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Gilead Sees Prospects For Declining HCV Revenues To Stabilize

By Joseph Haas

A CONFLUENCE OF FACTORS, INCLUDING

A higher proportion of patients covered by public payers, has caused Gilead's powerhouse hepatitis C franchise to slow down and now begin showing signs of decline.

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Despite offering clear-cut rationale for the decline and reasons to hope for stabilization, if not growth, **Gilead Sciences Inc.** could not change the narrative coming out of its July 25 earnings call, with market analysts across the board noting that while its hepatitis C franchise sales remain strong, the peak almost certainly is past.

Continuing a recent trend of flat or slightly decreased net sales for its HCV drugs *Sovaldi* (sofosbuvir) and *Harvoni* (sofosbuvir/ledipasvir), Gilead reported that during the second quarter, HCV sales totaled $4.0bn, down nearly 20% from $4.9bn in second-quarter 2015. This followed a first-quarter report in which US sales of Harvoni, the Foster City, Calif.-based firm's top-seller, decreased 50% from a year earlier. *(Also see "Gilead Not Bullet-Proof After All: Harvoni US Sales Tumble More Than 50%" - Scrip, 28 Apr, 2016.)*

Harvoni, which yielded global sales of nearly $13.9bn in 2015, brought in $2.564bn on the quarter, down more than one-third from $3.608bn in the second quarter of 2015. US sales again were approximately cut in half, year-over-year, from $2.826bn to $1.474bn. EU sales also fell off, from $623m a year before to $512m. Even the combo pill's strong launch in Japan abated, as sales declined sequentially from $887m to $448m.

Sovaldi, meanwhile, showed a slight uptick in sales, from $1.291bn worldwide in second-quarter 2015 to $1.358bn in the quarter just past, driven by a $160m increase in domestic sales year-over-year to $775m, but this increase was not nearly enough to offset the Harvoni erosion. Just-launched second-generation combo *Epclusa*, which combines sofosbuvir with the pan-genotypic NS5A inhibitor velpatasvir, posted sales of $64m on the heels of its June 28 FDA approval, which Gilead attributed to stocking. *(Also see "Gilead's Epclusa Approved As First Pan-Genotypic HCV Therapy" - Pink Sheet, 28 Jun, 2016.)*

These trends led Gilead to reduce its full-year sales guidance downward by $500m to a range of $29.5bn to $30.5bn. In a July 25 note, Credit Suisse analyst Alethia Young projected that Gilead would achieve aggregate net sales of $29.7bn this year and $26.2bn in 2017.

Several analysts said M&A activity was more likely to catalyze a return to growth for Gilead than approval of pipeline assets in hepatitis B, non-alcoholic steatohepatitis, oncology or cardiovascular disease. *(Also see "When Will Gilead Make Its M&A Move?" - Scrip, 26 Jul, 2016.)* CEO John Milligan said Gilead, which had $24.6bn cash in hand as of June 30, would continue to proceed slowly with its business development efforts, and indicated it was looking for assets outside of its virology sweet spot.

Lower Per-Patient Revenue In US

The gradual erosion in the HCV franchise derives from many factors, as Gilead execs detailed during the investor call. Domestically, these include reduced patient starts on HCV therapy, increased discounting in the US and lower per-patient revenue as public payer-insured patients comprise a higher proportion of the business. The US trend is exacerbated by European trends, which are seeing reduced patient starts and a greater percentage of the HCV business occurring in countries that have set lower net prices for sofosbuvir-based regimens.

"We still think this could be the toughest year for Gilead's HCV franchise, ahead of expected 2017 approval in China." – Morningstar analyst Karen Andersen

In a July 26 note, Morningstar analyst Karen Andersen asserted that Gilead remains the dominant player in the HCV space and predicted its revenue outlook in the space will stabilize after 2016 and a "readjustment period."

"We still think this could be the toughest year for Gilead's HCV franchise, ahead of expected 2017 approval in China," she wrote. "As in the first quarter, fewer US patients started Harvoni, and higher rebates and shorter duration of therapy (an eight-week regimen) also weighed on sales."

"This dynamic was expected to some extent, as first-quarter 2015 saw high patient starts as warehoused patients flooded the US market, and we saw a similar trend in Japan in the first quarter of 2016," Andersen continued. "Previously negotiated contracts (that include lower pricing with expanded access) are now starting to dominate sales, and public market sales are being driven by a heavily discounted VA market. We model a 54% discount to list price for Gilead's US HCV sales."

Credit Suisse's Young lowered her 2016 sales estimate for Harvoni from $11bn to $9.9bn, adding "Harvoni is becoming more difficult to model and accurately predict the moving pieces." The new estimate relies on more conservative projections for key drivers such as price, duration of therapy and volume, she explained. "We continue to decrease the net Harvoni price per patient as the US payer mix shifts from private to public, more patients are on 8-week vs. 12-week regimens and the EU mix shifts to Southern Europe, where prices are lower," she said.

On the earnings call, Gilead Chief Operating Officer Kevin Young noted that while US HCV revenue is down 33% year-over-year, it has risen 13% sequentially. "Since the beginning of the year, access has improved and almost all major commercial payers have [moved away from] fibrosis score criteria, joining Medicare and the VA in this regard," he said. "Medicaid remains the only payer segment where use is still generally restricted to the sicker patients. There are other significant barriers to access, but we are encouraged that some states have recently moved away from fibrosis restrictions towards more open access."

A recent study by the International Society of Pharmacoeconomic and Outcomes Research noted that restricting treatment to patients with cirrhosis or advanced fibrosis was going to increase costs in the long term. *(Also see "Full Access To HCV Drugs Would Save Money Long-Term, Study Finds" - Pink Sheet, 27 Jun, 2016.)*

According to Young, approximately 59,000 people started HCV therapy in the second quarter and around 90% of those began a sofosbuvir-based regimen. "Importantly, third-party databases suggest that new patients are being identified through increased screening efforts. As evidence, approximately 14m people were screened for HCV for the period of 2014 through 2015 and approximately 280,000 were confirmed RNA positive in that two-year period," Young continued. "These figures represent a significant increase from the years prior to the launch of Sovaldi. We estimate 3m individuals remain infected with HCV in the US, approximately half of whom are diagnosed."

Increased Access Offset By Less-Urgent Patients

Patient inflows into care in the US remain steady at about 30,000 a month, the exec pointed out, and Gilead now estimates that roughly 90% of commercially covered lives have access to HCV therapy regardless of fibrosis score. The company, however, is seeing a reduced trend of patient starts among insurers that have had full access in place for longer periods of time. Most of the sickest patients have been treated, and so treatment now tends toward less-ill patients who often qualify for an eight-week duration of therapy.

"In terms of all new HCV treatment starts in the second quarter, approximately 45% came from within the public-payer systems," Young said. "We anticipate this percentage will remain largely the same through the remainder of the year. The VA is one example of a payer within this

segment and their commitment to treating and curing veterans who have HCV, using budget allocated by Congress to do so, is truly groundbreaking. We are aware that in some cities, extra clinics have been scheduled to help shoulder the workload. However, we also expect that in the longer term, socially disadvantaged patients within the VA system will be harder to reach and bring to care, and that the rate of treatment will decline."

Roger Longman, CEO of the reimbursement consulting firm Real Endpoints, said in an interview that these trends demonstrate "the impact of an energized and powerful payer community." The FDA approval and launch in January of **Merck & Co. Inc.**'s *Zepatier* (grazoprevir/elbasvir), bringing a third competitor into the all-oral therapy market joined by **AbbVie Inc.** with its *Viekira Pak* (ombitasvir/paritaprevir/ritonavir; dasabuvir) in 2014, has effectively forced prices down in the US public-payer markets, he said. *(Also see "Sales Down, Discounts Up: Hepatitis C Market Feeling Zepatier Launch" - Scrip, 13 May, 2016.)*

"Merck's Zepatier came out and is really a Medicaid kind of product," Longman asserted. At launch, Zepatier had a wholesale acquisition cost of $54,800 for a 12-week course of therapy, about 30% below the pricing set initially for Harvoni. *(Also see "Merck Hep C Drug Zepatier OK'd " - Scrip, 29 Jan, 2016.)*

"Zepatier has forced down the prices in that market," he added. "It's easier for plans to buy the Merck drug for their Medicaid population without hurting the rebates that they get for their other businesses. It's an interesting situation. If it were the commercial world, plans that contracted for Zepatier would lose the rebates they get from Gilead because of their preference for Zepatier. But because Medicaid gets best price, they're not going to lose the best-price deals they get for Harvoni in that world. So there's no penalty to Medicaid plans for preferring Zepatier. And that really hurts Gilead."

On the Gilead earnings call, Milligan predicted that the patient flow in the US would remain strong for many years to come. He noted that only 13% of patients starting HCV drug therapy now have the most severe fibrosis score, F4, while the percentage was above 21% in years prior.

"With less severely ill patients, there's less urgency to immediately treat patients," the CEO said. "This may explain the slower rate of treatment versus last year. However, we do believe these patients will eventually benefit from treatment and this means the flow of patients will continue for many years to come."

Benefiting Gilead, he said, are HHS policies that support HCV testing – the company estimates that about 280,000 new patients were diagnosed in the past two years.

"So, while there's been a slowing of treatment compared with the rush of patients when Sovaldi and Harvoni were first approved, the HCV market is attractive over the longer term, providing good revenues, strong cash flow and earnings-per-share on top of our base business of chronic therapies," Milligan said.

Still to come from Gilead is a triple-therapy pill that includes sofosbuvir, velpatasvir and the pan-genotypic protease inhibitor voxilaprevir (GS-9857). Milligan noted that it is being tested in four Phase III trials, two in treatment-failure patients, and two others testing its potential to offer an eight-week regimen for treatment-naïve patients across all genotypes, with or without cirrhosis. Gilead hopes to have top-line data from those studies by year's end and intends to position the triplet as a salvage therapy for HCV patients who've failed on other therapeutic regimens.

Young said there might be a significant market opportunity for salvage therapy in Japan, where significant treatment resistance is being seen in patients who received a regimen of Sovaldi with **Bristol-Myers Squibb Co.**'s NS5A inhibitor *Daklinza* (daclatasvir). Elsewhere, however, Harvoni is providing a very high cure rate in genotype 1, while Epclusa now offers similar hope to patients with genotypes 2 and 3 of the virus. In the US and EU, the market opportunity for a salvage regimen likely will be "far more modest," the COO said.

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