage Morgan Stanley as an advisor.<sup>63</sup>

Pharmasset executives also continued to press the board for supplemental budget approvals to carry on development of PSI-7977.<sup>64</sup> Executives discussed and explored ways to turn a small firm focused on research into a company that sold HCV drugs internationally.<sup>65</sup> According to an internal slide presentation, the FDA told the company on August 18, 2011 that PSI-7977 "could enable [a] rapid transition away from interferon AND ribavirin," and that agency officials "were supportive of a rapid move to monotherapy in order to eliminate both interferon and ribavirin."<sup>66</sup> On November 6,

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<sup>57</sup> Pharmasset, Inc., Registration Statement (Form S-1), at F-21 (May 8, 2006), available at <http://www.sec.gov/Archives/edgar/data/1301081/000119312506103750/ds1.htm>.

<sup>58</sup> *Id.*

<sup>59</sup> Appendix F, Gilead Sciences, Inc., Response to Chairman Wyden/Senator Grassley letter dated July 11, 2014, narrative answer to question 6a (Sept. 9, 2014).

<sup>60</sup> *Id.*

<sup>61</sup> *Qualifying Therapeutic Discovery Project Grants for the State of New Jersey*, Internal Revenue Service (May 7, 2015), available at <http://www.irs.gov/Affordable-Care-Act/Affordable-Care-Act-Tax-Provisions>.

<sup>62</sup> Appendix E, Ex. 6, Pharmasset, Board of Directors meeting packet (July 21, 2010), GS-0014970 at GS-0015031-GS-0015039.

<sup>63</sup> Pharmasset, Inc. Solicitation/Recommendation Statement Under Section 14(d)(4) of the Securities and Exchange Act of 1934 (Schedule 14D-9) (Dec. 6, 2011), at 8-12, available at <http://www.sec.gov/Archives/edgar/data/1301081/000119312511331226/d265035dsc14d9.htm>.

<sup>64</sup> Appendix E, Ex. 7, Pharmasset, Board of Directors Memorandum (Sept. 16, 2011), GS-0017760.

<sup>65</sup> Appendix E, Ex. 8, *Global Commercialization Strategy Update to Pharmasset Board of Directors* (2011), GS-0003852.

<sup>66</sup> Appendix E, Ex. 9, PSI-7977 Phase II Clinical Trial Data Review (Oct. 3, 2011), GS-0011638, at GS-0011640.

2011, just two weeks before announcing its acquisition by Gilead, Pharmasset publicly unveiled the results of a Phase 2 FDA trial dubbed “ELECTRON,” which showed that PSI-7977 effectively cured all 40 of the genotype 2 and 3 participants, including 10 who had not used interferon.<sup>67</sup>

Jim Meyers, Gilead vice president of North American commercial operations, told investigative staff that the data release was better than Gilead expected. It provided a better view and a more bullish view of all of the variables that came into play, including assumptions about the drug’s launch year, its eventual market penetration, overall disease prevalence and geographic distribution.<sup>68</sup>

Pharmasset’s Phase 2 success with PSI-7977 came against a backdrop of stiff competition. In 2011, the first drugs that directly attacked HCV had been released, and a herd of pharmaceutical companies was racing to be the first with an interferon-free therapy, as described in a 2010 memo from Pharmasset’s executives to its board:

[M]ost big pharmaceutical companies with antiviral franchises are expecting HCV to be the next big antiviral market and are placing a strong emphasis on quickly establishing market leadership through the use of direct acting antivirals to improve the efficacy of current therapy with the hope of decreasing the duration of interferon therapy. This will be quickly followed by combinations of direct acting antivirals in hopes of eliminating interferon therapy.<sup>69</sup>

Given the promising data from clinical trials and the potential market for improved HCV therapies, Pharmasset’s PSI-7977 was well-positioned to be a market leader. Gilead was aware of this potential.

#### **Gilead’s Concern About a Weak Product Pipeline**

Gilead was not only concerned about ensuring it could acquire Pharmasset’s promising molecule, it was aware that it could move too slowly and miss the chance to purchase the company in a highly competitive industry. Gilead and its bankers code-named the acquisition “Project Harry,” with the companies named after characters from the children’s novel *Harry Potter*—Pharmasset was referred to as “Harry” and Gilead was “Gryffindor.” In a presentation titled “Introduction to Project Harry” on July 21, 2011, Gilead COO John Milligan stated that “Harry is the best, and most timely, way to bring a nucleotide to Gilead’s portfolio,” and the company was “unlikely to be available a year from now” because it is an “[a]ttractive acquisition for several companies.”<sup>70</sup>

Presentations to Gilead’s board suggest that absent its own promising drug compounds, the purchase of Pharmasset was the

<sup>67</sup> *Twelve Weeks Interferon-Free PSI-7977 Regimen Cures 100 Percent Hep C Genotype 2/3*, Hep Mag (Nov. 6, 2011), available at [http://www.hepmag.com/articles/psi7977\\_svr\\_hcv\\_2501\\_21405.shtml](http://www.hepmag.com/articles/psi7977_svr_hcv_2501_21405.shtml).

<sup>68</sup> Interview with Jim Meyers, Senior Vice President, North America Commercial Organization, Gilead Sciences, Washington, D.C. (Dec. 1, 2014).

<sup>69</sup> Appendix E, Ex. 6, Pharmasset, Board of Directors meeting packet (July 15, 2010), GS-0014970, at GS-0015031—0015042.

<sup>70</sup> Appendix E, Ex. 10, Gilead Sciences, Inc., *Introduction to Project Harry* (July 21, 2011), GS-0019211, at GS-0019214.

primary route for the company to compete in the HCV market. Barclays summarized the strategic rationale in the days before the acquisition was announced:

- Diversifies Gryffindor's business outside of **HIV** while leveraging Gryffindor's area of expertise
- Harry acquisition accelerates Gryffindor's development program in the treatment of **HCV**
- Harry's nucleotide analog PSI-7977 and portfolio of nucs have demonstrated potency and effectiveness in 700+ patients without safety or resistance concerns
- Gryffindor's expertise in anti-viral therapies positions it as the company uniquely capable of maximizing Harry's **HCV** commercial opportunity<sup>71</sup>

More than a year before acquisition talks began, Pharmasset executives presented a case study to the company's board that succinctly summarized their view of Gilead's difficulties in HCV drug development:

Today, Gilead is left wondering what to do in HCV. As a result of their lack of success in HCV, they hired John McHutchison to head their Hepatitis development efforts in June 2010. The very clear signals from Gilead and John are that they will be making some strategic moves in HCV.<sup>72</sup>

The expectation of a strategic move was partially due to Gilead's own difficulties in developing an HCV drug. As negotiations with Pharmasset began in September 2011, Gilead announced another setback for one of its HCV drugs, GS-9190, forcing the company to alter study protocols after patients in two studies reported adverse side effects.<sup>73</sup> A presentation to Gilead's board of trustees in October 2011 showed that as late as 2010, Gilead had been aiming for a "broad genotypic oral antiviral" in 2020, but that "the competitive nature of the field and speed of development has now compacted the timelines" to within just a few years.<sup>74</sup> Another presentation showed that Gilead's advisory board expected an all-oral therapy "very soon," that "[development] [t]imelines are shrinking rapidly," and that the "[f]ield is moving very fast; faster than anyone anticipated."<sup>75</sup> The presentation stated that Pharmasset was recruiting patients to its clinical trials faster than any other company, and concluded that the company "has established the fastest pathway forward with the simplest regimen that is furthest along."<sup>76</sup> These presentations made clear that Gilead's lack of success in its HCV

<sup>71</sup> Appendix E, Ex. 11, Barclays, Description of Fairness Opinion (Nov. 13, 2011), GS-0011877, at GS-0011880 (emphasis in original).

<sup>72</sup> Appendix E, Ex. 6, Pharmasset, Board of Directors meeting packet (July 15, 2010), GS-0014970, at GS-0015031—0015061.

<sup>73</sup> Press Release, Gilead Sciences, Inc., Gilead Amends Study Design for Ongoing Hepatitis C Clinical Trials That Include GS 9190, Pegylated Interferon and Ribavirin, and Another Direct-Acting Antiviral Agent (Sept. 4, 2011), available at <http://www.gilead.com/news/press-releases/2011/9/gilead-amends-study-design-for-ongoing-hepatitis-c-clinical-trials--that-include-gs-9190--pegylated-interferon-and-ribavirin-and-another--directacting-antiviral-agent>.

<sup>74</sup> Appendix E, Ex. 12, Gilead Sciences, Inc., *Gilead Liver Disease Franchise: BOD Strategic Review* (2011), GS-0019275, at GS-0019285—0019286.

<sup>75</sup> Appendix E, Ex. 13, Gilead Sciences, Inc., *Harry Update* (Oct. 7, 2011), GS-0019236, at GS-0019239.

<sup>76</sup> *Id.* at GS-0019246.

pipeline and its desire to remain competitive increased both the value and importance of acquiring Pharmasset's promising therapies.

### **The \$11.2 Billion Acquisition of Pharmasset**

On January 17, 2012, Gilead Sciences, Inc., announced the completion of its \$11.2 billion purchase of Pharmasset, Inc. Gilead executives were confident in Pharmasset's HCV drug candidate, which was entering the final phase of testing for regulatory approval. However, when the acquisition was first announced on November 21, 2011, it triggered a selloff of Gilead stock, and was panned by financial analysts who deemed the deal as extremely risky:

Investors balked at the deal on Monday, with shares of Gilead falling 9 percent on the announcement. "For Gilead to give up effectively one-third of their value for an unproven asset still subject to significant ongoing clinical risk seems remarkable," Geoffrey Porges, biotechnology analyst at Sanford C. Bernstein & Company, wrote in a note Monday. Thomas Wei of Jefferies & Company estimated that Gilead's sales of hepatitis C drugs would have to reach \$4 billion a year—difficult, but not impossible—to justify the purchase price.<sup>77</sup>

Despite doubts among analysts and investors, Gilead executives were confident that Pharmasset was developing a molecule that would revolutionize HCV treatment by potentially removing interferon from therapy in the future. Furthermore, executives were willing to pay a premium because, as noted above, Gilead's own efforts at developing HCV drugs were not succeeding and were not progressing as quickly as needed to keep up with competitor companies.

Although a company executive told investigative staff that Gilead was taking an extraordinary risk in buying Pharmasset,<sup>78</sup> documents provided by the company suggest that executives were very confident in sofosbuvir's ability to gain FDA approval. Gilead slides highlighted an "[e]xcellent safety profile (no measureable side effects in any patients to date)" headed into Phase 3 testing as well as high cure and response rates for genotype 1 patients with and without interferon.<sup>79</sup> The confidence stemmed from months that Gilead, in conjunction with advisors from Barclays and Bank of America, had spent studying the global HCV market and potential revenue streams from a hypothetical "Harry-Gryffindor" acquisition. The acquisition team had studied proprietary financial and research data provided by Pharmasset under non-disclosure agreements, and provided regular reports to executives and the Board of Directors at Gilead.

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<sup>77</sup> Andrew Pollack & Michael J. De La Merced, *Gilead to Buy Pharmasset for \$11 Billion*, N.Y. Times (Nov. 21, 2011), available at [http://dealbook.nytimes.com/2011/11/21/gilead-to-buy-pharmasset-for-11-billion/?\\_r=0](http://dealbook.nytimes.com/2011/11/21/gilead-to-buy-pharmasset-for-11-billion/?_r=0).

<sup>78</sup> Interview with Jim Meyers, Senior Vice President, North America Commercial Organization, Gilead Sciences, Inc., in Washington, D.C. (Oct. 30, 2014).

<sup>79</sup> Appendix E, Ex. 13, Gilead Sciences, Inc., *Harry Update* (Oct. 7, 2011), GS-0019236 at GS-0019240.

The information left Gilead's leadership sufficiently convinced of PSI-7977's promise, that the company increased its offer 37% during the 11 weeks spent negotiating the deal—from \$100 per share to the final offer price of \$137 per share.<sup>80</sup> That was a 59% premium to the all-time high price for Pharmasset stock.<sup>81</sup>

John McHutchison, who would be an important player in the eventual pricing of Sovaldi, was deeply involved in the acquisition process. A medical doctor and well-known HCV researcher, McHutchison had been a consultant to Pharmasset before joining Gilead as senior vice president, liver disease therapeutics, and a member of the company's executive team.<sup>82</sup> Shortly before the deal closed, McHutchison described the purchase of Pharmasset as a "bargain" in an email to Matthew Young at Barclays, which served as Gilead's acquisition advisor. In the same email, dated January 7, 2012, McHutchison wrote that Bristol-Meyers Squibb acted in "desperation" when the company paid \$2.5 billion to purchase another small biotechnology firm developing a different HCV drug.<sup>83</sup>

In 2014, the first year that Gilead marketed Sovaldi and Harvoni, the company reported \$12.4 billion in worldwide HCV sales,<sup>84</sup> more than three times the amount that Jefferies & Company projected being needed to justify the purchase of Pharmasset. The company expects sales of its HCV drugs to grow in 2015, having reported net product sales of \$14.3 billion during the year's first nine months.<sup>85</sup>

### **Pharmasset Expected 12-Week HCV Treatment to Cost \$36,000**

Gilead's eventual selling price for Sovaldi was substantially higher than what Pharmasset expected to charge. Specifically, after the acquisition was announced, Pharmasset filed with the Securities and Exchange Commission on December 6, 2011, showing it projected to sell PSI-7977 for \$36,000 per treatment regimen in the United States, with discounted prices in the European Union.<sup>86</sup> Gilead ultimately set the price of Sovaldi at \$84,000 for a single 12-week treatment course, more than twice as high as Pharmasset's public projection at the time the acquisition was announced.

Gilead claims that Pharmasset actually projected a higher selling price than \$36,000. In particular, Gilead's outside counsel directed

<sup>80</sup> Pharmasset, Inc. Solicitation/Recommendation Statement Under Section 14(d)(4) of the Securities and Exchange Act of 1934 (Schedule 14D-9) (Dec. 6, 2011), at 8–12, available at <http://www.sec.gov/Archives/edgar/data/1301081/000119312511331226/d265035dsc14d9.htm>.

<sup>81</sup> Press Release, Gilead Sciences, Inc., Pharmasset, Inc., Gilead Sciences to Acquire Pharmasset, Inc. for \$11 Billion (Nov. 21, 2011), available at <http://www.sec.gov/Archives/edgar/data/882095/000119312511317734/d259746dex991.htm>.

<sup>82</sup> Press Release, Gilead Sciences, Inc., John G. McHutchison, MD, to Join Gilead Sciences as Senior Vice President, Liver Disease Therapeutics (June 8, 2010), available at <http://investors.gilead.com/phoenix.zhtml?c=69964&p=irol-newsArticle&ID=1436018>.

<sup>83</sup> Appendix E, Ex. 2, Gilead Sciences, Inc., Emails between Matthew Young, Barclays Capital, and John McHutchison (Jan. 7, 2012), GS-0010634.

<sup>84</sup> Gilead Sciences, Inc. Annual Report (Form 10-K) (Feb. 25, 2015), available at <http://www.sec.gov/Archives/edgar/data/882095/000088209515000008/a2014form10-k.htm>.

<sup>85</sup> Press Release, Gilead Science, Inc., Gilead Sciences Announces Second Quarter 2015 Financial Results (July 28, 2015), available at <http://www.sec.gov/Archives/edgar/data/882095/000088209515000022/exhibit991earningspressrel.htm>.

<sup>86</sup> Pharmasset, Inc. Solicitation/Recommendation Statement Under Section 14(d)(4) of the Securities and Exchange Act of 1934 (Schedule 14D-9) (Dec. 6, 2011) at 32, available at <http://www.sec.gov/Archives/edgar/data/1301081/000119312511331226/d265035dsc14d9.htm>.

investigative staff to Pharmasset's amended 14-D filing, which projects a price range of \$36,000 to \$72,000 for U.S. customers, filed on December 20, 2011.<sup>87</sup> Investigative staff's review of documents provided during the course of the investigation show that Pharmasset's executives and board of directors were presented with this price range immediately before the acquisition was announced, but the \$72,000 price did not appear to play a role as the company considered selling to Gilead.

Documents show that the \$72,000 price for PSI-7977 first appeared on November 18, 2011, three days before the acquisition was announced. That day, Pharmasset CEO Schaefer Price emailed a presentation to the company's board of directors. The presentation states that the "price for 7977 + RBV ranges from \$36,000 (Victrelis only) to \$72K (Incivek + SOC). This does not reflect any price premium or cost savings to payers."<sup>88</sup> The presentation also states that the then-current cost to treat patients with protease inhibitors ranged from "\$65K to \$74K based on length" of treatment. Importantly, though, the price increases were not included in the presentation's forecast model.<sup>89</sup>

On the same day as the Price email, Morgan Stanley presented slides to the Pharmasset board containing a matrix titled "Pricing Sensitivity—Mgmt. Case."<sup>90</sup> In this matrix, unit pricing of \$72,000 translates to a price of \$290 per share.<sup>91</sup> This amount per share is more than twice the purchase price the board approved from Gilead less than 72 hours later. This suggests that Pharmasset did not view \$72,000 as a realistic price. Moreover, in that presentation, all of the management cases—downside, base, and upside—used \$36,000 as the price for PSI-7977. The management case "represents management's view of the most probable scenario in light of recent developments in the Hepatitis C landscape."<sup>92</sup>

Other documents from earlier in the year further demonstrate that Pharmasset had not contemplated pricing PSI-7977 nearly as high as Gilead would eventually price Sovaldi. One document contains a presentation prepared by Morgan Stanley with financial analysis prepared in its advisory role to Pharmasset. These presentations contained a matrix like the one below estimating the per-

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<sup>87</sup> Pharmasset, Inc., Amendment No. 2 to Solicitation/Recommendation Statement Under Section 14(d)(4) of the Securities Exchange Act of 1934 (Schedule 14D-9) (Dec. 20, 2011), available at <http://www.sec.gov/Archives/edgar/data/1301081/000119312511347237/d270458dsc14d9a.htm>.

<sup>88</sup> Appendix E, Ex. 14, Email from Schaefer Price to Herb Conrad, et al., "FW: Forecast Assumptions," November 18, 2011, GS-0018378; Appendix E, Ex. 15, Pharmasset, Inc., "Adjustments to Forecast Assumptions, Based on Learnings from AASLD" (Nov. 18, 2011), GS-0018379 at GS-0018380. At the time, clinical guidelines recommended using Victrelis (boceprevir) in combination with peg-interferon/ribavirin for 24 to 44 weeks; guidelines recommended that Incivek be used for 12 weeks in combination with peg-interferon/ribavirin, with an additional 12 to 36 weeks of peg-interferon/ribavirin. See Table 2 in Mark G. Ghany et al., *An Update on Treatment of Genotype 1 Chronic Hepatitis C Virus Infection: 2011 Practice Guideline by the American Association for the Study of Liver Diseases*, 54 Hepatology 1433, 1433–44 (Oct. 2011), available at <http://doi.org/10.1002/hep.24641>.

<sup>89</sup> Appendix E, Ex. 15, Pharmasset, Inc., "Adjustments to Forecast Assumptions, Based on Learnings from AASLD" (Nov. 18, 2011), GS-0018379, at GS-0018380.

<sup>90</sup> A management case is typically the financial model that executives believe is most likely reflective of a company's business on a go-forward basis or the model that management is using to make planning decisions.

<sup>91</sup> Appendix E, Ex. 16, Morgan Stanley, Project Royal Discussion Materials (Nov. 18, 2011), GS-0018382, at GS-0018396.

<sup>92</sup> *Id.* at GS-0018393.

share value of Pharmasset correlated with the expected prices for PSI-7977 and another drug candidate, PSI-938:<sup>93</sup>

## Pricing Sensitivity - Base Case

\$ / Share

		Price per Unit - 7977		
		\$24,000	\$36,000	\$50,000
Price per Unit - 938	\$24,000	\$84	\$123	\$168
	\$36,000	\$93	\$131	\$177
	\$50,000	\$103	\$141	\$186

The above pricing sensitivity matrix suggests that if Pharmasset expected PSI-7977 to sell for \$50,000, the company would have expected its market value to range from \$13.7 billion to \$15.2 billion—between 22.6% and 35.7% higher than the price that was actually garnered from Gilead.<sup>94</sup> Similarly, presentations in May 2011 and July 2011 show that the highest price points being discussed in modeling were \$24,000 and \$36,000, the latter of which was dubbed the “management case.”

Lastly, a presentation from September 2011 shows the price of manufacturing PSI-7977 in relation to the price of therapy. While the drug was being manufactured for testing, Pharmasset calculated the production cost to be \$32,000 per kilogram, or \$1 per 1,200-milligram caplet.<sup>95</sup> Pharmasset expected production costs to be cut by almost two-thirds to \$11,000 per kilogram when commercial-scale operations began.<sup>96</sup> The presentation shows that manufacturing costs for Pharmasset would be de minimis compared to

<sup>93</sup> Appendix E, Ex. 17, Morgan Stanley, Project Royal Discussion Materials (Oct. 6, 2011), GS-0002762.

<sup>94</sup> To determine this estimate, investigative staff compared the tender price Gilead offered Pharmasset shareholders when the 2011 transaction took place (\$137/share) with the Morgan Stanley pricing sensitivity matrix. *Id.* The matrix projected different share prices for Pharmasset based on prices for PSI-7977 and PSI-938. The column in which PSI-7977 was priced at \$50,000 had a range of share prices as low as \$168 (with PSI-938 at \$24,000) and \$186 (with PSI-938 at \$50,000), which are 122.6% and 135.7% of the tender price. Staff used those percentage differences to multiply the final purchase Gilead paid for Pharmasset (\$11.2 billion) to arrive at a range of \$13.7 billion and \$15.2 billion.

<sup>95</sup> Appendix E, Ex. 18, Pharmasset, Untitled Presentation by Pharmasset Executives (Sept. 2011), GS-0011557 at GS-0011588.

<sup>96</sup> *Id.* at GS-0011581.

the revenue each course of therapy would generate—ranging from 0.9% for a \$50,000 course to 1.5% for a \$30,000 course:<sup>97</sup>

### PSI-7977 12 week Regimen Cost of Goods

Price per Course of Therapy			
API Cost/kg	\$50,000	\$40,000	\$30,000
\$32,000	2.3%	2.9%	3.9%
\$11,000	0.9%	1.1%	1.5%

Assumptions:

- Every patient (all genotypes) is treated with 12 week 400mg QD regimen – 84 caplets
- Regimen manufacturing cost (84 caplets) is \$370 @ \$11,000/Kg and \$1075 @ \$32,000/Kg
- Drug product cost is ~\$1 per 400mg caplet
- API cost and price of therapy indicated above

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Thus, it appears that, based on internal presentations given between five months and three days before the announcement of Gilead's acquisition of Pharmasset, Pharmasset did not intend to sell PSI-7977 for prices exceeding \$50,000. In particular, the range that was presented to the board while the acquisition was in its final stages indicate that the financial impacts of the higher end of the drug price range would have meant Pharmasset was substantially undervaluing itself.

### Gilead Did Not Contemplate a Price Above \$75,000 Leading up to Acquisition

On November 13, 2011, less than two weeks before the deal was announced, Barclays gave a presentation to Gilead that suggests Gilead was considering a price range of \$55,000 to \$75,000 for Sovaldi treatment to ensure suitable financial returns. The presentation referenced a gross price per patient in the United States of \$65,000 and included sensitivity analysis showing the revenue effect of increasing or decreasing the price by \$10,000 (resulting in the \$55,000 to \$75,000 range).<sup>98</sup> It is important to recognize that the figures in the presentation were projected gross prices, which is the price point before discounting to payers which results in a net price.

<sup>97</sup>Id. at GS-0011590.

<sup>98</sup>Appendix E, Ex. 19, Barclays Capital, *Revenue/Valuation Models: Project Harry* (Nov.13, 2011), GS-0013466, at GS-0013467, GS-00013474.

These figures were developed over the course of several months by Barclays in close partnership with a Gilead project team. Emails show that the pricing model had been through numerous iterations with Gilead's employees studying the model for market assumptions with respect to infection rates, cure rates, market share and other data points related to the HCV population domestically and abroad.<sup>99</sup>

Jim Meyers told investigative staff that the molecule's ultimate price was not a major consideration during the run-up to the purchase of Pharmasset.<sup>100</sup> Gilead had a rough but conservative estimate for drug prices, primarily based on the Barclays model.<sup>101</sup> Treatment rates, flow of patients and flow of diagnosis were the company's primary concern at that point.<sup>102</sup> Price was not unimportant, but the number of patients was more important to making the deal acceptable.<sup>103</sup>

Meyers referred investigative staff to the last page of a presentation from July 20, 2011, and a summary of assumptions, including an \$80,000 "price-per-cure" (the total cost of prescribing drugs divided by the number of cured patients results in an average price per cured patient), which was based on the price of telaprevir and boceprevir.<sup>104</sup> Price per cure is higher than the price of these drugs because some number of patients taking the drug would not be cured, and the initial treatment regimen required the use of interferon and/or ribavirin to also be administered.<sup>105</sup> That presentation assumed that the gross price of DAA drugs would start at \$63,500, equaling a price per cure of \$80,000.<sup>106</sup> The pricing assumption model showed that the cost-per-cure was projected to increase 3% annually, and assumes an 8% "convenience bump" in pricing when an all-oral, single-tablet drug came to market.<sup>107</sup> This appears similar to the strategy, detailed later in this report, which Gilead employed when it priced Sovaldi and Harvoni. Lastly, Barclays expected that American patients would be charged a premium for HCV treatments, compared to patients in Japan and Europe (see slide below).<sup>108</sup>

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<sup>99</sup> Appendix E, Ex. 20, Email from John McHutchison to Jonathan Piazza, Re: Project Pyramid Assumptions (June 21, 2011), GS-0004809; Appendix E, Ex. 21, Gilead Sciences, Inc., *Project Harry—Model Discussion* (Aug 16, 2011), GS-0005511.

<sup>100</sup> Interview with Jim Meyers, Senior Vice President, North America Commercial Organization, Gilead Sciences, Inc., in Washington, D.C. (Dec. 1, 2014).

<sup>101</sup> *Id.*

<sup>102</sup> *Id.*

<sup>103</sup> *Id.*

<sup>104</sup> Appendix E, Ex. 22, Gilead Sciences, Inc., *Project Harry—Barclays Deck Backgrounder* (July 20, 2011), GS-0000207, at GS-0000228.

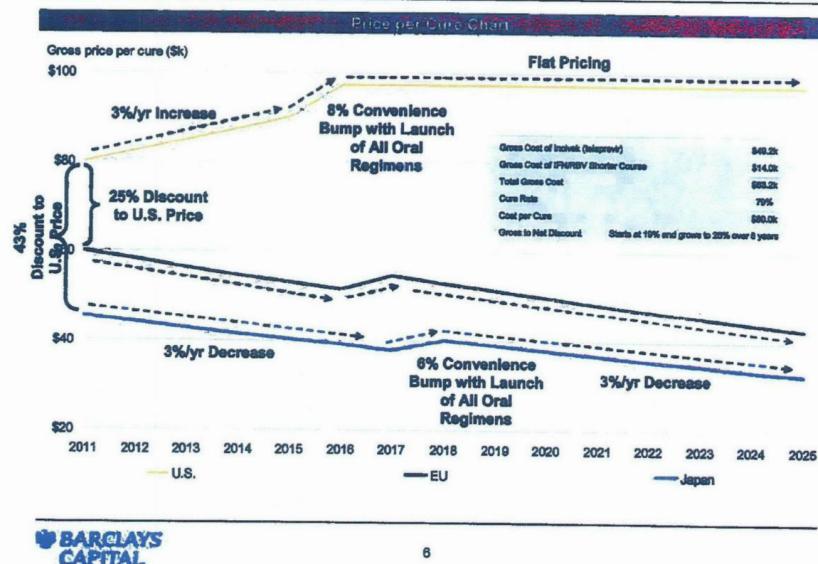
<sup>105</sup> *Id.* at GS-0000214.

<sup>106</sup> *Id.* at GS-0000219.

<sup>107</sup> *Id.*

<sup>108</sup> *Id.*

## Pricing Assumptions



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In sum, as the deal between Pharmasset and Gilead entered its final phase, Gilead executives believed that the purchase of Pharmasset would be profitable if the drug were sold for a gross price ranging from \$55,000 to \$75,000 before sales discounts were applied. A presentation one year after the sale suggests the company expected prices to be at the midpoint—i.e., \$65,000.<sup>109</sup> This was approximately \$20,000 less than what Gilead ultimately chose as the selling price.

### Complete R&D Costs for Gilead's Completion of the Approval Process for Sovaldi Were Not Provided

Gilead provided R&D spending data for “sofosbuvir-based regimens,” which include “any compound in R&D that uses sofosbuvir or is combined in development with sofosbuvir.”<sup>110</sup> Thus, the spending data may overstate the R&D costs associated with bringing Sovaldi to market because the data includes three compounds in addition to sofosbuvir as a single-agent drug.<sup>111</sup> Gilead failed to provide costs attributable solely to the development of Sovaldi, despite repeated requests to do so.

<sup>109</sup> Appendix E, Ex. 23, Gilead Sciences, Inc., *Hepatitis C and GS-7977 Development Update, HCV Strategy Review*, November 5, 2012, GS-0019442, at GS-0019461—GS-0019462.

<sup>110</sup> Appendix F, Gilead Sciences, Inc., Response to Chairman Wyden/Senator Grassley letter dated July 11, 2014, narrative answer to question 12 (Sept. 9, 2014).

<sup>111</sup> These four combinations were GS-7977 (sofosbuvir as a single-agent drug); GS-7977 in combination with GS-5885 (which would eventually become Harvoni); GS-7977 in combination with GS-5816; and GS-7977 in combination with GS-9813. Appendix E, Ex. 24, Gilead Sciences, Inc., *2012–2018 Financial Forecast* (Nov. 2012), GS-0019394 at GS-0019413.

Gilead said that its estimated R&D costs for sofosbuvir-based regimens would be \$880.3 million between 2012 and 2014.<sup>112</sup> The R&D costs that Gilead provided are detailed in table 1 below:

**Table 1—Gilead Sciences’ Research and Development Costs for Sofosbuvir-based Drug Regimens**

	2012	2013	2014 (estimated)
<b>Personnel Costs*</b> .....	\$45,195,000	\$51,770,600	\$74,765,423
<b>Clinical Studies/Contract Research Organization Costs**</b> .....	\$136,942,698	\$238,986,739	\$242,830,400
<b>Milestones/Licenses</b> .....	–	\$4,117,281	(\$2,907,678)
<b>Overhead Allocations/Facilities Costs/ Materials and Supplies</b> .....	\$27,859,182	\$29,339,061	\$31,367,638
<b>Total</b> .....	\$209,996,871	\$324,213,681	\$346,055,782
<b>Total 2012–2014</b> .....			<b>\$880,266,334</b>

Source: Gilead Sciences, Inc.

\* Gilead does not track expenses related to personnel costs, overhead allocation, facilities costs, and materials and supplies by therapeutic product candidate. Gilead estimated expenses by allocating based on a percentage of total employee headcount.

\*\* Section 14.1 of Sovaldi’s FDA label states “The safety and efficacy of SOVALDI was evaluated in five Phase 3 trials in a total of 1724 HCV mono-infected subjects with genotypes 1 to 6 chronic hepatitis C (CHC) and one Phase 3 trial in 223 HCV/HIV-1 co-infected subjects with genotype 1, 2 or 3 CHC.”<sup>113</sup>

As noted above, Pharmasset spent \$62.4 million between 2008 and 2011 researching and developing PSI-7977. Combined, this totals \$942.4 million. Gilead did note in its response to the senators’ letter that additional costs were expected for post-market release studies, but Gilead failed to detail those costs.<sup>114</sup>

By comparison, while negotiating its eventual sale to Gilead, executives for Pharmasset presented the company’s expected drug development costs for fiscal year 2012 (which began October 1, 2011):

Our budgeted development program expenses are \$125.0 million for fiscal 2012, up \$72.7 million from \$52.3 million in fiscal 2011. The main drivers of this substantial increase in our development expenses is the advancement of PSI-7977 into four Phase 2b studies (including the Phase 2b QUANTUM study), as well as 3 Phase 3 studies, and the advancement of PSI-938 into the QUANTUM study.<sup>115</sup>

<sup>112</sup> Appendix F, Gilead Sciences, Inc., Response to Chairman Wyden/Senator Grassley letter dated July 11, 2014, narrative answer to question 12 (Sept. 9, 2014).

<sup>113</sup> SOVALDI Prescribing Information, Section 14.1 (2013), available at <http://www.accessdata.fda.gov/spl/data/24e7ec0a-9f1b-4b63-8e48-53a63cd7c46f/24e7ec0a-9f1b-4b63-8e48-53a63cd7c46f.xml>.

<sup>114</sup> Appendix F, Gilead Sciences, Inc., Response to Chairman Wyden/Senator Grassley letter dated July 11, 2014, narrative answer to question 12 (Sept. 9, 2014).

<sup>115</sup> Appendix E, Ex. 25, Pharmasset, Inc., Board of Directors Packet (Oct. 11, 2011), GS-0017925, at GS-0017956.

Specifically, development costs for PSI-7977 were budgeted by Pharmasset to be \$90.5 million.<sup>116</sup> In the same presentation, Pharmasset executives projected that the Phase 3 studies for PSI-7977—the final clinical development needed for regulatory approval that Gilead was primarily engaged in after the merger—would total \$125.6 million.<sup>117</sup>

The spreadsheet on the following page provides specific, quarterly costs that Pharmasset budgeted for these studies.

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<sup>116</sup>*Id.*

<sup>117</sup>*Id.* at GS-0017966.

Development Programs	FQ1 '12 Budget	FQ2 '12 Budget	FQ3 '12 Budget	FQ4 '12 Budget	F '11 Budget	F '11 Actuals	Diff Ov (Und)	Total Study Costs
	\$	\$	\$	\$	\$	\$		
PSI-7977								
DMPK, Tox & Other	\$ 963	\$ 943	\$ 766	\$ 587	\$ 3,259	\$ 3,117	\$ 142	
Phase 1 & Clin Pharm	\$ 2,339	\$ 1,101	\$ 1,288	\$ 900	\$ 5,628	\$ 4,765	\$ 863	
Phase 2b - early studies	1,185	754	534	330	2,803	9,215	(6,412)	
Phase 2b - ATOMIC	2,615	1,670	1,156	693	6,134	9,465	(3,331)	
Phase 3 - Study 1	3,769	7,102	7,492	8,084	26,457	743	54,077	
Phase 3 - Study 2	428	3,124	5,624	6,588	15,764	-	36,286	
Phase 3 - Study 3		428	3,672	7,146	11,246	-	11,246	
Phase 3b - Rollover				500	500	-	500	
Phase 3b - Health Economics	7,251	4,088	5,137	1,729	18,205	10,339	7,866	
API	<u>\$ 18,550</u>	<u>\$ 19,210</u>	<u>\$ 25,669</u>	<u>\$ 27,067</u>	<u>\$ 90,496</u>	<u>\$ 37,644</u>	<u>\$ 52,832</u>	
PSI-938								
DMPK, Tox & Other	792	303	418	616	2,129	2,145	(16)	
Phase 1 & Clin Pharm	2,540	2,223	3,669	2,911	11,343	5,035	6,308	
Phase 2b - QUANTUM	3,421	4,541	4,205	5,678	17,845	2,251	15,594	\$ 49,480
API	<u>1,557</u>	<u>1,605</u>	<u>31</u>	<u>31</u>	<u>3,224</u>	<u>34,541</u>	<u>(742)</u>	
	<u>8,310</u>	<u>8,672</u>	<u>8,323</u>	<u>9,236</u>	<u>13,397</u>	<u>21,144</u>		
PSI-661	-	-	-	-	-	1,289	(1,289)	
Total	<u>\$ 26,860</u>	<u>\$ 27,882</u>	<u>\$ 33,992</u>	<u>\$ 36,303</u>	<u>\$ 125,037</u>	<u>\$ 52,330</u>	<u>\$ 72,707</u>	

### Gilead's Development Timeline Benefited from FDA Policies

Sovaldi was one in a series of HCV therapies that benefited from FDA policies designed to shorten the R&D process and broaden access to potentially lifesaving therapies (See Table 2). In the case of Sovaldi, the compressed timeline meant Gilead was afforded an opportunity to sell its therapy in the U.S. with minimal competition in the genotype 1 market for nearly a year.

Little more than a month before acquiring Pharmasset in 2011, Gilead executives reported to the board that changes to FDA standards regarding HCV testing protocols would benefit the purchase of Pharmasset and speed up the eventual approval of sofosbuvir. The agency would no longer require SVR to be tested 24 weeks after treatment ended. Instead, it would require an SVR follow-up at just 12 weeks.<sup>118</sup> Furthermore, studies using placebo-controlled trials would be accepted. As a result, Phase 3 studies would be “simpler and faster.”<sup>119</sup> Gilead executives believed that the probability of successfully reaching the market increased along with the “truncated timelines for approval.”<sup>120</sup>

By November 2012, McHutchison reiterated to the board that “the timelines have shortened considerably for both GS-7977 as a single agent and GS-7977 combinations,” in a presentation that referred to additional conversations with the FDA (when Gilead acquired Pharmasset, the PSI-7977 became GS-7977). A presentation made on the same day first referenced the company’s expectation that a new drug approval (NDA) for GS-7977 would be submitted by April 2013, and approval achieved by December of that year.<sup>121</sup>

In 2013, the FDA granted GS-7977 both “breakthrough therapy designation”<sup>122</sup> and GS-7977 “priority review”<sup>123</sup> status. The priority review, granted in June 2013, expedited the approval of Sovaldi.<sup>124</sup> The breakthrough status broadened the label’s treatment indication, as Martin explained in a memo that was drafted for the board of directors:

As highlighted by John McHutchison and Bill Symonds during our meeting last month/earlier this month, the FDA granted Sovaldi a Breakthrough Designation, which

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<sup>118</sup> Appendix E, Ex. 26, Gilead Sciences, Inc., *Harry Update: Board Meeting* (Oct. 24, 2011), GS-0019309, at GS-0019311.

<sup>119</sup> *Id.*

<sup>120</sup> Appendix E, Ex. 13, Gilead Sciences, Inc., *Harry Update: Board Meeting* (Oct. 7, 2011), GS-0019236, at GS-0019244.

<sup>121</sup> Appendix E, Ex. 23, Gilead Sciences, Inc., *Hepatitis C and GS-7977 Development Update*, November 5, 2012, GS-0019442, at GS-0019443, GS-0019469.

<sup>122</sup> The agency implemented the process based on instruction in the Food and Drug Administration Safety and Innovation Act of 2012 to “implement more broadly effective processes for the expedited development and review of innovative new medicines intended to address unmet medical needs for serious or life-threatening diseases,” Pub. L. No. 112–144, § 901(a)(1)(C), 126 Stat. 993.

<sup>123</sup> Authorized by the Prescription Drug User Act (PDUFA) of 1992, Pub. L. No. 102–571, priority review allows the FDA to act on an NDA within six months of submission, as opposed to the standard 10-month period. The FDA can grant priority review status if the NDA “treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness.” Food and Drug Administration, *Guidance for Industry: Expedited Programs for Serious Conditions—Drugs and Biologics*, at 7 (2014), available at <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm358301>.

<sup>124</sup> Press Release, Gilead Sciences, Inc., Gilead Announces U.S. FDA Priority Review Designation for Sofosbuvir for the Treatment of Hepatitis C (June 7, 2013), available at <http://www.gilead.com/news/press-releases/2013/6/gilead-announces-us-fda-priority-review-designation-for-sofosbuvir-for-the-treatment-of-hepatitis-c>.

allowed us to submit data from two additional Phase 3 studies beyond the four Phase 3 trials submitted with the initial New Drug Application.<sup>125</sup>

Martin appeared to be referring to the VALENCE and PHOTON-1 studies.<sup>126</sup> The FDA's summary review explained, "VALENCE provided data to support a 24-week treatment duration for GT3 subjects to improve relapse rates and PHOTON-1 provided data to support regimens for HCV/HIV-1 co-infected subjects along with an interferon-free regimen for GT1 subjects."<sup>127</sup>

Under section 506(a) of the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended, breakthrough designation is provided:

if the drug is intended, alone or in combination with 1 or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.<sup>128</sup>

When considering a breakthrough therapy designation request, the FDA evaluates the quantity and quality of the clinical evidence submitted, available alternative therapies to that drug, and magnitude of treatment effects shown.<sup>129</sup> For Gilead, expanding the label's indication meant that Sovaldi would be a viable therapy for more patients, expanding the market for the drug.

Financial documents filed a month after the Gilead-Pharmasset acquisition was announced show that Pharmasset's management expected that the drug would be launched in the U.S. sometime between the fourth quarter of 2013 and the second quarter of 2015.<sup>130</sup> The actual December 2013 FDA approval was at the front-end of these projections. The importance of this timing shift is underscored in pricing documents discussed in detail later in this report showing that Gilead officials believed a lack of competition would inform the eventual price for Sovaldi.

Table 2 shows the HCV drugs that received FDA approval.

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<sup>125</sup> Appendix E, Ex. 27, Gilead Sciences, Inc., Email from Cara Miller to Gregg Alton (Nov. 22, 2013), GS-0020826.

<sup>126</sup> Food and Drug Administration Center for Drug Evaluation and Research, Clinical Pharmacology and Biopharmaceutics Review(s): Application Number: 204671Orig1s000, at 2 (Nov. 22, 2013), available at [http://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2013/204671Orig1s000ClinPharmR.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/204671Orig1s000ClinPharmR.pdf).

<sup>127</sup> *Id.* at 8.

<sup>128</sup> Food and Drug Administration Safety and Innovation Act Pub. L. No. 112–114, § 902(a)(3), 126 Stat. 995 (2012).

<sup>129</sup> Center for Health Policy at Brookings, *Breakthrough Therapy Designation: Exploring the Qualifying Criteria* (2015) [hereinafter Brookings, *Breakthrough Therapy Designation*], available at [http://www.brookings.edu/-/media/events/2015/04/24-fda-breakthrough-therapy-designation/breakthrough-therapy-designation\\_final.pdf](http://www.brookings.edu/-/media/events/2015/04/24-fda-breakthrough-therapy-designation/breakthrough-therapy-designation_final.pdf).

<sup>130</sup> Pharmasset, Inc., Amendment No. 2 to Solicitation/Recommendation Statement Under Section 14(d)(4) of the Securities Exchange Act of 1934 (Schedule 14D–9) (Dec. 20, 2011), available at <http://www.sec.gov/Archives/edgar/data/1301081/000119312511347237/d270458dsc14d9a.htm>. Pharmasset, Inc.

**Table 2—HCV Drugs That Received FDA Approval**

<b>Drug</b>	<b>Approval Date</b>	<b>Breakthrough Therapy Designation for Approved Indication(s)</b>	<b>Priority Review (Y/N)</b>	<b>Indication(s) Approved</b>
Daklinza (daclatasvir) NDA 206843.	July 24, 2015	No	Yes	For the treatment of hepatitis C virus (HCV) genotype 3 in combination with sofosbuvir.
Technivie (ombitasvir, paritaprevir, and ritonavir) NDA 207931.	July 24, 2015	Yes	Yes	For use in combination with ribavirin for the treatment of hepatitis C virus (HCV) genotype 4 infections in patients without cirrhosis.
Viekira Pak (ombitasvir, paritaprevir, and ritonavir; dasabuvir) NDA 206619.	December 19, 2014	Yes	Yes	For use with or without ribavirin to treat patients with chronic hepatitis C virus (HCV) genotype 1 infection.
Harvoni (ledipasvir and sofosbuvir) NDA 205834.	October 10, 2014	Yes	Yes	For the treatment of chronic hepatitis C (CHC) genotype 1 infection.
Sovaldi (sofosbuvir) NDA 204671	December 6, 2013	Yes	Yes	For the treatment of chronic hepatitis C (CHC) infection as a component of a combination antiviral treatment regimen. [Labeling specifies efficacy established in genotype 1, 2, 3 or 4]
Olysio (simeprevir) NDA 205123	November 22, 2013	No	Yes	For the treatment of chronic hepatitis C (CHC) genotype 1 infection as a component of a combination antiviral treatment regimen.
Incivek (telaprevir) NDA 201917	May 13, 2011	No *	Yes	In combination with peginterferon alfa and ribavirin, the treatment of genotype 1 chronic hepatitis C (CHC) in adult patients with compensated liver disease, including cirrhosis.
Victrelis (boceprevir) NDA 202258.	May 13, 2011	No *	Yes	For the treatment of chronic hepatitis C (CHC) genotype 1 infection, in combination with peginterferon alfa and ribavirin, in adult patients with compensated liver disease, including cirrhosis.

**Source:** FDA.**Note:** \*Prior to Food and Drug Administration Safety and Innovation Act and creation of the Breakthrough Therapy designation.