Evaluate Vantage

March 31, 2016

Defitelio highlights a regulatory fault line

Jacob Plieth

US approval of Jazz Pharmaceuticals' Defitelio must have come as a welcome relief after years of disappointments. But it also put the spotlight on another quirk: while this orphan disease drug lurched from one US setback to another it was already available in Europe.

Defitelio is not alone in having scored such an accolade, and a search of *EvaluatePharma* reveals some 80 projects that have secured the green light in the EU but not on the other side of the Atlantic. These include one blockbuster, and another that could breach the $1bn threshold by 2020 (see table below).

The current blockbuster – Novartis's Galvus – looks unlikely ever to secure US approval owing to safety worries connected with liver enzyme elevations. This had also troubled EU regulators, though not excessively: the diabetes drug eventually got the go-ahead in 2008, and last year recorded global sales of $1.1bn.

Only yesterday another example of this divergence was seen when Newron's safinamide – available in Europe for over a year – added a US complete response letter to its refuse-to-file missive of 2014 (*Parkinson's developers go one for two, March 30, 2016*).

Safinamide does not appear in this analysis because its forecast sales are relatively insignificant. Not so the likes of Novo Nordisk's Xultophy – predicted to become a blockbuster by 2020 – or PTC Therapeutics' Duchenne muscular dystrophy drug Translarna.

Top 10 drugs available in Europe but not the US

				Sales ($m)	
Product	**Company**	**EMA approval**	**US status**	**2015**	**2020e**
Xultophy	Novo Nordisk	Sep 2014	Filed	20	1,561
Galvus	Novartis	Nov 2008	Phase III	1,140	1,429
Translarna	PTC Therapeutics	Jul 2014	Phase III	32	692
Brimica Genuair	AstraZeneca	Nov 2014	Phase III	27	345
DuoResp Spiromax	Teva	Apr 2014	Phase III	45	323
Lyxumia	Sanofi	Feb 2013	Filed	42	240
Teysuno	Otsuka Holdings	Mar 2011	Phase III	243	203
Imvamune	Bavarian Nordic	Aug 2013	Phase III	12	194
Zinforo	AstraZeneca	Aug 2012	Phase II	106	192
Esmya	Gedeon Richter	Feb 2012	Phase III	56	166

In fact, Xultophy is one of two diabetes drugs in this top 10, the other being Sanofi's Lyxumia.

The FDA sidelined Xultophy because of its Tresiba (basal insulin) element, which was delayed over three years ago owing to a cardiovascular signal. Meanwhile, Lyxumia, a GLP-1 agonist, was set back when the FDA said it wanted to see data from the Elixa outcomes study before approving.

Like safinamide Translarna got a rare US refuse-to-file letter; this came in February and stated that PTC's filing was incomplete.

Back in 2011 Defitelio, approved in the US yesterday for treating a rare complication of stem cell transplantation, was so badly knocked back by FDA requests that its then-developer, Gentium, withdrew the

application before selling itself to Jazz. Defitelio was approved by the EMA in 2013 after several years' sales as a "drug of last resort".

At one point these disparities might have been seen as proof of the EMA's soft touch versus its US opposite number. Since the EMA's refusal to follow the US regulator's lead on drugs like Kynamro and Belviq this is clearly no longer the case.

To contact the writers of this story email Jacob Plieth or Edwin Elmhirst in London at news@epvantage.com or follow @JacobPlieth or @EPVantage on Twitter