CLOSER LOOK

American Diabetes Association 76th Scientific Sessions

June 10-14, 2016; New Orleans, LA; Full Report - Exhibit Hall - Draft

Executive Highlights

This document contains our coverage of the exhibit hall and product theaters at ADA 2016. Immediately below, we enclose our high-level thoughts on what was often a bustling hall, followed by detailed coverage of company's booths and product theaters.

The ADA 2016 exhibit hall didn't have quite as much fanfare, attendance, and excitement as it has had in recent years - this has been a consistent theme over the last several years. We took particular note of a couple absentees from the hall - for a start, Roche and all obesity drug companies (aside from Novo Nordisk) - which we assume reflect both the challenging SMBG and obesity environments in the US and perhaps an evolving perception on the return on investment from exhibit hall booths. In the modern era of digital and social media marketing, an argument could be made that the ROI of exhibit hall booths has become harder to measure, at least relatively speaking. Our coverage includes the following companies and organizations: Abbott, Alere, Amgen, Ascensia, AstraZeneca, Becton Dickinson, BI/Lilly, Dexcom, Glooko, GSK, InSpark, Insulet, Intarcia, J&J/Animas, J&J/LifeScan, J&J/Janssen, LabStyle, Lilly, Mannkind, Medtronic, Merck, Novo Nordisk, Novo Nordisk (Saxenda), Sanofi, Sanofi-Regeneron, Takeda, Tandem, Valeant, and Valeritas.

Booths highlighted in yellow were among our favorites from ADA 2016; titles highlighted in blue are new full report additions from our daily coverage.

Table of Contents

J&J/Janssen
Lilly
Lilly/BI
MannKind
Merck
Novo Nordisk
Sanofi
Takeda

Exhibit Hall - Obesity

Novo Nordisk (Saxenda)

Exhibit Hall - PCSK-9 Inhibitors

Amgen
Sanofi-Regeneron

Product Theaters

The Efficacy Mirage in T2D - Why Do Clinical Trial Results Disappear in Clinical Practice (Sponsored by Intarcia) | *Steven Edelman, MD (University of California, San Diego, CA); William Polonsky, PhD, CDE (Behavioral Diabetes Institute, San Diego, CA)*

A Treatment Option for Patients who are Severely Insulin Resistant (Sponsored by Sanofi) | *Timothy Gilbert, MD (Texas Diabetes & Endocrinology, Dallas, TX) and Jeremy Pettus, MD (University of California San Diego, San Diego, CA)*

Options in Basal Insulin: Basaglar (Sponsored by Lilly/BI) | *Tom Blevins, MD (Texas Diabetes & Endocrinology, Austin, TX)*

Toujeo: A Once-daily Basal Insulin (Sponsored by Sanofi) | *Bruce Bode, MD (Atlanta Diabetes Associates, Atlanta, GA), Bill Polonsky, PhD (University of California San Diego, San Diego, CA) Steven Edelman, MD (TCOYD, Del Mar, CA), Debbie Hinnen, APRN, CDE (Touro University California, Vallejo, CA)*

Detailed Discussion and Commentary

Exhibit Hall - Devices

ABBOTT

A rotating, circular sign reading "FreeStyle Libre Pro" and accompanying a picture of the FreeStyle Libre Pro sensor and reader heralded BIG news in Abbott's spacious booth ... and the exhibit did not disappoint with a slew of updates: (i) the US debut of FreeStyle Libre Pro on an Exhibit Hall floor (still under FDA review); (ii) confirmation that the consumer version has not been submitted to FDA; (iii) an updated timeline on LibreLink - multiple EU launches slated for this month; (iv) the debut of Abbott's new LibreView data management software; (v) news that LibreLink will soon sync with LibreView; and (vi) confirmation that the company is working hard on LibreLink Apple compatibility and further discussion about the possibility of an iPhone adapter to power the NFC-reading capability. See details on all the highlights below:

- **Abbott has chosen ADA 2016 to debut its Libre Pro sensor at a US conference for the first time and came out with strong marketing intent.** Among many gizmos and gadgets on hand, the booth featured a touchscreen display complete with videos that introduced attendees to Libre Pro's features, seemingly omnipresent Libre Pro signage, and multiple demo sensors and readers on display. Reps and booth-goers alike shared huge enthusiasm for Libre Pro though the former were very quick to point out that the product remains at FDA with no timeline for approval. As a reminder, the product was most recently slated for a mid-2016 US launch (submitted in 2Q15),

which would mean an approval would have to come soon to meet this timeline. It sounds like there are plans to launch Libre Pro in additional international territories in coming months (it's currently available in India) though reps did not share any further details.

    - **We happened to drop by the Abbott booth at the same time as a noted KOL, who asked an interesting question: Will providers have the option to give the Libre Pro reader to patients unblinded? The answer was a firm "No,"** to which the KOL suggested that the professional version might see better uptake if this functionality was built in. He spoke to his positive experience giving Dexcom G4 CGMs to patients in a professional setting unblinded and the benefit of allowing them to see their data - he spoke in particular to the teachable moments unblinded CGM can create - e.g., connecting the dots between eating ice cream before bed and having a high morning fasting glucose. We, too, would love to see this functionality built in though can understand the counter-argument that the majority patients suitable for professional CGM/Libre might be overwhelmed if they were to go from intermittent BGM to continuous glucose data. We look forward to more discussion on this front.

- **There were no updates on the US timing of the FreeStyle Libre consumer version, and management confirmed today that the system has yet to be submitted to the FDA.** As a reminder, Abbott CEO Miles White said last year that the consumer version could be "optimistically" approved in time for an end of 2016 launch; that seems less likely at this point.
- **On the EU front, we learned an interesting new detail that FreeStyle Libre is available in readers that report in "mg/dl" or "mmol/l."** We had previously thought that only the latter was available. However, depending on the territory, management confirmed that there are Libre readers coded in both units, though individual readers do not allow patients to switch between mg/dl and mmol/l for safety purposes.
- **Reps confirmed that LibreLink has seen a successful launch in Sweden and the Netherlands and remarked that the mobile app would come to other EU countries where FreeStyle Libre is available (Italy, Spain, Germany, France, and the UK) by the "end of the month."** See our coverage from earlier this week. We're not sure if this was simply off-the-cuff commentary - especially given that Abbott said during Thursday's official Sweden/Netherlands launch that only the German launch would come this month - but hints that Abbott is pushing strongly to get this to more patients as quickly as possible.
- **Abbott continues to work "eagerly" on expanding LibreLink to Apple devices though reps reiterated ATTD commentary that the device may require an iPhone adapter to power the NFC-reading capability.** As a reminder, the iPhone franchise (up to and including iPhone 5S) has not had NFC built-in and it sounds like this solution would work for both existing iPhones and the iPhone 6 (that, in fact, does support NFC but - according to the rep - does not have the ability to read data from Libre.) As we understand it, the adapter would be plugged into the headphone jack, would scan data from the sensor, and would then send the data straight to the app. We applaud management for identifying a workaround though it is a less-than-deal solution - requiring an adapter negates the seamlessness and patient convenience of scanning with just a phone alone.
- **Abbott also unveiled its new LibreView cloud-based data management software - this is the first time we've seen the software on display in an exhibit hall.** According to reps, the platform soft-launched in September 2015 but the company is still building up compatibility to support a full launch. The software allows patients to download data from both Abbott and other proprietary BGMs using an appropriate USB cable and can give healthcare professionals access to glucose data. We didn't get the chance to explore the cloud-based software in depth, but it looks like the platform in its current form provides graphical displays with typical glucose trends and statistics - key for staying competitive with Medtronic CareLink and Dexcom Clarity. We did not see AGP graphs on any of the LibreView pictures, but assume this is part of the program.

- **We were told that LibreView will soon sync data from LibreLink,** a logical step to keep FreeStyle Libre competitive on the connectivity and software fronts with Medtronic (Guardian and CareLink) and Dexcom (G5 and Clarity).

ALERE

The Alere booth showcased the company's Afinion AS100 Analyzer, a high-performing, rapid (only three minutes) point-of-care A1c measurement device (it also does albumin-creatinine ratio). The importance of in-clinic, high-speed analysis was underscored by the slogan, "Knowing Now Matters." Coming down the pipeline, the company hopes to see the Afinion AS100 lipid panel testing approved in the US on the heels of last year's European launch. In other pipeline news, the rep did not mention the July 22 FDA Advisory Committee meeting that will discuss and vote on a 510(k) application for Alere's Afinion HbA1c Dx point-of-care test to be used for diagnosing diabetes. If cleared, Afinion would be the first point-of-care A1c test cleared for diabetes diagnosis. ADA guidelines currently specify that only lab A1c tests should be used to diagnose diabetes, which would make this an important marketing claim. This clearance could make it easier and faster to diagnose diabetes and prediabetes right in the clinic, or perhaps other locations like pharmacies. This is critical from our view given the importance of prevention and the ease of use with this test.

ASCENSIA

Ascensia has come to ADA 2016 with a bang! The company's large bold booth at the back of the exhibit hall was decked out in the new purple and blue colorway, and it was refreshing to see a big investment in ADA real estate after the company's absence at ADA 2015. Reps informed us that the transition to a standalone company has really allowed the teams to flourish, citing the company's recently launched Contour Next One and Contour Plus One Bluetooth-connected BGM systems (currently launched in Switzerland and Poland respectively; CE Mark in May 2016). Additional EU launches are planned for later in 2016. The Contour Next One system is still being reviewed by FDA and the company anticipate clearance before the end of 2016.

BD

Reps in BD's booth shared new news that the MiniMed Pro FlowSmart Infusion Set with exclusive partner Medtronic will launch in the US and France "by the end of 2016." This is the most concrete forecast we can recall hearing to date and confirms previously disclosed plans to orchestrate a "limited launch" in 2016. It's great to hear that patients in the US will have access during this soft launch period (we're hoping we'll have the chance to try it out!) but assume that this will be fairly low-key at first. The purpose of the soft launch is to gather feedback from early users to inform the subsequent full-scale rollout. Back to the booth, the infusion set itself was not on display as BD - per usual - focused its exhibit on injection counseling technique. We were sad to see that BD has retired its classic lipohypertrophy demo ("Lipo Larry") but very excited to see what he was replace with - two virtual reality simulations! The demo allowed us to experience an injection technique counseling session as a patient with type 2 diabetes who had just been instructed to go on insulin, with one video documenting common mistakes physicians make and the other documenting best practices. Kudos to BD for bringing this experience to attendees! We've heard the demo has been wildly successful, sharing that multiple providers have asked to have access to the videos in their clinic (to show peers) while one promised to change the way he addressed patients after watching the video - we'd very much hope to hear more of that.

- **Consistent with the injection technique theme, BD's booth also shared data that showed improved clinical outcomes at three months for type 1 and type 2 insulin-treated patients who optimized their injection technique.** Patients (n=346) in this uncontrolled study received intensive education on the value of rotating injection sites and instructions to switch to BD's Ultra-Fine Nano 4 mm x 32 gauge pen needles. Results looked encouraging - patients in the intervention cohort saw: (i) a 0.6% reduction in A1c (baseline not provided; $p<0.05$); (ii) a 14.2 mg/dl reduction in fasting glucose (baseline not provided; $p<0.05$);

(iii) a two units reduction in total daily dose (baseline not provided; p<0.05); and (iv) a 0.5 kg/m2 BMI reduction (baseline not provided; NS).

- **BD has unveiled new branding.** The company has: (i) embraced a "lighter, brighter" look following the acquisition of CareFusion; (ii) updated its logo - see the new look below; and (iii) has updated its slogan from "Helping people live healthy lives" to "Advancing the world of health."

DEXCOM

Dexcom's booth in the center of the hall was flanked around by iPhones showing off G5 mobile in all its glory - including versions in mmol/l for attendees. Reps took us through the new Professional version of Dexcom Clarity, which will launch this summer and has some slight improvements to consolidate multiple patient accounts on one page. Oddly, providers can't track their population of patients and easily identify those with dangerous glucose levels that need prioritization (like Glooko's Population Tracker) - we hope this is added over time, since it makes so much sense and is where digital must take diabetes. Dexcom will also add standard deviation to Clarity this summer, along with a seven-day modal day overlay plot (the infamous CGM spaghetti chart, with each day appearing in a different color). We've heard that providers are asking for the spaghetti chart to be put back into Clarity, a surprise to us since they are so hard to make sense of.

GLOOKO

Glooko had its largest exhibit hall presence at ADA ever, flanked by computers highlighting its next-gen work to optimize insulin dosing: the DreaMed partnership to develop a pump settings advisor (clinical trial starting later this year) and its own Mobile Insulin Dosing System (MIDS) to optimize long-acting insulin for type 2s (studies in 2H16, commercial launch in 2017). Both were first announced at ATTD, though we appreciated another look at MIDS in particular, which allows a clinician to select an insulin plan, and then allows patients to confirm fasting blood glucose values and receive constantly updated insulin doses in the app. Glooko and Medtronic also announced their integration work is complete and will officially launch in July. The user interface for displaying pump and CGM data looks great and adds Glooko's new "Personal Advisor," bringing new pattern recognition features in the patient-facing app (high and low trends by time of day, best day, fun emoji faces, etc.). This integration has been more than a year in the making (Medtronic invested in Glooko last March) and we give HUGE kudos to Glooko (and particularly Holly McGarraugh) for breaking open the Medtronic CareLink data silo. A massive win for diabetes data! Glooko is riding impressive momentum after its partnership with Insulet was announced in January, and management told us it is in more than 1,000 US clinics now. We love seeing all the new work on optimizing insulin dose titration and have very high hopes it will save the system massive costs, save providers time, and help patients more safely dose this very dangerous drug.

- **Glooko's mobile insulin dosing system (MIDS) for type 2 patients on long-acting insulin will help clinicians and patients continuously titrate insulin based on observed glucose readings.** A clinician will select and/or configure insulin-dosing titration instructions, with the option of selecting standard titration schemes (e.g., AACE geriatric dosing template). Clinicians enter a patient's basic information, type of insulin, glucose range, and time periods. A patient's mobile device then receives the personalized dosing configuration, with reminders to check glucose and to take insulin doses. Titration happens on a regular basis based on the glucose readings collected (e.g., from a Bluetooth-enabled meter) and the clinician's configuration of MIDS. Clinicians can monitor remotely, with everything integrated into EHRs. Glooko is naturally receiving

lots of interest from the pharmaceutical industry, medical device companies, and health systems in making this part of their standard of care for new insulin starts.

- **Patients will receive notifications such as,** "It's checkup time! Let's see if your insulin dose needs to be adjusted," "Your new dose is 12 units," and "Here's what to do next: take 12 units of Lantus at 9pm every day for the next three days. Check your fasting blood glucose at 7am every day. Your next insulin adjustment will be on Sunday, May 1."

INSULET

The Insulet booth showed off the company's snappy new branding, highlighted three major company goals: innovation ("commitment to pursue a hybrid closed loop artificial pancreas"), clinical benefits (72 continuous hours of insulin delivery), and quality of life (the tight-knit "podder community"). A corner of the booth showed off Insulet-branded Glooko, the data downloading product announced in January and now in over 1,000 clinics - wow! The company recently launched its new patient-facing app for reordering supplies, a precursor to its goal of viewing key pump data from the next-gen OmniPod on a smartphone app (FDA submission "later this year").

INSPARK TECHNOLOGIES

We were very pleased to see InSpark Technologies with a small booth at ADA 2016 following the recent launch of Vigilant, its Android and iOS blood glucose pattern recognition app based on technology developed at UVA. Reps shared a keen interest in expanding compatibility beyond Roche's Accu-Chek Connect BGM to other connected meters in the near future and possibility to CGM. Notably, Vigilant still cannot take data from Apple's HealthKit, though this is planned in the VERY near-term; they had been hoping to have this by ADA but it sounds like they barely missed their timeline. On the cost front, reps shared that Vigilant will move to a low-cost subscription model in the coming "six months or so" and is hoping to price the product at "less than a co-pay." A payer- or clinician-facing business model is also a near-term possibility and InSpark is currently in conversations on this front.

J&J/ANIMAS

Animas' booth occupied a small sliver of the J&J real estate. Excited reps eagerly provided us an overview of the Animas Vibe G4. They expressed great enthusiasm for the pumping accuracy of the product, suggesting that the solid foundation puts Animas at an advantage in the closed-loop game vs. Tandem (who also has its CGM-integrated t:slim G4). Reps also suggested that work on a G5-integrated pump is underway though did not provide any further specifics. Per J&J's Medical Device Business review two weeks ago, the goal is be in a pivotal study of the hypoglycemia-hyperglycemia minimizer (HHM) before the end of this year, with a launch targeted by November 2017. Reps could not comment on other pipeline updates, such as the OneTouch Via on-demand mealtime insulin delivery device (previously Calibra's Finesse). In the Medical Device Business review, a regulatory filing for the device is expected in 2H16, with an launch planned by May 2016.

J&J/LIFESCAN

LifesSan's booth aimed to get booth-goers thinking about the biggest challenges they face on a daily basis (e.g., reimbursement, access) and create an opportunity for reps to explain how LifeScan's portfolio solves these challenges - nice marketing! There were no major updates but we did notice that the OneTouch Verio Flex was on the floor, following the stateside launch in February 2016. Notably, the booth also featured a rep from WellDoc to talk about the companies' recent partnership and it sounds like there is a lot of internal enthusiasm on this front as well as for the paired Reveal mobile app, which was also on display.

LABSTYLE

LabStyle's modest booth showcased Dario, their all-in-one smartphone BGM (plugs into headphone jack), which launched in the US in March 2016 with a self-pay subscription model for strips. The rep didn't provide any substantial updates on the pipeline, but did mention that the Android smartphone app has been submitted to the FDA - the app is pending approval and he did not share a timeline for launch. The Dario

app remains available for free on Apple devices, and the reps shared great enthusiasm for the cloud-sharing feature, which allows patients to upload and share their glucose trends with family/friends. Despite the company's shoestring cash levels and the very challenging BGM environment, the rep spoke optimistically about ongoing efforts to bring Dario to additional markets in the near future (it is currently in US, UK, Netherlands, New Zealand, Australia, and Canada).

MEDTRONIC

Medtronic's expansive booth showed off its growing slew of products, including glass cases housing its MiniMed 670G/Enlite 3 (FDA submission by end of this month) and Bluetooth-enabled Guardian Connect mobile CGM (under FDA review, US launch expected by April 2017; EU launch this summer). We got a closer look at the next-gen CareLink report to optimize pump basal and bolus settings, which won't be quite as specific as the Glooko/DreaMed vision. Instead of specific changes (I:C should be 1:12 in the morning), the CareLink report will share which time of day and direction pump settings should change (Increase basal rate from 8am - 12pm). Slides around the booth highlighted the growing list of partners, including IBM Watson (SugarWise app launching this summer with retrospective data analysis), Glooko (compatibility launching in July), and Nutrino (food app + CGM beta launched yesterday). Signs showed a larger presence in type 2 diabetes, highlighting the iPro 2 professional CGM and positive pump data from Opt2mise.

TANDEM

In a surprise, Tandem's booth showed pictures of its predictive low glucose suspend device and t:sport patch pump. The latter was the first image shown in a couple years, appearing as a 50% smaller pump worn on the body with a short infusion set (it looked just like Cellnovo's pump), a "separate touchscreen controller or mobile app" (Tandem is presumably still in FDA discussions on this), waterproof, a rechargeable battery, and CGM integration. No timing was shared, but the 4Q15 call suggested an FDA submission would occur in 2017. The predictive low glucose suspend device looked just like the t:slim G4, but with a slightly updated interface to denote a suspend event (the color is really impactful). It is still expected to enter a feasibility study in summer 2016 and a pivotal study in late 2016. This product will be behind other AID systems that respond to hyperglycemia (MiniMed 670G, Animas Hypoglycemia-Hyperglycemia Minimizer, and many others), though perhaps the path to market is easier for PLGS. Signs on the top of the booth noted, "Having diabetes isn't a choice. How you manage it should be." The slogan was appropriate to describe Tandem's portfolio of three pumps, and of course, even more apt to respond to the Medtronic/UHC agreement that excludes Tandem pumps.

VALERITAS

Valeritas hosted a modest booth to expound upon their wearable insulin delivery device, V-Go. The disposable pump has been highly effective at: (i) increasing affordability; and (ii) improving diabetes health metrics such as A1c (1.59% decrease in 14 weeks in one study), A1c variability, and total daily insulin dose. Reps suggested that the product has been so successful because of its simplicity - patients adhere to their regimens, promoting better glycemic control and reducing the need for expenses on excess insulin. In addition, we were interested to see in-person the changes in branding that Valeritas has rolled out in the past year. They have adopted two double-entendre-laced taglines - "Suddenly it clicks" and "Get your V-Go On" - to encourage patients to try the wearable patch for better diabetes management.

Exhibit Hall - Drugs

ASTRAZENECA

AZ posted a large, centrally located booth that devoted essentially equal time to each of its diabetes products. Each featured drug - Farxiga (dapagliflozin), Xigduo (dapagliflozin/metformin), Bydureon (exenatide once weekly), Byetta (exenatide twice daily), Onglyza (saxagliptin), Kombiglyze (saxagliptin/metformin), and Symlin (pramlintide) - received its own block hanging from the ceiling, and most also had a small booth with a screen providing prescribing information. AZ's booth was one of our more interactive experiences in the exhibit hall today; we tried our hand at the "mechanism of action challenge" for GLP-1 agonists and SGLT-2 inhibitors (we did pretty well but couldn't beat the record time of nine seconds!) and

built a personalized recipe collection at the station featuring the company's Fit2Me patient support program.

GSK

GSK's booth was large but sparse, featuring a white theme with signature orange and purple accents. The booth's colors were carried through to the treats of mango and acai berry sorbet on offer. The booth was focused entirely on the company's sole approved diabetes drug: GLP-1 agonist Tanzeum (albiglutide). The marketing featured the slogan "Your experience may change theirs." Our sense (based on the most recent sales and volume data) is that Tanzeum has struggled to break into the crowded GLP-1 agonist market - we believe the market will continue to expand and it will be interesting to see how it evolves. Tanzeum has a more modest efficacy compared to other agents, but we are surprised that the company's strategy of competing on price has not paid off more in such a cost-conscious environment.

INTARCIA

Intarcia wins the award for the most significant exhibit hall upgrade at this year's ADA, posting two fairly sizable booths instead of the single small booth we have seen at recent conferences. One especially eye-catching booth focused on the newly branded Medici delivery device, with signage promising a "Renaissance in medicine delivery." The décor had a bit of a seventies vibe, with neon lights hanging above the booth, bright blue plush carpeting, and walls covered with graphics of the Medici device with colorful flowers, smiley faces, etc. emerging from the end. The booth centered around two stations where reps demonstrated the insertion and removal procedures for the device - this has been the mainstay of Intarcia's booth at previous conferences, though this time the reps went to great lengths to emphasize that they were promoting only the Medici device, not ITCA 650 (implantable exenatide mini-pump). Any questions about ITCA 650 were referred to the company's second booth across the hall, labeled "Is T2D Spiraling Out of Control?" and featuring a huge funnel hanging from the ceiling with words like "prevalence," "hypo," and "not to goal" going around and around in a downward spiral. Even that booth featured little mention of ITCA 650 specifically, focusing instead on the need for a paradigm shift in how type 2 diabetes is treated. Intarcia is clearly making a concerted effort to broaden its focus beyond a single product, and we can't wait to see what it has in store.

J&J/JANSSEN

As in the recent past, Janssen occupied the majority of J&J's booth, with approximately equal real estate devoted to Invokana (canagliflozin) and Invokamet (canagliflozin/metformin). The booth had several prominent signs promoting the recent expansion of Invokamet's indication to include use as a first-line therapy for type 2 diabetes. We see this as a major win for drug-naïve patients with a high A1c and believe it should spur greater use of Invokana in patients at earlier stages of the disease. The booth also had a substantial focus on ancillary programs for Invokana, including the CarePath patient support program and the Check Your Numbers Tracker App. We found it interesting that there seemed to be less of a focus on Invokana's strong formulary positioning compared to previous exhibit halls - management acknowledged during the company's 1Q16 update that Invokana has faced increased competition for formulary positioning this year but emphasized that it retains 80% preferred access in the combined commercial and Medicare Part D segments.

LILLY

Lilly's classically red booth was set up in a circular labyrinth-like layout with sections promoting each of its diabetes products surrounding a quiet inner oasis with (sugar-free) artisanal espressos and café seating. We especially loved the wall that asked attendees to fill out magnetic tiles answering the question "Whose diabetes do you have?" as a show of support for loved ones with diabetes (answers were in the format "I have ____'s diabetes"). The center portion also featured screens that encouraged participants to explore Lilly's extremely diverse product portfolio through the lens of the multi-organ pathophysiologies associated with type 2 diabetes - we previously saw this at the AACE 2016 exhibit hall. In terms of products, the booth devoted a sizable aqua-drenched section to its Humulin U500 KwikPen, the striking color scheme

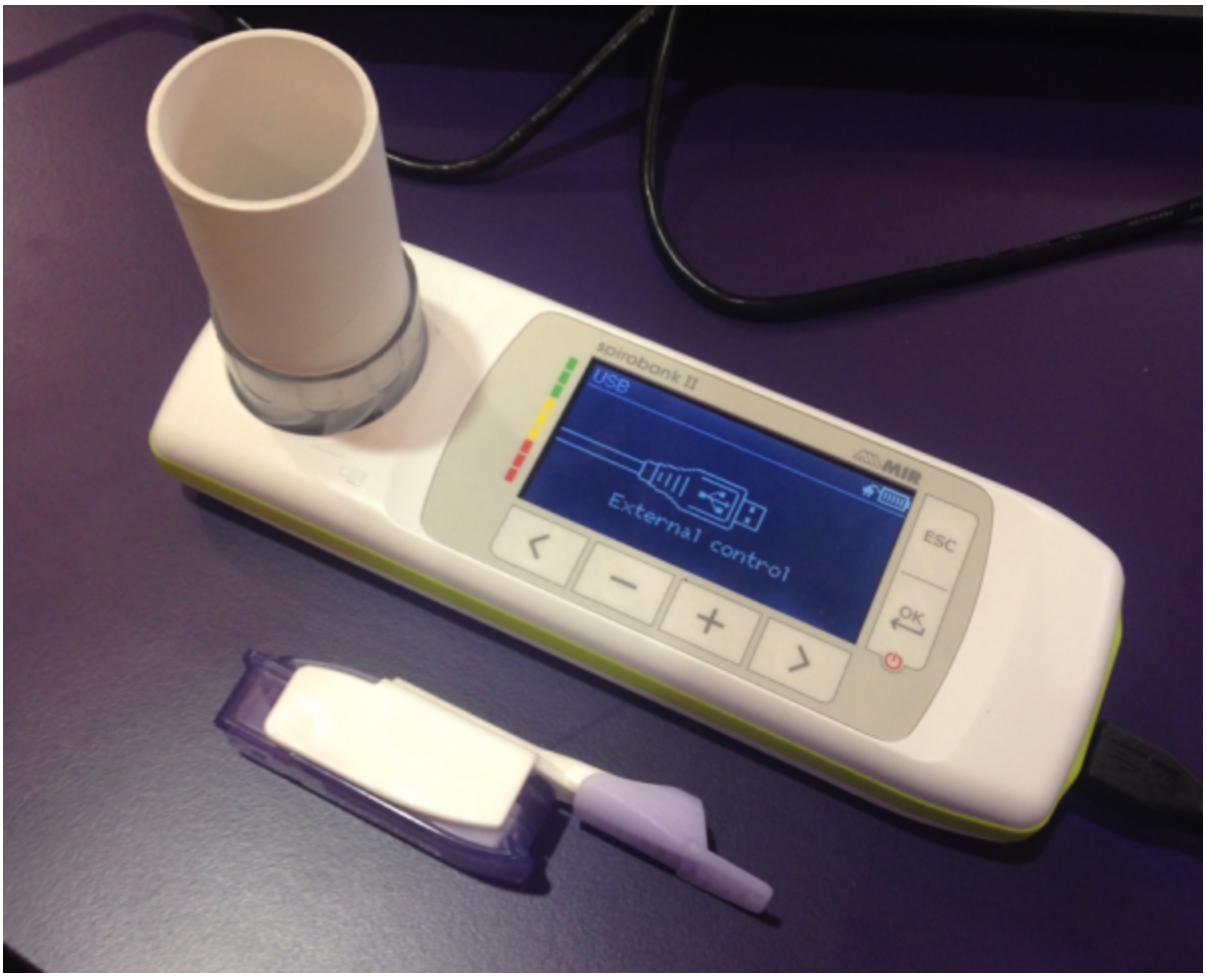
complementing the bright aqua body of the pen. We also got our first glimpse of Basaglar in a US exhibit hall - we love the minimalist logo that evokes A1c reduction with a single drop of a blood over a downward arrow. The screens for Basaglar drove home a single point: "Basaglar is coming December 15, 2016." Clearly, Lilly/BI is already starting to build the excitement for the product. The booth also devoted floor space to Jardiance (empagliflozin), Glyxambi (empagliflozin/linagliptin), Tradjenta (linagliptin), Jentadueto (linagliptin/metformin), Trulicity (dulaglutide), and the Humalog and Humalog U200 KiwkPens.

LILLY/BI

Lilly/BI's large, airy booth sported gray and teal accents against a predominantly white background - a contrast to the wood-paneled Scandinavian-modern-rustic look we'd become accustomed to. The booth's star product was clearly Jardiance (empagliflozin) whose materials took up a full half of the display (along with those of its sister product Synjardy [empagliflozin/metformin]). Several touchscreens featured the memory game seen at the Lilly standalone booth - we counted at least four stations where attendees could try their hand at matching pictures of Jardiance-related info within 60 seconds. On the more old-school side, the Jardiance section also featured a croquet game in which attendees attempted to navigate through hoops such representing healthy lifestyle choices while avoiding obstacles such as "Mom's Spaghetti" and "Desk Chair Dessert." The other half of the Lilly/BI booth was evenly split among Glyxambi (empagliflozin/linagliptin), Tradjenta (linagliptin)/Jentadueto (linagliptin/metformin), and Basaglar (biosimilar insulin glargine). Lilly/BI has also stepped up its promotional materials for Glyxambi with a Pixar-style cartoon of a two-person cleaning crew ("Dual inhibition, ready for action") to represent the dual empagliflozin and linagliptin components of the product. The exhibit even featured a photobooth area in which attendees would don props and pose with large statues of the two characters. We're glad to see Glyxambi garner more attention within Lilly/BI's marketing scheme - there have been high hopes for this product as the only incretin/SGLT-2 inhibitor fixed-dose combination on the market, but Lilly has been fairly quiet on its performance since its launch over a year ago.

MANNKIND

Our trip to the MannKind booth allowed us to experience the company's nifty new spirometry solution for healthcare providers to test lung function before prescribing Afrezza. The small, relatively inexpensive device (~$400) pays for itself quickly, as providers can bill $50 for each test. It plugs directly into a desktop computer and is factory calibrated, saving time. It's a massive improvement for endocrinologists that will now be able to do spirometry in-office, rather than sending patients to specialists. The MannKind team seemed enthusiastic and said they had "learned a lot" from the Sanofi partnership, and we look forward to seeing some commercial progress as MannKind takes over responsibility for the ultra-rapid inhaled insulin. We love seeing this new tool and think it will aid uptake significantly.



MERCK

Merck and its DPP-4 inhibitor empire had a decently sized booth, with the majority of marketing unsurprisingly focused on the Januvia (sitagliptin) franchise. The green and white booth included six boards on Januvia and two on Janumet (sitagliptin/metformin), with emphasis on the drugs' potential concomitant use with insulin, "strong" A1c reductions, and tolerability. The company also aimed to bring a patient-centric feel to the booth, with several large touch screens on images and stories of patients as well as a center to pick up patient education resources. In addition, Merck featured a yogurt parfait bar (which generated a decent amount of traffic) as well as a virtual reality experience on Januvia's mechanisms of action - an increasingly popular entity in exhibit halls. Other non-diabetes drugs promoted at the booth included LDL-lowering drug Zetia (ezetimibe) and vaccine Pneumovax 23 (pneumococcal vaccine polyvalent). The TECOS results appeared to not be as heavily featured as we've seen in the past, likely due to the upstaging of the more recent CVOTs. Nonetheless, Merck continues to hold onto leadership of the DPP-4 inhibitor class, although the company has notably directed more attention to other classes recently, with the decision to drop once-weekly omarigliptin and greater attention to SGLT-2 inhibitor candidate ertugliflozin. For more on Merck's latest, check out our 1Q16 update.

NOVO NORDISK

Novo Nordisk's bright, airy booth was hard to miss as one of the largest displays in the exhibit hall. In terms of products, the booth was focused almost entirely on Tresiba (insulin degludec), though there was a small amount of signage promoting Victoza (liraglutide) and NovoLog (insulin aspart). Promotional materials for Tresiba emphasized the product's long duration of action and the potential for flexible dosing ("schedules change, dosing can too"). The Tresiba section also included a few creative touches such as a large hanging

parachute labeled "A1c" and a "virtual representative" of sorts (a webcam on a motorized roving base) circulating around the booth. Aside from products, we were thrilled to see a sizable portion of the booth devoted to the company's Cities Changing Diabetes program; when we stopped by, a presentation was in progress about the contribution of environmental sustainability initiatives to Novo Nordisk's "triple bottom line." As usual at ADA, Novo Nordisk's booth also featured the popular A1c testing station, which was attracting a pretty substantial crowd.

SANOFI

Sanofi's large booth at the center of the exhibit hall was one of the largest and most elaborate Sanofi booths we've seen in recent memory. At the center of the booth, Sanofi created a COACH café, featuring dark wood floors, low-slung white sofas, and treats such as banana mint slushees and apple crisps. The café promoted Sanofi's COACH patient support programs that offer live diabetes education and more to patients with a prescription for Toujeo (U300 insulin glargine). Toujeo itself occupied much of the square footage of the booth, which signage simply asserting "All Day. Every Day." and characterizing Toujeo as "an insulin of today." Sanofi's other major insulin products, Lantus (insulin glargine) and Apidra (insulin glulisine), were also given sections of the massive booth. The giant SoloStar pens for Toujeo, Lantus, and Apidra returned to dominate a far corner of the booth. In a separate location, Sanofi's unbranded Glycemic Explorer booth made a reappearance.

TAKEDA

Takeda took up a good amount of real estate toward the back of the exhibit hall, promoting Nesina (alogliptin), Kazano (alogliptin/metformin), and Oseni (alogliptin/pioglitazone). The marketing centered around the theme of a puzzle ("diabetes management is a puzzle" and "every piece counts") while the booth included a few touch screens reviewing the products' information and a "personality quiz" that tested attendees' diabetes knowledge. Overall, the booth seemed to be lighter on promotional material, with approximately two-thirds of the booth's space blocked off for a lounging area for international delegates - a nod to the fact that most of Takeda's drugs are marketed ex-US. As expected, the booth had no mention of obesity drug Contrave (naltrexone/bupropion), as Takeda recently left the drug's partnership with Orexigen - see our coverage of this news for more.

Exhibit Hall - Obesity

NOVO NORDISK (SAXENDA)

Similar to recent meetings, Novo Nordisk had one booth focused exclusively on its obesity drug Saxenda (liraglutide 3.0 mg). In its typical purple color scheme, the promotional material emphasized Saxenda as the "first and only GLP-1 agonist" approved for chronic weight management, as reps walked attendees through clinical data and had demo pens on display. Imaging throughout the booth again featured a woman holding up a pair of old larger jeans inscribed with "excess weight," "high cholesterol," "large waistline," and "high blood pressure" - highlighting the versatility of Saxenda. Next to a smoothie bar, a video also played in the background, stressing the "science of Saxenda," with an emphasis on biology rather than willpower (we love this education piece for removing stigma). Not surprisingly, Novo Nordisk's Saxenda booth was the only obesity drug representation on the floor, with no booths from Arena/Eisai, Vivus, or Orexigen - a stark contrast from ADA 2014, when the obesity drug market seemed to be at the height of its anticipation. We believe Saxenda sales would improve if the price were not based on the dose.

Exhibit Hall - PCSK-9 Inhibitors

AMGEN

Amgen brought a relatively large booth to the ADA floor, with all eyes on its PCSK9 inhibitor Repatha (evolocumab). Buzzwords and phrases on the product included "maximize efficacy from the start," "intensive reduction," and "predictable response." We were very glad to see the Amgen booth and focus on PCSK-9 given the very high numbers of patients who need significant help on the cholesterol front. In a blue and white color scheme, several touch screens scattered throughout the booth showcased the product's

safety and prescribing information, while a video of PCSK9 inhibitors' mechanisms of action played in the background. To illustrate "who Repatha is for," the booth featured stacked blocks of "clinical ASCVD history," "current statin use," and "LDL-C levels." Similar to last year, Amgen also incorporated an element of fun, with a hands-on game simulating PCSK9 inhibitors' mechanism of action, as attendees threw stuffed LDL-C molecules onto Velcro-backed LDL receptors on two different walls, each representing either more functional (with fewer receptors available) or less functional PCSK9 (with more receptors available). In efforts to differentiate Repatha from Sanofi/Regeneron's Praluent (alirocumab), Amgen also highlighted that Repatha is the only PCSK9 inhibitor with 30-day room temperature storage for patients, no dose titration, and one 140 mg/ml sub-Q dose every two weeks. The company seemed to come to ADA in full force, with scientific affairs and medical booths, a scheduled product theater, and of course, a popular espresso bar. As a reminder, Amgen's recent calls have expressed strong enthusiasm for Repatha (first revenues released in 1Q16 at $16 million) and the company's significant presence at ADA gives us the impression that Amgen has its eyes on diabetes once the product can gain the momentum to expand its indication - see our 1Q16 report for more.

SANOFI-REGENERON

Sanofi-Regeneron, one of two PCSK9 inhibitor players on the ADA floor, had a decently sized booth focused on Praluent (alirocumab). The company marketed the product with an emphasis on its dosing flexibility, with repeated mentions of "power like never before…and more power if you need it," with giant down arrows in a green and turquoise color scheme. Additionally, the booth stressed this flexibility as a key differentiator, with the message that Praluent is the only PCSK9 inhibitor that "offers two levels of efficacy." Sanofi/Regeneron's imaging also appeared to bring the patient to life, as several touch screens featured different patient types and walls showed images of patients with shirts exclaiming their lower LDL levels. In addition, we were glad to see the patient support program, MyPraluent, make up a wall of the booth, promoting information on how to help patients with coverage support, cost, and adherence. We have heard of the complex paperwork and processes involved in authorization for PCSK9 inhibitors for both patients and providers, so we would imagine that such patient support programs are critical for the product's success - for more on this, see our 1Q16 update from Sanofi.

Product Theaters

THE EFFICACY MIRAGE IN T2D - WHY DO CLINICAL TRIAL RESULTS DISAPPEAR IN CLINICAL PRACTICE (SPONSORED BY INTARCIA)

Steven Edelman, MD (University of California, San Diego, CA); William Polonsky, PhD, CDE (Behavioral Diabetes Institute, San Diego, CA)

This exceptionally well-attended session in the exhibit hall - with attendance over 200 by our count - never mentioned Intarcia or its implantable exenatide mini-pump ITCA-650 - brilliant, in our view! Instead, very popular and highly regarded session leaders Dr. Steven Edelman and Dr. Bill Polonsky tackled a more general and very highly relevant question in diabetes care from our view: why real-world efficacy for new glucose-lowering therapies so rarely matches what is seen in clinical trials? The short answer is adherence, which some data suggest accounts for 75% of the clinical trial / real world discrepancy, though there are also other important factors at play - cultural and social determinants that are often masked in RCTs. Drs. Edelman and Polonsky hammered home the point that 40 new type 2 diabetes therapies have been approved since 2005 without any significant change in the percentage of patients with A1cs below 7%. Dr. Polonsky worked hard to shift blame away from the patient, noting that patients logically will not adhere to a regimen that they do not perceive as worthwhile, or that is too burdensome to manage. He challenged members of the audience to avoid seeing their non-adherent patients as chronically unmotivated; after all, he pointed out, nobody is unmotivated to live a long and healthy life. We will look forward to hearing more in the future about what will engage patients with traditional therapies and with ITCA 650, how taking adherence "off the table" to a large degree will result in different outcomes (how engaged patients are, whether they have more bandwidth to focus on diet/exercise, whether doctors and nurses are more

motivated by also receiving procedure payments, etc.) In the meantime, we heard a lot of audience enthusiasm from this less traditional and very absorbing session.

- **The product theater was part of a larger Intarcia-sponsored unbranded initiative called RethinkT2D (along with the "efficacy mirage" booth at the exhibit hall).** In what we thought was a nice touch, all session attendees were invited to visit RethinkT2D.com to download the presentation slide deck for their own use.

A TREATMENT OPTION FOR PATIENTS WHO ARE SEVERELY INSULIN RESISTANT (SPONSORED BY SANOFI)

Timothy Gilbert, MD (Texas Diabetes & Endocrinology, Dallas, TX) and Jeremy Pettus, MD (University of California San Diego, San Diego, CA)

Dr. Pettus characterized Toujeo (U300 insulin glargine) as a completely new basal insulin, with what he emphasized was a PK profile distinct from that of Lantus (U100 insulin glargine). He reviewed the basic characteristics of the drug, including its lower injection volume (one-third that of Lantus), the fact that it forms a smaller precipitate than Lantus, and the convenience offered by the one-to-one unit conversion between the Lantus and Toujeo pens. Both Dr. Pettus and Dr. Gilbert highlighted that Toujeo is more stable than Lantus over 24 hours. In reviewing the six-month non-inferiority phase 3 EDITION studies that compared Toujeo to Lantus, both physicians focused on EDITION 3, which recruited insulin-naïve type 2 diabetes patients uncontrolled on oral agents. They highlighted that both drugs had similar A1c reductions, and that Toujeo had improved rates of hypoglycemia. During the second half of the talk, the two physicians reviewed a patient example, walking the audience through the considerations of starting basal insulin.

- **For insulin-naïve patients, Dr. Gilbert recommended starting with a Toujeo dose of 0.2U/kg/day for type 2 patients and with one-third to one-half of the total daily insulin dose for type 1 patients.** For patients on once-daily long or intermediate acting insulin, he recommended a 1:1 conversion. Lastly for those on twice-daily NPH insulin, he recommended starting with 80% of the total daily NPH dose. Dr. Pettus suggested increasing the Toujeo dose every three to four days based on the patient's personalized fasting plasma glucose target.
- **In reviewing the EDITION 3 data, Dr. Pettus highlighted that both Lantus and Toujeo had similar A1c reductions,** and that the rates of severe hypoglycemia and documented symptomatic hypoglycemia with Toujeo were 0.9% and 8%, respectively. Dr. Pettus acknowledged that the data for Lantus were not shown, and stated that studies have indicated a trend toward less hypoglycemia with Toujeo. That said, hypoglycemia with Toujeo has not been studied in a dedicated trial as it has with Novo Nordisk's Tresiba (insulin degludec) in the SWITCH 1 and SWITCH 2 trials. We'll be curious to see if Sanofi initiates a similar trial of hypoglycemia in Toujeo as it vies with Tresiba within the next-generation basal insulin market.

OPTIONS IN BASAL INSULIN: BASAGLAR (SPONSORED BY LILLY/BI)

Tom Blevins, MD (Texas Diabetes & Endocrinology, Austin, TX)

In this Lilly/BI Saturday afternoon product theater, Dr. Tom Blevins reviewed Basaglar's (biosimilar insulin glargine) phase 3 efficacy and safety data, highlighting its non-inferiority vs. Sanofi's Lantus. Throughout the presentation, Dr. Blevins emphasized that while Basaglar is identical to Lantus in terms of amino acid sequence and dosing information, the FDA does not technically consider it a biosimilar - it was approved under the 505(b)(2) regulatory pathway, which will be consolidated with the newer "official" biosimilar pathway in 2020. Dr. Blevins also commented on the delivery device - Basaglar will be delivered in a uniquely-colored KwikPen that is compatible with BD's ultrafine needles. This is different than the delivery device for Lantus and could potentially make Basaglar more appealing for patients averse to needles. While Dr. Blevins did not comment on pricing during the presentation, he suggested during Q&A that the cost would "probably be more or less the same compared to Lantus." We would be surprised if this is the case given the widespread belief that biosimilar insulins do not provide better quality (quality will have to be proven) but will provide at least somewhat better access to many. Notably, although many call

Basaglar a "biosimilar" the company has not done so to date. So far, the product has been priced at about a 10%-20% discount compared to Lantus in the EU countries where it has launched. We had assumed that the discounts may be larger in the US given the higher list prices for basal insulin analogs there compared to Europe, though the discounts are still expected to fall well short of those for small-molecule generics compared to branded drugs. Dr. Blevins confirmed that Basaglar is expected to launch in the US launch around December 15, 2016 as per the terms of Lilly's patent lawsuit settlement with Sanofi. During the presentation, Dr. Blevins also reviewed results from the phase 3 ELEMENT I and ELEMENT II trials (presented at ADA 2014) demonstrating non-inferiority between Basaglar and Lantus in terms of A1c reduction and percentage of patients achieving an A1c <7% in type 1 and type 2 diabetes.

Questions and Answers

Q: Are there any differences in cost between Basaglar and Lantus?

A: The cost will probably be more or less the same. I'm not sure, as that information isn't available yet. I would suggest continuing to communicate directly with BI and Lilly to find out exact information on pricing.

Q: Can you speak to the interchangeability in treatment with Basaglar and Lantus?

A: Basaglar did meet the criteria for non-inferiority vs. Lantus. However, I don't believe that these two are officially interchangeable - that is not worked out. Basaglar is another option, that's my best answer. However, there is no difference in achievement; Basaglar is non-inferior to Lantus.

A: Because Basaglar is regulated through an NDA, and interchangeability is a regulatory status, this follow-on is not deemed interchangeable in the US. We know that for sure.

Q: What does the experience of someone who is pregnant and on Basaglar look like?

A: We haven't studied Basaglar in pregnancy.

TOUJEO: A ONCE-DAILY BASAL INSULIN (SPONSORED BY SANOFI)

Bruce Bode, MD (Atlanta Diabetes Associates, Atlanta, GA), Bill Polonsky, PhD (University of California San Diego, San Diego, CA) Steven Edelman, MD (TCOYD, Del Mar, CA), Debbie Hinnen, APRN, CDE (Touro University California, Vallejo, CA)

At a well-attended Sanofi product theater, the A+ team of Drs. Bruce Bode, Steve Edelman, Bill Polonsky, and Debbie Hinnen made a strong case for why providers should prescribe Toujeo (insulin glargine U300) in type 2 diabetes. The speakers began by taking turns presenting on Toujeo's pharmacology, clinical data, and administration before walking through different case studies to demonstrate how to dose for a wide range of patients, from those who are insulin-naïve to those on basal-bolus therapy. Notably, the formulation was characterized as a particularly "forgiving" insulin, both in terms of its smooth basal rate (which enables patients to get away with errors - Dr. Bode actually noted that the flat profile is just like "what you see with an insulin pump") and flexible dosing (which allows patients to get away with missing a morning dose). We got the sense that Toujeo fits better into patients' lives - rather than patients having to fit their lives around the insulin - which led Dr. Edelman, in particular, to highlight the potential adherence benefits - we have heard a lot about this anecdotally speaking. He also acknowledged the company's "very good" COACH program, stressing his view that more patient contact and support leads to better outcomes. Lastly, panelists spent time discussing the clinical transition from Lantus (insulin glargine) to Toujeo, stressing that it takes 3-4 days for the latter to achieve steady state - indeed, all the speakers had stories of patients who claimed Toujeo "didn't work" because they did not stick with it long enough, and with that in mind, stressed that setting expectations is key.

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