CLOSER LOOK

JP Morgan Healthcare Conference

January 11-14, 2016 San Francisco, CA; Day #1; Highlights - Draft

Executive Highlights

Greetings from Union Square and 804 Haight, where the conference comes to us for once! Downtown SF has turned into a sea of business suits, as the annual JP Morgan Healthcare Conference and Biotech Showcase has officially kicked off and life sciences globally descends on San Francisco. The first day brought in a slew of updates from Medtronic, Intarcia, Abbott, J&J, and more - please see below for our top ten highlights (and a couple honorable mentions) and check out our preview to see what's to come for the rest of the week.

1. Medtronic CEO Omar Ishrak enthusiastically highlighted plans to still launch the MiniMed 670G hybrid closed loop system in the US in FY17 (by April 31, 2017), but in major news, the 640G may not launch in the US beforehand. Management said the timelines are similar, so it may make sense to leapfrog the 640G in the US. We also learned for the first time that the iPro 3 (EU) and Guardian Connect with Enlite 3 (US; Bluetooth-enabled standalone CGM) are expected to launch by April next year. We're very excited about seeing professional CGM driving therapeutic change so will be very keen to watch the iPro in particular since that's where the therapy's benefits seems truly scalable.

2. The CVOT for Intarcia's ITCA 650 (implantable exenatide mini-pump) has completed and will report results in 2Q16. We also learned that Intarcia's collaboration with Numab will involve an antibody-based SGLT-2 inhibitor (!) to be combined with ITCA 650.

3. Abbott CFO Mr. Brian Yoor shared enthusiasm for FreeStyle Libre along with news that the company has - at long last - completed its capacity expansion to meet global demand.

4. J&J announced Monday morning that it has received FDA approval for the pediatric indication of the Animas Vibe integrated with Dexcom G4; the approval goes down to age two, the youngest available for a sensor-augmented pump in the US and we're very excited for parents about this news.

5. Down the road at the Biotech Showcase, ViaCyte presented encouraging preliminary results from the phase 1/2 trial of its VC-01 islet cell replacement therapy.

6. Merck CEO Mr. Ken Frazier characterized diabetes multiple times as a key growth area for the company, most notably announcing anticipated filings for Pfizer-partnered SGLT-2 inhibitor ertugliflozin in 2016. We were glad to hear the focus is still there!

7. A lunchtime panel discussion featured the compelling Dr. Susan Desmond-Hellmann (CEO, Bill & Melinda Gates Foundation), J&J CEO Alex Gorsky, JP Morgan CEO Jamie Dimon, and Fox News anchor Maria Bartiromo. The wide-ranging discussion addressed cost pressures, scientific innovation, the role of philanthropy, the challenges of Ebola, and more. Quotes below!

8. In a lively Panel Discussion on digital health, speakers expressed optimism for the seemingly inevitable fusion of the health and technology worlds, though noted that the medical industry still has a LOT to learn from Silicon Valley.

9. Gilead management: "The actual opportunity for meaningful change to drug pricing in the US is quite low. It's more of a campaign issue than an actual issue."

10. Results are expected this quarter (1Q16) from a phase 2 trial testing Midatech's MidaForm buccal insulin (single-use, dissolvable strip placed on the interior of the cheek). The company also plans to move a type 1 diabetes vaccine into phase 1 this year.

Honorable Mention: Novartis CEO Mr. Joseph Jimenez shared that the full details of a "turnaround plan" for Alcon, the division partnered with Google, will be announced during the company's 4Q15 call later this month.

Honorable Mention: Personal genetic testing company 23andMe is expanding beyond its direct-to-consumer tests to research and drug discovery efforts.

Table of Contents

Top Ten Highlights

1. Medtronic CEO Omar Ishrak highlighted plans to launch the MiniMed 670G hybrid closed loop system in the US in FY17 (by April 31, 2017, consistent with JPM 2015), and in major news, the 640G may not launch in the US beforehand. The company's near-term pipeline slide (see below) did not show the 640G predictive suspend system, and in Q&A, management said the two products are actually running on roughly similar US launch timelines. Leapfrogging the 640G and instead launching the 670G makes strategic sense: the 640G has still not been submitted to the FDA and the 670G pivotal study will wrap up soon (May); a single 670G launch means one PMA submission and no hassle of upgrading early 640G adopters; and the marketing will be far stronger for a hybrid closed loop. Still, getting the 670G approved and launched by April 2017 means less than one year at FDA - possible but not a certainty, given a new sensor (Enlite 3) and the first commercial product to increase insulin delivery based on CGM values. Otherwise, the pipeline slide showed two other major timelines of note: launches of Guardian Connect with Enlite 3 (US) and iPro 3 (EU) by April 31, 2017 (FY17). We assume the former is Medtronic's own standalone, Bluetooth-enabled CGM (first demoed at Health 2.0 in September 2014), a key answer to Dexcom's G5 mobile. Outside of the pipeline, Mr. Ishrak reiterated the company's plans to expand into type 2 diabetes ("we're committed"), while a company-wide partnership slide showed the slew of diabetes collaborations: BD (infusion set launching around March-April), DreaMed Diabetes (closed-loop beyond 670G), Glooko (data integration launching in 1H16), Diabeter (generating revenue), and IBM Watson Health (hypoglycemia prediction app launching this summer) - there was no commentary on any of them, though it's worth noting that all of these came about in the past year! More details and analysis below from a fascinating meeting we had with the Medtronic Diabetes management team.

2. The CVOT for Intarcia's ITCA 650 (implantable exenatide mini-pump) has completed and will report results in 2Q16. In a compelling and well-received presentation built (like last year's) around the theme of disruptive innovation, Intarcia CEO Mr. Kurt Graves shared that the FREEDOM-CVO trial reached its required number of events late last year. While this is substantially earlier than the expected completion date of July 2018 listed on ClinicalTrials.gov, Mr. Graves described it as a "stretch target" but one the company had hoped to meet. The trial began in March 2013 and aimed to enroll 4,000 patients with a

history of CVD. Mr. Graves stressed that this trial was designed as a safety study and is not powered to test for cardioprotection. We imagine that ITCA 650 would be one of the more likely GLP-1 agonists to demonstrate cardioprotection given its inherent adherence advantage but are keeping our expectations in check as the company reminds often that the trial was not designed to show cardioprotection. In his presentation, Mr. Graves also provided some insight into Intarcia's expected marketing strategy for ITCA 650, which involves positioning it early in the type 2 diabetes treatment algorithm and appealing to payers from the outset. The company plans to initially target 25,000 early adopters who represent 80% of the volume for most type 2 diabetes launches, which should require a sales force of 500 reps. We also learned that Intarcia's collaboration with Numab will involve an antibody-based SGLT-2 inhibitor, which the company hopes to combine with ITCA 650 for a "completely revolutionary" treatment. Mr. Graves also addressed the company's acquisition of Phoundry Pharmaceuticals, which includes glucagon and amylin as targets. See our full coverage below for more.

3. Abbott CFO Mr. Brian Yoor shared enthusiasm for FreeStyle Libre along with news that the company has - at long last - completed its capacity expansion to meet global demand. This expansion has been in the works for several quarters and it's great to hear that constraints should no longer hold marketing and sales back. Mr. Yoor noted that serious demand ("greatly exceeding expectations") drove the shortage - echoing commentary from recent earnings calls - and we're glad to hear that manufacturing hurdles have been overcome. Indeed, now that supply is unconstrained, we will be very curious to see if Abbott finally discloses FreeStyle Libre sales in its 4Q or 1Q updates. The expansion will clearly please many EU patients waiting to get on the system, and the wider launch this year of the LibreLink Android app (only available on an invite-basis in Sweden) should presumably accelerate uptake - once available, patients will only need to order sensors to use FreeStyle Libre. Unfortunately, Mr. Yoor was unable to comment on the timeline or plans for bringing FreeStyle Libre (consumer or pro version) to the US, though did express that the company is working hard on this front (a US launch of Pro is expected this year, per the 2Q15 submission). The attention to Libre from upper levels of management is terrific to see and stands as a clear sign the product will get the needed sales and marketing to drive adoption moving forward - ultimately, we hope that brings much better data and engagement to millions of people with diabetes. Other commentary on Diabetes Care was nearly nonexistent, though management did label the segment an "innovation-driven business" - a testament to the clear dedication to FreeStyle Libre.

- **As a reminder, Abbott has completed its US pivotal study for the FreeStyle Libre consumer version; the blinded Pro version was submitted to FDA in 2Q15, and we assume an approval is still on track for 2016.** The company's US pilot study of the Pro - which began recruiting type 2 participants in April (n=132) - did wrap up in August and results have not yet been posted.

4. J&J announced this morning that it has received FDA approval for the pediatric indication of the Animas Vibe integrated with Dexcom G4; the approval goes down to age two, the youngest available for a sensor-augmented pump in the US. The excellent news bodes well for J&J as it looks to stay ahead of the other two most recently launched sensor-integrated pumps in the US: Medtronic's MiniMed 530G (16 years and older) and the Tandem t:slim G4 (12 years and older). This is a competitive advantage for J&J and a great new option for young patients - less hassle to get on CGM! - though there are lots of factors for parents and young patients to weigh (e.g., waterproof vs. other pumps; worse user interface than t:slim G4; lacking Dexcom G5 smartphone integration and remote monitoring - see the pros and cons below). It was certainly clear during today's breakout session, however, that internal optimism is high. We heard both CEO Mr. Alex Gorsky and Group Worldwide Chairman Ms. Sandi Peterson (who oversees J&J's Diabetes Solutions business) allude to the approval, and there seems to be real belief that Vibe's success can help right some of the business's financial challenges. Disappointingly, management did not comment on the closed loop (termed a priority at AACE 2015) or plans to launch the Calibra Finesse bolus-only insulin delivery patch device this year. Ms. Peterson did allude to confidence in the future of the BGM business - we were a bit surprised by this characterization given the segment's recent performance - and we share more thoughts in the detailed write-up below.

- **While there was little specific discussion of diabetes in the context of J&J's pharmaceutical business, Invokana (canagliflozin) was highlighted as one of several blockbuster successes for Janssen in recent years.** Looking forward, CEO Mr. Alex Gorsky suggested that the company has "just scratched the surface" in areas of unmet need including type 2 diabetes. While he did not include any diabetes drugs in his list of promising mid- to late-stage pipeline highlights, the company has made several exciting efforts to refill its metabolic disease pipeline in the past year, including recent agreements with Hanmi and Intrexon.

5. Down the road at the Biotech Showcase, ViaCyte President and CEO Dr. Paul Laikind presented encouraging preliminary results from the phase 1/2 trial of the company's VC-01 islet cell replacement therapy. He shared that 12 patients have now received the therapy (encapsulated pancreatic progenitor cells derived from embryonic stem cells) at sub-therapeutic doses and that early safety/ tolerability and proof-of-concept results are promising. There have been no serious adverse events or severe hypoglycemic episodes in the trial thus far, and most of the milder adverse events have been related to the surgical procedure (e.g., pain and swelling at the implantation site). There has also been no off-target growth of the cells in unwanted locations or any evidence of immune rejection or sensitization. Beyond these safety endpoints, Dr. Laikind presented histological data demonstrating robust vascularization, cell survival, and expression of beta cell-specific markers in one of the devices when removed after 12 weeks. He acknowledged that this represents the best outcome the investigators have seen and implied that it has not been replicated in every patient. However, he stressed that the company's goal with this first cohort is only to demonstrate that the therapy is viable in humans. As stated in the past, ViaCyte then plans to use these initial results to optimize the therapy before beginning cohort two, which will evaluate efficacy in 36 patients.

- **ViaCyte is also developing a cell replacement therapy aimed at very high-risk patients that does not use the encapsulation device.** This therapy, PEC-Direct/VC-02, has flown under the radar relative to VC-01 and remains preclinical. It would not represent as great a leap forward as VC-01, as patients would still need to take chronic immunosuppressants after implantation. However, it would address the current shortage of cadaveric islet cells available for transplantation, and Dr. Laikind suggested that there would be a substantial market for the product among the 5-10% of patients with type 1 diabetes who are currently eligible for islet transplants. We are curious how this will compare, both in terms of efficacy and development timeline, to other stem cell-derived therapies like those being developed by Semma Therapeutics and BetaLogics, as the potential for differentiation is less clear than with VC-01.

6. Merck CEO Mr. Ken Frazier repeatedly referred to diabetes as a key growth area for the company, most notably announcing anticipated filings for Pfizer-partnered SGLT-2 inhibitor ertugliflozin in 2016. Throughout the presentation, Mr. Frazier highlighted Merck's commitment to diabetes, emphasizing the market opportunity of the disease's growing prevalence. He specifically pointed to DPP-4 inhibitor Januvia's (sitagliptin) consistent strong growth, stressing that Merck will "continue to invest in this important product and defend its market share." Notably, in discussing the company's "key potential catalysts for 2016," Mr. Frazier noted the completion of ertugliflozin's phase 3 studies (which we learned in the 3Q15 update) and shared that Merck anticipates filings in 2016 for the candidate both as a monotherapy as well as in fixed-dose combinations with Januvia and metformin. We especially see a DPP-4 inhibitor/ SGLT-2 inhibitor combination of great value in improving adherence and it will be interesting to see whether such a patient population will grow if guidelines change after more CVOT results. In addition, Mr. Frazier noted that Januvia's label may be updated with the TECOS results in 2016 - we believe the spot-on neutrality of these results have at least somewhat contributed to the product's growth over recent quarters and a label update will likely further support this trend. While diabetes received little attention during the breakout session, please see below for one response of management's confidence in the Januvia franchise and ertugliflozin moving forward.

7. A lunchtime panel discussion featured the impressive Dr. Susan Desmond-Hellmann (CEO, Bill & Melinda Gates Foundation), J&J CEO Alex Gorsky, JP Morgan CEO Jamie Dimon, and Fox News anchor Maria Bartiromo. The wide-ranging discussion touched on cost pressures, scientific innovation, the role of philanthropy, the challenges of Ebola, and more. We were

particularly impressed with Dr. Desmond-Hellman, who emphasized profound tension she lives in each day: bringing cutting-edge science to those who need it most around the world. Her remarks reinforced the value of public-private partnerships in overcoming market failures - areas of high need where there simply isn't enough investment. Her comments on polio were particularly striking - with the help of vaccine makers, the Gates Foundation has practically eliminated polio globally. We continue to wonder where such partnerships can move the needle in diabetes. What are the most important trials or pilots that could be funded with philanthropic dollars? See our top three favorite quotes from this lunchtime discussion immediately below, with the complete list in the detailed discussion section.

- **"The most profound thing that strikes me is the quality of the science - the ability to benefit patients is better now than it has ever been. But I live in tension in profound ways every day with the Gates Foundation. How do we take great science and innovation and help people be healthier?** The deal making is very exciting, but we want to bring deals that bring that science to the people who need it the most. We're excited to be part of this ecosystem. You can see the kinds of deals we make, like this morning with Lodo Therapeutics. They are looking at microbes in mud and whether we can find new antibiotics. The world needs new antibiotics, and we can use our capital to drive deals from market failures. The more this is a healthy, science driven industry, the better." - *Dr. Susan Desmond-Hellmann*
- **"In China right now, the average healthcare spend is $400 per person. In the US, it's $8,000-$9,000.** What's the right answer? It's probably not $400, but it's also not $9,000. We as an industry have to change the models. Over the next few years, it needs to become outcomes-based, episode of care based." - *Alex Gorsky*
- **"I have three metrics on my plate that will make this a great year. One is wiping polio off the globe. We're down to two countries - Pakistan and Afghanistan.** The second is to decrease again by half mortality in kids under five. Lots of companies are at this meeting, and we need great companies helping make affordable vaccines. The third is education - we have to increase the proportion of American high school students that are job or college ready. Those are my top three." - *Dr. Susan Desmond-Hellmann*

8. In a lively Panel Discussion on digital health, speakers expressed optimism for the seemingly inevitable fusion of the health and technology worlds, though noted that the medical industry still has a LOT to learn from Silicon Valley. "As Google and Apple get into healthcare, they have something very profound to teach us," said Evidation Health CEO Dr. Deborah Kilpatrick. "They know how to think of people as consumers of something in their daily lives, and that is not how we in healthcare have traditionally viewed patients." Indeed! Grand Rounds CEO Mr. Owen Tripp echoed this sentiment, stating that tech giants will not only speed the process of innovation but will expedite the "17-year lag time" between a health technology's development and adoption by physicians - yikes! [The stat is even more embarrassing relative to the technology world where it takes "18-24 months" for new software to be adopted by engineers!] Mr. Tripp advocated for simpler solutions that deliver instant gratification, suggesting rather provocatively that striving for "engagement" (which is too slow of a process) is actually the enemy. "I hope we can slay the word engagement," he said. "What patients really want is a big red button they can smash when they are worried. If you give patients something that easy, then you'll have your solution." We've seen companies succeed at offering close-to "instantaneous" services (e.g. OneMedical's online booking/appointment reminders, Walgreens' online prescription filling service) though are not as sure that the solution is quite that simple. The digitization of health requires providing insight and customizing care in a scalable, cost-effective manner. Having a chronic disease is zero fun, and too much of digital health asks more of patients without offering much in return. That said, we can appreciate Mr. Tripp's point -a solution lacking the automaticity and ease we have in tech (e.g., push a button, have a pizza delivered to your front door; open an app, get a ride in two minutes) may sit at the bottom of most patients' sock drawers. That does not help anyone, and we left the discussion even more appreciative of the many, many factors - instantaneous, scalable, cost-effective, regulated, easy for patients, valuable for providers, insightful for payers, and on and on - that must be integrated in order to achieve the Holy Grail in digital health. No wonder it's so difficult. For now, we wait.

9. Gilead management: "The actual opportunity for meaningful change to drug pricing in the US is quite low. It's more of a campaign issue than an actual issue." In a breakout session, Gilead management was adamant that the recent public and political discourse over high drug prices will not actually have a substantive impact, though the company expects the issue will garner a fair bit of attention on the 2016 campaign trail (indeed, both Secretary Hillary Clinton and Senator Bernie Sanders have already tackled the topic). Gilead also suggested that the press has been one-sided in its coverage of drug prices and emphasized that the company would focus on highlighting the value of its products to legislators in Washington. Gilead's controversial hepatitis C drugs Sovaldi (sofosbuvir) and Harvoni (ledipasvir/sofosbuvir) offer an unprecedented opportunity for a complete cure - but at an extremely high cost ($84,000 and $94,500 for a complete course of treatment, respectively). Gilead management noted the growing evidence of the cost savings associated with curing, rather than merely treating, hepatitis C. That said, its high cost has forced payers and healthcare systems to limit access to only the sickest of the 130-150 million people with hepatitis C worldwide. Public furor over the pricing was on clear display - protesters outside of JPM 2016 displayed signs with slogans such as "Gilead = Greed" and "Don't be Greedy! Treat the Needy!" We expect manufactures will see more of this as more inequality is evident.

- **The biggest diabetes-related news from Gilead's update was a mention of its ASK-1 inhibitor GS-4997, which is in phase 2 trials for diabetic nephropathy.** Management acknowledged that its anti-inflammatory portfolio, including GS-4997, has been more under the radar than its high-profile hepatitis C and HIV products. Gilead's 3Q15 update presentation slides noted that the phase 2 trial for GS-4997 in diabetic nephropathy is fully enrolled. In addition to diabetic nephropathy, Gilead is pursuing GS-4997 both alone and in combination with its cancer drug simtuzumab for NASH. With the combination, Gilead hopes to address both the anti-inflammatory and the anti-thrombotic components of NASH. The company did not mention its cardiovascular pipeline during its prepared remarks or breakout session. We found this disappointing as we've been eagerly awaiting an update on whether Gilead will pursue a type 2 diabetes indication for its sodium current inhibitor Ranexa (ranolazine; approved for angina) for some time.

10. Midatech Pharma CEO Dr. Jim Phillips said that results are expected this quarter (1Q16) from a phase 2 trial testing Midatech's MidaForm buccal insulin (single-use, dissolvable strip placed on the interior of the cheek). The company is focused on oncology and plans to license the insulin ("we are not a diabetes company"), presumably to one of the insulin manufacturers. Dr. Phillips said results that replicate phase 1 would be a home run, showing 25% of the bioavailability of injection, with 50% of the pharmacodynamic effect. Apparently, insulin companies are looking for >10% bioavailability. As we noted when the trial began in summer 2015, MidaForm insulin is a joint venture with MonoSol Rx. Dr. Phillips also disclosed plans to move a type 1 diabetes vaccine into phase 1 this year. The slide detailed the approach, which was not elaborated on: pancreatic beta cell T cell epitope (proinsulin C19-A3) combined with the tolerogenic cytokine IL-10 and targeted to antigen presenting cells via gold nanoparticles and delivery into the very superficial layers of the skin using microneedles. We look forward to following this company more closely, as they listed on the NASDAQ in December. Midatech has 105 employees, was founded in 2001 in the UK, and has four commercial products in oncology.

Honorable Mention

- **Novartis CEO Mr. Joseph Jimenez shared that the full details of a "turnaround plan" for Alcon, the division partnered with Google, will be announced during the company's 4Q15 call later this month.** As a reminder, we learned from Novartis' 3Q15 update that the company is planning to implement a growth acceleration plan as a response to the division's slow growth. Mr. Jimenez labeled Alcon's recent performance as an area where Novartis fell short, but highlighted that the division has potential as demographic trends support eye care as a significant growth area. Details around the "turnaround plan" remained mostly undisclosed, although Mr. Jimenez suggested during the breakout session that recognition of the differences in Alcon's pharma and device work will be a key component of the plan. In that vein, while he briefly

and ambiguously pointed to contact lens as an example of Alcon's device work, management provided no mention of the company's collaboration with Google on diabetes - see our 2Q15 report for more details on the latest we've heard on this front. Otherwise, Novartis' DPP-4 inhibitor Galvus (vildagliptin) received no attention during the company's presentation or Q&A, similar to recent financial updates, as we do not foresee the company devoting additional resources to the drug. Thus with regard to diabetes, while we have not heard any specific mention of the Google smart contact lens collaboration since the 4Q14 call, we will be listening most closely for any potential updates in the proposed Alcon growth acceleration plan on January 27. Please see below for a transcript of the Q&A on this.

- **Personal genetic testing company 23andMe is expanding beyond its direct-to-consumer tests to research and drug discovery efforts.** President Mr. Andy Page described how the company's three business units - direct-to-consumer genetic testing, research services, and drug discovery - collaborate to advance its mission of helping people access, understand, and benefit from the human genome. On the genetic testing front, 23andMe was recently able to relaunch its product following FDA approval and the creation of a pathway to allow for approval of future carrier status reports that the company (or other companies) may develop. Management emphasized the accuracy and impressive user engagement with the product - trials demonstrated over 90% user comprehension and a survey aimed at investigating a link between a particular genotype and prostate cancer garnered an astounding 10,000+ responses in just 12 hours. Looking to the future, the company plans to expand the report types available through the 23andMe platform (we hope diabetes and obesity will eventually be included, though the research in this area is very preliminary) and hinted at expanding to other types of testing beyond genetic testing. 23andMe has also built a thriving research services business unit using the genotypic and phenotypic data it has gathered through its genetic tests and survey responses. While the company works with third-party groups as well, Mr. Page noted that 23andMe's new drug discovery unit is its own largest client within research services. Headed by Genentech alumni Drs. Richard Scheller and Robert Gentleman, the drug discovery unit will develop new therapeutic targets based on "phenome-wide association studies (PheWAS)," which investigate the wide variety of phenotypes that may be associated with a particular genotype. Mr. Page shared that in the six months since its inception, the division has already identified several potential therapeutic targets. The company hopes to set up a wet lab for research in the Bay Area within the next year. The company has certainly grown up since its JPM 2013 showing and we're excited to see 23andMe expand its business focus beyond personal genetic testing to new frontiers in precision medicine. See our recent interview with Dr. Anne Peters for more on how 23andMe and genetic testing could revolutionize diabetes care.

Detailed Discussion and Commentary

JP Morgan Healthcare Conference

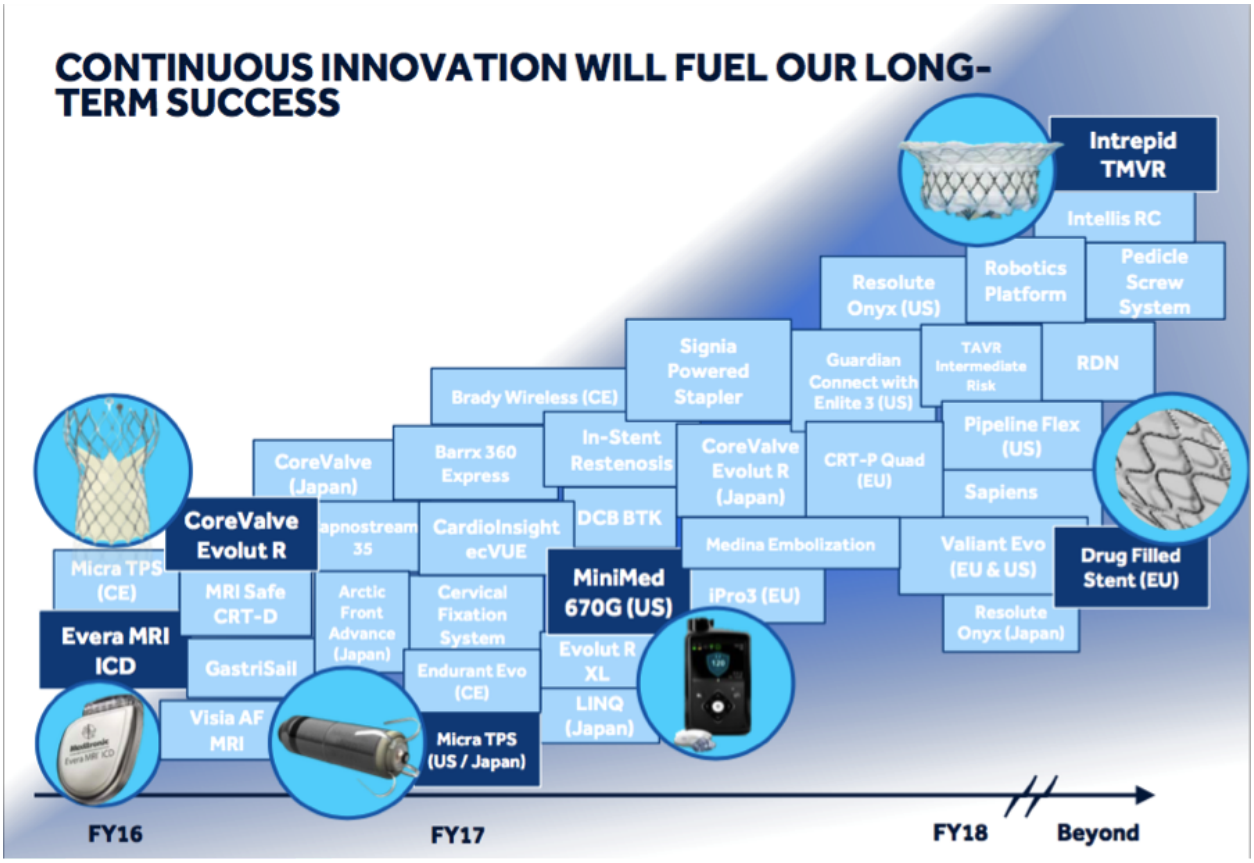
MEDTRONIC

Omar Ishrak (CEO, Medtronic, Minneapolis, MN)

Medtronic CEO Omar Ishrak enthusiastically highlighted plans to launch the MiniMed 670G hybrid closed loop system in the US in FY17 (by April 31, 2017, consistent with JPM 2015), but in major news, the 640G may not launch in the US beforehand. The company's near-term pipeline slide (see below) did not show the 640G predictive suspend system, and in Q&A, management said the two products are actually running on roughly similar US launch timelines. Leapfrogging the 640G and instead launching the 670G makes strategic sense: the 640G has still not been submitted to the FDA and the 670G pivotal study will wrap up soon (May); a single 670G launch means one PMA submission and no hassle of upgrading early 640G adopters; and the marketing will be far stronger for a hybrid closed loop. Still, getting the 670G approved and launched by April 2017 means less than one year at FDA - possible but not a certainty, given a new sensor (Enlite 3) and the first commercial product to increase insulin delivery based on CGM values. Otherwise, the pipeline slide showed two other major timelines of note: launches of Guardian Connect with

Enlite 3 (US) and iPro 3 (EU) by April 31, 2017 (FY17). We assume the former is Medtronic's own standalone, Bluetooth-enabled CGM (first demoed at Health 2.0 in September 2014), a key answer to Dexcom's G5 mobile. Outside of the pipeline, Mr. Ishrak reiterated the company's plans to expand into type 2 diabetes ("we're committed"), while a company-wide partnership slide showed the slew of diabetes collaborations. More details below!

- **Mr. Ishrak stated that the 670G will "come out a little earlier than we've talked about before," and his optimism was crystal clear:** "we are really excited about the early results" and "really excited about the prospects." The important pipeline slide (below) had 39 company-wide pipeline products listed over the next few years, though only five were called out - the 670G was one of them. That's a serious vote of confidence in the product, given that the diabetes division accounts for just ~6% of company sales. We'd note that the timeline is actually the same as shared at JPM 2015 ("FY17"), though perhaps the study and talks with FDA are progressing faster than expected.



- **The strategic decision to leapfrog the 640G and launch the 670G is sensible, all things considered.** Assuming the products are running on similar expected launch timelines, the 670G provides more functionality (hypoglycemia AND hyperglycemia minimization), will bring stronger marketing than the 640G ("closed loop!"), and will presumably cut down the PMA submissions from two to one. Medtronic is ahead of anyone else planning to launch an automated insulin delivery device (see our latest competitive landscape), meaning the company will likely be first to market with either predictive suspend or hybrid closed loop. The one area of risk is the 670G might have a longer timeline at FDA than the 640G (it shuts off AND delivers insulin vs. just shutting off), though the device division has shown a serious willingness to approve groundbreaking products quickly (e.g., Dexcom G5 approved in six months). At DTM 2015, we learned that the FDA granted 670G pivotal study participants continued access and use of the device, a positive sign for the eventual PMA review. The 670G is pretty customizable, so those who only want to use predictive suspend can set it up to do so.

- **Guardian Connect with Enlite 3: the FY17 launch timeline (by April 31, 2017) is the first we've ever heard.** The Bluetooth-enabled, standalone CGM device was demonstrated as "Guardian Mobile" in September 2014 at the Health 2.0 conference. The pivotal study was completed in August 2015, so we've been waiting for any updates on a submission or launch; the product was not mentioned in Medtronic's December call. We see this as an answer to Dexcom's standalone G5 and a bigger foray into MDI, as Medtronic's real-time CGM requires a paired pump.
- **The pipeline slide brought the first ever mention of iPro 3 (EU), also expected to launch by April 31, 2017.** We're not sure what this professional CGM product adds, but assume it includes improved accuracy, better provider analytics, fewer necessary calibrations, longer wear time, or perhaps a different on-body form factor (e.g., more like FreeStyle Libre Pro).
- **"In diabetes, we're looking at the broader market opportunity. We're committed to moving towards type 2 while maintaining our presence in type 1."** This statement came on a slide showing Medtronic's different business units, which in diabetes include intensive insulin management (type 1), non-intensive diabetes therapies (type 2 and prediabetes), and service and solutions. The past two quarterly calls have given the first breakouts for these divisions, with non-intensive diabetes therapies (type 2 and prediabetes) growing the fastest (60-100%, though from the lowest base).
    - **Medtronic asks three questions for every business segment:** Is there a line of sight to improving outcomes? What value does Medtronic add? Is Medtronic positioned to win?
- **A company-wide partnership slide showed the slew of diabetes collaborations that have come about in the past year**: BD (infusion set launching around March-April), DreaMed Diabetes (closed-loop beyond 670G), Glooko (data integration launching in 1H16), Diabeter (generating revenue), and IBM Watson Health (hypoglycemia prediction app launching this summer). There was no commentary on any of them, though we appreciated hearing the three Medtronic metrics for any partnership or acquisition: minimal to no dilution to net earnings per share, clear financial proposition, and mid-teens risk-adjusted return hurdle.
- **Medtronic also announced a partnership with the Chengdu government today to locally manufacture and launch its next-gen insulin pumps (e.g., 640G, 670G) in China.** Medtronic will partner with the Chengdu government to enable people with diabetes in Chengdu and the broader Sichuan province to access the new, locally produced technology with software displayed in Chinese language. The manufacturing facility is the second Medtronic plant announced in Chengdu over the past 18 months - the first for portable hemodialysis equipment was announced in August 2014. We're glad to see public private partnerships of this nature and hope it can expand access to historically expensive diabetes technology.
- **We were very impressed by the team** - we got to meet with Laura Stoltenberg who runs the type 2 business along with Alejandro Galindo who runs intensive diabetes management and were impressed with their ambition.

Questions and Answers

Q: In diabetes you mentioned the 670G; can you say more about that?

A: In the past, we've showed the 640G in that timeframe. The 640G is the same product in Europe, where insulin delivery is managed based on trending of glucose levels - the difference is it shuts off insulin, but doesn't deliver it. The 670G is a fully closed loop system that can deliver insulin too. The early results are very encouraging, and we're working with the FDA on zeroing in the trial process and approval process. This is close enough that perhaps instead of launching the 640G, we'll focus resources on the 670G, which would come instead of the 640G. Or we may do it together; we haven't fully decided yet. The 670G time frame is similar to the 640G right now.

INTARCIA

Kurt Graves (CEO, Intarcia, Boston, MA)

In a compelling and well-received presentation built (like last year's) around the theme of disruptive innovation, Intarcia CEO Mr. Kurt Graves shared that the FREEDOM-CVO trial for ITCA 650 (implantable exenatide mini-pump) reached its required number of events late last year and will report results in 2Q16. While this is substantially earlier than the expected completion date of July 2018 listed on ClinicalTrials.gov, Mr. Graves described it as a "stretch target" but one the company had hoped to meet. The trial began in March 2013 and aimed to enroll 4,000 patients with a history of CVD. We imagine that this trial is one of the more likely GLP-1 agonist CVOTs to demonstrate cardioprotection given the inherent adherence advantage with ITCA-650, though the usual limitations of a high-risk population and a relatively short duration still apply and as the company has emphasized, the trial was not designed to show cardioprotection.

- **Mr. Graves also provided some insights into Intarcia's expected marketing strategy for ITCA 650.** Much of his presentation emphasized the need for a truly disruptive innovation that can reverse the trends in type 2 diabetes prevalence and non-adherence that have not budged for over a decade. He confirmed that the company plans to position ITCA 650 very early in the type 2 diabetes treatment algorithm, helped by a price comparable to that of oral drugs. Intarcia will initially target 25,000 early adopters who represent 80% of the volume for most type 2 diabetes launches, which Mr. Graves stated would require a sales force of only 500 reps. The company is also deliberately appealing to payers from the outset, both with its price point and a set of head-to-head studies against several major type 2 diabetes drug classes. Upcoming studies in addition to FREEDOM-1 vs. placebo and FREEDOM-2 vs. Merck's Januvia (sitagliptin) include trials against an SGLT-2 inhibitor and a sulfonylurea slated to begin this year and a real-world study against Novo Nordisk's Victoza (liraglutide) post-approval.
- **We also learned that Intarcia's collaboration with Numab will involve an antibody-based SGLT-2 inhibitor.** The collaboration, announced last March, is aimed at developing new antibody-based therapies for diabetes, obesity, and autoimmune diseases, but specific targets had not previously been disclosed. In this presentation, Mr. Graves shared that the companies are developing an antibody fragment approach to SGLT-2, which they hope to combine with ITCA 650. He described such a combination as potentially "completely revolutionary" given the drugs' synergistic mechanisms and high potential for cardioprotection. Mr. Graves also confirmed that the most advanced candidate from Intarcia's acquisition of Phoundry Pharmaceuticals could enter clinical trials in 2017. Targets encompassed by that program include glucagon and a next-generation amylin, and Mr. Graves reiterated that the (ambitious) goal is to develop a new therapy for diabetes that can produce 15-20% weight loss.

J&J - ANIMAS/LIFESCAN

J&J announced this morning that it has received FDA approval for the pediatric indication of the Animas Vibe integrated with Dexcom G4; the approval goes down to age two, the youngest available for a sensor-augmented pump in the US. The excellent news bodes well for J&J as it looks to stay ahead of the other two most recently launched sensor-integrated pumps in the US: Medtronic's MiniMed 530G (16 years and older) and the Tandem t:slim G4 (12 years and older). This is a competitive advantage for J&J and a great new option for young patients - less hassle to get on CGM! - though there are lots of factors for parents and young patients to weigh (see the pros and cons below). It was certainly clear during today's breakout session, however, that internal optimism is high. We heard both CEO Mr. Alex Gorsky and Group Worldwide Chairman Ms. Sandi Peterson (who oversees J&J's Diabetes Solutions business) allude to the approval, and there seems to be real belief that Vibe's success can help right some of the business's financial challenges. Disappointingly, management did not comment on the closed-loop (termed a priority at AACE 2015) or plans to launch the Calibra Finesse bolus-only insulin delivery patch device this year. Ms. Peterson did allude to confidence in the future of the BGM business - we were a bit surprised by this characterization

given the segment's recent performance - and we dive into our thoughts on that and more in our detailed write-up below.

- **The lower age indication for the Vibe expands the potential market size, but also brings lots of tradeoffs and tough choices for patients (not a bad thing!).** Most important for parents and young patients, the Animas Vibe forces a choice between standalone G5 CGM with remote monitoring vs. the convenience of the G4-integrated Vibe. On the user interface front, the t:slim G4 interface is a stronger option than the Vibe for Dexcom users, something younger patients might particularly appreciate. On the other hand, the Vibe is waterproof, a feature neither the t:slim G4 nor MiniMed 530G can boast. Tandem expects to further reduce its age indication to six or seven years old in 2016, bringing a more competitive offering vs. the Vibe. As a reminder, neither the Vibe nor t:slim G4 have Dexcom's latest Software 505 algorithm (G4AP). Both companies are presumably working on G5 integration, though no specific timing has ever been announced.
- **J&J was silent on its Calibra Finesse bolus-only insulin delivery patch device; guidance in 2Q15 called for a Finesse launch in 2016, and we hope that has not changed.** Notably, J&J is recruiting for a 24-week clinical trial (n=312) of the device that will randomize type 2 diabetes patients not achieving glycemic targets (A1c 7.5-10%) to either Finesse or the Novo Nordisk FlexPen to initiate bolus insulin therapy. The primary endpoint is A1c at 24 weeks, with secondary endpoints that include time-in-range (YES!) and treatment satisfaction. Primary completion is slated for December 2016.
- **Management also did not comment on J&J's artificial pancreas project, which has moved at a glacial pace since signing its partnership with JDRF in 2010.** The company has said it is working on it, though at what pace and how it will compare to Medtronic MiniMed 670G and others is a big question.
- **Other relevant commentary included remarks on pricing pressure in the BGM business though management remains "very confident in the future."** It was encouraging to hear the commitment to the challenging BGM area, though the pricing pressures don't seem to be going anywhere - can J&J innovate its way to better sales? If so, what will carry the business going forward? We did find it a bit disconcerting to hear Ms. Peterson allude to "lapping" pricing pressures that have hampered the business to date. It's true that competitive bidding has anniversaried (it began July 2013), though at the same time, the business has seen nearly three straight years of YOY declines in the US (11 of the past 14 quarters).

MERCK BREAKOUT SESSION

Questions and Answers

Q: With the recent SGLT-2 cardiovascular outcomes data, what are your thoughts about Januvia and its growth prospects?

A: If you look at Januvia, it has continued to have strong growth throughout 2015 and into 2016. If you look at all the prescription data, Januvia continues to do well. Now there have been some share changes within the SGLT-2 inhibitor class. But we have not seen an impact on the DPP-4 inhibitor class. This is true for the US and also outside the US. As we start to think about the future, we believe Januvia's safety and efficacy profile and physicians' comfort with it will help maintain use of the product. If over time, guidelines and labels change, we'll monitor. But it's also important to remember that we have an SGLT-2 inhibitor in development and we're thinking about combining it. Since the average patient is taking 2.4 medications, a combination with an SGLT-2 inhibitor and Januvia would be the best and obvious choice. And we'll see how more CVOT results of SGLT-2 inhibitors go.

NOVARTIS BREAKOUT SESSION

Questions and Answers

Q: From your presentation, it sounds like with Alcon, you are not planning on selling any part of it?

A: Alcon is a good business because of basic trends. If you look at the current healthcare environment, it's good and the leading position looks good. We need to jumpstart innovation so you'll see a plan unveiled on January 27 and that'll show that this is our plan for a best shot at turning the business. We believe we can do that. It deserves a shot and we think we can turn it and make it a business.

Q: Regarding Alcon, are we seeing a lengthening of cycle from an innovation standpoint?

A: I think it's important to remember that Alcon is two business. They're two very different businesses: devices and pharma. One of the insights that we've pulled from our analysis is that these are two very different models. To be successful in pharma innovation, it requires a different investment, skillset, and different elements compared to medical devices such as contact lenses and the surgical business. The latter can be much more rapid in innovation. There are R&D people in operating rooms with surgeons. It's about identifying incremental changes to the equipment and the product that can improve outcomes for the surgeon. It's a very different process and what you're going to see is recognition of that in the plan.

Keynote

PANEL DISCUSSION

Panelists - Dr. Susan Desmond-Hellmann (CEO, Bill & Melinda Gates Foundation); Alex Gorsky (CEO, J&J); Jamie Dimon (CEO, JP Morgan); Moderator - Maria Bartiromo (Anchor, Fox News)

A lunchtime panel discussion featured the impressive Dr. Susan Desmond-Hellmann (CEO, Bill & Melinda Gates Foundation), J&J CEO Alex Gorsky, JP Morgan CEO Jamie Dimon, and Fox News anchor Maria Bartiromo. The wide-ranging discussion touched on cost pressures, scientific innovation, the role of philanthropy, and more. We were particularly impressed with Dr. Desmond-Hellman, who emphasized profound tension she lives in each day: bringing cutting-edge science to those who need it most around the world. Her remarks reinforced the value of public-private partnerships in overcoming market failures - areas of high need where there simply isn't enough investment. Her comments on polio were particularly striking - with the help of vaccine makers, the Gates Foundation has practically eliminated polio globally. We continue to wonder where such partnerships can move the needle in diabetes. What are the most important trials or pilots that could be funded with philanthropic dollars? Otherwise, cost was a major focus of remarks, headlined by Alex Gorsky's remark on disparities in spending: "In China right now, the average healthcare spend is $400 per person. In the US, it's $8,000-$9,000. What's the right amount?" See our favorite quotes from this lunchtime discussion below.

- **"The most profound thing that strikes me is the quality of the science - the ability to benefit patients is better now than it has ever been. But I live in tension in profound ways every day with the Gates Foundation.** How do we take great science and innovation and help people be healthier? The deal making is very exciting, but we want to bring deals that bring that science to the people who need it the most. We're excited to be part of this ecosystem. You can see the kinds of deals we make, like this morning with Lodo Therapeutics. They are looking at microbes in mud and whether we can find new antibiotics. The world needs new antibiotics, and we can use our capital to drive deals from market failures. The more this is a healthy, science driven industry, the better." - *Dr. Susan Desmond-Hellmann*
- **"In China right now, the average healthcare spend is $400 per person. In the US, it's $8,000-$9,000.** What's the right answer? It's probably not $400, but it's also not $9,000. We as an industry have to change the models. Over the next few years, it needs to become outcomes-based, episode of care based." - *Alex Gorsky*
- **"It's remarkable that as we get better phones and tablets, the price comes down. In healthcare, almost uniquely, as we innovate the price goes up. What does it look like to innovate in a world of cost constraints?** That isn't the environment in the US. Increasingly as patients pay for their own healthcare, there will be more burden on families and consumers. It will become part of the next product profile." - *Dr. Susan Desmond-Hellmann*

- **"We all want the same thing: a healthy world. Knowing that, but also knowing the pressures for shareholders, there are opportunity costs. [At the Gates Foundation], we want to use our capital to cover the risk.** Two tools have worked really well. Tiered pricing has been great for issues like HIV - it works for something that affects both the rich and poor parts of the world. The other tool, volume guarantees, works when there is a large market for things like vaccines. We can guarantee a pharma company will sell 2 million doses with our capital. Where we really struggle, and where there is a tough market failure, is for things like Ebola. Nearly two years ago, when Ebola hit, it was not a rich world disease, and there were less than 2,000 cases. We didn't have tool for that kind of market failure. Now we looking with colleagues to understand how can we be more ready next time." - *Dr. Susan Desmond-Hellmann*
- **"Polio is a disease of poverty - we cannot reach kids with two very effective vaccines. This year, Nigeria, went an entire year free of polio.** That is an enormous accomplishment. [Applause]" - *Dr. Susan Desmond-Hellmann*
- **"I have three metrics on my plate that will make this a great year. One is wiping polio off the globe. We're down to two countries - Pakistan and Afghanistan.** The second is to decrease again by half mortality in kids under five. Lots of companies are at this meeting, and we need great companies helping make affordable vaccines. The third is education - we have to increase the proportion of American high school students that are job or college ready. Those are my top three." - *Dr. Susan Desmond-Hellmann*
- **"If we look at the macro issues, we're living longer. The challenging thing is that costs more.** The older you get, the consumption of healthcare increases by almost a factor of five. It's daunting. How are we going to deal with that as a society? - *Alex Gorsky*
- **"This conference started in 1983: there were 20 companies presenting to 100 people. The combined market cap was $3 billion. Today there are 500 companies presenting to 10,000 people. The combined market cap is over $5 trillion.** I've come every single year, and every year there are more and more people, more and more technology, more equipment, more pharma, huge innovation, and huge growth. The industry will be twice as big 10 years from now, and it will be very vibrant." - *Jamie Dimon*

-- by Melissa An, Adam Brown, Helen Gao, Varun Iyengar, Emily Regier, Ava Runge, and Kelly Close