Closer Look

MEMORANDUM

Sanofi 3Q11 - Diabetes Division sales total $1.6 billion; new insulin glargine formulation to enter phase 3 in 1Q12 - November 3, 2011

Executive Highlights

- Diabetes Division sales totaled €1.16 billion ($1.64 billion), up 5.8% on a reported basis (12.4% operationally) year over year; Lantus sales increased 7.6% on a reported basis (14.6% operationally) to €968 million ($1.37 billion).
- Sanofi intends to advance its new insulin glargine formulation into phase 3 in 1Q12, bypassing phase 2 development altogether.

Earlier today, Sanofi announced its 3Q11 results in a call led by CEO Chris Viehbacher. Global sales for the company's Diabetes Division totaled €1.16 billion ($1.64 billion), a 5.8% reported increase (12.4% operational increase) from 3Q10. Lantus sales totaled €968 million ($1.37 billion) in 3Q11, a 7.6% year-over-year reported increase (14.6% operational increase). Growth in Lantus sales was attributable to strong growth in the US and in Emerging Markets, in particular Japan (15.1%), China (103.5%), and Latin America (31.4%). Although Takeda has not reported its sales figures for Actos yet, it is all but certain Lantus would retain its title as the world's #1 diabetes brand for the quarter. Even with upcoming patent expiries for Lantus and the potential introduction of biosimilars and other basal insulins, Sanofi remains confident that its product will continue to perform well in the market. During Q&A, management asserted that they "don't really see anything really putting Lantus off its perch any time soon," especially with the company's new formulation, combination with lixisenatide, and combination device in development. Apidra sales increased 17.8% on a reported basis (22.2% operationally) to €53 million ($75 million) for the quarter, while Amaryl sales decreased 12.4% on a reported basis (7.4% operationally) to €106 million ($150 million). Although BGStar and iBGStar sales were not broken out separately (the meters were launched in France and Germany in 2Q11), we estimate sales to be in the ballpark of €2 million ($5.8 million) in their first full quarter on the market. This compares to an estimated €4 million ($5.8 million) in 2Q11 - we assume it will take some time to get coverage for the products, which we look very forward to trying. .

On the R&D and pipeline front, on an excited, unexpected note, management announced that its new insulin glargine formulation would be progressing straight from phase 1 to phase 3 development in 1Q12. Significant interest in the formulation was voiced during Q&A; though few details were provided, we learned that the compound will have a unique PK/PD profile. During Sanofi's 3Q11 update, management also announced that the company submitted lixisenatide for regulatory approval in the EU in late October 2011. Zealand Pharma, the company from which Sanofi licensed lixisenatide, recently guided during its capital markets day that US filing would occur in 4Q12. As a reminder, if approved, lixisenatide will be the third GLP-1 agonist to market (the second once-daily one behind Victoza) and at least in Europe, will be entering a market where a once-weekly GLP-1 agonist, Bydureon, is already available. Given the strength of the Lantus franchise and valued GP relationships, we would expect this factor to translate into success. Further success, in our opinion, will be based on lixisenatide having a very good safety and tolerability profile, being delivered in a great pen, dominating through lixisenatide/Lantus combination sales, and/or having a cardioprotective benefit.

FINANCIAL & PRODUCT NEWS

- **Worldwide Diabetes Division sales (Lantus, Apidra, Amaryl, Insuman, BGStar, and iBGStar) increased 12.4% year over year on an operational basis (5.8% on a reported**

basis), driven by strong growth of Lantus in the US and in Emerging Markets. In 3Q11, Lantus accounted for 83.5% of total diabetes sales, up slightly from 83% in 1Q11 and 2Q11.

	3Q11 Sales (in millions)	Operational/Reported Growth from 3Q10
Diabetes Division Sales	€1,161 ($1,643)	12.4% / 5.8%
United States	€601 ($851)	15.1% / 5.4%
Western Europe	€235 ($333)	5.9% / 5.9%
Emerging Markets	€223 ($316)	19.1% / 12.1%
Rest of the World (ROW)	€102 ($144)	-0.9% / -3.8%

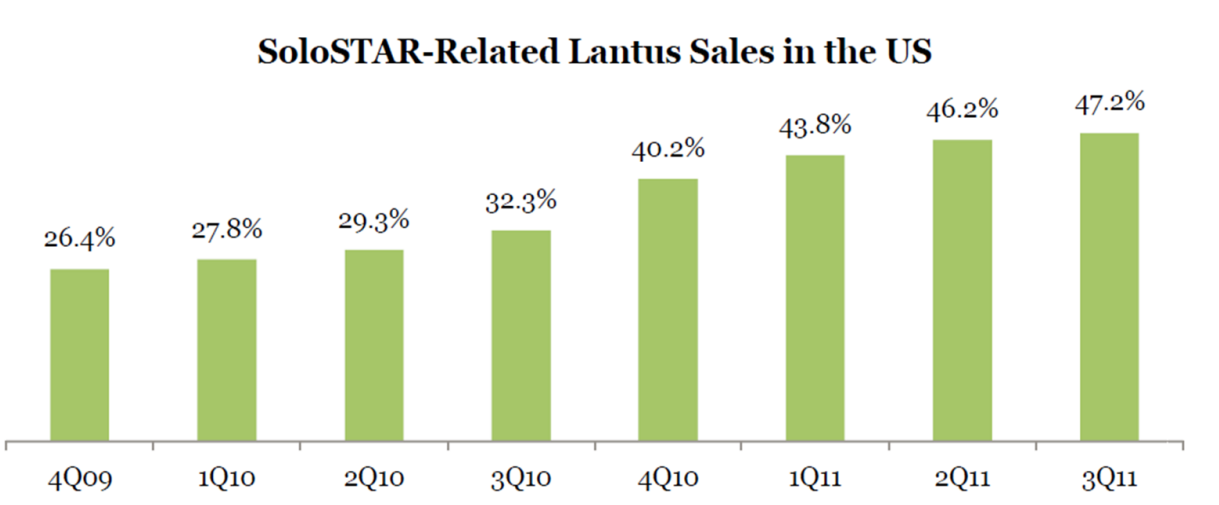
*USD estimates assume a conversion rate of €1 to 1.4155 USD; ROW consists of Japan, Canada, Australia, New Zealand

- **In 3Q11, Lantus sales totaled €968 million ($1.37 billion), driven by strong sales in the US and in Emerging Markets.** Sequentially, Lantus sales decreased 0.1% on a reported basis from €969 million ($1.39 billion) in 2Q11. Management noted that Lantus sales grew by 15.1% in Japan; meanwhile, in Emerging Markets, Lantus sales more than doubled in China (+103.5%), benefiting from inclusion into the reimbursement scheme in Shanghai (December 2010) and Beijing (July 2011). In Latin America, Lantus sales were up 31.4% for the quarter. For comparison, Novo Nordisk achieved DKK 1.9 billion ($366 million) in Levemir sales in 3Q11; like Lantus sales, Levemir sales increased 7.6% on a reported basis from 3Q10. During Q&A, management noted that Lantus maintains an approximate 75% market share in the US.

	3Q11 Sales (in millions)	Operational/Reported Growth from 3Q10
Worldwide Lantus Sales	€968 ($1,370)	14.6% / 7.6%
United States	€580 ($821)	14.6% / 4.9%
Western Europe	€182 ($258)	7.1% / 7.1%
Emerging Markets	€149 ($211)	23.4% / 16.4%
Rest of the World (ROW)	€57 ($81)	16.3% / 16.3%

*USD estimates assume a conversion rate of €1 to 1.4155 USD; ROW consists of Japan, Canada, Australia, New Zealand

In the US, the contribution of the SoloSTAR injection pen to Lantus sales continued to rise in 3Q11, accounting for 47.2% of Lantus sales, up from 46.2% in 2Q11 and up from 26% in 4Q09.



Even with upcoming patent expiries for Lantus and the potential introduction of biosimilars and other basal insulins, Sanofi remains confident that its products will continue to perform well in the market. We think this is more likely given that they should have a new insulin to launch before the patent expiry happens, if all goes to plan. During Q&A, management asserted that they "don't really see anything really putting Lantus off its perch any time soon," especially with the company's new formulation, combination with lixisenatide, and combination device in development. This makes sense from our view, especially given that basal insulin penetration has a lot of room to grow, globally - although it's also true that the introduction of GLP-1 is causing a one-time slow-down in movement to insulin overall. With this introduction of GLP-1, however, we would have to assume at this point that patients are also probably getting healthier earlier and staying older longer - this is pure speculation, of course, since there is not "duration of life" data on a type 2 population level that we know about. As expected, management also highlighted Sanofi's strength in emerging markets as a major asset - we would say that doubling sales in China, even from a small base, is a prime example of this. A major opportunity, of course, rests on the ORIGIN CV outcomes trial; if this is a positive trial, all bets are off, and Lantus could become the first insulin to garner a cardioprotective claim (topline results are expected in mid-2012) as well as the first insulin to move significantly earlier in disease therapy. Sanofi management predicted that the basal insulin market would grow with the addition of new entrants; that is, the market would not be a zero-sum game. We also believe this is true; too, the movement toward a greater focus on healthcare economics also should be a positive driver for insulin, as insulin is cheaper (for most dosages) than most non-generic oral drugs and incretins.

- **Worldwide Apidra sales increased 22.2% on an operational basis (17.8% on a reported basis), a very good result for this insulin.** Management noted that the gains observed in the US were driven by a new commercial approach - we would like to hear more about this. In addition, they stated that a temporary shortage of Apidra 3 ml cartridges will impact supplies in some markets potentially until early 2012; meanwhile, Apidra vials remain unimpacted.

	3Q11 Sales (in millions)	Operational/Reported Growth from 3Q10
Worldwide Apidra Sales	€53 ($75)	22.2% / 17.8%
United States	€20 ($28)	40.0% / 33.3%
Western Europe	€17 ($24)	0.0% / 0.0%
Emerging Markets	€11 ($16)	10.0% / 10.0%
Rest of the World (ROW)	€5 ($7)	100.0% / 66.7%

*USD estimates assume a conversion rate of €1 to 1.4155 USD; ROW consists of Japan, Canada, Australia, New Zealand

The rapid-acting insulin market experienced significant growth in 3Q11, with Apidra, Eli Lilly's Humalog, and Novo Nordisk's NovoLog all posting solid gains. As the third-to-market rapid- acting insulin, Apidra's sales are still significantly lower, given the lack of significant differentiation.

	3Q11 Sales (in millions)	**Operational/Reported Growth from 3Q10**
Sanofi's Apidra	~$75* (€53)	22.2% / 17.8%
Eli Lilly's Humalog	$593.2	-- / 20.1%
Novo Nordisk's NovoLog	~$616* (DKK 3,243)	-- / 7.0%

*USD estimates assume conversion rates of €1 to 1.4155 USD and 1 DKK to 0.190 USD

- **Amaryl sales decreased 7.4% operationally in 3Q11, due to generic competition in Japan.** This drop in sales was partially offset by strong performance in Emerging Markets, where Amaryl experienced low double-digit gains.

	3Q11 Sales (in millions)	**Operational/Reported Growth from 3Q10**
Amaryl Sales	€106 ($150)	-7.4% / -12.4%
United States	€1 ($1.4)	-50.0% / -50.0%
Western Europe	€8 ($11)	-20.0% / -20.0%
Emerging Markets	€56 ($79)	10.9% / 1.8%
Rest of the World (ROW)	€41 ($58)	-22.2% / -24.1%

*USD estimates assume a conversion rate of €1:$1.4155; ROW consists of Japan, Canada, Australia, New Zealand

- **Insuman sales reached increased 6.5% operationally to €32 million ($45 million).** Negative sales were reported in Japan, Canada, Australia, and New Zealand (we presume this is merely a necessary accounting measure), and the product is not currently sold in the United States.

	3Q11 Sales (in millions)	**Operational/Reported Growth from 3Q10**
Insuman Sales	€32 ($45)	6.5% / 3.2%
Western Europe	€26 ($37)	4.0% / 4.0%
Emerging Markets	€7 ($10)	16.7% / 16.7%
Rest of the World (ROW)	-€1 (-$1.4)	--

*USD estimates assume a conversion rate of €1:$1.4155; ROW consists of Japan, Canada, Australia, New Zealand

- **While BGStar and iBGStar sales were not reported, we estimate sales of €2 million ($2.8 million) for 3Q11.** For comparison, we estimated sales of €4 million ($5.8 million) in 2Q11. As a reminder, the meters were launched in France and Germany in 2Q11. Sanofi previously stated its intent to continue rolling out the meters in the rest of Europe in 2011, and anticipates launching the meters in the US before the end of the year as well; however, no updates were provided in the

company's 3Q11 update to this regard and we would assume there is some decent chance the launch could be delayed due to now-familiar unpredictability of the FDA. As a reminder, Sanofi has already received 510k clearance for the BGStar, and submitted a dossier for the iBGStar to the FDA in 4Q10; they do not plan to market the BGStar in the US. During Sanofi's recent Strategy and Outlook IR Thematic Seminar, management stated that the company is developing integrated advice for Lantus dosing into the meters, which should enable patients to manage their diabetes better. We think this could be a smart strategy to drive blood glucose monitoring sales and look forward to seeing, longer term, if this is a way that could move more people to start basal insulin earlier than they otherwise would.

PIPELINE & COMPANY UPDATES

- **On a very positive note, Sanofi announced that its new formulation of insulin glargine should move directly from phase 1 into phase 3 development in 1Q12.** During Q&A, management expressed confidence that Sanofi could skip phase 2 studies, based on their recent discussions with regulatory agencies. As stated during the company's Strategy and Outlook Thematic IR Seminar in September, this formulation has already completed phase 1 trials. In one of these phase 1 trials (n= 30; ClinicalTrials.gov Identifier: NCT01349855), the PK/PD properties of two dose levels of the new insulin glargine formulation were compared with those of 0.4 U/kg Lantus used in a once-daily multiple dosing regimen. In another of these trials (n=24; ClinicalTrials.gov Identifier: NCT01195454) the formulation's safety, tolerability, dose response, and dose-exposure relationship of the new glargine formulation were evaluated and its metabolic effect ratios, exposure ratios, and duration of action were compared to those of Lantus. Significant interest in the compound was voiced during Q&A; while few details were disclosed, we did learn that the compound will have a unique PK/PD profile. It is currently unclear whether this profile will give it an ultra-long half-life, improve its stability, enable more flexible dosing, or provide some other novel feature - we'll look for more hints of this during the first half of next year when, as management guided in today's call, phase 3 protocols are disclosed and results from phase 1 trials are presented at a diabetes congress. We see increasing the speed of development of this new insulin glargine as a very smart move by Sanofi, as it signals that the company is not resting on any laurels about Lantus' impressive basal insulin market share (75% in the US according to management) or base sales of several billion per year. The strategy, of course, is not set in stone and could change significantly as degludec and Lilly's version of glargine enter the market.
- **The company filed for regulatory approval of its GLP-1 agonist lixisenatide (Lyxumia) in the EU in late October 2011.** Given a standard 13-month EMA review cycle, we expect to hear a decision on the compound by around November 2012. Though no specific mention of this was made during today's call, Zealand Pharma, the company from which Sanofi licensed lixisenatide in 2003, said in their recent Capital Markets Day (see our October 28, 2011 Closer Look at https://closeconcerns.box.net/sharhttps:/closeconcerns.box.net/shared/b8uquexdd661n1ofknh1ed/b8uquexdd661n1ofknh1that US regulatory submission of lixisenatide is expected in 4Q12 (Sanofi and Zealand had previously guided for 2H12). If approved, lixisenatide will be the third GLP-1 agonist to market (the second once-daily behind Victoza) and at least in Europe, will be entering a market where a once-weekly GLP-1 agonist, Bydureon, is already available. Although in clinical trials lixisenatide has been shown to be non-inferior to exenatide in its A1c lowering efficacy and Zealand management has suggested that lixisenatide has a stronger postprandial effect than Victoza, we think that in order for lixisenatide to succeed in this established GLP-1 arena, it will have to succeed on a couple of other fronts. We expect, for example, that it will be delivered in what patients perceive as a "standout" pen - Sanofi's current pens are very popular and challenging to copy. It goes without saying that the drug will have to have a very good safety and tolerability profile; another area that it may be differentiated, of course, is through a Lantus combination product (see below for our discussion of Sanofi's upcoming lixisenatide/Lantus combination). A major opportunity could also be the chance for it to be the first GLP-1 to show cardioprotective benefits - this may help reimbursement and we are not sure, however, if this is

shown, whether it would be considered a class effect or something compound-specific.. Given that diabetes is a risk factor for cardiovascular disease, we would assume a diabetes drug or class with the latter characteristic would be extremely appealing to physicians, patients, and payors alike and we look forward to seeing how assumptions play out once data is shown. Numerous animal studies have suggested a cardioprotective effect of GLP-1s and in a pre-clinical ex vivo study presented at ADA (0968-P), lixisenatide was shown to protect against myocardial reperfusion ischemic injury in an isolated rat heart model. ELIXA, the cardiovascular outcomes trial for lixisenatide, is assessing whether lixisenatide has discernible cardioprotective effects in humans, and could help lixisenatide be the first GLP-1 with a cardioprotective claim - we'll be eagerly waiting for its results in 2013. As a reminder, LEADER and EXSCEL, liraglutide's and exenatide-once-weekly's cardiovascular outcomes trials, are anticipated to report results in 2015 and 2017, respectively.

- **During Q&A, management reaffirmed its plan to start phase 3 trials with its lixisenatide/Lantus combination product in early 2013.** It also restated that the combination will not be a fixed-dose combination, but rather, it will allow for insulin dose individualization - we are really interested in learning how this will be possible. As we reported in our coverage of Sanofi's Diabetes and Oncology IR Seminar (see our October 3, 2010 Closer Look at https://closeconcerns.box.net/shared/sco26zvpbnylr1uy46j8the lixisenatide/Lantus phase 3 program is comprised of three trials. One of these trials (ClinicalTrials.gov Identifier: NCT00975286, n=446), which examined the relative glycemic benefits of adding lixisenatide versus placebo to insulin glargine and metformin treatment for 24 weeks (a "free combination" of lixisenatide/Lantus), was completed in August 2011. We look forward to hearing its results in the near future. In order to comply with FDA and EMA requirements, the pivotal trial required for registration of the lixisenatide/Lantus combination will have to use the pen in which Sanofi plans to eventually market the combination. Management had previously guided for this pivotal trial to initiate in October 2011-April 2012, but we learned during Sanofi's 2Q11 update that initiation of this trial had been delayed until early 2013; we assume this delay was due to development of the pen intended for commercial use being slower than expected. Due to this delayed start, the combination could now at earliest be submitted to regulatory authorities by late 2013 or the beginning of 2014. In our view, this timing is unfortunate for lixisenatide. We have heard significant clinician support for use of short-acting GLP-1s with basal insulin, understood that many physicians have been using GLP-1 plus insulin off-label for many years with very positive results, and therefore think that lixisenatide would have gained important traction from being part of the first product to market that simplified dosing of this quite popular combination. Novo Nordisk is now slightly ahead in the process. As a reminder, Novo Nordisk has already initiated a phase 3 trial (DUAL I) for its degludec/Victoza combination (Clinicaltrials.gov Identifier: NCT01336023) that is expected to complete before October 2012 - this trial timeline could place filing for Novo Nordisk's combination by the end of 2012 and an FDA decision in 4Q13, right around the time the lixisenatide/Lantus combination might be submitted. However, the degludec/Victoza combination would not allow for individualized dosing of insulin, as the doses of degludec and Victoza would be set at a fixed ratio in the pen for the combination product.
- **Sanofi highlighted results from the GETGOAL-F1 trial that were presented at EASD 2011.** The 24-week study evaluated the safety and efficacy of two different lixisenatide dose regimens versus placebo. Patients were randomized to receive lixisenatide 20 ug with a one-step dose increase regimen (n=161), lixisenatide 20 ug with a two-step dose increase regimen (n=161), or placebo (n=160). At baseline, patients had an approximate A1c of 8.0%, fasting plasma glucose of 9.5 mmol/l (171 mg/dl), and weight of 90 kg (198 lbs). Patients in the lixisenatide treatment arms also experienced significant reductions in A1c, fasting plasma glucose, and weight compared to placebo. Specifically, at the study's end, mean changes in A1c of -0.92, -0.83, and -0.42 were observed for the lixisenatide one-step, lixisenatide two-step, and placebo groups, respectively. We note that while this isn't a head-to-head trial and lixisenatide has previously been shown to be non-inferior to exenatide in its glucose-lowering efficacy, the placebo-adjusted A1c reduction of less than 0.5% seen in this trial seems low for the GLP-1 class. Overall, in the trial, the one-step and two-step

dose increase regimen treatment arms were comparable in terms of efficacy and safety and according to the company, this finding supports simplified treatment initiation of lixisenatide (i.e. with a one-step dose regimen). Adverse events were generally balanced between the two lixisenatide treatment arms and placebo. Finally, the rate of hypoglycemia was 1.9% in the one-step group, 2.5% in the two-step group, and 0.6% in placebo; no severe hypoglycemic events were reported. For more details on these results, see our EASD 2011 Full Report at bit.ly/ozzbgG. As a reminder, lixisenatide is being tested in nine phase 3 GETGOAL trials in addition to GETGOAL-F1. Results from six of the ten GETGOAL trials have thus far been released, and aside from two trials in Japan and China (which will complete in 1H12), results from the remaining GETGOAL trials are expected in 4Q11.

- **No updates were provided during the call regarding the rest of Sanofi's metabolic pipeline.** FOV2304, the company's bradykinin B1 antagonist for diabetic macular edema, remains in phase 2; meanwhile both SAR407899 (a RHO kinase inhibitor) and SAR101099, (a urotensin II receptor antagonist) remain in phase 1 for the treatment of diabetic nephropathy. Again, no updates were provided on Pancreate (the human proislet peptide Sanofi acquired from CureDM), so we assume that the compound remains in preclinical studies. Management had previously guided during Sanofi's October 2010 Diabetes and Oncology IR Thematic Seminar that Sanofi intended to advance the candidate into phase 1 development in 2011, so we look forward to seeing in 4Q11 whether the company remains on track with its timeline.

Questions and Answers

Q: Can you remind us what the potential benefits of your new insulin glargine formulation might be?

A: We're not going to say an awful lot at this point on the new glargine formulation. It will offer a different and unique PK/PD profile. Once we get the phase 3 protocols, we'll disclose those once we get studies that begin to recruit. We are going to show the phase 1 results at one of the future diabetes congresses. So, I think you can look towards first half of next year for more information on it, but this has become a pretty competitive space, so we're not to say an awful lot.

Q: As a follow-up to the previous question on Lantus... just playing devil's advocate, if you're bypassing phase 2, would it be right to assume this is more of an ultra-long-acting once-daily formulation that you've got it mind, rather than something that's longer acting for Lantus? Could give any sense as to why you are confident that you can bypass phase 2 studies? I realize there's a strong incentive to get this product in the market sooner rather than later.

A: Again, I don't want to say too much about our new insulin glargine. Since we talked last on September 6th, we've had regulatory interactions that gave us the confidence that we can go straight through to phase 3.

Q: Just yet another one on glargine. It looks like Lilly is now is now in phase 3 with a biosimilar Lantus. So, what are your thoughts on the timing of your program - how is it going to stack up in relative terms?

A: So, I don't know what timeline Lilly is on. It would be too early to start commenting on our own timeline. I think one thing we have said is that Lilly is obviously doing full clinical. So, we don't really see Lilly coming up with a fully substitutable biosimilar at this stage. Lilly comes into a market that's got Lantus as market leader. There is Levemir, and degludec will get there, so it's going to be a fourth entry into the market and we'll see what happens. Thus far, Lantus has maintained roughly 75% market share in the United States despite Levemir. I don't really see anything really putting Lantus off its perch any time soon. We have a new formulation, a combination with our GLP-1, and a different device [in development]. Given the sheer volumes of this market - remember that it's only a small portion of the market that is treated with modern insulins, certainly with long-acting basal insulins - I think the market is certainly big enough. I would actually suspect that you're going to see some market expansion. I mean really because Levemir hasn't been a phenomenal success for Novo, they haven't really been putting all that much commercial effort behind it. When you get to degludec and a few others, you're going to have an awful lot of commercial effort going to really converting towards basals. We've certainly seen this in plenty of other categories. When you actually have new entrants

coming in, it helps it to accelerate the convergence process. So I wouldn't see this as a zero-sum game in the marketplace. I think you're going to see market growth, and you're going to see everybody get a little bit of share. But, first of all, nobody has the emerging market presence that Sanofi does - certainly Lilly doesn't and Novo is clearly strong in a few key BRIC markets, but for the most part doesn't have our presence either. I think this is one of the biggest and most important markets out there. You have a few players in it. I'm not too worried about it, and we've got plenty of innovation coming along to keep our franchise going.

Q: Apologies for yet another question about the insulin glargine, but will the new insulin glargine be a full NDA or a 510(k)? What is the patent protection?

A: I can tell you that we have filed patents on that, but that's all that I can really give you. On what regulatory filing, I actually don't know the answer to that, so we can follow up with you on that.

Q: Any update on the Lantus lixisenatide-pen device?

A: I'll remind you that our combined device will contain both products, which means both products will be injected together. We believe that we have an interesting concept because it will allow, contrary to other concepts, to individualize the insulin dose, which we feel is imperative given the mode of action of insulin. We feel it would be not adequate to put it in a fixed dose and make some titrations very complex. Given our large background in developing and producing devices in-house, we have done very well and we are very optimistic that we will run the phase 3 clinical trials with the combination as foreseen starting very early in 2013 approximately in, let's say, 15 or at the latest 18 months from today.

--by Vincent Wu, Lisa Rotenstein, and Kelly Close