Closer Look

MEMORANDUM

Merck 2Q13 - Januvia franchise sales rise 5% to $1.5 billion - August 1, 2013

Executive Highlights

- Januvia/Janumet sales totaled $1.5 billion in 2Q13, up 5% from 2Q12 and 20% from 1Q13.
- Merck continues to support studies in China to pursue reimbursement for the Januvia franchise.
- Pfizer/Merck's SGLT-2 inhibitor remains on track for 2H13 initiation of phase 3.

Merck reported 2Q13 financial results Tuesday in a call led by CEO Kenneth Frazier. The call had a positive tone as the Januvia franchise (Januvia, Janumet, and Juvisync) showed major signs of rebounding since 1Q13 when it posted its first year-over-year (YOY) decline (1%) - although most of the gains come from pricing and inventory and won't necessarily be repeated. Still, in 2Q13, the franchise posted sales of $1.55 billion, up 5% YOY as reported (10% in constant currencies) and 20% sequentially, and notably, the second best result ever for the franchise, which is now back annualizing at $6 billion. We note that Merck's payment schedule from Japan distorts the sequential growth, since $100 million in sales from Merck's Japanese co-marketing partner are only reported to during 2Q and 4Q. Had the $100 million paid in 2Q13 been split evenly between 1Q13 and 2Q13, the sequential rise in 2Q13 would have been 11%. Management painted its entire portfolio's results, including the Januvia franchise's, as "more accurately reflecting" its "underlying" strength compared to 1Q13's results. While these results were certainly positive, increasing competition and cost-pressures remain major concerns - even to Merck, as well as the entire diabetes ecosystem. Access is an especially big concern in the EU..

Both US and ex-US sales strengthened in 2Q13 and since slowing US sales seemed to have underpinned Januvia's loss in 1Q13, the US rebound was particularly encouraging - and this also received more attention on the call. US franchise sales totaled $806 million in 2Q13, up 9% YOY and 22% sequentially. Management attributed four-of-the-nine percentage points of YOY growth to higher price, four to inventory benefits, and one to growing script demand. Script volume, of course, is a better predictor of demand than either inventory or price. International sales in 2Q13 grew 2% YOY (11% ex-exchange) and 17% sequentially to $740 million. Normalizing for the Japanese payment schedule, ex-US sales rose 1% between 1Q13 and 2Q13, though the Januvia franchise did better ex-US than in the US during 1Q13, with YOY growth of 3%. Surprisingly, Japan was the only region in which Januvia sales did not increase; as recently as 4Q12, Japan was one of two key drivers of growth (the other being the US). Explaining this decline, Merck cited a challenging yen, highlighting that script volume grew in Japan.

On sitagliptin's development, Merck has studies in China to pursue reimbursement in the large and growing market. Merck also appears to be pursuing pediatric indications for the Januvia franchise. Turning to Merck's diabetes pipeline, consistent with Pfizer's, past comments, Merck reaffirmed that the SGLT-2 inhibitor ertugliflozin, is on track to begin phase 3 in 2H13. Pfizer has not released much detailed data on the agent to date, though Merck has characterized its results as extremely strong. According to Q&A, fixed-dose combinations (FDCs) of ertugliflozin and Januvia or Janumet remain a goal for Merck. We also gleaned several updates from ClinicalTrials.gov, where Merck's once-weekly DPP-4 inhibitor MK-3102 has 11 (!) active phase 3 trials. A number of these trials compare the agent to sulfonylureas, reflecting Merck's goal of moving patients from SUs to DPP-4 inhibitors. A phase 2 trial of MK-6096 for painful diabetic neuropathy, was completed in April. No updates were provided on the SmartCells glucose-responsive insulin program, or on potential development of a GPR40 agonist.

FINANCIAL UPDATE

- **In 2Q13, sales of the Januvia franchise rebounded 19.6% sequentially to $1.55 billion with YOY growth of 5.3%.** This result seemed to relieve investors and management alike on the call since 1Q13 was the first negative YOY growth in the franchise's history (for more details on the 1Q13 results, please see our Merck 1Q13 report at http://www.closeconcerns.com/knowledgebase/r/foe5540f). In contrast, 2Q13 Januvia franchise revenue was over the $1.5 billion mark and only $40 million shy of its highest revenue ever ($1.59 billion in 4Q12).
- **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, revenue is superficially high every 2Q and 4Q, and low in 1Q and 3Q. The ~$100 million difference between 2Q13 and 1Q13 resulting from this payment schedule accounts for ~40% of the $253 million jump in sales seen between the two quarters. Had this $100 million been evenly distributed between the two (i.e., an additional $50 million being reported in 1Q13 and $50 million less being reported in 2Q13), the sequential decline would have been 11% (rather than the 20% posted).
- **The Januvia franchise's US sales were the highest in the franchise's history at $806 million.** Until 2Q13, the highest US sales were 4Q12's $802 million. The domestic result is particularly impressive since the 1Q13 decline in the Januvia franchise's worldwide sales stemmed largely from slower sales in the US (for more details, please see our Merck 1Q13 report at http://www.closeconcerns.com/knowledgebase/r/foe5540f). To accomplish this, domestic Januvia franchise sales rose 8.6% YOY (compared to their 5.2% YOY decline in 1Q13) and 22.3% sequentially (compared to their 17.8% drop in 1Q13). The YOY comparison in 2Q13 was pretty challenging as US Januvia franchise revenue rose 24.5% in 2Q12 to reach $742 million. Additionally, YOY growth of ~9% in 2Q13 was slightly higher than the mid-single digits the Merck guided for during its 1Q13. Merck attributed this difference to a $30 million inventory increase (details below) and continued to guide for mid- single digit growth in the US, excluding inventory changes. The Januvia franchise continues to have 75% of the US DPP-4 inhibitor market.
- **Merck cited three factors to explain the rise in domestic revenue: 1) higher price over last year, 2) a $30 million inventory benefit, and 3) growth in script volume.** Management attributed four percentage points of the 9% YOY growth to both price and inventory, and the remaining point to script volume. We wish that script volume had represented a larger share of YOY growth, since it is a more robust predictor of future demand than either inventory, whose fluctuations are difficult to predict, or price, which will likely be increasingly difficult to raise given intensifying competition and cost pressures. Notably, these reasons largely contrast with the reasons given for 1Q13's drop: 1) greater price competition, 2) a $70 million inventory reduction, and 3) weakening growth in script demand.
    - **Price** increases over last year accounted for four percentage points of the 9% YOY growth. Merck cautioned, however, that it continues to see increased rebate and pricing pressures, as competitors seeks to improve their formulary positions. In Merck's 1Q13 update, the company cited these increased levels of price competition as a reason why domestic Januvia franchise sales slipped. Januvia has preferred formulary status in "over 80%" of US patients (in the Merck's 1Q13 update, management stated that Januvia had about 85% preferred formulary status).
    - **Inventory** levels increased by about $30 million during 2Q13. This trend contrasted with the $70 million reduction seen during 1Q13, which caused US Januviawholesalers' inventories 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 increased inventory during 2Q13, Januvia's YOY growth would have been ~5% (instead of 9%) - the same level of growth that would have been seen in 1Q13 had the $70 million inventory reduction not occurred. Without the $30 million benefit, the sequential increase would have been ~18% (instead of 22%). During Q&A, Merck explained that inventory movements on the order of $30 million or $50 million are difficult to anticipate, as they

represent only about half-a-day of sales. Merck therefore excluded channel movements from its continuing guidance for US growth in the mid-single digits.

    - **As a reminder, during the 1Q13 update, management hypothesized that the $70 million reduction was a one-time adjustment** by wholesalers who had overestimated Rx demand growth based on the acceleration seen after thiazolidinone (TZD) safety concerns arose.

  - **Demand** for Januvia continues to grow but not as rapidly as it had about one year ago following growing concerns over TZDs' safety. Januvia prescription growth was slight at only 1%, which was down compared to 1Q13's ~4%. When considering the underlying strength of the Januvia franchise, we find this weakening script demand to be most concerning. Indeed, Merck also appears to be most concerned about this trend emphasizing during Q&A, "the real key is changing the TRx trend and that's what we're frankly focused on." During Merck's 1Q13 update, it stated that 4% YOY script demand growth was significantly lower than demand growth in 1H12 (Merck did not disclose absolute script numbers). Management explained during the 1Q13 Q&A that demand growth has been a challenging comparison. Around the time of 1Q12, Januvia Rx growth was between 11% and 16% because increasing concerns over TZDs' safety prompted greater Januvia uptake. Merck has previously stated that before TZD safety concerns arose, Januvia's Rx growth was closer to 8% and 9% and from a lower base.

- **Consistent with Merck's updates since at least 1Q12, the company believes the Januvia franchise can gain market share from sulfonylureas (SUs).** In 1Q12, SUs accounted for 37% of patient days on therapy - a number that has remained stable to date at~35% of patient days. We note, however, that Merck's tone around this issue appears to beintensifying; during yesterday's Q&A, Merck management emphasized, "All of our focus now is on of the sulfonylurea utilization" and explained that up until 1Q14 "most of [its] focus was on the TZD opportunity that's no longer there." Thus, we are hopeful they will make inroads into SU's market share in the future.

    - **During the 1Q13 update, 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. Additionally, yesterday, Merck remarked during Q&A that it has increased promotion spending and print direct-to-consumer advertising.

- **International Januvia franchise sales of $740 million in 2Q13 grew 1.9% YOY (11% operationally) and 17.0% sequentially.** YOY growth as reported in 2Q13 was the slowest in the franchise's history; previously, the lowest growth was 1Q13's 2.8% and before that it was3Q12's 14.4%, though the comparison was more challenging in 2Q13 than in 1Q13 (YOY growth in 2Q12 was 44% vs. in 1Q12 it was 36%). We note that correcting for the Japanese payment schedule, international sales grew 1% sequentially. Merck explained that the 11% operational increase was largely driven by volume growth. In 1Q13 and again in the 2Q13 call, management guided for international revenue growth in the low-double digits excluding exchange rates. Merck focused its comments on operational growth ex-US and characterized its underlying international business performance as being "very strong." For comparison, operational growth was up from 7% in 1Q13.
- **Management cited the challenging yen for why the "big difference" existed between reported and operational growth.** A "very significant amount" of Januvia sales are in Japan and Japan was the only region in which Januvia sales did not grow (we assume YOY, since Japan supply sales are not posted in 1Q) despite Januvia script volume increasing in Japan, as well as all other regions. Merck explained that the large share of Januvia sales in Japan combined with its revenue coming in "lumpy" (i.e., only in 2Q and 4Q) causes the yen-exchange rate to have a "very significant" impact on international sales not adjusted for the exchange rate.

    - **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. During the 1Q13 update, Merck warned that this high-market penetration was leading to lower YOY growth in the country. We are curious how Januvia reimbursement and price in Japan compares to that in the US and the EU where cheaper generics still account for more patient days on therapy.

- **Turning to Europe, Merck painted the reimbursement environment as "tough" and that it will likely "continue to be tough."** However, Merck expressed confidence that European governments see the implications of not treating diabetes and that Januvia has "strong potential" in Europe as a second-line to metformin, particularly if a person has side effect issues with a sulfonylurea. We note, however, that at least Germany's drug evaluation and reimbursement environment seems to be more challenging than Merck's comments suggest. For example, Merck was pleased with the German Institute for Quality and Efficiency in Health Care's (IQWiG) July 1, 2013 ruling that Januvia in combination with metformin has "hints of a minor added benefit" when compared to sulfonylureas, if the goal is to lower blood glucose levels tonear-normal levels. Indeed, this ruling is positive compared to Germany's Federal Joint Committee's (G-BA) prior decision that BI/Lilly's Tradjenta has "no additional benefit", causing its price to be non-negotiable. Thus, Tradjenta would likely have been priced similar to that of SUs and BI/Lilly decided to not launch the drug in Germany. Similarly, on July 1, 2013 IQWiG found that Novartis's Galvus or BMS/AZ's Onglyza have "no additional benefit." If G-BA confirms these findings, these agents' reimbursement will also become non-negotiable. Merck expects the G-BA to make a decision on Januvia's added medical value (and thereby reimbursement) in 4Q13. Management noted that Germany accounts for less than 5% of the Januvia franchise's sales
    - **For background, IQWiG is the German agency that evaluates drugs' quality and efficiency for German society.** Considering IQWiG's recommendation, the G-BA then decides on what drugs' added medical value is and how it should be reimbursed.
- **Januvia alone had a fine 2Q13, posting $1.1 billion in worldwide revenue.** This revenue was up 1.4% YOY and 21% sequentially. Domestic revenue for Januvia totaled $571 million, the highest in franchise history (until 2Q13 the record was $565 million in 4Q12). To achieve this, revenue grew 7.3% from 2Q12 and 24% from 1Q13. In contrast, Januvia ex-USrevenue did not rebound above pre-1Q13 levels, decreasing 4.6% YOY and increasing 18.7% sequentially to reach $501 million. In 4Q12, Januvia's international sales were $568 million.
- **Janumet had a strong 2Q13, with worldwide sales totaling $474 million. This was Janumet's highest-ever revenue; until 2Q13, 4Q12's $452 million held the record.** Worldwide Janumet sales were up 15.3% from 2Q12 and 16% from 1Q13. In the US, Janumet posted revenue of $235 million. This represented a 11.9% rise from 2Q12 and a 19.3% jump 1Q13. Janumet revenue also faired well internationally, growing 18.9% YOY and 12.7% sequentially.
- **Concerns about incretins potentially being associated with pancreatic events was not discussed during the call.** However, as a reminder, last Friday the EMA's CHMP issued a press release stating that current data does not adequately support an association between incretin-based therapies and pancreatic adverse events. In response, Merck released a response emphasizing that it will continue monitoring the safety of Januvia. For details on these press releases, please see our July 30, 2013 *Closer Look* at http://www.closeconcerns.com/knowledgebase/r/72400858. The KOL consensus surrounding incretins and pancreatic events seems to be that not enough evidence exists to alter prescribing behavior. However, we believe that the media coverage could be impacting DPP-4 inhibitor sales, particularly with the launch of SGLT-2 inhibitors offering an alternative.

DEVELOPMENT UPDATES: SITAGLIPTIN

- **According to ClinicalTrials.gov, Merck is supporting a number of studies investigating the use of sitagliptin in pediatric type 2 diabetes patients,** consistent with guidance that

Merck wants to pursue a pediatric indication for sitagliptin and associated co- therapies. We believe that sitagliptin would likely be a good fit for pediatric populations, given its relatively easy administration. We are, however, mindful of the words of Dr. Philip Zeitler (University of Colorado, Aurora, CO) at Keystone this year - he noted that clinical trials in pediatric type 2 diabetes patients generally do not fare well due to poor enrollment. We hope that Merck's scientific team finds a way to surmount this obstacle.

    - **Three active studies are investigating the use of Janumet (MK-0431A), a sitagliptin/metformin fixed-dose combination, in pediatric populations.** A phase 1 study (ClinicalTrials.gov Identifier: NCT01557504) assessing the pharmacokinetics and swallowing tolerability of the candidate is currently recruiting. It is scheduled to end in November 2013. Two phase 3 trials investigating the safety and efficacy of MK-0431A are also recruiting: the first tests the basic formulation, and is scheduled to end in December 2017 (Identifier: NCT01472367); the second uses the extended release formula, and has a scheduled primary completion date of January 2016 (Identifier: NCT01760447).
    - **Merck is also conducting a phase 3 study investigating the safety and efficacy of sitagliptin as an initial monotherapy for children with type 2 diabetes.** The trial (ClinicalTrials.gov Identifier: NCT01485614) is currently recruiting, and is estimated to end in July 2018. An indication for sitagliptin as a first-line therapy will likely be a tougher sell to payers than an indication for an FDC with metformin, given that most type 2 patients (pediatric and adult) start on the much cheaper metformin, though it could be used for children who do not tolerate metformin.

- **Merck's pipeline also reflects its interest in gaining reimbursement in China, which has the largest type 2 diabetes patient population in the world.** Interestingly, at this year's Keystone conference, we learned from Dr. Linong Ji (Peking University People's Hospital, Beijing, China) that DPP-4 inhibitors might have significantly greater efficacy in East Asian populations than in Caucasian populations - early meta-analyses demonstrate a significant average A1c differential of 0.24%. If confirmed by future studies, this finding could enhance the potential of Merck's DPP-4 inhibitor in this market.

    - **To the best of our knowledge, there are three currently ongoing trials investigating the use of sitagliptin in China.** The studies will not only provide valuable data on the efficacy and safety profiles of sitagliptin in Chinese populations, but also include comparators that are more frequently prescribed in China (such as SFUs and acarbose). One phase 3 study aims to evaluate the safety and efficacy of adding sitagliptin to stable-dosage insulin therapy with or without metformin (ClinicalTrials.gov Identifier: NCT01590797; recruiting). A second phase 3 study will investigate the usage of sitagliptin as an add-on to SFU treatment, again with or without metformin (NCT01590771; recruiting). The first study is scheduled to end in January 2014; the second in August 2014. An interesting phase 4 study will test the safety and efficacy of adding glimepiride, gliclazide, repaglinide, or acarbose to Janumet (sitagliptin/metformin FDC) therapy (NCT01709305). We are interested in knowing why Merck is testing a number of existing drugs as add-ons to the chief therapeutic candidate, and not the other way around. The decision may anticipate the need for patients to be placed on additional agents given the modest efficacy of the DPP-4 inhibitor class.

- **Other interesting active sitagliptin trials include:** TECOS (sitagliptin's CVOT, estimated to end in December 2014; ClinicalTrials.gov Identifier: NCT00790205), a phase 3 study of a sitagliptin/simvastatin FDC in type 2 diabetes patients (NCT01678820; recruiting), and a study assessing the safety and efficacy of the drug in type 2 diabetes patients who have recently undergone a gastric bypass operation (NCT01512797; recruiting).

PIPELINE UPDATES: MK-3102

- **Management provided no new updates on Merck's diabetes pipeline, although ClinicalTrials.gov shows several new developments.** A number pertain to MK-3102, Merck's phase 3 once-weekly DPP-4 inhibitor candidate. The clinical trial program for MK-3102 (save for a CVOT) is scheduled to end in October 2016, placing the earliest potential approval in late 2017. As background, Merck has stated that MK-3102 has a long half-life because it is not metabolized - see our report from Merck's November 2011 R&D day for more information: http://www.closeconcerns.com/knowledgebase/r/4d18c66c.
    - **We noticed one new phase 3 study since Merck's 1Q13 update,** investigating the safety and efficacy of MK-3102 versus glimepiride (a sulfonylurea) in patients who cannot take metformin (ClinicalTrials.gov Identifier: NCT01863667). The study is currently recruiting with an estimated primary completion date of October 2016. The appearance of this study lines up with Merck's stated goal of moving patients to DPP-4 inhibitors from SFUs. Having long-term data on the safety and efficacy of MK-3102 compared to SFUs should help the candidate gain a competitive edge in a crowded DPP-4 inhibitor market.
    - **Merck has 10 additional existing phase 3 studies on MK-3102 registered on ClinicalTrials.gov, with the first estimated primary completion set for April2014 and the last for October 2017.** These 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. glimepiride as an add-on to metformin (NCT01682759; recruiting); 4) MK-3102 vs. placebo as a third-line add-on to metformin and a sulfonylurea (NCT01704261; recruiting); 5) MK-3102 vs. sitagliptin as an add-on to metformin (NCT01841697; recruiting) 6) MK-3102 as first-line monotherapy vs. placebo (NCT01717313; recruiting);7) MK-3102 in people with moderate or severe chronic kidney disease or kidney failure ondialysis (NCT01698775; recruiting); 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); 9) MK-3102 safety and efficacy in patients age 18 to 45 (NCT01814748; recruiting); and 10) cardiovascular outcomes associated with MK-3102 use (NCT01703208; recruiting). For more details on these trials, see our Merck 1Q13 report at http://www.closeconcerns.com/knowledgebase/r/f0e5540f.
    - **Merck presented the results of a discrete-choice experiment on oral antihyperglycemics at ADA this year (sponsored by Merck):** the results of the market research do not necessarily bode well for MK-3102. Dr. Brett Hauber (RTI Health Solutions, Durham, NC), who directed the study and presented the results, shared that 67% of patients (especially the young and treatment naïve) preferred once-weekly to daily administration, but that the average patient was only willing to pay $5.86 more per month for a once-weekly agent. We anticipate that Merck might target the young and treatment naïve when it launches MK-3102, who may be willing to pay a higher premium for the once-weekly administration - we feel that Merck will find it unpalatable to market the agent at only $5 more per month. However, if Merck is willing to convince payers that the once-weekly administration will substantially improve adherence, insurance coverage could prevent patients' out of pocket expenses from rising too much. Targeting younger groups may help MK-3102 capture a demographic for whom resistance to once-daily treatment represented a barrier to Januvia uptake. For more information on Dr. Hauber's presentation, see page 10 of our ADA 2013 Report (http://www.closeconcerns.com/knowledgebase/r/76f49d51).

OTHER PIPELINE UPDATES

- **To the best of our knowledge, the rest of Merck's diabetes pipeline remains the same:**

- **Ertugliflozin, Merck's SGLT-2 inhibitor co-developed with Pfizer, has completed phase 2 testing.** Management indicated that phase 3 testing should begin in 2H13 - Pfizer leadership corroborated this timeline during its 2Q13 update. Merck is leading the clinical program, with Pfizer overseeing certain (undisclosed) trials of the program. Although neither Merck nor Pfizer have formally commented on the candidate's longer-term regulatory timeline, an FDA submission in 2016 at the earliest appears reasonable. If approved, ertugliflozin could enter a crowded SGLT-2 market: BMS/AZ's Forxiga was recently launched in Europe and resubmitted to the FDA this summer. Lilly/BI filed empagliflozin in the US and EU in March. Several other companies are developing SGLT-2-based therapies, including Astellas/Kotobuki (ipragliflozin; filed in Japan this past March), Lexicon (phase 3 initiation for the SGLT-1/SGLT-2 dual inhibitorLX4211 slated to begin later this year), and Novartis (SGLT-1/SGLT-2 dual inhibitor LIK066; phase 2). Ertugliflozin-based FDCs - for example, with Januvia (sitagliptin) or Janumet (sitagliptin/metformin) could help differentiate the product, and FDCs have been a stated area of interest for Merck management.
- **Merck is still developing a candidate for painful diabetic neuropathy (MK-6096).** The field of diabetic neuropathy has been relatively active of late, with the launch of NeuroMetrix's Sensus transcutaneous electrical nerve stimulator (TENS) device in January and the approval of J&J's Nucynta ER (extended-release tapentadol) for this indication last year. ClinicalTrials.gov indicates that a phase 2 study on the candidate was completed in April - results have not yet been made available (ClinicalTrials.gov Identifier: NCT01564459). See our Merck 1Q13 report (http://www.closeconcerns.com/knowledgebase/r/f0e5540f) for more information.
- **We remain eager to hear about progress in the company's SmartCells glucose-responsive insulin program, given its exciting potential for both type 1 and type 2 diabetes patients.** We believe that Smart Insulin (the specific candidate) remains in preclinical development. As a reminder, Merck acquired SmartCells in December 2010 - for more on that acquisition, see our coverage: http://www.closeconcerns.com/knowledgebase/r/f121fcfe.

Questions and Answers:

Q: We recently saw a rebound in reported 2Q growth, but it looks like prescription volume growth, at least in the US, is still fairly low. My question is do you believe you're seeing a benefit from the additional resources you put in the franchise earlier this year?

A: We're pleased that we saw the product perform better this quarter vs. 1Q. We think it's rebounding, and we're continuing to provide tremendous support behind it.

Q: Can you more broadly, talk about the overall DPP-4 inhibitor market at this point. As you start to annualize the TZD benefit, do you belief you can reaccelerate growth for this category?

So, as I discussed, in the US we had 9% growth. And I tried to give you some context on that by breaking it down, where we had 1% that was volume, 4% was inventory, and the rest was price. The real key is changing the TRx trend, and that's what we're frankly focused on. So the real issue is that we have a 75% market share in the US despite a very significant number of competitors. So it's not about trying to gain more market share. It's really about getting sulfonylurea use over into DPP-4s, of which we're the lion's share. Typically with multiple new entrants in a market, you see a lot of class growth. We don't see a lot of class growth despite all the new competitors that have come into the marketplace. So a way for us to change the trend is really to focus on the switch from sulfonylureas. And sulfonylureas still represent about 35% of the patient days of therapy, so there's still a big opportunity there for us to go after. So what we've done is increased our focus. We now have a dedicated sales force, and they're out there. They are promoting; they are engaged. In addition to that, we have increased our promotion spending and our print direct-to-consumer advertising. All of our focus now is on the sulfonylurea utilization. Up until 1Q this year, most of our focus was on the TZD opportunity that's no longer there, so it really is about sulfonylureas. The good news is that we've maintained our strong

managed care access in the US, so we have access to our product. In over 80% of the patients, we have preferred access. And now it really is about executing on the sulfonylurea strategy in the United States.

Outside the United States, we still have a very significant opportunity, and every region outside the US had strong volume growth. Although we had 11% growth ex-[foreign exchange], the big difference between ex-[foreign exchange] and [foreign exchange] was the yen. We have a very significant amount of our sales in Japan for Januvia. In Japan you may recall the DPP-4 class is the number one class of oral diabetics in Japan. It's ahead of metformin. It's ahead of sulfonylureas. And we have by the far the leading market share. At the same time, every other quarter we get supply sales from our co-marketing partner, which happened this quarter. So when you look at our success in Japan plus the supply sales coming in lump, you can see how the yen would have a very significant impact on our sales when you don't adjust for exchange. That's the primary difference for the underlying business performance being very strong from what you see including foreign exchange. Outside the US, we continue to anticipate low double-digit growth. And we see that we're getting that in volume, and I think the opportunity remains very strong there for us.

Q: First of all, congratulations especially on the US Januvia numbers. You probably know there was a lot of consternation around that number on the Street, and you guys delivered. So my questions are mainly around that. So number one, you said that there was $30 million inventory benefit in the quarter. I believe there was $70 million drawdown last quarter, so there has been a fair bit of movement here. Should we expect further movements going forward?

A: It's important that I try to give you as much specifics as we can because it's such a big growth driver for us. If you look at Januvia, what I said was that of the 9% US growth, about 1% from volume, 4% was from inventory, the rest was from price, so that makes about 4% price. You have to be careful extrapolating that over every quarter, because mix can have a significant impact on how much price comes through at any point in time. Also, the timing of price increases makes it a little difficult for you to try and predict and look for it to be the same, quarter over quarter. With regard to the inventory, we did see about $30 million of inventory movement this month, which I mentioned. On the base of business that we have, it's very, very small at $30 million. So, it's very difficult to predict the channel movements from one quarter to another. We're not seeing large channel movements in terms of how big the product is in the United States; they're relatively small. But small channel movements can have $30 to $50 million impact. So, that's why for the guidance that I gave for the rest of the year, I said mid-single digits for the US, but I excluded the movement of channel in there because you can't predict $30 to $50 million of channel movement. It's within a half-a-day sales or something like that. So that's how I think about the inventory moving forward.

Q: Ex-US, can you update us on what's going on with AMNOG and IQWiG in Germany? I guess you guys came out a little bit ahead of your computers. I know no one knows what's going to happen, but what are some of the potential outcomes?

A: With regard to IQWiG, on July 1, they announced the outcome of their assessment of Januvia when added to metformin. We were very pleased with that. That's the beginning of the process. The next step is a decision on the added medical value by the G-BA, and that's expected in 4Q this year. Once that happens, you actually go into the reimbursement discussions. So we're happy with where we are today. But there's still a lot more work for us to do, and it will be another six months before we probably know the final outcome of that. Just to put that in perspective for you, if you look at Germany, it represents less than 5% of our Januvia family sales to just give you a sense of the magnitude of that. So, we're excited with what has happened thus far, but there's still a long way to go.

Q: First, on the DPP-4 class within Europe, the Transparency Commission in France just yesterday announced they're going to be focusing on the class. On IQWiG, while Merck may benefit from the ongoing discussions there, it's clear that some of your competitors are going to have the pricing dragged down. The first outcomes trial failed to show any DPP-4 benefits compared to much older drugs. And healthcare systems in my part of the world are still struggling, and DPP-4s make a soft target, and obviously a reference to Japan. Am I being too negative here, when I think about the pressures on the franchise outside the US?

A: I'll focus on the DPP-4 inhibitor class outside the US because that's where you focused, and I spoke a lot about the US already. I just want to reiterate that we had good volume growth in all regions and we had very strong growth in the five core European markets, not only in volume but also in dollars. I believe the environment in Europe is tough and I think it will continue to be tough. But I also believe that the value that physicians and patients see in a product like Januvia is very strong. And also when you talk to the governments, I do believe that they see the value that a product like Januvia can bring into the marketplace. The marketplace tends to show you the value of the product based on utilization. When you look at the utilization of Januvia, I think it's because physicians see not only the great efficacy that you can see on A1c, but they also feel comfortable with the safety profile that they've been accustomed to. And if you look at the cost of the implications of diabetes, they're very significant. In Europe, typically the DPP-4 inhibitors are utilized after metformin. So, it's not threatening the largest generic in Europe; it's actually being utilized after the generics are used in Europe. So I think that it shows that there is a way to try to use a low-cost metformin. But since many patents can't get to goal on a low-cost metformin or if a sulfonylurea has safety or side effect issues that the physicians are looking for a way to control diabetes such as with Januvia. And then the governments see the implications of not treating diabetes in terms of the macrovascular disease, microvascular disease, in terms of hospital admissions, and so forth. So, I still think that there's a strong potential for Januvia in Europe. In addition to that, we still have markets that we're waiting for reimbursement outside of Europe such as in China, where we think there are also opportunities for the future.

Q: Are you doing any co-formulation work to combine the SGLT-2 inhibitor you got from Pfizer with Januvia as a fixed-dose combination, similar to what your competitors are doing?

A: We're just moving forward with that program. We expect to advance that program into phase 3 this year. As I said last quarter, that one of the things that's extremely attractive about this program is it's very well behaved pharmaceutically, and hence we expect it to play nicely with others. We've always had an interest in the idea that this could be used in combination with our existing programs, and so we're looking at those things very closely. That would be something, of course, that we would include in our registration programs.

Q: Could you please provide us an update on your once-weekly DPP-4 inhibitor, and is there any possibility for a co-formulation there?

A: We continue to make progress on our once-weekly program. Our phase 3 program is ongoing and we're enthusiastic about it, and we think it's a very, very good opportunity.

Close Concerns Questions

- Reflecting on DPP-4 inhibitors having a larger share of patient days on therapy, how do pricing and reimbursement of Januvia in Japan compare to that in the US and EU? Do patients in Japan pay branded prices for metformin?
- What was the international growth excluding Japan?
- How well are the pediatric trials of sitagliptin enrolling?
- How well is the Januvia franchise is growing in China, Latin America, and the Middle East?
- Is Merck still interested in developing a GPR40 agonist, perhaps in combination with sitagliptin or ertugliflozin?

-- by Hannah Deming, Manu Venkat, Jessica Dong, Ewuradjoa Gadzanku, and Kelly Close