DIABETES CLOSE UP

Diabetes Close Up, V3, #2
January 16, 2004

1. **Abbott reported 4Q and 2003 results this morning**. Worldwide reported MediSense 4Q sales increased approximately 10% year over year on a reported basis, bolstered by a currency tailwind; on a performance basis, growth was a more muted 2.4%. Notably, 100% of 4Q's growth stemmed from international sales (see related stories below). Clearly there is excitement over prospects for 2004. Management forecasts 30% growth next year, including the impact of TheraSense, which should close in 2Q. Depending on a range of factors addressed below, we believe this projection could be conservative, even given current industry challenges.
2. **Great conference! JP Morgan Tidbits** on Amylin, Andrx, Aventis, BMS, Medtronic, and Pfizer.
3. **J&J Gets Tough on Distributors**: Details on the new policy at J&J and implications for the industry.
4. **Our next issue: On the Road - Conference Roundup.** Interesting conferences of late - our next two issues of DCU on Conferences will examine recent conferences including the following:
    a. **1st Annual World Congress on the Insulin Resistance Syndrome**, Los Angeles, CA, Nov. 21-22. *Interest is growing in metabolic syndrome – here's why.*
    b. **Sociedad Puertorriqueña de Endocrinología y Diabetología (SPED) / American Association of Clinical Endocrinologists (AACE) International Endocrine Clinical Update** and the 26th SPED Post Graduate Diabetes Course, Río Grande, Puerto Rico, December 10-14, 2003. *This was perhaps the most impressive lineup of speakers we've ever seen at a conference of this size – literally experts from every corner of diabetes. A fantastic success for AACE/SPED*.
    c. **Consensus Development Conference on Inpatient Diabetes and Metabolic Control**, Washington, DC, December 14-15, 2003. *We believe this conference could have profound positive implications on insulin use, insulin application, and blood glucose monitoring. Implementation will be key to watch.*
    d. **The Diabetic Foot Update**: A Multidisciplinary Course, San Antonio, TX, December 11-14. *Again, an impressive lineup and incredible focus on this complication area*.
    e. **From Clinical Trials to Community: The Science of Translating Diabetes and Obesity Research**. January 12-13, 2004, Washington DC. *This conference at the NIH had interesting complications for the industry – stay tuned.*
5. **Our next issue, part 2: Literature/Media Roundup coming next Tuesday, in DCU #3**:
    a. JAMA on being young and fat
    b. JAMA – TZD Circulation Statement
    c. *The Economist* on obesity ("Filling the World's Belly, December 13, 2003)
    d. *Time* on diabetes ("Diabetes: Are You At Risk?" December 8, 2003)
    e. *The New York Times* on teen obesity
6. ***Diabetes Close Up* commercial**! *DCU's Diabetes 2004 Roundup* will publish its first annual diabetes/obesity roundup in the coming weeks! Ordering information to follow shortly on our website. Please let us know if you are interested by e-mailing info@closeconcerns.com. The volume will contain:
    a. Detailed notes on 20 conferences in 2003, including ADA, AADE, EASD/IDF, NAASO
    b. Top ten research articles of 2003
    c. Top diabetes/obesity themes we saw in 2003
    d. Key conferences in 2004
    a. DCU High Five Awards – the best products of 2003

---

1. **More Abbott details**: **Abbott MediSense sales reached $141 million in the fourth quarter (slightly below last quarter's $145 million but up from $128 million in Q1 and Q2), up ~10% on a reported basis and 2.4% on a performance basis.**
    a. **US sales fell 4% to $50 million and international sales rose a 21%** to $92 million; excluding FX benefit, int'l sales rose 7%. Asia Pacific and Latin America represented areas of strength internationally.
    b. **Hospital sales have represented another area of relative strength for MediSense** – recent estimates put MediSense at 25% market share. Implications of the recent Consensus Development Conference on Inpatient Diabetes and Metabolic Control, in mid-December in Washington, DC, will be interesting to watch, as MediSense's hospital presence *could* put it in a stronger position as insulin use increases among inpatients as hospital use increases and consumer use at home increases.
        1. **Profoundly compelling evidence was shown in Washington last month on the impact of mortality and morbidity resulting from good glucose control**. For details prior to this month's conference report, see www.aace.com/pub/ICC/inpatientStatement.php. Our early assumption is that insulin manufacturers, insulin application manufacturers, and blood glucose monitoring manufacturers will see benefit from this meeting – more to follow on how this will emerge.
        2. **Our assumption is based on evidence shown, but it's complicated in our view.** Although it seems very likely that hospital glucose monitoring will start to increase as a result of more insulin taken, the real monitoring profits are in consumer use. Hospital margins are notoriously low, and it takes a lot to set up a hospital, etc. Because regulations require "lab" sort of monitors to be used in hospitals, the bigger question in our view is what happens when patients leave the hospital – assuming many are new to insulin, will they keep monitoring, and if so, using whose products?
            a. **In other words, if patients go on insulin at the hospital and stay on insulin**[1] and therefore need monitors to help with dosing decisions (they aren't labeled for this, by the way, but they are commonly used for this) both in the hospital and when they leave, there may be a higher likelihood that they will stick with the hospital brand (if in a slightly different meter form).
            b. **While some say implementation will make change in hospitals all but impossible**, others believe that we're in the midst of the start of a sea change. Our early perspective is that we agree we're at the beginning of a change - the evidence is basically unassailable, after all. The real question probably involves the *rate* of change, which we need to do more thinking on.
    c. **Look for stronger 2004 MediSense growth:** After annual growth of 10% in 2003 at MediSense (which was pretty impressive given that spending was probably restrained due to the consent decree, and the challenges in the industry related to pricing), management expects 30% growth for Medisense in 2003 assuming MediSense's 2003 base of $542 million. We believe this is conservative, though given industry pressures conservative is understandable.
        i. **Still, we would wager on higher growth given the following back of envelope math**:
            1. **Even if** TheraSense reports the low end of $200-$210 million for 2003 *and* even if the deal closes doesn't close until June (rather than April/May expectations) *and* even if Abbott's 2004 internal growth is only 6%, *and* even if TheraSense's 2004 internal growth is only 20%, we calculate growth for the combined entity would *still* hit nearly 30%. Still!

[1] This is another key question. High glucose sometimes occurs in those that are not diabetic who are in the ICU – while it makes sense to monitor and use insulin with such patients, they are not "long term" patients that will use insulin and monitors at home. How big is this group? That's just one of the big questions coming out of the conference ~ stay tuned on this front.

2. **On the other hand**, if Abbott gets nine months of THER 2004 sales, if THER has a better than expected 2003 and achieves growth of ~35% in 2004, and if Abbott's 2004 organic growth reaches 10%, overall MediSense 2004 growth would exceed 50%. So there's a lot that would have to go right, but then again there's a lot that *could* go right, which could render MediSense close to a billion dollar business long before anyone expected.
3. **Whether it's 30% growth or higher, we believe the match is a helpful one for both players** – among other things, Abbott gets better technology, a sexy new product, and a more robust pipeline, while TheraSense gets expertise that may prove very helpful, expertise that a Fortune 50 company can offer, on a variety of fronts like regulatory, reimbursement, etc. Although some say Abbott's FDA relationships couldn't be that great due to the consent decree, we believe that the FDA relationships company wide have improved – plus, MediSense wasn't part of the consent decree, although it certainly bore some of the downside. Success of the deal will depend on the success of continuous – needless to say, we believe Abbott is probably much happier with an option play for this area than without. Onward for both! THER reports January 22 – stay tuned.

- by Kelly Close

2. **JPMorgan Tidbits**: JPM had a very successful conference this week – lots of standing room only rooms, lots of energy, more optimism than has been seen in a long while. Of note to diabetes watchers:
    a. **Amylin said** it would begin testing exenatide in patients with Type 1 diabetes (with the NIH) and that it was testing Symlin in patients with Type 2 diabetes (phase 2 trials). Additionally, lower A1C results and lower weight was sustained in 52 patients at 52 weeks in the open label trials, and antibodies were seen in a lower percentage of patients.
    b. **Andrx** is launching a generic version of **Pfizer's Glucotrol XL** and also announced collaboration with **Takeda**, combining **Takeda's Actose** with once-daily metformin **Fordamet.** More combo therapy – good news for patients.
    c. **Aventis** chatter in the hallways focused largely on a potential bid by P&G, while in its presentation, Aventis stuck to numbers:
        i. **It showed 2002 ratings** that elevated the rank of the role of Aventis in the diabetes market from #6 in 2001 to #1 in 2002 (versus Eli Lily, which dropped from #2 in 2001 to #5 in 2002) – we're searching more for how they calculated this though certainly by any measure Lantus has helped hugely.
        ii. **On the positive Lantus front**, Aventis noted successful launches worldwide, including Brazil, Sweden, Germany, Ireland, the United Kingdom, and particularly in France, as well as its more recent success in American markets.
        iii. **On the negative Lantus front,** while at the conference, we heard that more than 1,000 people in the UK have complained of difficulties using Aventis' Optipen Pro insulin pen injection system, also known as the "Lantus" pen, which has been available in the UK since August 2002 (130,000 pens have apparently been distributed there). Reported problems apparently included plunger jams, dose setting problems, injection problems, and even DKA.
        iv. Meanwhile, **Aphidra** is a fast-acting insulin for both type 1 and type 2 diabetic patients; expect FDA approval in mid/late 2004.
    d. **BMS officially termed Muraglitzar** one of its "big 3 filings" for next year - said it is on track for filing end of 04. Said early clinical studies show good glucose control.
    e. **Medtronic said** it expects to see Guardian 1 (alarm product) approved in the next few weeks and that it would submit its real-time product by the end of this fiscal year, in late April.
    f. **Pfizer said** very little in its breakout about Exubera, the inhaled insulin formulation that it's working on with Aventis and Nektar, except "(*SIGH*) *This is one of three questions we can <u>always</u> count on. What we have said has been pretty consistent … things are going well with clinical development, and we want to make sure to provide a complete clinical package to maximize turnaround. We have not gone public with a specific timeframe.*"

--by Martha Nelson and Kelly Close

3. J&J Gets Tough on Distributors

Counterfeit drug and medical supply scams have increased sharply in recent years. During the late 1990s, FDA averaged about five investigations into counterfeit drugs per year, according to the agency. Since 2000, such FDA investigations have swelled to an average of over 20 per year.[2] While the majority of such scams have focused on pricey drugs like Lipitor, Procrit, Epogen, and Neupogen, a similar swindle in the diabetes industry involves a related problem known as product diversion - this has also been termed parallel importing, third party importing, the grey market, secondary sourcing, alternate sourcing, and our favorite, reimportation.

Product diversion strikes when wholesalers or distributors purchase product in one country (where prices are lower, such as Russia or Australia or France) and sell it in a country where prices are higher (like the US or the UK or Japan), thus taking advantage of pricing "arbitrage." Little known to some, but a box of strips could be as much as 150-200% higher or more in one country versus another. Strict labeling requirements in most regions prohibit product diversion, although product diversion until recently was legal in Europe (replicating package inserts, repackaging goods, etc.)

While multiple factors influence domestic and international growth, and while the specific impact of diversion is impossible to track precisely, the fact that international blood glucose revenues have grown at faster rates than domestic corroborates the suspicion that diversion has influenced results, perhaps significantly. For example, J&J's LifeScan international revenues over the last four quarters have increased an impressive 33%, while domestic revenues have fallen 3% on average[3]. As announced today, in 2003, Abbott's domestic sales were flat, while international revenues increased an average 17%. While a range of factors clearly influences such results, relating to competition, payors, promotions, currency, market fluctuations, etc. we believe sans product diversion, domestic growth rates would have been higher across the industry, perhaps significantly higher.

Both product diversion and counterfeiting are clearly more prevalent in developing countries - prices are lower there, for a kickoff, and regulation tends to be sketchier, in a word. The FDA estimates, in fact, that upwards of 10% of drugs worldwide are counterfeit and in some countries more than half the drug supply is made up of counterfeit product. An FDA task force plans to release a final report on drug counterfeiting later this month. While product diversion is a bigger problem in devices than is counterfeiting, we believe some manufacturers have experienced both. Importantly, we note that diversion and counterfeiting are very different; the latter is clearly illegal and the intent is to defraud the ultimate consumer rather than the manufacturer.

Like counterfeiting, product diversion is difficult to identify, investigate, and quantify. In addition to bottom line impact, product diversion creates other potential problems: If distributors do not purchase products directly from the manufacturer, it is uncertain how the product may be transferred, handled and stored, which ultimately may compromise product integrity. Further, there can be differences in product calibration by region for some products. For example, if LifeScan's One Touch Basic product, which is plasma calibrated, comes into whole blood markets via the secondary market, this could produce a result that is 12% higher or lower – not a big deal with a blood glucose of 120, maybe, but not so great at a blood glucose of 70.

Perpetrators have been tough to thwart, although industry has attempted to do so by various means, such as designing unique packaging security features, "both overt and covert," stepping up due diligence in selection, review, audit, and contract enforcement, and even by offering slightly different products in different regions, using slightly different strip technology, rendering strips not interchangeable.

---

[2] See http://www.fda.gov/oc/initiatives/counterfeit/qa.html.

[3] Below is a summary of recent LifeScan growth – 4Q03 results will be announced January 20.

- 4Q02 LifeScan domestic revenues increased 16%, while international revenues rose 33%;
- 1Q03 domestic revenues fell 1%, while international revenues increased 31%;
- 2Q domestic revenues fell 27% while international revenues increased 35%; and
- 3Q03 domestic revenues increased 0.3% while international revenues increased 32%.

What else can companies do? In mid-December, Johnson & Johnson took the proverbial bull by the horns and initiated a new policy requiring wholesalers and distributors to purchase prescription medications and medical devices directly from J&J rather than from secondary distributors. While the initiative may have originally stemmed from problems with high-growth, high-margin drugs like Procrit that are being counterfeited or otherwise diverted, it also has clear implications for areas like blood glucose monitoring. Pfizer followed suit a week later issuing a similar policy for its distributors.

What's the impact of J&J's new policy for diabetes products?

- For diabetes drugs, counterfeiting drugs aren't as much of an issue as in other therapeutic areas, by and large– in fact, come 2004, the majority of oral diabetes drugs will be generic (Actos, Avandia, and Amaryl, and Glucotrol XL, plus some combos, are exceptions).
- On the blood glucose monitoring side, this initiative could have key bearing on the diversion problem. For LifeScan itself, assuming the policy can be enforced, we would expect international sales to decline and for U.S. sales to climb back up, as more domestic distributors are forced to buy from J&J direct - through the US[4]. As noted, while multiple factors influencing the market make it impossible to isolate the impact of product diversion precisely, we expect net revenue from blood glucose monitoring products to climb as average selling prices effectively increase[5] as a result of J&J's new policy.
- Enforcement and implementation will be key to watch. Although it's always possible that distributors could refuse to buy direct, we think the risk is probably too big for most of them to do this since many of them rely on access to Procrit and other key J&J products such as atypical anti-psychotic Risperdal and Cypher stents, to name a couple.

The distributor list on JNJ's site (www.jnjgateway.com/public/USENG/Distributor_List_01.pdf) **bears watching**. While the deadline to express intent to sign letters is not until January 19, as of January 13, 2004, 26 LifeScan distributors have agreed to the policy; although the total number of LifeScan distributors is a proprietary number, we believe the total exceeds at least 50. For close readers who wonder what the status is for McKesson, Bergen, and other large distributors, note that this site shows the med/surg list only, although J&J believes the "Big 3" is close to signing, "…in the interest of public health and a vision of a secure supply chain." So far 60% of the Pharmaceutical Sourcing Group of North America and 50% of J&J's Health Care Systems distributors have signed the letters; those that haven't signed will not receive shipments beyond March 5. We believe it is likely that more distributors will be checked off the list in the coming days; we understand that although a distributor may have indicated his/her intention to sign the agreement, this is not noted as official until the letter is received. Additionally, since LifeScan shares distribution across various J&J companies, it's an administrative task to ensure that all covered companies are updated.

In general, J&J appears to believe that a majority of its distributors share their concern about protecting the public and their customers from counterfeit products and believe the policy will be widely adopted. According to J&J spokesman David Swearingen, J&J doesn't expect the policy, short- or long-term, to have a disruptive effect on its business and the company expresses deep concern about the threat that counterfeit products pose to public health.

Ultimately, we believe J&J's new product diversion policy is a positive for the rest of the industry as well as LifeScan, as well as for patients and we applaud the aggressive move. Although J&J possesses more power to make and enforce such policies than do most other industry players, overall, we look for bogus distributors to start running at least a little lower on products and perhaps a little more scared.

-- by Janet Ng and Kelly Close

---

[4] Another factor influencing international revenue could stem from a recent European Court of Justice ruling that struck down the European Commission's decision to fine Bayer for preventing its distributors from shipping drugs priced lower in one country to another country with a higher price. This decision appears a positive because it could help lower the risk of diversion, since pharmaceutical companies may now have more leverage for refusing to sell to those who profit from such price differentials. Ultimately, we believe the costs of enforcing it will be below the money lost due to diversion in the first place, and thus we view this as a positive move for the industry overall.

[5] This would stem from less lower-priced internationally-priced product sold and more higher-priced domestic product sold.

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.

Disclosure: Kelly L. Close is a specialized consultant to the medical technology/pharmaceutical/biotech industries. Companies 1) in which Kelly Close has a personal investment; 2) that are clients of Close Concerns, Inc.; and/or 3) on which Kelly Close serves on a speaker's bureau, including Abbott, Animas, Amylin, Aventis, Johnson & Johnson, SimpleChoice, and TheraSense. All observations expressed are the opinions of Close Concerns alone and should not be viewed as recommendations to investors on any companies in the industry.