CLOSER LOOK

MEMORANDUM

Lilly 2018 Financial Guidance - Trulicity, Basaglar, Jardiance highlighted as growth drivers; Optimism for REWIND readout; Biosimilar competition for Humalog; Nasal glucagon filing + Jardiance in CKD study + data from two DPP-4 CVOTs to come in 2018 - December 13, 2017

Executive Highlights

- **Financial guidance:** Lilly presented strong financial guidance for 2018, confirming that it expects ~5% annual revenue growth through 2020, totaling $23-$23.5 billion in expected revenue. The company is on track to meet its ~$22 billion revenue guidance for 2017. So far, the diabetes business has contributed $5.6 billion, and for the full year, should easily surpass the $5.9 billion recorded in 2016.
- **Growth drivers for 2018:** Management highlighted GLP-1 agonist Trulicity, biosimilar insulin Basaglar, and SGLT-2 inhibitor Jardiance, among other "recently-launched" products. Due to ongoing and intensifying pricing pressure, Lilly is focused on volume expansion to drive growth rather than changes to list price. This is a win from the patient perspective, though muted profits for industry (via higher rebates to PBMs) also constrain R&D for the next generation of advanced diabetes therapies, a clear negative.
- **A year of CVOTs:** Lilly expects three major readouts in 2018 - (i) topline data from REWIND for Trulicity, (ii) full results from CARMELINA for DPP-4 inhibitor Tradjenta, and (iii) topline data from CAROLINA comparing Tradjenta vs. SU glimepiride. Management shared a positive outlook on REWIND, suggesting good chances of showing CV efficacy. Management also acknowledged competition from Victoza's CV indication and the anticipated 1Q18 market entry of Novo Nordisk's Ozempic (semaglutide), but argued that this will do more to grow the GLP-1 class than to compete with Trulicity.
- **Planned regulatory filings:** In 2018, Lilly will submit nasal glucagon to the FDA as well as a combination of SGLT-2 empagliflozin, DPP-4 linagliptin, and metformin extended-release.
- **New phase 3 studies:** Lilly announced that a dedicated outcomes study of Jardiance in CKD will begin in 2018 - this is the first concrete timing disclosed since the initial announcement of this planned trial in June. Phase 3 studies of high-dose dulaglutide (3.0 and 4.5 mg) in type 2 diabetes will also be launched in 2018.

Lilly provided 2018 financial guidance in a call this morning led by CEO Mr. Dave Ricks. You'll find seven highlights from us on this page, and you can also see the press release and presentation slides on the company's website. We conclude our report with Q&A from the call relevant to Lilly's diabetes business, and we note particular interest from investors in GLP-1 and REWIND (the CVOT for Trulicity expected to complete mid-2018, with topline results expected by end of 2018).

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Top Seven Highlights

1. LILLY'S OVERALL BUSINESS ON TRACK WITH ~5% ANNUAL REVENUE GROWTH 2015-2020; EMPHASIS ON GROWING VOLUME IN 2018 RATHER THAN LIST PRICE; TRULICITY, BASAGLAR, JARDIANCE HIGHLIGHTED AS CURRENT AND FUTURE GROWTH DRIVERS

Lilly confirmed that it expects its overall pharmaceutical business to grow ~5% annually from 2015-2020, and predicted 2018 revenue between $23 and $23.5 billion. The company is on track to meet its 2017 revenue guidance of ~$22 billion. The diabetes portfolio has posted $5.6 billion so far this year ($1.7 billion in 1Q17, $1.9 billion in 2Q17, and $2 billion in 3Q17), and for the full-year 2017, will easily surpass last year's $5.9 billion. Due to ongoing and intensifying pricing pressure (particularly in the US, but also in Japan), management explained that growth in 2018 will come primarily from volume increases, and mentioned high expectations for new products including GLP-1 agonist Trulicity (dulaglutide), biosimilar insulin Basaglar (biosimilar glargine), and SGLT-2 inhibitor Jardiance (empagliflozin). This pricing pressure has been no secret among diabetes companies, with management from Lilly as well as Novo Nordisk, Sanofi, AZ, J&J, and Merck citing lower net prices for their diabetes drugs - as PBMs and payers take higher rebates, the price recorded by the manufacturer is lower per prescription. On previous earnings calls, Lilly has also discussed segment mix (or a higher proportion of prescriptions going to patients on Medicaid) and higher patient discounts in the context of pricing pressure around Humalog (insulin lispro), specifically. Some of this is great news for patients - presumably better savings programs, greater access within Medicaid, and Lilly's focus on growing volume rather than list price for advanced medicines like Trulicity, Basaglar, and Jardiance. That said, the lack of transparency around PBMs is only becoming more frustrating (and simultaneously more complex), and lower profits to industry puts constraints on innovation for the next generation of diabetes therapies. Notably, management clarified that this 2018 financial guidance assumes no major changes to the US healthcare system or the US corporate tax system. "Obviously, some of this legislation is unstable," said CEO Mr. Dave Ricks, "and this could change our guidance."

- **Management discussed the competitive threat of new market entries in diabetes, referring to Novo Nordisk's once-weekly GLP-1 agonist Ozempic (semaglutide) and to Sanofi's just-approved biosimilar insulin lispro Admelog, but asserted that Lilly's diabetes portfolio is expected to grow in all major markets next year.** Both of these new

products received FDA approval only in the past week or so. Ozempic will launch in US pharmacies early next year, in 1Q18, while Admelog's launch timing remains unclear but will probably come sometime in 2018. We provide a deeper dive on GLP-1 and insulin below (highlights #2 and #3).

2. "WE FEEL GOOD ABOUT OUR CHANCES TO HAVE A POSITIVE STUDY WITH REWIND"; TRULICITY CVOT TO REPORT TOPLINE RESULTS BY END OF 2018; LILLY'S ORAL GLP-1 REMAINS PRECLINICAL BUT A DEFINITE PIPELINE PRIORITY

Head of Diabetes Mr. Enrique Conterno fielded many questions on Lilly's GLP-1 business during Q&A, ultimately expressing a positive outlook for Trulicity (once-weekly dulaglutide), for REWIND (CVOT expected to complete July 2018), and for underlying class growth. Yes, he acknowledged, competition is fierce. Novo Nordisk's Victoza (liraglutide) became the first GLP-1 agonist with a CV indication on its label in August, and Ozempic (once-weekly semaglutide) has shown incredible potency throughout its clinical program, including superiority over Trulicity in the head-to-head SUSTAIN 7 trial. That said, Mr. Conterno seemed unfazed, in part because Trulicity has shown a strong clinical profile and comes in a very patient-friendly, IDEO-designed pen. He didn't comment specifically on SUSTAIN 7, nor did this come up at all during prepared remarks or Q&A - we've only seen topline data so far, and we await full results before making any firm conclusions, although it does seem like this could turn into a headwind for Lilly and we'll be eager to hear management's take once all the data is public. Mr. Conterno suggested that Victoza's CV indication and Ozempic's market entry are important steps toward growing the entire GLP-1 agonist class. Both regulatory victories mean more promotion of GLP-1 agonists to patients and providers, and more understanding in the diabetes community of residual CV risk and how to treat it. These milestones could also prove useful in payer negotiations, to improve reimbursement prospects for GLP-1 agonists. For the most part, payer contracts have been less exclusive for GLP-1 vs. other diabetes drug classes (Mr. Conterno mentioned some restrictions, but very few that are totally exclusive, forcing all patients onto one GLP-1 agent or another), perhaps because there are substantial differences between GLP-1 products in terms of clinical profile (level of A1c-lowering and weight loss), dosing schedule (from twice-daily Byetta to once-weekly Trulicity, Ozempic, Bydureon, and Tanzeum), injection device (reconstitution kits, pens, autoinjectors), and demonstrated cardioprotection. Mr. Conterno highlighted this "open access environment" and maintained confidence that Trulicity will be able to compete by differentiating itself. We see the within-class differences for GLP-1 agonists as a tremendous opportunity for more personalized care decisions, and we were glad to hear that exclusive contracts are rare in the GLP-1 segment, as this implies expanded patient choice. We appreciated management's emphasis on whole class growth rather than in-class competition, because we agree that many more patients could be benefiting from GLP-1 therapy. According to a recent Diabetes Care paper, only 7% of second-line diabetes prescriptions in the US were for a GLP-1 agonist in 2016, which is far, far too low considering the many advantages to this class of medicines (profound A1c reductions, weight loss, anti-atherosclerotic effects, possible CV and renal protection). Lilly management called out an opportunity to position Trulicity as the first injectable treatment for people with diabetes - currently, the large majority of patients start basal insulin as their first injection, but earlier initiation of a GLP-1 agonist could more swiftly promote weight loss and A1c decline without hypoglycemia risk, enhancing patient satisfaction and quality of life.

- **Lilly anticipates that the required number of CV events for REWIND will be accrued by mid-2018, leading to a topline data release toward the end of the year.** The company is committed to getting a slot at a major medical meeting for the full results presentation, perhaps ADA 2019. Mr. Conterno seemed enthusiastic about the chances for positive results, indicating CV efficacy for dulaglutide vs. placebo, in which case Trulicity would join the ranks of Victoza as a GLP-1 agonist with demonstrated CV benefit (the SUSTAIN 6 study for semaglutide was smaller and shorter, and FDA will likely require a larger post-approval CVOT for Ozempic before granting a CV indication). Notably, during Novo Nordisk's 3Q17 earnings call, CSO Dr. Mads Thomsen was skeptical that REWIND will produce positive data due to certain elements of trial design - namely, a majority primary prevention cohort (only 31% of participants have established CV disease at baseline), a relatively low mean baseline A1c (~7.3%), and a relatively short mean duration of diabetes (~10 years). This topic arose in interpreting EXSCEL results as well for AZ's Bydureon

(exenatide once-weekly), which were "marginally positive" and might have been definitively positive were the study population "more sick" or higher-risk at baseline. Considering the entire, motley mix of neutral, positive, and marginally positive CVOTs for GLP-1 agonists, Mr. Conterno still claimed that "we feel good about our chances to have a positive study with REWIND." To be sure, showing cardioprotection and other benefits beyond glucose-lowering is becoming increasingly important - if not essential - for new diabetes drugs. There are definite advantages to getting a CV indication on a product label, which determines what companies can say to real-world patients/providers. If REWIND results don't support a label change, this could pose another challenge to Trulicity going forward. We'll be watching closely to see how Bydureon sales/volume are affected by the neutral, though marginally positive, EXSCEL readout.

- **Mr. Conterno declined to comment extensively on future commercial competition from Novo Nordisk's oral semaglutide, but confirmed that Lilly has an oral GLP-1 agonist in preclinical stages.** This was first announced officially during Lilly's R&D update in May 2016, and Mr. Conterno provided reassurance that this candidate is still a priority within the company's diabetes pipeline. Novo Nordisk plans to report results from 10 phase 3 PIONEER studies on oral semaglutide in 2018, and indeed, characterized oral GLP-1 as a very important future growth driver during the company's recent Capital Markets Day. Eliminating injection burden could be the next big frontier for GLP-1 agonist therapy - how terrific would it be if patients could reap all the same benefits of A1c-lowering, weight loss, and cardio/renal protection with a pill instead of a needle? Mr. Conterno cautioned that oral semaglutide's side-effect profile must be carefully evaluated in phase 3 data.

3. UPCOMING COMPETITION FOR HUMALOG FROM SANOFI'S BIOSIMILAR LISPRO (ADMELOG); LILLY UNCONCERNED ABOUT INTERCHANGEABILITY OF INSULINS

Lilly anticipates competition ahead from Sanofi's Admelog (biosimilar insulin lispro), the first-to-market biosimilar mealtime insulin approved earlier this week by FDA. Although this is factored into 2018 financial guidance, Humalog (insulin lispro) sales and prescriptions may not be meaningfully impacted until 2019. Sanofi hasn't yet announced launch timing for the US, and due to timing of the contracting cycle, Admelog may not be covered by many payers until 2019. Of note, no biosimilar insulins to-date have been approved with an interchangeability designation, which would allow pharmacists to switch patients from the originator product to the generic without consulting the prescriber (for that matter, products like Basaglar and Admelog are considered "follow-on biologics" from FDA's perspective, and are not true biosimilars). During Q&A on Sanofi's 3Q17 earnings call, management shared their assumption that biosimilars will be interchangeable in the US by 2020 - Mr. Conterno strongly disagreed on today's call. He explained that the clinical studies required for an interchangeability designation are much more involved than those conducted in phase 3 for Admelog or for Basaglar (biosimilar basal insulin glargine). Per FDA's guidance on interchangeability of biosimilars, this includes RCTs showing safety and sustained efficacy with at least two back-and-forth switches between the biosimilar and the originator. In addition, to be interchangeable, the biosimilar must be dispensed in the same type of device as the originator. In fact, Lilly chose not to pursue patent infringement litigation against Sanofi because the only remaining patents on Humalog pertained to the KwikPen device, and management recognized that this is "fundamentally different" from Sanofi's SoloStar device - the flip side is that this might stand in the way of an interchangeability designation for Admelog. In sum, Lilly management is prepared for some adverse impact on the Humalog franchise - although this could be delayed slightly depending on when Sanofi launches Admelog in US pharmacies - but doesn't seem too worried about the additional decline in volume that would come from interchangeability between Humalog and Admelog.

- **Management noted during Q&A that Humulin U500 has grown into a very important product within Lilly's insulin portfolio.** This fits with what we've seen on the conference circuit, with Lilly product theaters dedicated to Humulin U500, in some cases instead of Basaglar or Humalog. Mr. Conterno underscored that human insulin remains a "key franchise" for the company.

- **Overall, insulin received little air time on this call, besides Basaglar being listed as a volume growth driver in 2018.** The company recently initiated a phase 3 program for its ultra-rapid-acting insulin candidate, but there was no mention of this. There was significantly more focus on the GLP-1 agonist business, and as we've gathered from all the major insulin manufacturers (Novo Nordisk, Sanofi, Lilly), they can no longer expect rising insulin profits to fuel growth given immense pricing pressure.

4. OUTCOMES STUDY OF SGLT-2 INHIBITOR JARDIANCE IN CKD TO BEGIN IN 2018; REGULATORY SUBMISSION PLANNED FOR COMBINATION OF EMPAGLIFLOZIN, DPP-4 LINAGLIPTIN, & METFORMIN XR

Lilly/BI have been silent on the planned CKD outcomes study for SGLT-2 Jardiance (empagliflozin) since the initial press release in June, but management shared today that this study will definitely begin in 2018. As background, empagliflozin showed a significant 39% risk reduction for nephropathy in EMPA-REG OUTCOME (HR=0.61, 95% CI: 0.53-0.70; p<0.001). J&J's Invokana (canagliflozin) showed a similarly positive result for renal protection in CANVAS, pointing to a possible class effect for SGLT-2 inhibitors, which has sparked interest from manufacturers in a potential chronic kidney disease (CKD) indication for these drugs. J&J's CREDENCE study is investigating canagliflozin in people with type 2 diabetes and kidney disease (expected to complete June 2019). AZ's Dapa-CKD trial is investigating Farxiga (dapagliflozin) in people with CKD with or without diabetes (expected to complete November 2020). Lilly/BI's still-unnamed study will also enroll participants with or without diabetes. No other details on study design were discussed, and boy are we curious. This is certainly an area to watch: For one, diabetes-related nephropathy is an area of high unmet need, and no new treatments have been approved since the beginning of the century (irbesartan and losartan in 2000). Thought leaders have expressed distinct enthusiasm for the renal protective properties of SGLT-2 inhibitors, and Dr. David Fitchett suggested at ESC 2017 that data from these renal outcomes studies could help remove the contraindication for these agents in patients with lower eGFR - this would extend SGLT-2 inhibitors, an advanced class of therapies with profound clinical benefits, to a much wider spectrum of the diabetes population.

- **While not discussed on the call, Lilly/BI have also launched the EMPEROR clinical program to investigate empagliflozin in heart failure.** Jardiance's CV benefits received little attention, which stands in stark contrast to Lilly's 2017 financial guidance update (this was right after the FDA approved a new CV indication for Jardiance, the first of its kind for a diabetes product).
- **Lilly's presentation slides also noted that an empagliflozin/linagliptin (DPP-4 inhibitor Tradjenta)/metformin XR combination will be submitted to FDA in 2018.** To our knowledge, this would be the first triple combination in a single oral tablet for diabetes - it's so exciting! The potential benefits to patients are tremendous, including substantially reduced pill burden, a milder side-effect profile due to lower doses of component monotherapies, and superior efficacy from complementary mechanisms of action. That said, Lilly/BI's fixed-dose combination Glyxambi (empagliflozin/linagliptin) hasn't gained much commercial traction since launch, in part because the companies haven't invested heavily in the combo product vs. standalone Jardiance, so we're somewhat surprised to see this triple combination pop up in the late-stage pipeline. We were disappointed not to hear more details on this planned regulatory filing, but we'll keep our eyes and ears peeled in 2018.

5. NASAL GLUCAGON FILING CONFIRMED FOR 2018; LILLY BECOMES THE LEADER IN GLUCAGON COMPETITIVE LANDSCAPE

Management announced that Lilly will submit its nasal glucagon candidate to the FDA in 2018. We previously heard from Dr. Jessica Castle at DTM 2016 that the candidate would be filed in 1H18, but this is the first confirmation of timeline directly from the company. No more specific details were provided, so an FDA decision could be expected anytime between 1Q19 and 1Q20 (assuming a standard 10-12 month regulatory review period). Very notably, Dr. Elizabeth Seaquist presented real-world data on Lilly's nasal

glucagon at ADA 2017, showing a 96% recovery rate from hypoglycemia within 30 minutes and extremely high satisfaction scores from caregivers. Based on these findings, nasal glucagon would be a huge step up from current options for hypoglycemia rescue treatment - native glucagon kits place immense burden on caregivers, requiring a lengthy, complicated reconstitution process and leaving too much room for error. With a 2018 filing, Lilly would forge ahead as the leader in the glucagon competitive landscape. Phase 3 studies are ongoing for Xeris' advanced glucagon and for Zealand's dasiglucagon, but these candidates presumably won't reach FDA's desk until after 2018.

6. A DATA-HEAVY YEAR COMING UP FOR DPP-4 INHIBITOR TRADJENTA: RESULTS EXPECTED FROM CARMELINA AND CAROLINA CVOTS

Lilly's 2018 will feature three major CVOT readouts: In addition to highly-anticipated REWIND results for GLP-1 Trulicity, we'll see full results from CARMELINA for BI-partnered DPP-4 inhibitor Tradjenta (linagliptin) and possible topline results from CAROLINA comparing linagliptin vs. SU glimepiride. According to ClinicalTrials.gov, CARMELINA is expected to complete this month. Data will likely be presented at a major diabetes meeting next year, perhaps ADA 2018 in Orlando or EASD 2018 in Berlin, though management provided no hints. CAROLINA was listed in the company's presentation as an internal readout for 2018, which means the findings may not be announced publically, but we're hoping for at least a topline release by year-end (REWIND was also listed as an internal readout, and management promised topline data by late 2018 - see above). We're particularly looking forward to CAROLINA results as they could finally tip the scale away from sulfonylureas as the most common second-line diabetes therapy (and a frequently-prescribed first-line therapy). As we've said many times, we do not think that SUs should even be available, given that they would surely not be approved today, although they are cheap, that should not be a good enough reason to prescribe them (TZDs have lots of issues too but we'd rather see them as the generic of choice after metformin). Head-to-head outcomes data that highlights the safety issues associated with SUs - CV harm, hypoglycemia, weight gain, and beta cell burnout over the long term - and shows Tradjenta to be a safer, more effective alternative could have major implications on treatment guidelines and real-world standards of care. As Dr. Robert Ratner explained at CMHC 2016, sulfonylureas retain their place in the ADA treatment algorithm because of their low cost, but compelling outcomes data could make the case for their removal. To this end, we also look forward to results from the ongoing GRADE study, sponsored by NIH.

7. HIGH-DOSE DULAGLUTIDE MOVING INTO PHASE 3 FOR TYPE 2 DIABETES; NEW STUDIES SET TO LAUNCH IN 2018

Phase 3 trials of high-dose dulaglutide (3.0 mg and 4.5 mg) in type 2 diabetes are slated to begin in 2018. This comes on the heels of positive phase 2 data: Management did not share any specific results, but expressed distinct excitement around this study on Lilly's 3Q17 earnings call. We're eager for more information on both phase 2 and phase 3. When can we expect the full phase 2 data? How will the phase 3 trial be designed, and what characteristics will be important in the patient population enrolled? Notably, Lilly's presentation stipulates that this soon-to-begin phase 3 trial will be a type 2 diabetes study, whereas Novo Nordisk branded its high-dose GLP-1 agonist liraglutide (Saxenda) for obesity. Lilly has previously shown a laser focus on type 1 and type 2 diabetes rather than obesity, and this seems to persist for the time being. That said, weight loss is one of the key benefits to GLP-1 agonist therapy, and we imagine the body weight effects of high-dose dulaglutide are even more powerful than what we've seen for Trulicity (available at 0.75 mg and 1.5 mg doses). Again, we await the data.

LILLY DIABETES PIPELINE SUMMARY

Candidate	Phase	Timeline/Notes
Jardiance (empagliflozin) in type 1 diabetes	Phase 3	EASE-2 and EASE-3 trials completed in September 2017 per ClinicalTrials.gov

Jardiance (empagliflozin) in heart failure	Phase 3	EMPEROR HF-Preserved and EMPEROR HF-Reduced trials initiated March 2017, both expected to complete June 2020
Jardiance (empagliflozin) in chronic kidney disease	Phase 3	Dedicated kidney outcomes trial announced June 2017; Scheduled to begin 2018
Nasal glucagon	Phase 3	Acquired from Locemia; FDA submission planned for 2018; Real-world data presented at ADA 2017
LY900014 (ultra-rapid-acting insulin lispro)	Phase 3	Phase 3 initiated 3Q17: PRONTO-T1D expected to complete September 2019, PRONTO-T2D expected to complete February 2019; Phase 2 data presented at ADA 2017 (type 1, type 2)
DACRA-042 (dual amylin calcitonin receptor agonist)	Phase 2	Acquired through partnership with KeyBioscience in June 2017; No study timing shared
High-dose dulaglutide (3 mg and 4.5 mg once-weekly)	Phase 2	Phase 3 studies in type 2 diabetes to begin 2018; Phase 2 trial completed August 2017
GIP/GLP-1 dual agonist	Phase 2	Phase 2 study ongoing, expected to complete May 2018; Phase 1 trial completed June 2017
LY3015014 (PCSK9 inhibitor)	Phase 2	Highlighted in May 2016 R&D update; Potential for greater durability and less frequent dosing than others in class
Soluble glucagon	Phase 1	Announced in May 2016 R&D update; Candidate is a short-acting, soluble, stable glucagon; Potential use in bi-hormonal closed-loop systems
Basal insulin/dulaglutide fixed-ratio combination	Phase 1	Likely a combination of once-weekly "next-generation basal insulin" and Trulicity to support once-weekly dosing; Added to pipeline in 4Q16

DACRA-089 (dual amylin calcitonin receptor agonist)	Phase 1	Acquired through partnership with KeyBioscience in June 2017; No study timing shared
GLP-1/glucagon dual agonist (once-weekly)	Phase 1	Announced in May 2016 R&D update; Oxyntomodulin analog; Under development for type 2 diabetes and NASH; Advanced into phase 1 in 4Q16
GPR142 agonist	Phase 1	Highlighted during company's 2Q17 update and listed on pipeline page
Next-generation basal insulin	Preclinical (unclear if standalone development is still ongoing)	Announced in May 2016 R&D update; Potential for combination with Trulicity
Long-acting once-weekly glucagon	Preclinical	Announced in May 2016 R&D update; Potential for co-formulation with Trulicity or with GIP/GLP-1 dual agonist
Oral GLP-1 agonist(s)	Preclinical	Confirmed in May 2016 R&D update; Remains a key pipeline priority according to 2018 financial guidance call

Questions and Answers

ON TRULICITY, REWIND, AND THE GLP-1 AGONIST CLASS

Q: How are you thinking about the growth trajectory for Trulicity in 2018? How does this fit into market growth for GLP-1 as a class?

Mr. Enrique Conterno (Head, Lilly Diabetes): Expansion of the GLP-1 class is one of the biggest opportunities in diabetes therapy, given the benefit that these agents offer. We expect continued strong growth of the class. We don't provide exact commentary on that, but we see important catalysts including the CV indication for Victoza and increased promotion due to the market entry of semaglutide. Both of these changes, we see as positive for class growth. And quite frankly, these changes are really important as we think about the long-term future of the GLP-1 class. We expect significant growth for Trulicity in 2018.

Mr. Phil Johnson (SVP of Finance and Treasurer, Lilly): I'd add that we see GLP-1 agonists, and particularly a drug with a profile like Trulicity, as very strong products for first injection. Most of these prescriptions are still going to basal insulin. That could be flipped to GLP-1 as a patient's first injectable therapy rather than basal. That's a huge opportunity to grow the class.

Q: GLP-1 seems to be one of the few segments of the diabetes market where there hasn't been that much formulary restriction to-date. Do you expect that to continue in 2018, 2019, 2020?

Mr. Conterno: We do see some restrictions that have happened in the GLP-1 class. Maybe contracts aren't going totally exclusive, but we do see trends of narrowing. In those instances, the chosen products have been

the market-leading products. It's fair to say that there's more differentiation in the GLP-1 class than mealtime insulins, DPP-4s, and so forth - that is to say, our perspective has always been that we like to compete in a more open access environment, because our product will differentiate itself. We're pleased that Trulicity continues to have good access, and even improved access, as we look to 2018.

Q: REWIND is listed as an internal readout for 2018, and I'm wondering why that's not an external readout? What should we read into that, if anything?

Mr. Conterno: In mid-2018, we expect to reach the number of required events for REWIND. As you all know, this is an event-dependent trial. Beyond just an internal readout, we also expect to issue a topline press release late in 2018. There's nothing more to read into that. We want to get into an important medical meeting to disclose these results, and we'll do that as soon as we can.

Q: Do you think we're at the point in GLP-1 where you *need* to show CV benefit, given Victoza having it on its label?

Mr. Conterno: Look, based on the data we've seen - positive studies, marginally positive studies, and neutral studies in the GLP-1 class - we feel good about our chances to have a positive study with REWIND. That's our current thinking, but of course we need to wait for the results. Victoza does have a CV indication. Semaglutide does not at this stage. I've shared what my thinking is, and I believe our chances are good.

Q: I know this isn't relevant to 2018 guidance per se, but what are your thoughts on Novo Nordisk's oral GLP-1 program? What impact would this have down the line?

Mr. Conterno: Oral GLP-1 is an area of interest to us. We're working close on this in preclinical development. When it comes to Novo Nordisk's product in development, we really need to wait and see all the data - not just on glycemic control, but also side-effect profile, and what they're able to show from a CV perspective as well.

Q: With the semaglutide approval, there's this belief out there that it's going to take some time to get payers on board, and that the real impact won't be until 2019. What visibility do you have on Trulicity coverage for 2019, as a defense already?

Mr. Conterno: Clearly, Trulicity is performing well. It is becoming more and more relevant, and that's a great strength for us as we look at our contracting for 2019. That process has already started within Part D, but commercial tends to lag a bit. There are few comments I can make on this. The questions around semaglutide access? Those are questions for Novo Nordisk. We're well-prepared for their entry, and we're focused on the great experience that our product provides to patients and their physicians.

ON INSULIN

Q: You mentioned Humulin and Humalog being about flat. What are your expectations around pricing, moving forward?

Mr. Conterno: On Humalog and Humulin, the business right now is pretty stable, but of course we have an important competitor coming in with follow-on lispro from Sanofi (Admelog). It's unclear to us when they're launching this product. So, it would be premature for me to speculate on what we expect when it comes to pricing dynamics. Human insulin is another key franchise for us. We do see continued growth, particularly from Humulin U500, which is becoming more and more important within our insulin portfolio.

Q: During the Q3 earnings season, I asked Sanofi if they expect substitutable biosimilar insulins anytime soon. Their candor surprised me - they said by 2020. And, they explained that this was factored into their guidance already. I'm wondering your thoughts on this.

Mr. Conterno: Some may say that when we look at insulins even today, they're already considered to be substitutable, because we do see payers treat them as such based on formulary access. As I understand it, you're referring to interchangeability of insulins, where pharmacists can make the switch without physician intervention. You'll have to ask Sanofi for the basis of their forecast. We don't see this as a possibility in the very near term - a number of studies would need to be conducted to meet all the requirements of interchangeability. It could happen over time, and maybe insulin is one of the places where this will happen

first, but we don't have a prediction for significantly soon. There's already significant pricing pressure on insulin, and we already have US pricing pressure baked into our guidance.

-- by Payal Marathe and Kelly Close