COWEN AND COMPANY

Quick Take

Hyperion Therapeutics — Outperform (1)

HPTX: $10.67

Quick Take: Ravicti's HE Data Presented At AASLD

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Yesterday at the 63rd Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) the data from Ravicti's Phase IIb trial in hepatic encephalopathy (HE) were presented. Last night the data were discussed at a Hyperion analyst event. Overall, the data were consistent with that previously disclosed by Hyperion. The trial succeeded with Ravicti statistically significantly reducing the proportion of patients with at least one HE event. Ravicti significantly reduced the proportion of patients experiencing at least one HE event, with 19 of 90 Ravicti patients (21%) experiencing an event vs. 32 of 88 (36%) of placebo patients (42% reduction, p = 0.02). Ravicti also significantly reduced the total HE events on study and the number of subjects with a symptomatic day, and produced a numerical reduction in the total HE-related hospitalizations.

Ravicti's Overall Phase II Efficacy In HE

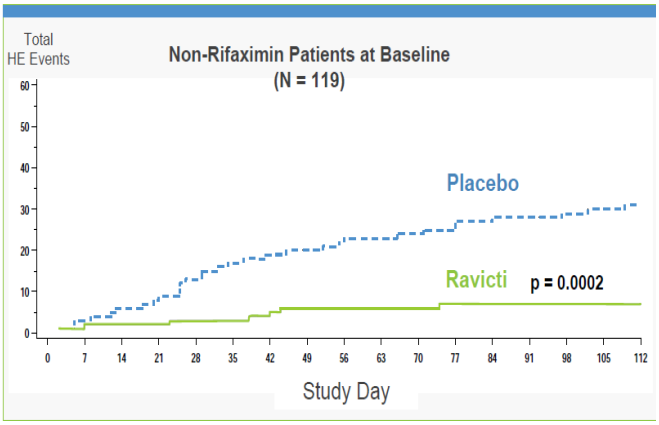
	Ravicti N=90	Placebo N=88	% Reduction	p value
Primary Efficacy Endpoint: Patients with at least one HE event # of subjects and %	19 21.1%	32 36.4%	42%	0.021
Total HE Events	35	57	37%	0.035
Subjects with a Symptomatic Day*	13	27	52%	0.015
Total HE Hospitalizations	13	25	48%	0.064

* Corresponds generally to West Haven ≥2

Source: Hyperion Therapeutics

Ravicti's data in patients not on Rifaximin at baseline were particularly striking. Among the 119 patients in the trial not on Rifaximin at baseline, Ravicti reduced the number of patients with HE events (32% on placebo vs 10% on Ravicti, p<0.001) and the total number of HE events (7 vs 31, p < 0.001).

Ravicti's Phase II Subset Analysis in HE



Source: Hyperion Therapeutics

In those patients who were receiving rifaximin at study baseline, the Phase II data are somewhat murkier as to whether Ravicti can offer an additional efficacy benefit on top of background rifaximin. Ravicti patients who were on rifaximin at baseline (n = 30), 43.3% experienced at least one HE event, similar to the 44.8% of placebo patients on rifaximin at baseline (n = 29). Ravicti patients in this group did experience numerically fewer HE hospitalizations (11 for Ravicti vs. 20 for placebo), but not fewer patients with HE events (13 vs. 13). Hyperion has suggested that the requirement that this subset of patients have failed rifaximin within the pre-trial months may have selected unusually difficult patients, which would be consistent with the rather high HE event rate on both arms.

Consultants believe Ravicti's efficacy data on the background of lactulose alone convincingly show that the drug is active at lowering the risk of HE attacks, and looks at least as effective as rifaximin. They also see no evidence of major red flags on safety. They therefore think Ravicti has a good chance of being approved for this indication, assuming Hyperion pursues development.

However, they say the limited evidence thus far for Ravicti's potentially additive efficacy on top of rifaximin may make it challenging to find the right trial design and patient population for a pivotal study. Hyperion may conduct a Phase III trial in which patients on rifaximin at study entry may not need to have failed rifaximin, which could reduce selection of more difficult patients. However our consultants point out that patients really need to be having breakthroughs on baseline treatment, or it would be difficult to define an efficacy endpoint. Consultants have suggested that a Phase III trial simply pitting Ravicti against lactulose could be sufficient to support approval (although we think this would perhaps not optimize commercial uptake). Alternative trial designs they suggest could be (1) conducting a trial designed to replace lactulose in the typical lactulose/rifaximin regimen; (2) conducting a trial in lactulose-refractory patients; (3) a head to head trial vs. rifaximin. We await further clarity on Ravicti's pivotal trial design following the end of Phase II meeting over the next couple of months.

Our opinion of Ravicti and Hyperion's stock is unchanged. Ravicti has been shown to be at least as potent as the current standard of care, but with much better tolerability and dosing convenience, in the treatment of urea cycle disorders (UCD). Our consultants expect Ravicti to be approved based on its current filing, and for it to quickly capture majority share of the UCD market. Based on Ravicti's potential in

UCD alone, with no contribution from HE, we think Hyperion is significantly undervalued, and remain at Outperform.

Addendum

STOCKS MENTIONED IN IMPORTANT DISCLOSURES

Ticker	Company Name
HPTX	Hyperion Therapeutics

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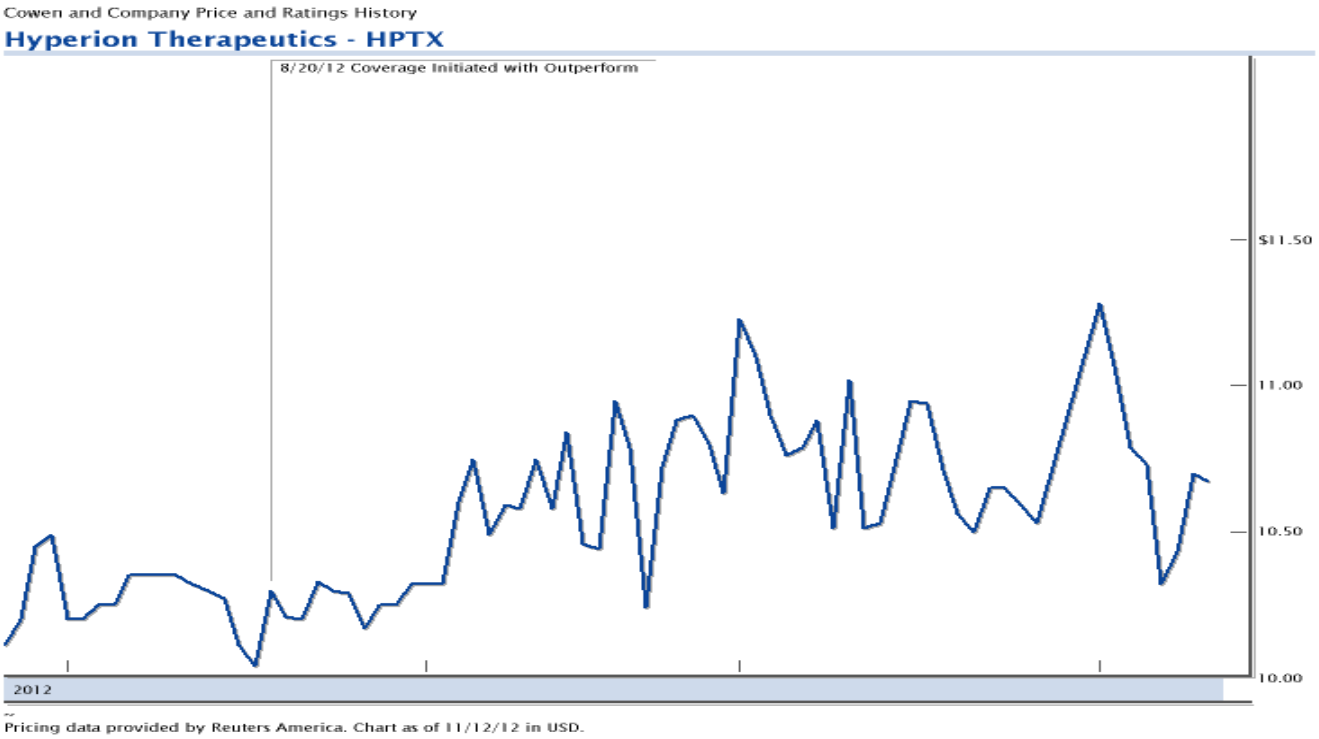
Cowen and Company Price and Ratings History
Hyperion Therapeutics - HPTX
8/20/12 Coverage Initiated with Outperform
$11.50
11.00
10.50
10.00
2012
Pricing data provided by Reuters America. Chart as of 11/12/12 in USD.