Evaluate Vantage

May 17, 2023

Market shrugs off PTC's latest success

Jacob Plieth

The success of PTC Therapeutics' sepiapterin in the phase 3 Aphenity study in phenylketonuria (PKU) has left investors unimpressed, and for good reason: a positive hit was always the likely outcome. Aphenity had stacked the deck in sepiapterin's favour, enrolling relatively mild PKU patients, comparing not against an approved treatment like Biomarin's Kuvan or Palynziq, and including a 14-day run-in during which PKU patients received only sepiapterin, and on the basis of which only those who responded were selected for the placebo-controlled part. Aphenity's primary endpoint was met, with sepiapterin-treated patients showing a 63% mean reduction in blood phenylalanine, versus a 1% increase for placebo. Sepiapterin and Kuvan have the same mechanism of action, effectively replacing an enzyme that breaks down phenylalanine and reduces its build-up, and on a cross-trial basis PTC's project wins: Kuvan's label cites placebo-adjusted phenylalanine reduction of just 32%. However, Biomarin's trial enrolled PKU patients with much higher phenylalanine levels, around 850µmol/l versus 650µmol/l in Aphenity. Kuvan is approved only in BH4-responsive PKU, and while PTC argues that sepiapterin could be used in a broader population it has some way to go to show that it has a better drug.

Cross-trial comparison in phenylketonuria				
Company	Biomarin		PTC Therapeutics	
Trial	Study 2		Aphenity	
Treatment	Kuvan	Placebo	Sepiapterin	Placebo
Mean baseline Phe	843µmol/l	888µmol/l	646µmol/l	654µmol/l
Mean 6wk Phe change	-239µmol/l	+6µmol/l	-410µmol/l	+16µmol/l
	-29%	+3%	-63%	+1%
Source: Kuvan label & PTC press release.				