Evaluate Vantage

February 16, 2015

With FDA action nearing biosimilar agents begin to shake US market

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A move last week could presage how copies of biological drugs are about to disturb the US market in 2015: shares in Pfenex nearly doubled after the group signed a deal on a Lucentis biosimilar with Hospira.

One biosimilar has the backing of a US expert panel and appears headed for approval, a second has a vote slated, and yet a third was submitted to the FDA in January. The regulatory pathway established five years ago looks like it could be well trodden in the coming months as several other agents near critical milestones.

Pfenex's Lucentis copycat, PF582, has completed enrolment in a phase I/II trial and will report interim safety and tolerability data by the end of March. This is progress enough to satisfy Hospira, which will hand over $51m up front and an additional $291m in developmental and sales milestones could follow.

When PF582 enters phase III in the mid-year it will join a lengthening queue of projects gathering pivotal data for regulatory submission. Agents mimicking the actions of inflammation-fighting antibodies like Humira and cancer antibodies like Avastin are approaching critical readouts, and soon afterwards should join biosimilars of Neupogen, Remicade and Epogen in having reached the US regulator.

Rich pipeline

Given how long it has taken for candidates to reach the regulator, it might seem surprising to see how rich the late-stage pipeline is. Then again, the targets are attractive, given that among them is the biggest-selling drug in the world: Humira.

Selected biosimilar projects now in phase III			
Reference product	**Candidate**	**Company**	**Forecast launch**
Humira	ABP 501	Amgen	2017
	BI 695501	Boehringer Ingelheim	–
	SB5	Samsung	–
	Adalimumab	Novartis	2016
Remicade	PF-06438179	Pfizer	2017
Rituxan	BI 695500	Boehringer Ingelheim	–
	GP2013	Novartis	2016
	CT-P10	Celltrion	2016
	PF-05280586	Pfizer	2017
Herceptin	PF-05280014	Pfizer	2017
	Trastuzumab	Hospira	2016
	ABP 980	Amgen/Actavis	2017
	SB3	Samsung	–
Avastin	ABP 215	Amgen/Actavis	2017
	BI 695502	Boehringer Ingelheim	–
Enbrel	Etanercept	Novartis	2016
	CHS-0214	Coherus BioSciences	2017

Last week, Citi analyst Andrew Baum published a note warning that launches of lookalikes to some of the biggest biological blockbusters were “closer and more competitive than [the] market appreciates”. Mr Baum estimates that innovative drugmakers stand to lose $360bn in revenue in the next 10 years, with biosimilar makers likely to grab $110bn of that.

Companies Mr Baum identifies that are now positioned to benefit are Novartis, Amgen, Actavis and Pfizer. The latter company’s takeout of Hospira is well-timed to capture even more of a presence, as its Remicade and Epogen are poised to become the second and third biosimilars to get an FDA nod (*Hospira moves the needle for Pfizer spin-out, February 5, 2015*).

Status of biosimilars submitted to the FDA		
Zarxio (Neupogen)	Novartis	Passed adcom, PDUFA March, injunction hearing March 2
Remsima (Remicade)	Hospira	Submitted to FDA, adcom March 17
Epoetin alfa (Epogen)	Hospira	Announced as submitted to FDA Jan 12

On the other hand, AbbVie is looking vulnerable as its $14bn-a-year Humira loses market exclusivity next year. Mr Baum writes that sales of the rheumatoid arthritis treatment will drop to just $3bn by 2022 because of heavy discounting, payer pressure and the potential for direct pharmacist substitution.

So sue me

The regulatory issues look to be very nearly ironed out, but some legal matters still need to be decided – and the pace of rulings could have some effect on the launch of the first US biosimilar. Amgen is suing Novartis’s Sandoz division over the launch of the Neupogen copycat Zarxio, and the possibility of an injunction could prevent Sandoz from launching on approval (*Not so fast on that first US biosimilar launch, February 10, 2015*).

Amgen alleges that Sandoz has refused to take part in the data disclosure procedures laid out in the biosimilars law – nicknamed the “patent dance” – to determine whether any remaining intellectual property is infringed.

How this case proceeds could set precedent for future launches. A judgement that the law does not require participation in the patent dance could require the innovative product makers to sue to achieve the data disclosure in future cases.

Legal action can only slow the march of biosimilars into the US. The phase III pipeline is impressive, and serious disruption is only months away.

Since publishing, the Remsima advisory committee has been postponed.

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