Evaluate Vantage

August 22, 2019

Astra could use a voucher to cement roxadustat's head start

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Spending $95m to speed up the anaemia project's path to approval could be worth the investment for Astrazeneca.

The market for priority review vouchers isn't what it used to be. And Astrazeneca looks like it has bagged a relative bargain, paying Sobi $95m to get a head start for one of its pipeline candidates.

Astra has not yet said if it has a particular therapy in mind for the voucher, but its anaemia project roxadustat seems like a good bet. The Fibrogen-originated asset is vying with several others in the same class for a piece of what is expected to be a multi-billion dollar market.

Under priority review the US FDA aims to make an approval decision within six months, versus the standard 10-month review. Companies have therefore used the vouchers when there is a good reason to hasten a drug to market, for example where competition is set to be fierce and first-mover advantage could be vital.

Another contender for the voucher might be trastuzumab deruxtecan, an Her2-targeting antibody-drug conjugate that Astra licensed from Daiichi Sankyo in March. However, the companies are pitching this as a better version of the well-established drug Herceptin, so time is not exactly of the essence here.

It is worth remembering that Astra now has two priority review vouchers, having gained another, still apparently unused, from Wellstat in 2014.

Perhaps Astra just saw a chance to get its hands on a voucher at a good price, particularly as these were changing hands for as much as $350m at their peak. But as more US priority review vouchers have been issued following the programme's 2016 reauthorisation their resale value has fallen. The $95m Astra has given Sobi is in the $80-105m range of this year's three other disclosed voucher sales.

A net total of eight existing vouchers are thought not to have been sold on or redeemed, though additional vouchers might have been issued without this fact having been disclosed.

Anaemia race

Roxadustat does look like an ideal candidate for the voucher. The project is one of several HIF-PHI inhibitors in late-stage development, and the market could be very large indeed: Stifel analysts note that the erythropoiesis-stimulating agents HIF-PH developers are hoping to displace sell around $6bn per year.

Roxa currently leads the race, but cementing this head start could be invaluable. The project is set to be submitted to the FDA in October; if approved, Astra will be responsible for US commercialisation.

Competitors are not too far behind. Akebia's vadadustat and Glaxosmithkline's daprodustat are both filed in Japan, but the US will be the main battleground, and both projects are due to yield phase III data in late next year.

The late-stage HIF-PH inhibitor race

Project	Companies	Status	2024e sales ($m)	Note
Roxadustat	Astrazeneca/Fibrogen/ Astellas	Approved in China, US filing due Oct 2019	1,373	Full US/EU data to be presented at ASN in November
Vadadustat	Akebia/Mitsubishi Tanabe/Otsuka	Filed in Japan, US phase III data due 2020	929	Inno2vate (NCT02865850, dialysis-dependent); Pro2tect (NCT02648347, non-dialysis-dependent)
Daprodustat	Glaxosmithkline/ Kyowa Kirin	Filed in Japan, US phase III data due 2020	383	Ascend-D (NCT02879305, dialysis-dependent); Ascend-ND (NCT02876835, non-dialysis-dependent)
Molidustat	Bayer	Japanese phase III trials ongoing	29	Miyabi ND-C (NCT03350321, non-dialysis-dependent); Miyabi HD-M (NCT03543657, dialysis-dependent)
Enarodustat	Japan Tobacco/Torii	Korean phase III trial recruiting	-	NCT04027517, dialysis-dependent
Desidustat	Zydus Cadila	Phase III not yet recruiting	-	Dream-ND (NCT04012957, non-dialysis-dependent)

Source: EvaluatePharma, clinicaltrials.gov.

However, there are still question marks over roxa's safety following a confusing update from a pooled analysis earlier this year (*Roxadustat safety analysis provokes more questions than answers, May 10, 2019*). Toxicity concerns look like the only thing that might scupper roxa, which has met efficacy endpoints in pivotal trials in various settings. A priority review voucher would not be much help if the FDA did have worries here.

The safety question might be answered by the further US and European data that are due to be presented at the American Society of Nephrology meeting in Washington, DC, in November. Roxa is also likely to be the subject of a US FDA adcom next year.

Meanwhile, roxa was approved in China today for a new use: patients with anaemia caused by chronic kidney disease who are not dependent on dialysis. This adds to its Chinese approval last December in dialysis-dependent patients. Astra and Fibrogen plan to launch roxa in China, where they have a 50/50 profit share agreement, in the second half of this year.

Astra reckons it is several years ahead of its HIF-PHI rivals in China. In the US the stakes are higher, and timelines look tighter, so using the voucher could be a good move.

The fate of disclosed priority review vouchers

Date sold	Price	Date issued	Issued company	Action
–	–	Apr 2009	Novartis	Redeemed by Novartis in BLA for Ilaris (gout)
–	–	Dec 2012	J&J	Redeemed by J&J in BLA for Tremfya (psoriasis)

The fate of disclosed priority review vouchers				
–	–	Oct 2015	Alexion	Redeemed by Alexion in BLA for Ultomiris (PNH)
–	–	Aug 2017	Novartis	Redeemed by Novartis in BLA for brolucizumab (AMD)
–	–	Jul 2018	Glaxosmithkline	Redeemed by Viiv in NDA for Dovato (HIV)
Jul 2014	$68m	Feb 2014	Biomarin	Sold to Sanofi & Regeneron
Sep 2014	Not disclosed	Sep 2015	Wellstat	Transferred to Astrazeneca in licensing deal
Nov 2014	$125m	Mar 2014	Knight	Sold to Gilead, which redeemed it in NDA for Odefsey (HIV)
May 2015	$245m	Mar 2015	Asklepion	Asset sold to Retrophin, which sold PRV to Sanofi, which redeemed it in NDA for insulin glargine (T2D)
Aug 2015	$350m	Mar 2015	United	Sold to Abbvie, which redeemed it in NDA for Rinvoq
Q2 2016*	~$200m**	Jun 2016	Paxvax	Likely sold to Gilead and redeemed in NDA for Descovy (HIV)*
Feb 2017	$125m	Sep 2016	Sarepta	Sold to Gilead, which redeemed it in NDA for Biktarvy (HIV)
Nov 2017	$125m	Apr 2017	Biomarin	Sold to undisclosed party
Dec 2017	$130m	Nov 2017	Ultragenyx	Sold to Novartis, which redeemed it in NDA for Mayzent (MS)
Apr 2018	$110m	Dec 2017	Spark	Sold to Jazz Pharmaceuticals
Jul 2018	$81m	Apr 2018	Ultragenyx	Sold to undisclosed party
Nov 2018	$80m	Jul 2018	Siga	Sold to Lilly
Mar 2019	$105m	Jun 2018	GW Pharma	Sold, presumably to Biohaven[#]
Aug 2019	Not disclosed	Jun 2018	Medicines Development	Sold to Novo Nordisk[##]
Aug 2019	$95m	Nov 2018	Novimmune	Asset sold to Sobi, which sold PRV to Astrazeneca
–	–	Dec 2015	Alexion	None
–	–	Dec 2016	Biogen/Ionis	None
–	–	Feb 2017	Marathon	None; asset sold to PTC Therapeutics
–	–	Nov 2017	Chemo Research	None
–	–	Oct 2018	Leadiant	None
–	–	Feb 2019	Novartis	None
–	–	Feb 2019	Vertex	None
–	–	May 2019	Sanofi	None
–	–	May 2019	Novartis	None
–	–	Aug 2019	TB Alliance	None

*Notes: Glaxosmithkline and Teva have bought PRVs from undisclosed sellers, for $130m and $150m respectively; these were redeemed in 2017 filings for Juluca (HIV) & Ajovy (migraine). *Gilead revealed purchase of undisclosed PRV in SEC statement; **based on Gilead disclosure of $624m increase in R&D spend, less $400m Nimbus purchase and undisclosed clinical trial progression; [#]to be used with Rimegepant*

Zydis; ##Novo redeemed a second PRV, obtained from an undisclosed source, in its NDA for oral semaglutide (T2D).

The fate of disclosed priority review vouchers

The table in this story has been updated to reflect information from Novo Nordisk about the company's two separate vouchers.