Closer Look

MEMORANDUM

J&J 3Q14 - Invokana sales reach ~$128 million; new trial in obesity; Global, US LifeScan-Animas see encouraging growth - October 14, 2014

Executive Highlights

- Invokana continued its strong performance, with continued gains in prescriber share and ~$128 million in sales in 3Q14, up ~45% sequentially from ~$90 million in 2Q14.
- A trial investigating Invokana in combination with phentermine as a treatment for obesity is currently recruiting with a May 2015 completion date; a phase 2 study of Invokana in type 1 diabetes patients is also ongoing.
- Global Diabetes Care (LifeScan/Animas) revenue was flat as reported and up 1% operationally year-over-year; the US business rose 3%.

Early this morning, Johnson and Johnson CFO Mr. Dominic Caruso led the company's 3Q14 financial update, stepping in for CEO Mr. Alex Gorsky (no reason was specified). Overall, Invokana continues to perform well, with little concern from management on how an expanding SGLT-2 inhibitor class will impact Invokana sales; the drug continues to be the focus of the company's diabetes discussion during the financial update, with devices once again barely acknowledged in either the call or prepared materials. Below, we bring you our top ten highlights from the call:

Top Five Drug Highlights

1. We estimate that US Invokana (canagliflozin) sales were ~$123-$132 million in 3Q14, up ~45% sequentially from our $84-$93 million estimate in 2Q14. J&J said that Invokana represented "over" 3.5% of pharma growth this quarter.

2. Management expressed confidence that Invokana's performance will not suffer as more SGLT-2 inhibitors are introduced to the market; it remains to be seen whether patients and prescribers will perceive any key differentiating factors between the various options. From what we understand, there is a bit of a price war, and consumers with insurance all pay between $0 and a maximum of $10 co-pay.

3. Management confirmed during Q&A that, unlike competitors AstraZeneca and Lilly/BI, J&J is not currently pursuing an SGLT-2 inhibitor/DPP-4 inhibitor fixed-dose combination. This is clearly a strategic choice in our view; it will be interesting to see how the branded fixed dose combination drugs are priced and reimbursed and prescribed.

4. Notably, a new trial investigating Invokana in combination with phentermine for patients who are overweight or obese is currently listed as recruiting on ClinicalTrials.gov (Identifier: NCT02243202).

5. A phase 2 study investigating Invokana in type 1 diabetes continues to recruit participants, with an estimated primary completion date in May 2015.

Top Five Device Highlights

6. Global Diabetes Care revenue (LifeScan and Animas) totaled $558 million, flat as reported and up 1% operationally year-over-year (YOY), marking the first quarter of positive growth in worldwide Diabetes Care in two-and-a-half years (albeit from an easy comparison to 3Q13).

7. US Diabetes Care sales reached $244 million, up 3% YOY. Declines are tapering as competitive bidding has more than annualized at this point.

8. International Diabetes Care sales totaled $314 million, declining 2% as reported and flat operationally YOY.

9. We are eager to glimpse the financials for the rest of the Big Four blood glucose monitoring companies (Abbott, Bayer, and Roche), particularly to see whether the improvements in US Diabetes Care revenues are mirrored across the board.

10. The call was noticeably void of remarks on the device pipeline; management was silent on the ongoing 18-month FDA review for the Animas Vibe integrated with the Dexcom G4 Platinum CGM and on the Calibra Finesse insulin delivery device.

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TOP FIVE DRUG HIGHLIGHTS

1. Invokana continues to do well. We estimate that US sales of Invokana (canagliflozin) were $123-$132 million in 3Q14. Management said that Invokana contributed "over 3.5 percentage points" to the company's overall US pharmaceutical growth (which was 33.1%) in 3Q14; by our calculations (assuming that values up to 3.75 would be rounded to 3.5), this gives a range of $123-$132 million for 3Q14, representing an impressive~45% sequential increase from the $84-$93 million range we estimated in 2Q14. Invokana sales have shown a strong positive trajectory for the past three quarters after rising dramatically from $45-$75 million in 4Q13 to $80-$97 million in 1Q14. Management continued to characterize Invokana as a strong driver of growth in its sixth full quarter on the market. We had previously forecast $500 million for 2014 for Invokana - it would need a very strong 4Q14 to reach this level!

- **Invokana has achieved 3.2% of total prescription (TRx) share in the US diabetes market (excluding insulin and metformin), up from 2.3% in 2Q14.** TRx among US endocrinologists grew from 7% in 2Q14 to 9.2% in 3Q14.
- **Management did not provide an update on international launches of Invokana; as of 2Q14, the drug had been approved in 45 countries.** Invokana has received mixed reimbursement decisions in Europe (where it was approved in November 2013). The UK's National Institute for Health and Care Excellence (NICE) granted the drug a positive recommendation that preserves optimal reimbursement for most patients; by contrast, the German G-BA determined that Invokana provides "no additional benefit" compared to other drug classes and relegated the product to generic-level pricing (as it has done for multiple other diabetes drugs). The G-BA issued a similar negative ruling from the G-BA on AZ's Forxiga (dapagliflozin), causing AZ to withdraw the product from the market; however, earlier this year, AZ shared that it had successfully re-arbitrated with the G-BA on pricing and was re-launching Forxiga. We wonder if J&J will be able to follow a similar path, and would imagine that the possibility is likely. Bigger picture, we believe patient political advocacy is needed in Germany to slow or reverse the G-BA's campaign, which has significantly impeded patient access to new therapies.

2. J&J will be under increasing pressure in the coming years to differentiate Invokana from its competitors in a more crowded SGLT-2 inhibitor market. The drug's first-in-class status in the US will certainly remain an advantage, as many HCPs and patients learned about SGLT-2 inhibitors from experience with Invokana. Management argued during Q&A that the introduction of more SGLT-2 inhibitors will benefit Invokana by increasing overall awareness of the class - we agree with this. The main competitive threat to Invokana's US market leadership, in our view, are not the competing SGLT-2 inhibitor monotherapies, but rather will be the future SGLT-2 inhibitor/DPP-4 inhibitor fixed-dose combinations that J&J's competitors (including AZ, Lilly/BI, and Pfizer/Merck) are pursuing (see #3 below). That said - we also

understand that Lilly/BI and AZ have lower co-pays associated with their prescription cards in the US - this has prompted a price war that has most patients paying $10 or $5 or nothing.

- **Invokana's current competitors in the US and European markets are AstraZeneca's Farxiga (dapagliflozin) and Lilly/BI's Jardiance (empagliflozin).** Farxiga was approved in the US in January 2014 following its approval in Europe under the trade name Forxiga in November 2012, ahead of Invokana. Jardiance was approved in the US in August 2014 following European approval in May. Other earlier stage SGLT-2 inhibitors in development include Pfizer/Merck's ertugliflozin (phase 3), Astellas/Kotobuki's ipragliflozin (approved in Japan), Taisho's Lusefi (luseogliflozin; approved in Japan), Islet Sciences/BHV Pharma's remogliflozin etabonate (phase 2), Theracos' THR1442 (phase 2), Lexicon's SGLT-1/SGLT-2 dual inhibitor LX4211 (phase 2 for type 1 and type 2 diabetes), and Novartis' SGLT-1/SGLT-2 dual inhibitor LIK066 (phase 2).
    - **One potentially key point of differentiation among the three SGLT-2 inhibitors on the market is the indication for patients with renal impairment.** Farxiga is completely contraindicated in patients with eGFRs below 30 ml/min/1.73 m² and not recommended in patients with eGFRs between 30 and 60 ml/min/1.73 m². With Invokana, patients with eGFRs between 45 and 60 ml/min/1.73 m² are limited to the lower 100 mg dose, while both doses of Jardiance are indicated for patients with eGFRs down to 45 ml/min/1.73 m². We have previously speculated that Invokana might benefit from the looser restrictions when Farxiga was the only competitor on the market, but that advantage will likely be reduced at least to some degree by the even more permissive indication for Jardiance. Of course, Invokana is also currently being investigated for a diabetic nephropathy indication in the CREDENCE renal outcomes trial (scheduled to complete in 2019), and the results of that trial could completely alter the conversation around SGLT-2 inhibitors and renal impairment.

3. Although J&J recently received approval for Invokamet (canagliflozin/metformin IR), the point was raised during Q&A that, unlike AZ, Lilly/BI, and Pfizer/Merck, J&J *does not* have plans for an SGLT-2 inhibitor/DPP-4 inhibitor fixed-dose combination (FDC). CFO Mr. Dominic Caruso stated that he is not aware that J&J is studying the combination (this is code for "we're not doing that"; frankly, we also thought Mr. Caruso sounded rather uninformed when he referred to the class as "DPP-2 inhibitors"). Management later noted that 50% of Invokana prescriptions are being used as part of triple therapy, meaning that patients are able to pursue the combination themselves (although still in the form of separate pills).

- **SGLT-2 inhibitor/DPP-4 inhibitor FDCs have attracted a great deal of excitement in the field in recent years due to the compelling promise of combining insulin-dependent and insulin-independent modes of action for strong efficacy without the need for injections.** Thus far, phase 3 results for AZ's "saxa/dapa" (saxagliptin/dapagliflozin) and Lilly/BI's "empa/lina" (empagliflozin/linagliptin) have generally demonstrated superior efficacy with the combinations compared to the individual components alone. Of course, unlike AZ and Lilly/BI, J&J would need to pursue a partnership in order to develop such an FDC since it does not have a DPP-4 inhibitor in its portfolio, and the company may have concluded that the potential benefits of this new class do not warrant such a substantial investment. We wonder whether this assessment will change in the future - if SGLT-2 inhibitor/DPP-4 inhibitor FDCs eventually pull a significant percentage of patients away from the SGLT-2 inhibitor market, J&J may be forced to develop a combination to stay competitive.
- **Management highlighted the recent US approval of Invokamet (Invokana/metformin immediate release) during the call; the product was approved in Europe in April under the trade name Vokanamet.** Invokamet is the first SGLT-2 inhibitor/metformin fixed-dose combination to reach the US market and the second such combination to launch in the EU behind AZ's Xigduo (Forxiga/metformin).

- **J&J's Invokana/metformin extended release (XR) FDC remains in phase 3 in the US.** This compound would allow for once-daily dosing, as opposed to the twice-daily dosing recommended with Invokamet. AZ currently has a Xigduo XR FDC under review in the US, with a decision expected in 4Q14. The XR combinations are not being pursued in Europe given that metformin XR is not available there.

4. We noticed a new J&J-sponsored trial investigating Invokana in combination with phentermine as a treatment for obesity is currently listed as recruiting on ClinicalTrials.gov (Identifier: NCT02243202). Although not a fixed-dose combination (the two drugs are being tested as separate pills), we imagine this study could lay the groundwork for a FDC in the future. The double-blind, 26-week phase 2 trial aims to enroll 344 overweight and obese patients without diabetes, who will be randomized to receive one of four oral, once-daily treatment regimens: (i) Invokana 300 mg and phentermine 15 mg; (ii) Invokana 300 mg and placebo; (iii) phentermine 15 mg and placebo; and (iv) double placebo. The primary endpoint is percent change in body weight from baseline after 26 weeks, and secondary endpoints include the percentage of patients achieving at least a 5% weight loss, as well as changes in systolic blood pressure and pulse rate. Primary completion is expected in May 2015.

- **The phentermine molecule (in a different time-release formulation) is half of Vivus' weight loss medication Qsymia (phentermine/topiramate XR).** Earlier this year, Vivus acquired certain topiramate-related patents from J&J, covering uses of topiramate to treat obesity (1997), lower blood pressure and lipids, and reduce blood glucose (2000), both in monotherapy and in combination with other agents. Previously, J&J had an active topiramate-related lawsuit against Vivus.
- **The lines between diabetes and obesity therapy continue be blurred by agents like SGLT-2 inhibitors and GLP-1 agonists that cause weight loss (and other pleiotropic benefits).** Among companies in the diabetes arena, Novo Nordisk has taken some substantial steps in the obesity direction recently - first with the development of Saxenda (liraglutide 3.0 mg for obesity), which received a 14-1 vote in favor of approval at an FDA Advisory Committee meeting in September, and more recently with the establishment of a new obesity research unit in Seattle, WA. While enormous knowledge gaps still exist with regard to the best ways to define and treat obesity (see our coverage of the AACE/ACE Consensus Conference on this issue in March), we suspect that as the condition becomes more widely accepted as a disease with related pathophysiology to type 2 diabetes and metabolic syndrome, the repurposing of diabetes drugs for obesity (and the use of obesity drugs in diabetes and/or prediabetes) will become an increasingly appealing avenue for industry to pursue.

5. A phase 2 trial investigating Invokana in type 1 diabetes is also currently recruiting participants (ClinicalTrials.gov Identifier: NCT02139943). The trial has an expected enrollment of 330 patients and an estimated primary completion date of May 2015. This was one of the more exciting news items from J&J in 2Q14 and we believe it is part of a larger trend of exploration of type 2 diabetes drug classes (especially SGLT-2 inhibitors) in type 1 diabetes. A trial of Farxiga/Forxiga in type 1 diabetes is also currently recruiting participants (ClinicalTrials.gov Identifier: NCT02211742) and has an expected primary completion date of January 2015. Although SGLT-2 inhibitors will not allow type 1 diabetes patients to completely forego insulin, they show promise in reducing patients' daily insulin dose, yielding weight benefits, and reducing glycemic variability, thereby improving time in range.

TOP FIVE DEVICE HIGHLIGHTS

6. Worldwide Diabetes Care revenue from LifeScan BGM and Animas insulin pumps totaled $558 million in 3Q14, flat as reported and rising 1% operationally year-over-year (YOY); this marks the first quarter of positive growth in worldwide Diabetes Care since 1Q12. However, this was an easy comparison to 3Q13, when worldwide sales declined ~11%. Additionally, accompanying slides attributed the positive overall business growth to adjustment to previously established reserves as opposed to business growth - as we understand it, the company appears to have set aside excess revenue reserves in 3Q13 (i.e., underreporting 3Q13 revenue) thereby enhancing the YOY comparison; unfortunately, it is impossible to

know from which geographies J&J held these reserves, therefore, whether or not US or international growth benefited more from these established reserves. Excluding the impact of that adjustment, worldwide Diabetes Care revenue fell ~3.5% YOY. Still, we'd note that even a 3.5% decline is encouraging, as it would represent the smallest deficit since 2Q12. Sequentially, revenue similar remained flat from 2Q14. Leaving the call, our overall take on LifeScan/Animas is that the business is trending in a better direction, though it has not fully recovered.

7. US Diabetes Care sales in 3Q14 reached $244 million, up 3% YOY. This was against a particularly easy comparison, as US Diabetes Care revenue declined a striking 27% in 3Q13. (As a reminder, US sales totaled just $237 million in that quarter - the lowest quarterly revenue since we began reporting J&J financials in 2006.) Sequentially, 3Q14 US revenue grew 10%, following 16% sequential growth observed in 2Q14, and indicating a promising sales trajectory.

- **The declines in US Diabetes Care appear to be tapering as competitive bidding has more than annualized at this point (the program went into effect July 1, 2013).** These financials mark the first quarter of growth for J&J's US business since 2Q12, and the second consecutive quarter of sequential growth following eight consecutive quarters of sequential decline. While management did not comment on these points during the call, the slide deck echoed the 2Q14 comment on the diabetes care business word-for-word: "Lower prices in US related to competitive bidding partially offset by volume growth" - we would expect that volume growth partially refers to the continued penetration of OneTouch VerioSync, which launched in the US in January. Understandably, management has a a conservative and cautious outlook on the Diabetes Care business; we hope pipeline innovations, such as the Animas Vibe and Finesse, could bring a more positive outlook on the device business.

8. International Diabetes Care sales totaled $314 million, declining 2% as reported and remaining flat operationally YOY. Revenue fell 7% sequentially from 2Q14. The decline came on a challenging comparison, as international sales rose 6% in 3Q13, the largest gain in the past two years. We wonder whether instability in some of J&J's fast-growing international markets (Russia and Ukraine) has contributed to this decline and how continued instability might impact sales for the foreseeable future.

9. We are eager for the remaining Big Four blood glucose monitoring companies (Roche [Thursday], Abbott [October 22], and Bayer [October 30]) to report later in the quarter, particularly to see whether these other comparable companies experience similar growth in the US. As of their respective 2Q14 updates, companies were still commenting on the challenges of competitive bidding implementation - Bayer, in fact, commented in its 2Q14 update that "we are planning to see a continuous decline of our Diabetes Care, mainly driven by the US..." which implies that pricing pressures and competitive bidding will continue to impact company revenues in a very real way this quarter. For background, Abbott US Diabetes Care revenue fell 27% in 2Q14 and 9% in 3Q13; Roche North American revenue fell 19% in 2Q14 and 7% in 3Q13 (USD); and though Bayer does not report US Diabetes Care revenue, the overall business has struggled, falling ~10-16% in 2Q14 and 7% in 3Q13. Roche reports its 3Q14 financial results on Thursday (October 16), Abbott reports October 22, and Bayer reports October 30.

10. The call was noticeably void of remarks on the device pipeline. In 2Q14, we heard disappointing news that management was not "projecting an approval time" on the Animas Vibe integrated with the Dexcom G4 Platinum CGM (an ongoing 18-month FDA review at this point). The FDA review has now tripled the statutory six-month PMA review cycle; Ms. Ashley McEvoy (Chair of Diabetes Care and Vision Care) called the product a competitive "sore spot" at the Medical Devices and Diagnostics Day this past May. Similarly, there were no updates on Calibra's three-day, wearable, bolus-only Finesse insulin delivery device, which, according to management at the Medical Devices and Diagnostics Day, would be launched in what is now ~19 months (originally 24 months at the Medical Devices and Diagnostics Day). There also continues to be no timing updates on the status of the company's automated insulin delivery efforts, a partnership that was originally signed with JDRF in 2010; a small feasibility study was presented at ADA 2014, though this whole part of the pipeline has moved very slowly indeed. We hope to see J&J jump in full force, since it will be a

requirement to stay competitive with Medtronic, and presumably other pump companies like Asante, Roche, Tandem, Insulet.

- **Over the past year, J&J has tended not to divulge device pipeline updates during earnings calls** - opting instead to provide more details at gatherings with slightly more of a focus on diabetes (e.g., Medical Devices and Diagnostics Day) - so the silence is not particularly surprising.

Pipeline Product	Timeline
Finesse insulin delivery device (acquired from Calibra Medical)	Expected to launch within the next ~19 months; Medical Devices and Diagnostics Day timeline
Animas Vibe Insulin Pump with integrated Dexcom G4 Platinum CGM	Health Canada approval received September 2013. FDA PMA filing submitted in April 2013, and J&J recently responded to FDA questions. Not "projecting approval timing" as of 2Q14.
OneTouch Ping Verio Insulin Pump with Remote Meter	Planned US submission in 2013; no recent updates - potential 2014 filing?
Next Generation OneTouch UltraVue Verio	Planned Japan submission in 2013; no recent updates - potential 2014 filling?
Next Generation Glucose Testing Platform	Planned US and EU submission in 2013; no recent updates - potential 2015 filing?
Predictive Low Glucose Suspend	Inpatient feasibility study of algorithm presented at ADA 2014
Hypoglycemia-Hyperglycemia Mitigation (HHM) System	Feasibility study presented at ADA 2013; no recent updates
Metabolics (surgical care product)	Planned submission in 2013; no recent updates

QUESTIONS AND ANSWERS

Q: Can you comment on what you're hearing from physicians around the differentiation for your product [Invokana] vs. some of the competitors that are now in the market? Are you envisioning tougher pricing dynamics going forward with that class given that there are new competitors?

A: With respect to differentiation of Invokana to the new competitors, Invokana of course continues to do very well. And the data as filed was a result of something like eight different clinical trials, which showed both the safety and efficacy of Invokana. It seems to continue to do well even in the face of new competition, so we're still growing share even with new competitors coming to the market. We don't see much of a price issue in the marketplace. Drugs in this class are all priced relatively competitively. You need to remember that this is a very large market, and we think it is a good thing that more SGLT-2 inhibitors are coming to market because it increases physicians' awareness of the use of that particular mechanism of action. I think the market can withstand a number of competitors, and therefore we think that overall there will be market growth as a result.

Q: Are you working on a combination of SGLT-2s and DPP-4s? I think that would be a good strategy to maintain your position, and your competitors certainly are working on those combination agents.

A: I'm not aware that we are studying the combination. Invokamet was just approved, and if you look at the usage of Invokana right now, about 50% is in triple therapy so they are actually able to get the combination themselves.

-- by Varun Iyengar, Emily Regier, Adam Brown, Hannah Martin, Manu Venkat, and Kelly Close