January 04, 2011

Clinical and regulatory events over the Christmas period

While the holiday period is not generally busy, some interesting clinical and regulatory developments emerged that prompted some fairly significant share price movements for a handful of companies.

While the four-week delay to the FDA's decision on Mannkind's inhaled insulin Afrezza robbed 2010 of potentially one of its biggest drug approvals, there was disappointing news for the class of antibodies which target nerve growth factor (NGF). On a more positive note, Endo Pharmaceuticals and ProStrakan's testosterone gel, Fortesta, finally gained approval while BioTie Therapies announced decent phase III data for its alcohol dependence drug, nalmefene, which could transform the company's fortunes in 2011.

Regulatory

December 29

FDA approval of Fortesta sent Endo's shares up 3% to $35.71, while ProStrakan rose 15% to £1.05. This provides a much-needed $12.5m milestone payment for ProStrakan, with further milestones to come next year. NomuraCode analysts pencil in peak sales of $100m, while UBS sees $45m in 2016; pre-approval consensus saw $59m in 2016. NomuraCode says Fortesta could capture a "significant share" of an under-diagnosed market, estimated at $700m.

This is a big plus for ProStrakan, which has recently seen financial difficulty and product delays (*ProStrakan's debt pile casts dark shadow on drug delays, September 7, 2010*). Now it has a better financial outlook and early-2011 launch for Fortesta in the US and Sancuso in Europe to look forward to. Furthermore, says NomuraCode, heightened interest shown by Paladin Labs and Norgine could see ProStrakan as a possible takeover target.

The FDA requested four additional weeks to review approval of MannKind's inhaled insulin Afrezza. Interestingly, this sent shares up 11% to a six-month high of $8.70, with investors seemingly encouraged the FDA did not outright reject the device, as many anticipated (*Event - MannKind holds its breath as FDA decision approaches, December 1, 2010*). However, safety and the device's efficiency versus injectable insulin – bioequivalence data to support this were not submitted – remain issues. Rodman & Redshaw analysts read little into the FDA's delay, still predicting approval in January. Conversely Avik Roy, Monness, Crespi, Hardt & Co analyst and contributor to Forbes, is not so sure, reckoning the FDA will either ask for large, lengthy new trials, sending stock to record lows, or request extensive additional safety data, as with Bydureon (*FDA crashes party of three with Bydureon rejection, October 20, 2010*).

December 28

Santarus and Pharming filed for US approval of recombinant human C1 inhibitor Rhucin for hereditary angioedema (HAE); Santarus shares jumped 16% to $3.67, and Pharming will receive a $5m milestone payment with the acceptance of the submission. Pivotal studies demonstrated significant improvement in time to relief of symptoms. Global sales of Rhucin are predicted to reach $50m by 2016 . Pharming and European partner Swedish Orphan Biovitrum also announced the first European sales – in Denmark and Norway – for the drug, sold as Ruconest in the region.

December 27

After a complete response two years ago, King Pharmaceuticals and Pain Therapeutics have resubmitted for US approval their application for controlled release analgesic Remoxy; Pain shares rose 3% to $6.66, while capsule technology developer Durect's stock has rallied since September in anticipation of this re-filing. The technology is designed to stop abuse of the oxycodone formulation – a sticking point for the FDA first time around. Analysts at Zacks think that approval will be granted in six months as abuse-resistant analgesics are in demand, although mitigating risk could still remain the thorn in Remoxy's side (*Remoxy headache continues as FDA delays approval, December 12, 2008*). Remoxy is predicted to sell $458m in 2016 globally.

Cephalon has scrapped development of Nuvigil (armodafinil) tablets for jet lag-associated sleepiness, after receiving a complete response from the FDA, sending shares down a total of 3.5% over the Christmas period to $63. This, say analysts at UBS, puts pressure on the franchise. The additional indication would have been a

welcome boost as sales on Nuvigil and predecessor Provigil had been declining by 5% over 2010. Nuvigil is already approved for sleep apnoea and narcolepsy, predicted to sell nearly $600m in 2016 globally; UBS attributed no sales to the jet lag indication. The next catalyst will be data in late-2011 for bipolar depression, although UBS does not expect great things in this setting.

December 23

Alimera Sciences received a complete response from the FDA for its fluocinolone acetonide-releasing ocular implant Iluvien for diabetic macular oedema, after discrepancies emerged between the whole-population phase III data set versus a modified set. Observers think this signals only a delay, and still expect an approval. Mercifully for Alimera no further trials were requested (*Alimera gets unwelcome Christmas message from FDA, December 24, 2010*). Shares dipped 14% at the start of trading after Christmas from $11.22 to $9.69 although began to recover quickly, currently trading at $11.72. Partner pSividia on the other hand was hit a little harder; shares lost 24% to open on Monday 27 December at $4.83, and have barely recovered since.

Novartis applied for European approval of its broad-coverage meningitis B vaccine Bexsero (formerly 4CMenB). Consensus sales of $725m in 2016, based on forecasts made prior to the submission, could increase significantly with an approval of the first vaccine of its kind; a decision is expected in mid-2011 (*Therapeutic focus – Novartis set to dominate meningitis vaccine market, November 4, 2010*). Bexsero is said to cover 77% of meningitis B strains that have been isolated in Europe, with results in other strains to be further reported in 2011.

Johnson & Johnson filed for US, European and Canadian approval of abiraterone acetate plus prednisone for metastatic, advanced prostate cancer in patients previously treated with taxane chemotherapy. A phase III, placebo-controlled 1,200-patient trial reported results in October 2010, showing the drug significantly increased overall survival. The drug is expected to sell $289m in 2016 globally.

Novartis' Bcr-Abl inhibitor Tasigna was approved in Europe as a first-line treatment for patients newly-diagnosed with Philadelphia chromosome-positive chronic myeloid leukaemia, after phase III results showed superiority over Glivec in delaying progression of the cancer, and in a wide array of Bcr-Abl mutations normally resistant to Glivec.

Clinical

January 3

Shares in Inspire Pharmaceuticals lost over half their value at the start of trading yesterday, hitting an 18-month low of $3.50, after topline phase III results showed its cystic fibrosis drug denufosol failed to meet its primary endpoint of demonstrating improvement in lung function. Data from the 466-patient Tiger-2 trial will continue to be evaluated, with a full report expected mid-February. *EP Vantage will provide a full analysis of this in the coming days.*

Lundbeck shares rose 4% yesterday to DKr 110, on the back of news that its tablet for alcohol addiction, nalmefene, was safe and efficacious, and is expected to be submitted for European approval in the second half of this year. Preliminary data from two out of three European phase III studies – the Esense-1 and Sense trials – showed the drug reduced alcohol consumption in the short-term while being safe in the long-term. Another short-term efficacy study – Esense-2 – is expected to report in the second quarter. The full data set will then be presented at an upcoming scientific conference, with a submission for European approval anticipated soon after. Partner Biotie Therapies shares rose 36% on the news to €0.68, hugely significant for a company running its cash reserves dangerously low. *EP Vantage will provide a full analysis of this in the coming days.*

December 29

CEL-SCI and Teva Pharmaceutical Industries initiated an open-label pivotal trial, It-Matters, of Multikine in head and neck cancers – the largest in head and neck cancer ever with 880 patients. It is due to complete in May 2015, although preliminary data could be reported in mid-2012.

Merck & Co confirmed plans to progress with Cardiome Pharma's oral formulation of vernakalant for atrial fibrillation. It will continue clinical development in 2011, although it is unclear whether the drug will move straight into phase III. Shares in Cardiome were up 5% to C$6, and investor relief caused an upward trend to C$6.70 at the start of New Year's Eve. The disappointment of Merck's announcement it would not be starting trials last summer wiped 13% off Cardiome's share price, which had been trading at C$9.50 prior to this setback (*Merck calls a go-slow on oral vernakalant, August 12, 2010*).

December 27

AVI BioPharma's incoming chief executive Chris Garabedian, joining January 1, said he is evaluating "alternative development options" to accelerate Duchenne muscular dystrophy (DMD) program AVI-4658, which was due to start pivotal US trials before the end of 2010. The announcement appeared to support

investor confidence in the new appointment – stock has rallied since news of AVI's new leader broke, now trading close to a 12-month high at $2.16. This could rise considerably higher with promising guidance from the new chief (*Failure for PTC muscular dystrophy drug leaves few treatment options, March 4, 2010*).

The FDA has placed a clinical hold on Regeneron Pharmaceuticals and Sanofi-Aventis' analgesic anti-nerve growth factor (NGF) inhibiting antibody REGN475/SAR164877, after a similar, undisclosed compound in a separate trial caused one case of avascular necrosis, or bone tissue death.

The company thinks the problem also reads through the entire class of anti-NGF therapies. When certain trials of Pfizer's tanezumab were placed on clinical hold mid-last year after joint problems emerged, consensus sales for 2016 plunged from $608m to just $81m (*Safety concerns narrow tanezumab's potential further, July 21, 2010*).

The FDA also placed phase II trials of Johnson & Johnson's fulranumab on hold last week while AstraZeneca suspended its phase I studies of MEDI-578 as soon as the safety signal for tanezumab was revealed.

Which only leaves Abbott Laboratories' PG110 in active clinical development for general pain indications. Phase I trials are said to be proceeding as planned but recent developments will certainly be a worry for the company that splashed out $170m on the asset from PanGenetics just over a year ago (*PanGenetics cashes in on Abbott's early stage bet, November 13, 2009*).

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