CLOSER LOOK

MEMORANDUM

Novo Nordisk 4Q16 - Overall diabetes and obesity portfolio up 3% as reported to DKK 23.8 billion (~$3.9 billion); Strong performance continues for Tresiba, Victoza, and Saxenda; Faster-acting insulin aspart re-submission expected in next three months - February 6, 2017

Executive Highlights

- Novo Nordisk's overall diabetes and obesity portfolio grew 3% year-over-year (YOY) as reported (5% operationally) and 6% sequentially to DKK 23.8 billion (~$3.9 billion). Full year sales totaled DKK 85.6 billion (~$13.2 billion), a 4% YOY increase (6% operationally). Management highlighted Tresiba (insulin degludec), Victoza (liraglutide), and Saxenda (liraglutide 3.0mg) as key drivers of growth.
- Tresiba continued to be a bright spot for Novo Nordisk, growing 46% sequentially to DKK 1.6 billion (~$218 million) in 4Q16. Full year revenue for this growing star of the company's insulin portfolio totaled DKK 4.1 billion (~$608 million), a greater than three-fold YOY increase. It accounted for a whopping 49% of the company's overall diabetes/obesity portfolio growth for the year.
- Victoza revenue grew 10% YOY as reported and operationally to DKK 5.4 billion ($774 million) in 4Q16, a 6% sequential increase. Victoza posted DKK 20.0 billion (~$2.9 billion) in sales for full year 2016, an 11% rise as reported (12% operationally) from 2015. It was responsible for 33% of the company's overall diabetes/obesity portfolio growth in 2016.
- Saxenda's (liraglutide 3.0 mg for obesity) success continued with DKK 540 million (~$77 million) in 4Q16 revenue, more than tripling YOY and increasing a whopping 29% sequentially. The obesity drug posted DKK 1.6 billion (~$233 million) in sales for 2016, its first full year on the market. Saxenda was responsible for 19% of Novo Nordisk's overall growth (including non-diabetes products) in 2016.
- On the pipeline front, Novo Nordisk shared that faster-acting insulin aspart will be resubmitted to the FDA in the next three months, fixed-ratio combination Xultophy (insulin degludec/liraglutide) will be launched in the US in 1H17, and a phase 2 trial of once-daily injectable GLP-1 agonist semaglutide has completed. Management also highlighted a number of phase 1 and 2 trial initiations for the company's diabetes and obesity pipeline candidates.

Novo Nordisk just provided its 4Q16 and full year earnings update in a call led by newly-minted CEO Mr. Lars Jørgensen. Below we detail our top highlights and commentary on the performance of Novo Nordisk's diabetes products and the progress of its diabetes pipeline. You can also check out the company's press release and presentation slides and access a webcast replay.

Top Financial Highlights

1. Novo Nordisk's overall diabetes and obesity portfolio grew 3% year-over-year (YOY) as reported (5% operationally) and 6% sequentially to DKK 23.8 billion (~$3.9 billion). Full year sales totaled DKK 85.6 billion (~$13.2 billion), a 4% YOY increase (6% operationally). Management highlighted the GLP-1 agonist Victoza (liraglutide), its obesity counterpart Saxenda (liraglutide 3.0mg), and the company's new generation insulin portfolio (Tresiba [insulin degludec], Xultophy [insulin degludec/liraglutide], and Ryzodeg [insulin degludec/insulin aspart)) as key drivers of growth. Novo Nordisk's new-generation insulins accounted for the lion's share of growth in the company's diabetes portfolio at 52% in 4Q16 (49% for 2016), while Victoza was responsible for 24% of growth in 4Q16 (33% for 2016) and Saxenda was

responsible for 16% of growth in 4Q16 (18% for 2016). Modern insulins did less well - not surprising given pricing pressure and the loss of a key contract for NovoLog, and given the movement of some patients from Levemir to Tresiba.

2. Tresiba continued to be a bright spot for Novo Nordisk, growing 46% sequentially to DKK 1.6 billion (~$218 million) in 4Q16. Full year revenue for this growing star of the company's insulin portfolio totaled DKK 4.1 billion (~$608 million), a greater than three-fold YOY increase. Revenue for Novo Nordisk's overall new generation insulin portfolio (consisting of Tresiba, Xultophy [insulin degludec/liraglutide], and Ryzodeg [insulin degludec/insulin aspart]) tripled YOY and rose 33% sequentially to DKK 1.7 billion (~$232 million) in 4Q16. In full year 2016 the portfolio grew three-fold to DKK 4.4 billion (~$661 million). We expect the portfolio will be further bolstered in future quarters by the recent US approval of Xultophy, which management specified is expected to launch in the first half of 2017.

3. Victoza revenue grew 10% YOY as reported and operationally to DKK 5.4 billion ($774 million) in 4Q16, a 6% sequential increase. Victoza posted DKK 20.0 billion (~$2.9 billion) in sales for full year 2016, an 11% rise as reported (12% operationally) from 2015. Novo Nordisk is benefiting from underlying GLP-1 agonist class growth (which now accounts for nearly 10% of the value share of the total diabetes care market) even though its TRx share, now at 50% by volume, is declining from the 60% range as more competitors enter the market.

4. Saxenda's (liraglutide 3.0 mg for obesity) success continued with DKK 540 million (~$77 million) in 4Q16 revenue, more than tripling YOY and increasing a whopping 29% sequentially. The obesity drug posted DKK 1.6 billion (~$233 million) in sales for 2016, its first full year on the market. Saxenda was responsible for 19% of Novo Nordisk's overall growth (including non-diabetes products) in 2016 - quite impressive given the falling sales of virtually every other obesity drug on the market.

5. Novo Nordisk's modern insulins (Levemir [insulin determir], NovoLog [insulin aspart], and NovoMix) experienced another tough quarter, largely due to underlying challenges in the insulin market, particularly in the US. The company's modern insulin portfolio as a whole experienced a 10% YOY decline in 4Q16 as reported (falling 8% operationally). This was largely driven by Levemir's 19% YOY drop as reported (-17% operationally) to DKK 4.1 billion ($586 million), as well as NovoLog's 3% drop as reported (-2% operationally) to DKK 5.5 billion ($794 million), and NovoMix's 8% drop as reported (-5% operationally) to DKK 2.6 billion ($372 million). For the full year, Novo Nordisk's modern insulin portfolio fell 5% as reported (-3% operationally) to DKK 47.5 billion (~$7 billion). We would, of course, expect declines for Levemir as patients (the lucky ones) move to Tresiba but the pricing pressure and competition has obviously never been as intense on the rapid acting analog front.

6. Human insulin experienced a relatively strong quarter with revenue growing 6% YOY as reported (8% operationally) to DKK 2.9 billion (~$422 million) in 4Q16. Sequentially sales grew 6%. Full year revenue for human insulin remained steady at DKK 11.1 billion (~$1.6 billion), a 1% decline as reported and 2% uptick operationally. We wonder if this is due to payers wanting to see more human insulins versus analogs prescribed and/or patients who have very high co-pays looking for cheaper options.

Pipeline Highlights

7. Novo Nordisk shared that it has met with the FDA regarding the Complete Response Letter for faster-acting insulin aspart and a class II resubmission of the New Drug Application (NDA) for the product is expected in the next three months, with an approval hopefully by the end of 2017. The product is already approved in the EU and Canada under the trade name Fiasp and will be launched in these markets in the first half of 2017.

8. The US launch of basal insulin/GLP-1 agonist fixed-ratio combination Xultophy (insulin degludec/liraglutide) is expected in the first half of 2017. Management emphasized that the somewhat later launch is due to its current focus on impressing upon payers the value of Xultophy in order to establish strong market access prior to launch without conceding too-large rebates that may undermine Victoza and Tresiba. As a reminder, Sanofi's basal/GLP-1 Soliqua is already out and we look forward to hearing about this when

Sanofi reports - it is priced lower than Xultophy will be and we know they are also very intent on strong access.

9. Management highlighted the December 2016 US and EU submission of once-weekly injectable GLP-1 agonist semaglutide (decisions expected in 4Q17) and that the Japan submission is expected in the next three months. In Q&A, management continued to emphasize that the finding of increased retinopathy in the SUSTAIN 6 trial is likely due to the very rapid substantial glucose-lowering produced by semaglutide rather than a characteristic of semaglutide itself. That said, the company acknowledged that regulatory agencies may require additional data on this front.

10. A phase 2 trial (n=706) for a once-daily injectable formulation of semaglutide has completed, with 0.3 mg of daily semaglutide producing a mean A1c reduction of 1.9% (vs. 1.3% with liraglutide) and a very impressive mean weight loss of 8.2 kg (~18.1 lbs, vs. 3.7 kg [~8.2 lbs] with liraglutide). Notably, Novo Nordisk initiated a phase 2 trial of once-daily semaglutide in NASH in November 2016, with an expected completion date in 2019, and a phase 2 trial in obesity is expected to report in the next six to nine months.

11. All ten trials in the phase 3 PIONEER program for oral semaglutide have initiated, with some expected to begin completing in 2018.

12. In terms of Novo Nordisk's obesity pipeline, management highlighted the initiation of a phase 1 trial of a once-weekly FGF21 analog (NN9499) for the treatment of obesity. The company also appears to have added a novel GLP-1/glucagon dual agonist (NN9277) to its phase 1 pipeline for obesity.

13. Novo Nordisk's treatment combination of anti-IL-21 and GLP-1 agonist liraglutide for type 1 diabetes with residual beta cell function received an orphan drug designation from the FDA in January 2017. We're excited to see Novo Nordisk continue its efforts in non-insulin therapies and liraglutide for type 1 diabetes following the somewhat disappointing results from the ADJUNCT ONE and TWO trials.

Table 1: 2016 Financial Results for Novo Nordisk's Major Diabetes and Obesity Products

Product	2016 Revenue (billions)	Year-Over-Year Reported (Operational) Growth
Modern Insulins	DKK 47.5 (~$7.0)	-5% (-3%)
- NovoLog	DKK 19.9 (~$2.9)	-4% (-2%)
- NovoMix	DKK 10.5 (~$1.5)	-6% (-2%)
- Levemir	DKK 17.1(~$2.5)	-7% (-4%)
Human Insulin	DKK 11.1 (~$1.6)	-1% (2%)
Next-Generation Insulins (Tresiba, Xultophy, Ryzodeg)	DKK 4.4 (~$0.7)	210% (212%)
- Tresiba	DKK 4.1 (~$0.6)	221% (219%)
Victoza	DKK 20.0 (~$2.9)	11% (12%)
Saxenda	DKK 1.6 (~$0.23)	(245%)
Total Diabetes/Obesity Portfolio	DKK 85.6 (~$13.2)	4% (6%)

Table 2: 4Q16 Financial Results for Novo Nordisk's Major Diabetes and Obesity Products

Product	4Q16 Revenue (billions)	Year-Over-Year Reported (Operational) Growth	Sequential Reported Growth
Modern Insulins	DKK 12.2 (~$1.8)	-10% (-8%)	4%
- NovoLog	DKK 5.5 (~$0.8)	-3% (-2%)	13%
- NovoMix	DKK 2.6 (~$0.4)	-8% (-5%)	2%
- Levemir	DKK 4.1 (~$0.6)	-19% (-17%)	-6%
Human Insulin	DKK 2.9 (~$0.4)	6% (8%)	6%
Next-Generation Insulins (Tresiba, Xultophy, Ryzodeg)	DKK 1.5 (~$0.2)	231% (269%)	33%
- Tresiba	DKK 1.5 (~$0.2)	--	46%
Victoza	DKK 5.4 (~$0.8)	10% (10%)	6%
Saxenda	DKK 540 (~$0.08)	148%	29%
Total Diabetes and Obesity Portfolio	DKK 23.8 (~$3.9)	3% (5%)	6%

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Financial Highlights

1. DIABETES/OBESITY PORTFOLIO: MODEST GROWTH CONTINUES WITH 3% YOY RISE

Novo Nordisk's overall diabetes and obesity portfolio grew 3% year-over-year (YOY) as reported (5% operationally) and 6% sequentially from 3Q16 to DKK 23.8 billion (~$3.9 billion). Full year sales totaled DKK 85.6 billion (~$13.2 billion), a 4% YOY increase as reported (6% operationally). Management highlighted the GLP-1 agonist Victoza (liraglutide), its obesity counterpart Saxenda (liraglutide 3.0 mg), and the company's new generation insulin portfolio (Tresiba [insulin degludec], Xultophy [insulin degludec/liraglutide], and Ryzodeg [insulin degludec/insulin aspart]] as key drivers of growth. Novo Nordisk's new-generation insulins accounted for the lion's share of growth in the company's diabetes portfolio at 52% in 4Q16 (49% for 2016), while Victoza was responsible for 24% of growth in 4Q16 (33% for 2016). Saxenda was responsible for 19% of growth in Novo Nordisk overall product portfolio (including diabetes, obesity, and hemophilia) in 2016. Modern insulins did less well - not surprising given pricing pressure and the loss of a key contract for NovoLog, and given the movement of some patients from Levemir to Tresiba. Much more on this below.

- **2016 has been a more modest year for Novo Nordisk, with low single digit growth in 2Q16, 3Q16, and now 4Q16 to contrast the ~20-25% growth that characterized 2015.** This was reflected in a fairly substantial adjustment to Novo Nordisk's financial guidance in 3Q16, in which operating profit target growth was reduced to 5%, down from 10% as per Novo Nordisk's 4Q15 update. Management attributed this change also to the challenging pricing environment in the US (by far Novo Nordisk's largest commercial market), especially as it pertains to insulin. This is further indication of how challenging the diabetes arena has become even for leaders like Novo Nordisk with decades of experience and a robust portfolio of clinically differentiated products.

Figure 1: Total Diabetes/Obesity Sales (1Q12-4Q16)

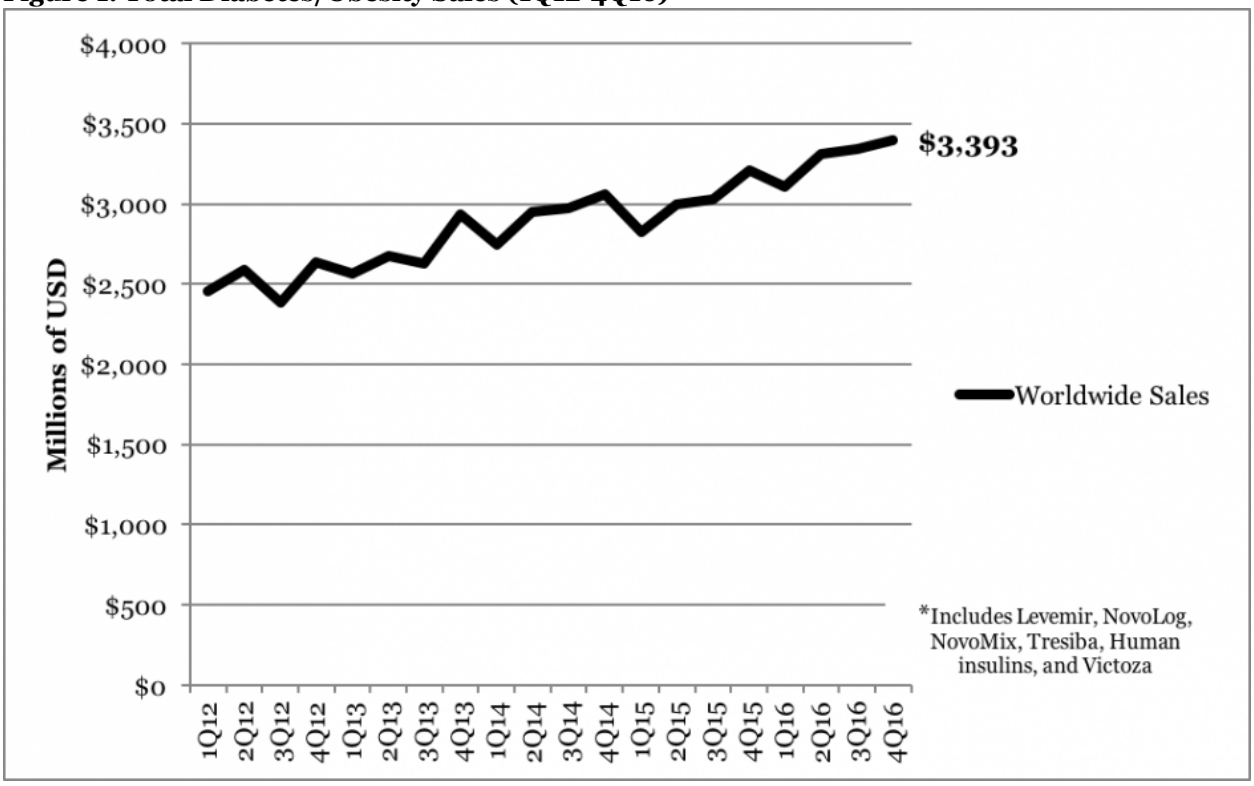


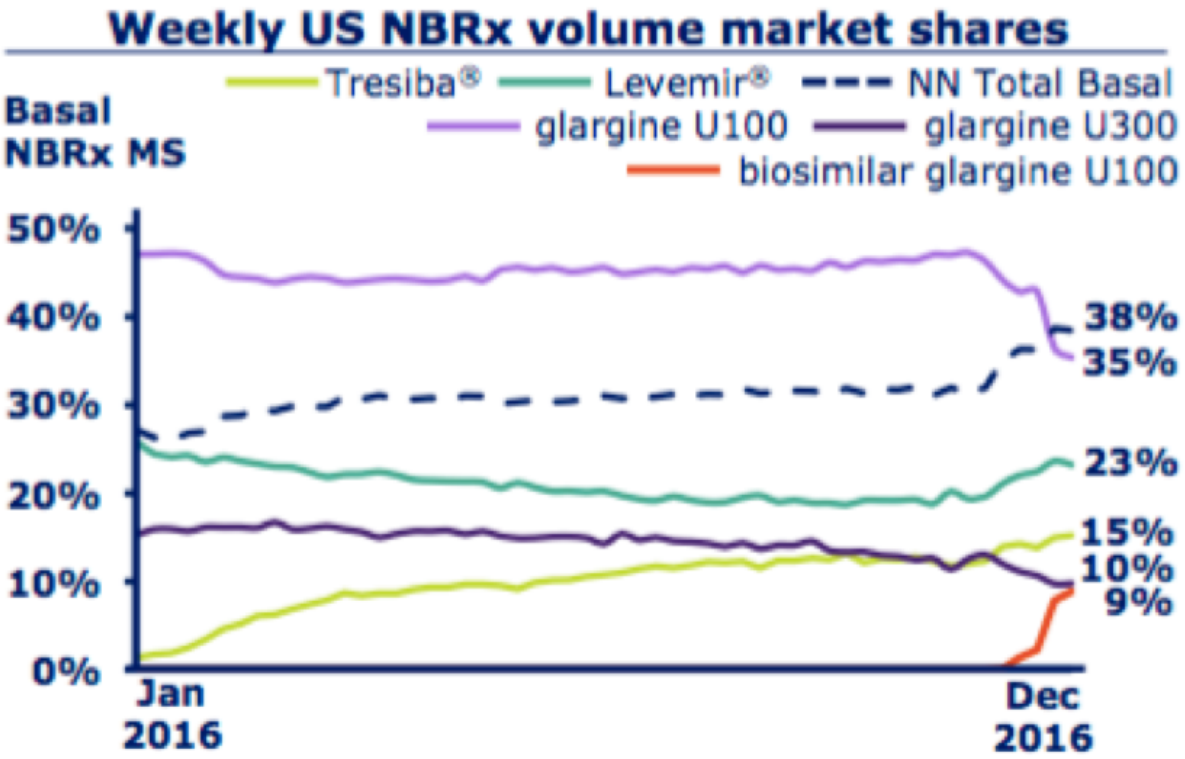
Table 3: Whole-Company Sales and Growth by Geography (2016 full year)

	Share of Sales	Reported (Operational) Growth	Share of Growth
USA	51%	4% (4%)	37%
Europe	19%	-1% (2%)	5%
International Operations	13%	2% (14%)	32%
Region China	9%	6% (12%)	19%
Pacific	8%	10% (5%)	7%
Total	100%	4% (6%)	100%

2. TRESIBA: 46% SEQUENTIAL GROWTH TO DKK 1.6 BILLION (~$232 MILLION)

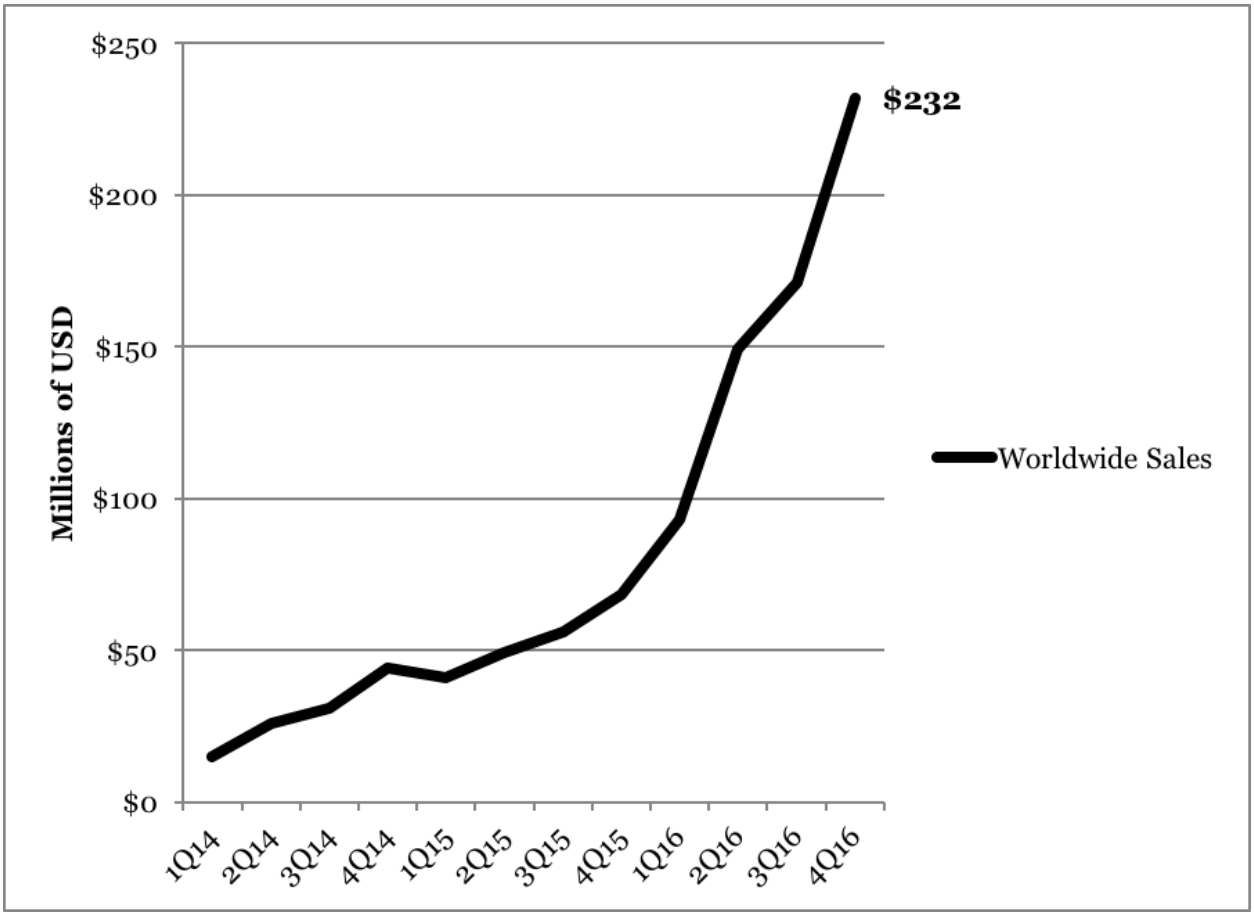
Tresiba (insulin degludec) continued to be a bright spot for Novo Nordisk, growing 46% sequentially to DKK 1.6 billion (~$218 million) in 4Q16. Full year revenue for this growing star of the company's insulin portfolio totaled DKK 4.1 billion (~$608 million), a greater than three-fold YOY increase. We think it is safe to say that Tresiba will be a blockbuster in 2017 based on this result. Management highlighted encouraging feedback on Tresiba from patients and prescribers and noted that the product's rollout continues, with Tresiba available in 52 countries to date. Following its US launch in January 2016, Tresiba currently holds nearly 6% of the basal insulin market share by volume, a figure management believes will only increase following advantageous formulary positioning for Tresiba with CVS Health, where it is favored above the next-generation competitor Sanofi's Toujeo (U300 insulin glargine). Management also highlighted Tresiba's accessibility, with approximately 75% coverage for patients in commercial channels and Medicare Part D combined. In international markets, the product is performing particularly well in Japan, where it holds a 39% share of the basal insulin market by value (notably Tresiba has comparable reimbursement as Lantus in this market). Value share is also strong in Italy (30%), Switzerland (29%), Greece (24%), and Mexico (21%), but less so in markets such as the UK (4%) and Brazil (9%) where market access for Tresiba is more restricted. See slide 7 of the company's presentation for a full rundown of the drug's market penetration by geography.

- **Novo Nordisk outlined the shifting dynamics of the US basal insulin market (slide 8 below).** In terms of the new generation basal insulins, Tresiba holds an edge over Toujeo, with 15% NBRx share and 10% NBRx share, respectively. Novo Nordisk's combined basal insulin portfolio new-to-brand prescription (NBRx) share of 38% now outstrips that of Sanofi's Lantus (U100 insulin glargine). As of December 2016, Lantus held 35% of the NBRx share (down sharply from nearly 50% at the beginning of 2016). On the other hand, Sanofi's combined basal insulin franchise (with Lantus and Toujeo) still leads the market with 45% NBRx share. We found the rapid uptake of Lilly/BI's newly-launched Basaglar (biosimilar insulin glargine) impressive - the product was only launched in mid-December 2016 and already won 9% of the NBRx share - nearly as much as Toujeo's share - after only two weeks on the market. In our view, this is clearly an indication of the demand for lower-cost insulin analogs, also reflected in the immense public frustration over rising insulin prices throughout 2016.



- **Management highlighted the recent announcement of topline results from the DEVOTE CVOT, in which Tresiba demonstrated non-inferiority to Sanofi's Lantus (insulin glargine U100) on a primary endpoint of three-point MACE (non-fatal MI, non-fatal stroke, and CV death).** The hazard ratio for CV events was 0.91 in favor of Tresiba, though the difference was not statistically significant. Tresiba additionally showed 40% reduced risk for severe hypoglycemia and a 54% reduced risk for severe hypoglycemia overnight vs. Lantus. 27% fewer participants in the Tresiba treatment arm experienced an episode of severe hypoglycemia - a matter of huge many real-world importance to patients, in our view. These resoundingly neutral results are long-awaited - the DEVOTE trial was initiated in response to the Complete Response Letter issued by the FDA for Tresiba in 2013. The requirement for a CVOT delayed Tresiba's launch to early 2016, following the product's late 2015 approval on the basis of interim data from DEVOTE. The neutral results from DEVOTE are not unexpected given the product's earlier approval, but are reassuring nonetheless.
- **Revenue for Novo Nordisk's overall new generation insulin portfolio (consisting of Tresiba, Xultophy [insulin degludec/liraglutide], and Ryzodeg [insulin degludec/ insulin aspart]) tripled YOY and rose 33% sequentially to DKK 1.7 billion (~$232 million) in 4Q16.** In full year 2016 the portfolio grew three-fold to DKK 4.4 billion (~$661 million), accounting for 49% of Novo Nordisk's diabetes portfolio growth for the year (and 52% for the quarter). We expect the portfolio will be further bolstered in future quarters by the US approval of Xultophy, which management specified is expected to launch in the first half of 2017 (it is currently on pharmacy shelves in Switzerland, the UK, Sweden, Hungary, Greece, Cyprus, and most recently the Czech Republic, France, and the Netherlands). Much more on Xultophy below in our discussion of Novo Nordisk's pipeline updates.

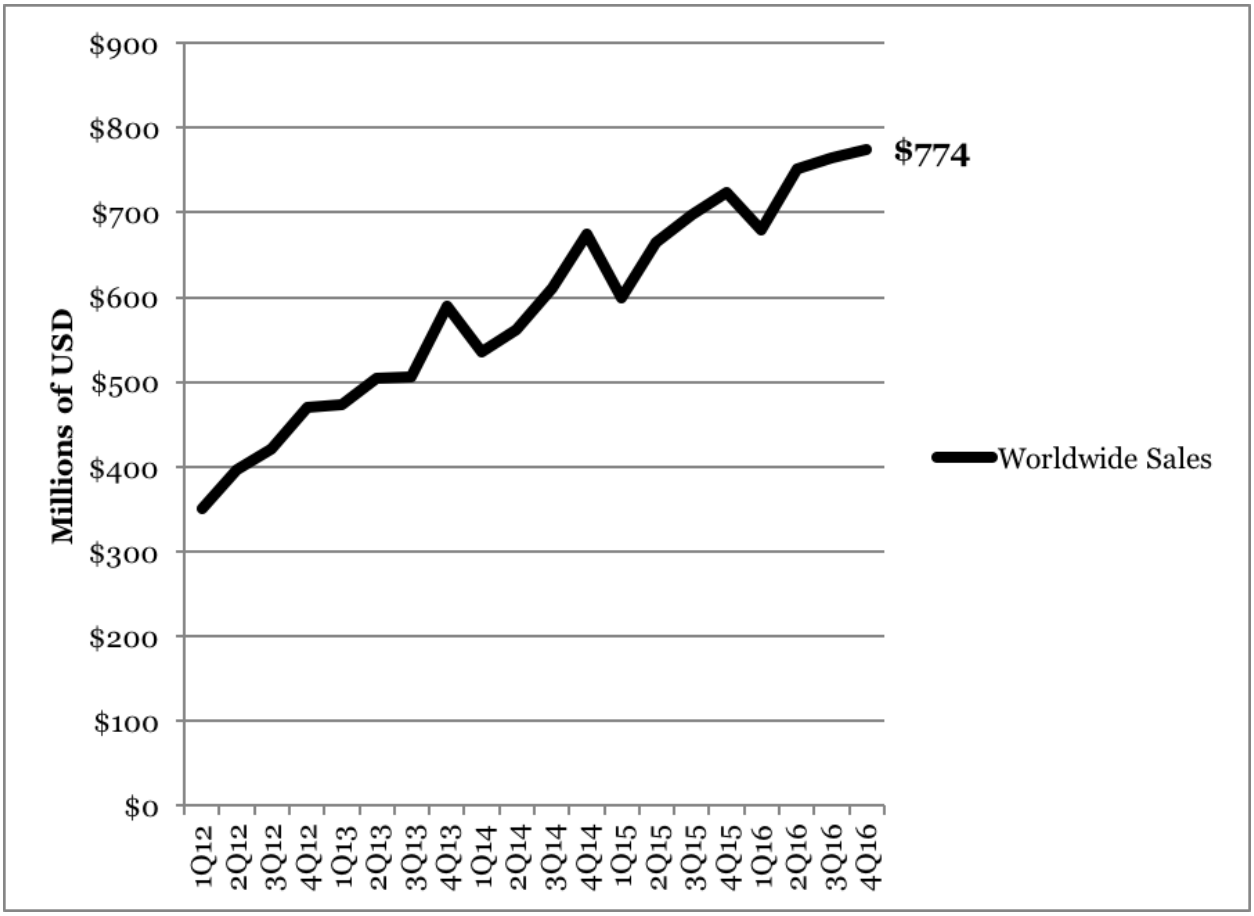
Figure 2: New-Generation Insulin Sales (1Q14-4Q16)



3. VICTOZA: 10% YOY GROWTH DRIVEN BY STRONG MOMENTUM OF GLP-1 AGONIST CLASS

Victoza revenue grew 10% YOY as reported and operationally to DKK 5.4 billion ($774 million) in 4Q16, a 6% sequential increase. The drug posted DKK 20.0 billion (~$2.9 billion) in sales for full year 2016. This represents an 11% rise as reported (12% operationally) from 2015. By geography 4Q16 sales totaled DKK 3.9 billion ($554 million) in the US, DKK 857 million ($123 million) in Europe, DKK 295 million ($42 million) in the Pacific, DKK 60 million ($9 million) in China, and DKK 323 million ($46 million) in international operations. Victoza experienced YOY growth in all regions in 4Q16, with the highest magnitude of growth in international operations (35% as reported, 39% in constant currencies). For the full year, Victoza experienced YOY growth in all regions except Europe (which remained flat), with the highest magnitude of growth again coming from international operations (23% as reported, 32% in constant currencies), followed by China (20% as reported, 25% in constant currencies). Victoza contributed substantially to Novo Nordisk's overall diabetes and obesity portfolio growth, both in 4Q16 (24%) and for the full year (33%).

Figure 3: Victoza Sales (1Q12-4Q16)

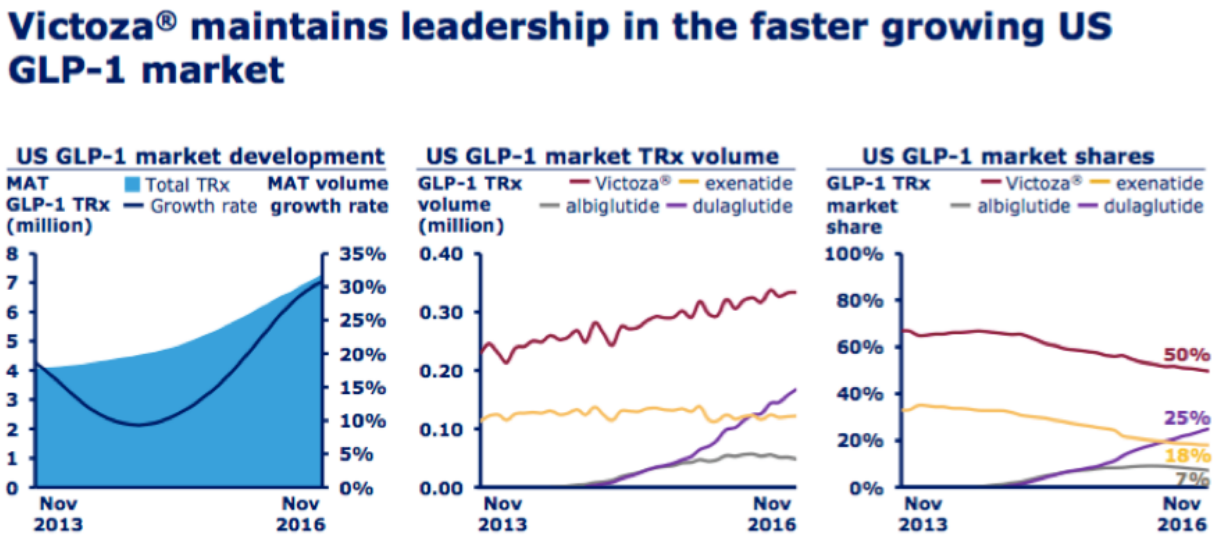


- **Novo Nordisk is benefiting from strong underlying GLP-1 agonist class growth.** The overall GLP-1 agonist market has grown to nearly 10% of the value share of the total diabetes care market (from 8% at the end of 2015). This figure is higher (close to 12% as shown in Table 4 below) in the US GLP-1 agonist market, where overall volume growth continues to hover around 30%. Novo Nordisk boasts 58% of the overall GLP-1 agonist market by value, with especially strong penetration in international operations (80%), Europe (66%), and Japan (61%). By volume, total prescriptions (TRx) for the GLP-1 agonist class grew 30% YOY in 4Q16, down slightly from ~32% in 3Q16.

Table 4: GLP-1 Agonist Market Share

	GLP-1 Agonist Share of Total Diabetes Market (by value)		Victoza Share of GLP-1 Agonist Market (by value)	
	November 2016	**November 2015**	**November 2016**	**November 2015**
US	11.5%	9.3%	56%	64%
Europe	9.6%	8.7%	66%	74%
International Operations	2.9%	2.4%	80%	85%
China	0.9%	0.8%	56%	54%
Japan	5.2%	2.8%	61%	69%
Global Totals	**9.8%**	**8.0%**	**58%**	**66%**

- **Though Novo Nordisk is the longstanding market leader in the GLP-1 segment by total prescription (TRx) volume (300,000 prescriptions, versus <200,000 for all other competitors, as shown below) its dominance is declining somewhata in terms of TRx market share - we are not particularly concerned at this point as the class is growing.** As of November 2016, Victoza held 50% TRx market share for the GLP-1 agonist class, down from high in the 60% range several quarters back. As shown in the figure of slide 9 below, this decline for Victoza is largely due to increasing TRx share for Lilly's once-weekly Trulicity (dulaglutide) which now holds 25% TRx. Indeed, in January 2017, Lilly management commented that Trulicity has surpassed the TRx volume that Victoza demonstrated at the corresponding two year timepoint after launch. Indeed, Trulicity's TRx trajectory is noticeably steeper than Victoza's. As for the other players in the GLP-1 agonist field. We're eager to see updated graphs of GLP-1 TRx market share that include January 2017 and beyond in Novo Nordisk's next earnings update. AZ's exenatide franchise (twice-daily Byetta and once-weekly Bydureon) and GSK's Tanzeum (albiglutide) respectively hold 18% and 7% TRx market share. We are interested to see how Intarcia fares; we think the adherence benefits could make that a disruptive product (to say nothing of the potential impact of lower pricing).



4. SAXENDA: UP 29% SEQUENTIALLY TO DKK 540 MILLION (~$77 MILLION)

Saxenda's (liraglutide 3.0 mg for obesity) success continued with DKK 540 million (~$77 million) in 4Q16 revenue, more than tripling YOY and increasing a whopping 29% sequentially. The obesity drug posted DKK 1.6 billion (~$233 million) in sales for 2016, its first full year on the market. Saxenda is now launched in 15 countries and was responsible for 19% of the growth of Novo Nordisk's overall product portfolio (including diabetes, obesity, and hemophilia) in 2016 - quite impressive given the falling sales of virtually every other obesity drug on the market (refer to our 1H16 Industry Roundup for more; we will be back soon with an updated analysis of the obesity market once more companies have reported their 4Q16 updates). Although Novo Nordisk has yet to split Saxenda sales by geography, management has attributed overall growth in the company's US diabetes/obesity business in part to this obesity treatment, suggesting that Saxenda is an especially valuable player in the US market. Given that nearly 40% of American adults have obesity (very few of whom are receiving adequate , if any, care), we expect this trend to grow increasingly stronger, and look forward to learning more about the geographical distribution of Saxenda sales in future earnings updates.

- **Novo Nordisk management has expressed confidence in Saxenda and has previously stated its commitment to developing the product further in the short- and long-term. This only sharpens our expectation that Saxenda's indisputable stronghold of the**

obesity drug market will continue in 2017. Saxenda's success also derives from its strong clinical profile. Cumulatively, presentations and publications from the SCALE program (seen at major conferences including ADA, EASD, and Obesity Week) have shown that liraglutide 3.0 mg leads to clinically-meaningful weight loss, maintenance of weight loss over at least three years, improved quality of life, and reduced incidence of new-onset type 2 diabetes. Together, these are tremendously valuable outcomes from both an individual and a broader public health perspective. It's comforting, given the challenges that plague the obesity drug arena and the persistent lack of adequate treatment options for people with obesity, to see a chronic weight management agent doing well commercially.

- **Pricing and reimbursement remain significant challenges that restrict patient access to Saxenda (and obesity therapy more generally).** Obesity drugs across the board are not well-reimbursed in the US and as we learned from Dr. Ken Fujioka (Scripps Health, San Diego, CA), only about one-third of patients taking Saxenda are reimbursed through their insurance plan - the rest are self-pay, we assume. Saxenda is priced proportionally to the dose of liraglutide, which makes it much more costly than Victoza (liraglutide 1.2 mg or 1.8 mg), and prohibitively expensive for many. Novo Nordisk was relatively quiet on this issue during the call, and we're curious if any plans are in the works to increase Saxenda's availability. Management has previously underscored its commitment to growing the obesity market as a whole and investing in greater promotional efforts for Saxenda - we assume that improving reimbursement and access is included in these plans.

5. MODERN INSULINS: CHALLENGES CONTINUE WITH 10% YOY DECLINE

Novo Nordisk's modern insulin portfolio (Levemir [insulin determir], NovoLog [insulin aspart], and NovoMix) experienced another tough quarter with sales declining 10% YOY as reported (falling 8% operationally). This was largely driven by Levemir's 19% YOY drop as reported (-17% operationally) to DKK 4.1 billion ($586 million), as well as NovoLog's 3% drop as reported (-2% operationally) to DKK 5.5 billion ($794 million), and NovoMix's 8% drop as reported (-5% operationally) to DKK 2.6 billion ($372 million). For the full year, Novo Nordisk's modern insulin portfolio fell 5% as reported (-3% operationally) to DKK 47.5 billion (~$7 billion). By geography, the falling revenues in Novo Nordisk's modern insulin portfolio were primarily driven by the US sales, which fell 15% YOY as reported in 4Q16 (versus only a 3% YOY decline for ex-US sales) - not a surprise given the challenging US pricing environment, for insulin especially. Levemir sales took a particularly deep dive, declining YOY by double digits in all regions except China (up 40%) and international operations (up 3%); US and European revenues were hit the hardest, with YOY declines of 20% and 32%, respectively. Management pointed out that some of these declines in Levemir sales are attributable to patients (the lucky ones) moving to Tresiba, particularly given this next generation product's favorable 2017 formulary positioning.

- **These challenges underscore management's overarching message that Novo Nordisk, like many diabetes companies, continues to face a very tough pricing environment in the US, particularly surrounding insulin.** As was also the case in 3Q16 and 2Q16, negative growth among Levemir, NovoLog, and NovoMix offset Tresiba's strong performance, the net result of which is merely modest sales growth globally and in the US, specifically. Even bright spots in the modern insulin portfolio, such as revenue gains in China (where in 4Q16 NovoLog sales increased 26% YOY and NovoMix sales increased 16% YOY), seem to be constantly overshadowed by sluggish sales in the US. Nevertheless, Novo Nordisk remains a true giant in the insulin arena, capturing 46% of the total insulin market and 45% of the modern and new-generation insulin market as shown in the table below.

Table 5: Novo Nordisk Insulin Market Share

	Share of Total Insulin Market		Share of Modern and New-Generation Insulin Market	
	November 2016	November 2015	November 2016	November 2015

US	37%	38%	38%	38%
Europe	45%	47%	45%	47%
International Operations	55%	45%	51%	52%
China	54%	55%	61%	62%
Japan	52%	52%	50%	50%
Global Total	**46%**	**47%**	**45%**	**45%**

6. HUMAN INSULIN: RELATIVELY STRONG PERFORMANCE WITH 6% YOY GROWTH

Human insulin experienced a relatively strong quarter with revenue growing 6% YOY as reported (8% operationally) and 6% sequentially to DKK 2.9 billion (~$422 million) in 4Q16. Full year revenue for human insulin remained steady at DKK 11.1 billion (~$1.6 billion), a 1% decline as reported and 2% uptick operationally. Positive growth was driven primarily by the US and China, where 4Q16 sales increased 11% and 19% YOY - quite the contrast from the double digit negative growth and flat growth respectively seen in these markets earlier in 2016. We wonder if this is due to payers wanting to see more human insulins versus analogs prescribed and/or patients who have very high co-pays looking for cheaper options.

Pipeline Highlights

7. FASTER-ACTING INSULIN ASPART: FDA RESUBMISSION EXPECTED IN NEXT THREE MONTHS

Novo Nordisk shared that a class II resubmission of the New Drug Application (NDA) for faster-acting insulin aspart is expected in the next three months, with an approval hopefully by the end of 2017. The FDA had previously issued a Complete Response Letter for the product in October 2016 and management characterized its December meeting with the FDA over the letter as "constructive." Coming out of the meeting, management shared that Novo Nordisk and the FDA are now "totally in agreement" with regards to the assay for assessment of faster-acting insulin aspart and that the required new data is already available. As such, management express optimism that a US approval of the product would be possible in the second half of 2017. Given this timeline, faster-acting insulin aspart will be the first-to-market next-generation rapid-acting insulin analog to reach the US market. Just last week, Lilly terminated its partnership with Adocia for phase 3-ready ultra-rapid insulin BioChaperone Lispro, suggesting that the phase 3 program for BioChaperone Lispro will be delayed while Adocia searches for a new partner. Lilly is instead advancing its own internally-developed ultra-rapid insulin candidate, which is expected to enter phase 3 trials in 2017. We have not seen any data on Lilly's internally-developed candidate thus far and we're curious to see how it might compare to faster-acting insulin aspart and BioChaperone Lispro - the data for the latter two candidates at ADA 2016 suggest that while these next-generation insulins offer meaningful advantages for patients, they're certainly not as much of a paradigm-shifting leap forward as insulin analogs were from human insulins.

- **Faster-acting insulin aspart was approved in the EU and Canada under the trade name Fiasp in January 2017 and will be launched in these markets in the first half of 2017.** The product will be available in vial, Penfill, and FlexTouch pen formulations and is approved for use in insulin pumps as well. We certainly look forward to early real-world patient and provider feedback on Fiasp as it rolls out in these countries and look forward to its hopefully speedy approval and launch in the US.

8. XULTOPHY: US LAUNCH IN FIRST HALF OF 2017

The US launch of basal insulin/GLP-1 agonist fixed-ratio combination Xultophy (insulin degludec/liraglutide) is expected in the first half of 2017. Notably, this projected timeline is several months behind that of Sanofi's combination Soliqua (insulin glargine/lixisenatide), which was approved by the FDA on the same day as Xultophy and launched in early January. Novo Nordisk management underscored that Xultophy boasts a very strong clinical profile and emphasized that the somewhat later launch is due to its current focus on making sure payers understand the value proposition of Xultophy compared to Soliqua and other available type 2 diabetes therapies. Novo Nordisk hopes to steadily establish strong market access prior to launch without conceding too-large rebates that may undermine Victoza and Tresiba. Sanofi, on the other hand, has embraced a lower list price strategy for Soliqua's launch - based on early reports, Soliqua will be priced lower than Xultophy and we know they are also very intent on strong access. Sanofi has a history of accepting higher rebates in exchange for achieving or maintaining broad formulary access to its products, as it did with Lantus (insulin glargine). Soliqua is clearly among the top priorities for Sanofi as it aims to revitalize its sagging diabetes franchise. Novo Nordisk management, on the other hand, acknowledged that resources will be largely prioritized toward Victoza and Tresiba and that Xultophy may not be broadly promoted until possibly after next-generation GLP-1 agonist semaglutide is established. This suggests to us that Xultophy may not be a top priority for Novo Nordisk's diabetes portfolio for a number of years. In the meantime, however, management emphasized that Xultophy's launch will still benefit from "significant" resources and that the launch would focus on prescribers that have a high likelihood prescribing Xultophy, based on the company's experience with Xultophy in Europe (we assume this refers largely to KOLs and endocrinologists), and in geographical areas with strong market access. Outside of the US, management noted that Xultophy is currently available in nine countries and that additional launch activities are progressing as expected.

- **Novo Nordisk highlighted topline results from the DUAL VII phase 3b trial of Xultophy compared to basal-bolus therapy.** The 26-week trial (n=506) evaluated once-daily Xultophy vs. basal-bolus therapy of Lantus (insulin glargine) and NovoLog (insulin aspart) and found that Xultophy demonstrated similar glucose control to basal-bolus therapy with hypoglycemia and weight benefits. Xultophy demonstrated a superior 89% reduction in the rate of severe or blood glucose confirmed symptomatic hypoglycemia compared to basal-bolus therapy. In addition, patients on Xultophy experienced a mean weight loss of 0.9 kg (~2 lbs), compared to a mean weight gain of 2.6 kg (~5.7 lbs) in the basal-bolus arm. Patients on Xultophy also had lower insulin requirements at the end of the trial - 40 units per day compared to a total 85 units in the basal-bolus arm.

9. ONCE-WEEKLY SEMAGLUTIDE: SUBMITTED IN THE US AND EU

Management highlighted the December 2016 US and EU submission of once-weekly injectable GLP-1 agonist semaglutide and shared that decisions expected in 4Q17. Furthermore, the Japan submission is expected in the next three months. In Q&A, management continued to emphasize that the finding of increased retinopathy in the SUSTAIN 6 trial is likely due to the very rapid substantial glucose-lowering produced by semaglutide rather than a characteristic of semaglutide itself. In fact, the company shared that it had conducted a mediation analysis that found that adjusting for precipitous fall in glucose from a high baseline A1c could completely mitigate the effect of increased retinopathy observed in SUSTAIN 6, suggesting statistically that this may be the cause. That said, the company acknowledged that regulatory agencies may require additional data on this front and signaled its willingness to work with the FDA on this. We're curious of the semaglutide submission will elicit an FDA Advisory Committee meeting - the SUSTAIN 6 certainly included a number of both highly positive (cardioprotection) and more worrisome (increased retinopathy) results.

10. ONCE-DAILY INJECTABLE SEMAGLUTIDE: PHASE 2 TRIAL IN TYPE 2 DIABETES COMPLETED; PHASE 2 IN OBESITY AND NASH ONGOING

Novo Nordisk shared that the once-daily injectable formulation of GLP-1 agonist semaglutide has completed a phase 2 dose-ranging trial, with impressive A1c efficacy and weight reduction results. The 26-week, double-blind phase 2 trial (n=706) enrolled participants with type 2 diabetes who were either treatment-naïve or treated with metformin. The trial evaluated daily doses of 0.05 mg, 0.1 mg, 0.2 mg, and 0.3 mg injectable semaglutide compared to placebo and liraglutide (Victoza). Daily semaglutide produced a mean A1c reduction of up to 1.9% (vs. 1.3% with liraglutide; mean A1c 7.9%-8.2% for all groups). Even more impressively, semaglutide demonstrated a mean weight loss of up to 8.2 kg (~18.1 lbs, vs. 3.7 kg [~8.2 lbs] with liraglutide). Notably, the weight reduction produced by the highest daily dose of semaglutide is about twice as much as the weight reductions produced by once-weekly 1.0 mg semaglutide in the SUSTAIN phase 3 program. Regarding adverse events, management emphasize in Q&A that the main determinant of GI side effects is the titration rate, rather than the actual dose, and that nausea and other effects could be managed with appropriate titration.

- **Novo Nordisk announced that it had initiated a phase 2 trial of once-daily semaglutide in NASH in November 2016, with an expected completion date in 2019.** According to ClinicalTrials.gov, the trial will enroll 372 patients with NASH randomized to 0.1 mg, 0.2 mg, or 0.4 mg semaglutide or volume-matched placebos. The primary endpoint of the trial is NASH resolution without worsening of fibrosis and the trial also includes a number of secondary endpoints related to liver fibrosis or NAFLD, as well as A1c and fasting plasma glucose. ClinicalTrials.gov lists an expected completion date of July 2019 for the trial - NASH trials are notoriously long, which has historically been a contributor to the very high unmet need in this area. We're extremely pleased to see Novo Nordisk invest in this very important indication - the company joins a number of others in a robust competitive landscape for NAFLD/NASH.
- **The company also shared that results from the ongoing phase 2 trial of daily semaglutide in obesity are expected in the next six to nine months.** According to ClinicalTrials.gov, the study is expected to complete in April 2017. The company announcement stated that next steps related to daily semaglutide will be determined once the obesity results are available. Based on the phase 2 type 2 diabetes results, semaglutide clearly has potential as an extremely potent option for patients with high A1c and overweight or obesity. That said, Novo Nordisk appears to be learning toward obesity and NASH indications for once-daily semaglutide, based on its product pipeline, which lists both obesity and NASH as potential indications for the once-daily formulation, but not type 2 diabetes.

11. ORAL SEMAGLUTIDE: ALL TRIALS IN PIONEER PHASE 3 PROGRAM INITIATED

Novo Nordisk confirmed that all ten trials in the phase 3 PIONEER program for the oral formulation of semaglutide have initiated. Many of the trials are expected to begin reporting out in 2018. See below for an overview of the large and ambitious program, which includes head-to-head comparisons with Lilly/BI's SGLT-2 inhibitor Jardiance (empagliflozin), Merck's DPP-4 inhibitor Januvia (sitagliptin), and Novo Nordisk's own leading GLP-1 agonist Victoza (liraglutide).

Table 6: PIONEER Phase 3 Trial Program for Oral Semaglutide

Trial	Estimated Enrollment	Comparator/Design	Estimated Completion
PIONEER 1	704	Placebo	November 2017
PIONEER 2	816	Lilly/BI's Jardiance (empagliflozin)	March 2018

PIONEER 3	1,860	Merck's Januvia (sitagliptin)	March 2018 (enrollment complete)
PIONEER 4	690	Novo Nordisk's Victoza (liraglutide)	April 2018
PIONEER 5	324	Moderate renal impairment	January 2018
PIONEER 6	3,176	CVOT	April 2018
PIONEER 7	500	Flexible dose escalation	March 2019
PIONEER 8	720	Insulin add-on	August 2018 (not yet recruiting)
PIONEER 9	240	Placebo and liraglutide in Japan	September 2018
PIONEER 10	455	Lilly's Trulicity (dulaglutide) as an add-on to orals in Japan	August 2018

12. PHASE 1 OBESITY PIPELINE PROGRESS

Novo Nordisk also shared that it has initiated a phase 1 trial of a new once-daily FGF21 analog (NN9499) in obesity. The trial will enroll 56 male participants with overweight or obesity and has an expected completion date of August 2017, according to ClinicalTrials.gov. FGF21 has been hailed as a therapeutic target with vast potential, but the initial enthusiasm for the target as a type 2 diabetes medication has diminished somewhat in recent years as candidates from Pfizer and Lilly failed to demonstrate significant glucose lowering. Despite the lackluster results for type 2 diabetes, FGF21 is promising an obesity treatment, given that it increases energy expenditure and possibly even causes "browning" of white adipose tissue. Novo Nordisk is usually very, very smart about its product pipeline and this addition to its pipeline is a strong vote of confidence in FGF21 as a therapeutic target.

- **A novel phase 1 GLP-1/glucagon dual agonist, NN9277, has also been added to Novo Nordisk's obesity pipeline.** A phase 1 trial for the candidate was initiated in October 2016 and is currently recruiting participants, according to ClinicalTrials.gov. The trial plans to enroll 288 male participants with overweight or obesity and the expected completion date in September 2017. The company has also previously stated its interest in eventually co-formulating its phase 1 glucagon analog G530L/NN9030 (currently under investigation for obesity) with GLP-1 agonist liraglutide. In fact, management had previously expressed a preference for this approach over the development of a single compound that activates both GLP-1 and glucagon receptors, positing that animal studies have not indicated exactly what ratio of GLP-1 vs. glucagon action is necessary for optimal human dosing and that a co-formulation allows more flexibility in the dose ratio. Thus, the decision to advance a single dual agonist compound into phase 1 likely indicates a strong vote of confidence in the preclinical data for this candidate. There is a flurry of industry interest in GLP-1/glucagon dual agonists, though most candidates are investigating a type 2 diabetes indication. The exception is OPKO Health's phase 2 TT401 - following its acquisition from Transition Therapeutics, OPKO Health has pivoted the candidate to an obesity indication with a modified dose for its upcoming phase 2b trial.
- **Two new phase 1 trials for obesity have been posted for glucagon analog G530S (NN9030) on ClinicalTrials.gov, including a co-administration trial with GLP-1 agonist liraglutide.** The first is a trial of standalone G530S and will enroll 48 participants with overweight or obesity, with an expected completion date of June 2017. The second trial, very notably, is of the co-administration of G530S and GLP-1 agonist liraglutide. This trial will enroll 180

participants and is expected to complete in September 2017. Management had previously expressed interest in co-formulating G530S with liraglutide and we're pleased to see these plans progressing despite the addition of the single compound dual agonist to Novo Nordisk's pipeline. We imagine Novo Nordisk is hedging its bets to some extent to see which method may produce better results in obesity - certainly the single compound method has been more popular on the GLP-1/glucagon dual agonist competitive landscape, and we imagine Novo Nordisk has the resources to explore both options in the early stage.

- **Long-acting amylin analog AM833 (NN9838) for obesity is also being investigated in a new phase 1 trial.** According to ClinicalTrials.gov, the trial initiated in November 2016 and will enroll 84 participants with overweight or obesity. Participants will be randomized to either once-daily or once-weekly doses of AM833. The trial is expected to complete in December 2017.
- **We're excited to see Novo Nordisk continue to expand its commitment to obesity through the development of novel obesity compounds.** The company clearly intends to be in the obesity field for years to come (further evidenced by the company's recently updated R&D strategy to focus on diabetes-adjacent indications like obesity). Furthermore, we're encouraged that Novo Nordisk certainly has the resources to both develop new obesity medications and grow the market through educational efforts aimed that increasing the acceptance of obesity pharmacotherapies.

13. ADDITIONAL PIPELINE UPDATES: TYPE 1 ORPHAN DRUG DESIGNATION, SEVERAL NEW PHASE 1 TRIALS; NO MENTION OF BETA BIONICS PARTNERSHIP

Novo Nordisk announced that its combination treatment of anti-IL-21 and GLP-1 agonist liraglutide (together known as NN9828) has received an orphan drug designation from the FDA for the treatment of type 1 diabetes with residual beta cell function. A phase 2 trial of the combination was initiated in 4Q15; the trial's primary completion date is November 2018 according to ClinicalTrials.gov (full completion in April 2019). The trial hopes to demonstrate preservation of beta cell function in newly-diagnosed patients with type 1 diabetes with this combination. There is growing consensus in the field that disease-modifying therapies for type 1 diabetes will require the use of multiple agents in combination. In addition, Novo Nordisk previously declined to pursue a type 1 diabetes indication for standalone Victoza (liraglutide) following positive but modest results from the ADJUNCT ONE and TWO trials. The trials also demonstrated a number of worrisome safety signals for liraglutide in type 1 diabetes, particularly for hyperglycemia with ketosis and DKA. Notably, however, all eight cases of DKA in ADJUNCT ONE occurred in patients treated with liraglutide with no detectable C-peptide levels, suggesting that there may be differential effects in patients with type 1 diabetes with and without C-peptide. Increasingly, it's becoming clear that disease modification in type 1 diabetes will require personalized treatment based on patient characteristics, rather than a "one-size-fits-all" cure and we're eager to see the effects of liraglutide+anti-IL-2 in this particular subset of patients. We're also pleased that the FDA recognizes the unmet need for type 1 diabetes disease-modifying therapies and appreciate the agency's support in the form of this orphan drug designation.

- **We noticed that a new phase 1 trial for once-weekly basal insulin LAI287 (NN1436) has been posted on ClinicalTrials.gov.** The trial was initiated in November 2016 and is currently recruiting for 48 participants with type 2 diabetes. The trial will compare LAI287 to insulin degludec (Tresiba) and is expected to complete in December 2017.
- **A new phase 1 trial for liver-preferential prandial insulin PI406 (NN1406) has also been posted on ClinicalTrials.gov.** The trial was initiated in October 2016 and hopes to enroll 44 participants with type 1 diabetes. The trial involves insulin aspart (NovoLog) as the active comparator and is expected to complete in July 2017.
- **There was no mention of Novo Nordisk's brand-new partnership with Beta Bionics.** Just this week, Close Concerns broke the news that Novo Nordisk has invested $5 million in closed loop company Beta Bionics, gaining a seat on the Beta Bionics Board of Directors in the process.

Lilly previously made a $5 million investment in Beta Bionics a year ago and also holds a seat on the board - a virtually unprecedented move. Beta Bionics intends to make its iLet system compatible with pre-filled cartridges of both NovoLog (in the form of the prefilled NovoRapid PumpCart, available in Europe) and Lilly's Humalog (insulin lispro), a big win for patient choice. Beta Bionics CEO Dr. Ed Damiano emphasized that Novo Nordisk is interested in both the research and commercial aspects of the iLet Bionic Pancreas: from the research angle, the dual-chamber pump will provide scientists a platform upon which to study new drugs and new autonomously delivered dual-drug interactions, and from the commercial angle, it would help to optimize delivery of Novo Nordisk insulins. Despite the lack of mention in Novo Nordisk's earnings update, this news is just the latest in a string of moves in diabetes technology and digital health for the company: Novo Nordisk also announced a partnership with Glooko last month and announced a partnership with IBM Watson in late 2015. While these partnerships are clearly not Novo Nordisk's main focus or core business currently, the company certainly seems to be looking to the future and diversifying beyond its traditional insulin+peptides business model.

- **The table below contains an overview of all of Novo Nordisk's diabetes and obesity-related pipeline projects of which we are aware.**

Table 7: Novo Nordisk Diabetes and Obesity Pipeline Candidates

Candidate	Indication	Class/Mechanism of Action	Phase	Timeline/Notes
Xultophy (insulin degludec/liraglutide)	Type 2 diabetes	GLP-1 agonist/basal insulin fixed-ratio combination	Approved	FDA approved in December 2016; US launch expected in 1H17
Faster-acting insulin aspart (approved as Fiasp in EU and Canada)	Type 1 and type 2 diabetes	Next-generation rapid-acting insulin analog	Received Complete Response Letter (CRL)	Received CRL in October 2016; Resubmission expected by May 2017
Once-weekly injectable semaglutide	Type 2 diabetes	Once-weekly GLP-1 agonist	Phase 3 in type 2 diabetes	US and EU submission in December 2016
Oral semaglutide	Type 2 diabetes	Once-daily oral GLP-1 agonist	Phase 3	10-trial phase 3 PIONEER program initiated; Phase 2 data presented at EASD 2016
Once-daily injectable semaglutide	Obesity, NASH	Once-daily GLP-1 agonist	Phase 2	Phase 2 results in type 2 diabetes reported 4Q16; Phase 2 trials in obesity and NASH ongoing (expected completion April

				2017 and July 2019, respectively)
NN9828	Type 1 diabetes (newly-diagnosed)	Anti-IL 21/GLP-1 agonist (liraglutide) combination for beta cell preservation	Phase 2	Phase 2 trial initiated in 4Q15; Expected completion November 2018; FDA orphan drug designation in January 2017
LAI287 (NN1436)	Type 1 and type 2 diabetes	Once-weekly injectable basal insulin	Phase 1	Phase 1 trial completed 3Q15; New phase 1 trial initiated in November 2016 with completion expected in December 2017
PI406 (NN1406)	Type 1 and type 2 diabetes	Liver-preferential prandial insulin analog	Phase 1	Phase 1 trial initiated 4Q15; Completed June 2016; New phase 1 trial initiated in October 2016 with completion expected in July 2017
PYY1562 (NN9748)	Type 2 diabetes	PYY	Phase 1	Added to pipeline in 4Q15
PYY1562 (NN9747)	Obesity	PYY; Under development both as a standalone therapy and in combination with semaglutide	Phase 1	Advanced into phase 1 3Q15; Phase 1 trial expected to complete February 2017
AM833 (NN9838)	Obesity	Long-acting amylin analog	Phase 1	Announced in 4Q14; Completed phase 1 trial in March 2016; New phase 1 trial initiated in November 2016

				and expected to complete in December 2017
G530S (NN9030)	Obesity	Glucagon analog	Phase 1	Announced in 3Q14; Completed phase 1 trial in July 2016; Phase 1 trials of standalone and co-administration with liraglutide expected to complete in June 2017 and September 2017, respectively
NN9277	Obesity	GLP-1/glucagon dual agonist	Phase 1	Phase 1 trial expected to complete in September 2017
FGF21 Obesity (NN9499)	Obesity	FGF21 analog	Phase 1	Phase 1 trial expected to complete in August 2017

Questions and Answers

Q: On the guidance around operating profit and sales, what is the upside opportunity from Victoza in terms of potentially gaining the CV benefit label?

A: We have in our assumption that the CV benefit from the impressive LEADER results will get into the Victoza label. From there, we expect this to have some impact on our sales. If any change in momentum occurs earlier, that would be an upside for Victoza. There is also upside opportunity for Tresiba. Our guidance assumes a gradual increase in our market share, continuing the current trend of gaining approximately 5% market share YOY. This is also linked to the improved market access we see currently for Tresiba.

Q: What downside do you see in terms of US healthcare reform and pricing pressure in the government channel?

A: It's unpredictable, but the Trump administration acknowledges Pharma as an important sector that drives jobs and represents innovation in the US. It's the general uncertainty we're pointing out as something that may drive a downside.

Q: You seem to have a lot of resources behind Tresiba and Victoza, but what is your strategy in for the US launch of Xultophy?

A: The way we're handling Xultophy is a clear indication that the market has changed. Five years ago we would have prepared for a major launch as soon as possible, but now we need to first establish a certain level of market access and take the time to convince payers about the value of Xultophy compared to Sanofi's Soliqua and other alternative therapies for type 2 diabetes. We will launch in the first half of 2017 when we've

ensured we have solid momentum. If you look broadly at the market, we will have an overwhelming priority of resources behind Victoza and Tresiba. In the backside of semaglutide, we may return to Xultophy as a major priority when it's more broadly established and clinically accepted and we can promote it more broadly in the market. This is a more of tactical short-term approach to optimize delivery on the 2017 plan.

Q: What are the potential challenges you'll see for semaglutide going forward? What do you expect in terms of your label?

A: The background literature on GLP-1 would, if anything, indicate protection rather than aggravation of retinopathy, and there was absolutely no difference in the occurrence of retinopathy in the SUSTAIN 1 through 5 trials. SUSTAIN 6 was not designed to look at retinopathy. Nonetheless, there was an over representation of people who had complications to their retinopathy, at least transiently. We went on to do a mediator analysis where the mediator was assumed to be precipitous fall in glucose from the high baseline A1c. With this there is no longer any effect whatsoever in SUSTAIN 6. It is basically a consequence of people dropping very, very fast. We may need and are highly willing to discuss with agencies the possibility of post-approval studies. We do not see any risk with semaglutide other than it's a highly efficacious product.

Q: With changes coming to US healthcare, is it correct to think about the dual eligibles shifting back to the Medicaid as the biggest risk to Novo Nordisk?

A: We don't really know. Obviously, there would be an impact, but in our view it's not likely that there will be a short-term change in where the dual eligibles will be heading.

Q: Are you still confident in your statement that ongoing pricing pressure across the portfolio for Novo in the US to be less severe going forward than what you've seen this year?

A: In terms of overall impact of prices, we have hinted an operating profit of about 5% beyond 2017. We have included an assumption of a 2- 3% negative global pricing impact, expected largely from the US, but there is also a balanced negative impact expected from rest of world. That remains the same.

Q: We've recently seen Sanofi launching a $10 maximum co-pay strategy with access to Lantus and Toujeo. Can you talk to us about the impact you're seeing from this? How do you think this will affect the price competition for the 2018 formulary negotiations?

A: We've not been able to detect any significant signal that they have had success with these cards so I think it doesn't appear to be a dynamic in the market that will have any sort of significant influence when we negotiate contracts going forward.

Q: Can you offer a bit more about the discussions you've had with the FDA about Fiasp re-submission?

A: The conference with the FDA on the CRL was highly constructive as to what should be included in the resubmission, and we will resubmit in the next three months. We are now totally in agreement regarding the assay for the fast-acting aspart assessment. And the new data going into the resubmission are now available. We hopefully can have an approval in the second half of this year.

Q: We've recently seen Lilly terminate their partnership with Adocia for ultra fast-acting insulin. Are you still confident in your ultra fast-acting insulin opportunity?

A: I think it's fair to say that Lilly has not abandoned an ultra rapid-acting approach to insulin because they have an internal formulation. This tells me that they're still interested in the physiological mealtime insulin for type 1 diabetes and type 2 diabetes, and also for pump usage - I think they are still in the game.

Q: How fast do you actually see the market moving towards value-based contracting, and what would that mean for potential pricing development?

A: We've signed a number of value-based contracts so far in the GLP-1 agonist area where it has been the easiest to implement metrics we could use. We still need to find ways to implement that on the insulin side, so that's for us a development, but the SWITCH data and DEVOTE data for Tresiba gives us confidence for value-based contracting here. I would say the development is very fast: there's already an expectation that

with the increased competition in the basal insulin/GLP-1 agonist segment in particular, better value is going to fall through to some improved rebate from a payer point of view. In the medium term, I think we're going to see that the payments for products are going to reflect the result delivered for patients. We get a vested interest in further investing in digital health in ways to help the patients achieve glycemic targets and get support in the everyday diabetes care. I think it's going to be a couple of years before it plays in, but we need to make the contracts work very fast right now.

Q: We have seen recently quite a strong uptake of both Levemir and Tresiba, but Basaglar and the exclusion of Sanofi's Lantus came very late in the process. Would you assume that the next time we see a large contract swing, you would not see a similar effect for Tresiba and Levemir again?

A: You're right, and I think we have to be cautious with reading these dynamics because Basaglar has been only briefly in the market. On the other hand, CVS letters have not specified Tresiba as an alternative, but have positioned it prominently in their internal communication on the Basaglar offering. The performance we've seen delivered is also because of our presence in the field. We are continuing to promote Tresiba, so the average prescriber will have a more positive view. When there's an opportunity to prescribe, because it's covered, that will play in our favor. I remain very, very optimistic about the future, particularly because we still have great data from SWITCH and DEVOTE.

Q: The semaglutide once-daily phase 2 study is a little bit more than double the dose on a weekly perspective versus semaglutide once-weekly. If we look at a comparable dose on a weekly basis, are we then seeing more powerful or less powerful semaglutide when administered once-daily?

A: We wanted to investigate: (1) whether this more subtle once-daily dose is able to get to higher doses and higher levels of efficacy; and (2) whether once-daily as opposed to once-weekly would be able to achieve higher levels of efficacy. This is being studied both in the trial that you're hinting at, but also in phase 1 studies not yet reported. You can titrate once-weekly and achieve basically the same efficacy as from once-daily application. From a convenience perspective, the patients tend to prefer once-weekly application of injectables if they are safe, tolerable, and efficacious. The data today tells me that once-weekly application of semaglutide is a good way to go by the injection route as long as you titrate in the adequate manner.

Q: You saw some retinopathy in SUSTAIN 6, which you explained as a possible consequence of the rapid blood glucose lowering effect. Do you see something similar on the semaglutide safety profile? Or nausea?

A: We have not seen anything on the once-daily application. The GI side effects are simply a question of how fast you titrate and how aggressively you titrate, once-daily or once-weekly. Once you're in steady state, there's no difference whatsoever in tolerability between once-weekly and once-daily.

-- by Abigail Dove, Helen Gao, Hae-Lin Cho, and Kelly Close