Evaluate Vantage

December 20, 2011

Pipeline setbacks hurt AstraZeneca

Evaluate Vantage

AstraZeneca's Christmas of 2011 is shaping up to be just as disappointing as its festive season last year. Two significant pipeline setbacks announced today, TC-5214 in depression and olaparib for ovarian cancer, mimic the double-blow Astra suffered a year ago when heart drug Certriad and RSV treatment motavizumab were scrapped in quick succession.

A $382m impairment charge related to TC-5214 and olaparib, which will hurt full-year earnings, knocked 3% off Astra's share price today to £28.55 and brought fresh calls from analysts for the UK pharma giant to re-think its relatively narrow strategic focus on innovation. After all, Astra's track record in bringing new products to market is far from enviable. Despite spending $23bn on R&D in the last five years, cumulative sales from new products over the ten year period between 2007-2016 is just $11.5bn – a somewhat meagre 49% return rate which ranks Astra as the worst performer on this measure among its big pharma peers (see table below).

Latest setbacks

Astra and partner Targacept announced that a second pivotal phase III trial of TC-5214 failed to improve the symptoms of patients with major depressive disorder – this follows a similarly negative result last month from the first trial to report from its so-called Renaissance programme (*Targacept investors severely depressed by TC-5214 failure, November 8, 2011*).

The first two failed trials enrolled around 300 patients each and used flexible doses of TC-5214, whereas two further studies due to read out in the first half of 2012 tested a fixed dose regimen in a greater number of patients with around 680 in each trial. As such, there is potential for a magical recovery – the companies have said that two of the four efficacy studies need to be positive to support a regulatory filing – but the chances seem slim at best.

Targacept shares fell 25% in early trade today to a two-year low of $5.82, below a year-end cash per share value of $7, as estimated by Leerink Swann analysts.

As for olaparib, Astra decided against taking the one-time promising PARP inhibitor candidate into phase III trials for ovarian cancer (*Therapeutic Focus - Disappointment a recurring theme in ovarian cancer pipeline, December 20, 2011*). Unfortunately, detailed analysis of a phase II study in serous ovarian cancer, which had shown an encouraging progression free survival benefit, indicated this was unlikely to translate into an overall survival benefit.

Astra continues to study olaparib in other cancers - phase II studies are ongoing in colon and gastric tumours - but having previously scrapped development for breast cancer the omens are not good.

Of the impairment charge, $285m related to olaparib and $97m for TC-5214, means Astra's full-year earnings per share will now be at the lower end of its $7.20 to $7.40 guidance.

Improvement required

Sticking to its innovative R&D knitting has seen Astra aligned with the likes of Bristol-Myers Squibb, Eli Lilly and Merck & Co, but somewhat at odds with the diversification strategies adopted by other such as GlaxoSmithKline, Sanofi and Novartis.

Focusing on innovation is a plausible and commendable strategy, one which should offer greater returns in the long run, but is inherently much riskier and only viable if Astra's pipeline delivers the goods.

The table below shows a number of metrics by which a return on R&D can be measured. Although they may be somewhat crude and simplistic, by any yardstick Astra does not score particularly well compared with its big pharma peers.

Aside from only returning half a dollar in sales for every dollar invested in the last five years, the potential value of its pipeline is slightly disappointing. Valued at $5.5bn according to *EvaluatePharma's NPV Analyzer*,

this is greater than the likes of Johnson & Johnson and Abbott Laboratories, but for a company throwing all its resources behind innovative R&D this is a cause for concern. Similarly, Astra's enterprise value of $57.5bn is just 2.5 times greater than its five-year R&D spend, better than only Eli Lilly's 2.2 times value.

	Total sales from new products (07 - 16) $bn	5yr (07-11) pharma R&D spend ($bn)	% 10yr Sales/ 5yr R&D spend	Pipeline NPV ($bn)	Count of clinical pipeline projects	Enterprise value ($bn)	EV / 5yr Group R&D Spend
Bristol-Myers Squibb	26.5	16.4	162%	4.7	115	55.5	3.4
GlaxoSmithKline	38.4	28.5	135%	15.2	248	130.2	4.5
Johnson & Johnson	30.5	24.1	126%	1.6	121	160.9	4.4
Pfizer	54.9	47.5	116%	13.7	212	179.3	4.4
Novartis	41.8	36.7	114%	13.9	195	148.8	4.0
Merck & Co	38.5	40.1	96%	6.0	134	113.7	3.7
Abbott Laboratories	8.9	9.8	91%	3.0	63	94.0	6.2
Eli Lilly	16.1	21.3	75%	7.6	127	47.5	2.2
Roche	27.7	44.6	62%	9.5	157	173.4	3.6
Sanofi	18.0	32.0	56%	6.1	128	117.4	3.7
AstraZeneca	11.5	23.3	49%	5.5	104	57.5	2.5

Of course, sales are only one measure and can also be misleading. For example, the analysis above does not account for new diabetes treatments that Astra developed in partnership with Bristol-Myers Squibb – Onglyza, launched in 2009 and dapagliflozin, which could gain FDA approval next year although the odds are low. BMS books the sales for both products, with Astra receiving a profit-share. Estimated global sales of Onglyza of $447m this year are expected to reach $1.73bn by 2016, according to *EvaluatePharma* forecasts.

Nevertheless, Astra certainly appears to suffer more than its fair share of pipeline setbacks. Some high profile failures around five years ago, to the likes of Exanta and Iressa which were developed in-house at Astra, led to a greater desire to look outside its research labs for innovative products.

Some big pharma companies are pursuing this strategy more aggressively than others, with the theory being there is greater chance of R&D and regulatory success with licensed or acquired products (*Big pharma push on with externalisation strategies, October 18, 2011*).

Yet with Astra paying a staggering $200m upfront for TC-5214 and sourcing olaparib through its $210m purchase of KuDOS Pharmaceuticals in 2006, externally derived products are just as vulnerable to failure.

Pivotal trial results next year from oral RA drug, fostamatinib (R788), also licensed at considerable expense by paying $100m upfront to Rigel Pharmaceuticals, are taking on greater significance.

If there is another high profile pipeline setback the calls for Astra to alter its strategic course will grow even louder.

Evaluate APAC
+81-(0)80-1164-4754