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Gilead: Hepatitis C Access Strategy (A) Abridged

Founded in 1987, and headquartered in Foster City, California, Gilead Sciences, Inc., was a research-based biopharmaceutical company with revenues of $11.2 billion and net income of $3.1 billion in 2013. As can be seen from its financial history (**Exhibit 1**), the company grew dramatically from 2003 to 2013, mainly by virtue of its breakthrough antiretroviral (ARV) medication for HIV/AIDS. Nearly 80% of the company's revenues and profits came from this line of innovative medicines, which were the therapy of choice in both developed and developing countries. Over the years, through a series of acquisitions, the company had built a wide product portfolio that extended to drugs targeting cardiovascular, respiratory, cancer, and liver diseases. By 2013, that portfolio included 18 commercially available drugs, with another 30 in the research pipeline.

In December 2013, the company's direct-acting antiviral drug (DAA), sofosbuvir (brand name: *Sovaldi*), gained United States Food and Drug Administration (USFDA) clearance for the treatment of hepatitis C, for which existing treatments, plagued with severe side effects, showed a limited ability to cure. *Sovaldi* obtained European Commission clearance in January 2014.

The hepatitis C virus (HCV) was considered one of the most prevalent blood-borne infections in the world, currently affecting over 3 million in the U.S. and approximately 185 million people globally. HCV was implicated in over 500,000 liver-related deaths worldwide every year. *Sovaldi* promised to deliver a safe, simple, and highly effective cure. It had all the makings of being another Gilead blockbuster drug. The company was contemplating how to price a full course, 12-week *Sovaldi* treatment in the U.S. market.

Another quandary for the company than its U.S. pricing, however, was how to price the drug in global markets, especially in low-income countries that were the hardest hit by the disease. On the one hand, if the company charged a uniform global price based on its U.S. price, then patients in low-income countries would likely not be able to afford it, which could hamper Gilead's market penetration and could lead to a critical backlash. On the other hand, if it charged a differential price, then insurers and payers in developed markets could balk, and the company would also have to worry about the parallel importation of goods into higher-priced countries.

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The question of how to price *Sovaldi* was complicated by the company's outstanding record in making HIV/AIDS medicines available at affordable prices. Nearly 6 million people, or 60% of all patients who needed Gilead's ARV medications worldwide, especially in sub-Saharan Africa and South Asia, were able to afford and receive them. One of the highlights of the company's "access" strategy was its proactive engagement of key generic drug manufacturers in India and South Africa, to whom it transferred production technology. As a result, prices of front-line ARV medications dropped steeply. Having earned kudos for its innovative access program, expectations were naturally high for the company as it announced the USFDA clearance of *Sovaldi*.

As head of Gilead's newly constituted Access Operations and Emerging Markets (AOEM) division, Clifford Samuel knew that attention would be focused on his team. AOEM was responsible for the 130 low-income and emerging market countries (see **Exhibit 2**) where the bulk of the incidence of the HCV disease occurred. His boss, Gregg Alton, Executive Vice President, Corporate and Medical Affairs, and the architect of Gilead's access program, was very clear that the role of the AOEM division was to ensure that Gilead's medicines reached as many people in the world as who needed them. Its mandate was different from that of the commercial side of the business. "Access is the goal, not profits," emphasized Alton. Samuel and his team were charged with developing a market entry strategy for the hardest-hit countries, such as Egypt, which had an HCV prevalence rate of 15%. Samuel and AOEM had to grapple with the following questions: What should *Sovaldi's* price be? In which affected countries should Gilead start? How should it time the entry? And how would AOEM's answers to these questions align with the rest of the company, which was already preparing for launches in the U.S., UK, and Canada?

Access Operations and Emerging Markets—Background

Founded in 1987, it was 14 years before Gilead launched its first ARV drug for HIV/AIDS. Since then, it had been at the forefront of innovative ARV (Anti Retroviral) medicines for HIV/AIDS, with a continuing stream of medicines forming the backbone of safe, effective, and convenient ARV therapies. In 2001, there were roughly 30 million people worldwide who were living with HIV, with about 2.5 million new infections and 2 million deaths reported that year. An estimated 10 million people infected with the virus would develop AIDS and face certain death, unless they were treated with ARV medicines. Although HIV was a global pandemic, low- and lower-middle-income countries in sub-Saharan Africa and South Asia were the most affected, bearing 80% of the global disease burden. The cost of a year's supply of ARVs in 2001 was $10,000, clearly beyond the reach of most individuals and governments in lower income countries.

This affordability gap attracted the attention of civil society, activists, and the United Nations (UN), leading to multiple relief initiatives. In the early 2000s, several international organizations were created with the goal of enabling developing countries to access medicines to help treat their citizens: the Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria (Global Fund), established with nearly $7.5 billion, and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), with nearly $15 billion, were the two major entities created in 2003.[1] Other organizations, too, like the Clinton HIV/AIDS Initiative (CHAI) and UNITAID (founded in 2006 by the governments of Brazil, Chile, France, Norway, and the United Kingdom to leverage market purchasing power to achieve quantity discounts) played a role as mediators between national governments and pharmaceutical companies in negotiating affordable prices for medicines.

[1] Since then, the Global Fund had swelled to $20 billion and PEPFAR to $50 billion from 2008 to 2013.

Simultaneously, in 2000, the Accelerating Access Initiative (AAI) was created as a partnership among the UN, the World Bank, and research-based pharmaceutical companies (all based in the West). The members of AAI worked with governments, international organizations, and other stakeholders to find ways to broaden access to ARVs. Under the aegis of AAI, pharmaceutical company members decided to offer tiered pricing programs to increase access to ARVs in the developing world. For example, Merck established a two-tiered pricing strategy, meaning that it offered its ARVs to the least-developed countries and those hardest hit by AIDS at not-for-profit prices; countries with higher levels of economic development and/or lower prevalence rates were charged prices above not-for-profit levels, but still heavily discounted from the regular price. GlaxoSmithKline also implemented a similar tiered pricing strategy. Through such a pricing structure, by 2008, second- and third-generation HIV/AIDS medicines were made available to the poor countries hardest hit by the epidemic at $300 per person per year.

Generic manufacturers, like Cipla in India, which were shielded by liberal patent laws, became active in offering ARV drugs at prices significantly lower than those typically offered by research-based pharmaceutical companies. The introduction of generic ARVs, and the competition among its manufacturers, led to a steep reduction in the price of first-generation ARVs (2000 to 2008): from roughly $10,000 annually to $100 annually. Countries like South Africa that were hardest hit by the disease preferred the cheaper generics to AAI drugs, which, in spite of the tiered pricing, still cost two to three times more than the generic medicines.

Gilead approached the challenge somewhat differently. Essentially, Gilead structured dual channels to serve the needs of the low- and lower-middle-income countries. The first channel established 11 distributors to sell Gilead's branded products in the 130 low-income and emerging economies using the same, two-tiered formula as the AAI member companies. These distributors could purchase Gilead products at "non-profit" pricing, and were allowed to earn a profit margin of around 15% to cover their costs of registering the product in their respective countries, managing local logistics, cultivating the medical network, and providing the network with the appropriate clinical and scientific information. This channel was aimed at serving the sizable middle- and upper-income consumers in developing countries like India, South Africa, and Thailand.

The second channel was the more radical one: the company offered its know-how (including that for its active ingredient) to generic[2] drug manufacturers in India and South Africa on a licensing basis. The licensees paid a 5% royalty on sales and were allowed to sell in local markets and also export products to 95 low-income countries with high HIV prevalence. Gilead's strategy was considered unusual because it held the patent on the most innovative second- and third-generation ARV drugs, yet it was willing to license that technology, bringing down the price of these groundbreaking medicines to about $125 per person per year.

A leading supplier of such Gilead-generic HIV/AIDS medicines was Matrix Labs in Hyderabad, India.[3] Matrix had a broad portfolio of drugs, including (non-HIV) generics, as well as contract manufacturing. Gilead's HIV license added a third dimension to its portfolio and was considered profitable, even if somewhat less so than the other two components of its business. In 2012, Matrix was subsequently acquired by Mylan Labs, a $7.5 billion U.S. company with expertise in generic drug manufacturing. Generic manufacturers such as Mylan and Aspen (South Africa) had their own independent distribution channels to take their broad portfolio of drugs to market. In addition, they

[2] Generic products, with respect to pharmaceuticals, were copies of patented drugs or drugs whose patents had expired.

[3] The original generic license was issued to Matrix Labs, which was then acquired by U.S. generic drug manufacturer Mylan Labs.

had built specific capability in bidding for government tenders, which generally called for producing large quantities of the necessary medicines and supplying them in a timely fashion to serve public health needs.[4]

In summary, mainly through its generic licensees, Gilead's ARV formulations had reached 60% of the 10 million individuals with HIV/AIDS who needed the medicines, at prices as low as $100 per year. Meanwhile, the company continued to be the market leader in North America, Western Europe, and other developed countries, with a market share of close to 80% among the 1.6 million individuals on ARV therapy.[5]

Creation of the Access Operations and Emerging Markets (AOEM) Organization

With the visible success of Gilead's International Access Operations for ARV medicines, the company chose to formalize its structure by creating the AOEM organization, with Samuel as its head. The team reported to Alton, and not to the company's commercial head. The division was responsible for accelerating drug access in the 130 low-income, lower-middle-income, and even some upper-middle-income countries. The unit's mandate was to expand access using differential market methods. Gilead's CEO and Chairman, John Martin, had repeatedly said that the division's number-one goal was to expand access and make *Sovaldi* available to any patient in the world who needed it, regardless of economic circumstance. Thus, the AOEM organization was charged with providing access first and foremost, and running it as a financially sustainable operation that could make a profit if possible, but certainly not a loss. (The division's income statement is shown in **Exhibit 3**.)

Hepatitis C: Background

HCV was a chronic infection that affected 185 million people worldwide, approximately 3 million of whom lived in the United States. Roughly 60% of those infected fell within the footprint of Gilead's AOEM. The highest prevalence worldwide was in China (30 million—not part of AOEM), followed by India (20 million), and Egypt (15 million). As noted previously, HCV was responsible for over 500,000 global deaths yearly and approximately 10,500 annual deaths in the U.S.

The HCV infection was relatively benign in the initial stages, and many patients were unaware of their infection. However, most of those infected usually did not clear the virus entirely and patients who had been infected with HCV usually progressed to a chronically infected state over their lifetime, sometimes two to three decades later. The virus caused liver inflammation in the majority of these patients. Chronic inflammation progressed to a condition called cirrhosis, in which a significant portion of the liver was damaged and replaced by scar tissue, affecting its normal functioning. HCV was the world's dominant cause of liver failure leading to liver transplantation. Additionally, patients with cirrhosis were at significantly increased risk of developing liver cancer, which carried a poor long-term prognosis. The highest prevalence of infection in the U.S. was in the baby-boomer generation, those born between 1946 and 1964. Injection drug use was currently the dominant transmission mechanism for spreading the disease.[6]

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[4] In addition to Mylan and Aspen, Gilead's licenses included another 13 generic manufacturers in India.

[5] In 2014, of the 35 million people infected with HIV, nearly 90% were in developing countries.

[6] Historically, blood transfusions were a common vector of transmission, but since HCV testing became standard for transfused blood in 1990, transmission from blood transfusion had become extremely rare. Sexual contact with infected patients and

HCV was a small virus consisting of genetic material called ribonucleic acid (RNA). There were six known genotypes of the HCV virus, essentially consisting of minor variations in the virus's RNA sequence. Genotypes 1–3 had a worldwide distribution, but genotype 1 predominated in North America, Europe, and Japan. India and Pakistan were mainly genotype 3, whereas genotype 4 predominated in 90% of Egyptians diagnosed with HCV. Low- and middle-income countries accounted for nearly 60% of the global HCV burden.[7] (See **Exhibits 4-5** for a snapshot of AOEM market countries with the highest HCV prevalence.

Previous Standard of Treatment

HCV was a treatable disease, but in the two decades since the virus was first identified in 1989, treatment for it had been far from ideal. The historical mainstay of treating hepatitis C was a combination of two drugs: pegylated interferon (known as peginterferon) and ribavirin. The former (generally considered to be the workhorse of the regimen) was a weekly subcutaneous injection and acted by inducing the patient's own antiviral response (this treatment did not directly act on the virus). Two pharmaceutical giants, Merck and Roche, were the main global suppliers of the injectable. Ribavirin was an oral drug that acted synergistically with peginterferon through a mechanism not fully understood. These two drugs remained the backbone of HCV treatment until 2011.

For many reasons, this regimen was far from optimal. For one, it was associated with a very high rate of adverse side effects (up to 80%). Since the regimen primarily worked by inducing the body's immune response, one inherent side effect was flu-like symptoms throughout the course of treatment. Since the duration of therapy was 24–48 weeks, patients were often sick for a large part of the year while on this therapy. Additionally, this combination was associated with anemia (a decrease in the body's red blood cell count, which subsequently caused fatigue), neutropenia (a decrease in the body's white blood cell count and ability to fight other infections), rash, and depression. Almost half of all HCV patients were ineligible for interferon therapy (often due to coexisting medical conditions, such as autoimmune disease and depression, which tended to worsen with interferon therapy), and for those that qualified, this poorly tolerated regimen carried only modest cure rates. Treatment efficacy was generally measured using a marker called sustained virologic response (SVR). Patients with undetectable viral loads in their blood 12 weeks after treatment were said to have demonstrated an SVR to therapy and were considered to be cured. While SVR rates varied by study for the traditional peginterferon/ribavirin combination, they were generally cited as being only 70%–80% effective for genotypes 2 and 3 and only 45%–70% effective for genotype 1. Given the poor tolerability and limited success, treatment was generally offered only to those patients with evidence of liver damage.

2011: The Introduction of DAA Therapies

In 2011, a major advancement in the treatment of viral hepatitis C was made, with the approval of two new drugs: boceprevir (Merck & Co.) and telaprevir (Vertex Pharmaceuticals). Rather than acting indirectly against HCV via the body's immune system, these two drugs acted directly on the virus[8] and were associated with a dramatic improvement in the effectiveness of hepatitis C treatment. In a landmark clinical trial comparing peginterferon-ribavirin to peginterferon-ribavirin plus the new drug

tattooing (particularly among incarcerated individuals) were potential but unlikely modes of transmission. Finally, perinatal transmission (from an infected mother to a newborn baby) was a possible vector of infection, too.

[7] Perspective, *New England Journal of Medicine*, April 10, 2014, pp. 1–3.

[8] Both of these drugs belonged to a class known as protease inhibitors; these drugs blocked a specific enzyme (NS3/4A protease) that was crucial to the replication of the virus inside of an infected human liver cell.

telaprevir (ADVANCE Trial)[9], the latter achieved an SVR rate of 75%, compared to 44% in patients randomized to peginterferon-ribavirin only. The two new drugs were approved for treatment in 2011. Their launch was a dramatic success, with the Vertex drug approaching $2 billion in sales in its first full year on the market.

Despite this significant advance, treatment for HCV remained problematic. For one, despite the improvement in efficacy, these two new drugs still needed to be taken with peginterferon and ribavirin, which retained their associated side effects. Furthermore, both drugs carried side effects of their own. For example, both drugs were associated with anemia. Vertex's drug was also associated with the development of rash, which in some cases compelled discontinuation of treatment. The initial excitement of these new drugs gave way to mild disappointment because of the significant side effects. Finally, both of these drugs were restricted to treating genotype 1, which was the most prevalent genotype in the U.S., but less prevalent in other global settings.

Pharmaceutical Drug Development and Gilead's Efforts at Developing HCV Drugs

U.S. pharmaceutical companies spent about $60 billion a year (average expenditures from 2005 to 2013) on drug development, or roughly 17% of sales. Typically, only one in 5,000 chemical compounds in the research and development (R&D) pipeline was successfully commercialized, putting the cost of an average new drug at $1.5 billion, or at least that had been the inherited wisdom. A new study by Tufts University in Massachusetts put it at $2.6 billion, which included the opportunity cost of the capital employed in R&D.[10] This cost included not only the laboratory and scientific research, but also the three phases of clinical trials that were required before a drug was cleared by regulatory authorities. Bringing a drug to market could take up to 12 years. The USFDA reviewed data from each step and allowed, or disallowed, the continuation to the next stage. The first two years were usually spent on basic research and drug development. The next two were spent on pre-clinical and translational research, wherein the drug would be tested on animals. The drugs that were successful at that stage then moved into human trials over three phases.

Of the 20 to 25 new drugs launched by the industry each year, only one or two reached "blockbuster status," i.e., achieved sales of over $1 billion in its first year. Knowing how expensive it was to conduct R&D from "idea-generation to commercial launch," Gilead had followed a policy of watching trends and acquiring and/or licensing the hottest emerging technology at the most opportune time rather than doing basic research to develop early stage drugs itself. Indeed, that strategy had led to the acquisition of Pharmasset for a record $11 billion, which gave Gilead sofosbuvir[11] (eventually marketed as *Sovaldi*) and piloted it through Phase 3 clinical testing.

2013: A Major Advance in DAAs; Sovaldi Is Born

A major milestone in HCV therapeutics came in 2013, with the approval of two new drugs: Gilead's *Sovaldi* and *Olysio*, developed by Medvir and Janssen, the pharmaceutical arm of Johnson & Johnson.[12]

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[9] Jacobson IM, McHutchison JG, Dusheiko G. Telaprevir for Previously Untreated Chronic Hepatitis C Virus Infection. New England Journal of Medicine. 2011 Jun 23; 364(25):2405-16.

[10] "The Price of Failure," *Economist*, November 29, 2014, p. 59.

[11] Sofosbuvir, an RNA polymerase inhibitor, acted by inhibiting the enzyme that enabled HCV to replicate its genetic material.

[12] The latter drug, simeprevir, was a second-generation protease inhibitor, with the same mechanism of action as the two initial direct-acting antivirals: boceprevir and telaprevir.

These two medications were preferred over first-generation DAAs. In addition to the improvement in treatment efficacy, these two drugs were well tolerated and did not carry the large side-effect profile that plagued telaprevir and boceprevir. Gilead's *Sovaldi*, however, demonstrated higher efficacy with a cure rate of 95%, fewer adverse effects, and fewer adverse drug interactions than *Olysio*.[13] It emerged as the front-runner among the two novel treatments for HCV.

Based on several clinical trials,[14] the American Association for the Study of Liver Diseases (AASLD) recommended a 12-week course of *Sovaldi* + ribavirin + weekly peginterferon as the preferred treatment.[15]

Cost Burden to Society of HCV

National health expenditures in the U.S. (GDP: $16 trillion, population: 315 million) were about $3 trillion in 2012, of which hospital care was 32%; physician and clinical services, 20%; and prescription drugs, 10% or $300 billion. Of that $300 billion, private insurance accounted for 45%. Medicare (government insurance for senior citizens) covered 30%, and Medicaid (government insurance for low-income Americans) covered 10%.

As stated previously, 3 million Americans were infected with HCV and approximately 10,500 died every year from liver diseases caused by the virus. Most patients were now in their 50s and 60s, having been infected primarily through experimentation with injection drugs in the 1960s and 70s. Estimates marked the *annual* cost of treating a patient with non-cirrhotic liver disease at $8,000; one with a more complicated stage (compensated cirrhosis) at $13,000; and one with end-stage liver disease at $42,000.[16,17] The typical number of years in treatment for each patient was ten years in the non-cirrhotic stage, then two years in the more advanced compensated cirrhosis stage, and finally, two years in end-stage liver disease.

Because the age group most frequently diagnosed with HCV (people aged 30 to 49 years) were likely to be employed and enrolled in an employer-based insurance plan, the direct cost burden of HCV in the U.S. was projected to fall largely on private health insurance companies.

Sovaldi Launch in Developed Countries

Sovaldi was projected to launch in the U.S. in late 2013 and would compete against the available standard of care for patients with genotype 1 hepatitis C. (See **Table A**.) The cost of the ribavirin + weekly peginterferon, which would be needed alongside *Sovaldi* in the new treatment regimen,

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[13] In particular, simeprevir had been shown to have notable drug-drug interactions with a large number of therapies used to treat the HIV virus, which was a common co-infection in HCV patients. Additionally, patients taking simeprevir required monitoring of HCV viral load over the course of HCV treatment (in order to ensure treatment efficacy), while patients being treated with sofosfubir did not (in the NEUTRINO trial of sofosbuvir, virtually all patients were shown to have undetectable viral loads after four weeks of treatment).

[14] Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. N Engl J Med 2013;368:1878-1887.

[15] Up-to-date AASLD guidelines are available at http://www.hcvguidelines.org/.

[16] Gordon SC, et al., Hepatology, 2012, 56, 1651-1660.

[17] Wong JB, et al., Estimating future hepatitis C morbidity, mortality, and costs in the United States. *American Journal of Public Health*, 2000; 90: 1562-1569.

generally ran around $10,000 for the 12 weeks). The older treatment regimen (peginterferon injection plus ribavirin) was estimated to cost $25,000.[18]

Table A HCV Treatment Costs[a]

Regimen	Cost	Duration of Therapy (weeks)
OLYSIO ™ + PEGASYS (R) + ribavirin	$106,673	48
INCIVEK(R) + PEGASYS + ribavirin	$106,468	48
VICTRELIS(R) + PEGINTRON(R) + ribavirin	$95,845	48
OLYSIO + PEGASYS + ribavirin	$86,516	24
INCIVEK + PEGASYS + ribavirin	$86,312	24
VICTRELIS + PEGINTRON + ribavirin	$85,257	36
VICTRELIS + PEGINTRON + ribavirin	$64,825	28

Source: Company documents.

[a] OLYSIO = Janssen's Simeprevir, INCIVEK = Vertex's Telaprevir, VICTRELIS = Merck's Boceprevir.

Health Canada approved *Sovaldi* in December 2013, and shortly thereafter, the European Medicines Agency (EMA) granted approval for the drug in January 2014. As required by local regulation, Gilead and local governments entered into discussions on pricing in these localities. In Canada and most western European countries, universal healthcare was the norm and, as such, national health agencies negotiated prices that were traditionally at a 20% to 30% discount off the U.S. price.[19]

Gilead's CEO Martin explained the company's pricing rationale: "We bring innovative solutions to human needs. Price levels in each country are determined by the social-political-economic context of the situation. Even within each country, prices are different. In the U.S. our prices for Medicare, Medicaid, Veterans Administration, Kaiser, Private Insurers etc., are different, and of course there is tremendous value at every price point," he added.

Mario Molina, President and CEO of Molina Healthcare, one of the nation's largest Medicaid-managed companies, said, "It's superior to anything we have had to treat hepatitis C. The problem is it's extraordinarily expensive."[20] His firm had decided not to cover the drug if it was priced too high. California, the state in which the company operated, spent about $7 billion a year covering roughly 2 million citizens who had incomes too low to carry private insurance or were too young to access Medicare insurance for the elderly.

It was not just healthcare providers that were concerned about *Sovaldi's* expected price. Spurred on by the advocacy group Campaign for Sustainable Rx Pricing, senators from both political parties started an investigation into Gilead's expected pricing of *Sovaldi*. The *New York Times* said the

[18] "KHN Original Stories: 2014," *Kaiser Health News*, http://www.kaiserhealthnews.org/stories/2014/, accessed August 19, 2014.

[19] Saw Swee Hock School of Public Health, "Financing One-Off High Cost Treatments." White Paper, https://cpb-us-w2.wpmucdn.com/blog.nus.edu.sg/dist/e/9820/files/2020/11/Financing-One-Off-High-Cost-Treatments_for-website-2.pdf, accessed July 2024.

[20] Julie Appleby. "There's a Life-Saving Hepatitis C Drug. But You May Not Be Able To Afford It." *Kaiser Health News*, March 3, 2014. https://khn.org/news/insurers-debate-who-should-get-costly-hepatitis-c-drug/, accessed August 19, 2014.

investigation showed that Pharmasset, original developers of the drug, had planned a $36,000 price point.[21] According to a news report, "The public call to Gilead from Congress has sent shock waves through the biotech investment community, raising concerns that other leading drug makers could face pressure on pricing new medicines."[22]

Sovaldi Launch in Developing Countries

Gilead adopted a more liberal income tier range than the World Bank for classifying countries as low-income (GNI/capita $2,000 or less), lower-middle-income ($2,001 to $7,000), and upper-middle-income ($7,001 to $12,500). Using this classification, the 55 countries in the low-income category accounted for a little over 65% of the HCV-infected population; the 40 lower-middle-income countries accounted for a little over 25%; and the 33 upper-middle-income countries accounted for 7%. (See **Exhibit 6** for a list of countries with potential for DAA intervention.)

Challenges associated with attempts to increase access to HCV treatment in these settings included the high cost, perceived complexity of treatment, and insufficient political commitment. Access to treatment was severely limited in these countries primarily by the fact that the main medicine used, pegylated interferon, was priced out of reach for most people, and their governments.[23] In countries like Russia, a 48-week course was available at roughly $12,000 to $16,000. In other countries, however, activist governments and civil society had been able to selectively bring these prices down on a case-by-case basis. Pakistan, for instance, paid $1,500 for the same treatment; Brazil, $5,000; and Thailand, $4,000.[24]

Nowhere was the issue of cost more acute than in Egypt, which had the world's third-highest prevalence of the virus, at 15%, as a consequence of the use of poorly sterilized needles in campaigns, dating back to the 1970s, to stamp out the parasitic disease schistosomiasis. The government in Egypt, however, had made significant efforts to facilitate access to treatment for HCV-infected patients. Reiferon Retard, which was biosimilar to pegylated interferon, had been used to overcome the high cost of HCV treatment and to increase the number of patients treated. Whereas dual therapy with ribavirin remained expensive in many developing countries, its cost in Egypt, due to active government intervention, was estimated to be $1,750 for 48 weeks of treatment. In addition, since 2006, the Egyptian government had opened 26 national treatment centers, subsequently treating 190,000 patients.[25]

Given the Egyptian government's eagerness to address HCV infection, it waived the requirements for independent human trials before drug registration, making *Sovaldi* available for treatment in an accelerated manner (within seven months of USFDA approval).

Unlike Egypt, the Indian government had not yet waived the requirements for Phase 3 clinical trial testing with local patients before registration.

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[21] Sanger-Katz, "$1,000 Hepatitis Pill Shows Why Fixing Health Costs Is So Hard."

[22] Reuters Health Information, http://www.medscape.com/view article/822442, accessed July 24, 2014.

[23] Saw Swee Hock School of Public Health, "Financing One-Off High Cost Treatments." White Paper, https://cpb-us-w2.wpmucdn.com/blog.nus.edu.sg/dist/e/9820/files/2020/11/Financing-One-Off-High-Cost-Treatments_for-website-2.pdf, accessed July 2024.

[24] A. Momenghalibaf, "Hepatitis C Treatment: Price, Profits, and Barriers to Access" (New York: Open Society Foundations, 2013).

[25] Effectiveness and Cost-effectiveness of Immediate Versus Delayed Treatment of Hepatitis C Virus-Infected Patients in a Country With Limited Resources: The Case of Egypt (Clinical Infectious Diseases 2014: 58 (15 April) Obach et al. (pp. 1064 to 1071).

The receipt of that approval—registration—gave a pharmaceutical firm the green light to sell its product in that country; but without corresponding patent protection, it also opened the doors for copycat drug makers to produce generic versions of that drug. This was a particularly significant problem in India, which had a strong domestic generic manufacturing capability. A leading Indian newspaper, *The Hindu*, captured the dilemma facing low-income countries: "While one side of the debate argues that stronger patent protection incentivizes innovation, the other side has argued that a strong patent regime results in a monopolization of production of essential medicines, accompanying high prices, and consequent exclusion of large sections of the population from essential medicines."[26] According to World Trade Organization (WTO) rules (adopted in 1995, and amended in 2006) called the Doha Declaration, a country was allowed to grant compulsory licenses in cases of national emergency or public interest.[27] Under the compulsory licensing law, the patent holder was entitled to payment of fair royalties by the licensee. Invoking the clause, the Indian government in 2012 permitted a local company (Natco Pharma Ltd.) to manufacture and sell a cancer drug, Nexavar (sorafenib tosylate), at a price of $200/month, compared to the $6,000/month charged by its patent holder, Bayer.

As a way to address such challenging patent issues, pharmaceutical companies attempted alternative approaches, even though there was no clear evidence by which to judge their success. For example, Roche slashed the price of two expensive cancer drugs, Herceptin (from $2,000/month to about $1,300/month) and MabThera (from $1,456/month to $682/month), and arranged to produce them locally in India, at Emcure Pharmaceuticals, and sell them under different brand names.[28] Merck, too, took a similar approach: it granted a non-exclusive license to Cipla, a local pharmaceutical manufacturer, to market and distribute its HIV/AIDS drug, raltegravir, under a different brand name in India at a much lower price.

Meanwhile, Mylan Labs in India had indicated to Gilead that it was eager to take on the generic license for *Sovaldi*, in the same the way it had with Gilead's line of ARVs for HIV/AIDS. Mylan had the capability to synthesize the API, but the process was complicated and would take at least 12 months to master and calibrate, so it was urging Gilead to engage in early discussions on the matter. In addition to Mylan, there were six other generic manufacturers in India, including Cipla and Hetero, that had indicated an interest.

The Future of Competition in Hepatitis C Medicines

Competition was heating up. Gilead was well on its way to launching a second novel compound, ledipasvir. This compound demonstrated that the combination of sofosbuvir and ledipasvir without interferon and ribavirin carried an efficacy rate of approximately 95% or greater.[29] The sofosbuvir/ledipasvir combination (as a once-daily combination pill) branded *Harvoni* was under priority review by the USFDA and, if approved, could become available in the fall of 2014. The duration

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[26] "Losing Ground to Big Pharma, bit by BIT," *The Hindu*, http://www.thehindu.com/opinion/op-ed/losing-ground-to-big-pharma-bit-by-bit/article5097, accessed September 5, 2013.

[27] This amendment was covered by TRIPS (Trade Related Aspects of Intellectual Property Rights) in January 1995.

[28] Eric Palmer, "Roche dropping Herceptin price in India by 30%," *FiercePharma*, March 1, 2013, http://www.fiercepharma.com/story/roche-dropping-herceptin-price-india-30/2013-03-01, accessed September 16, 2014.

[29] Three studies examined various subsets of genotype 1 patients (including those with cirrhosis, and those who had previously failed an attempt at treatment), as well as different durations of treatment (ION-3 examined 8- vs. 12-week courses of treatment), as well as the sofosbuvir/ledipasvir combination with and without ribavirin. Similar efficacy rates were noted in all of these treatment groups.

of the treatment, too, could be shorter (only eight weeks) in patients not exposed to previous HCV therapy.

Multiple non-Gilead HCV drugs were also currently in clinical trials as well. Of these, the one furthest along the development pipeline was a three-drug, direct-acting antiretroviral combination produced by AbbVie (spun off from Abbott Pharmaceuticals), which had demonstrated efficacy rates similar to that of *Harvoni*. Bristol-Myers Squibb and Merck, too, had HCV drugs under review that they hoped to take to market soon.[30]

With many new drugs and treatments for Hepatitis C on the horizon, a leading medical journal, the *New England Journal of Medicine*, wrote in its editorial: "The charge is onerous, but seldom in the history of medicine have such definitive, curative therapies been developed for a disease so widespread and consequential to human health. We believe that robust efforts toward equitable access to these advancements are imperative."[31]

What Strategy for AOEM?

Gilead took its role in producing innovative medicines and bringing it to market seriously. What strategy should Samuel and his team propose to EVP Alton and the company's chairman and CEO, John Martin? How should they price the treatment? Which countries should they lead in first? What should their marketing strategies be within each country? Should they allow generic licenses, as was done with HIV/AIDS drugs? And, importantly, how should they justify their strategy to their commercial division counterparts in the U.S.?

[30] Lynn C. Klotz, PhD, "Why Is Everybody Picking On Sovaldi?" *Genetic Engineering & Biotechnology News*, September 3, 2014.

[31] Treating Hepatitis C in Lower-Income Countries, *New England Journal of Medicine*, April 10, 2014, pp. 1–3.

Exhibit 1 Gilead Sciences, Inc., Selected Consolidated Financial Data

GILEAD SCIENCES, INC.
SELECTED CONSOLIDATED FINANCIAL DATA
(in thousands, except per share data)

	Year Ended December 31,				
	2013	2012	2011	2010	2009
CONSOLIDATED STATEMENT OF INCOME DATA:					
Total revenues	$ 11,201,688	$ 9,702,517	$ 8,385,385	$ 7,949,420	$ 7,011,383
Total costs and expenses [1]	$ 6,677,689	$ 5,692,342	$ 4,595,544	$ 3,987,198	$ 3,482,162
Income from operations	$ 4,523,999	$ 4,010,175	$ 3,789,841	$ 3,962,222	$ 3,529,221
Provision for income taxes	$ 1,150,933	$ 1,038,381	$ 861,945	$ 1,023,799	$ 876,364
Net income attributable to Gilead	$ 3,074,808	$ 2,591,566	$ 2,803,637	$ 2,901,257	$ 2,635,755
Net income per share attributable to Gilead common stockholders-basic	$ 2.01	$ 1.71	$ 1.81	$ 1.69	$ 1.46
Shares used in per share calculation-basic	1,528,620	1,514,621	1,549,806	1,712,120	1,809,208
Net income per share attributable to Gilead common stockholders-diluted	$ 1.81	$ 1.64	$ 1.77	$ 1.66	$ 1.41
Shares used in per share calculation-diluted	1,694,747	1,582,549	1,580,236	1,746,792	1,868,218

	December 31,				
	2013	2012	2011	2010	2009
CONSOLIDATED BALANCE SHEET DATA:					
Cash, cash equivalents and marketable securities	$ 2,570,590	$ 2,582,086	$ 9,963,972	$ 5,318,071	$ 3,904,846
Working capital [2]	$ 948,332	$ 1,918,450	$ 11,431,584	$ 3,271,267	$ 2,963,066
Total assets [3]	$ 22,496,785	$ 21,239,838	$ 17,303,134	$ 11,592,630	$ 9,698,559
Other long-term obligations [2]	$ 156,647	$ 249,973	$ 175,325	$ 55,536	$ 58,057
Convertible senior notes, senior unsecured notes and credit facility [4]	$ 6,635,678	$ 8,223,988	$ 7,605,734	$ 3,477,564	$ 1,155,443
Retained earnings	$ 6,105,244	$ 3,704,744	$ 1,776,760	$ 1,183,730	$ 1,995,272
Total stockholders' equity [2]	$ 11,744,501	$ 9,543,722	$ 6,867,349	$ 6,121,837	$ 6,505,158

(1) During 2012, we recorded $100.1 million and $93.8 million of stock-based compensation in research and development (R&D) expenses and selling, general and administrative expenses, respectively, related to the acquisition of Pharmasset, Inc. (Pharmasset).
During 2011, we recorded $26.6 million of impairment charges in R&D expenses related to certain in-process research and development (IPR&D) assets acquired from CGI Pharmaceuticals, Inc.
During 2010, we recorded $136.0 million of impairment charges in R&D expenses related to certain IPR&D assets acquired from CV Therapeutics, Inc. (CV Therapeutics).

(2) Certain prior period amounts have been reclassified to conform to the current presentation.

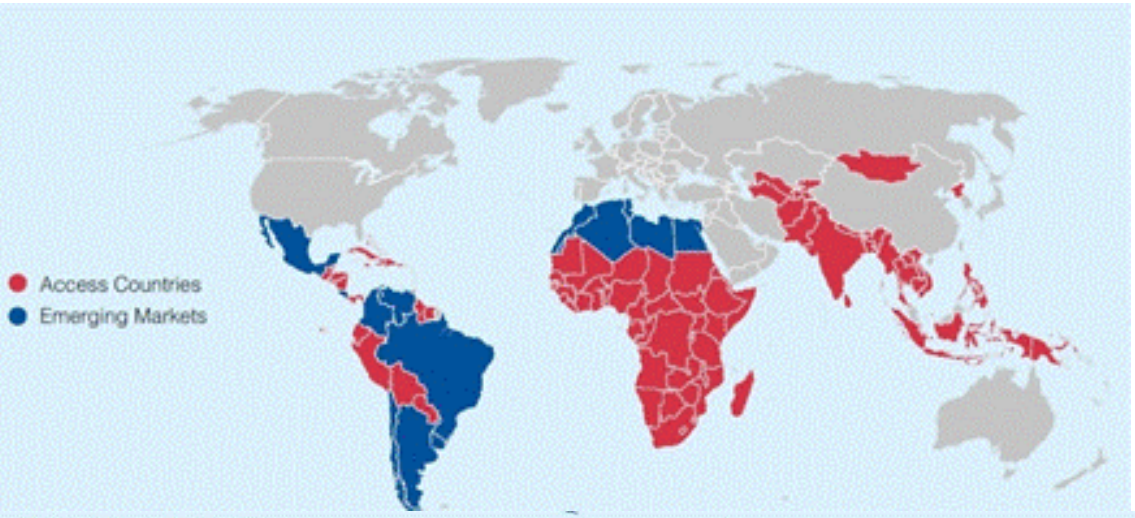
(3) During 2012, we completed the acquisition of Pharmasset and we recognized consideration transferred of $11.05 billion which was primarily recorded in intangible assets. We financed the transaction with approximately $5.20 billion in cash on hand, $2.15 billion in bank debt issued in January 2012 and $3.70 billion in senior unsecured notes issued in December 2011.
During 2009, we completed the acquisition of CV Therapeutics and we recognized consideration transferred of $1.39 billion which was primarily recorded in intangible assets.

(4) During 2013, we repaid $1.52 billion of principal balance of convertible senior notes and repaid $150.0 million under the five-year revolving credit facility credit agreement (the Five-Year Revolving Credit Agreement).
During 2012, we borrowed $750.0 million under our Five-Year Revolving Credit Agreement.
During 2011, we issued $4.70 billion principal amount of senior unsecured notes in registered offerings.
During 2010, we issued $2.50 billion principal amount of convertible senior notes in a private placement.

Source: Gilead Sciences, 10-K, http://investors.gilead.com/phoenix.zhtml?c=69964&p=irol-sec, accessed February 2015.

Note: Gilead Sciences' gross margin in 2013 was 74%. (Gilead Sciences Inc., Form 10-K, 2023, https://www.sec.gov/Archives/edgar/data/882095/000088209514000013/a2013form10-k.htm, accessed September 2024.)

Exhibit 2 Gilead Access and Emerging Market Countries



Gilead Access Countries

Afghanistan
Angola
Anguilla
Antigua & Barbuda
Aruba
Bahamas
Bangladesh
Barbados
Belize
Benin
Bhutan
Bolivia
Botswana
British Virgin Islands
Burkina Faso
Burundi
Cambodia
Cameroon
Cape Verde
Cayman Islands
Central African Rep
Chad
Comoros
Congo, Democ. Rep
Congo, Republic of
Cuba
Curacao
Djibouti
Dominica
Dominican Republic
Ecuador
El Salvador
Equatorial Guinea
Eritrea
Ethiopia
Gabon
Gambia
Ghana
Grenada
Guatemala
Guinea
Guinea Bissau
Guyana
Haiti
Honduras
India
Indonesia
Ivory Coast
Jamaica
Kenya
Kiribati
Kyrgyzstan
Laos
Lesotho
Liberia
Madagascar
Malawi
Maldives
Mali
Mauritania
Mauritius
Mongolia
Montserrat
Mozambique
Myanmar
Namibia
Nauru
Nepal
Nicaragua
Niger
Nigeria
North Korea
Pakistan
Palau
Panama
Papua New Guinea
Paraguay
Peru
Philippines
Rwanda
Saint Kitts and Nevis
Saint Lucia
Samoa
Sao Tome & Principe
Senegal
Seychelles
Sierra Leone
Solomon Islands
Somalia
South Africa
South Sudan
Sri Lanka
St. Maarten
St. Vincent & Grenadines
Sudan
Suriname
Swaziland
Tajikistan
Tanzania
Thailand
Timor-Leste
Togo
Trinidad and Tobago
Turkmenistan
Turks and Caicos
Tuvalu
Uganda
Uzbekistan
Vanuatu
Vietnam
Zambia
Zimbabwe

Emerging Markets

Algeria
Argentina
Brazil
Chile
Colombia
Costa Rica
Egypt
Libya
Mexico
Morocco
Tunisia
Uruguay
Venezuela

Source: Company documents.

Exhibit 3 Gilead's Access Operations and Emerging Markets (AOEM) P&L

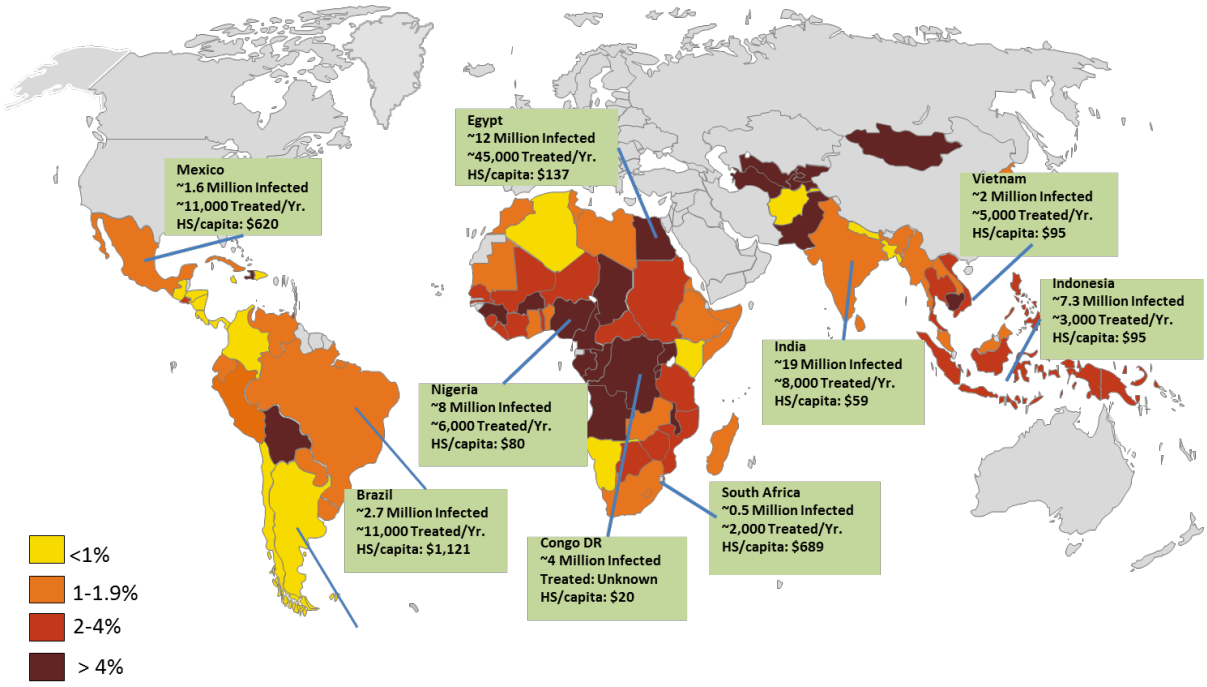
	(in $ 000's)		
	2011	**2012**	**2013[a]**
1. Revenue from Product Sales	$34,453	$55,244	$232,521
2. Revenue from Licensees	5,619	7,001	5,323
3. Total Revenues	40,072	62,245	237,844
4. Gross Profit	11,183	16,328	165,609
5. Operating Profit	4,980	4,825	145,229
6. Number of Managerial & Support Staff	7	7	17

Source: Gilead Sciences, Inc.

[a] In 2013, China was removed from AOEM; Mexico, Argentina, Brazil, Chile, Colombia, Costa Rica, and Venezuela were added.

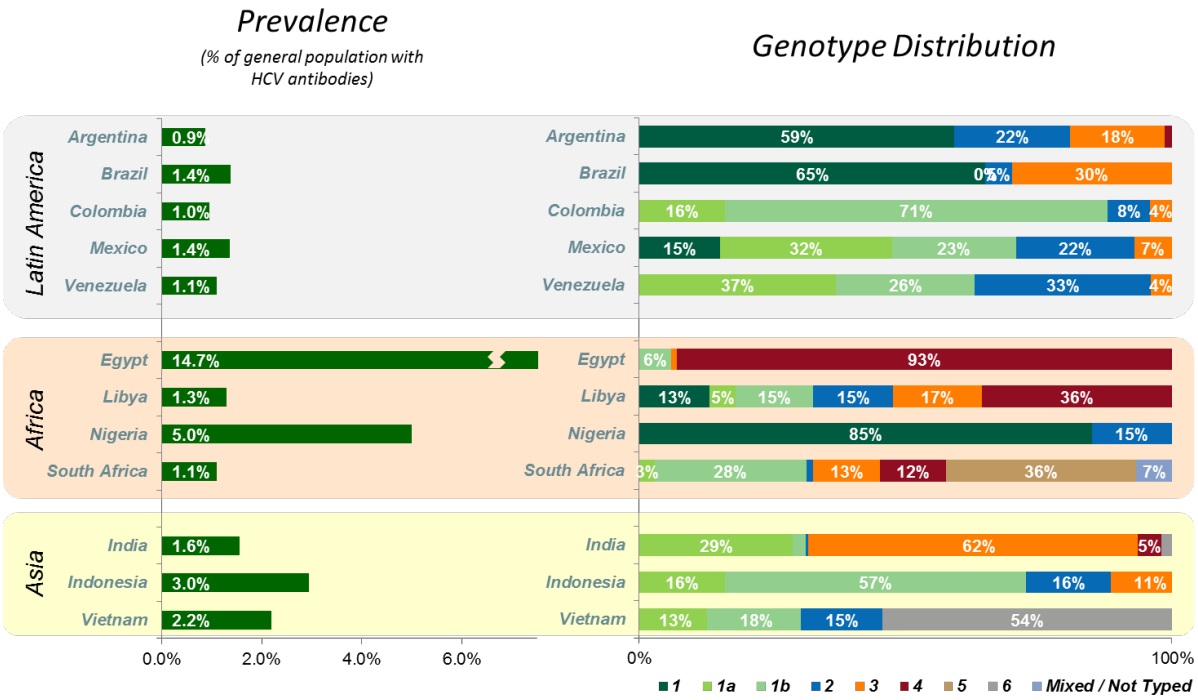
Exhibit 4 HCV Prevalence in Hardest-Hit AOEM Countries

HCV Example: Current spend per capita is very low (all figures based on Interferon treatment)



Source: Gilead Sciences, Inc.

Exhibit 5 Prevalence and Genotype Diversity



Source: Gilead Sciences, Inc.

Exhibit 6 List of Countries by Each Region with Potential for DAA Intervention

Country	Population (K)	$GNI/capita	5Y GNI Growth	Health Spending/ GDP	HCV Prevalence
AFRICA					
Angola	20,821	4,580	79%	3%	5.00%
Cameroon	21,700	1,170	18%	5%	13.80%
Congo, DR	65,705	220	47%	9%	6.40%
Egypt	80,772	3,000	84%	5%	14.70%
Ethiopia	91,729	410	86%	5%	1.90%
Nigeria	168,834	1,430	49%	5%	5.00%
South Africa	51,189	7,610	32%	9%	1.10%
Sudan	37,195	1,450	67%	8%	2.80%
Tanzania	47,783	570	39%	7%	3.20%
Uganda	36,346	440	33%	9%	6.60%
ASIA					
Bangladesh	154,695	840	65%	4%	0.60%
India	1,236,687	1,530	59%	4%	1.56%
Indonesia	246,864	3,420	112%	3%	2.95%
Mongolia	2,796	3,160	no data	5%	10.70%
Pakistan	179,160	1,260	48%	3%	5.90%
Philippines	96,707	2,470	64%	4%	2.20%
Thailand	66,785	5,210	59%	4%	2.20%
Turkmenistan	5,173	5,550	138%	3%	4.00%
Uzbekistan	29,777	1,720	126%	5%	6.50%
Vietnam	88,776	1,400	77%	7%	2.20%
LATIN AMERICA					
Argentina	41,087	11,576	41%	8%	0.87%
Bolivia	10,496	2,220	83%	5%	4.70%
Brazil	198,656	11,630	91%	9%	1.38%
Colombia	47,704	6,990	73%	6%	0.97%
Cuba	11,271	6,106	23%	10%	1.80%
Ecuador	15,492	5,190	57%	7%	1.40%
El Salvador	6,297	3,580	13%	7%	2.50%
Mexico	120,847	9,740	10%	6%	1.36%
Peru	29,988	5,880	74%	5%	1.00%
Venezuela	29,955	12,470	66%	5%	1.10%

Source: Gilead Sciences, Inc.