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LEERINK SWANN

HEALTHCARE EQUITY RESEARCH

## HYPERION THERAPEUTICS, INC.

### Full Phase II Data Suggest Good Activity of Ravicti in Difficult HE Patients

• **Bottom Line:** HPTX announced full results of the Phase 2 HALT-HE Study presented in an oral presentation at the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) in Boston. The HALT-HE study was a Phase II, multi-center, randomized, double-blind trial of Ravicti vs. placebo in 178 patients with episodic hepatic encephalopathy (HE) on background standard of care therapy. Ravicti shows promise as a novel therapeutic agent for HE based on Phase IIb data and has a potentially complementary mode of action compared to Xifaxan (SLXP, MP), the current standard of care. We see HE as a significant source of upside for HPTX. We are updating our estimates to reflect 3Q:12 financial results. **Reiterate OP rating and \$18 FVE.**

• **Ravicti shows promise as a novel therapeutic agent for HE based on Phase IIb data.** The study met its primary endpoint: significantly fewer patients in the active arm experienced HE events, 21% vs. 36% ( $p = 0.021$ ). Compared to placebo, patients randomized to Ravicti also had significantly fewer total HE events (35 vs. 57  $p=0.035$ ), significantly lower ammonia values (46 vs. 58  $\mu\text{mol/L}$   $p=0.036$ ), and significantly fewer symptomatic days (13 vs. 27;  $p=0.015$ ). There were non-statistically significant trends in favor of fewer HE-hospitalizations and fewer total HE-hospital days. Safety appeared satisfactory (76% and 79% of subjects in the placebo and Ravicti groups, respectively, reported AEs), and the adverse event profile was consistent with that expected for the study population. Ammonia was significantly lower on Ravicti (45.7 vs. 58.15  $\mu\text{mol/L}$ ,  $p = 0.036$ ) and correlated with the likelihood of HE events whether measured at baseline or during the study ( $p < 0.01$ ).

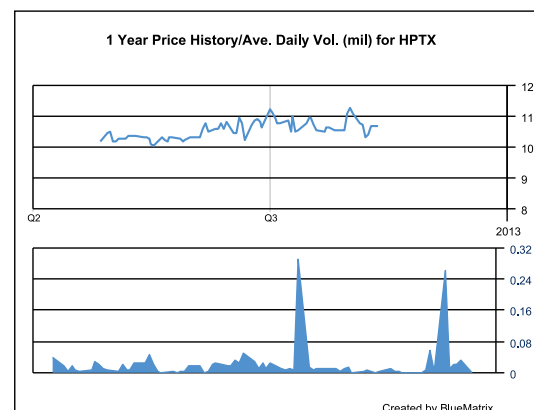
• **Efficacy in sicker patient population than studied in Xifaxan pivotal trials is encouraging.** The study enrolled 178 total patients, of whom 59 were on Xifaxan at baseline, including 29 in the placebo arm and 30 in the active arm. Among the 119 patients not on Xifaxan at baseline, there was a highly statistically significant reduction among Ravicti treated patients in both the percentage of patients with events (10% vs 32%;  $p=0.003$ ) as well as the total number of HE events (7 vs. 31;  $p<0.001$ ). Among patients on Xifaxan at baseline, there was no difference in the number of patients with events or total events. Potentially confounding, patients on Xifaxan at baseline had higher ammonia levels than those not on Xifaxan and the study was not powered enough to detect a difference.

• **Next up:** 4Q:12 end-of-Phase 2 FDA meeting; HPTX expects to start Phase 3 program in 2013. Our [analysis](#) suggests a \$500MM market opp via 25% peak penetration of est. 20% of 140k severe HE patients.

#### Key Stats:

(NASDAQ:HPTX)

S&P 600 Health Care Index:	795.34
Price:	\$10.67
52 Week High:	\$12.00
52 Week Low:	\$9.95
Shares Outstanding (mil):	16.6
Market Capitalization (mil):	\$177.1
Book Value/Share:	\$0.00
Cash Per Share:	\$2.28
Dividend (ann):	\$0.00
Dividend Yield:	0.0%
Valuation:	\$18 on DCF analysis



Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	P/E
2011A	0.0	0.0	0.0	0.0	0.0	--	--	--	--	(\$62.68)	NM
2012E - New	0.0A	0.0A	0.0A	0.0	0.0	(\$25.33)A	(\$15.26)A	(\$0.44)A	(\$0.32)	(\$4.05)	NM
2012E - Old	0.0A	0.0A	0.0A	0.0	0.0	(\$25.33)A	(\$15.80)	(\$0.68)	(\$0.67)	(\$5.24)	NM
2013E - New	\$19.7	\$21.1	\$23.1	\$24.5	\$88.3	(\$1.13)	\$0.23	\$0.30	\$0.31	(\$0.29)	NM
2013E - Old	\$19.7	\$21.1	\$23.1	\$24.5	\$88.3	(\$1.13)	\$0.22	\$0.30	\$0.31	(\$0.30)	NM
2014E - New	--	--	--	--	\$126.1	--	--	--	--	\$2.87	3.7x
2014E - Old	--	--	--	--	\$126.1	--	--	--	--	\$2.90	NM

Source: Company Information and Leerink Swann LLC Research  
Revenues in millions. HPTX completed an IPO on 7/31/12.



## INVESTMENT THESIS

We believe that HPTX shares present an attractive opportunity to invest in the orphan drug business model and rate the stock Outperform. Lead agent Ravicti is in late-stage development for urea cycle disorders (UCD) and hepatic encephalopathy (HE), two rare diseases characterized by elevated levels of ammonia in the bloodstream, which can cause significant neurological complications. HPTX generated positive Phase III data for Ravicti in adult urea cycle disorder patients pursuant to a special protocol assessment (SPA) and has a PDUFA date of 1/23/13. HPTX has also completed Phase II trials for Ravicti in HE with an end-of-Phase II meeting planned in 4Q:12. Ravicti has a similar mechanism of action to MRX's FDA-approved Buphenyl, the use of which is constrained by a large dose burden, frequent (3-6 times/day) administration, unpleasant taste and smell, tolerability issues, and high sodium content. Easier patient compliance to Ravicti therapy may enable better disease management ultimately translating into fewer hyperammonemic (HA) crises relative to what is currently available with Buphenyl. The rate of HA crises with Ravicti was 40% lower than that seen for Buphenyl in the 12-month safety extension study following HPTX's pivotal Phase III trial. HPTX is led by seasoned orphan drug company executives who have stayed close to key physicians and patient support organizations who are expected to influence Ravicti uptake. HPTX expects to launch Ravicti in early 2013 with a field staff of 10 people and 10 individuals running back-office operations. We project that HPTX achieves breakeven by 2014 and generates peak sales around \$150MM in UCD in 2019. HPTX may influence the conversion and expansion of the UCD market since the company has the option to purchase worldwide rights to Buphenyl and Ammonul from MRX for \$22MM, which may be funded by drawing on a loan commitment from MRX. HE presents an upside market opportunity of around \$500MM, in our estimation. In contrast to SLXP's Xifaxan, which blocks nitrogen absorption in the gut for HE patients, Ravicti lowers ammonia systemically by increasing its clearance. Ravicti could thus potentially be complementary to currently approved agents that limit the local production of ammonia. HPTX completed a Phase II clinical study of similar design to the pivotal trial used to evaluate Xifaxan, the only therapy approved by the FDA for episodic HE within the last 30 years. Phase II data indicate that Ravicti may have superior efficacy compared to Xifaxan and may improve outcomes when given in combination.

## VALUATION

Our 12-month fair value estimate for HPTX is \$18/share based on discounted cash flow (DCF) analysis. We assume a 12% discount rate and 5% terminal growth rate. We discount free cash flow until early 2020E, when orphan drug exclusivity for Ravicti for treating UCD expires.

## RISKS TO VALUATION

The key risks to HPTX's valuation include the potential for disappointing clinical data, regulatory setbacks, and commercial and financial shortfalls. Since HPTX presently has only one late-stage product candidate, any of those possible setbacks may impact the stock significantly.

HPTX P&L (\$MM)	2010	2011	1Q12	2Q12	3Q12	4Q12E	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E
Revenue	-	-	-	-	-	-	-	19.7	21.1	23.1	24.5	88.3	126.1	147.0
COGS	-	-	-	-	-	-	-	3.0	3.2	3.5	3.7	13.2	18.9	22.1
R&D	23.1	17.2	8.9	2.7	2.4	2.5	16.5	5.0	5.0	5.0	5.0	20.0	25.2	29.4
SG&A	3.5	8.9	2.3	2.0	2.4	2.5	9.2	8.0	8.5	9.0	10.0	35.5	31.5	36.8
Operating expenses	26.6	26.2	11.2	4.8	4.8	5.0	25.7	16.0	16.7	17.5	18.7	68.7	75.6	88.2
Operating income	(26.6)	(26.2)	(11.2)	(4.8)	(4.8)	(5.0)	(25.7)	3.7	4.4	5.6	5.8	19.6	50.4	58.8
Interest income	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.2	0.3	0.4
Interest expense	(0.0)	(2.6)	(1.0)	(1.3)	(0.8)	(0.2)	(3.4)	(0.5)	(0.7)	(0.7)	(0.7)	(2.6)	(2.9)	(1.4)
Other income (expense)	1.1	(0.7)	0.4	(1.1)	0.6	-	(0.1)	(22.0)	-	-	-	(22.0)	-	-
EBT	(25.5)	(29.4)	(11.9)	(7.2)	(4.9)	(5.2)	(29.2)	(18.7)	3.7	4.9	5.1	(4.9)	47.8	57.8
Tax expense	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Net income (loss)	(25.5)	(29.4)	(11.9)	(7.2)	(4.9)	(5.2)	(29.2)	(18.7)	3.7	4.9	5.1	(4.9)	47.8	57.8
<b>Diluted EPS</b>	<b>(61.70)</b>	<b>(62.68)</b>	<b>(25.33)</b>	<b>(15.26)</b>	<b>(0.44)</b>	<b>(0.32)</b>	<b>(4.05)</b>	<b>(1.13)</b>	<b>0.23</b>	<b>0.30</b>	<b>0.31</b>	<b>(0.29)</b>	<b>2.87</b>	<b>3.44</b>
Basic shares outstanding	0.4	0.5	0.5	0.5	11.3	16.6	7.2	16.6	16.6	16.6	16.6	16.6	16.7	16.8

HPTX BS	2010	2011	1Q12	2Q12	3Q12	4Q12E	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E
Cash	6.6	7.0	3.7	7.3	56.5	51.5	51.5	55.9	60.7	66.8	73.1	73.1	126.7	169.0
Debt	-	23.4	30.7	40.5	12.0	10.0	10.0	32.0	32.0	32.0	32.0	32.0	32.0	-
Convertible notes	-	23.4	30.7	31.2	-	-	-	-	-	-	-	-	-	-
Venture debt	-	-	-	9.4	12.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0	-
Ucyclyd loan	-	-	-	-	-	-	-	22.0	22.0	22.0	22.0	22.0	22.0	-

HPTX CFS	2010	2011	1Q12	2Q12	3Q12	4Q12E	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E
Change in cash	(3.5)	0.4	(3.3)	3.6	49.2	(5.0)	44.5	4.4	4.8	6.1	6.3	21.6	53.5	42.4
Cash from operations	(25.9)	(24.5)	(10.7)	(5.8)	(5.7)	(5.0)	(27.2)	(17.6)	4.8	6.1	6.3	(0.4)	53.5	64.4
Net Income	(25.5)	(29.4)	(11.9)	(7.2)	(4.9)	(5.2)	(29.2)	(18.7)	3.7	4.9	5.1	(4.9)	47.8	57.8
SOE	0.2	0.3	0.1	0.2	0.3	0.3	0.9	1.0	1.1	1.1	1.2	4.4	5.7	6.6
Other	(0.6)	4.5	1.1	1.1	(1.1)	-	1.1	-	-	-	-	-	-	-
Cash from investing	(0.0)	(0.0)	(0.1)	0.2	(0.0)	-	0.0	-	-	-	-	-	-	-
Option to purchase Buphenyl	-	-	(0.3)	-	-	-	(0.3)	-	-	-	-	-	-	-
Other	(0.0)	(0.0)	0.2	0.2	(0.0)	-	0.3	-	-	-	-	-	-	-
Cash from financing	22.4	25.0	7.6	9.2	55.0	-	71.7	22.0	-	-	-	22.0	-	(22.0)
Issuance (buyback) shares	22.5	-	(0.0)	0.1	53.4	-	53.5	-	-	-	-	-	-	-
Issuance (repay) debt	-	25.0	7.5	10.0	2.5	-	20.0	22.0	-	-	-	22.0	-	(22.0)
Other	(0.0)	-	0.1	(0.9)	(0.9)	-	(1.7)	-	-	-	-	-	-	-

Source: SEC filings and Leerink Swann Estimates

HPTX DCF (Scenario 1)	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	TV
FCF	(27)	(0)	54	64	46	43	44	44	22	0	
Discount periods	-	0.2	1.2	2.2	3.2	4.2	5.2	6.2	7.2	8.2	
NPV	(4)	(0)	54	64	46	43	44	44	22	0	2
Valuation	314										

Discount Rate	12%
Terminal Growth	5%

Valuation		Valuation	per shr	Probability	P/W
Scenario 1, Ravicti approved for UCD	1	314	\$ 16.10	50%	157
Scenario 2, Ravicti NOT approved	2	78	\$ 3.97	30%	23
Scenario 3, Ravicti approved for UCD and HE	3	588	\$ 30.13	20%	118
<b>Blended Valuation</b>					<b>298</b>
Net cash					44.6
Diluted Shares Outstanding					19.5
Per share valuation					\$ 18

Source: SEC filings and Leerink Swann Estimates

Hyperion Therapeutics, Inc. (HPTX) Expected Milestones			
Ravicti	UCD	PDUFA	1/23/2013
Ravicti	HE	End of Phase II meeting	4Q12
Ravicti	HE	Phase III initiation	1H13
Ravicti	HE	Phase III data	2014
Ravicti	HE	sNDA filing	2015
Ravicti	HE	sNDA approval	2016
Ravicti	UCD	Orphan drug expiration	1Q20
Ravicti	HE	Orphan drug expiration	2H21

*Source: Company reports, Leerink Swann LLC estimates*



## Disclosures Appendix

### Analyst Certification

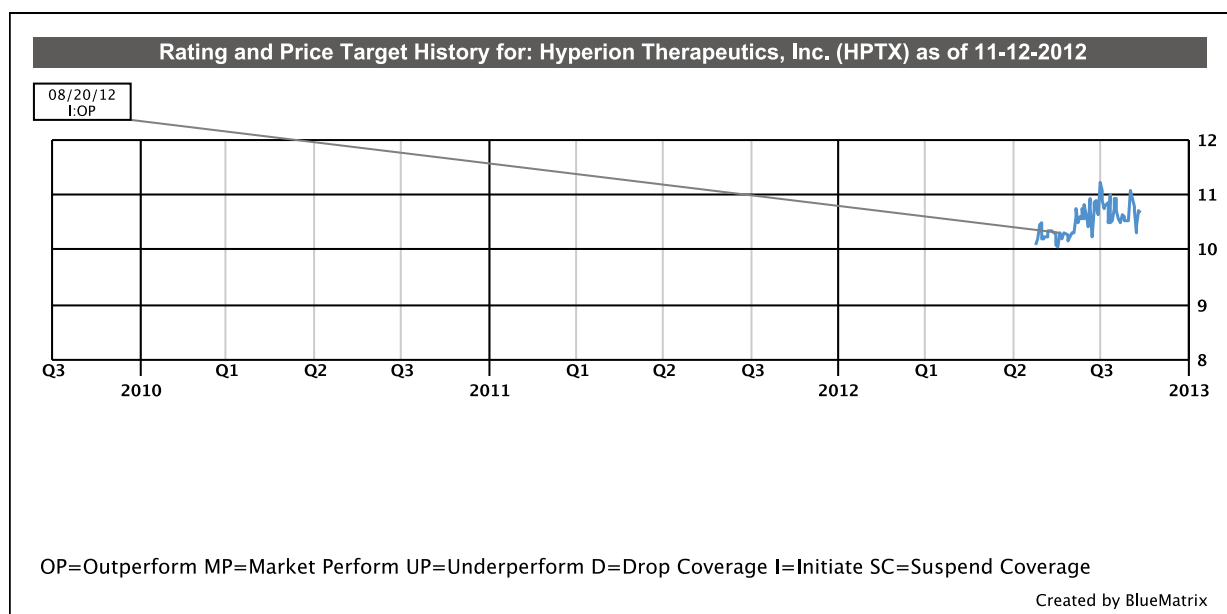
I, Joseph P. Schwartz, certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

### Valuation

Our 12-month fair value estimate for HPTX is \$18/share based on discounted cash flow (DCF) analysis. We assume a 12% discount rate and 5% terminal growth rate. We discount free cash flow until early 2020E, when orphan drug exclusivity for Ravicti for treating UCD expires.

### Risks to Valuation

The key risks to HPTX's valuation include the potential for disappointing clinical data, regulatory setbacks, and commercial and financial shortfalls. Since HPTX presently has only one late-stage product candidate, any of those possible setbacks may impact the stock significantly.





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**Rating and Price Target History for: Medicis Pharmaceutical Corp. (MRX) as of 11-12-2012**

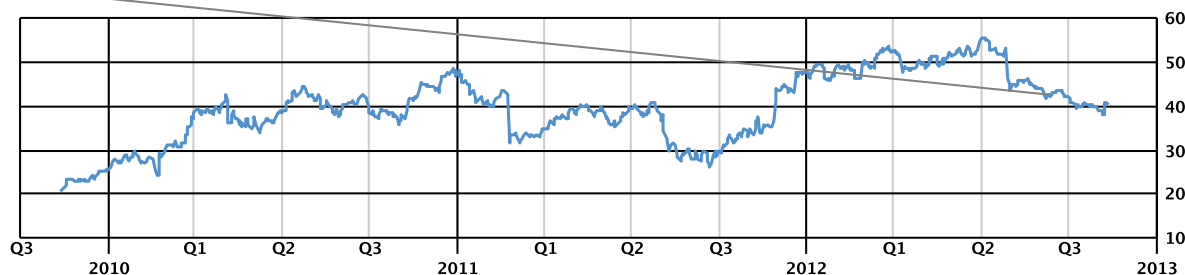
 06/01/10  
SC


Leerink Swann placed a Market Perform rating on MRX on November 8, 2006.

OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage

Created by BlueMatrix

**Rating and Price Target History for: Salix Pharmaceuticals, Ltd. (SLXP) as of 11-12-2012**

 09/10/12  
I:MP


OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage

Created by BlueMatrix



Distribution of Ratings/Investment Banking Services (IB) as of 09/30/12				
Rating	Count	Percent	IB Serv./Past 12 Mos.	
			Count	Percent
BUY [OP]	102	58.30	29	28.40
HOLD [MP]	73	41.70	3	4.10
SELL [UP]	0	0.00	0	0.00

## Explanation of Ratings

**Outperform (Buy):** We expect this stock to outperform its benchmark over the next 12 months.

**Market Perform (Hold/Neutral):** We expect this stock to perform in line with its benchmark over the next 12 months.

**Underperform (Sell):** We expect this stock to underperform its benchmark over the next 12 months. The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company.

For the purposes of these definitions the relevant benchmark will be the S&P 600® Health Care Index for issuers with a market capitalization of less than \$2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over \$2 billion.

From October 1, 2006 through January 8, 2009, the relevant benchmarks for the above definitions were the Russell 2000® Health Care Index for issuers with a market capitalization of less than \$2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over \$2 billion.

Definitions of Leerink Swann Ratings prior to October 1, 2006 are shown below:

**Outperform (Buy):** We expect this stock to outperform its benchmark by more than 10 percentage points over the next 12 months.

**Market Perform (Hold/Neutral):** We expect this stock to perform within a range of plus or minus 10 percentage points of its benchmark over the next 12 months.

**Underperform (Sell):** We expect this stock to underperform its benchmark by more than 10 percentage points over the next 12 months.

For the purposes of these definitions, the relevant benchmark were the Russell 2000® Health Care Index for issuers with a market capitalization of less than \$2 billion and the S&P 500® Index for issuers with a market capitalization over \$2 billion.





## Important Disclosures

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**Leerink Swann Consulting LLC, an affiliate of Leerink Swann LLC, is a provider of evidence-based strategy and consulting to the healthcare industry.**

**In the past 12 months, the Firm has received compensation for providing investment banking services to Hyperion Therapeutics, Inc.**

**Leerink Swann LLC makes a market in Hyperion Therapeutics, Inc. and Salix Pharmaceuticals, Ltd.**

**Leerink Swann LLC is willing to sell to, or buy from, clients the common stock of Medicis Pharmaceutical Corp. on a principal basis.**

**Leerink Swann LLC has acted as the manager for a public offering of Hyperion Therapeutics, Inc. in the past 12 months.**

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