August 20, 2012

OUTPERFORM

Reason for report:

INITIATION

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HEALTHCARE EQUITY RESEARCH

HYPERION THERAPEUTICS, INC.

Attractive Ammonia Orphan Disease Markets: Initiating at OP

• **Bottom Line:** We believe that HPTX shares present an attractive opportunity to invest in the orphan drug business model, and are **initiating coverage of HPTX with an Outperform rating and $18/share fair value estimate in 12 months.**

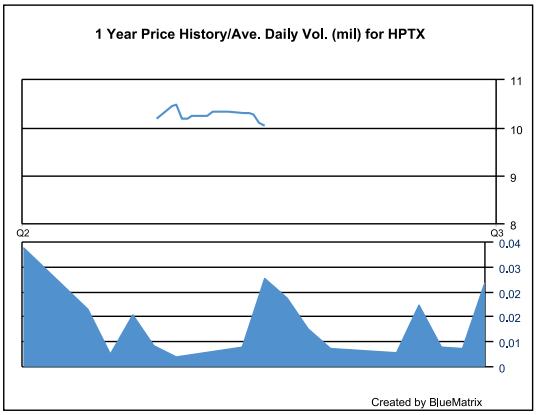
• **Lead agent Ravicti is in late-stage development for urea cycle disorders (UCD) and hepatic encephalopathy (HE),** two rare diseases characterized by elevated levels of ammonia in the bloodstream, which can cause significant neurological complications. HPTX generated positive Phase III data for Ravicti in adult urea cycle disorder patients pursuant to a special protocol assessment (SPA) and has a PDUFA date of 10/23/12. HPTX has also completed Phase II trials for Ravicti in HE with an end-of-Phase II meeting planned in 4Q12.

• **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 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 indicates that Ravicti may have superior efficacy compared to Xifaxan and may improve outcomes when given in combination.

Key Stats:	**(NASDAQ:HPTX)**
S&P 600 Health Care Index:	**840.54**
Price:	**$10.04**
52 Week High:	$11.99
52 Week Low:	$9.95
Shares Outstanding (mil):	16.6
Market Capitalization (mil):	$166.7
Book Value/Share:	$0.00
Cash Per Share:	$3.16
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	0.0A	0.0	0.0	0.0	0.0	($25.33)A	($15.80)	($0.68)	($0.67)	($5.24)	NM
2013E	$19.7	$21.1	$23.1	$24.5	$88.3	($1.13)	$0.22	$0.30	$0.31	($0.30)	NM
2014E	--	--	--	--	$126.1	--	--	--	--	$2.90	3.5x

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

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The Healthcare Investment Bank™

Hyperion Therapeutics, Inc (NASDAQ: HPTX) Attractive Ammonia Orphan Disease Markets: Initiating at Outperform

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Hyperion Therapeutics (HPTX) Investment Thesis and Company Overview

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- We believe that HPTX shares present an attractive opportunity to invest in the orphan drug business, and are initiating coverage with an OP rating and $18/share fair value estimate.
- Hyperion Therapeutics (NASDAQ: HPTX) is a biopharmaceutical company that is developing Ravicti (glycerol phenylbutyrate) to treat two rare (orphan) diseases: urea cycle disorders (UCD) and hepatic encephalopathy (HE).
- UCD and HE are characterized by elevated levels of ammonia in the bloodstream, which can cause significant neurological complications known in the two disease fields as hyperammonemic (HA) crises and hyperammonemic events, respectively.
- Ravicti is an ammonia scavenging (lowering) agent with a similar mechanism of action to FDA-approved Buphenyl (sodium phenylbutyrate), 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.
- Approximately 1 tablespoon of Ravicti oral solution is equivalent to the FDA-approved maximum daily dose of 40 tablets of Buphenyl. Ravicti is nearly tasteless and odorless and does not contain any sodium.
- Easier patient compliance to Ravicti therapy may enable better disease management ultimately translating into fewer HA crises vs. what is currently available with Buphenyl.

HPTX Is an Attractive Opportunity To Invest in the Orphan Drug Business Model

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- We expect HPTX to execute a lean orphan drug business model, which may result in a fast route to profitability.
- Management 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. HE presents an upside market opportunity around $500MM in our estimation.
- We believe that orphan drug companies have advantages over non-orphan "mass-market" companies, providing unique opportunities for investors.
  - Based on our prior work, we believe orphan drugs have higher odds of regulatory success.
  - We believe orphan drug launches may be more rewarding for investors than “mass-market” drug launches.
  - Marketed orphan drugs tend to have less competition, lower marketing costs, and a longer life-cycle with less risk of generic erosion.
  - As a result, orphan drug company stocks have outperformed their mass-market drug company peers and benchmark indices over the past 10 years.

Hyperion Pipeline Catalysts

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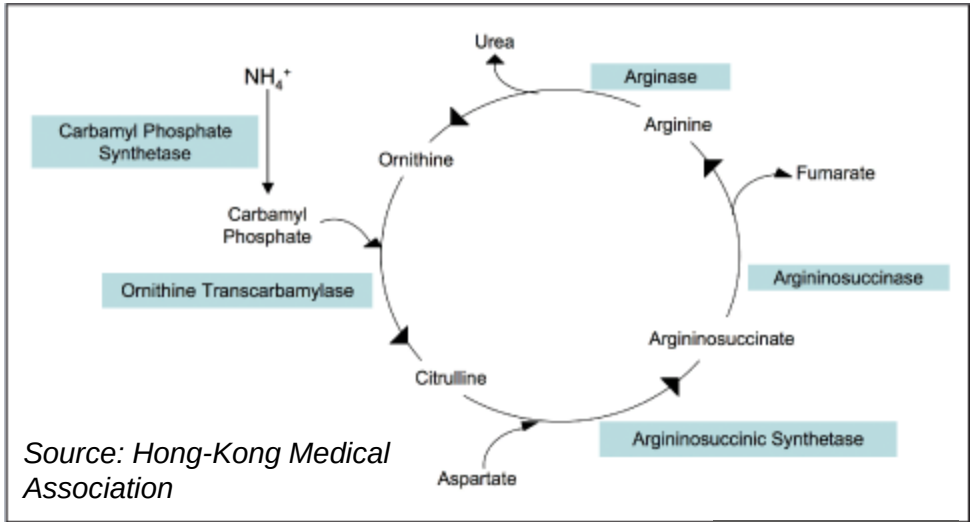
- On December 23, 2011, HPTX submitted an NDA for Ravicti for the chronic management of UCD with a PDUFA date on October 23, 2012.
- HPTX has also completed Phase II trials for Ravicti in HE with an end-of-Phase II meeting planned in 4Q12.
- HPTX currently expects to commercially launch Ravicti in UCD in 1H13.

Hyperion Therapeutics, Inc. (HPTX) Expected Milestones			
Ravicti	UCD	PDUFA	10/23/2012
Ravicti	HE	End of Phase II meeting	4Q12
Ravicti	HE	Phase III initiation	1H13
Ravicti	HE	Phase III data	2H13
Ravicti	HE	sNDA filing	1H14
Ravicti	HE	sNDA approval	2H14
Ravicti	UCD	Orphan drug expiration	4Q19
Ravicti	HE	Orphan drug expiration	2H21

Source: Company reports, Leerink Swann LLC estimates

Urea Cycle Disorder (UCD) Background

- The urea cycle is a vital function of the liver in the metabolism of protein. Our bodies are unable to store nitrogen, an element found in protein, so excess nitrogen must be excreted.
- The excess nitrogen is normally converted to urea in the urea cycle, and then transported via the bloodstream to the kidneys, where it is excreted.
- When the body is deficient in an enzyme of the urea cycle, it cannot efficiently remove the accumulating nitrogen, which ultimately forms ammonia in the bloodstream (NH3), which is a neurotoxin.
- The urea cycle is controlled by a series of six enzymes, which do not work correctly in various UCD.
- Patients with moderate to severe UCD are generally candidates for Buphenyl (sodium phenylbutyrate; currently manufactured by the Ucyclyd division of Medicis), which provides an alternative mechanism for removing glutamine from the body via its conversion to phenylacetylglutamine. Ammonul contains sodium phenylacetate plus sodium benzoate.



Source: Hong-Kong Medical Association

Ravicti's De-risked MoA Is Similar to Buphenyl

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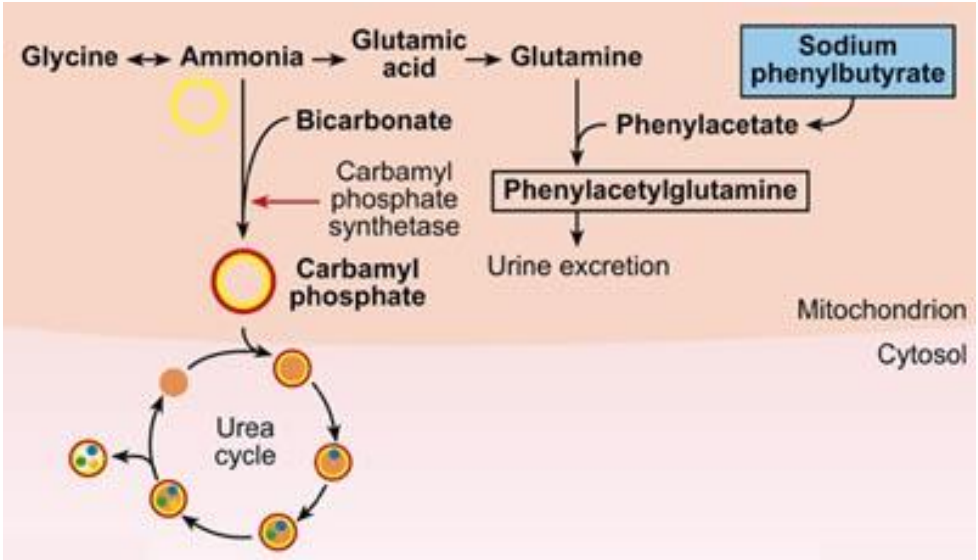
- Ravicti functions as a systemic ammonia lowering agent and provides an alternate pathway to the urea cycle for removing ammonia from the bloodstream.
- Ravicti consists of glycerol phenylbutyrate (glycerol-PBA), which is a pre-pro-drug of the active ingredient PAA.
- Buphenyl (sodium PBA) is the pro-drug of PAA.
- PAA facilitates the removal of ammonia when it is converted to phenylacetylglutamine, or PAGN, which is excreted in urine and replaces urea as a vehicle for ridding the body of ammonia.
- In contrast to Buphenyl, Ravicti is nearly tasteless and odorless and requires a much smaller volume of drug to achieve similar efficacy.



Source: National Urea Cycle Disorders Foundation (NUCDF)

Ravicti Addresses Most Urea Cycle Disorders (UCD)

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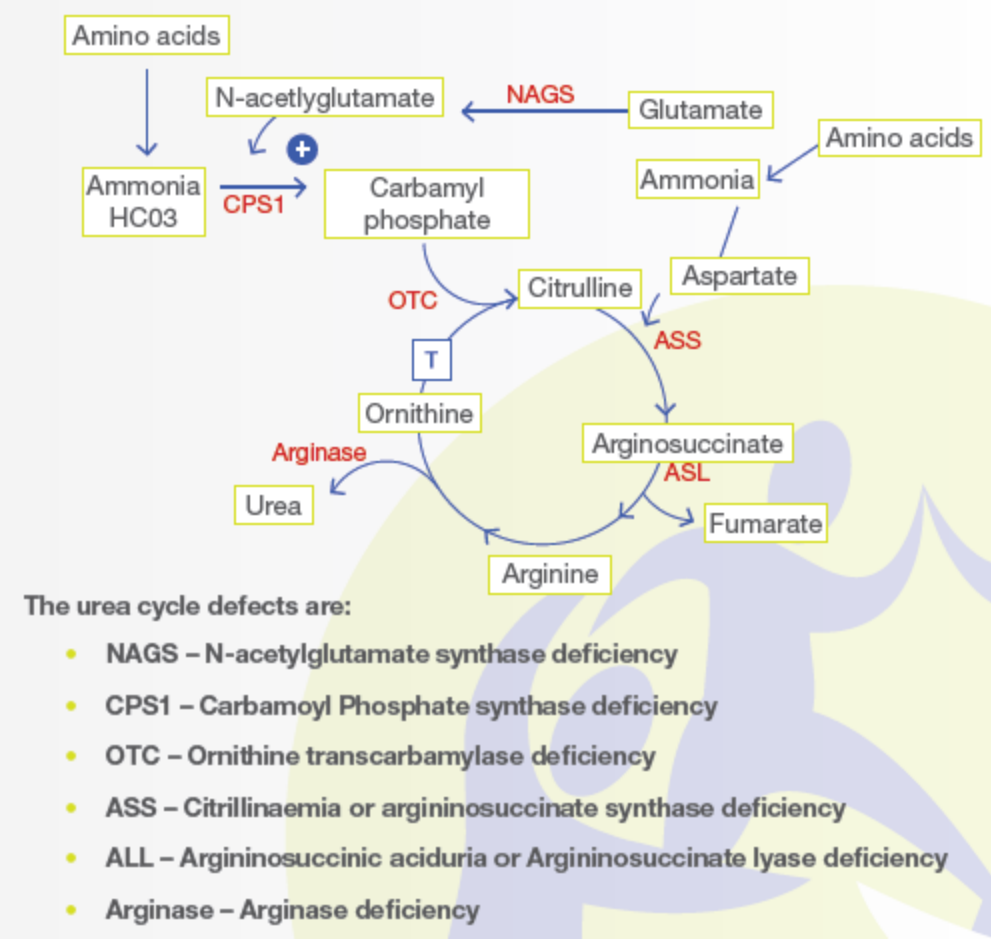
- Subtypes of UCD that may benefit from Ravicti therapy include CPS1 deficiency (carbamyl phosphate synthetase deficiency), OTC deficiency (ornithine transcarbamylase deficiency), ASS (citrullinemia or argininosuccinic acid synthetase deficiency), ALL (argininosuccinic aciduria or argininosucciate lyase deficiency), and arginase deficiency.
- Carbaglu (carglumic acid) was approved by the FDA in 2010 for patients with deficiency of the hepatic enzyme N-acetylglutamate synthase (NAGS).



Source: National Urea Cycle Disorders Foundation (NUCDF)

The Goal of UCD Therapy Is To Avoid Hyperammonemic (HA) Crises

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- Infants with a urea cycle disorder rapidly develop cerebral edema and the related signs of lethargy, anorexia, hyperventilation or hypoventilation, hypothermia, seizures, neurologic posturing, and coma. Liver transplantation is an option reserved for the most severely affected patients, typically those who present very early in life.
- UCD are estimated to occur in approximately 1 in 10,000 births in the US, and 1,000 diagnosed UCD patients are estimated to be currently living in the US. Because many cases of UCD remain undiagnosed and/or infants die without a definitive diagnosis, the exact incidence of these cases is unknown and underestimated. It is believed that up to 20% of Sudden Infant Death Syndrome (SIDS) cases may be attributed to an undiagnosed inborn error of metabolism such as UCD. Some children with autism spectrum and behavioral disorders may have undiagnosed UCD.
- In milder (or partial) urea cycle enzyme deficiencies often seen in adults, ammonia accumulation may be triggered by illness or stress at any point in life, resulting in multiple mild elevations of plasma ammonia concentration that may go undiagnosed.
- Accumulated ammonia can cause HA crises, which may result in irreversible brain damage, coma or death. Metabolic stressors -- viruses, high protein intake, excessive exercise or dieting, surgery, or a drug (valproic acid, prednisone or other corticosteroid) -- can create excessive ammonia in the body and overwhelm the individual's urea cycle enzyme function, resulting in severe neurological symptoms.

The Goal of UCD Therapy Is To Avoid Hyperammonemic (HA) Crises (continued)

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- Anything that places increased stress on the patient can trigger a HA episode. Viral infections are probably the most common cause, but episodes can be triggered by physical or emotional stress, dehydration, trauma, broken bones, the menstrual cycle, certain medications (like valproic acid), and changes in diet.
- Most patients presenting with a hyperammonemic coma have some degree of delay in their development. Mental retardation is defined as a measurable delay in the normal development of skills and intellect. Some of these children have delayed speech, or learning disabilities. Patients with severe defects in their urea cycle require treatment with many drugs and strict dietary controls. While this will complicate their daily routine, they can grow up and participate in school, play, and work.
- Most patients who experience a severe hyperammonemic episode will have some degree of developmental delay. The duration of the hyperammonemic episode (particularly coma) does affect the outcome, with longer episodes causing worse damage to the brain. In addition to developmental delay, urea cycle patients are also at risk for milder disabilities such as attention deficit disorder or learning disabilities. With developmental intervention programs and careful medical management, UCD patients can catch up with their peers.

Buphenyl Is the Mainstay Therapy for UCD Today

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- Sodium phenylbutyrate (trade name Buphenyl) is the primary medication being used today to treat urea cycle disorders. H-blockers (antacids) are often used in conjunction to minimize the gastrointestinal side effects (stomach ache, reflux, etc.) of Buphenyl treatment. It is estimated that around 425 UCD patients are currently treated with Buphyenyl in the US, often at suboptimal doses due to poor tolerability.
- Sodium benzoate is used in some patients, solely or in conjunction with Buphenyl; both are “ammonia scavengers” that provide alternative pathways for removal of ammonia from the bloodstream thereby helping to prevent hyperammonemia (elevated blood ammonia). One or both of these medications is administered three to four times per day in order to ensure continual removal of toxic ammonia from the bloodstream.
- Pharmaceutical grade L-citrulline (for OTC and CPS deficiency) or L-arginine free base (for ASA and citrullinemia) is also required by some patients (not to be used in Arginase Deficiency). These supplements help catalyze the urea cycle enzymes and promote optimal removal of ammonia.
- Carbaglu (carglumic acid) was approved by the FDA in 2010 for patients with deficiency of the hepatic enzyme N-acetylglutamate synthase (NAGS).

Buphenyl Is Generally Very Poorly Tolerated

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- Buphenyl use is constrained due to the combination of high pill burden or large quantity of powder that must be taken, frequency of dosing (3-6 times per day), the unpleasant taste, smell and tolerability issues. The usual total daily dose of Buphenyl tablets and powder for patients with urea cycle disorders is 450–600 mg/kg/day in patients weighing less than 20 kg, or 9.9–13.0 g/m2/day in larger patients.
- Children with urea cycle disorders often lack appetite (due to excess serotonin in the brain suppressing appetite) and have difficulty tolerating/complying with Buphenyl therapy. Hence, some patients receive medications and feedings either via gastrostomy tube (surgically implanted into the stomach) or nasogastric tube (manually inserted through the nose into the stomach).
- HPTX management believes that around a third of physicians use less drug than they would like their patients to take for optimal disease management, and 80% of patients experience HA crises as a result.

Ravicti Addresses Shortcomings of Buphenyl

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- Ravicti, if approved, will offer benefits over the current standard of care that enhance tolerability and increase compliance in support of improved disease management.
- Ravicti was designed to contain the same quantity of the active ingredient as Buphenyl in a much smaller drug volume and it also has a longer half-life. For example, approximately 1 tablespoon of Ravicti liquid is equivalent to the FDA-approved maximum daily dose of 40 tablets of Buphenyl.
- Ravicti is also nearly tasteless and odorless and does not contain any sodium.
- Ravicti has been shown to have non-inferior efficacy in terms of mean blood ammonia levels compared to Buphenyl, while providing convenience advantages, such as less frequent dosing, lower drug volume, and no taste or odor, which ultimately may result in better control of patients' ammonia levels.
- 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.

Skilled Orphan Drug Management Team

- Hyperion is led by seasoned biotech industry veterans with a proven track record in clinical, operational and financial execution, particularly in the field of orphan diseases.
- Importantly, we believe that management has stayed close to key physicians and patient support organizations, who are expected to influence Ravicti uptake.

Hyperion Therapeutics, Inc. (HPTX) Management		
Donald Santel	Chief Executive Officer	CoTherix, Reflow, Cardiac Pathways, Medtronic
Jeffrey Farrow	Chief Financial Officer	Evotec, Renovis, KPMG
Bruce Scharschmidt, M.D.	Chief Medical Officer	Novartis, Chiron, UCSD
Klara Dickinson	Regulatory Affairs	CoTherix, Scios, Dey
Christine Nash	Chief Commerical Officer	CoTherix, Genesoft, Oncology Therapeutics Network, Eli Lilly, Imana
Dion Coakley, Pharm. D.	Clinical Operations	Virobay, Gilead, Burroughs Wellcome
Masoud Mokhtarani, M.D.	Clinical Development	Limerick, Pfizer/Rinat Neurosciences, Immune Tolerance Network

Source: Leerink Swann Research and SEC Filings

Generic Buphenyl Unlikely To Be Significant Threat

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- Buphenyl is off patent and sodium phenylbutyrate has been produced and "marketed" as part of Dr. Burzynski's controversial "antineoplaston" cancer therapy for many years in Houston, TX. The tablets are not sold "a la carte" separate from his services, and we do not expect UCD specialists to obtain drug supply from him given their sophistication, fragile nature of their patients, and his multiple run-ins with the FDA.
- Our checks with reimbursement specialists indicate that payors will not go out of their way to limit access to Ravicti to UCD patients who prefer and are prescribed it as an alternative to Buphenyl, so we do not view generic Buphenyl as a meaningful threat to the Ravicti franchise. We expect HPTX to offer financial (i.e., co-pay) support to patients who lack adequate insurance, which is subsidized by premium prices for others.
- Current Buphenyl sales of roughly $24MM are not sufficient enough to attract additional generic competition, in our opinion. We believe HPTX will be able to successfully convert the vast majority of patients currently on Buphenyl to Ravicti. Hence, we do not expect Buphenyl peak sales to exceed $40MM in our base case scenario that Ravicti is approved on 10/23/12, or $65MM if Ravicti is not approved and HPTX raises the price of Buphenyl. This should support attractive pharmaceutical market dynamics for Ravicti.

Clear Registration Plan for Ravicti

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- HPTX submitted an NDA for Ravicti for the chronic management of UCD patients aged 6 years and above on December 23, 2011.
- As part of an April 2012 update to the FDA, HPTX submitted a revised draft package insert requesting approval of Ravicti for UCD patients down to 29 days of age.
- In the original NDA package, HPTX included data from Phase II and Phase III trials in patients aged 6 years and above as well as safety data from 69 UCD patients with 12 months of treatment on Ravicti and the results of two nonclinical carcinogenicity studies in the NDA submission.
- HPTX is currently in the process of conducting a clinical trial in UCD patients aged 29 days through 5 years. The efficacy portion of this trial is complete and was submitted to the FDA in April 2012.
- Data from the 12-month safety extension portion of the age 29 days – 5 years study will not be available until the second quarter of 2013.

Ravicti Premium Price Justifiable

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- The treatment of patients with UCD requires a highly coordinated team of specialists trained in caring for patients with inborn errors of metabolism.
- Emergency management of patients in hyperammonemic coma resulting from a UCD is based on three interdependent principles:

1. Physical removal of the ammonia by dialysis or some form of hemofiltration;
2. Reversal of the catabolic state through caloric supplementation and in extreme cases, hormonal suppression (glucose/insulin drip);
3. Pharmacologic scavenging of excess nitrogen.

Figure 2: Treatment Team and Organization

- Metabolic Specialist
  - coordinate treatment and management
- Intensive care team
  - assist with physiologic support
  - ventilator management
  - sedation and pain management
- Nephrologist or dialysis team
  - manage dialysis
  - manage renal complications
- Surgical team
  - large bore catheter placement
  - liver biopsy as necessary
  - gastrostomy tube placement (if indicated)
- Pharmacy staff
  - formulate nitrogen scavenging drugs
  - cross check dosing orders in complex management
- Laboratory staff
  - analyze large volume of ammonia samples in acute phase
  - analyze amino acids and other specialty labs
- Nursing staff
  - execute complex and rapidly changing management plan
  - closely monitor patient for signs of deterioration or change
- Nutritionist
  - maximize caloric intake with neutral nitrogen balance
  - educate family in management of complex very low-protein diet
- Social work
  - rapidly identify resources for complex outpatient treatment regimen
  - work with families in highly stressful clinical situation
- Genetic Counselor
  - educate family in genetics of rare metabolic disease
  - identify other family members at potential risk (OTC particularly)
  - ensure proper samples are obtained for future prenatal testing
  - contact research/diagnostic centers for genetic testing

Source: Rare Diseases Clinical Research Network

Buphenyl License Option With Ucyclyd Raises the Floor for HPTX

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- HPTX entered into an option agreement with Ucyclyd/Medicis to purchase worldwide rights to Buphenyl and Ammonul for $22MM, which may be funded by drawing on a loan commitment from Ucyclyd.
- Option period runs from January 1, 2013, to June 30, 2013.
- Ucyclyd has the right to retain Ammonul for $32MM.
- If the Ravicti NDA for UCD is not approved by January 1, 2013, then Ucyclyd is obligated to make monthly payments of $0.5MM to HPTX until FDA approval of Ravicti or June 30, 2013.

Pivotal Ravicti Phase III Trial in Adult Patients Was Conducted Under an SPA

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- A four-week, multi-center, randomized, double-blind, placebo-controlled cross-over study was designed to evaluate the non-inferiority of Ravicti to Buphenyl.
- The primary efficacy measure was blood ammonia control, assessed as 24-hour area under the curve on days 14 and 28, the last day of each two-week treatment period.
- Subjects were administered a Buphenyl dose equivalent to their prescribed dose before study enrollment or a dose of Ravicti that delivered the same amount of PBA. All patients received active or placebo Buphenyl tablets or powder, as well as either active or placebo Ravicti, throughout the study. The drugs were administered three times a day with meals, and diet was strictly controlled.
- Based on the study design, non-inferiority of Ravicti would be demonstrated if the upper 95% confidence interval of ammonia on Ravicti was not more than 25% higher than that seen on Buphenyl.
- The study enrolled 46 adults at 19 sites in North America. Of the 46 adults enrolled, 45 subjects received at least one dose of study drug and 44 subjects completed the study and are included in the primary efficacy analysis. Subjects were required to be on a stable dose of Buphenyl before enrollment.

Phase III Met the Primary Endpoint

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- **Ravicti demonstrated non-inferiority vs. Buphenyl in the pivotal Phase III trial.**
- Ravicti was generally well tolerated. Twenty-three subjects reported at least one adverse event during Buphenyl treatment, and 27 subjects reported at least one adverse event during Ravicti treatment.
- There was one serious adverse event (SAE), gastroenteritis, during treatment with Ravicti, which was deemed not to be drug related. No deaths occurred during the study, and no clinically significant lab or electrocardiogram changes were observed for either treatment.
- One patient experienced an HA crisis during Buphenyl treatment.
- One subject withdrew early from the study during Buphenyl treatment because of high ammonia and headache.
- There were no HA crises or subject withdrawals from the study during dosing with Ravicti.
- Forty of the 44 patients in Phase III agreed to continue treatment and monthly monitoring with Ravicti in the 12-month open-label extension (OLE).

Positive Phase II Adult Trial Demonstrated Ravicti Efficacy and Safety

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- **Ravicti was well tolerated and exhibited a similar safety profile to Buphenyl in the adult Phase II study.**
- There were 2 SAEs related to HA crises, both occurred during Buphenyl treatment.
- It was an open-label, switchover study of the safety, tolerability, pharmacokinetic profile, & ammonia control of Ravicti compared to Buphenyl.
- There were 13 adult UCD patients, 10 of whom completed the trial.
- Subjects were required to be on a stable dose of Buphenyl before enrollment
- Upon enrollment, all subjects received Buphenyl for 7 days and were then admitted to a monitored clinical setting for overnight observation and 24-hour pharmacokinetic (PK) and ammonia measurements and urine collection.
- Subjects were then switched over to Ravicti, stayed on the Ravicti dose for seven days and were then re-admitted to the monitored clinical setting for repeated PK and ammonia measurements, and urine collection.

Positive Phase II Pediatric Trial Age 6 – 17 Years Demonstrated Ravicti Efficacy and Safety

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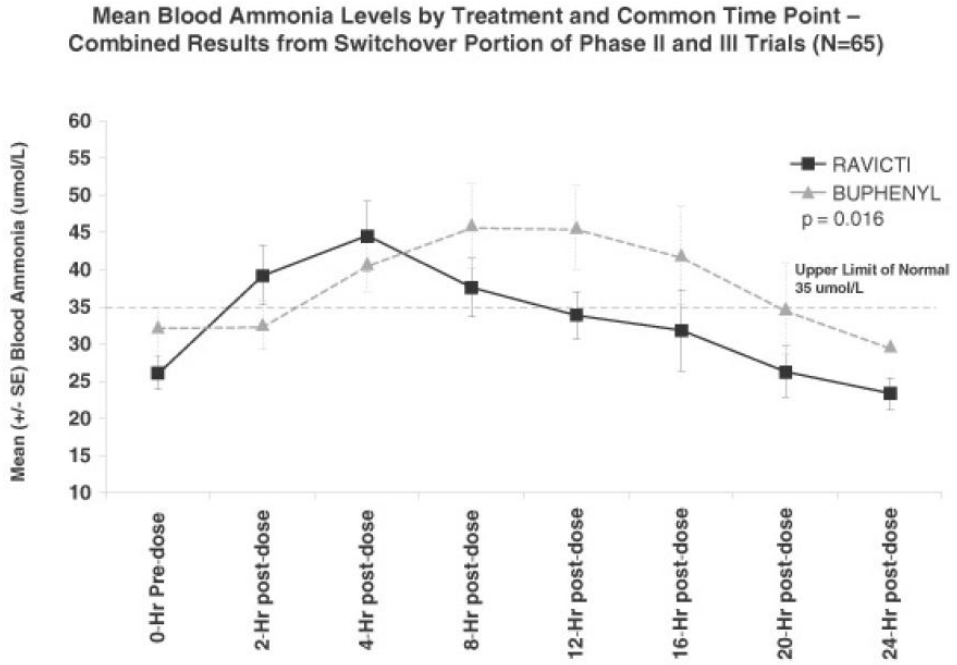
- **Ravicti was well tolerated and exhibited a safety profile similar to Buphenyl in the pediatric Phase II study.**
- Trial included two phases: a two-week, open-label, switchover comparison of the safety, tolerability, PK characteristics and ammonia control of Ravicti compared to Buphenyl, and a 12-month safety extension.
- Eleven UCD were enrolled in the study, all of whom completed the study and enrolled in the extension phase. The extension portion of the trial enrolled an additional 6 patients for a total of 17 patients.
- Subjects were required to be on a stable dose of Buphenyl before enrollment. Upon enrollment in the switchover phase, all subjects received Buphenyl for 7 days and were then admitted to a monitored clinical setting for overnight observation and 24-hour PK and ammonia measurements and urine collection.
- Subjects were then switched over to Ravicti. Subjects stayed on the Ravicti dose for 7 days and were then re-admitted to the monitored clinical setting for repeated pharmacokinetic, ammonia and urine collection.

Pooled Efficacy Results Show More Favorable PK Profile of Ravicti

- The slow release profile of Ravicti may result in lower ammonia blood levels over late afternoon and nighttime hours, pooled data analysis showed.
- During these Phase II and Phase III trials, Ravicti demonstrated a differentiated rate of gastrointestinal absorption and PK profile as compared with Buphenyl. This was demonstrated by PBA (active ingredient) entering the circulation more slowly when administered as Ravicti.



Source: SEC Filings

Open-label Extension Studies Demonstrate Durable Effect of Ravicti and Better Outcomes

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- Ravicti continues to demonstrate a durable effect on ammonia control, with mean fasting ammonia values well below the upper limit of normal.
- During one year of treatment with Ravicti, patients experienced 40% fewer HA crises versus the prior 12 months and their peak ammonia values during crises were lower.
- Neuropsychological evaluations at baseline and after 12 months of treatment with Ravicti also show evidence of clinically significant improvements in executive function among pediatric patients, including behavioral regulation and metacognitive skills.
- Seventy-seven adult and pediatric UCD patients were enrolled in two 12-month OLE safety studies, 69 of whom completed the studies.

Pediatric Study in Children Aged 29 Days – 5 Years Shows Drug Exposure Same as Buphenyl

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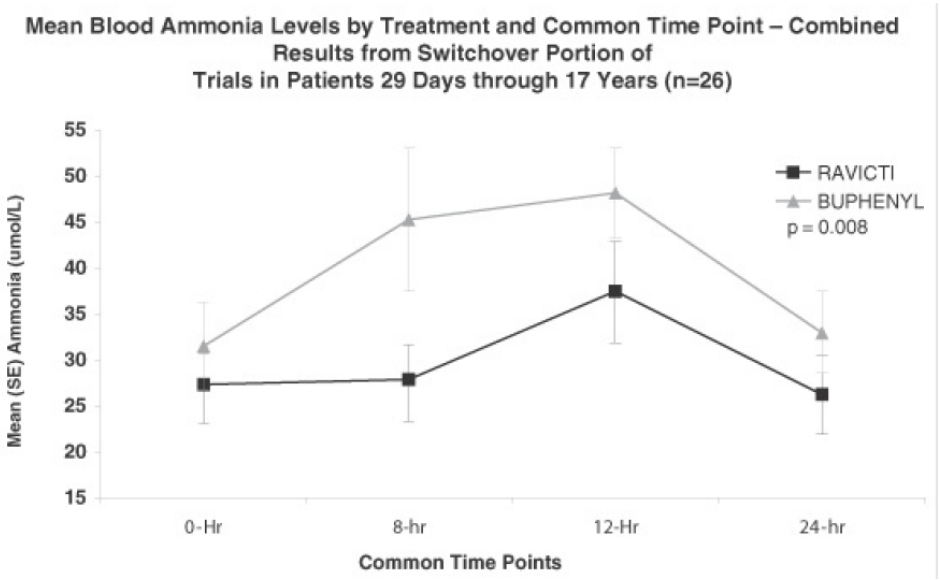
- A trial in 15 pediatric UCD patients aged 29 days - 5 years demonstrated similar age-dependent drug exposure between Ravicti and Buphenyl. Similar to the findings in prior studies, blood ammonia tended to be lower on Ravicti as compared with Buphenyl.
- HPTX initiated this open-label Buphenyl to Ravicti switchover comparison of the safety, PK and ammonia control during treatment with the two drugs followed by a 12-month open-label extension study, following FDA concerns raised during a pre-NDA meeting.
- Data from Ravicti Phase II and Phase III studies indicate that metabolism and elimination of Ravicti and Buphenyl varies with body surface area. Exposure to both drugs' active moiety, PAA, tends to be higher among pediatric patients versus adults. In addition, HPTX Phase II data in children age 6-17 years showed that patients receiving Ravicti had higher PAA levels than patients receiving Buphenyl.
- The FDA raised concerns, because very high levels of PAA have been associated with reversible toxicity in previously published studies involving patients who received intravenously infused PAA; however, PAA exposure among UCD patients administered Ravicti has been below the range associated with toxicity in these previously published studies.
- HPTX submitted a proposed REMS program with the NDA package which is intended to support informed dosing and treatment decisions between patients and their healthcare providers by educating them on the safe use of Ravicti and to limit access to Ravicti only to patients aged 6 years and over until such time as the Ravicti label is expanded to include this patient population.



Source: SEC Filings

Carcinogenicity Signal in Preclinical Data Potentially a Fluke

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- In a 24-month carcinogenicity study in male and female rats, six different tumor types occurred at an incidence suggestive of a relationship to Ravicti administration.
- Based on specialist feedback, HPTX believes study results are not predictive of human risk because:
  - Ravicti and its metabolites have been demonstrated not to damage DNA in a wide range of in vitro tests.
  - There was no evidence of tumors in the targeted tissues in transgenic mice rendered susceptible to cancer, primates or in shorter duration rat studies.
  - Tumors seen in the higher dose groups in the study were of the same type seen in control rats and all were late occurring and of low incidence.
  - Metabolic consequences of long-term exposure to Ravicti in normal rats, and UCD patients are substantially different.
  - The HPTX specialist panel also noted that certain types of the observed tumors are extremely rare in humans and there are no known chemicals that cause abnormal growth in these organs.
- HPTX also has not observed incidence of cancer in any of the UCD clinical trials and is not aware of any reported cases of cancer in patients taking Buphenyl.
- Liver cancer was identified in three patients in HPTX's HE study, two of whom had a predisposing history of hepatitis C and one of whom had cirrhosis of unknown cause. Two of these patients were exposed to Ravicti and one patient received placebo.

Sales & Marketing To Target UCD

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- The two current branded products FDA-approved for UCD -- Buphenyl and Ammunol -- are not currently promoted in the US by a sales force, and market education and support efforts are limited.
- If Ravicti is FDA-approved HPTX plans to establish sales, marketing, and reimbursement functions in the US.
- HPTX plans to hire approximately 10 representatives to reach the specialists involved in treating the majority of patients with UCD.
- A cornerstone of HPTX's strategy will be to facilitate the rapid transition of patients approved under FDA-labeling from Buphenyl to Ravicti. Based on MEDACorp feedback, we believe that most Buphenyl patients will rapidly transition to Ravicti if it is approved by the FDA for commercial sale.
- HPTX will continue to sell Buphenyl for any patients who are not included in the FDA-approved Ravicti label or who may prefer Buphenyl.

UCD Revenue Trajectory Should Benefit From Established Patient Base & Pent-Up Demand

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- We estimate that there are around 90 UCD patients currently receiving Ravicti in the US following their participation in clinical trials. We expect HPTX to convert all of these patients to commercial status within two years following FDA approval.
- We estimate that there are around 425 UCD patients currently receiving Buphenyl in the US. We expect HPTX to convert all of these patients to Ravicti within three years following FDA approval.
- We believe there are around 575 UCD patients in the US who are not currently treated with Ravicti or Buphenyl. We assume that HPTX penetrates 20% of these patients within 3 years following FDA approval.
- We expect HPTX to raise the price on Buphenyl after acquiring rights to the product. Assuming Ravicti is approved contemporaneously, we expect both products to be priced in the "'zyme" range of other ultra-orphan drugs (200-450k/patient/year). If Ravicti approval is delayed, we expect HPTX to implement more gradual price increases of 50% per year.
- We model an average price of $250k/patient/year for the estimated 60% of UCD patients with commercial insurance. For the estimated 40% of UCD patients with government insurance (Medicare/Medicaid) we assume the average realized price will remain flat at $56k/patient/year since HPTX will have to rebate the excess.

7 Years Orphan Drug Exclusivity a Base Case Scenario

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- Ravicti was granted orphan drug designation for the maintenance treatment of UCD and for the intermittent or chronic treatment of patients with cirrhosis and any grade HE.
- Orphan Drug exclusivity would protect the franchise until late 2019, assuming FDA approval in late 2012.
- HPTX has licensed the rights to the Ravicti composition of matter patents (from Brusilow) that have been issued in the United States, Canada, and the primary countries of the European Union, with expiration in 2018 including patent term restoration.
- HPTX also expects to obtain three years of data exclusivity.

Scharschmidt Patents Would Offer Upside Beyond Orphan Drug Exclusivity, If Issued

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- Because HPTX Ravicti composition of matter patent (U.S. Patent 5,968,979) is expected to expire in 2018 including Hatch-Waxman extension, management is mainly relying on orphan drug exclusivity until late 2019 to protect the franchise.
- Issuance of the pending “Scharschmidt” patent applications would be a major surprise and a significant source of upside, in our view. These patents could extend the franchise by at least 10 years until 2032.
- HPTX has a pending patent application for methods of using, administering, and adjusting the dosage of drugs, including Ravicti and Buphenyl, which operate via the active chemical entity PAA. The patent would expire in 2029 if granted (application #12/350,111).
- HPTX also own pending patent applications that incorporate fasting ammonia level measurements into methods of treating and determining dosage for UCD patients, which if issued would expire in 2032 (application #13/061,509).
- The ’111 application, filed in 2009, is in advanced prosecution, whereas the ’509 application is in early prosecution steps. HPTX recently filed a request for continued examination (RCE) for the ’111 application, and the next office action could be key for allowability of this application.
- We believe the recent Promethius supreme court decision raises the hurdle for this application. To date, the patent examiner has not raised a 101-rejection, but HPTX’s claim structure resembles Promethius methods claims, in our view, making it tougher for HPTX to prevail with the USPTO, beyond the limited traction HPTX has already gained with the patent office.

Hepatic Encephalopathy (HE) May Be a Significant Label Extension Opportunity for Ravicti

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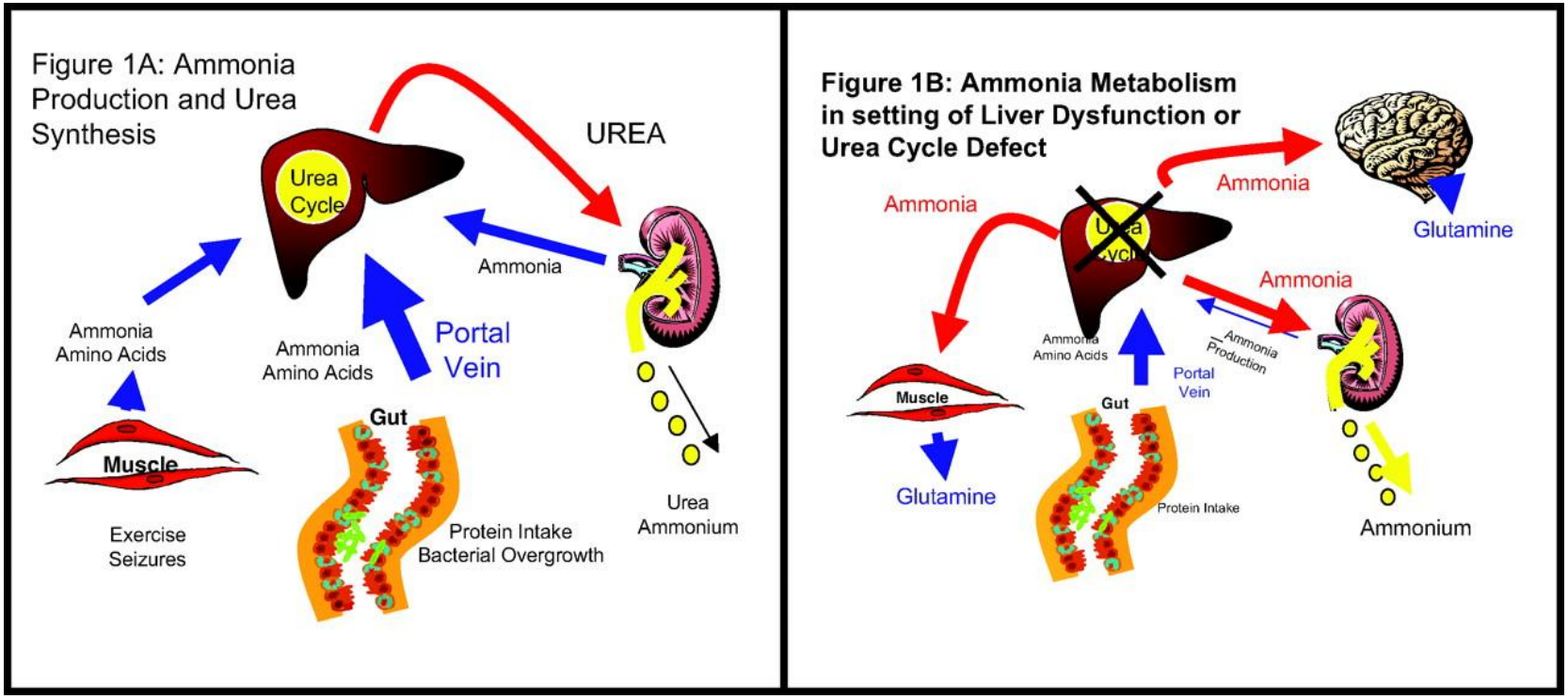
- HE is a serious but potentially reversible neurological disorder that can occur in patients with cirrhosis or acute liver failure.
- HE is believed to occur when the brain is exposed to gut-derived toxins including ammonia that are normally removed from the blood by a healthy liver.
- The spectrum of symptoms that constitute HE is very similar to that for UCD, including neuropsychiatric abnormalities and motor disturbances that are associated with varying degrees of disability ranging from subtle to lethal.
- Similar to UCD patients who may experience HA crises, patients with episodic HE often experience periods when their symptoms worsen. HE events are manifested by symptoms ranging from disorientation to coma, and frequently require hospitalization.
- HPTX's HE development program is targeting patients with episodic HE who have experienced past HE events and is designed to determine whether treatment with Ravicti will reduce the number of HE events.
- There are approximately 1 million patients in the US with cirrhosis, of whom an estimated 140,000 have clinically recognizable episodic HE.

Hepatic Encephalopathy Has a Similar Disease Mechanism as UCD

- Hepatic encephalopathy (HE) is a brain disorder that is caused by liver damage (hepatic cirrhosis).
- Liver damage leads to accumulation of toxic substances including ammonia in the bloodstream that are normally removed by the liver.
- HE is thought to cause secondary (or acquired) hyperammonemia, vs. UCD, which causes primary (or inherited) hyperammonemia.



Source: Google Images

HE Prevalence Is Significantly Higher Than UCD

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- Published epidemiological data suggest that there are approximately one million patients in the US with cirrhosis.
- Episodic overt HE, which is a complication of cirrhosis is clinically recognizable in 140,000 patients can occur without warning, render the patient incapable of self-care, and frequently result in hospitalization.
- In 2003, more than 40,000 patients were hospitalized with HE -- a number that increased to over 50,000 in 2004.
- HE is a neuropsychiatric syndrome for which symptoms, manifested on a continuum, are deterioration in mental status, with psychomotor dysfunction, impaired memory, increased reaction time, sensory abnormalities, poor concentration, disorientation, and -- in severe forms – coma.
- HE is diagnosed based on the presence of compatible signs and symptoms in a patient with cirrhosis in whom other causes of brain dysfunction have been excluded.
- Physicians focus on two concurrent types of symptoms: impaired mental status, as defined by the Conn score (also called West Haven criteria) (on a scale from 0 to 4, with higher scores indicating more severe impairment), and impaired neuromotor function.
- Stable patients with Grade 1 or 2 HE are typically ambulatory and can usually be managed as outpatients. By contrast, Grade 3 and 4 patients are hospitalized and often require intensive support.

HE Disease Can Be Triggered by Precipitating Factors

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- Patients with HE are subject to episodes of worsened encephalopathy (HE crisis).
- Common precipitating factors are:
  - Renal failure: Renal failure leads to decreased clearance of urea, ammonia, and other nitrogenous compounds.
  - Gastrointestinal bleeding: The presence of blood in the upper gastrointestinal tract results in increased ammonia and nitrogen absorption from the gut. Bleeding may predispose to kidney hypoperfusion and impaired renal function. Blood transfusions may result in mild hemolysis, with resulting elevated blood ammonia levels.
  - Infection: Infection may predispose to impaired renal function and to increased tissue catabolism, both of which increase blood ammonia levels.
  - Constipation: Constipation increases intestinal production and absorption of ammonia.
  - Medications: Drugs that act upon the central nervous system, such as opiates, benzodiazepines, antidepressants, and antipsychotic agents, may worsen hepatic encephalopathy.
  - Diuretic therapy: Decreased serum potassium levels and alkalosis may facilitate the conversion of NH4+ to NH3. At the author's institution, diuretic-induced hypovolemia is the most common reason for patients with previously well-controlled hepatic encephalopathy to present to the emergency room with worsening mental function.
  - Dietary protein overload: This is an infrequent cause of hepatic encephalopathy.

Current Treatment of HE Has Limitations

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- Currently, treatment of HE is focused on controlling precipitating factors combined with decreasing the nitrogenous load from the gut, according to MEDACorp specialists.
- Suppressing the production of ammonia and other toxic substances in the intestine is most commonly done with the laxative lactulose or with non-absorbable antibiotics such as rifaxamin (Xifaxan, SLXP), but both agents have limitations.
- Abdominal cramping, diarrhea and flatulence are common side effects with lactulose, making the drug difficult for many patients to tolerate. Moreover, a published review of clinical trials involving lactulose and lactitol in the treatment of HE concluded that those agents failed to demonstrate a statistically significant benefit.
- Although Xifaxan represents the current standard of care, approximately 20% of patients experienced breakthrough HE events while taking rifaximin over a period of six months in a pivotal study. Based on KOL feedback, we believe Xifaxan is well tolerated, but patients face the risk of antibiotic colitis and believe the effects may be fairly short lived. This may be due to development of resistance to rifaxamin over time as the gut flora changes over time.
- Buphenyl is not an appropriate treatment for most HE patients given the FDA warning regarding the use of the drug in patients with sodium retention and edema, which is common for patients with HE.
- The treatment of any underlying liver condition may improve the symptoms, in severe cases, such as acute liver failure, the onset of HE may indicate the need for a liver transplant.

Xifaxan (Rifaximin) Represents the Current Standard of Care for HE

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- Xifaxan (rifaximin) 550 mg marketed by Salix is an antibiotic that was FDA approved in March 2010 to reduce the risk of overt hepatic encephalopathy (HE) recurrence in adults.
- Xifaxan 550 mg has been shown to work in overt HE by altering bacteria in the intestines, which produce ammonia. As these bacteria decrease, fewer and fewer toxins are able to pass through the body and this reduces the risk of HE flare-ups.
- The efficacy of Xifaxan 550 mg taken orally two times a day was evaluated in a 6-month trial of adult subjects who were defined as being in remission from HE. Eligible subjects had ≥ 2 episodes of HE associated with chronic liver disease in the previous 6 months.
- Breakthrough overt HE episodes were experienced by 31 of 140 subjects (22%) in the Xifaxan group and by 73 of 159 subjects (46%) in the placebo group during the 6-month treatment period. Comparison of Kaplan-Meier estimates of event-free curves showed Xifaxan significantly reduced the risk of HE breakthrough by 58% during the 6-month treatment period.
- HE-related hospitalizations (hospitalizations directly resulting from HE, or hospitalizations complicated by HE) were reported for 19 of 140 subjects (14%) and 36 of 159 subjects (23%) in the Xifaxan and placebo groups respectively. Comparison of Kaplan-Meier estimates of event-free curves showed Xifaxan significantly reduced the risk of HE-related hospitalizations by 50% during the 6-month treatment period.

Ravicti Therapy for HE Would Represent a New Mode of Action

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- In contrast to available agents that block nitrogen absorption in the gut, 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 indicates that Ravicti may have superior efficacy compared to Xifaxan when compared to placebo/lactulose and may improve Xifaxan efficacy when given in combination.

Positive Phase IIb Data Suggests Ravicti May Have Superior Efficacy Compared to Xifaxan

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- The Phase II trial in 178 patients met its primary endpoint: the proportion of patients experiencing at least one HE event was significantly lower on Ravicti versus placebo (21.1% vs. 36.4%, p = 0.0214). HPTX conducted the 4-month, multi-center, randomized, double-blind trial of Ravicti vs. placebo in 178 patients with episodic HE. Patients enrolled in the trial were allowed to continue standard of care therapy (including lactulose and/or rifaximin).
- Patients receiving Ravicti also experienced fewer total HE events in the course of the study versus placebo (35 vs. 57; p = 0.0354) and fewer patients on Ravicti experienced one or more symptomatic days versus placebo (13 vs. 27; p = 0.0148).
- There were also trends favoring Ravicti in numbers of patients hospitalized for HE events, total HE-related hospitalizations and total hospital days for HE-related admissions, suggesting a potentially important pharmacoeconomic benefit to the treatment of HE with Ravicti.
- Among patients who received rifaximin at any time during the study (n=69), those receiving Ravicti as well experienced fewer total HE events, fewer patients hospitalized for HE events and fewer total HE hospitalizations, suggesting combination therapy may be beneficial.
- The population most similar to that enrolled in the rifaximin pivotal trial was the subgroup of patients on no therapy or lactulose only at study entry. In this population, Ravicti significantly reduced the proportion of patients experiencing at least one HE event versus placebo (10% vs. 32.2%; p = 0.0031) as well as the proportion of patients who experienced the more severe West Haven grade > 2 events versus placebo (5% vs. 25.4%; p = 0.0017), and the total number of HE events on study (7 vs. 31; p = 0.0002). Among these patients, this corresponds to an 82% reduction in the risk of experiencing a grade 2 HE event on Ravicti as compared with placebo.
- Detailed data will be presented at AASLD being held in Boston, Nov. 9-13, 2012.

Safety/Tolerability Profile in HE Looks Good

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- The rate of adverse events in the HE Phase II trial was similar on Ravicti versus placebo.
- There were three deaths in the study -- two on Ravicti and one on placebo -- all of which were judged by the clinical investigators to be unrelated to the study drug.
- There were 20 serious adverse events (SAEs) on Ravicti, of which one was deemed possibly related to Ravicti by blinded assessment at the time of the study, and 12 SAEs on placebo, of which four were deemed possibly related to the placebo by blinded assessment at the time of the study.
- The higher number of SAEs in the Ravicti group may reflect the greater number of Child-Pugh C patients (i.e., the most severely ill patients) randomized to Ravicti versus placebo (21 vs. 8).

HPTX Plans To Design a Pivotal Phase III HE Trial in 2013

LEERINK SWANN

- HPTX is currently conducting additional data analyses ahead of the end-of-Phase II FDA meeting in 4Q12 to discuss these findings and gain the agency's input on plans for a Phase III trial in HE.
- HPTX does not expect to conduct a head-to-head trial vs. Xifaxan since efficacy vs. placebo already looks significantly stronger based on Phase II data.
- In order to rapidly complete a Phase III trial, HPTX expects to enroll a similar, US-based patient population as in Phase II, including patients on Xifaxan.
- Phase III could be completed by 2015, with potential sNDA approval in 2016.

Ultra Orphan Drug Pricing Strategy

LEERINK SWANN

- HPTX expects to raise the price of Buphenyl after acquiring it from MRX to levels that more closely correspond to its ultra-orphan market opportunity. We model an average price of $250k/patient/year for the estimated 60% of UCD patients with commercial insurance. For the estimated 40% of UCD patients with government insurance (Medicare/Medicaid), we assume the average realized price will remain flat at $56k/patient/year since HPTX will have to rebate the excess.

- Management has retained experienced industry specialists from an early stage to support premium pricing, channel design, reimbursement strategy and communications. HPTX has set clear expectations with key stakeholders, such as the NUCDF patient advocacy group, that Ravicti will be a premium-priced product, given the significant R&D expenditure that has been required to bring it to market. HPTX is focused on building and communicating the value of new patient support programs, which have not existed for this community before and often drive success for orphan drugs.

- We see key differences from the situation with McKenna from KV Pharma, who was not prepared, executed poorly, and only positioned communications toward investors' point of view. We do not believe that KV Pharma emphasized the benefit of having access to a FDA-approved drug vs. a compounded one, and KV Pharma addressed a much larger patient population and could not justify its economic return since the company did not pay much for development.

Assume Lower Ravicti Price If Launched for HE Given Higher Prevalence

LEERINK SWANN

- If Ravicti is approved in HE, HPTX would take a price decrease vs. UCD given the significantly larger market size but still price at a premium over Xifaxan ($60k/year), which is currently on a $450MM sales run-rate of which 30-40% of sales are thought to be derived from HE.
- We believe HPTX could make a solid pharmacoeconomic case for payors considering the average cost of $37,000/per hospitalization for an HE crisis.
- Key opinion leaders (KOLs) we spoke to believe Xifaxan was received well in the market but there is room for further improvement and growth. We believe that, if Ravicti is approved in HE based on similar data as seen in Phase II, the drug would experience fast adoption, given potentially superior efficacy and tolerability.
- HPTX could monetize HE rights in Europe, given the lack of an established market, which would make commercialization there less straightforward.

Significant Market Opportunity for HPTX in UCD

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UCD Scenario 1: Ravicti approved	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Total US pts diagnosed	1,000	1,002	1,004	1,006	1,009	1,005	1,014	1,022	1,031	1,040	1,049	1,058	1,067
Total untreated pts	575	576	577	579	580	578	583	588	593	598	603	608	613
patients < age 6	161	161	162	162	162	162	163	165	166	167	169	170	172
patients age 6-17	184	184	185	185	186	185	187	188	190	191	193	195	196
adults	230	230	231	231	232	231	233	235	237	239	241	243	245
Total Buphenyl treated pts	425	426	427	428	429	427	431	435	438	442	446	450	453
patients < age 6	119	119	120	120	120	120	121	122	123	124	125	126	127
patients age 6-17	136	136	137	137	137	137	138	139	140	141	143	144	145
adults	170	170	171	171	171	171	172	174	175	177	178	180	181
Untreated pts on Ravicti	-	12	23	35	46	29	87	118	119	120	121	122	61
penetration, patients < age 6	0%	2%	4%	6%	8%	5%	15%	20%	20%	20%	20%	20%	10%
penetration, patients age 6-17	0%	2%	4%	6%	8%	5%	15%	20%	20%	20%	20%	20%	10%
penetration, adults	0%	2%	4%	6%	8%	5%	15%	20%	20%	20%	20%	20%	10%
Prior Buphenyl treated pts on Ravicti	-	85	107	150	171	128	323	435	438	442	446	450	227
penetration, patients < age 6	0%	20%	25%	35%	40%	30%	75%	100%	100%	100%	100%	100%	50%
penetration, patients age 6-17	0%	20%	25%	35%	40%	30%	75%	100%	100%	100%	100%	100%	50%
penetration, adults	0%	20%	25%	35%	40%	30%	75%	100%	100%	100%	100%	100%	50%
Total Ravicti pts	-	97	130	184	218	157	411	552	557	562	566	571	288
Avg cost/pt($mm)	-	0.063	0.063	0.063	0.063	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250
Ravicti US sales in UCD ($MM)	**-**	**6**	**8**	**12**	**14**	**39**	**103**	**138**	**139**	**140**	**142**	**143**	**72**

Buphenyl Model Private Payors	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Patients on Buphenyl	425	341	320	278	257	299	108	-	-	-	-	-	227
Branded Buphenyl market private payor	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*10%*	*0%*	*0%*	*0%*
Avg cost/pt	0.056	0.063	0.063	0.063	0.063	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250
Buphenyl US sales in UCD ($MM)	**10**	**9**	**8**	**7**	**6**	**30**	**11**	**-**	**-**	**-**	**-**	**-**	**-**

Buphenyl Model Medicare/Medicaid	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Patients on Buphenyl	425	341	320	278	257	299	108	-	-	-	-	-	227
Branded Buphenyl market public payor	*60%*	*60%*	*60%*	*60%*	*60%*	*60%*	*60%*	*60%*	*60%*	*10%*	*0%*	*0%*	*0%*
Avg cost/pt	0.056	0.014	0.014	0.014	0.014	0.056	0.056	0.056	0.056	0.056	0.056	0.056	0.056
Buphenyl US sales in UCD ($MM)	**14**	**3**	**3**	**2**	**2**	**10**	**4**	**-**	**-**	**-**	**-**	**-**	**-**

Total Buphenyl US sales ($MM)	**24**	**11**	**11**	**9**	**9**	**40**	**14**	**-**	**-**	**-**	**-**	**-**	**-**

Ammunol US sales ($MM)	**9**	**2**	**2**	**2**	**2**	**9**	**9**	**9**	**9**	**-**	**-**	**-**	**-**

Total sales Ravicti + Buphenyl	**33**	**20**	**21**	**23**	**24**	**88**	**126**	**147**	**148**	**140**	**142**	**143**	**72**

Source: SEC filings and Leerink Swann Estimates

Ucyclyd Agreement Limits Downside If Ravicti Not Approved

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UCD Scenario 2: Ravicti not approved	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Total US pts diagnosed	1,000	1,002	1,004	1,006	1,009	1,005	1,014	1,022	1,031	1,040	1,049	1,058	1,067
Total untreated pts	575	576	577	579	580	578	583	588	593	598	603	608	613
patients < age 6	161	161	162	162	162	162	163	165	166	167	169	170	172
patients age 6-17	184	184	185	185	186	185	187	188	190	191	193	195	196
adults	230	230	231	231	232	231	233	235	237	239	241	243	245
Total Buphenyl treated pts	425	426	427	428	429	427	431	435	438	442	446	450	453
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patients age 6-17	136	136	137	137	137	137	138	139	140	141	143	144	145
adults	170	170	171	171	171	171	172	174	175	177	178	180	181
Untreated pts on Ravicti	-	-	-	-	-	-	-	-	-	-	-	-	-
penetration, patients < age 6	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
penetration, patients age 6-17	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
penetration, adults	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Prior Buphenyl treated pts on Ravicti	-	-	-	-	-	-	-	-	-	-	-	-	-
penetration, patients < age 6	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
penetration, patients age 6-17	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
penetration, adults	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Total Ravicti pts	-	-	-	-	-	-	-	-	-	-	-	-	-
Avg cost/pt/year	-	0.063	0.063	0.063	0.063	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250
Ravicti US sales in UCD ($MM)	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**

Buphenyl Model Private Payors	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Patients on Buphenyl	425	426	427	428	429	427	431	435	438	442	446	450	453
Branded Buphenyl market private payor	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*10%*	*0%*	*0%*	*0%*
Avg cost/pt	0.056	0.021	0.021	0.021	0.021	0.085	0.127	0.191	0.286	0.429	0.429	0.429	0.429
Buphenyl US sales in UCD ($MM)	**10**	**4**	**4**	**4**	**4**	**14**	**22**	**33**	**50**	**19**	**-**	**-**	**-**

Buphenyl Model Medicare/Medicaid	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Patients on Buphenyl	425	426	427	428	429	427	431	435	438	442	446	450	453
Branded Buphenyl market public payor	*60%*	*60%*	*60%*	*60%*	*60%*	*60%*	*60%*	*60%*	*60%*	*10%*	*0%*	*0%*	*0%*
Avg cost/pt	0.056	0.014	0.014	0.014	0.014	0.056	0.056	0.056	0.056	0.056	0.056	0.056	0.056
Buphenyl US sales in UCD ($MM)	**14**	**4**	**4**	**4**	**4**	**14**	**15**	**15**	**15**	**2**	**-**	**-**	**-**

Total Buphenyl US sales ($MM)	**24**	**7**	**7**	**7**	**7**	**29**	**36**	**48**	**65**	**21**	**-**	**-**	**-**
Ammunol US sales ($MM)	**9**	**2**	**2**	**2**	**2**	**9**	**9**	**9**	**9**	**-**	**-**	**-**	**-**
Total sales	**33**	**9**	**9**	**9**	**10**	**38**	**45**	**57**	**74**	**21**	**-**	**-**	**-**

Source: SEC filings and Leerink Swann Estimates

Significant Upside on Successful Ravicti Label Extension in HE

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UCD Scenario 3: Ravicti approved in HE	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Total US UCD pts diagnosed	1,000	1,002	1,004	1,006	1,009	1,005	1,014	1,022	1,031	1,040	1,049	1,058	1,067
Total untreated pts	575	576	577	579	580	578	583	588	593	598	603	608	613
patients < age 6	161	161	162	162	162	162	163	165	166	167	169	170	172
patients age 6-17	184	184	185	185	186	185	187	188	190	191	193	195	196
adults	230	230	231	231	232	231	233	235	237	239	241	243	245
Total Buphenyl treated pts	425	426	427	428	429	427	431	435	438	442	446	450	453
patients < age 6	119	119	120	120	120	120	121	122	123	124	125	126	127
patients age 6-17	136	136	137	137	137	137	138	139	140	141	143	144	145
adults	170	170	171	171	171	171	172	174	175	177	178	180	181
Untreated pts on Ravicti	-	12	23	35	46	29	87	118	119	120	121	122	61
penetration, patients < age 6	0%	2%	4%	6%	8%	5%	15%	20%	20%	20%	20%	20%	10%
penetration, patients age 6-17	0%	2%	4%	6%	8%	5%	15%	20%	20%	20%	20%	20%	10%
penetration, adults	0%	2%	4%	6%	8%	5%	15%	20%	20%	20%	20%	20%	10%
Prior Buphenyl treated pts on Ravicti	-	85	107	150	171	128	323	435	438	442	446	450	227
penetration, patients < age 6	0%	20%	25%	35%	40%	30%	75%	100%	100%	100%	100%	100%	50%
penetration, patients age 6-17	0%	20%	25%	35%	40%	30%	75%	100%	100%	100%	100%	100%	50%
penetration, adults	0%	20%	25%	35%	40%	30%	75%	100%	100%	100%	100%	100%	50%
Total Ravicti pts	-	97	130	184	218	157	411	552	557	562	566	571	288
Avg cost/pt($mm)	-	0.063	0.063	0.063	0.063	0.250	0.250	0.250	0.070	0.070	0.070	0.070	0.070
Ravicti US sales in UCD ($MM)	**-**	**6**	**8**	**12**	**14**	**39**	**103**	**138**	**39**	**39**	**40**	**40**	**20**

Buphenyl Model Private Payors	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Patients on Buphenyl	425	341	320	278	257	299	108	-	-	-	-	-	227
Branded Buphenyl market private payor	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*40%*	*10%*	*0%*	*0%*	*0%*
Avg cost/pt	0.056	0.063	0.063	0.063	0.063	0.250	0.250	0.250	0.070	0.070	0.070	0.070	0.070
Buphenyl US sales in UCD ($MM)	**10**	**9**	**8**	**7**	**6**	**30**	**11**	**-**	**-**	**-**	**-**	**-**	**-**

Buphenyl Model Medicare/Medicaid	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Patients on Buphenyl	425	341	320	278	257	299	108	-	-	-	-	-	227
Branded Buphenyl market public payor	*60%*	*60%*	*60%*	*60%*	*60%*	*60%*	*60%*	*60%*	*60%*	*10%*	*0%*	*0%*	*0%*
Avg cost/pt	0.056	0.014	0.014	0.014	0.014	0.056	0.056	0.056	0.056	0.056	0.056	0.056	0.056
Buphenyl US sales in UCD ($MM)	**14**	**3**	**3**	**2**	**2**	**10**	**4**	**-**	**-**	**-**	**-**	**-**	**-**

Total Buphenyl US sales ($MM)	24	11	11	9	9	40	14	-	-	-	-	-	-

Ammunol US sales ($MM)	9	2	2	2	2	9	9	9	9	-	-	-	-

Ravicti for HE	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Total US HE pts diagnosed	140,000	140,297	140,594	140,892	141,190	140,743	141,939	143,146	144,363	145,590	146,827	148,075	149,334
Total severe HE patients	28,000	28,059	28,119	28,178	28,238	28,149	28,388	28,629	28,873	29,118	29,365	29,615	29,867
% severe HE patients	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*
% Ravicti patients	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*5%*	*10%*	*15%*	*25%*	*6%*
Ravicti pts in HE	-	-	-	-	-	-	-	-	1,444	2,912	4,405	7,404	1,867
Avg cost/pt($mm)	-	-	-	-	-	-	-	-	0.070	0.070	0.070	0.070	0.070
Ravicti US sales in HE ($MM)	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**101**	**204**	**308**	**518**	**131**

Total sales Ravicti + Buphenyl	33	20	21	23	24	88	126	147	149	243	348	558	151

Source: SEC filings and Leerink Swann Estimates

HPTX P&L Model (Ravicti UCD Approval Scenario)

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HPTX P&L ($MM, except per share)	2010	2011	1Q12	2Q12E	3Q12E	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	3.0	3.5	4.0	19.4	5.0	5.0	5.0	5.0	20.0	25.2	29.4
SG&A	3.5	8.9	2.3	3.0	4.0	7.0	16.3	8.0	8.5	9.0	10.0	35.5	31.5	36.8
Operating expenses	26.6	26.2	11.2	6.0	7.5	11.0	35.7	16.0	16.7	17.5	18.7	68.7	75.6	88.2
Operating income	(26.6)	(26.2)	(11.2)	(6.0)	(7.5)	(11.0)	(35.7)	3.7	4.4	5.6	5.8	19.6	50.4	58.8
Interest income	0.0	0.0	0.0	0.0	0.1	0.1	0.2	0.0	0.0	0.0	0.0	0.1	0.9	1.4
Interest expense	(0.0)	(2.6)	(1.0)	(1.4)	(0.6)	(0.2)	(3.3)	(0.5)	(0.7)	(0.7)	(0.7)	(2.6)	(2.9)	(1.4)
Other income (expense)	1.1	(0.7)	0.4	-	-	-	0.4	(22.0)	-	-	-	(22.0)	-	-
EBT	(25.5)	(29.4)	(11.9)	(7.4)	(8.0)	(11.1)	(38.4)	(18.7)	3.7	4.9	5.1	(5.0)	48.4	58.7
Tax expense	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Net income (loss)	(25.5)	(29.4)	(11.9)	(7.4)	(8.0)	(11.1)	(38.4)	(18.7)	3.7	4.9	5.1	(5.0)	48.4	58.7
Diluted EPS	**(61.70)**	**(62.68)**	**(25.33)**	**(15.80)**	**(0.68)**	**(0.67)**	**(5.24)**	**(1.13)**	**0.22**	**0.30**	**0.31**	**(0.30)**	**2.90**	**3.50**
Basic shares outstanding	0.4	0.5	0.5	0.5	11.8	16.6	7.3	16.6	16.6	16.6	16.6	16.6	16.7	16.8
Dilutive securities					2.4	2.4		2.4	2.4	2.4	2.4	2.4	2.4	2.4
Diluted shares outstanding					14.2	19.0		19.0	19.0	19.0	19.0	19.0	19.1	19.2

Source: SEC filings and Leerink Swann Estimates

HPTX Balance Sheet and Cash Flow Model (Ravicti UCD Approval Scenario)

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HPTX BS	2010	2011	1Q12	2Q12E	3Q12E	4Q12E	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E
Cash	**6.6**	**7.0**	**3.7**	**6.6**	**52.5**	**41.9**	**41.9**	**46.2**	**51.0**	**57.1**	**63.4**	**63.4**	**116.3**	**158.4**
Debt	**-**	**23.4**	**30.7**	**40.7**	**10.0**	**10.0**	**10.0**	**32.0**	**32.0**	**32.0**	**32.0**	**32.0**	**32.0**	**-**
Convertible notes	-	23.4	30.7	30.7	-	-	-	-	-	-	-	-	-	-
Venture debt	-	-	-	10.0	10.0	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	2Q12E	3Q12E	4Q12E	2012E	1Q13E	2Q13E	3Q13E	4Q13E	2013E	2014E	2015E
Change in cash	**(3.5)**	**0.4**	**(3.3)**	**2.9**	**45.9**	**(10.6)**	**34.9**	**4.3**	**4.8**	**6.0**	**6.3**	**21.4**	**53.0**	**42.0**
Cash from operations	**(25.9)**	**(24.5)**	**(10.7)**	**(7.1)**	**(7.6)**	**(10.6)**	**(36.0)**	**(17.7)**	**4.8**	**6.0**	**6.3**	**(0.6)**	**53.0**	**64.0**
Net Income	(25.5)	(29.4)	(11.9)	(7.4)	(8.0)	(11.1)	(38.4)	(18.7)	3.7	4.9	5.1	(5.0)	48.4	58.7
SOE	0.2	0.3	0.1	0.3	0.4	0.6	1.3	1.0	1.1	1.1	1.2	4.4	4.5	5.3
Other	(0.6)	4.5	1.1	-	-	-	1.1	-	-	-	-	-	-	-
Cash from investing	**(0.0)**	**(0.0)**	**(0.1)**	**-**	**-**	**-**	**(0.1)**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
Option to purchase Buphenyl	-	-	(0.3)	-	-	-	(0.3)	-	-	-	-	-	-	-
Other	(0.0)	(0.0)	0.2	-	-	-	0.2	-	-	-	-	-	-	-
Cash from financing	**22.4**	**25.0**	**7.6**	**10.0**	**53.5**	**-**	**71.0**	**22.0**	**-**	**-**	**-**	**22.0**	**-**	**(22.0)**
Issuance (buyback) shares	22.5	-	(0.0)	-	53.5	-	53.4	-	-	-	-	-	-	-
Issuance (repay) debt	-	25.0	7.5	10.0	-	-	17.5	22.0	-	-	-	22.0	-	(22.0)
Other	(0.0)	-	0.1	-	-	-	0.1	-	-	-	-	-	-	-

Source: SEC filings and Leerink Swann Estimates

Valuation: HPTX Blended Probability-Weighted DCF

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HPTX DCF (Scenario 1)	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	TV
FCF	(36)	(1)	54	65	46	44	45	46	24	2	
Discount periods	-	0.5	1.5	2.5	3.5	4.5	5.5	6.5	7.5	8.5	
NPV	(18)	(1)	54	65	46	44	45	46	24	2	14
Valuation	323										

Discount Rate	12%
Terminal Growth	5%

Valuation		Valuation	Probability	P/W
Scenario 1, Ravicti approved for UCD	1	323	50%	**161**
Scenario 2, Ravicti NOT approved	2	73	30%	**22**
Scenario 3, Ravicti approved for UCD and HE	3	611	20%	**122**
Blended Valuation				**305**
Net cash				42.5
Diluted Shares Outstanding				19.5
Per share valuation				**$ 18**

Source: SEC filings and Leerink Swann Estimates

- We arrive at a valuation of ~$18 per share through blended probability-weighted discounted cash flow (DCF) analysis.
- We assume a 12% discount rate and 5% terminal growth rate.
- We assume generic competition after Ravicti orphan drug exclusivity for treating UCD has expired in early 2020.

Risks to Valuation

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- 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.

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.

Distribution of Ratings/Investment Banking Services (IB) as of 06/30/12				
			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OP]	92	57.1	23	25.0
HOLD [MP]	69	42.9	4	5.8
SELL [UP]	0	0.0	0	0.0

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.

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