CLOSER LOOK

MEMORANDUM

J&J 3Q16 - Invokana sales total $328 million, down 4% YOY; CANVAS to report mid-2017; Prediabetes CVOT planned; LifeScan-Animas sales decline 9%; No major device pipeline updates - October 18, 2016

Executive Highlights

- The Invokana (canagliflozin) SGLT-2 inhibitor franchise posted $328 million in sales, marking a 4% year-over-year (YOY) decline as reported and a 14% sequential decline. Management maintained a positive outlook on future franchise growth, attributing 3Q16 numbers to a temporary increase in costs associated with administration of co-pay access programs. We did not find out as much as we would've liked about the program.
- There were two very surprising things on the call today. First, management outlined major opportunities for Invokana franchise growth, including the recent FDA approval of Invokamet XR and upcoming results from CANVAS, CANVAS-R, and CREDENCE. Based on comments made during the call (predicting similar data to EMPA-REG OUTCOME), we are more excited than ever for full CANVAS results to be presented at ADA 2017, given that management said it expected results similar to EMPA.
- Notably, management also disclosed preliminary plans for a cardiovascular outcomes trial for Invokana enrolling individuals with prediabetes. This is the first CVOT in prediabetes that we know of, and says a great deal about J&J's views on potential prevention potential of Invokana.
- Global LifeScan/Animas sales fell to $427 million, down 9% year-over-year as reported and operationally and 5% sequentially. *This marks 17 of the past 18 quarters with global sales declines*. US sales fell 7% ($191 million), and the OUS business fared worse, down 11% ($236 million).
- There were no technology pipeline updates on the call, though we know from a recent call with management that an Animas Vibe with Dexcom G5 integration was submitted to the FDA in June. The OneTouch Via (formerly Calibra Finesse) was previously expected to launch outside the US late this quarter, with a US launch in early 2017. The automated insulin delivery pivotal trial was previously slated to begin in 4Q16, but is not posted online yet.

This morning, J&J provided its 3Q16 financial update in a call led by Vice President of Investor Relations Mr. Joseph Wolk. Below, you'll find highlights from the call followed by Q&A. You can also view the press release here and the presentation slides here.

Janssen Highlights

1. Invokana (canagliflozin) SGLT-2 inhibitor franchise sales fell 4% year-over-year (YOY) as reported and 3% operationally to $328 million. This is the first quarter in which Invokana revenue has declined YOY since the product launched in 2Q13. For context, the overall SGLT-2 inhibitor class experienced robust ~48% YOY growth in 1H16, including growth of 17%-20% for Invokana for the first half of the year. J&J management attributed the dip to a temporary increase in costs to administer co-pay access programs and cited Invokana's favorable formulary positioning, leading share of total prescriptions (56%), and recent FDA approval of Invokamet XR as encouragement that the franchise will "swing back" in 2017. Presumably, strong EMPA results prompted some of the downturn.

2. On that note, full results from the CANVAS and CANVAS-R cardiovascular outcomes trials (CVOTs) for Invokana will read out in mid-2017, and management confidently forecasted that canagliflozin will show

similar cardioprotection to empagliflozin - wow! This kind of commentary was unexpected: "We have very strong reason to suspect that the combination of CANVAS and CANVAS-R will give data very similar to what was reported with EMPA-REG OUTCOME." CANVAS is slated to report full results at ADA 2017 in June.

3. The company announced plans for a trial investigating the potential cardioprotective effects of Invokana in people with prediabetes and highlighted prediabetes as an opportunity for franchise growth. We applaud J&J's decision to focus on prediabetes as well as type 2 diabetes. A CVOT enrolling participants with prediabetes could be instrumental in showing compelling evidence for cardioprotection among a broader patient population.

4. Though not mentioned during the call, Janssen recently reported positive results for canagliflozin/ phentermine coadministration as an obesity treatment, and is involved in several other diabetes and obesity projects as well - see below for an overview.

LifeScan/Animas Financial Highlights

5. Global LifeScan/Animas revenue totaled $427 million in 3Q16, down 9% as reported and operationally year-over-year (YOY) on a very easy comparison to 3Q15 (when sales fell 16% as reported and 6% operationally). 3Q16 now marks 17 of the past 18 quarters with global sales declines. Sequential sales fell 5% from 2Q16. This was LifeScan/Animas' lowest global quarterly revenue in more than a decade.

6. US Diabetes Care sales totaled $191 million in 3Q16, dropping 7% YOY as reported and operationally against a very easy comparison (sales fell 16% YOY in 3Q15). This marked the third lowest US revenue ever recorded in our J&J model. US sales grew 8% sequentially against a very low base, but the field continues to struggle at the hands of CMS price cuts, and competitive headwinds took a toll on Animas insulin delivery revenue, which declined 10%.

7. International Diabetes Care revenue totaled $236 million in 3Q16, down 11% as reported and operationally YOY. Sequentially, OUS sales fell a striking 20% against a relatively high base of $294 million in 2Q16. Management cited a reduction of inventory levels from category slowdown in China as a chief contributor to poor performance, causing LifeScan SMBG sales specifically to decline 13% outside of the US.

LifeScan/Animas Pipeline Highlights

8. Through discussions with management, we learned last month that J&J submitted a PMA in June for the Animas Vibe pump integrated with Dexcom G5. As we understand it, the application was submitted for use in patients with type 1 diabetes ages two and over. The company has not speculated on an approval timeline, but the Vibe with G4 took ~20 months for approval.

9. Management did not comment on its OneTouch Via (formerly Calibra Finesse) bolus-only insulin delivery patch device. Guidance from ADA 2016 called for a commercial launch in select markets outside the US by late 4Q16, followed by the US in early 2017. The 24-week trial of the device (n=280) is fully enrolled, though primary completion has been pushed back to April 2017 from the previous December 2016. This study will be a positive for marketing and reimbursement (A1c, time-in-range data), though is not a gating factor to launch.

10. Animas' automated insulin delivery plans were not mentioned, though as of Keystone 2016, the trial was expected to begin in 4Q16. The single-arm trial will test the hypoglycemia-hyperglycemia minimizer with Dexcom's G5 CGM in 200 adults, adolescents, and pediatrics. Animas hopes to launch between November 2017-May 2018, behind Medtronic but potentially ahead of other competitors.

11. Neither prepared remarks nor Q&A mentioned the WellDoc BlueStar integration partnership (including a J&J investment), signed in March 2016 and "finalized" in September 2016. As of WellDoc's update last month, the first integration is still by the end of 2016.

12. Earlier this month, Animas sent a letter to customers informing them that the OneTouch Ping insulin pump has some cybersecurity vulnerabilities: it may be accessed wirelessly to deliver extra insulin (via the unencrypted RF communication that connects the meter and pump). The likelihood of unauthorized access is

extremely low, and the letter suggests helpful mitigations (very strong in our view). We would underscore the low absolute risk, though clearly, companies will have to make secure AID systems, particularly once Bluetooth is added.

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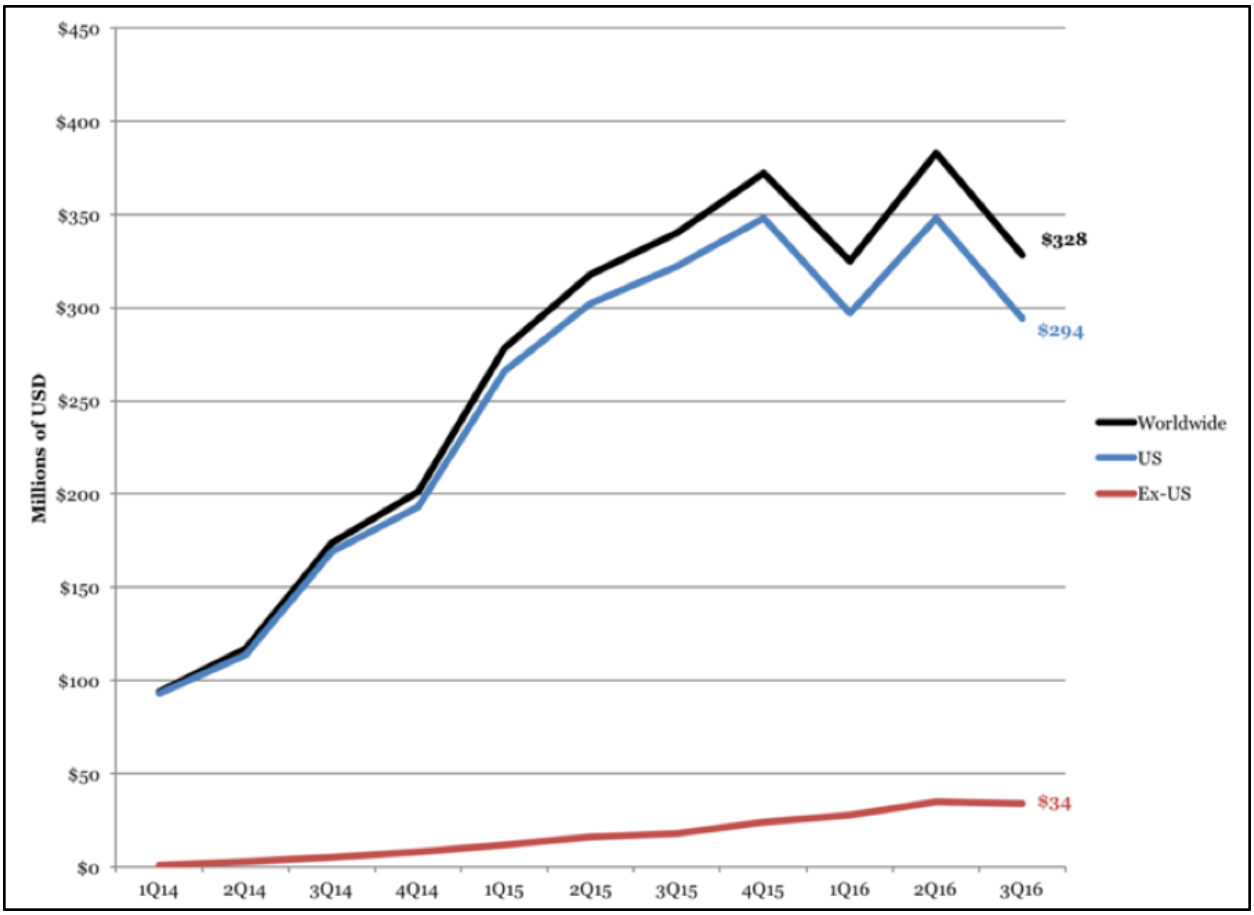
Janssen Highlights

1. Sales of the SGLT-2 inhibitor Invokana (canagliflozin) franchise fell 4% year-over-year (YOY) as reported and 3% operationally to $328 million. This marks a decline from $340 million in combined revenue for Invokana and fixed-dose combination Invokamet (canagliflozin/metformin) in 3Q15. This is the first quarter in which Invokana revenue has declined YOY since the product launched in 2Q13, and for context, the overall SGLT-2 inhibitor class experienced robust ~48% YOY growth in 1H16. Sequentially, sales fell 14% from $383 million in 2Q16. The decline in revenue was driven entirely by Invokana's US performance, by far its largest market with 90% of the franchise's worldwide revenue. By geography, US sales fell 9% YOY as reported and operationally to $294 million, which also represents a 16% sequential decline. Ex-US sales, totaling $34 million, grew 89% YOY as reported (94% in constant currencies). Sequentially, ex-US revenue fell 3% against a tough comparison, as international sales of the franchise rose 25% sequentially in 2Q16 - in fact, the franchise has posted consistent sequential growth ex-US since 2Q14. See the graph below for a visual display of Invokana's worldwide, US, and international sales. Management was not at all discouraged by the YOY or sequential decreases, attributing the dip to a temporary increase in costs to administer co-pay access programs. We're very curious what the magnitude of the cost increase was and how much of the additional cost went toward direct co-pay assistance versus administrative costs - we're certainly glad to see J&J investing in greater patient access to this relatively new branded medication. This was only a "transient expense," and management remained confident that Invokana sales will "swing back" in 2017, given (i) Invokana's favorable formulary positioning, (ii) its high share of total prescriptions (TRx), (iii) the recent FDA approval of Invokamet XR, and (iv) upcoming results from the CANVAS and CANVAS-R cardiovascular outcomes trials (CVOTs).

- **The company's presentation slides highlighted that Invokana is preferred by >70% of commercial insurance plans and by >90% of Medicare Part D plans in the US.** This represents a slight increase in coverage from what was reported in 2Q16 ("nearly" 70% and 90% of commercial and Medicare Part D plans, respectively), and further underscores J&J's particular savvy on the formulary front. The company's concerns over competition for formulary positioning have fluctuated somewhat - management explained sequential decline in 4Q15 as a result of increased competition, but shared during the 2Q16 update that Invokana had not faced substantial formulary competition thus far. It's a wait-and-see for how a label update for Lilly/BI's Jardiance (empagliflozin) and Synjardy (empagliflozin/metformin) will affect relative formulary positioning among the available SGLT-2 inhibitors. An FDA decision on whether or not to include positive cardiovascular (CV) data from EMPA-REG OUTCOME on the Jardiance/Synjardy labels is expected by end of year.

- **Management emphasized that Invokana remains the leading SGLT-2 inhibitor by volume.** TRx share for the franchise in the US type 2 diabetes market was 6.4%, which was described during the call as "essentially flat" (TRx share was 6.3% in 2Q16, 6.1% in 1Q16, and 6.5% in 4Q15) and which was further broken out into 11% TRx share among endocrinologists and 6% among primary care providers. However, management also noted that Invokana is now the third-largest non-insulin branded diabetes medication by volume in the US (we assume first and second place go to Merck's DPP-4 inhibitor Januvia [sitagliptin] and Novo Nordisk's GLP-1 agonist Victoza [liraglutide]), with >1.3 million patients treated to-date and more prescriptions filled than all other SGLT-2 inhibitors combined. According to the company's slides, the Invokana franchise held 56% of the SGLT-2 inhibitor market by volume as of August 19, compared to 26% for AZ's Farxiga (dapagliflozin) and 18% for Lilly/BI's Jardiance (empagliflozin) franchises. Invokana does benefit from being the first-to-market agent in this drug class in the US, the largest market for diabetes drugs, which affords greater familiarity and an edge in the competition for formulary positioning. Stay tuned for our whole class analysis of SGLT-2 inhibitors in 3Q16, available following Lilly's 3Q16 update on October 25 and AZ's on November 10. In the meantime, see our 1H16 diabetes industry round-up for the big picture on SGLT-2 inhibitors from 1Q16 and 2Q16.
- **Invokamet XR (canagliflozin/metformin extended-release) was recently approved by the FDA.** Invokamet XR is indicated as a first-line therapy for adults with type 2 diabetes and joins Invokana and Invokamet within the franchise. Management remarked that this addition to the franchise expands Janssen's diabetes portfolio, which now offers a "range of solutions to meet patient needs." Indeed, during an interview we conducted with J&J's VP of Medical Affairs Dr. Paul Burton, he emphasized that this latest-to-market agent sets up the franchise to cater to a wider spectrum of patients. It's too soon to tell exactly how Invokamet XR is influencing Janssen's diabetes sales (after all, the product only recently hit pharmacies at the very, very end of 3Q16 on September 28!), so this is something to watch for in future quarters.

FIGURE 1: INVOKANA SALES (1Q14-3Q16)



2. Full results from the CANVAS cardiovascular and the CANVAS-R renal outcomes trials for Invokana will read out in mid-2017, and management confidently forecasted that canagliflozin will demonstrate similar cardioprotection to empagliflozin. ADA's Chief Medical Officer Dr. Robert Ratner recently announced at CMHC 2016 that CANVAS results will be presented at ADA 2017, and today, J&J put forth a very (!) positive forecast: "We have very strong reason to suspect that the combination of CANVAS and CANVAS-R will give data very similar to what was reported with EMPA-REG OUTCOME." Management hinted at a potential class effect for SGLT-2 inhibitors, commenting that CANVAS findings will "further strengthen the importance of the SGLT-2 inhibitor class in diabetes care." J&J's CVOT will be the second to report for an SGLT-2 inhibitor, and data in line with what was seen in EMPA-REG OUTCOME could support a cardioprotective class effect, which has been a central topic of discussion and speculation of late. Moreover, management shared that the two trials on cardiovascular and renal outcomes, respectively, will be analyzed together and that discussions are ongoing with the FDA to determine an appropriate degree of statistical confidence. The focus on cardiovascular and renal outcomes in this call underscores the continuing recognition in the diabetes field that drugs in this day and age must go beyond glucose-lowering, offering protective benefits to the heart and kidneys as well. To this end, J&J management listed cardio- and renal protection as opportunities for growth in the Invokana franchise. In addition to CANVAS and CANVAS-R, results from the CREDENCE trial for Invokana in diabetic nephropathy will be available in 2019 (this study could potentially support a diabetic nephropathy indication for the product, which would be incredibly valuable given that nephropathy remains a therapeutic area of high unmet need - see our competitive landscape for more). Management suggested that the company plans to file for Invokana line extensions based on data from these three trials in the near-future. In conjunction with line extensions planned for J&J's Xarelto (rivaroxaban, for blood clots), expanded indications for Invokana have the potential to drive $3-5 billion in incremental sales for the company's cardiovascular franchise, according to management.

- **As in 2Q16, there was no mention of the ongoing safety review of Invokana, initiated in response to an observed increase in lower limb amputations in interim CANVAS results.** The initial EMA notice stated that the incidence of lower limb amputations (mostly affecting the toes) in CANVAS is currently 7/1,000 patient-years with the 100 mg dose of Invokana and 5/1,000 patient-years with the 300 mg dose vs. 3/1,000 patient-years with placebo after a mean 4.5 years follow-up. No significant difference in amputations has been observed in CANVAS-R. Patients requiring amputations were mostly high-morbidity cases, and there is no mechanistic evidence that points to SGLT-2 inhibitors as a risk factor for amputations. We continue to watch the safety review closely; some experts with whom we have spoken believe there are too many safety red flags, though we believe numbers are by far too early to assess in areas like amputation risk. We expect patient education can also similarly mitigate the DKA risk and the bone fracture risk associated with SGLT-2 inhibitors in type 2 diabetes treatment.

3. The company announced plans for a trial investigating the potential cardioprotective effects of Invokana in people with prediabetes. This was highlighted as one of four opportunities for Invokana franchise growth, alongside CANVAS and CANVAS-R in the CV realm and CREDENCE in the realm of kidney disease. This is the first concrete steps we've heard to pursue a potential prediabetes indication for Invokana - J&J first expressed its interest in such a move in a Pharmaceutical Business Review in May 2015. We're thrilled to see this focus on prediabetes and expanding the scope of cardiovascular outcomes results to evaluate their impact on a larger, potentially primary prevention population. We also expect such a trial would also evaluate the impact of canagliflozin on type 2 diabetes prevention and would love to see a company invest in pursuing a prediabetes indication for a medication. The pronounced weight loss benefit of Invokana and the entire SGLT-2 inhibitor class piques our interest about use of these agents in prediabetes, which in our view, is an area that demands more attention and viable therapies - after all, there are currently no medications indicated for diabetes prevention in prediabetes, though some providers are putting pressure on the FDA to expand metformin's label to include such an indication. These preliminary trial plans were shared as part of J&J's discussion of how Invokana can address obesity and prediabetes. We're eager to learn more details (there was no specific timeline outlined during the call), and we applaud J&J's commitment, despite what we expect will be a very high cost for running this CVOT (particularly given that those enrolled will likely have far lower risk of heart disease so the trial could take far longer though this is speculative at best).

- **We're especially looking forward to details of the patient population that will be enrolled in this trial.** To reach a minimum threshold of statistical significance, a CVOT typically requires a high number of CV events - 1,302 in LEADER for Novo Nordisk's GLP-1 agonist Victoza (liraglutide) and 772 in EMPA-REG OUTCOME for Lilly/BI's Jardiance (empagliflozin) - and thus the FDA-required post-marketing CVOTs to date have tended to enroll participants with type 2 diabetes with existing cardiovascular disease or at high risk in order to accrue the necessary number of events in a reasonable timeframe. Accordingly, we expect J&J's proposed trial will likely necessitate a much longer follow-up period if it is enrolling individuals with prediabetes, who generally have a lower risk of cardiovascular events (that said, it's possible the trial could choose to enroll patients with prediabetes and a history of cardiovascular disease, similar to how the IRIS trial for TZD pioglitazone enrolled patients with prediabetes and a history of stroke). We do hope that this trial chooses to investigate primary prevention of cardiovascular events in a prediabetes population - some thought leaders, including Dr. Juris Meier (Ruhr University of Bochum, Germany) at EASD 2016, have argued that CVOTs should examine primary prevention to make a more compelling case for cardioprotection in an even broader patient population. Overall, we see this plan for a prediabetes CVOT as a sign of the company's great confidence in the CANVAS results.

4. Though not mentioned during the call, Janssen recently reported positive results for canagliflozin/phentermine coadministration as an obesity treatment, and is involved in several other diabetes and obesity projects as well. Data from the phase 2 obesity trial was showcased first in a late-breaking poster at ADA 2016, with more details elucidated during an oral presentation at EASD 2016. Participants with obesity but without type 2 diabetes experienced significantly greater weight loss if treated with canagliflozin/phentermine together (7.5% body weight reduction) vs. placebo (0.6% reduction).

We are interested in the potential of this combination for the treatment of obesity, though its success will depend largely on broader education to drive a shift away from patient/provider reluctance to consider pharmacotherapies for obesity. With the exception of Novo Nordisk's Saxenda, a high-dose of liraglutide, obesity drugs have experienced a tough market in recent quarters, and an Invokana product targeted to obesity will likely face these same challenges. That said, the familiarity of canagliflozin among endocrinologists and other providers who treat patients with diabetes will likely be a plus - we expect Saxenda's success is partly attributable to similar widespread familiarity with liraglutide. We also expect Novo Nordisk is laying much of the groundwork with regards to changing patient and provider attitudes toward obesity pharmacotherapies and Janssen may encounter a less challenging landscape in a few years. Janssen's other diabetes-related projects include:

- **In type 1 diabetes,** Janssen has been active in beta cell replacement therapy through subsidiary BetaLogics and an option to license/acquire ViaCyte's VC-01 cell replacement therapy. In a consolidation move, ViaCyte also acquired the rights to Janssen subsidiary BetaLogics' assets in February of this year.
- **In type 2 diabetes,** the company has presented preclinical data on phase 1 long-acting, once-weekly GLP-1/glucagon dual agonist HM12525A, licensed from Hanmi in November 2015. Another ADA 2016 poster introduced GLP-1/glucagon dual agonist JNJ-54728518, which showed efficacy in mouse models vs. Novo Nordisk's Victoza (liraglutide). In addition, Janssen is part of ongoing collaborations with Intrexon to develop oral biologics for type 2 diabetes, obesity, and other metabolic disorders.
- **In obesity,** the company has another ongoing trial investigating canagliflozin's mechanism of weight loss in adults with type 2 diabetes and obesity. According to ClinicalTrials.gov, the study is expected to complete in August 2017. See the table below for a summary of Janssen's pipeline and ongoing trials.

JANSSEN PIPELINE AND ONGOING TRIALS

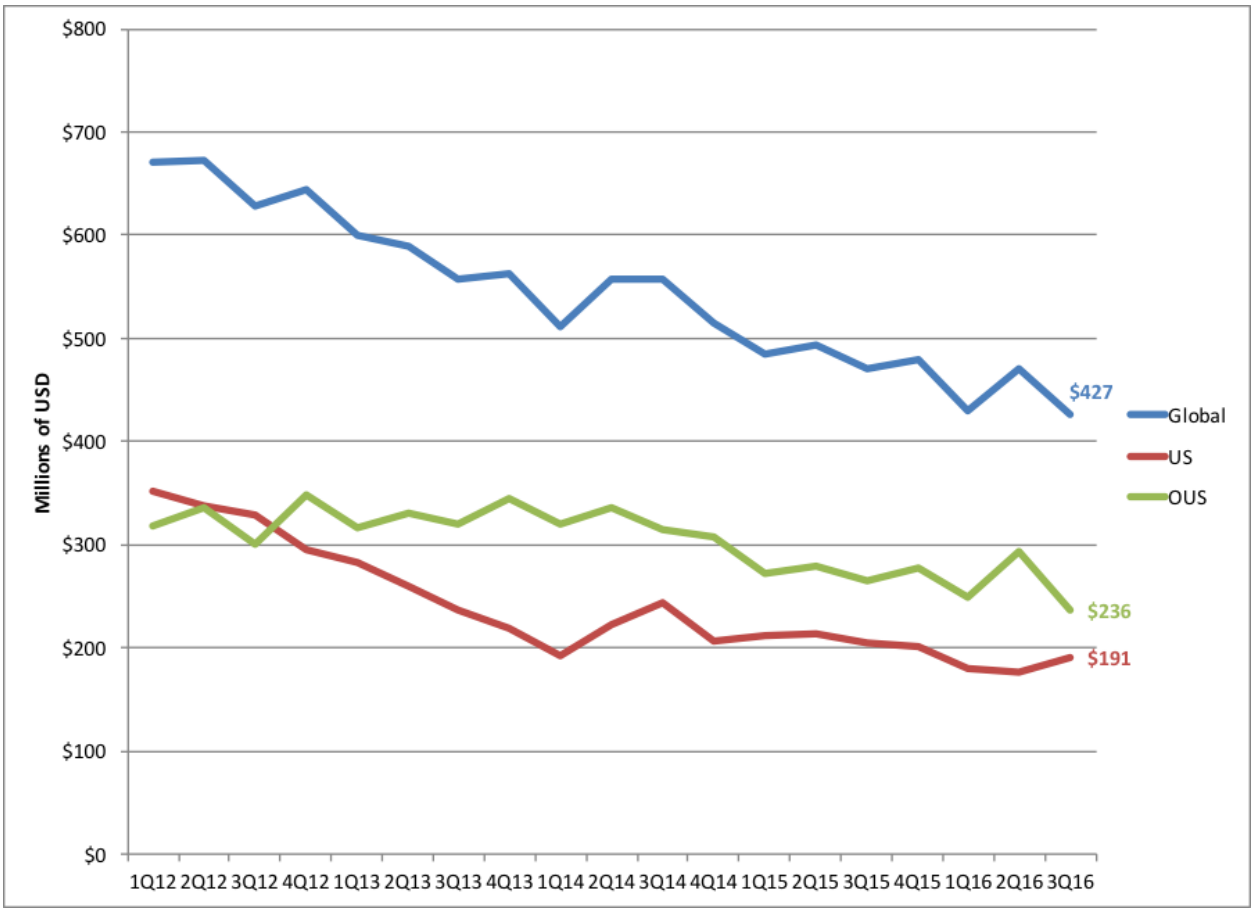
Product	Updates/ Timeline
Invokana (canagliflozin)	CANVAS cardiovascular outcomes trial to report mid-2017; CANVAS-R to report mid-2017; CREDENCE trial on diabetic kidney disease to report 2019; CVOT for prediabetes planned as of 3Q16 update; Trial investigating mechanism of weight loss scheduled to complete August 2017; Phase 2 for type 1 diabetes
canagliflozin/phentermine	Phase 2 trial in obesity reported positive results at ADA 2016
HM12525A (glucagon/GLP-1 dual agonist)	Phase 1; Licensed from Hanmi in November 2015
JNJ-54728518 (glucagon/GLP-1 dual agonist)	Preclinical; Data presented on ADA 2016 poster showing efficacy vs. Novo Nordisk's Victoza (liraglutide)

LifeScan/Animas Financial Highlights

5. Global LifeScan/Animas revenue totaled $427 million in 3Q16, down 9% as reported and operationally year-over-year (YOY) on a very easy comparison to 3Q15 (when sales fell 16% as reported and 6% operationally). This marked LifeScan/Animas' lowest global quarterly revenue in more than a decade in our model, including 17 of the past 18 quarters with global sales declines (3Q14 was the lone

exception and that was an easy comparison). Part of this has been currency-driven in recent history, though the negligible effect this quarter (negative 0.1%) shows that the underlying business is still struggling. Sequential sales fell 9% against $471 million in 2Q16.

FIGURE 2: GLOBAL, US, INTERNATIONAL QUARTERLY SALES (1Q12-3Q16)



6. US Diabetes Care sales totaled $191 million in 3Q16, dropping 7% YOY as reported and operationally against a very easy comparison (sales fell 16% YOY in 3Q15). The quarterly performance marks the third lowest US revenue ever recorded in our J&J model - only outperforming revenue from 1Q16 ($180 million) and 2Q16 ($177 million) - and the fourth-ever quarterly revenue to dip below $200 million. For context, US LifeScan/Animas sales peaked at $362 million in 4Q07, nearly double this quarter's sales - a striking testament to how devastating the impacts of competitive bidding have been. On the bright side, sales grew 8% sequentially from a low base in 2Q16, the first quarter of sequential growth since 2Q15.

- **The slide deck attributed some of the steep US decline to negative impacts from the second round of CMS's competitive bidding program**, which led to a 7% decrease in US SMBG sales. As of this past July, competitive bidding established lower payment amounts for mail order and retail blood glucose strips- $8.32 per 50-count box ($0.17 per strip), down 20% from the current allowable payment of $10.41 ($0.21 per strip), and a striking 76% reduction from the pre-competitive bidding price (~$35). The pricing pressure has hurt LifeScan in a major way and will weaken sales for the next year at least (when new prices will "anniversary"). Given the CMS and payer pressure, we applaud J&J for working so hard to keep its business strong and helping patients. We hope that Janssen can give some funds to LifeScan/Animas to help the weaker organizations.
    - **Competitive bidding is not only hurting industry, but is also be hurting patients.** Earlier this year, *Diabetes Care* published a compelling investigation of the program, concluding that reduced access to testing supplies resulted in an increase in

mortality in competitive bidding test sites. In addition, we heard DA leader Dr. Des Schatz at Keystone in July acknowledge that, though the program was implemented with good intent to reduce overall costs and co-pay, there has been a dearth of education, resulting in patients and providers who do not know how to access strips.

- **There is also a higher bar to now get new BGMs approved in the US, as the FDA finalized tighter guidance last week.** We assume this business is cash generating, but we are not feeling positive about potential for incremental spending on innovation. What will J&J's BGM business look like in two years? In five years? In ten years?
- **Insulin delivery sales fell 10% due to competitive headwinds, according to the accompanying slide deck.** Though J&J is the first insulin delivery company to report, there is clearly stiff competition from Medtronic, Tandem, and Insulet - the former two have products launching this quarter (see below) and all three have been public about their plans to automate insulin delivery (see our most recent competitive landscape). The Vibe secured FDA pediatric approval in 4Q15 (down to age two) though this is apparently not driving growth. We assume many pediatric patients and their families are electing to go with the MiniMed 530G/Connect (remote monitoring), waiting for the 670G, opting for Insulet's tubeless OmniPod, or getting the Dexcom G5 standalone CGM.
    - **Medtronic** started shipping the 630G/Enlite (threshold suspend on new pump platform) in September, and is offering an upgrade program to enable new users to get on the just-approved MiniMed 670G hybrid closed loop system for $0-$299. The product will launch in Spring 2017 and we have to imagine lots of pent-up demand from current pumpers, including frustrated Animas pumpers that have been waiting years for the company to move on automation.
    - **Tandem** began taking orders for the new t:slim X2 pump earlier this month, which is compatible with the Device Updater, allowing users to remotely update the pump's software (from a personal computer) and eventually add Dexcom G5/G6 CGM integration and automated insulin delivery algorithms (PLGS, TypeZero). The pump will begin shipping later this month.
    - **Insulet** had a strong 1H16, including record-high OmniPod sales in 2Q16; the company will report 3Q16 shortly.
- **We are eager for the remaining Big Three blood glucose monitoring companies (Abbott [October 19] and Roche [October 20]) to report later this week, particularly to see whether these companies experienced comparable US challenges.** For our summary of what happened in BGM in 1Q16 and 2Q16, see our latest Industry Roundup here.

7. International Diabetes Care revenue totaled $236 million in 3Q16, down 11% as reported and operationally YOY. The decline came relative to a very easy comparison, as sales fell 16% as reported and grew 1% operationally in 3Q15. With this quarter's performance, the two-year-long trend of negative growth in the International Diabetes Care business resumes after a brief reprieve in 2Q16 (5% growth YOY, though, admittedly, against an easy comparison). Sequentially, sales outside of the US fell a striking 20% against a relatively high base (international sales of $294 million in 2Q16 were the highest since 4Q14, the last quarter in which international sales surpassed $300 million). According to our model, the international segment tends to decline between Q2 to Q3 (per the past five years), though this is easily the greatest negative sequential growth that we have ever observed.

- **The accompanying slide deck attributed the International headwind to SMBG sales (down 13% YOY) outside of the US primarily to a reduction of inventory levels from category slowdown in China.** While we assume Europe is a bigger driver of international sales than the US, clearly the slowdown in China was large enough to make a dent on sales.

LifeScan/Animas Pipeline Highlights

8. We learned from J&J last month that it submitted a PMA in June for an Animas Vibe pump integrated with Dexcom's Bluetooth-enabled G5 CGM. As we understand it, the application was submitted for use in type 1s ages two years and over. The company has not speculated on an approval timeline, but for context, the Vibe with G4 took ~20 months for approval. J&J has never commented publicly that this integrated product would be a precursor to the automated insulin delivery (AID) device, but we see it as a critical move for several reasons: (i) regulatory experience getting a Bluetooth-integrated pump approved before its AID device; (ii) the first pump company to integrate Dexcom's G5 (Tandem and Insulet are both in development, though Tandem seems to be moving faster); (iii) gives pumpers flexibility to view CGM data on the pump AND phone simultaneously; (iv) adds a remote monitoring for pediatric pumpers, which is sorely lacking in the current G4 integrated Vibe; and (v) sets up a potential upgrade program to the automated system, particularly if the new pump can be remotely software updated like the Tandem t:slim X2.

9. J&J did not comment on its OneTouch Via (formerly Calibra Finesse) bolus-only insulin delivery patch device. Guidance from ADA 2016 called for the "discreet, wearable, on-demand, mealtime insulin delivery device" to be commercially available in select markets outside the US by late 4Q16, followed by a US launch in early 2017. This timeline is accelerated from the Medical Device Business review, which originally called for a launch within the next 12 months (by May 2017).

- **According to the clinicaltrials.gov page, the OneTouch Via's 24-week clinical trial (n=280) is fully enrolled, though primary completion has been pushed back to April 2017 (back from the previous December 2016).** The study will randomize type 2s not achieving glycemic target (A1c 7.5-10%) to either OneTouch Via or the Novo Nordisk FlexPen to initiate bolus insulin therapy. The primary endpoint is A1c at 24 weeks, with secondary endpoints including time-in-range and treatment satisfaction. This study should be a positive for reimbursement and marketing, though is not a gating factor to launch.
- **Per the Medical Device Business Review, there are two OneTouch Via products in the pipeline: a smart version with connectivity and a version with a larger reservoir.** These both seem like logical expansions to improve the convenience factor of the device. We also hope a one-unit bolus version is in development, as many type 1s will be very interested.
- **As a reminder, the OneTouch Via is a three-day, very slim profile (2 inches long, 1 inch wide, and 0.25 thick), bolus-only delivery device.** J&J acquired the device from Calibra Medical in July 2012 and it secured FDA clearance way back in 2010 for type 1 and type 2 diabetes. The clearance was updated in 2012. We assume J&J has spent this time mastering the design and scaling up manufacturing. The FDA database does not list any new clearances related to this product.

10. Animas' automated insulin delivery plans were not mentioned, despite the fact that the pivotal trial, as far as we know, will begin in 4Q16 (per July's Keystone conference). The single-arm trial will test the hypoglycemia-hyperglycemia minimizer with Dexcom's G5 CGM in 200 adults, adolescents, and pediatrics. The trial, which we could not find on clinicaltrials.gov, will include a several-day in-clinic assessment, followed by a three-month home portion, and will take place at 25-30 centers in the US in children as young as two years old - this sounds very similar to Medtronic's MiniMed 670G pivotal, though the population is much larger. We got a first glimpse of the device at *the* Medical Device Business review in May, which aggressively slated launch by November 2017. Based on an ADA update, Animas now hopes to launch the product between November 2017-May 2018. See our detailed coverage from Keystone for more information.

- **Assuming the pivotal does start this quarter, Animas could be second to market after the MiniMed 670G launches** in Spring 2017; see our latest AID competitive landscape here.
- **The trial will include children as young as two years old, which could position Animas with an early market advantage in pediatrics** - Medtronic's MiniMed 670G pivotal only went down to 14 years, and Medtronic is currently enrolling for a pediatric study in 7-13 year olds that will

wrap up in December 2016, which it hopes will expand the initial FDA label for the 670G. The 670G is contraindicated in children under the age of seven due to the system's design and daily insulin requirements.

11. Neither prepared remarks nor Q&A mentioned the WellDoc BlueStar integration partnership (including a J&J investment), signed in March 2016 and "finalized" in September 2016. The latter suggested an integrated product launch will occur by the end of 2016. The system will integrate the BlueStar mobile app (Android, iOS) with LifeScan's OneTouch Verio Flex BGM and paired Reveal app (Android, iOS). It's still not clear what the integration will actually look like (e.g., two side-by-side apps vs. a single integrated app), what the business model will look like (e.g., traditional BGM vs. WellDoc's prescribed-as-a-drug model vs. something else?), or how the product will be branded (e.g., "LifeScan Verio powered BlueStar"?), but we're glad to see the product will launch soon. WellDoc will benefit from the commercial scale provided by the partnership ("a home run," said WellDoc CEO Kevin McRaith) and J&J's Reveal app and Flex BGM will receive a boost from the clinically proven BlueStar software. We see this as a critical project to enhance patient feedback and make glucose data far more actionable for type 2s. See our deep dive from March, when the agreement was first announced, for more details.

12. Earlier this month, Animas sent a letter to OneTouch Ping users informing them that the pump has some cybersecurity vulnerabilities: it may be accessed wirelessly to deliver extra insulin (via the unencrypted Radio Frequency communication that connects the meter and pump). None of the users of the 114,000 OneTouch Ping pumps circulating around the US and Canada (the first we heard this number) complained about being hacked, but the vulnerability was exposed by Jay Radcliffe, a security researcher at Rapid7 - see his blog post disclosing the findings here. Both Animas and Mr. Radcliffe emphasized that the likelihood of such unauthorized access is "extremely low" (Animas) and "relatively low" (Mr. Radcliffe), requiring technical expertise, sophisticated equipment, and RF proximity to the pump (since the Ping is not connected to the internet). In addition, the mitigations suggested in the letter should eradicate risk altogether: Patients can turn off the pump's radio frequency feature (disabling the ability to control the pump remotely via the OneTouch meter), program the pump to limit the amount of bolus insulin that can be delivered (at one time, within two hours, over the course of a day), and/or set the pump to vibrate whenever a dose is initiated by the meter remote. Animas is working with the FDA and Department of Homeland Security, among others, to ensure patient safety.

- **This issue continues to get attention, which presents a challenge: what are the unintended consequences of publicizing this issue, particularly if the absolute risk is low?** There is a risk to everything, and as Mr. Radcliffe wrote, "Removing an insulin pump from a diabetic over this risk is similar to never taking an airplane because it might crash." For those with malicious intent, there are easier ways than RF hacking to harm someone with diabetes wearing a pump.
- **This finding, however, does serve as a reminder to industry that cybersecurity is crucial, particularly as Bluetooth connectivity becomes standard in pumps**. Bigfoot's announcement of $35.5 million in Series A funding (see our coverage prior to tomorrow's press release) certainly emphasizes the security in its cloud-connected system.

LIFESCAN/ANIMAS PIPELINE SUMMARY

Pipeline Product	Timeline
OneTouch Via insulin delivery device (acquired from Calibra Medical)	*Launch in select markets outside the US by late 4Q16, followed by a US launch in early 2017 (ADA 2016 update).*
Automated Insulin Delivery (Hypoglycemia-Hyperglycemia Minimizer)	Pivotal study to begin in 4Q16 (per Keystone 2016); Launch expected between November 2017-May 2018

WellDoc Partnership to integrate BlueStar into Verio BGM and Reveal App	Integrated product to launch by the end of 2016. Commercial partnership finalized in September.
Animas Vibe System integrated with Dexcom G5 technology	PMA submitted to FDA in early June 2016 for patients with type 1 diabetes ages 2+ years.

Questions and Answers

Q: For Invokana, I saw in the presentation that you expect to present CANVAS and CANVAS-R data in mid-2017. Are you going to present each separately before that? Do you have plans to issue a press release with topline results? What's your confidence that we'll see a similar cardiovascular benefit as we did with EMPA-REG OUTCOME? Do you have a comment on the amputation risk?

A: Invokana remains the leading SGLT-2 inhibitor, as I described in the conference call. As for CANVAS and CANVAS-R: We plan to evaluate both together as one meta-analysis. We're in discussion right now about degrees of statistical confidence with FDA. We have very strong reason to suspect that the combination of CANVAS and CANVAS-R will give data very similar to what was reported with EMPA-REG OUTCOME.

Q: With the upcoming election, I'm curious as to your thoughts on Proposition 61, which might actually pass in the state of California. I'm wondering what you think the industry's response will be? (Editor's note: Proposition 61, if passed, would require state agencies to pay the same prices that the US Department of Veterans Affairs [VA] pays for prescription drugs.)

A: There are several vocal opponents. We would prefer to have pricing that is more related to outcomes. Evidence-based medicine is something that we're advocates of, and outcomes-based pricing is a component of that. Our view is that Proposition 61 is a misguided action, and it would be difficult to operationalize and would create access barriers for patients.

-- by Brian Levine, Payal Marathe, Adam Brown, Helen Gao, and Kelly Close