Good evening from San Francisco! We have several updates for you tonight, especially on the SGLT-2 inhibitor front: our full report on the FDA Advisory Committee meeting on BMS/AZ's Forxiga, an update on Forxiga's status in Germany, and regulatory news on J&J's canagliflozin/metformin fixed dose combination in the US. On the technology side, we have disappointing news just in from CMS on the insulin pump front, news on the FDA's disappointing clearance of Prodigy's Choice BGM, Insulet and Amgen's partnership, and Dexcom's G4 Platinum on CNBC. Last, we have a short preview of what we're looking forward to at the Consumer Electronics Show (CES) in early January.

Diabetes Drugs

1. FDA Advisory Committee votes 13-1 to approve BMS/AZ's Forxiga (dapagliflozin) - big picture panelist comments on CV guidance and more
2. BMS/AZ withdraw Forxiga (dapagliflozin) from German market - The only SGLT-2 inhibitor on the German market becomes the latest victim of Germany's challenging comparative effectiveness review process
3. FDA issues CRL for J&J's canagliflozin/metformin IR fixed dose combination (summary below; press release)

Diabetes Technology

4. Breaking news: CMS declines new HCPCS code request for integrated insulin pumps with CGM (summary below)
5. FDA clears Prodigy Choice BGM with warning label despite notable system inaccuracy - label states that the meter is too inaccurate for dosing insulin or calibrating CGMs
6. Insulet announces five-year commercial agreement to supply Amgen with an oncology medication delivery device - net positive for Insulet's diabetes business
7. Dexcom's G4 Platinum featured on CNBC's Fast Money - pediatric approval hopefully in "next several weeks" (summary below; video clip)

Conferences

8. CES 2014 sees 40% rise in digital health exhibitors - Dexcom, iHealthLab, Misfit Wearables, Telcare, Yofimeter to exhibit (summary below; press release; digital health summit; exhibitors)

SUMMARIES

1. FDA Advisory Committee votes 13-1 to approve BMS/AZ's Forxiga (dapagliflozin) - We are back with our full commentary on the Advisory Committee meeting for BMS/AZ's SGLT-2 Forxiga (dapagliflozin) - our report contains some of our big picture musings on the day's discussions and final votes as well as a supremely comprehensive set of details. In one of the more conclusive voting results at a diabetes drug Advisory Committee meeting in recent memory, the FDA's EMDAC voted 13-1 to approve dapagliflozin. It was a nail-biter until the very end - there was plenty of debate on the divergent cardiovascular safety results from the drug's phase 2b/3 program and on the imbalance of bladder cancer cases between groups, which had worsened since the drug's first Ad Comm but were

still non-significant. We thought BMS did a notable job assuaging panelists' concerns on the bladder cancer issue, using an analysis of the bladder cancer cases in the dapagliflozin arm to demonstrate that it was unlikely that the drug directly caused all of the cancer cases. It was too bad more of this information wasn't available at the first Ad Comm. Regarding CV safety, BMS met the FDA's pre-approval requirement in terms of ruling out unacceptable CV risk, and the panel voted 10-4 that dapagliflozin fulfilled the FDA's CV safety requirement. Interestingly, portions of the discussion touched upon big-picture issues in the diabetes drug regulatory process. Three of the four panelists who voted that the drug did not meet the FDA's CV guidance still ultimately voted to approve the drug, which suggests that they may not think adherence to the CV guidance was necessary for approval. We may be getting closer and closer to FDA calling a follow-up for the 2008 CV guidance - it seems to be getting less relevant (following Avandia's redemption) and more ambiguous (e.g., Novo Nordisk's CRL for insulin degludec) all the time to current approval decisions, although of course it will be very helpful to see all the CVD data as it emerges. Also quite notably, we were very pleased that we didn't see our worst case scenario, where panelists would use the presence of J&J's Invokana (canagliflozin) on the market as a reason to hold dapagliflozin to a higher bar - in our minds, doing so would have set a problematic precedent by effectively overtly discouraging competition. Read our full report for more of our big-picture musings and the specific details on the day's deliberations.

2. BMS/AZ withdraw Forxiga (dapagliflozin) from German market - On Friday, BMS/AZ announced that the removal of their SGLT-2 inhibitor Forxiga (dapagliflozin) from the market in Germany following a failure to reach an agreement with German authorities on the product's pricing. As background, the German Federal Joint Committee (G-BA) ruled earlier this year that Forxiga showed "no additional benefit" over currently available therapies, namely *sulfonylureas*. Disappointingly, the decision was based on the failure of the drug's clinical trial program to meet the G-BA's strict guidelines for comparator therapies, rather than on the drug's proven efficacy. The G-BA's ruling effectively subjects the drug to generic-level pricing. Novartis' Galvus (vildagliptin) and BI/Lilly's Trajenta (linagliptin) franchises also received "no additional benefit" rulings from the G-BA; BI/Lilly did not launch Trajenta in Germany, and Novartis is considering withdrawing Galvus. The withdrawal of Forxiga is particularly notable, in our view, as the drug is the first and only SGLT-2 inhibitor available to patients in Germany. Read our full report for more details and context.

3. The FDA has issued a complete response letter (CRL) to J&J for its canagliflozin/metformin IR fixed dose combination (FDC). We feel confident that J&J should be able to meet the FDA's request for additional information on whether the twice-daily dosing regimen of the canagliflozin/metformin FDC is comparable to the once-daily dosing of the approved canagliflozin single agent. There are no safety issues associated with this inquiry. We are curious whether most doctors would prefer to titrate metformin separately before initiating an FDC given that titration can reduce the gastrointestinal side effects associated with metformin; it doesn't really matter though some may be associated with higher fees for the patients. As a reminder, metformin IR is typically dosed twice-daily, while canagliflozin as a single agent is approved for once-daily dosing at 100 mg or 300 mg. To our knowledge, J&J has not disclosed what doses of canagliflozin will be available in the metformin

IR FDC. J&J is also working on a canagliflozin/metformin extended release (XR) FDC (in phase 3), which will allow for once-daily dosing. In some patients, metformin XR is also associated with fewer GI side effects.

4. Breaking and discouraging news just in on insulin pumps: As we understand it, CMS has just turned down the request for a new HCPCS Code for insulin pumps integrated with CGM. The decision is reportedly based on its view that CGM is not essential for proper management of blood glucose levels. This isn't good news on the competitive bidding front. At present, we don't know any manufacturers that will supply patients with pumps, either with or without CGM, at greatly reduced rates (rumors of very low pricing have been shared). We expect to see major patient advocacy and activity on this front in the coming months...

5. The FDA cleared the Prodigy Choice Blood Glucose Monitoring System late last month. Notably, the clearance carries quite a strong warning label (unprecedentedly strong) with it, stating that the meter is "less accurate than most other blood glucose meters sold today." Furthermore, the owner's manual and strip insert will include language specifically advising patients NOT to dose insulin or calibrate a CGM with the new meter. We salute the FDA for noting the device's inaccuracy (given that due to 510(k) laws, they had no choice but to approve it) and note that the FDA was in quite a tough spot on this one. Though the device is not very accurate by recent standards, it is technically substantially equivalent to an earlier Prodigy meter and complies with 2003 ISO Standards (the FDA has not adopted the newer 2013 ISO standards or released its own updated standards, which are due out soon). In effect, the FDA was forced to clear an inaccurate meter, and thus, did the best it could by alerting patients to the risks of using it. Luckily, we understand that Prodigy does not plan to market the meter. Read our report for more details on the new device's accuracy, thoughts on what the approval means for patients, and a summary of recent regulatory happenings on the BGM accuracy front.

6. Insulet to supply Amgen with drug delivery device for oncology medications - **On December 10, Insulet announced a five-year commercial agreement to supply Amgen with a delivery device to deliver oncology drugs.** While the press release was light on detail, we believe this agreement refers to Neulasta and Neupogen, Amgen's white blood cell boosters that are used after chemotherapy. The expansion is good news for Insulet, as the partnership could increase the company's gross and net margins, provide more money for R&D, give Insulet additional Big Pharma experience for the existing Lilly U-500 partnership, and broadly expand visibility of the OmniPod. Read our report for why the deal makes good strategic sense for Insulet, how oncology drugs could benefit from this type of delivery, and what modifications could be made to the OmniPod.

7. Last Wednesday, Dexcom CEO Terry Gregg discussed **the G4 Platinum and Dexcom's upcoming catalysts in a three-minute spot on CNBC's Fast Money.** Mr. Gregg described the basics of CGM vs. fingersticks, showed off the G4 Platinum receiver, and addressed stock-related questions from the show's hosts. Most importantly, he remarked that pediatric approval is hopefully expected "within the next several weeks," on par with the "end of 2013" estimate shared in Dexcom's

3Q13 financial update. As a reminder, discussions with the FDA have centered on labeling; as such, a pediatric approval is likely a "when," not "if" question. Additionally, Mr. Gregg highlighted the company's next catalyst, Dexcom Share, a remote monitoring product that should particularly appeal to parents (as of the 3Q13 call, Dexcom was responding to FDA questions). The segment concluded with host questions surrounding Dexcom management's recent sale of stock - Mr. Gregg was unfazed, noting that the executive team has been "too heavily weighted" with the "bulk of their net worth in a single stock." Mr. Gregg's confident appearance on CNBC certainly speaks volumes about Dexcom's recent success (the stock is up 147% year-over-year) and expectations for the future, as well as the growing public interest in CGM.

8. Earlier this month, the Consumer Electronics Association announced **that the 2014 Consumer Electronics Show will see a 40% increase in the number of digital health exhibits** - wow! The TechZone, focused on the intersection of technology, health and wellness, will showcase more than 65 exhibitors, including Dexcom, iHealthLab, Misfit Wearables, Telcare, and Yofimeter. We'll be on site covering all the happenings, including everything we expect to learn during the two-day digital health summit conference track (schedule here). We will hear sessions entitled "How Digital Health Saved My Life" (Dexcom's CEO Mr. Terry Gregg and VP of Global Access Dr. Claudia Graham), a keynote on breakthrough business models in digital health, and a luncheon entitled "Beyond Wearable - It's Invisible" (Medtronic Diabetes; CTO Dr. John Mastrototaro), among several others. Please let us know if you'll be at CES or what you'd be interested to hear more about.

Take good care, and we hope you are having a fantastic start to the week!

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