

Astellas set back highlights need for pipeline expansion



Amy Brown

The spectre of approval for generic versions of transplant drug Prograf, which has been stalking Astellas for some months now, has materialised in the realms of reality with news that Novartis's Sandoz unit is about to launch a copycat version of the product in the US.

Forecasts for Prograf suggest that this is not entirely unexpected; analysts were assuming that sales in the US peaked last year at \$887m and have pencilled in gradual erosion from now, with consensus slipping to \$500m by 2014, according to data from EvaluatePharma. Still, although it was on the cards this attack on Astellas' biggest product serves to illustrate that like its Western peers, the company is going to struggle to report anything close to exciting growth over the next few years. A fairly recent splurge on licensing deals needs to continue.

Prograf is an immunosuppressant approved to help prevent the body from rejecting transplanted organs, mainly livers and kidneys. The US patent expired last year, and Astellas itself anticipates that sales will start to fall more rapidly from this year, due to patent expiry in a number of other major markets last June.

The approval of Sandoz's version followed the FDA's rejection of Astellas' citizen petition, which it filed in 2007, lobbying for the regulator to require that generics are subject to bioequivalence tests in organ transplant patients, rather than just healthy volunteers, before approval. The FDA also threw out a label change that would have seen doctors informed if pharmacists were substituting Prograf for a generic.

The Japanese company intends to fight both decisions in court, but with Astellas shares dropping 5% on the news, hopes for victory are clearly low.

Familiar predicament

Global sales of Prograf touched \$1.88bn in fiscal 2008, accounting for almost a quarter of group revenues. Despite the loss of patent protection, analysts do not believe the product will be subject to the savage erosion some other medicines see, mainly because doctors may be cautious to switch such sick patients onto a different medicine.

As such, consensus for sales in 2014 sits at \$1.64bn leaving Prograf as Astellas's biggest product, although this number might come down now that the loss of the US has been confirmed.

Vesicare for urinary incontinence is now the biggest growth driver for the company, and the product is projected to become a blockbuster in 2011. However, with Prograf clearly under threat, and the patent on another key product, Flomax for enlarged prostate, also running out later this year, the predicament facing Astellas is horribly familiar. Compound annual growth is forecast to be a meagre 1% over the next five years, whilst profits are seen contracting by 3%.

Remedy

As the table below shows, Astellas has been trying to remedy this situation and has struck a number of in-licensing deals since the beginning of 2007, although these are mostly early stage.

Hopefully, these will progress more swiftly than a deal that was signed by Astellas' predecessor Fujisawa in 2003, over the US rights to Cardiome Pharma's atrial fibrillation drug Kynapid. The companies have failed to win approval in the US since first filing in 2006, an abysmal record, and today announced that another phase III trial would be required which will not report until 2011.

Astellas' product deals since 2007

Deal Date	Deal Type	Product	Deal Partner/Product Source	Pharmacological Class	Status on Deal Date	Phase (Current)	Deal Comment
-----------	-----------	---------	-----------------------------	-----------------------	---------------------	-----------------	--------------

2009	Co-promotion	Symbicort Turbohaler	AstraZeneca	Beta 2 agonist & corticosteroid	Filed in Japan	Filed in Japan	AstraZeneca and Astellas to co-promote, Astellas distribute in Japan. AstraZeneca to receive \$31.5m upfront plus milestones.
	Co-promotion	Sumavel DosePro	Zogenix	5HT1B (serotonin) & 5HT1D (serotonin) agonist	Approved	Approved	AUG09 Co-promote deal in US, Astellas to focus on primary care and Zogenix focus on neurology market. Terms undisclosed.
	In-licensed	TMX-67	Teijin	Xanthine oxidase inhibitor	Marketed	Filed	MAY09 In-licensed Taiwan rights from Teijin for gout, Teijin receives licensing fee and milestones.
	In-licensed	Qutenza	NeurogesX	Non-narcotic analgesic	Approved	Approved	JUN09 In-licensed European the Middle East & African rights from NeurogesX. Astellas to pay €30m (\$42m) as upfront.
	In-licensed	NGX-1998	NeurogesX	Non-narcotic analgesic	Phase I	Phase I	JUN09 In-licensed European the Middle East & Africa option rights form NeurogesX. Astellas to pay €5m (\$7m) as upfront.
2008	In-licensed	Front blockers project	Effector Cell Institute	CCR2 antagonist	Research project	Research project	Astellas license WW rights from ECI in return for an undisclosed upfront fee, milestones & royalties.
	In-licensed	CTS-21166	CoMentis	Beta secretase (BACE) inhibitor	Phase I	Phase I	APR08 WW rights in-licensed from CoMentis. CoMentis will receive an upfront payment of \$80m an equity

							\$500m, an equity investment of \$20m & up to \$660m in milestones.
	In-licensed	Next Generation Beta Secretase Inhibitor	CoMentis	Beta secretase (BACE) inhibitor	Pre-clinical	Pre-clinical	APR08 WW rights in-licensed from CoMentis.
	In-licensed	MAXY-4	Maxygen	B7 integrin antagonist	Pre-clinical	Pre-clinical	JUN09 Joint venture agreement with Astellas to develop & commercialise protein therapeutics including MAXY-4.
2007	In-licensed	ASKP1240	Kirin	Anti-CD40 MAb	Pre-clinical	Phase I	JAN07 In-licensed WW rights from Kirin.

Company acquisitions have been rare, other than the purchase of antibody company Agensys in 2007 for \$537m and the failed attempt to buy CV Therapeutics earlier this year ([Astellas walks away from CV but hunt for deals likely to continue, March 16, 2009](#)). This potential \$1bn takeover would have been the Japanese company's biggest deal since it came into being in 2005, following the merger of Yamanouchi and Fujisawa.

The next table shows that compared with its big pharma peers in Japan, relative to its size Astellas has not exactly been on a spending spree recently. Admittedly, the group does have a stated policy to return cash to investors via a substantial share buyback programme, but whilst this effort will no doubt be appreciated shareholders also want to see top line growth.

The reluctance of Astellas to raise its bid for CV Therapeutics, which was ultimately snapped up by Gilead Sciences, and the seemingly tentative in-licensing efforts perhaps suggests a high level of caution among the Astellas ranks. With the likes of smaller peers such as Eisai and Shionogi keeping their foot on the deals pedal, Astellas needs to start ratcheting up its business development activities, and possibly look for another deal the size of CV.

Japanese company licensing activity		
	Count of Licensed Products	Market Cap (\$bn)
Eisai	17	10.7
Takeda	17	31.8
Shionogi	16	7.8
Otsuka Pharmaceutical	11	Private
Astellas Pharma	10	19.1
Daiichi Sankyo	8	13.3
Kyowa Hakko Kirin	7	6.6
Mitsubishi Tanabe Pharma	6	6.5
Taisho Pharmaceutical	4	5.7
Ono Pharmaceutical	3	5.5
Chugai	2	10.1
Dainippon Sumitomo Pharma	1	3.8
Santen Pharmaceutical	1	2.6