



Diabetes Close Up, V2, #13
July 22, 2003

Greetings. We've got a flurry of reports in the coming days, so let's get started!

- 1. **Roche 1H03 results** – Diabetes business up 4% overall, 12% in the US, but less excluding Disetronic
 - 2. **Upcoming earnings reports** with implications for diabetes/obesity markets
 - 3. **Upcoming diabetes/obesity – related conferences**
 - 4. **Diabetes News of Note**
- Appendix: More Roche ~

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1. **Roche 1H03 results:** Roche's 1H03 conference call ended about half an hour ago; it's late, but at least we were able to see the slides before the show, since they were posted early (good tip for next time). My comments below relate to Roche's diabetes unit.

a. **Diabetes Business Results – US and overall:**

- **Total diabetes care sales rose just under 4%, from 1,235 million CHF in 1H02 to 1,280 million in 1H03. However, this includes 31 million (2% of total diabetes care revenue) from Disetronic, as of May 2003 – so “same store” sales would appear to be closer to 1% (the US percent of total Disetronic sales wasn't disclosed).**
- **Management stressed that US diabetes sales grew 12% in 1H (sales excluding pumps not broken out). No mention of relative weakness, but note that LifeScan's international results were robust in 2Q¹.**
- **“Local” sales grew 14%. Roche doesn't give the actual dollar split in its diabetes business.**
- **On its Compact launch, “No cannibalization of the Advantage and Active was seen and we're gaining share in the US.” Roche plans to launch the Advantage III meter and the Accu-Chek Go – in 3Q03 and 4Q03, respectively.**
- **Comment on industry growth – Management took an opportunity to confirm that the US diabetes market is slowing. They estimated the last two consecutive quarters saw growth of 5-6% - considerably down from double digits in recent years, saying “We would be surprised if it improved significantly” –growth might bump up to 8-9% later this year, but still far below recent mid-teens growth. Why the slowdown?**
 - a. **Potential price pressure** from managed care companies;
 - b. **The economy** - I spoke to a super smart pharma analyst today who agreed they are seeing slowness as well and I am now speculating that it might be *co-pay* pressure – perhaps people are trying to save more on co-pays by buying less frequently. That perhaps people are testing less (and taking fewer drugs) for economic reasons has been posited before and bears close watch in my view;
 - c. **Another conjecture is that some patients might be using cost as an “excuse” to check less** – some demographics may dislike testing more than others (I'm thinking of Type 2's but realize generalization is dangerous!) and they might use the expense

¹ LifeScan's Int'l sales rose 35% (14% operationally) to \$157 mm from \$117 mm in 2Q02.

as an excuse to test less. This may be ‘out there’ – the theory clearly needs some testing! Stay tuned on this ~

- d. **This one needs more thought** - something odd is happening in the Type 2 market with oral agents that would slow demand?
- **Competitive landscape** – J&J total blood glucose monitor sales fell 6% in 2Q and Abbott sales rose 3% - we understand Bayer sales were also weak in the US (results not disclosed) and we await BD and TheraSense on Thursday to get a better/more-detailed picture of the industry.
- b. **More on pumps:** Some interesting data on both the market and Disetronic emerged on the call:
 - **As you likely know, Disetronic is not shipping pumps in the US currently² – Roche shed some light on its Disetronic business:**
 - **Roche senior management was aware of the problems at Disetronic before its purchase announcement (“It has already received three FDA letters...” it was pointed out. “...We changed management immediately on May 5.”)** Do we hear too much protesting? It seemed a little odd to hear that the Disetronic integration was absolutely on track in light of the FDA issues. Investors were advised to expect resolution within 12 months and that an FDA inspection should happen 2Q04. “No other country has followed the FDA, not even Canada. We’re working closely with FDA to get compliance in order.” The big question to me is what impact the FDA action will have in Europe – no news yet on this but no question that int’l non-Disetronic reps see this as a big opportunity.
 - **There has been wide speculation that the Disetronic sales force would sell another pump during this “time off” but it appears the sales force here in the US will focus only on sale of disposables.** Given that the sale of an insulin pump is highly complex– and much more higher-margin than a disposable sale – I wonder how Disetronic will keep its best reps. In my experience, most patients decide early on which disposable set to buy (and stick with the decision – until now, there hasn’t been that much differentiation among sets though we should be seeing some new innovative ones soon), and a salesperson is typically not the main influence (patients tend to buy what they like). Most likely this is an attempt to keep sales force in front of clinicians, but again, the sales pitch is less compelling without the pump. Although clinicians definitely influence these purchases, the purchases are less high margin than the pumps. In addition, I suspect it will be very challenging (and not that profitable even if successful) to convince patients with Animas or Medtronic or Deltec pumps to buy Disetronic sets.
 - **In the meantime, plans are to launch the first Accucheck branded pump in the second half of 2004.** With this device, Roche hopes to leverage the Accucheck brand, achieve new growth by entering this market, gain greater access to high frequency testers and be the first company to create an artificial pancreas by combining monitoring and insulin delivery. With the Disetronic purchase (notwithstanding the FDA action), I believe they also hope to protect their blood glucose brand – they don’t to lose the pumpers! Page 57 of the slides shows an illustration of the planned pump lifecycle progress; interestingly, continuous monitoring, though not discussed on the call, is very near the pump/BG connectivity icon³.
 - **Management estimated the cost of the lost potential US sales at US\$60 million** and the cost of the restructuring was estimated at 10 mm (assume CHF).
 - **Management said it had 65,000 patients in the US on Disetronic pumps – I would not have guessed an estimate this high.** They send two pumps to each patient and I am wondering if that is somehow in the numbers – traditionally I believe Disetronic has had about 15% of the US market.

² For copy of tough-minded June 11 FDA letter, see http://www.fda.gov/foi/warning_letters/g4120d.pdf.

³ There should be interesting information on this at the Nov 6-8 Diabetes Technology meeting; at last year’s meeting, we saw a great live CM patient case (www.diabetestechology.com)

- **Plans for the next generation integrated pump/meter include a launch in the second half 2004** – clearly this assumes its FDA issues will be resolved within 12 months. It was noted that with this new pump. Disetronic would go after US market share aggressively, seeking 50% of new pump users. Although I do think that percentage sounds awfully high, I think we will start to see pump market expansion with the new “smart” pumps already on the market and those coming soon, with impressive pump “miniaturization”, etc.
 - **Points for puns:** Did anyone else notice that Roche said early on in its call: “*We acquired Disetronic to change the paradigm in diabetes care.*” That’s pretty clever! www.minimed.com/patientfam/pf_ipt_paradigm_pump_overview.shtml
- c. Roche pharma** – Roche is clearly trying to work the diabetes pharma angle – It has two Type 2 drugs in Phase 0, two in Phase 1, and one in Phase 2. Our appendix this week includes an interesting story on some of Roche’s efforts on this front.

2. Upcoming earnings reports with implications for diabetes/obesity markets:

- GSK** – Wednesday, July 23, 7:30 am EST www.gsk.com
- BDX** – Thursday, July 24, 8:30 am EST www.bd.com
- THER** – Thursday, July 24, 5:00 pm EST www.therasense.com
- BMY** – Thursday, July 24, 10:30am EST <http://www.bms.com/investors/data/>
- LLY** – Thursday, July 24, 9:30am EST <http://investor.lilly.com/calendar.cfm>
- PFE** – Friday, July 25, 11:00 EST <http://www.pfizer.com/main1.html>
- AVE** – Tuesday, July 29. Earnings press release on the website (www.aventis.com) as early as 1 am EST (7am Central European Time)
- IMDC** – July 30, 4:30 pm EST www.inamed.com
- NVO** - Aug 5, 15:00 Danish time - will be webcast on homepage. <http://www.novonordisk.com/investors/default.asp>
- NKTR** – Wednesday, August 6, 5 pm EST www.nektar.com
- AMLN** – Thursday, August 14, 12 am EST www.amylin.com
- MDT** – Week of August 11 (estimated); annual meeting occurs August 28 www.medtronic.com
- Already reported: JNJ, ABT, Roche, GSK.**

3. Upcoming diabetes/obesity – related conferences:

- AADE:** August 5-9, Salt Lake, www.aadenet.org.
- EASD/IDF:** August 24-29, Paris, www.easd.org.
- NAASO Annual Scientific Meeting:** October 11 – 15, Ft Lauderdale, www.naaso.org/meetings/
- Canadian Diabetes Association:** October 15-18, Ottawa, Canada. www.diabetes.ca **Early bird discount – ends August 18.**
- Diabetes Technology:** November 6-8, San Francisco. www.diabetestechology.org
- American Heart Association:** Diabetes symposium led by the great Dr. Steve Marso: November 8, Orlando – www.scientificsessions.org.

4. Diabetes news of note:

- **Novo discontinuing insulin - a move to free up capacity?** Novo is discontinuing its Novolin Lente insulin – this is a “long-acting” insulin that had much wider use before Lantus, Aventis’ powerhouse ‘basal insulin’ was approved in 2000. A smart investor noted that they might need extra manufacturing capacity for their Lantus-like product – stay tuned on this front. “Drug Shortage: Drug to be Discontinued; Novolin L” <http://www.fda.gov/cder/drug/shortages/default.htm#disc>
- **WSJ July 16, 2003: U.S. Government to Study Weight-Loss Successes** The National Institutes of Health last week announced the launch of a three-year, two-phase study of 1,600 people to answer the question of how to lose weight permanently. The study will be comprised of roughly 60% women and ~40% African-Americans. So far, Americans seem to manage initial weight loss fairly well; the real challenge lies in maintaining the weight loss. The study will take place at four centers across the US: Duke University, Pennington Biomedical Research Center at LSU - Baton Rouge, Kaiser Permanente Center for Health Research - Portland, Oregon, and Johns Hopkins Medical Institutions - Baltimore. www.wsj.com

- **Relationship of Walking to Mortality Among US Adults With Diabetes** *From Archives of Internal Medicine Vol 163, June 23, 2003 (1440-1447)* Data collected from the National Health Interview Survey (NHIS) of 1990 and 1991 was recently used to determine the relationship between walking and the risk for all-cause and cardiovascular disease (CVD) mortality among diabetics. In this prospective cohort study representative of the US population, 2,896 adults with diabetes from the NHIS were included in this additional research. **Results and Conclusions:** When compared to sedentary individuals, people who walked at least 2hr/week had a **39%** lower all-cause mortality rate and a **34%** lower CVD mortality rate. Mortality rates were lowest among people who walked an average of 3-4hr/week and for people who moderately increased their breathing and heart rates while walking. In summary, walking was associated with reduced mortality rates among a diverse population of adult diabetics. In downtown SF unexpectedly? Call me for a walk!
- **NYTimes July 17th: Europe Seeks Firm Limits on Health Claims for Food** The European Commission, amid strong opposition from food companies, recently proposed strict regulations aimed at making it harder for companies to make health and nutritional claims for their products, especially for foods high in sugar, salt or fat. David Byrne, the health commissioner for the European Union, says the proposed rules are necessary to prevent food companies from continuing to mislead consumers. Among the proposed amendments are mandatory backing of all health claims on food, drinks, or food supplements by independent experts and the refusal of health claims to be made regarding alcoholic beverages.

I hope this finds you well - it's a beautiful evening in San Francisco, and hope it's gorgeous wherever you are! Take good care.

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APPENDIX *More on Roche*

From July 22 *Diabetes In Control*

“New Drug Targets Liver and Pancreas”

Researchers said on Thursday they had found a new class of drugs that might attack diabetes on more than one front -- and that could be taken as a pill.

They have only tested the drugs in rats and mice so far, meaning years of development are needed, but said the medications could offer an alternative to some of the drugs that many diabetes patients must take.

"At this point in time, this type of drug will not allow us to replace insulin," cautioned Joseph Grippo, a vice-president at Swiss drug giant Roche who led the research. The drug is targeting type-2 diabetes populations before they get to insulin.

Patients with type 2 diabetes make too little insulin and have too much glucose in their systems. The new compound stimulates the pancreas to release more insulin and keeps the liver from producing too much glucose. Diabetes patients often take two drugs for this -- sulfonylureas and metformin. Roche's drug, known by the experimental name RO-28-1675, is a glucokinase enzyme activator. It acts on GK, an enzyme that diabetes researchers have known about for years.

The glucokinase enzyme is the body's first step in breaking down or metabolizing glucose. "When the enzyme is functioning normally, GK helps the body maintain glucose levels by controlling the release of insulin from the pancreas as well as the disposal of glucose in the liver."

HOPES FOR HUMAN TESTS WITHIN A YEAR

In 1992 researchers discovered a mutation in the GK gene caused a certain type of diabetes called maturity onset diabetes of the young type 2. But, it did not seem like a good target for a drug. "In order to make it effective you have to activate the enzyme. If you look at many of the drugs out there the activators are rare. Most drugs inhibit enzymes.

But when Roche scientists started screening through a library of compounds -- a common way to look for drugs -- they found one that seemed like it would activate GK.

Reporting in the journal *Science*, they said it worked both in lab dishes and in mice. Grippo said they hope to get approval to start testing it in people within a year.

"There have not been that many new drugs for the treatment of diabetes ever discovered, and this one is unique in its mechanism of action," said Mark Magnuson, a researcher at Vanderbilt University in Nashville, Tennessee who worked with GK for years. "No one ever thought we would find a drug that directly targets the enzyme and activates it," Magnuson added in a statement.

One big question is whether early treatment with drugs can prevent the development or progression of type-2 diabetes. A class of drugs called TZDs or glitazones, which includes GlaxoSmithKline's Avandia, are being tested with prevention in mind. Grippo said the new Roche drug would not compete with these drugs, but said its mechanism of action might help prevent the deterioration of the pancreatic cells that produce insulin.

"If we catch people early enough, it will possibly have some benefit," Grippo said. "It's something we will look for."

Diabetes Close Up is an occasional newsletter that highlights notable goings-on related to selected companies with diabetes/obesity businesses. This newsletter is put forward as an unbiased commentary on the industry. If you have any suggestions that you think should be included, please contact info@closeconcerns.com. Many thanks!

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