Closer Look

MEMORANDUM

Merck 1Q13 - Januvia franchise sales fall 1% to $1.3 billion, first year-over-year decline in franchise history - May 7, 2013

Executive Highlights

- Worldwide 1Q13 Januvia/Janumet sales totaled $1.3 billion in 1Q13, down 1% from 1Q12 and down 18% sequentially
- On the Pfizer/Merck partnership, Merck highlighted the potential ertugliflozin/sitagliptin fixed-dose combination as a key differentiating factor for the SGLT-2 inhibitor.
- Merck has initiated two additional phase 3 trials for its once-weekly DPP-4 inhibitor MK-3102.

Merck reported 1Q13 financial results last week in a call led by CEO Kenneth Frazier. In contrast to the excitement surrounding Merck and Pfizer's partnership for the SGLT-2 inhibitor ertugliflozin, the call had a somber tone due to the first quarter ever of weaker-than-expected sales of the Januvia franchise (Januvia, Janumet, and Juvisync). The franchise posted sales of $1.3 billion, down 1% year-over-year (YOY) as reported and down 18% sequentially. The 1Q13 results mark the first YOY decline in the franchise's history and the worst performance sequentially ever; indeed, previously, its weakest YOY growth was 15% in 3Q12 - Merck's weakest performance sequentially was also that quarter, down 6%. Operationally, things didn't look too much better, though sales did increased 1% YOY on this metric. We do point out that Merck's payment schedule from Japan distorts the sequential growth, since $100 million in sales are only reported to Merck's Japanese co-marketing partner during 2Q and 4Q. Had the $100 million paid in 4Q12 been split evenly between 4Q12 and 1Q13, the sequential decline in 1Q13 would have looked slightly better, at 14%, though still weak, relatively speaking. Global franchise sales in 1Q13 were split between $884 million in Januvia sales (down 4% from 1Q12 and down 22% from 4Q12) and $409 million in Janumet sales (up 4% from 1Q12 and down 10% from 4Q12) - both products experienced the lowest YoY and sequential growth rates in their history. Merck stated that it was "not satisfied with [its] overall number for the Januvia franchise."

Both US and ex-US sales weakened in 1Q13; however, slowing US sales appeared to have underpinned the worldwide loss. US franchise sales totaled $659 million in 1Q13, down 5% YOY and down 18% sequentially. Management attributed the reduced sales to slowing growth in demand due to reduced potential to take market share from thiazolidinediones, increased levels of discounting due to more price competition (though Januvia continues to have over a 75% market share in the US and 85% preferred formulary status), and a $70 million inventory reduction, which Merck believes was a one-time event in response to stabilizing demand. Management estimated that had this inventory reduction not occurred, US sales would have increased about 5% YOY. Merck is addressing weakness in a number of ways, including, to counter these slowing sales, training and reassigning additional full-time dedicated sales personnel in the US to Januvia. While management did not comment on the increasing concern over incretins and pancreatitis, we believe that this issue could have played a significant role in dampening domestic (and international) sales growth. International sales in 1Q13 grew 3% YOY and declined 19% sequentially. Normalizing for the Japanese payment schedule, ex-US sales declined 7% sequentially. Management highlighted that in Japan, DPP-4 inhibitors (Merck has a ~70% market share) are the leading oral anti-diabetic class - ahead of sulfonylureas and, strikingly, metformin (we are curious about the co-pay for DPP-4 inhibitors relative to sulfonylureas and metformin, and whether the class' price is less of a concern in Japan as it is in other countries).

Front and center on the pipeline front was Merck and Pfizer's new collaboration to develop and commercialize Pfizer's "phase 3-ready" SGLT-2 inhibitor ertugliflozin. While management did not provide

new details, they stated that Merck is "very pleased" to be collaborating with Pfizer and that ertugliflozin has "very desirable properties and an extremely strong phase 2 profile" - we hope to hear more details on this front, as few clinical results have been presented thus far. Merck believes that the "importance of combination [therapies] just can't be overemphasized" and that ertugliflozin can be differentiated from other SGLT-2 inhibitors (they were not specific on this although expressed great enthusiasm for its fixed-dose combination (FDC) potential with sitagliptin - we wonder if it means Merck believes the Pfizer SGLT-2 has a cleaner side effect profile than other SGLT-2 inhibitors in development). Interestingly, Merck has conducted market research in Europe that suggests that SGLT-2 inhibitors will be used after DPP-4 inhibitors. We imagine this will differ by patient group but could see more patients and providers being interested in fixed dose combinations since the two should work well together (pending the side effect profile of ertugliflozin). We are not surprised that Merck owns the phase 3 clinical program for ertugliflozin ~ we imagine that if it enters a partnership where Januvia and Janumet will be combined, it will want control of the formulaton.

Management did not provide any other updates to the diabetes pipeline, but we note that two of ten phase 3 trials for the once-weekly DPP-4 inhibitor MK-3102 have completed recruitment, and that another six are now recruiting. The latest primary completion date listed is now July 2016 (with the exception of the cardiovascular outcomes trial, whose completion date is 2017) - this timeline makes a mid-to-late-2017 approval possible, should all go well. No updates were provided on SmartCells, Merck's interest in the GPR40 mechanism, or Merck's candidate for the treatment of painful diabetic neuropathy MK-6095.

FINANCIAL UPDATE

- **In 1Q13, sales of the Januvia franchise totaled $1.3 billion, down 1.4% as reported (up 1% operationally), the first negative YOY growth in the franchise's history.** Prior to 1Q13, the franchise's weakest YOY growth was 15.4% in 3Q12. Sequentially, the franchise's revenue decreased 18.5%; this was also the franchise's weakest sequential growth result. Similar to YoY results prior to 1Q13, the franchise's weakest sequential growth was a negative 6% in 3Q12.
- **As a reminder, the franchise's sequential growth is impacted by its payment schedule in Japan.** Merck records $100 million in sales from its Japanese co-marketing partner Ono Pharmaceutical only in 2Q and 4Q. Thus, Merck overstates revenue every 2Q and 4Q, and understates revenue for 1Q and 3Q. The ~$100 million difference between 1Q13 and 4Q12 resulting from this payment schedule accounts for about one-third of the $293 million reduction in sales seen between 4Q12 and 1Q13. Had this $100 million been evenly distributed between the two quarters (i.e., an additional $50 million being reported in 1Q13 and $50 million less being reported in 4Q12), the sequential decline would have been 14% (rather than the 18% posted).
- **The decline in the Januvia franchise's worldwide franchise sales stemmed largely from slower sales in the US.** Domestic Januvia franchise sales of $659 million declined 5.2% YOY and dropped 18.2% sequentially. Similar to the franchise's worldwide trends, 1Q13's YOY drop was the first negative growth reported to date; prior to 1Q13, the weakest YOY growth had been ~12.0%, observed in both 2Q10 and 4Q10.
- Management cited three factors to explain the drop in domestic revenue: 1) weakening growth in demand, 2) increasing price competition, and 3) their customers making a ~$70 million inventory reduction. Management expressedconfidence that the franchise's domestic sales will improve; however, they guided for YOY rebounding (over an undefined time period) to mid-single digits, opposed to the ~18% domestic growth seen the last two years.
    - **Demand** for Januvia has is not growing as rapidly as it had about one year ago following growing concerns over thiazolidinedione's safety, according to Merck. Januvia prescription growth was ~4% during 1Q13, which Merck stated was significantly, lower than demand growth in 1H12 (Merck did not disclose absolute script numbers). Management explained during Q&A that this was a challenging comparison since around this time last year, Januvia Rx growth was between 11-16% as increasing concerns over TZDs' safety prompted

greater Januvia uptake. In 1Q13, there was less TZD share to erode and its Rx growth was closer to the 8% and 9% growth that the franchise was experiencing before "the TZD opportunity," which was also from a lower base.

- **Price competition** in the US caused Merck to put forward additional discounting and rebates. Management stated that Merck increased its price consistent with the market; however, they explained that their "new competitors" are offering more rebates in an attempt to improve their formulary positions. Merck has maintained its "very strong" managed care access, with about 85% preferred formulary status. Despite the market being "very competitive," the Januvia franchise still has ~75% of the US DPP-4 inhibitor market albeit likely at a lower average selling price.
- **Inventory** reductions of ~$70 million during 1Q13 caused Januvia wholesalers' inventories in the US to be at their lowest in about two years and had a significant impact on the franchise's bottom line, according to management. Had Merck's customers not made these reductions, Januvia's YOY growth would have been ~5% (which still would have been a record low for the franchise) and its sequential drop would have been ~9%. Management hypothesized that the reductions were a one- time adjustment by wholesalers who had overestimated Rx demand growth based on the acceleration seen after TZD safety concerns arose. Merck believes that the current levels can consistently supply the market and does not expect there to be an inventory bump in the future.

- **While management did not mention the growing concern over incretins and pancreatitis, we believe this issue could have dampened franchise sales growth.** As a reminder, this topic received greater focus after *JAMA Internal Medicine* published a case-controlled database study that found that sitagliptin and exenatide are associated with an increased risk of hospitalization for acute pancreatitis (our report on the article is available at http://www.closeconcerns.com/knowledgebase/r/70054620). One day following the article's publication, the ADA and AACE issued a strongly worded joint statement that highlighted the study's lack of rigor and declared that the *JAMA* article "does not provide the basis" for changing diabetes treatment protocols. KOLs have generally agreed, remarking that because of the trial's flawed study design, the results are not compelling. Since then, Dr. Peter Butler's (USC) group has published a morphological study on incretins and pancreatitis in *Diabetes* that prompted the FDA to examine this potential risk more seriously (for details, please see our April 18, 2013 *Closer Look* at http://www.closeconcerns.com/knowledgebase/r/b03ed6a2). The debate continued in the latest issue of *Diabetes Care*, in which incretin-expert Dr. Michael Nauck and Dr. Peter Butler wrote contrasting Point:Counterpoint articles (see our reports for details: http://www.closeconcerns.com/knowledgebase/r/6d3e6d53). We hope to gain a greaterunderstanding of this potential risk during the NIDDK workshop on pancreatitis, diabetes, and pancreatic cancer, which will be held June 12-13, 2013 in Bethesda Maryland.
- **International Januvia franchise sales of $634 million in 1Q13 grew 2.8% YOY (7% operationally) and down 19.0% sequentially.** Growth as reported was the slowest in the franchise's history; previously, the lowest growth was 3Q12's 14.4% (from a lower base of $540 million in 3Q11 versus 1Q12 international revenue of $617 million). We note that, correcting for the Japanese payment schedule, international sales declined 7.2% sequentially. Management expects the Januvia franchise's international growth to return to the low double-digits (they did not explain what would prompt this rebound).
- **Management noted that they are starting to see lower YOY growth in Japan due to high market penetration.** According to Merck, DPP-4 inhibitors are the leading oral anti-diabetic class in Japan (over SUs and, surprisingly, metformin) in terms of patient days on therapy, and Januvia accounts for nearly 70% of the DPP-4 inhibitor market. Curiously, in Merck's 4Q12 update, the company identified Japan (along with the US) as a driver of the franchise's growth; we are surprised the impact of this market would change so quickly.

- **Januvia alone posted $884 million in worldwide revenue, declining 4% YOY and down a striking 22% sequentially.** Domestic revenue for Januvia totaled $462 million, down 6% from 1Q12 and down 18% from 4Q12. Januvia posted international sales of $422 million, down 1% from 1Q12 and down 26% from 4Q12.
- **Janumet worldwide sales totaled $409 million, up 4% from 1Q12 and down 9% from 4Q12**. In the US, Janumet posted revenue of $197 million. This represented a 2.5% decline from 1Q12 and a 17% drop from 4Q12. Janumet revenue faired better internationally, growing 12% YOY and declining 1% sequentially.
- **Consistent with Merck's recent financial updates, the company believes the Januvia franchise can gain market share from sulfonylureas (SUs)**. SUs have accounted for a stable ~35% of patient days on therapy since at least 2Q12. Merck remarked that it has been more difficult to erode SU's market share in the US than in other regions, like Japan (where DPP-4 inhibitors have a larger market share than SUs). As a result, Merck has trained and reassigned additional full-time dedicated sales personnel in the US to Januvia; we look forward to hearing more about this strategy.

MERCK/PFIZER COLLABORATION

- **Merck is "very pleased" to be collaborating with Pfizer on the phase 3 ready SGLT-2 inhibitor ertugliflozin.** In describing Merck and Pfizer's historical relationship, Merck VP, US Medical Affairs, Dr. Sethu Reddy remarked at GTCBio's Diabetes Summit, "Some have said that it is a marriage between the Yankees and the Red Sox." Thus, we believe that the willingness and enthusiasm of the two rivals to partner on ertugliflozin speaks to the important role Pharma expects SGLT-2 inhibitors to play in diabetes care. Additionally, we think that this partnership is a striking example of effective risk- and cost-sharing between pharmaceutical companies.
- **Merck pressed that "the importance of combination therapy cannot be overemphasized."** This corroborates statements made by other big Pharma managements, including Lilly's CEO Dr. John Lechleiter around the time of the JP Morgan conference. Management indicated that ertugliflozin will be differentiated from other SGLT-2 inhibitors; we look forward to hearing more about its fixed-dose combination (FDC) availability with Januviaand eventually Janumet. We believe FDCs will be much more common in future years and that Merck's ability to combine Januvia with ertugliflozin puts it in an even stronger position going forward - without the partnership, Merck may have been on the defensive without access to an SGLT-2 inhibitor.
- **Still, it is quite novel to see the two powerhouse PCP companies (and erstwhile competitors) teaming up on this front;** it further validates the SGLT-2 inhibitor mechanism and certainly provides valuable risk-sharing and cost-sharing. During the call, Merck commented that its market research in Europe found that SGLT-2 inhibitors are being used after DPP-4 inhibitors. It will be interesting to see if this holds true (it's still early days); this would certainly be to Merck's advantage, as it would imply a lower chance of ertugliflozin-based products cannibalizing Januvia sales. By and large, it's too early to say; some HCPs will prefer greater efficacy and some weight loss and some risk of side effects while others will prefer a very clean side effect and safety profile and lower efficacy. At GTCBio 2013, Dr. Lauren Shearman (Executive Director of Scientific Licensing & Acquisitions, Merck) commented that Merck believes J&J is positioning Invokana (canagliflozin) as a second-line therapy to go head-to-head with Januvia (our GTCBio 2013 report is available here; our report on Invokana's recent FDA approval can be found at http://www.closeconcerns.com/knowledgebase/r/89751926). In our view, this could result in patients being moved onto therapy sooner - and to the next therapy - sooner, which is certainly a win for patients if their overall care is optimized.
- **As we have noted before, while Merck and Pfizer have not commented on the regulatory timeline, an FDA submission in 2016 appears reasonable.** For background, BMS/AZ's Forxiga recently launched in Europe (an FDA resubmission is targeted for mid-2013) and

the FDA approved J&J's Invokana in March (an EU decision is expected in 3Q13). Lilly/BI filed empagliflozin in the US and EU in March 2013 and plan to present phase 3 data at ADA 2013 (our ADA preview can be found at http://www.closeconcerns.com/knowledgebase/r/a05a11f0). Several other companies are also developing SGLT-2-based therapies, including Astellas/Kotobuki (ipragliflozin; phase 3), Chugai (tofogliflozin; phase 3 in Asia), Lexicon (phase 3 for the SGLT-1/ SGLT-2 dual inhibitor LX4211 slated to begin in 1H13), and Novartis (SGLT- 1/SGLT-2 dual inhibitor LIK066; phase 2).

- **We have heard little data on ertugliflozin; at the moment, it is unclear how Pfizer/Merck will differentiate their candidate from other SGLT-2 inhibitors as a monotherapy.** Given ertugliflozin's late market entry (at least four years after Forxiga), showing superior outcomes (better efficacy or tolerability or safety) will be key, especially for reimbursement. We imagine that Merck's brand name recognition and established patient base will complement Pfizer's expertise in primary care; however, BMS/AZ and J&J also have quite strong and broad-reaching brand recognition. Still, the Januvia franchise has been more successful than any other primary care franchise in the last 15 years that we can remember; this is tough competition for any company!
- **What does the data show? We last heard data on ertugliflozin at MDDD 2012:** The phase 2 data presented showed that ertugliflozin provided an average A1c reduction of 0.8% (for the 5 mg dose; baseline A1c is unknown), an average weight loss of ~2.5 kg(5.5 lbs; 3% body weight reduction for this cohort of patients), and reductions in blood pressure (~4 mmHg). For full details, please see page 25 of our MDDD report at http://www.closeconcerns.com/knowledgebase/r/208ea837.

PIPELINE UPDATES: MK-3102

- **Management provided no updates on Merck's diabetes pipeline, though ClinicalTrials.gov shows several new developments** for phase 3 studies of the once- weekly DPP-4 inhibitor MK-3102. Aside from MK-3102's cardiovascular outcomes trial (which is scheduled to complete in late 2017), the July 2016 completion of MK-3102's clinical trial program could place a potential approval around mid-to-late-2017.
  - **Two new phase 3 studies have been added since Merck's 4Q12 update:** one is a non-inferiority study comparing MK-3012's and sitagliptin's safety and efficacy in combination with metformin. The trial will have a two-week run-in period with placebo plus metformin before a 24-week double-blind treatment period (n=600). The trial has three primary outcomes: change in A1c, the number of participants who experienced at least one adverse event, and the number of people who discontinued the study due to an adverse event. The study is not yet open to enrollment - it is expected to begin in June 2013 and to complete in December 2014 (ClinicalTrials.gov Identifier: NCT01841697). The other trial will asses the safety and efficacy of MK-3102 in people 18-44 years old who have type 2 diabetes and inadequate glycemic control (n=200). This trial is expected to begin this May and to end in December 2015 (ClinicalTrials.gov Identifier: NCT01814748).
  - **Additionally, all eight studies that had been listed at the time of Merck's 4Q12 update are either recruiting or have completed recruitment.** As a reminder, these eight studies listed in order of time to primary completion are 1) MK-3102 compared to Januvia and placebo in Japanese patients with type 2 diabetes (ClinicalTrials.gov Identifier NCT01703221; active not recruiting); 2) MK-3102 as a second-line add on to oral therapy compared to placebo in Japanese patients with type 2 diabetes (NCT01697592; active not recruiting); 3) MK-3102 vs. placebo as a third-line add-on to metformin and a sulfonylurea (NCT01704261; recruiting); 4) MK-3102 vs. sulfonylurea as an add-on to metformin (NCT01682759; recruiting); 5) cardiovascular outcomes associated with MK-3102 use (NCT01703208; recruiting); 6) MK-3102 as monotherapy vs. placebo (NCT01717313;

recruiting); 7) MK-3102 in people with moderate or severe chronic kidney disease or kidney failure on dialysis (NCT01698775; recruiting); and 8) MK-3102's safety and efficacy as an add-on to metformin vs. placebo for 24 weeks and then vs. sulfonylurea for 80 weeks (NCT01755156; recruiting). For more detail on these trials, see our Merck 4Q12 report at http://www.closeconcerns.com/knowledgebase/r/400ebea2 and our Merck 3Q12 report at http://www.closeconcerns.com/knowledgebase/r/4a9d4587.

- **For background, Merck has previously stated that MK-3102 has a long half-life that enables once-weekly dosing because it is not metabolized** (for more information on MK-3102, please see our report from Merck's November 2011 R&D day at http://www.closeconcerns.com/knowledgebase/r/4d18c66c).

PIPELINE UPDATE: REMAINING DIABETES PIPELINE

- **To our knowledge, the rest of Merck's diabetes pipeline remains the same:**
  - **We believe its SmartCells glucose-responsive insulin program remains in preclinical development.** As a reminder, Merck acquired SmartCells (andSmartInsulin, the company's glucose-responsive insulin) in December 2010. For more details on SmartInsulin, see our report on the Smart Cells acquisition at http://www.closeconcerns.com/knowledgebase/r/f121fcfe and our Merck R&D and Business Briefing coverage at http://www.closeconcerns.com/knowledgebase/r/4d18c66c. While Merck has historically declined to comment on a possible indication for Januvia in type 1 patients, the SmartCells collaboration certainly demonstrates Merck's strong interest in and focus on type 1 diabetes.
  - **Merck is still developing a candidate for painful diabetic neuropathy (MK-6096) that completed a phase 2 trial in May 2013** (ClinicalTrials.gov Identifier: NCT01564459). MK-6096 is also in phase 2 development for insomnia, depression, and migraines. The diabetic neuropathy field has been relatively active of late with the launch of NeuroMetrix's Sensus pain management device (more specifically, a transcutaneous electrical nerve stimulations [TENS] device) in January 2013 and the approval of J&J's Nucynta ER (extended-release tapentadol) for this indication in August 2012. DPN represents a field with great-unmet medical need: the disease is notoriously difficult to treat due to its complex pathogenesis and due to the wide variation in patient responsiveness to available treatments. Other approved products for DPN include Pfizer's anticonvulsant Lyrica (pregabalin) and Lilly's antidepressant Cymbalta (duloxetine). Pregabalin is the only level "A" recommended treatment (pharmacologic or otherwise) for DPN in the guideline developed by the American Academy of Neurology, the American Association of Neuromuscular & Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. Several other options (both approved and off-label) are recommended as level "B" (including TENS devices), with no algorithmic guidance for which of the options should be used because patient responsiveness is so variable.
  - **In the past, management has expressed interest in the GPR40 mechanism, but we have not heard any updates on this front.** Looking forward, we're curious whether a GPR40 agonist/Januvia fixed-dose combination or a GPR 40 agonist/Januvia/ertugliflozin fixed-dose combination could be possible. As a reminder, GPR40 is an orphan G-protein coupled receptor expressed in pancreatic islets. Its agonists stimulate insulin secretion in a glucose-dependent manner. Takeda is the main company currently developing a GPR40 agonist for type 2 diabetes. Its compound TAK- 875 has completed phase 3 testing, with US, European, and Japanese filings expected in 2Q15-1Q16.

Questions and Answers

Q: On Januvia, can you give us a little bit more detail on what happened here? It seems like we've had competitors in this space for some time. Did something change recently? And without this TZD kind of tailwind, do you think you need to do a better job highlighting to physicians to really get the class of Januvia back on track?

A: I want to first start off by saying we remain confident that there are growth opportunities for Januvia and for the DPP-4 class moving forward. The opportunities are that diabetes prevalence is growing. Sulfonylureas still represent a huge amount of patient days of therapy, about 35% of patient days of therapy. We've been successful in some markets. In Japan, for example, DPP-4 inhibitors now represent more patient days of therapy than the sulfonylureas do. We have to continue to talk with physicians and show them the benefits that you can get by adding Januvia to metformin and I think with the additional dedicated resources that we're putting behind Januvia in countries like the United States - where we now have full-time dedicated people in discussion with physicians - that will give us some additional momentum.

I also want to give you additional perspective on what has occurred and what we see as we move forward. I'll go back to demand and I'll give you a little bit more color on demand. So if you look at IMS data, you can see about 4% growth. But if you look prior to TZD events, you can see Januvia volume growth was in the single digits. It was somewhere between 8% and 9%. When the TZD opportunity occurred, we increased our resources, we focused on the opportunity and we saw growth between 11% and 16%, so we saw a very big acceleration. It is very difficult to compare now to back then when this acceleration was occurring. So we believe that there is room for us to continue to grow and as we get through this summer when the acceleration started to go away, we'll start to see better comparisons year-over-year in terms of Rx growth.

In terms of price, we have increased our price consistent with the market. The rebates and discounts have increased because new competitors are seeking to try to improve formulary positions by lowering price or offering more rebates. So our discounts have gone up since last year, but we manage them closely and we manage them to maximize access. And the good news is, we have very strong managed care access, with about 85% preferred formulary status, and if you look at our share in the US, we still have about a 75% share, despite all the competition.

And then the last thing, which I mentioned before, our customers did reduce inventory levels in the US by about $70 million for the Januvia franchise in the first quarter. This is the lowest days of supply that they've been running for about 2 years. So if you excluded that, we would have seen sales growth of about 5% in the US.

Outside the US, the underlying growth remains in the low double-digits, and that's what leads us to feel confident that we anticipate mid-single digit growth in the US, and we expect this return to low double- digit growth outside the US. So we believe that there is an opportunity for Januvia moving forward. (Editor's note - this is still far lower growth than seen in recent years.)

Q: Regarding the $70 million inventory reduction, you mentioned that you think it's a one-time thing; can you just elaborate on why you think it's one time? And should we thus expect to commence a return to more normal wholesaler levels next quarter so we can expect a sequential bump up and should we be thinking about that in our models?

A: We believe there was a $70 million inventory reduction in the US, and we base that upon days of supply on hand that we receive data on. And I think what happened was with the very strong acceleration that we saw with the TZD volume, wholesalers were buying in based upon that volume growth. Now that we've seen less of a volume growth, they've kind of taken the inventory down to, I think, manageable levels. They're at levels where they can consistently supply to the market, but they're at days of supply that are lower than they've been before. So we don't expect them to go lower but I would not necessarily expect a bump up in the future. What we expect is mid-single digit sales growth in the US and that's reflective of the current Rx trends and the current marketplace competition and then outside it's low double-digit growth and that's really what we're seeing with underlying growth in demand for the first quarter.

Q: Regarding your recent partnership with Pfizer, where do you see the SGLT-2 inhibitors fitting in diabetes, particularly relative to the DPP-4 inhibitors?

A: So let me give you some background on the SGLT-2 inhibitors. The first US launch was less than a month ago, so it's still pretty early. In Europe the first launch was in late 2012, so it's early but we have some data on that. We've done some market research in Europe and what we see is that in most cases, the SGLT-2 inhibitor class is being used by specialists after the DPP-4 inhibitor class. And you know diabetes is a progressive disease. Most of the patients are on more than one prescription over time. The physicians typically begin treatment with metformin and then they add on therapies until a patient ultimately gets to insulin. So we believe there's room for another class.

However, we believe the SGLT-2 inhibitors will be used as an oral option after the DPP-4 inhibitors. And we believe that Januvia will continue to be the preferred choice as an add on to metformin because of the efficacy profile, the proven tolerability, and the five years of experience that physicians have with the product already. (Editor's note - Januvia has been approved since 2006.) But we're very pleased to be collaborating with Pfizer. We think that there is room to commercialize an SGLT-2 inhibitor and we're excited about the potential combination because after utilizing Januvia, we think a nice combination with a high quality SGLT-2 will be a very attractive option for physicians when they want to continue to use oral therapies prior to insulins.

I looked in detail at the materials, of course, from Pfizer before we went forward with that deal. Their molecule - that we're pleased to be collaborating on - has very desirable properties and an extremely strong phase 2 profile. So there's reason to want to go forward with a leading molecule like that in developing combinations.

Q: What kind of differentiation do you see in ertugliflozin given the fact that you may be number four or later to market?

A: We're excited about that opportunity. As I mentioned, we see SGLT-2 inhibitors as a potentially important class that will be utilized in an oral diabetic agent after DPP-4s, in particular, after Januvia. We think having a combination with the market leader Januvia will represent a very significant opportunity. So it's early to see the exact data from the product as a monotherapy, although we're excited about the initial phase 2 data. We think the combination also represents a very significant opportunity because of the success of Januvia in the marketplace. The importance of combination therapy just can't be overemphasized. Again, we have a compound that - based on what we can see - plays nicely with others. That's really important and provides us with a big advantage. Going forward, we have a number of programs that we're going to be talking about.

-- by Hannah Deming, Nina Ran, and Kelly Close