DIABETES CLOSE UP

Diabetes Close Up, V2, #21
October 14, 2003

Greetings from Florida, where I'm taking a break from NAASO (national obesity meeting) – this has been a really interesting week. Johnson & Johnson reported this morning; details are below, along with a couple of comments on recent media of note.

1. **J&J:**
   - **Worldwide reported LifeScan sales increased approximately 11% year over year, and 7% on an operational basis.** This is the first reported double-digit growth this year – nice to see a comeback in the midst of a sluggish US market. Fully 98% of the growth stemmed from LifeScan's international business.
   - **Topamax sales rose 37% worldwide to $253 – on an annualized basis, the drug is now officially a blockbuster.** The label covers anti-epileptic use, although doctors are free to use the drug for other indications where they see fit. J&J is at work on a new formulation for obesity.
2. **Media update**
   - **JAMA, October 7, 2003.** *Lifetime Risk for Diabetes Mellitus in the United States*
   - **Wall Street Journal, October 14, 2003**. *Americans Start to Shape Up, Eat Healthier*
   - **Wall Street Journal, October 14, 2003**. *Study Says Ranks of the Very Obese Widen Sharply*.
3. **Upcoming company reports of note**
4. **Upcoming conferences of note**

More on J&J ~

1. **For LifeScan, the U.S. blood glucose market in particular continues to be challenging, while internationally, results remain very strong.**
   - **LifeScan's worldwide sales increase of 11% (7% excluding FX) reflected a nice turnaround after last quarter's ww 6% decline**. Excluding the Can Am and LXN divestitures, operational growth would have hit 10% worldwide and 5% in the US.
   - **US sales rose 0.3% to $214 mm from $213 mm a year ago – this follows declines of 1% and 27%, respectively, for the first two quarters of the year. Excluding the Can Am/LXN divestures, US growth hit about 5%. CFO Bob Darretta** noted that LifeScan US growth was more in line with the market, pegged by JNJ at about 3% in the second quarter.
   - **Int'l sales rose 32% (20% operationally) to $148 mm from $111 mm a year ago.** LifeScan growth in Europe appears to be especially strong – indeed, the LifeScan booth was bustling at IDF[1], and it appears the core countries such as France, the UK, and Italy are doing particularly well.
   - **Easing comparisons helped the quarter**: A year ago (3Q02), US LifeScan sales rose 7%, following 26% and 31% increases in 1Q02 and 2Q02, respectively. Worldwide,

[1] The booth had head to head surveys comparing LifeScan strips to Roche and TheraSense – let me know if you would like survey summaries.

3Q02 LifeScan sales rose 13%, following 23% and 34% increases in 1Q02 and 2Q02, respectively.

- **Last quarter, LifeScan had discussed strength coming from the mail order segment and new products** – we didn't hear anything about these today, but we'll be on the lookout at the Canadian Diabetes Meeting, starting Wednesday.
- **Pricing appears to be impacting the market more than a unit slowdown**, as noted in DCU V2, #20 (www.closeconcerns.com). Managed care pressure is mighty and competition to attract and retain patients is tough – and expensive.
- **Therapy intensification continues – but blind blousing persists:**
    a. All that said about price, it seems that there should be opportunities in unit growth for the entire market. I often wonder why the companies in the industry don't get together and do a campaign on the benefits of testing. That patients only test on average ~1-1.5x/day is unbelievable to me.
    b. While clearly a segment exists of well-managed Type 2s not on insulin who do *not* need to test frequently, there are many others that should be on insulin and aren't, and another segment that, whether they are or are not on insulin, don't test as often as they should.
    c. Testing is important for insulin dosage and for "corrections" – while hyperglycemia in any form is a negative, hyperglycemia for one hour, followed by an insulin "correction" dose is far better than hyperglycemia for eight hours – or maybe for a day, til the next test.
    d. So it is said that therapy intensification is a growing trend, particularly for Type 2s, and so one would think, as more patients go onto insulin, more patients *would* test before meals to determine insulin dosage. BUT, this is all theoretical – in reality, I don't have data on this and anecdotal evidence suggests there's a lot of blind blousing going on. Anecdotally, I recently met a Type 1 patient that had just gone on the pump – she now tests her blood glucose prior to every meal, but prior to the pump (and despite the fact that she was on MDI), she noted that she checked "a couple of times per month." While I don't think this is common behavior among Type 1 patients, it does underscore the ongoing need for education.
    e. Continuous (especially once it is reimbursed) may really increase tests ~ I believe that the advent of continuous monitoring will results in more news about big excursions and the value of intensive management – namely, MDI and pumps. This in turn I would guess would drive more testing – even among those that don't go on continuous monitors themselves.
- **Back on the topic of education** – you know, the US healthcare system is really set up to address acute problems, not chronic problems. This is why reimbursement is straightforward for problems like the common cold but not for blood glucose data analysis. The other thing – although there's been a lot of growth in designer insulins (Lantus, Novalog, Humalog), interviews I had with CDEs at the AADE suggest that some non-endo, non-diabetes-specialist docs really don't know how the insulins work and they don't have a lot of time to spend with patients on them – so movement toward insulin is still slower than it should be, even given the more recent Lantus success. Unsurprising, given that docs have all of 15 minutes, often less, to spend with a patient.
- **And this is why it seems we're headed for even more trouble** – we think the obesity epidemic is bad now but just wait til all the adolescent /young adults getting diabetes now start getting heart attacks and strokes in a decade's time. Not to editorialize too much, and I hate to sound alarmist…but the public health implications are worrisome at best.
- **See Appendix for a few notes on Topamax.**

2. **Media Update**:
    a. **JAMA, October 7, 2003. *Lifetime Risk for Diabetes Mellitus in the United States* was published.** If you wonder why I go on and on about the importance of education, all you need to do is to read this article to understand why – this is the first time that "lifetime risk" for diabetes has been quantified and the findings are disturbing.
        i. The study estimated lifetime risk of developing diabetes for individuals born in 2000 at 32.8% at for males and 38.5% for females. 38.5%!! Females have higher residual risks at every age. In terms of ethnicity, the highest estimated lifetime risk for diabetes is among Hispanics - 45.4% for males and 52.5% for females.
        ii. Unsurprisingly, individuals diagnosed with diabetes have significant reductions in life expectancy. The study estimates that if an individual is diagnosed at age 40 years, men will lose 11.6 life-years and 18.6 quality-adjusted life-years and women will lose 14.3 life-years and 22.0 quality-adjusted life-years.
        iii. JAMA noted that primary prevention of diabetes and its complications are important public health priorities.
        iv. One bright light. I heard a fantastic talk by noted endocrinologist Irl Hirsch last spring at the AACE meeting. He noted DCCT data that showed for the same A1C over time, very different rates of diabetic retinopathy (DR) were seen between the groups intensively and conventionally managed (as a reminder – intensive patients were on MDI, with most taking prandial insulin, or on a pump). An A1C of even as high as 9, for example, results in significantly less retinopathy for patients on the pump or on multiple injections, versus an A1C of 9 for a patient on only 1-2 shots per day. The question posed by Dr. Hirsch - are the lower rates of DR seen with more physiologic insulin resulting in less postprandial hyperglycemia, or is it due to the decrease in glycemic variation? One could argue, he says, that a HbA1c of 9% in a CSII patient led to little DR since there was much less variability than a 9% on a BID NPH/Reg. insulin regimen. This of course leads to the importance of standard deviation (SD), which Dr. Hirsch pioneered and has discussed for some years now and which was more widely discussed at the 2003 meetings than ever before. I think the advent of continuous monitoring will contribute to much more focus on SD.
        v. Please let me know if you'd like a copy of the JAMA piece.
    b. **Wall Street Journal, October 14, 2003**. *Americans Start to Shape Up, Eat Healthier.* Amazing – some relatively positive news about Americans and food. The top line – Americans ate fresh fruit 6% more often in 2003 versus a year ago (based on a 14-day survey by NPD Group) and they exercised more – 55% exercised strenuously at least once a week, compared to 63% the year before. Self-reported obesity ranks fell. I actually wonder whether the self – reporting was as 'pure' this year – maybe all the media has made Americans feel more guilty about overeating/lack of exercise. It should also be pointed out that although the data is better versus a year ago, eating habits are still worse than they were a year ago. www.wsj.com.
    c. **Wall Street Journal, October 14, 2003**. *Study Says Ranks of the Very Obese Widen Sharply*. Rhonda Rundle points out that the number of Americans who are more than 100 pounds overweight has grown twice as fast as overall obesity trend hitting the US. The study she quotes, available in the current issue of the Archives of Internal Medicine, points out that between 1986 and 2000, the number of people clinically obese quadrupled to about 1 in 50 adults in the US. As a reminder – BMI typically defines obesity. Overweight is a BMI between 25-30, obese is 31-35, morbidly obese is 35-40, and super obese is over 40.
3. **Upcoming earnings reports with implications for diabetes/obesity markets**
    a. **Roche – Thursday, October 16,** 1:00 am EST – 3Q03 results www.roche.com
    b. **PFE – TBD; likely the week of October 13**
    c. **LLY - Wednesday, October 22,** 5:00 pm EST www.lilly.com. Note new info.
    d. **THER – Wednesday, October 22,** 5 pm EST. www.therasense.com
    e. **AVE** – Details TBD, likely week of Oct 27. www.aventis.com
    f. **Novo** – Wednesday, October 29, 9:00 am EST www.novonordisk.com Note new info.
    g. **BDX** – TBD; likely week of November 3 – F2Q03 results www.bdx.com Note new info.
    h. **IMDC** – Details TBD; www.inamed.com

i. **AMLN** – Details TBD; www.amylin.com.

4. Upcoming diabetes/obesity-related conferences.

a. **October 11-15, NAASO Annual Scientific Meeting**: Ft Lauderdale www.naaso.org
b. **October 15 – 18, Canadian Diabetes Association**: Ottawa, Canada. www.diabetes.ca
c. **October 25, Diabetes Research Institute, 4th Annual Conference,** New York http://www.drinet.org/html/4th_annual_research_conference.htm
d. **November 4-8**, **Rachmiel Levine Symposium: Advances in Diabetes Research**: From Cell Biology to Cell Therapy. Universal City http://levinesymposium.coh.org
e. **November 6-8**, **Diabetes Technology:** San Francisco www.diabetestechnology.org
f. **November 8, American Heart Association**: Diabetes symposium led by the esteemed Dr. Steve Marso. Orlando www.scientificsessions.org.
g. **November 14**, **Designing an Accelerated Cure for Type 1 Diabetes: Integrating Biology with Bioengineering.** Symposium at Sunsun, Santa Barbara.
h. **February 6-8, 2004**, ADA 51st Annual Postgraduate Course. San Francisco, CA http://www.diabetes.org/main/professional/conferences/default.jsp

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Appendix

A few notes on Topamax:

- **Sales grew a robust 37% worldwide – 35% in the US and 47% overseas.** Apparently there's been an increase in use of seizure drugs for other problems, including obesity. Topamax is not now labeled for obesity but doctors are free to use it for what they like, although the FDA obviously doesn't support off –label use encouraged by companies. Apparently for binge eating disorder, Topamax has seen some wide use. There have been a few interesting posters/talks at the summer meetings on Topamax, related to obesity. An intriguing presentation was given at NAASO – "*Effects of Topiramate on Body Fat after Low – Calorie Diet-Induced Weight Loss*."
- **There were three arms in the study** – those on a 96 mg and 182 mg doses of Topamax, and those on placebo. The presenter was noted that the study was halted by J&J, who is working on an improved formulation to enhanced tolerability and simplify dosing. Data shared:
  - **At week 44**, the mean percent change in weight for the two Topamax arms were 15% and 17% reductions, compared to a 9% reduction for those on placebo (there has been a run-in during which everyone was on a low-calorie diet-induced weight loss regimen in which an 8% weight loss was required in order to continue).
  - **Adverse events**: 13% dropped out in the Topamax arms compared to 8% in the placebo arms. In discussions with doctors, I have heard discussion of nausea, reduced activity levels, ability to function, etc. I understand that some populations, particularly those younger patients with no cognitive problems, appear to tolerate the drug well, though others have had major problems with the current formulation, which, *again* is not the formulation that J&J ultimately intends for obesity use. Anecdotally, to date, I have heard more caution on this drug than anything – clearly, it will be interesting to see results with new formulation in large populations over a longer time period.

Diabetes Close Up is a newsletter highlighting notable information and events related to selected companies with diabetes/obesity businesses. This newsletter is put forth as an unbiased commentary on the industry. If you have any suggestions or comments regarding content, please contact info@closeconcerns.com. If you would like to 1) unsubscribe; 2) receive a monthly digest rather than real-time updates; 3) add a name to the DCU mailing list; or 4) offer any suggestions or comments regarding content, please contact info@closeconcerns.com.