Executive Highlights

This sub-section of the report contains our coverage of the ATTD 2013 Exhibit Hall. Our themes are below, followed by our coverage of company booths from Abbott, Animas, CeQur, Debiotech, Dexcom, Diasend, Medtronic, Roche, Sanofi Diabetes, and Ypsomed.

- **ATTD's exhibit hall was replete with new product displays and timeline updates.** Medtronic's booth was front and center in the hall and a definite highlight. We saw three new products for the first time in person: an integrated CGM sensor/insulin infusion set, the recently CE Marked Sentrino critical care CGM, and a mobile hub that wirelessly sends pump and sensor data to CareLink and smartphone apps ("Connected Care"). Meanwhile at the CeQur booth, sales representatives shared timeline details on the company's PaQ insulin delivery device for people with type 2 diabetes (EU launch in 2013-2014, preparing a 510(k) submission for US regulatory clearance). Updates abounded at other companies as well: Dexcom's booth emphasized the G4 Platinum's newly approved pediatric indication in the EU (US approval pending); Abbott had its updated FreeStyle Navigator II handheld on display, the first time we'd ever seen the new receiver in person (in contrast to the absence of a booth and no specifics on the device at EASD in October); Roche sales representatives indicated that the company is planning to submit the Aviva Expert blood glucose monitor with built in bolus advisor to the FDA this year (already available in the EU); Debiotech intends to outlicense its Jewel Pump after regulatory clearance; and Diasend is launching a mobile app later this year.
- **As much as the exhibit hall made us excited for the years ahead, so too did it remind us of the contrast in US and EU regulatory processes.** The discrepancy has led to companies employing a step-wise device submission strategy, whereby EU submission often occurs before US submission. We remain curious whether discussions about the safety-related shortcomings of the CE Mark process will translate into changes in the near-term, what those changes will look like, and whether they would have tangible effects on diabetes device submissions and approvals - would approvals take longer? Would they be less likely to occur? Would companies be more likely to submit in the US first? Would submission in the US become harder as gathering real-world data ex-US also becomes harder? Would independent safety and accuracy evaluations be required? Would changes in the EU motivate broader international changes? Especially in light of the EASD's recent statement urging an overhaul of the CE Mark system (see our *Closer Look* email at http://www.closeconcerns.com/knowledgebase/r/2184fbc3), these questions are at the front of our minds.

Exhibit Hall Report

- **Abbott**: Bright yellow arches adorned with orange butterflies drew the boundary of Abbott's exhibit hall booth, and one couldn't help but envision a sunny Sunday afternoon. Complementing the butterflies above, vases of orange and yellow flowers stood topped four white stands beneath the arches. Each stand displayed one of Abbott's blood glucose meter offerings (FreeStyle InsuLinx, FreeStyle Precision, FreeStyle Freedom Lite, and FreeStyle Lite). While no sales representative manned the booth when we made our visit, Abbott's exhibit seemed to have three focuses. Large digital displays drew attention to the FreeStyle Navigator II continuous glucose monitor, about which we've heard a lot of good things, Ambulatory Glucose Profile (AGP) analysis system, and FreeStyle InsuLinx insulin bolus calculator.

- **FreeStyle Navigator II**: Abbott's display emphasized the "security" provided by the early-warning alarm system of the Navigator II and its small transmitter with extended range (30 meters, according to the display). The Navigator II receiver looked quite sleek in silver and black and bore a rough resemblance in form to a blackberry phone (though this was difficult to discern from a picture-only display). It was exciting to see the CGM front and center at the booth after its low-key launch just prior to the European Association for the Study of Diabetes (EASD) conference and notable absence from the EASD booth. We wonder, of course, whether Abbott has any intentions to pursue FDA clearance - the company already has a third-generation CGM slated for EU entrance by year-end 2014. For background, the company's pivotal trial of the Navigator II showed 97.7% of readings in the Clark Error Grid A- and B-Zones (83% and 14.7%, respectively). For more details on the study, please see our Abbott 3Q12 report at http://www.closeconcerns.com/knowledgebase/r/54fc41b3.
- **AGP**: Abbott positioned AGP as the diabetes ECG and the means to which data could become actionable. Abbott's corporate symposium on the topic dives into this topic in greater detail (see above).
- **FreeStyle InsuLinx**: Abbott advertised that the meter's dose calculator could help alleviate the challenges associated with manual insulin dose calculations ("In a study, 63% of insulin calculations done manually were incorrect," read the sign. "With FreeStyle InsuLinx there were 10x fewer errors.") As a reminder, the built-in bolus calculator is only available in the EU and no timeline or intention for FDA submission has been disclosed. We suspect that the FDA harbors concern for dose calculators that depend on patients correctly inputting their insulin data; though, there are certainly patients who could benefit from this feature.

- **Animas**: "Hello. We're Animas," read the blue sign at the top of the company's exhibit booth. "Meet CGM-enabled Animas Vibe." The display's blue, green, and white color scheme inspired an aquatic feel that spoke to the waterproof quality of the Vibe - two pumps were submerged completely in vertical water cylinders. The sales representative present explained that this characteristic is especially good for small children or those times when you sit down on the toilet and your pump falls out. The representative explained that the high-contrast color screen, intuitive design, and CGM were patients' three favorite features of system. Interestingly, she explained that where CGM reimbursement is poor or lacking (she pointed to Germany as an example), the company will market the Vibe for its pump-specific benefits, as many patients may not be willing to pay out-of-pocket for the CGM. Indeed, during Dr. Joroen Hermanides' afternoon talk, he showed just how challenging the CGM reimbursement environment in Europe is (see above).
- **CeQur:** The CeQur booth was small in size but grand in excitement, as many visitors (including us!) got their first hands-on experience with the company's PaQ insulin delivery device for people with type 2 diabetes, which received CE Mark in November 2012 (see our report at http://www.closeconcerns.com/knowledgebase/r/a314eba7). The booth's handouts included two ATTD abstracts about PaQ, one of which highlights patient satisfaction scores from CeQur's feasibility study. (Of 20 patients with type 2 diabetes in the six-week trial, 83% were "very satisfied" and 17% were "satisfied" with PaQ). Additional data from the study, including glycemic efficacy and patient-reported outcomes, will be presented at ATTD 2013. Meanwhile management continues to raise Series B funding, scale up manufacturing in anticipation of a "focused" European launch in 2013 or 2014, and prepare a 510(k) submission for US regulatory clearance. The company is targeting a large-scale launch for 2015, when it would debut a new version of the PaQ (optimized for large-scale manufacturability). As for pricing, we understand that CeQur intends the PaQ to be competitive with pens and cheaper than traditional pumps. Management mentioned that they are closely watching Valeritas, whose already-marketed V-Go delivery device is PaQ's most similar competitor. (Notable differences include the V-Go's one-day wear time vs. PaQ's three days, as well

as the absence of electronics in the V-Go). Management would not comment on partnership talks but said that they remain "fully prepared to go solo."

- **As a reminder, the PaQ (pronounced "pack") holds a reservoir of 330 usable units and is designed for three days of use.** It will be available in seven different versions, each with a different pre-set basal rate (16, 20, 24, 32, 40, 50, or 60 units per day); every version will also allow bolus dosing with the push of a button. The round, white device is roughly the length and width of a business card and roughly the thickness of a smartphone (we left our tape measurer stateside!). It has two components that fit together along an S-shaped intersection. The bigger, disposable piece contains the reservoir (an elastomeric bladder), the cannula, a window to indicate visually whether the cannula has successfully been inserted, and a button for bolus dosage. A smaller, reusable part sits atop the disposable piece. This reusable part contains the PaQ's only electronics and features a button that patients can press for an audible indication of how much longer their insulin supply will last. (A "happy tone" plays for the first 48 hours of reservoir use; one vibration indicates that between six and 24 hours are left; three vibrations occur during the last six hours; four vibrations indicate an empty reservoir.) The battery for this electronic messenger lasts roughly six-to-12 months.
- **Only one button must be pressed to deliver insulin; to prevent unintentional dosing this button is indented into the curvature on the lower side of the PaQ and counterweighted so that a firm press is needed.** The button's click is barely audible, but CeQur's engineers designed the button to give very clear tactile feedback when a bolus is delivered.
- **We learned that CeQur's name is an acronym:** the Ce stands for CE Mark (gained in November), the Q stands for quality, and the ur stands for "user requirements" (specifically, the user requirements for a simplified insulin delivery device in type 2 diabetes). CeQur lists these user requirements as follows: simple, effective, comfortable & discreet, freedom from daily injections.
- **The CeQur booth featured pictures of three elderly, heavy people, each smiling and holding PaQ -** real patients from the device's feasibility study who were also featured in a video that played continuously on a TV screen. Though this is only a superficial indication, we certainly liked that the company featured the images and experiences of real people with diabetes rather than models or actors. The booth was mostly white, with CeQur written in dark blue, PaQ written in violet, and a column of text that consisted of the word "freedom" written in multiple different languages. Blue, purple, and white M&Ms were available for booth visitors seeking glycemic excursions, and most excitingly - as noted above - the PaQ and its user guide were on hand for close inspection.

- **Debiotech:** In a prominently located booth as large as any in the exhibit hall, Debiotech reps showcased their company's Jewel patch pump. The specifications of the 500-unit semi-disposable device and its accompanying handheld, a custom-designed Android smartphone with an integrated blood glucose meter, remain largely unchanged - and still quite impressive - since our EASD 2012 exhibit hall report (see http://www.closeconcerns.com/knowledgebase/r/208ca0cc). However, we did hear some updates on the company's business plan. Debiotech's main goals are to gain CE mark and 510(k) clearance and to license the Jewel Pump to a large partner that could bring the technology to market. (No timelines for these events have been announced externally.) The license agreement would also include access to the closed-loop algorithm developed by Debiotech and studied by a consortium of seven French endocrinologists using the Jewel pump and a Dexcom CGM sensor. (We understand that data from these "Diabeloop" experiments will be published soon.) Buzz also surrounded a recently completed study with 35 patients; the company has characterized the results as successful but is waiting to release results (we hope at ADA or sooner).

    - **Debiotech recently finished lining up all the partners necessary to manufacture Jewel pumps on a large scale.** In the week prior to ATTD, Debiotech announced that its fellow Switzerland-based company Valtronic will manufacture the electronics in the patch pump's controller unit, which is designed to last for roughly two years. Longtime partner ST Microelectronics will provide the microfluidics for the pump's disposable unit. Other confirmed partners include companies that will make the disposable unit's cannula, produce the phone's glucose meter and its strips, and create the "Jewel Card" that is placed in each phone to enable secure communication with a single unique patch pump. Management noted that as part of the clearance and regulatory process before they ultimately out-license the Jewel Pump, they will perform clinical studies in France and the US.

- **Dexcom:** From across the exhibit hall, we couldn't miss the four young children gracing a billboard on the back of Dexcom's booth - the sparkling, and quite compelling (lots of people stopped to say so including typically hard-to-impress US diabetes advocates) new ad announced the very recent CE Mark of the G4 Platinum in children as young as two years old (previously, it was >18 years). A brochure displayed the clinical accuracy results comparing the G4 Platinum accuracy in adults and pediatrics; results were largely similar, with an overall MARD (40-400 mg/dl) of 13% in adults, rising slightly to 15% in pediatrics. Hypoglycemia accuracy (MARD 40- 80 mg/dl) was also a tad better in adults at 19%, compared to 23% for pediatrics. A-Zone accuracy reflected these small differences (80% in adults, 76% in pediatrics). Sensor life was the most noticeable metric that declined in pediatrics, with 81% of sensors lasting up to seven days vs. 94% in adults. We think many factors make pediatrics a tougher population for sensor accuracy, so these fairly comparable results are a testament to the G4 Platinum's strong innovation. A brochure noted that the G4 Platinum is only approved for use on the abdomen in adults, while pediatrics can use the abdomen or the upper buttocks. As a reminder, Dexcom has submitted the PMA supplement to the FDA for a pediatric indication, and approval is expected in 2H13. Elsewhere in the booth, a concise eight-page handout succinctly summarized Dexcom's new Studio software, with the tagline, "Help take the guesswork out of glucose pattern management." Arrows and directions in the handout did a good job of highlighting what different things mean and how to interpret them, especially the new pattern recognition feature on the Portrait report. On the international front, a sign in the back of the booth displayed Dexcom's geographic spread- we certainly took note of "Coming Soon" captions for India, Saudi Arabia, Canada, andSlovenia. On our way out, we were surprised not to see any signage for the Animas Vibe; according to the representative we talked to, this is Animas' product, so Dexcom is only supplying sensors.
- **Diasend:** In its ongoing quest to create a total system for diabetes management, Diasend had good news to report and is expecting more on the way. As a reminder, the company's products include a multi-cabled box for downloading of multiple different devices in diabetes clinics, as well as a web-based software for patients to transmit data from home. We were told that the latest list of compatible devices, which includes dozens of glucose meters and most pumps besides Medtronic's, now includes the two newest CGM systems - Abbott's FreeStyle Navigator II and Dexcom's G4 - as well as the "intelligent" insulin pen Pendiq. (A Diasend rep lamented that, despite the clinical demand, insulin pens with memory do not seem to be a big development priority among the major insulin manufacturers - we share this lament.) The company is also expanding its integration into electronic medical records (especially in US clinics) and its overall presence worldwide (roughly 2,000 clinics in 16 countries use Diasend's boxes, all of which can be wirelessly updated whenever the company changes its software or becomes compatible with a new device). Perhaps most excitingly to us, Diasend plans to launch a mobile app later in 2013 - one more step toward a future world where healthcare are stored primarily in the cloud and accessed largely through handheld devices.
- **Medtronic:** Medtronic's spacious booth was one of the biggest headlines in the exhibit hall, showcasing three products we had never before seen in person: an integrated CGM sensor/insulin

infusion set, a mobile hub that wirelessly sends pump and sensor data to CareLink and smartphone apps ("Connected Care"), and the recently CE Marked Sentrino critical care CGM. A video playing on the side of the booth also displayed the future improvements for the Enlite sensor (we presume this is the next-gen Enlite referred to in Medtronic's pipeline) and the company's closed-loop research system. Details on each are below.

- **"The world's first integrated sensor and infusion set":** We saw a poster on Medtronic's Combo-set at ADA 2012 in Berlin, though this was the first time we had ever seen it in person. It incorporates an insulin infusion catheter and a CGM sensor separated by a short distance (i.e., two skin punctures under a single adhesive patch). The set uses a single insertion device that is similar in look and feel to the Enlite inserter. From a top view of the integrated set, it looks like a Mio infusion set fused with the clamshell-shaped Guardian/Enlite transmitter. A video advertised a "small footprint" and "improved comfort, convenience, and patient acceptance." The Medtronic rep showed us the set behind a glass case and let us handle the inserter, despite a small label on the bottom of the case noting that it is "non CE-marked." According to the rep, the combined set is beginning early trials now.
    - **As a reminder from our Medtronic F3Q13 report, the company plans to begin a 50-patient study in March of the integrated sensor and infusion set** (ClinicalTrials.gov Identifier: NCT01775059). Each subject will wear five sets for three days each, and completion is slated for July 2013. While we do think the convenience of an integrated set will be appreciated by many patients, a key challenge in our view is matching disparate lengths of wear - a three-day integrated set would require a CGM sensor with a fast startup and good accuracy for the first 72 hours, an R&D barrier to date (i.e., sensors typically get more accurate over time, with the worst accuracy on day one). Our Medtronic F3Q13 report is at http://www.closeconcerns.com/knowledgebase/r/b5a0fd92.
- **"Connected Care"** is a mobile hub that wirelessly and automatically sends insulin pump and sensor data to CareLink Personal and a smartphone app (the booth had an iPhone). The hub itself is a bit larger than a hockey puck, though the rep assured us that it was a prototype and the final commercial product will be smaller. As we understand it, the device's battery is rechargeable and the hub would not have to be plugged into a wall (i.e., it could be carried in a backpack and pump/CGM data would be wirelessly sent to CareLink). We did not confirm whether the device operates on a cellphone or Wi-Fi - based on the symbol on the outside of the device, we assume it sends data over Wi-Fi. The smartphone app itself displayed a standard CGM screen: a large sensor glucose value, a trend arrow, trend graphs (three, six, 12, and 24-hours), and a red bar with details on a hypoglycemia alarm. The system seems to make good use of alerts, as "care partners [are] alerted to glucose highs or lows" on their cell phones. A poster displayed a woman on her cellphone and a caption stating, "Message from CareLink about Gary: LOW SG 65 mg/dl at 13:18 30-July 2012." The device is currently in two early trials in the EU, so it also displayed the "non-CE Marked" label. It was developed in partnership with eDevice (http://www.edevice.com). We're glad to see Medtronic improving on its mySentry system - though that device was certainly an excellent foray into the nascent remote monitoring space, we believe pump/CGM data wirelessly and automatically sent to smartphones is the way of the future (certainly, that's where Dexcom is going with its new Share product and Gen 5).
- **Sentrino critical care CGM:** Freshly CE Marked in December 2012, Medtronic had its new in-hospital CGM on display. We got to play with the device's bedside monitor, and liked the touchscreen interface and color alerts. The screen readability was quite good, though the alarms did not strike us as particularly loud. The rep gave no details beyond those in our initial Closer Look - as a reminder, the Sentrino was launched in the UK and

Germany following CE Marking (no reimbursement yet, though Medtronic is pursuing studies). The device incorporates redundant sensing (two novel subcutaneous sensors, not Enlite nor Sof-Sensor), a wired cable, and a bedside monitor. (EHR integration could come down the road, but is not supported in this version.) Medtronic is working with the FDA to support US commercialization, though there is no timeline yet. Patients can wear the Sentrino for up to 72 hours before the sensors need to be replaced. It is accurate within 10-15% of reference glucose and is approved for adjunctive use. The device is calibrated using the hospital's standard of care blood glucose measurement. Warm-up time is 30 minutes (pretty fast!) and a blood glucose calibration is required upon insertion, at one hour, two hours, eight hours, and then every eight hours thereafter. One hundred patients were studied prior to CE Mark submission, and 50 of them were critically ill patients. We look forward to understanding how hospitals like using the device, whether they feel it improves outcomes, and ultimately, whether it is cost-effective technology. For more on Sentrino, see our report on the CE Mark at http://www.closeconcerns.com/knowledgebase/r/9ac84bcc.

- **Next-gen Enlite:** A TV screen played a video cycling through Medtronic's various pipeline initiatives, including improvements in the Enlite sensor. Future Enlite improvements include: 1) an 80% size reduction from the current sensor; 2) a new electrode design; and 3) removed tubing. NO further details were given. In Medtronic's pipeline as of the 2011 Analyst Day, a next-gen Enlite launch was slated for May 2014-April 2016.
    - **Closed-Loop Research System:** The same video showcased Medtronic's closed-loop research system, which seems to have one change from the portable glucose control system we've previously seen in conference presentations: what looks like an iPhone controller (the picture seemed to show an iPhone, though the caption vaguely called it a "smartphone"; in the original portable glucose control system we saw at DTM 2011, this was a Blackberry smartphone). As a reminder, the system also includes the MiniMed Veo sensor-augmented pump system, "a translator" (a square one inch by one inch piece of hardware), and a tablet PC for physician monitoring. We've always anticipated that a commercialized closed-loop device from Medtronic would put the algorithm in the pump, alleviating the smartphone and translator.

- **Roche**: The company's exhibit booth touted a pastel pallet of maroon, yellow, blue, and orange. Five standing screen displays, each manned by a sales representative, presented Roche's Accu- Chek products. The DiaPort (intraperitoneal insulin infusion device; available in EU only), Combo (Aviva meter and Spirit insulin pump), Aviva Expert (blood glucose meter with built-in bolus calculator; available in EU only), Accu-Chek Mobile (strip-free glucose meter; available in EU only), and 360 diabetes management system were on display. Roche's "scientific center" was located towards the center of the booth and featured an array of scientific publications, including the results of its Automated Bolus Advisor Control and Usability study (ABACUS), which tested the effect on the Aviva Expert's insulin bolus advisor on glycemic control in patients on MDI. (For previous coverage of the first results from this study, see page 94 of our Diabetes Technology Society Meeting 2012 full report at http://www.closeconcerns.com/knowledgebase/r/c81dc4ef.) The Aviva Expert is currently available in eight countries, and according to the sales representative, seven more country launches and FDA submission are slated for this year. From another sales representative we learned that Roche is also in the process of exploring the US regulatory process for its Accu-Chek Mobile System. Meanwhile, Roche is readying for a small April launch of the second-generation DiaPort in Centers of Excellence in France, Germany, Australia, and the UK. One of the biggest improvements of the second-generation, explained the sales representative, is the polyester felt band that surrounds the flower-shaped plate (the piece inserted under the skin). The felt is designed to reduce irritation with the DiaPort by minimizing movement of the plate. (For additional detail on the technical

improvements of the second- generation DiaPort, see page 67 of our Diabetes Technology Meeting 2012 full report at http://www.closeconcerns.com/knowledgebase/r/c81dc4ef.)

- **Sanofi Diabetes:** Here on its home French soil, Sanofi used the ATTD 2013 exhibit hall to launch a new branding initiative: MyStar Diabetes Care. We understand that the MyStar name will eventually be associated with all of Sanofi's insulin delivery devices (e.g., ClikStar and SoloStar) and glucose meters (e.g., iBGStar and BGStar), as well as decision-support algorithms and all customer service for diabetes patients. (Given that a chief purpose of the MyStar label is to shore up Sanofi Diabetes' worldwide brand identity, the name "MyStar" will apparently be used even in non-English-speaking countries.) In light of Sanofi's eclectic range of diabetes products, we think that the company is smart to try to unify its image - especially with the friendly-looking MyStar logo (which includes the outline of a 5-pointed star, playfully askew and with a single missing line, which the company says is the open star inviting consumers). The MyStar umbrella will eventually cover the company's entire plethora of region- and nation-specific "patient services and solutions" - from patient education programs, call centers, and digital tools; to a recently launched Italian diabetes management software called MyStar Connect, which can integrate glucose data with lab results, comorbidity data, and other health records. We were told that the MyStar family would welcome a few other notable additions in 2013, but we were left to wonderabout the specifics. Sanofi also presented some of its collaborations with diabetes societies and academia, such as the E-Diabetes telemedicine training project for 1,000 physicians in 18 African countries, and the basal-bolus titration software Diabeo, which is being studied with some success in 700 type 1 and type 2 diabetes patients in France (Charpentier et al., Diabetes Care 2011).
- **Ypsomed:** Ypsomed's small booth had a clear focus on the second-generation mylife OmniPod and the compact mylife Unio blood glucose meter. The little pod was getting rave reviews from management and a promotional video emphasized both products' simplicity, discretion, and design with taglines such as "making diabetes a smaller part of life," "simple to use when out and about," "simple and private," and many others. We also saw Ypsomed's ServoPen on display, and a rep emphasized that it's a business-to-business (B2B) product for Ypsomed - despite the company's growing number of business-to-consumer products, B2B still represents the majority of the company's revenues. A glass case and demonstration table also showcased mylife Clickfine pen needles and Roto infusion sets.

-- by Adam Brown, Joseph Shivers, Nathan Nakatsuka, Kira Maker, John Close, and Kelly Close