Conatus Pharmaceuticals Inc. (CNAT)

Initiating Coverage of Conatus Pharmaceuticals at Market Outperform; Intervening in Liver Disease

MARKET DATA

Price	$9.29
52-Week Range:	$8.26 - $11.24
Shares Out. (M):	16.0
Market Cap ($M):	$148.6
Average Daily Vol. (000):	23.0
Cash (M):	$74
LT Debt (M):	$1

Source: Thomson Reuters and JMP Securities LLC

FY DEC		2012A	2013E	2014E
Revenue ($M)	1Q	$0.5	$2.7A	--
	2Q	$1.3	$2.2	--
	3Q	$2.5	$1.8	--
	4Q	$3.2	$1.8	--
	FY	**$7.6**	**$8.5**	**$13.4**
EPS	1Q	($0.54)	($0.30)A	--
	2Q	($0.46)	($0.19)	--
	3Q	($0.35)	($0.36)	--
	4Q	($0.30)	($0.46)	--
	FY	**($1.64)**	**($1.30)**	**($1.55)**
	P/E	NM	NM	NM

Source: Company reports and JMP Securities LLC

STOCK PRICE PERFORMANCE

MARKET OUTPERFORM | Price: $9.29 | Target Price: $14.00

INVESTMENT HIGHLIGHTS

Intervening in liver disease; initiating coverage of Conatus Pharmaceuticals with a Market Outperform rating and $14 price target. Conatus is about to initiate a three-pronged clinical program in serious liver conditions with limited treatment options for its novel oral pan-caspase inhibitor, emricasan. Emricasan was originally developed by Idun and purchased by Pfizer in 2005. After discontinuing development due to pre-clinical carcinogenic indications in 2007, Conatus, formed by several members of Idun, acquired the asset from Pfizer in 2010 and in 2013 obtained FDA clearance to re-initiate clinical development. Our analysis of the existing data suggests emricasan is active and supports the rationale for moving into proof of concept studies, which we believe will shore up the compound's clinical benefit. Conatus has $74M in cash following a recent successful IPO and we believe shares contain significant value. We believe Conatus could generate significant value for shareholders if emricasan can safely deliver improvements in morbidity and mortality in trials that should read out in the 2015-2017 timeframe. In the meantime, we see modest upside in shares with a positive Phase 2b study next year, which we believe should confirm the dramatic reductions in liver enzymes observed in earlier studies. Our $14 price target is based on a risk-adjusted, discounted cash flow analysis.

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INVESTMENT THESIS

Conatus is developing a novel oral pan-caspase inhibitor, emricasan, for the treatment of serious liver diseases. Caspases play an important role in the regulation of apoptosis (programmed cell death) and inflammation, both central to the pathology underlying liver fibrosis. Emricasan was originally developed by Idun and purchased by Pfizer. Following suspension of development due to pre-clinical carcinogenic indications in 2007, Conatus, founded by several of members of the Idun leadership team, purchased the asset in 2010. In 2013, on the basis of a mouse carcinogenicity study conducted by Conatus, the FDA lifted the clinical hold, freeing the company to resume development. Our analysis of data in humans suggests a low probability of cancer risk for short-term acute therapy, but safety has not yet been evaluated for long-term chronic therapy.

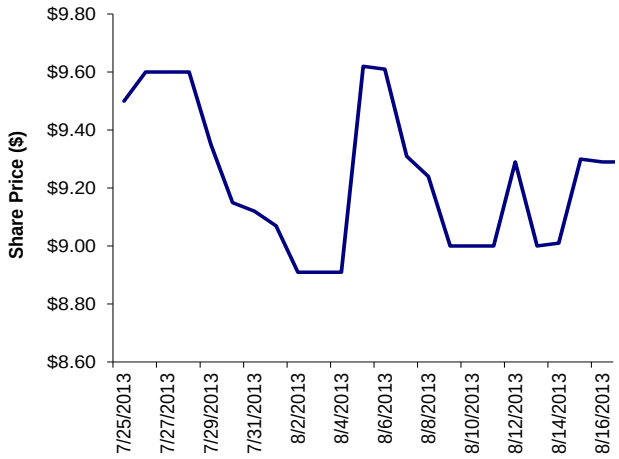
Conatus is currently preparing to initiate a series of proof of concept studies in three liver diseases characterized by fibrosis for which there are limited treatment options: acute-on-chronic liver failure (ACLF), chronic liver failure (CLF), and HCV post-orthotopic liver transplant (HCV-POLT). Our analysis of the existing data suggests the drug is active, in that it appears to induce a significant reduction in biomarkers indicative of liver damage. In our opinion, this supports the rationale for moving into proof of concept studies. It is unknown whether or not the biomarker changes reflect a change in the disease progression in these patients and forthcoming studies will address this head on by quantitating improvements in liver fibrosis, organ failure, transplant, or death. Following the IPO, we believe shares of Conatus reflect the leap affiliated with achieving the clinical hurdle described above and could generate significant value for shareholders if the studies read out positive in 2015, 2016, and 2017. In the meantime, we see modest upside in shares with positive Phase 2b study in ACLF next year, which we believe should confirm the dramatic reductions in liver enzyme observed in earlier studies.

FIGURE 1. Important Catalysts

Timing	Catalysts	Program	Importance
2H13	Initiate ACLF Phase 2b study	ACLF	low
2H13	Initiate HCV-POLT study	HCV-POLT	low
2014	Phase 2b ACLF data	ACLF	Medium
2014	Initiate CLF study	CLF	low
2015	CLF data	CLF	High
2016	ACLF data	ACLF	High
2017	HCV-POLT data	HCV-POLT	High

Source: Company reports and JMP Securities LLC

FIGURE 2. CNAT Price Chart



Source: Thompson Reuters and JMP Securities LLC

VALUATION

Our $14 price target is based on a risk-adjusted, discounted cash flow analysis (Figure 4). We assign a 12.5% discount rate based on CAPM and use a terminal growth rate of 0%, given our assumption that peak sales are achievable within five years of launch and the fact that patents expire in 2028.

Central to our valuation is our patient-based revenue model and assessment of clinical risk. Below, we summarize our assessment for each of the three target indications.

ACLF

Of the three indications that Conatus plans to pursue, ACLF is the largest with 150,000 patients in the U.S. and EU combined. Given our expectation that new HCV regimens introduced next year will cure the vast majority of patients, we anticipate a reduction in the size of the ACLF patient population, partially offset by an increase in other factors contributing to ACLF, including an aging population (alcoholic cirrhosis) and obesity (NASH). Despite this market contraction, the ACLF indication drives almost 80% of revenue in our model and is therefore the most important indication for the program, at least commercially.

The greatest swing factors in our model are the price and duration of therapy, both of which are unknown today. Benchmarking price against drugs used to treat similarly serious and deadly conditions, we assume a price of $8,000 per month which will ultimately be determined by the relative efficacy of the drug. Based on the acute nature of this indication, we assume three months of therapy. Given the dearth of available therapies and relatively concentrated hepatology community, we believe emricasan will be rapidly and widely adopted and we currently assign peak penetration of 50% three years post launch. As such, our peak sales estimate for emricasan in ALCF is $389M and $363M in 2024 in the U.S. and EU, respectively.

We see two primary risks to the ALCF development program: 1) will the biomarker efficacy data demonstrated in mostly HCV patients translate to the ALCF population and 2) will the data reflect a change in disease progression. We view the first as relatively low risk as our analyses of the data suggest the biomarker data should be translatable. The second is higher risk and applicable to the entire emricasan development program given and there are no other drugs we can point to that made this leap thus far. Weighing these factors, we currently assign a 25% probability of success to development of emricasan in ACLF. We expect Phase 2b data evaluating biomarkers in 2014 and Phase 3 data evaluating disease progression in 2016.

CLF

CLF is a more gradual course of decline than ACLF but the diseases are closely related. CLF is a more limited population encompassing about 5% of patients with liver failure, or about 4,700 and 6,500 patients in the U.S. and EU respectively. There are no disease-modifying agents for the treatment of CLF, so if emricasan can prolong mortality, we think the drug will be widely used. Assuming 50% penetration, three months of therapy, and pricing similar to ALCF, we arrive at peak penetration two years after launch in the U.S. (five in the EU) with sales of $32M in the U.S and $30M in the EU in 2024, contributing 7% to the emricasan franchise. We view the characteristics of ACLF and CLF as similar and thus we similarly assign 25% probability of success to the CLF indication. We expect data in 2015.

HCV-POLT

There are currently 15,000 liver transplants annually between the U.S. and E.U., half of which are the result of chronic HCV infection. In almost all of these cases, reinfection of the new liver with HCV occurs, creating a need for anti-fibrotic therapy in this population. In contrast to ACLF and CLF where there is no competition, in HCV-POLT, we anticipate the arrival of significant competition in 2014 HCV-POLT from new all-oral HCV regimens which promise to deliver high cure rates of greater than 90%. While the cure rate in the post-transplant setting is unknown at this time, we model 50%, which will shrink the available pool of patients for emricasan. For that reason, we limit our penetration to 50% post-transplant patients who fail to achieve cure. Assuming pricing of $8,000 per month, used chronically for 12 months in this indication, we arrive of peak sales of $67M and $68M in 2024 in the U.S. and EU, respectively.

We view the HCV-POLT development program as the riskiest of the three targeted indications. We specifically point to the ubiquitous use of immunosuppressive therapy in this setting as creating an environment ripe for cancer development, a potential on target toxicity of emricasan, which is compounded by the need for chronic emricasan therapy. That being said, we think the risk-benefit equation for this population may be more tolerant to safety risk. While emricasan has been safe and well tolerated in twelve week studies, we do not yet know what the longer term dosing will reveal. That being said, should emricasan prove to be safe and efficacious in this at-risk patient population, we believe any concerns over increased cancer risk will be quashed.

Beyond safety, there are other risks to this study as well, including a potential for a high dropout rate, at least in the U.S. sites as new HCV regimens are introduced and utilized, which will exclude them from the emricasan study. We believe the company is trying to mitigate this risk by enrolling in ex-U.S. sites where new HCV therapies will likely not be available for at least one year after the U.S. launch. We believe there is also efficacy risk, similar to that described in the ACLF and CLF programs, where the relationship between the observed impact on biomarkers and ultimate clinical benefit has yet to be described.

For these reasons, we assign a 10% chance of success to HCV-POLT program. We expect data in 2017. Unlike ACLF and CLF, the HCV-POLT program will focus on change in fibrosis as the primary efficacy endpoint. In our opinion, a positive outcome in the HCV-POLT indication could be a bridge to larger indications characterized by liver fibrosis including NASH, which would be significant upside to our model.

Following its recent initial public offering, we estimate Conatus has $74 million of in cash, which will be used to fund development of emricasan in all three indications. Based on our expense projections, most of which are R&D, we believe this cash is sufficient to support the company through registration. As the company approaches commercialization, its cash needs will increase and so we model additional capital raises in 2014, 2016, and 2017, acknowledging that the company may choose to partner, which could partially offset its longer term cash needs.

Separately, our comps analysis suggests that Conatus is undervalued compared to other companies also developing anti-fibrotic agents (Figure 3).

FIGURE 3. Comparable Companies Analysis

Ticker	Stock Price	Market Cap ($mil.)	EV ($mil)	Lead fibrosis indication	Indication	Stage of Dev.
ICPT	$44.25	$848.8	$744.8	OCA	PBC	Phase 3
ITMN	$14.34	$1,175.1	$1,050.5	pirfenidone	IPF	Approved EU Phase 3 US
RPTP	$11.40	$680.1	$655.4	Procysbi*	NASH	Phase 2
OCRX	$6.81	$76.9	$56.9	OCR-002	HE	Phase 2
			$626.89			
CNAT	$9.29	$144.7	$87.7	Emricasan	ACLF/CLF	Phase 2

** Procysbi approved for Cystinosis*

Source: Company reports and JMP Securities LLC

FIGURE 4. Discounted Cash Flow Analysis ($000's)

Discounted Cash Flow Valuation														
			2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Terminal
Revenues			0	0	0	0	942	33,491	177,219	374,268	530,740	652,698	652,698	817,902	
COGS			-	-	-	-	-	3,349	14,178	29,941	26,537	32,635	32,635	40,895	
R&D			4,700	20,000	40,000	50,000	40,000	25,000	20,000	20,000	20,000	20,000	20,000	20,000	
SG&A			6,800	6,936	7,075	12,000	20,000	26,000	33,800	43,940	57,122	71,403	71,403	78,543	
Operating Income (EBIT)			**(11,500)**	**(26,936)**	**(47,075)**	**(62,000)**	**(59,058)**	**(20,858)**	**109,242**	**280,387**	**427,081**	**528,661**	**528,661**	**678,464**	
Weighted Risk		**Prob of Success**	0%	0%	0%	0%	0%	25%	24%	23%	22%	22%	22%	22%	
	ACLF	25%	0%	0%	0%	0%	0%	19%	21%	21%	20%	20%	20%	20%	
	CLF	25%	0%	0%	0%	0%	0%	6%	3%	2%	2%	2%	2%	2%	
	HCVPOLT	10%	0%	0%	0%	0%	0%	0%	1%	1%	1%	1%	1%	1%	
Tax			0%	0%	0%	0%	0%	0%	5%	15%	30%	35%	35%	35%	
Risk adjusted Net Income			(11,500)	(26,936)	(47,075)	(62,000)	(59,058)	(5,214)	24,518	54,860	65,258	74,903	74,903	95,851	765,951
NPV			**$ 166,880**												
+ Current Cash & Equivalents			$ 73,759.4												
Value of the Company			**$240,639.1**												
- L-T Debt			$ 1,000												
Value of Equity			**$239,639.1**												
Value per Share			**$ 13.60**												

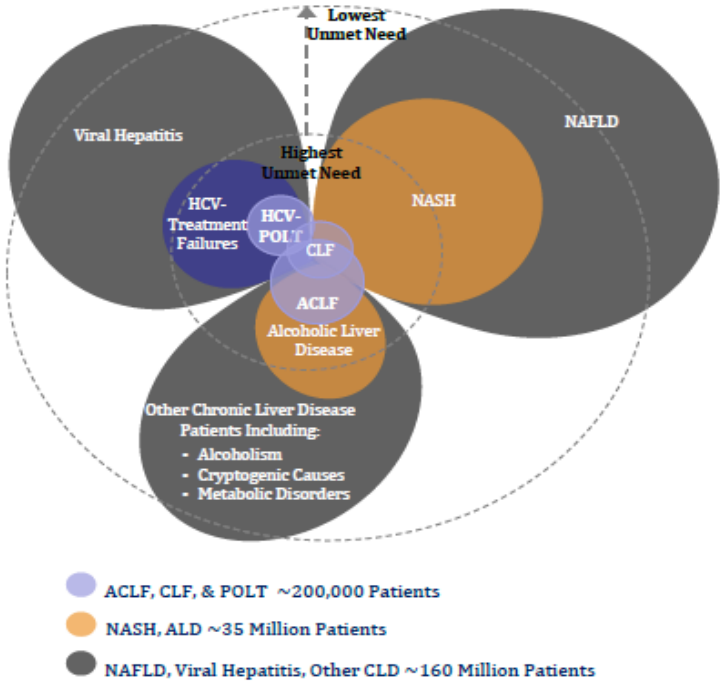
Source: JMP Securities LLC

LIVER FIBROSIS – HIGH MORTALITY AND POOR TREATMENT OPTIONS

Liver disease is among the 15 most common causes of death in the U.S. and EU and is a major burden on the healthcare system, representing in approximately $1.2 trillion in total annual healthcare costs in the U.S. Many of these patients suffer from liver fibrosis that occurs due to repeated liver injury. Many types of injury can result in fibrosis, but the most common causes include viral hepatitis, alcohol abuse, and non-alcoholic steatohepatitis (NASH). While common biological processes are involved in all cases of liver fibrosis, the diseases encompass several distinct patient populations, which differ in the underlying cause and stage of the disease (Figure 5).

Liver injury results in fibrosis, characterized by inflammation, remodeling of the extracellular matrix, and scarring of the liver, but symptoms in the early stages of the disease are relatively minor. Over time, continued damage can cause progression to cirrhosis, at which point liver function is significantly inhibited by scarring and tissue damage and increases the risk of hepatocellular carcinoma, portal hypertension, liver failure, multi-organ failure, and death. In some cases, progression can be halted by stopping the underlying pathology (i.e., HCV treatment, alcohol abstinence); however, there are no direct treatments to reverse the damage and once liver failure has set in, the only effective direct treatment is transplant which is supply limited to about 6,000 per year in U.S. Therefore, we believe there is strong rationale and large commercial opportunity for an effective anti-fibrotic drug.

FIGURE 5. Categories of Liver Fibrosis and Patient Size in U.S. and EU



Source: Company reports

Conatus is preparing to pursue development of emricasan in three specific liver diseases characterized by fibrosis: ACLF, CLF, and HCV-POLT. Below we review the characteristics of each.

Acute-on-chronic liver failure (ACLF)

ACLF is characterized by chronic cirrhosis catapulted into rapid liver failure by an acute event and is associated with high mortality. Current treatment of ACLF involves stabilization of the patient using a liver support device to temporarily replace liver function, followed by treatment with anti-inflammatory drugs and antibiotics to prevent additional complications and other organ support if additional organ failure occurs. With this intervention, only 60% of patients are stabilized, while 10% receive transplants, and 30% die as a direct result of liver failure. Even stabilization is only a temporary solution as 50% of stabilized patients will be re-hospitalized within 12 months. As such, there is a clear need for drugs that can maintain stable liver function in cirrhosis patients and reduce morbidity and demand for transplants. Key opinion leaders relay that there is a significant interest in a drug that can improve outcomes, even marginally.

Chronic liver failure (CLF)

CLF is similar to ACLF in that patients experience liver failure as a result of chronic cirrhosis; however, rather than being precipitated by an acute event, liver function slowly deteriorates over time. Treatment goals are similar to ACLF: reducing inflammation and infection while supporting liver and other organ function. Compared to ACLF, this patient population has a lower mortality rate of 25% over three months because of their more gradual decline. The unmet medical need is as critical given that no disease modifying treatment options exist. Most CLF patients are on a transplant list, although about 10% of the population is too sick to qualify.

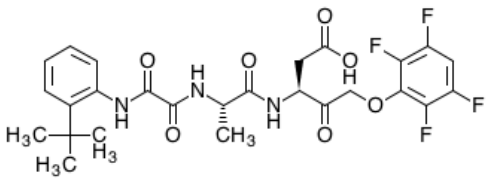
HCV-POLT

Approximately half of the 15,000 liver transplants in the U.S. and EU are performed in patients with HCV. Unfortunately, the livers of nearly all of these patients are re-infected after transplantation where viral loads can reach pre-transplant levels within four days. As a result, 60% percent of these patients will have graft fibrosis within two years and 20% will progress to cirrhosis within five years, despite treatment with anti-inflammatory drugs and use of currently available HCV regimens. 30-40% of patients are treated with interferon/ribavirin, limited by low efficacy (cure rate of 25-45% in this population) and poor tolerability. Newer agents, telaprevir and boceprevir, have been used in pilot studies in this population, but are limited by drug-drug interactions between the protease inhibitors and drugs used for transplantation. In our view, the introduction of more tolerable and efficacious all oral HCV therapies could drive cure rate beyond 90% in HCV patients, reducing the pool of patients requiring liver transplant and improving treatment options for curing HCV in the post-transplant setting. We expect a lower HCV cure rate in the HCV-POLT population; therefore, there will still be a need for anti-fibrosis to treat patients who fail to be cured.

EMRICASAN

Emricasan is an orally active pan-caspase inhibitor (Figure 6), which irreversibly binds caspases 1-10 (Figure 7). Caspases are enzymes that regulate the function of proteins expressed in most cells that play a central role in apoptosis (programmed cell death) and inflammation signaling. Although emricasan has a short half-life in the serum (about two hours), irreversible binding of emricasan to the active site of caspases shuts down apoptotic caspases for about 8-10 hours, the time it takes for apoptotic caspase turnover. Inflammatory caspases are more temporal and turn over in less than one hour, making the half-life of emricasan more relevant for fibrosis. Since emricasan is not metabolized by CYP enzymes and is excreted through the bile as an intact molecule, it can be reabsorbed, leading to a longer pharmacodynamic effect than would be assumed by half-life alone. We also note that animal studies demonstrate that the compound concentrates in the liver, kidney, and pancreas. Emricasan is peptide based and broken down through hydrolysis and not in the liver, which we believe is appropriate in the target populations who are likely compromised.

FIGURE 6. Emricasan



Source: Company reports

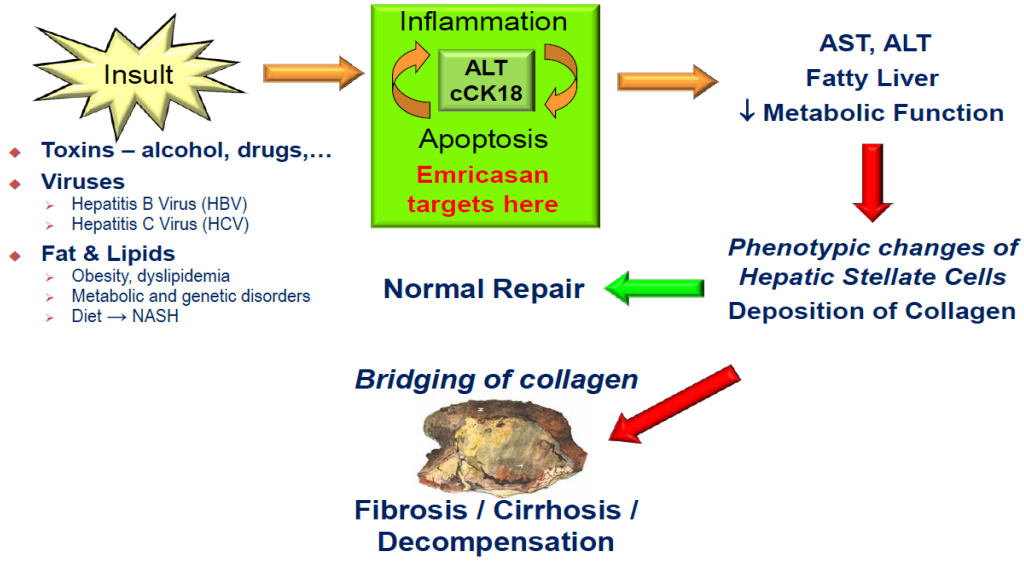
FIGURE 7. Emricasan Inhibition of Caspases

Caspase	IC_{50}(nM)*	Activation mechanism	Functions
Initiators:			
Capase-2	20.0	ER stress	Activate executioner caspases
Caspase-8	0.2	Receptor mediated	Death receptor signaling, cell proliferation and non-enzymatic functions
Caspase-10	1.4	Receptor mediated	Death receptor signaling
Caspase-9	0.3	Cytochrome c / apoptosome	Caspase 3/7 activation – post-mitochondrial stress
Executioners:			
Caspase-3	2.0	Caspase-8 and 9	Cleavage of cellular substrates
Caspase-6	4.0	Caspase-3 and 7	Cleavage of cellular substrates
Caspase-7	0.2	Caspase-8 and 9	Cleavage of cellular substrates
Cytokine Activators:			
Caspase-1	0.4	Inflammasome complex	IL-1β and IL-18 maturation
Caspase-4	0.06	Inflammasome complex	IL-1β and IL-18 maturation
Caspase-5	0.01	Inflammasome complex	IL-1β and IL-18 maturation
* k3/Ki ($M^{-1}s^{-1}$): 10^7 - 10^3			

Source: Company reports

Inhibition by emricasan can interfere with the processes of liver cell apoptosis and inflammation, two processes closely related to liver fibrosis. Inflammation and apoptosis create a positive feedback loop, driving disease progression (Figure 8). Thus, emricasan could have a role in reducing injury in liver fibrosis. In vitro, Emricasan appears to be selective for caspases with IC50 values > 100uM for other classes of enzymes such as kinases or receptors, which may limit the risk of off-target toxicities. However, we note that suppression of apoptosis may also have unwanted on-target, long-term side effects, including carcinogenesis and immune dysregulation.

FIGURE 8. Pathology of Liver Fibrosis



Source: Company reports

Emricasan development history

Emricasan was originally developed by Idun and purchased by Pfizer in 2005 for $350 million. Pfizer voluntarily discontinued development in 2007 following an observation of mixed inflammatory cell infiltrates in the liver and kidneys of emricasan treated mice, indicating potential carcinogenesis. These results were surprising, as no similar findings had been observed in rats and monkeys which suggested a potential species specific effect. In light of this observation, Pfizer chose to discontinue development. Conatus, formed in 2005 with many members of the leadership team at Idun, purchased the asset from Pfizer in 2010 for $250,000, a $1 million note, and $18 million in potential milestone payments associated with emricasan development. To further evaluate the mouse finding, Conatus tested emricasan in a carcinogenesis model using rasH2 transgenic mice, a recently validated murine model with high susceptibility to tumor formation requiring only six months of dosing. No increase of carcinogenesis was found, which compelled the FDA to remove the clinical hold in January 2013, clearing Conatus to proceed with studies in the U.S.

Conatus decided to proceed with the Pfizer Phase 3 development plan for HCV post-orthotopic liver transplant (HCV-POLT), adding two indications within liver fibrosis to the plan, namely ACLF and CLF. While our analysis of the Phase 2 clinical data supports the activity emricasan, we do not yet know if treatments with emricasan will improve morbidity and mortality. Conatus intends to address this question head on in its planned clinical studies.

CLINICAL DATA ANALYSIS

Biomarkers lowered by emricasan correlate with worse clinical outcomes

Emricasan has been evaluated in 432 patients with liver disease – mostly patients infected with HCV (Figure 9). Substantial changes in key biomarkers of liver cell damage were observed, confirming that the compound is active. Below we analyze the results in greater detail.

FIGURE 9. Completed Phase 2 Emricasan Trials

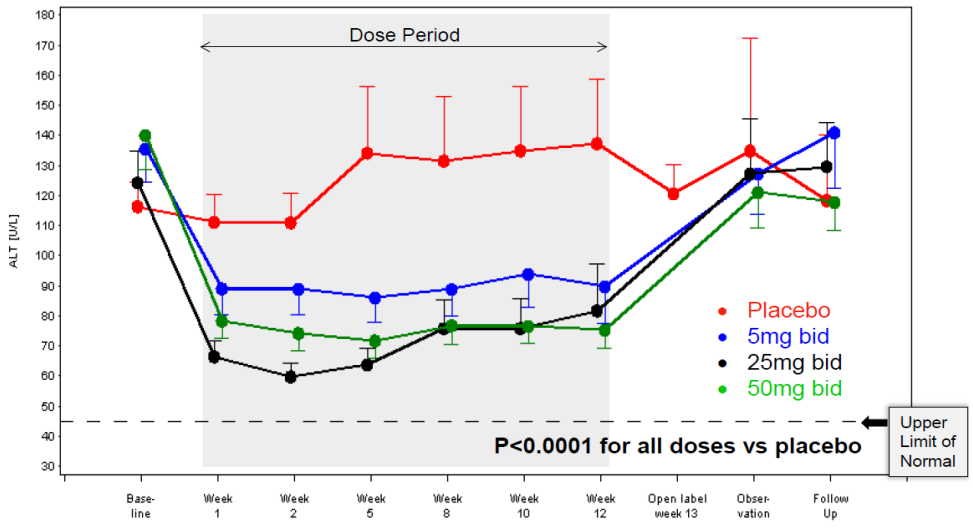
Subject	Numbers	Treatment Groups	Duration	Outcome
Liver disease (primarily chronic HCV)	105	Randomized, placebo-controlled, double blind, ascending dose trial	2 weeks	Well tolerated; improved liver function a measured by reduced ALT and other biomarkers
Chronic HCV	204	Randomized, placebo-controlled, double blind parallel group, multicenter dose response trial	12 weeks	Well tolerated; improved liver function as measured by reduced ALT, cCK18, and other biomarkers
Chronic HCV	24	Randomized, placebo-controlled, double blind, multicenter crossover dose response trial	2 weeks	Well tolerated; improved liver function at low dosing regime, as measured by reduced ALT and other biomarkers
Liver transplants	99	Randomized, placebo-controlled, double blind trial	1 day	Well tolerated; reduced post-transplant apoptosis as measured by ALT and other biomarkers

Source: clinicaltrials.gov and Company reports

Impact on key markers of cell damage - ALT and AST

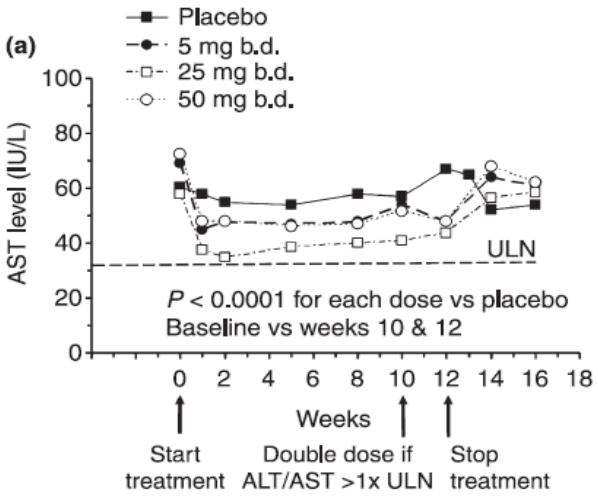
Alanine aminotransferase (ALT) is a liver enzyme and a clinically validated marker for liver disease progression and inflammation. Patients with liver disease have elevated plasma ALT over 100U/L (normal range: 30-50 U/L) due to release into the blood from damaged cells. Data from three Phase 2 studies in chronic HCV patients (who have failed previous treatment with interferon/ribavirin) have shown that treatment with emricasan is associated with a rapid reduction in ALT, dropping over 50% in some cases, with maximum inhibition reached by day 10. In our view, this rapid onset of activity could be important for future studies planned in acute indications like ACLF. Similar results were achieved with aspartate aminotransferase (AST), a closely related biomarker (Figure 10), although the change appears less striking, partially because baseline AST is generally lower than ALT (Figure 11).

FIGURE 10. Representative ALT Response with Emricasan Therapy



Source: Company reports

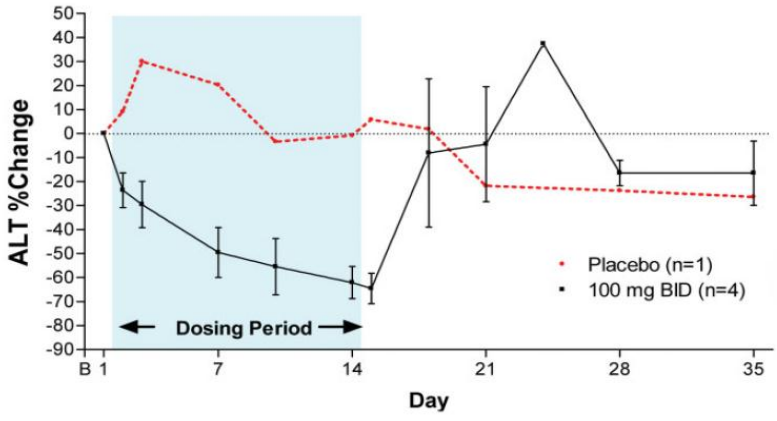
FIGURE 11. Emricasan Reduces AST Levels



Source: Aliment Pharmacol Ther, 2010

Importantly, similarly impressive reductions in ALT were observed in other diseases characterized by liver fibrosis. In one of the Phase 2 studies, patients with NASH (n=5), chronic hepatitis B (HBV) (n=13), and chronic cholestatic disorders (n=7) were included. Due to the small patient numbers, no formal statistical analysis was performed, nonetheless, we are pleased with the consistently high reduction in ALT reaching 59% and 47% in NASH and HBV, respectively, with baseline levels similar to the HCV populations (Figure 12), although we point out there was only one placebo patient in the NASH study, which weakens the argument somewhat. Furthermore, patients with chronic cholestatic disorder did not have a biomarker response to emricasan, although the numbers in the study were small, and fibrosis in these patients is mediated by bile ducts and therefore, may have less in common with the other indications. Taken together, we view these data as reasonably supportive of the activity of emricasan in liver fibrosis.

FIGURE 12. ALT Response in NASH Patients



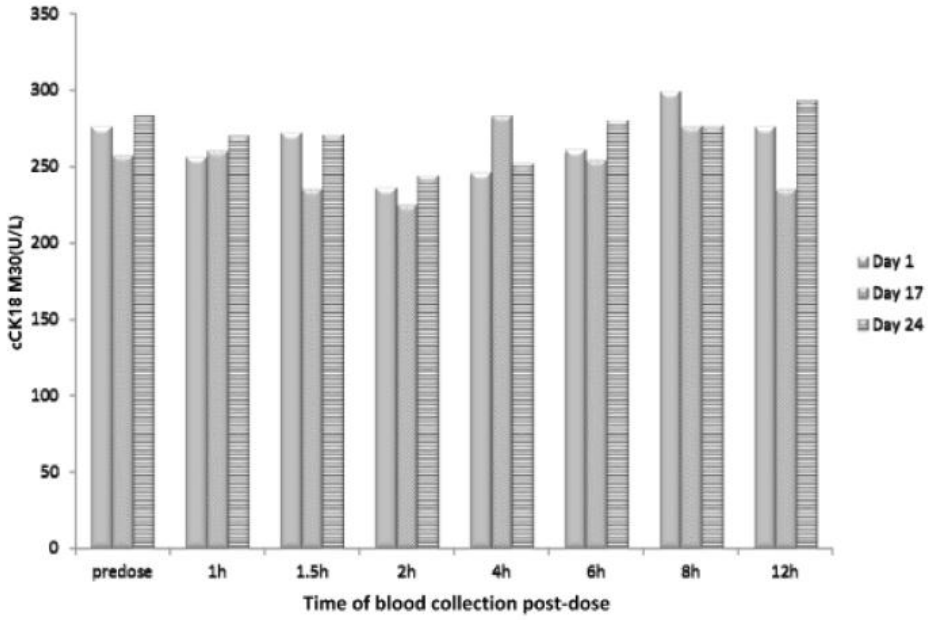
Source: Hepatology, 2007

Cytokeratin 18 (cCK18) – a marker of apoptotic activity

Cytokeratin 18 (cCK18) is an intracellular structural protein that is specifically cleaved by caspases, generating cCK18 that is released into the blood and is, therefore, a marker specific to caspases involved in apoptosis. Conatus management believes cCK18 is a relevant biomarker for the activity of emricasan; following our review of the evidence, we look to the next series of data to reach a similar level of conviction. In normal patients, cCK18 levels measured by Conatus (around 275 U/L) do not appear impacted by emricasan therapy, although we do not know the degree of viability amongst healthy individuals (Figure 13).

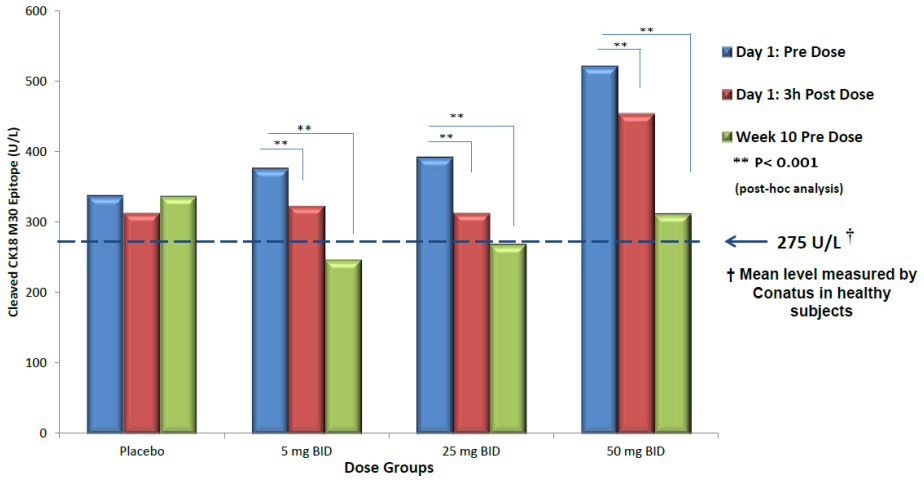
In HCV patients, cCK18 levels appear to be elevated by ~25% (Figure 14), though the baseline values vary amongst the groups, potentially indicating differences between the cohorts. We view this as a modest increase, particularly as we do not have a sense of natural variability. Upon emricasan treatment, cCK18 levels were reduced after ten weeks (Figure 14), although there appear to be variability at baseline amongst the groups and the lack of error bars make assessment difficult. We are encouraged that all drug cohorts appear to decrease cCK18 to normal levels without obliterating production, which could suggest that apoptosis can be restored to normal levels, but not de-regulated to an extent that would increase a risk of cancer, at least through 12 weeks of therapy.

FIGURE 13. cCK18 Levels in Healthy Individuals Through 24 Days of Dosing



Source: Company filings

FIGURE 14. Emricasan Reduces cCK18 Levels



Source: Company reports

Profile of emricasan appears safe and tolerable

Our analysis of the safety data from Phase 2 studies suggests that emricasan is well-tolerated and safe through 12 weeks of dosing. These studies include six Phase 1 trials with 191 patients (primarily healthy volunteers) and four randomized Phase 2 trials with 432 patients (primarily with HCV). Adverse events observed in studies to date were mostly mild or moderate in severity and were similar between the treatment and control groups (Figure 15). Across three Phase 2 studies, the most common adverse events include headache, fatigue, and nausea and we are encouraged that no dose response was observed. We believe these data support a tolerable profile for emricasan.

FIGURE 15. Representative Adverse Events

Double-blind treatment period	Placebo (n = 51)	5 mg b.d. (n = 55)	25 mg b.d. (n = 50)	50 mg b.d. (n = 48)
Adverse events	97	118	99	129
Patients with adverse events	30	42	31	36
Patients with adverse events occurring in >6 PF-03491390 recipients				
Headache	8	6	5	5
Fatigue	4	7	4	7
Nausea	2	6	1	6
Diarrhoea	6	2	2	4
Back pain	1	1	4	5
Upper respiratory tract infection	1	2	2	5
Insomnia	2	4	2	1

PF-03491390 = emricasan

Source: Aliment Pharmacol Ther, 2010

Adverse events of special interest include those expected based on the mechanism of emricasan such as increase in viral load resulting from reduced hepatocyte turnover and continued HCV replication in the increased number of viable hepatocytes. We are pleased that no viral susceptibility was observed in HCV or HBV patients. Another important safety issue is the potential for on-target carcinogenicity

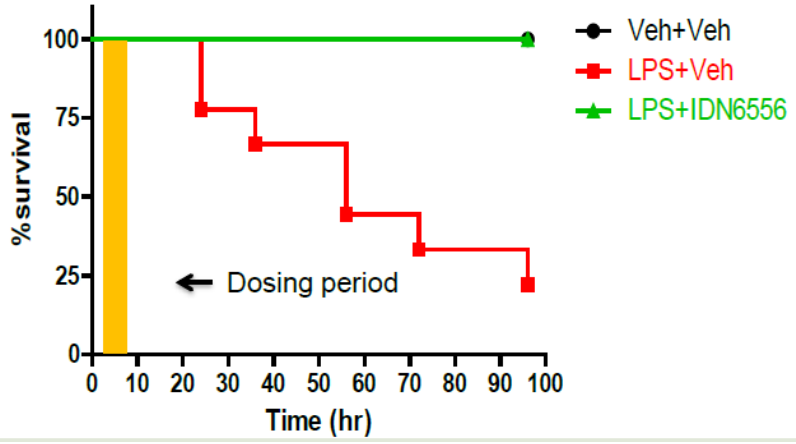
given emricasan inhibits apoptosis which could lead to deregulation of cell growth. We have some comfort with the profile of the drug after the FDA hold and subsequent release and no issues through 12 weeks of dosing. However, we cannot yet rule out the possibility of increased cancer risk with longer term treatment and longer term studies will be required to generate data to pursue chronic dosing. In our opinion, the existing data supports safety in high-mortality patient population, particularly in ACLF and CLF, where treatment duration is likely to be one to three months.

The Phase 1 studies also included a drug-drug interaction (DDI) study with ketoconazole (a CYP3A4 inhibitor) and cyclosporine (an immunosuppressant used to prevent transplant rejection). In our opinion, the ability to be dosed without interaction with other key drug classes is critical for emricasan as patients in the targeted indications will likely be receiving a host of other medications, including those that are metabolized via the CYP pathway.

Pre-clinical studies support potential for emricasan to modify disease progression

Animal models of liver fibrosis and liver injury support our thesis that emricasan is an active drug. In particular, we point to the rat study where liver failure was induced by lipopolysaccharide (LPS)-induced endotoxic shock (Figure X). Emricasan, administered by IV at 1, 4, and 7 hours after the administration of LPS reduced ALT and cCK18 levels and translated to lower mortality in the rat model (Figure 16). Taken together, we believe these pre-clinical data suggest a link between reduction of ALT and cCk18 levels and liver failure induced mortality, at least in rats, which supports our thesis that there could be a similar link in patients.

FIGURE 16. Emricasan Reduces Mortality from Liver Failure in Mice



Source: Company reports

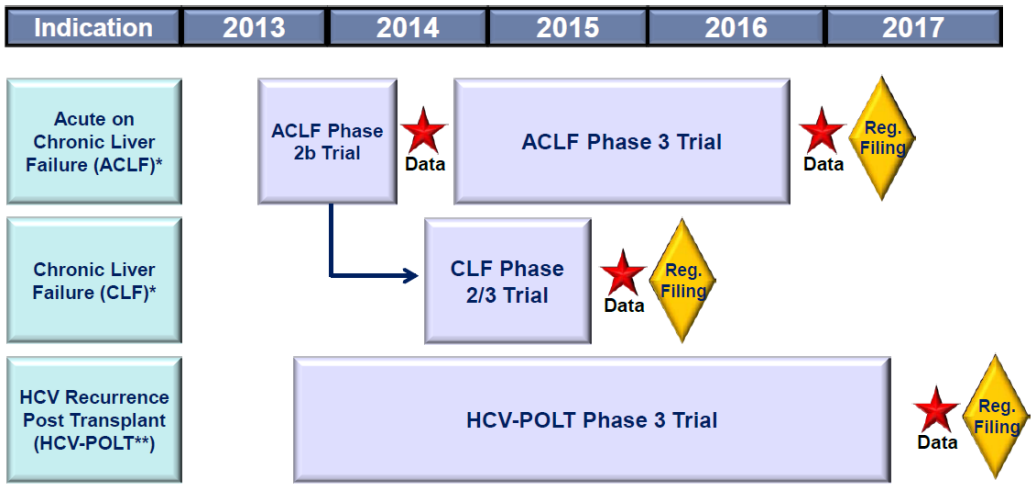
EMRICASAN CLINICAL DEVELOPMENT STRATEGY

Conatus is focusing its initial development efforts on ACLF, CLF, and HCV-POLT, and we anticipate the initiation of several Phase 2b and Phase 3 trials in all three areas over the next 12 months (Figure 17). In our view, the need for drug options for these indications opens up the possibility for Conatus to apply for breakthrough status and accelerated development/regulatory timelines.

Based on our analysis of data generated to date, we have modest expectations for the upcoming studies, mostly because while the relevant biomarkers point in the right direction, we have yet to know if these biomarker changes reflect a change in the underlying disease trajectory that can drive improvements in morbidity and mortality. Moreover, the biomarker analysis was conducted largely in HCV and NASH patients, a different population than the planned studies in CLF, ACLF, and HCV-POLT. While we are encouraged that substantial impact on biomarkers observed in two different drivers in liver fibrosis (virus and metabolic disorder) we note there was no impact in chronic cholestatic disorders. Therefore, we look to data from the forthcoming studies to discern the potential *clinical* impact of emricasan in the relevant patient populations.

In the Phase 2b ACLF study, three doses will be investigated: 5, 25, and 50 mg BID. These doses were chosen based on prior clinical studies in mostly HCV patients. A significant effect on ALT levels has been observed with as little as 5 mg BID. Doses above 50mg will not be tested in Phase 2b despite minimal adverse events, as little to no incremental benefit has been observed in past trials above 25 mg BID (as measured by ALT levels). The results of this study will guide dosing for both the Phase 3 ACLF and CLF trials. The HCV-POLT Phase 2b/3 study will use 25 mg BID dosing, again, as the highest dose that demonstrated an increased benefit in decreasing liver enzymes and biomarkers.

FIGURE 17. Clinical Strategy



*New indications based on extensive input from the hepatology community
** Pfizer Phase 3 indication

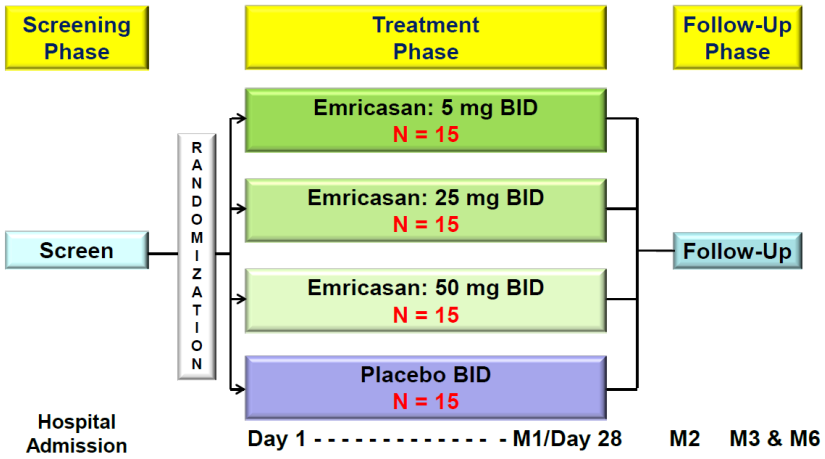
Source: Company reports

ALCF

Conatus intends to initiate a dose-ranging Phase 2b emricasan trial for ACLF in 2H13 (Figure 18) in the UK, as the IND for ACLF has not yet been submitted to FDA. Conatus has opened an IND for the HCV-POLT indication in the US based on the prior history of emricasan in this indication and will await an end of Phase 2 meeting for ALCF with the FDA to discuss the regulatory path for ALCF and CLF. Conatus conducted the emricasan drug-drug interaction (DDI) studies in the UK and will, therefore, leverage these sites for the Phase 2b ALCF study. The study will enroll 60 patients in 15 sites assigned to four treatment regimens: 5 mg BID, 25 mg BID, 50 mg BID, and placebo. Patients must meet the following criteria to be included in the study: hospitalized for at least 24 hours, have underlying cirrhosis, and a MELD score of 20-30. These criteria are designed to ensure a high-risk patient population, but not patients on the verge of multi-organ failure and death.

Patients will receive standard treatment including antibiotics, anti-inflammatories, and medical devices may be used to support organ function as needed. Changes in ALT and cCK18 levels from baseline are the primary endpoints at 28 days with other endpoints, such as IL-18 and caspase 3 and 7 activity monitored as well to ensure the drug is working on target. Follow-up at two, three, and six months post-treatment will be done by phone to monitor for outcomes. However, we point out that the study is not powered to detect a difference on this front. We anticipate data in 2H14. In our opinion, this trial has a high likelihood of success, based on positive data from previous trials using these biomarkers, with the key risk being the ALCF disease setting, whereas earlier positive studies focused on viral hepatitis and NASH. Given the similarity in underlying disease pathology, we believe the data should be consistent.

FIGURE 18. ACLF Phase 2b Trial

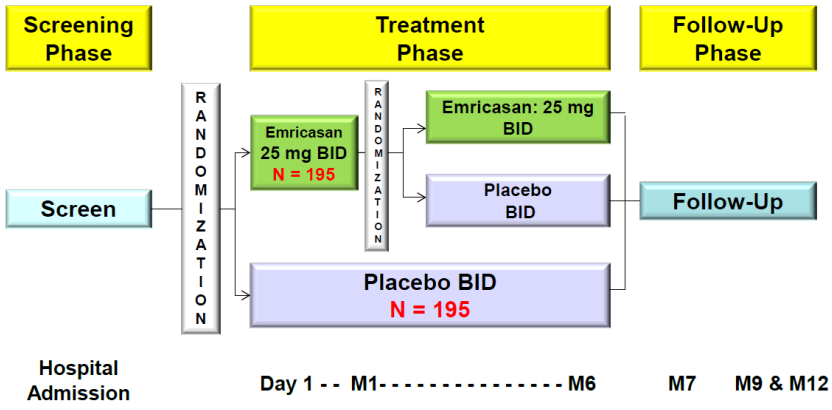


Source: Company reports

Conatus plans to initiate a pivotal study in ACLF in 2H14 after opening the IND in the U.S. and procuring a special protocol agreement (SPA) with the FDA. The target primary endpoint is time to clinical worsening, defined as the time to the first occurrence of transplant, death, or additional organ failure. Conatus anticipates enrolling ~400 patients in multiple sites in the U.S. and EU. We think patient selection will be critical to a successful outcome as the mortality rates for ALCF patients vary widely with disease severity.

Conatus is targeting enrollment of a population with 25% mortality and 45% worsening, defined as organ failure, transplant, or death. This will be accomplished by restricting enrollment to patients with Child Pugh scores of A or B and MELD scores in the range of 20-30, a group with three-month mortality of ~20%. Patients will be randomized 1:1 to twice-daily emricasan (dose to be determined by the Phase 2b dose-ranging study described above) or placebo for the first 28 days of the trial, at which point, the treatment group will be re-randomized 1:1 to emricasan or placebo and treated for an additional five months (Figure 19). Follow-up will occur at 7, 9, and 12 months. All patients will receive background standard of care: treatment with antibiotics, anti-inflammatories, and organ support, if needed. Feedback from KOLs suggest that lowering the worsening in this population from 45% to 30% is clinically meaningful and the study is powered at 80% to see this effect at a level of p = 0.025.

FIGURE 19. ACLF Phase 3 Trial



25 mg is a placeholder pending Phase 2b results

Source: Company reports

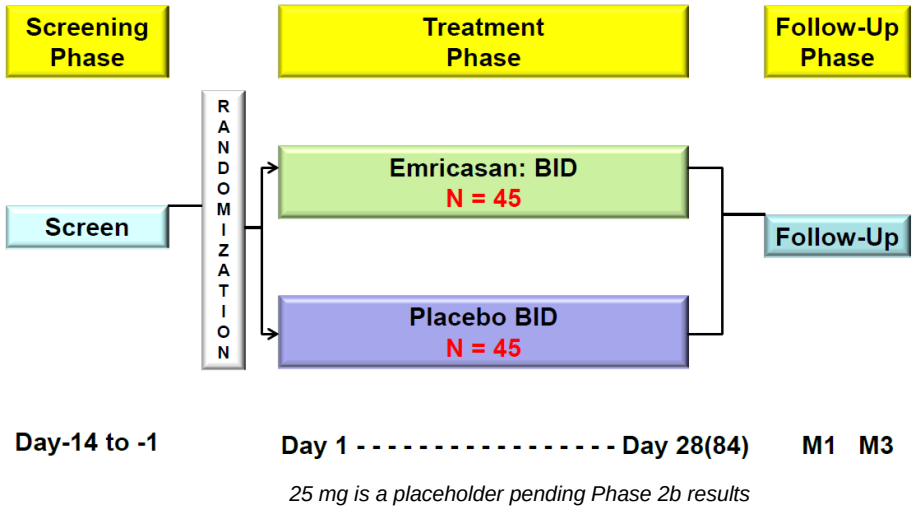
CLF

Successful completion of the Phase 2b ALCF study will be a gating factor for initiation of a Phase 3 study in CLF in 2H14 (Figure 20). The dose chosen from the ALCF dose-ranging study will also be applicable in CLF, given the similarity in underlying pathology, which we believe is a reasonable assumption. Similar to the ACLF study, the primary endpoint for the CLF study is expected to be time to clinical worsening (i.e., death, transplant, or next organ failure). Key biomarkers, including ALT and cCK18, will also be tracked.

Although the study design is still under review, we currently anticipate it will enroll at least 100 patients randomized 1:1 to or emricasan or placebo, although powering assumptions and final patient numbers have not been finalized. Dose and duration of therapy will be determined by the ACLF Phase 2b study and continuing KOL feedback regarding the treatment period. As with ALCF, patients will receive background standard of care: treatment with antibiotics, anti-inflammatories, and organ support, if needed. Conatus is targeting a population that should experience 20-30% clinical worsening in 28 days using a similar set of criteria to the ACLF study, and accounting for ~10% of the total CLF population.

In this population, MELD score is particularly important to physicians because it is used to select the transplant pool. If a patient's MELD score drops too low they may be deemed too healthy for transplant and if it is too high they are deemed too sick for transplant. As such, physicians closely monitor MELD scores and one of the factors in planning the CLF study is that physicians do not want to compromise their patients' position on transplant list. Therefore, the study may have two drug arms - one 28-day dosing cohort for transplant eligible CLF patients and one three-month cohort for those patients not eligible for transplant. Conatus intends to secure a SPA for this study prior to initiation and work with the FDA at the end of phase 2 meeting to clarify study design. Although this is a small population and a small commercial opportunity, Conatus believes this patient pool is similar enough to the ALCF that regulators will also want safety data in this population to support approval.

FIGURE 20. CLF Pivotal Trial Design



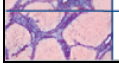
25 mg is a placeholder pending Phase 2b results

Source: Company reports

HCV-POLT

Conatus plans to initiate a Phase 2b/3 study in HCV-POLT in 2H13 (Figure 23) which could morph into a registration study should the FDA and the company come to agreement on the primary endpoint. The clinical goal for emricasan in HCV-POLT is to delay progression from fibrosis to cirrhosis. The proposed primary endpoint is response as measured by a one point change in the Ishak Fibrosis Score, a histology measure that rates fibrosis from 0-6 (6 being the worst (Figure 21)). Ishak has been incorporated into fibrosis clinical trials because of the relatively precise scoring. In a recent study of over 1,000 HCV patients treated with a long course of interferon, the Ishak score was found to predict clinical outcomes in patients with non-fragmented biopsies - patients without cirrhosis (Figure 22).

FIGURE 21. Ishak Fibrosis Staging Scale

General Appearance	Categorical Description	Categorical Assignment	Fibrosis Measurement*
	No fibrosis (normal)	0	1.9%
	Fibrous expansion of some portal areas (+/-) short fibrous septa	1	3.0%
	Fibrous expansion of most portal areas (+/-) short fibrous septa	2	3.6%
	Fibrous expansion of most portal areas with occasional portal to portal (P-P) bridging	3	6.5%
	Fibrous expansion of portal areas with marked bridging (P-P) as well as portal to central (P-C)	4	13.7%
	Marked bridging (P-P and/or P-C), with occasional nodules (incomplete cirrhosis)	5	24.3%
	Cirrhosis, probable or definite	6	27.8%

Source: Gilead company reports

The proposed study is currently not considered a registration study by the FDA as there is still a debate on the appropriate endpoints for trials measuring fibrosis. We think an FDA workshop entitled, "Trial Designs and Endpoints for Liver Disease Secondary to Nonalcoholic Fatty Liver Disease (NAFLD)" scheduled for early September could provide some clarity on this front, even though the workshop is focused on NAFLD, measurements for fibrosis could apply across diseases characterized by liver fibrosis including HCV-POLT. One of the ancillary takeaways from this workshop could be acceptance of a one point change in Ishak as the relevant hurdle for HCV-POLT, which could qualify the Phase 2b study as a pivotal study for this indication and Conatus will seek a SPA following this meeting although they plan to initiate the Phase 2b at risk without an SPA in hand. Further, we note that Pfizer had requested an SPA for the HCV-POLT study, submitted a protocol and received comments from the FDA on endpoints, study size, and statistical analysis, which have been incorporated into the current trial design.

While the design is in flux ahead of the September meeting, management believes the study will enroll about 300 patients randomized 1:1 to 25mg emricasan or placebo for two years of treatment. To be included in the study, patients must have an Ishak score of between two and four in the first six months to five years after transplant. We believe this represents about 60-70% of HCV-POLT patients and the cutoff is designed to ensure a population with moderately progressing fibrosis at a relatively early stage of the disease (pre-cirrhotic). All patients will receive standard of care, including antibiotics and post-transplant immunosuppressants. Feedback from KOLs suggests that in this population, 55% of patients will progress in two years and that lowering this to 35% is considered clinically meaningful. The HCV-POLT study is powered at 80% to see a one point change in the Ishak score over two years. Although the study will be blinded for the entire two year period, data will be periodically reviewed by the data safety monitoring board (DSMB), giving some visibility into safety and futility.

A potential risk for the POLT trial is the potential for high amounts of dropouts, especially in the U.S., due to the introduction of new HCV regimens. Patients who may want to receive treatment with the new HCV direct-acting antiviral (DAA) combinations can leave the study, but will be included in the final analysis as long as they have a biopsy taken at the one-year time point. Conatus plans to mitigate this risk of dropouts by running the study in Canada, Australia, and the five major EU markets, in addition to the U.S., where it will take at least one additional year for HCV DAAs to be launched.

Of the three tracks, we see the HCV-POLT trial as the study with the greatest risk. Specifically, we are concerned that this high-risk population on immunosuppressive therapy could be more vulnerable to cancer development, particularly given the longer 24-month exposure in this population. With respect to efficacy, we believe there is risk with the use of an endpoint, Ishak, which has not yet been evaluated in any clinical study of emricasan. Due to the relatively small market opportunity in HCV-POLT relative to the other targeted indications, we see the HCV-POLT indication as a strategy to establish long-term safety and efficacy in liver fibrosis and if successful, we see it as a gateway to larger liver diseases characterized by fibrosis, including NASH, which would be upside to our model if successful.

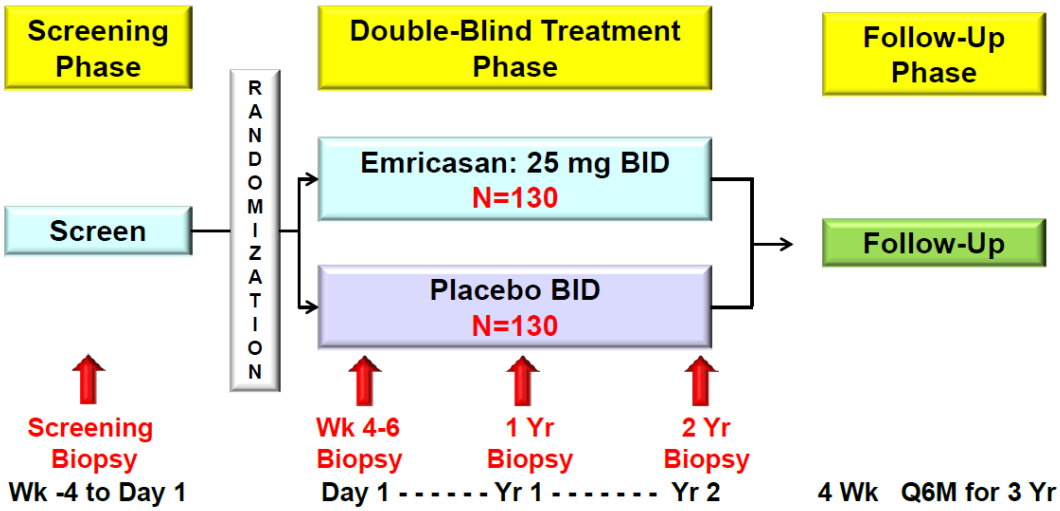
FIGURE 22. Ishak Fibrosis Stage and Liver Transplantation/Liver-related Death

	Ishak Stage					
	2	3	4	5	6	*P* Value for Trend
	Cumulative Incidence of Transplant or Death (N with Outcomes)					
All biopsies	4.3% (2)	8.1% (23)	10.2% (16)	21.3% (40)	27.8% (45)	<0.0001
Nonfragmented (NF)	2.4%	4.4%	8.2%	21.1%	28.1%	<0.0001
Fragmented (F)	16.7%	20.0%	22.3%	21.9%	27.0%	0.31
F versus NF: HR* (95% CI) and *P* value	–	4.4 (1.9-10.1) 0.0004	2.4 (0.8-7.0) 0.10	1.1 (0.6-2.1) 0.83	0.9 (0.5-1.7) 0.79	–

*Hazard ratio. Ishak 2 not compared because too few outcomes.

Source: HEPATOLOGY, Vol. 51, No. 2, 2010

FIGURE 23. HCV-POLT Trial



Source: Company reports

Intellectual property

Emricasan is protected by composition of matter and method of use patents that expire in the U.S. in 2018 before Hatch Waxman extensions which could add an additional five years. In the EU, composition of matter expires in 2017. A polymorph composition patent and methods patent has been granted that claims all crystalline forms discovered by Pfizer, as well as methods for treating liver fibrosis that should extend protection of emricasan until 2028 in the U.S. and 2027 internationally, prior to any extensions. Management believes that because it has identified all crystalline forms, it does not anticipate a successful challenge to the patent estate, although in our view, this is a source of risk.

We believe orphan exclusivity could provide an added an addition layer of protection of emricasan for the first seven years of sales in the U.S. and ten years in the EU. Conatus intends to file for orphan designation in the U.S. for HCV-POLT and potentially ACLF, as U.S. orphan designation is based on population size and unmet need. In the EU, orphan designation is more closely tied to the size of the population and recently the COMP (Committee for Orphan Medicinal Products) provided feedback to Conatus suggesting that although the HCV-POLT population is orphan in size, they see it as a bridging study to larger populations, prompting Conatus to withdraw the application.

Manufacturing

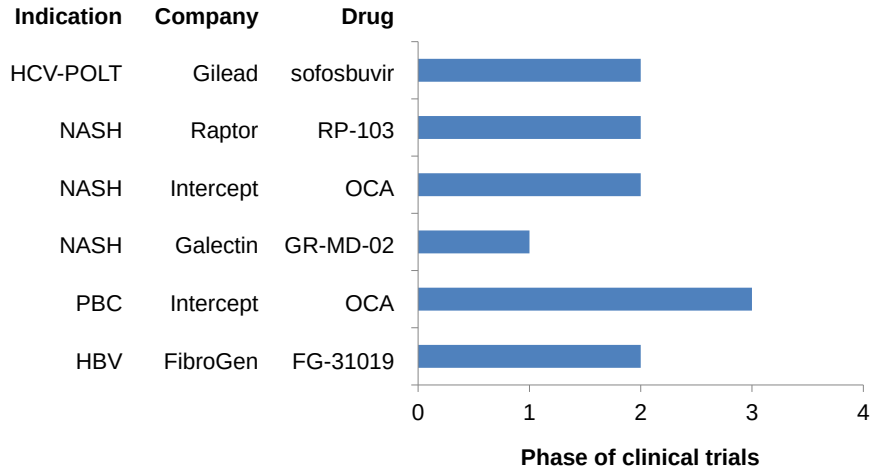
Emricasan is currently being manufactured in 50,000 capsule batches (5 and 25 mg capsules) by Metrics, a global contract development and manufacturing organization based in North Carolina. We believe this process is scalable and that Conatus has a sufficient inventory of active pharmaceutical ingredient (API) to meet the needs of all planned clinical trials. However, it will need to validate a second manufacturer and API supplier in order to launch commercially.

COMPETITIVE LANDSCAPE – OPPORTUNITIES IN ACLF, CLF, AND HCV-POLT

Our pipeline review suggests that there are no other small molecule caspase inhibitors in active development. Gilead was evaluating GS-9450, a pan-caspase inhibitor, in Phase 2 studies in both HCV and NASH; however, development was suspended following undisclosed adverse events and laboratory abnormalities in some patients. We believe this compound is structurally distinct from emricasan and therefore, toxicities cannot necessarily be attributed to a class effect, although we point out that GS-9450 had a tolerable profile through four weeks of dosing but was discontinued in a 26-week study, which stresses the need for caution in longer term evaluation of emricasan.

There are several promising anti-fibrotic drugs in the pipeline however, none are yet being pursued on ACLF, CLF, or HCV-POLT and therefore, we do not consider them direct competitors to emricasan at this time. We see tangential read-through to emricasan as data from these pipeline programs read out (i.e., data supporting the correlation between shift in biomarkers (ALT, AST) and clinical outcomes). Below, we summarize the compounds currently in development for liver fibrosis indications (Figure 24).

FIGURE 24. Liver Fibrosis Drugs

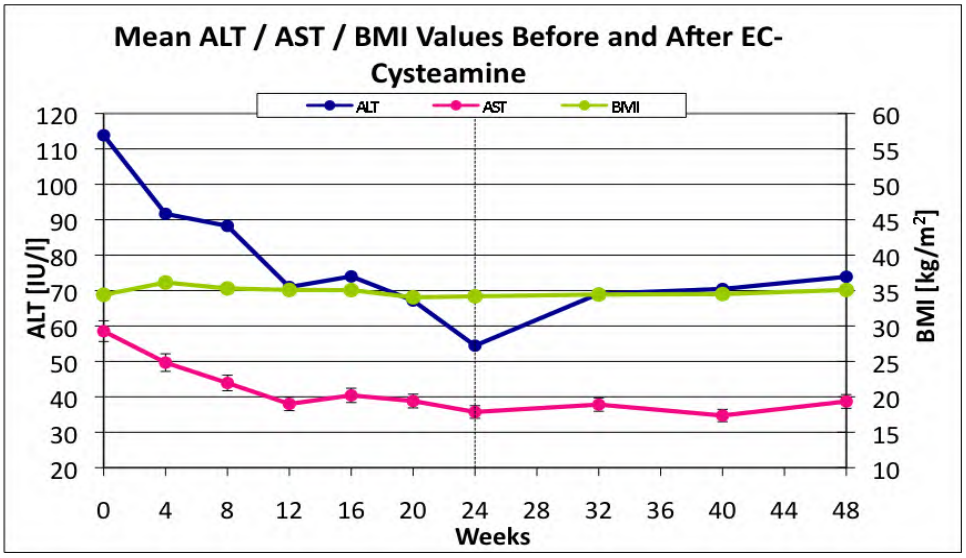


Source: Company reports and JMP Securities

- **Sofosbuvir**. Gilead's nucleotide inhibitor for HCV has been tested in the HCV-POLT population for 24 weeks with ribavirin with and without interferon, and the study has now been rolled over into an expanded access program, suggesting to us that the therapy has shown some efficacy, though the cure rates in this population have not yet been disclosed. A case report also suggests that sofosbuvir plus an NS5a HCV inhibitor can be efficacious in the HCV-POLT population, with a patient being cured after 24 weeks of all oral therapy; however, it is an n=1 study and hard to extrapolate at this time to an entire population.

- **RP-103**. Raptor (RPTP, MO, $15 PT) is currently testing a tablet formulation of its delayed release formulation of cysteamine called Procysbi (RP-103), in juveniles with NAFLD with the primary endpoint of improvement of liver biopsy. Similar to Conatus, Raptor conducted a Phase 2a study with RP-103 dosing of 6 months and observed a significant reduction in liver enzymes (Figure 25). The current Phase 2b study in about 160 juveniles is expected to complete enrollment in 1H2014 and read-out data. Our discussions with management suggest that if these data are positive, the company would then move into Phase 3 development.

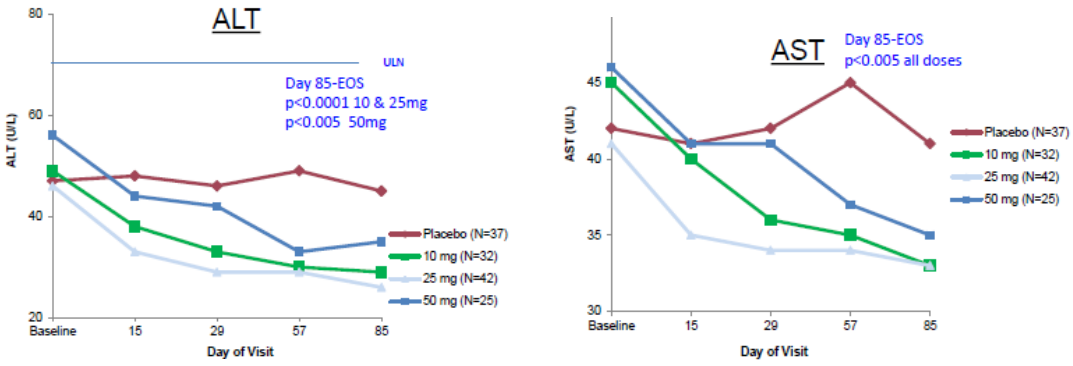
FIGURE 25. RP-103 and Liver Enzymes



Source: Company reports

- **Obeticholic acid (OCA)**. Intercept is developing OCA, a farnesoid X receptor agonist, for primary biliary cirrhosis (PBC), portal hypertension, and NASH. The compound reverses liver cirrhosis in animal models and dosing of drug in patients has led to declines in alkaline phosphatase (ALP) and liver enzyme levels (Figure 26). Similar to emricasan in HCV-POLT, the current study in PBC is considered pivotal in the EU but not in the U.S., although Intercept is considering an accelerated approval pathway using ALP as a surrogate. The National Institute of Diabetes and Digestive and Kidney Diseases is sponsoring a study of OCA in NASH with biopsy as the primary endpoint with data expected in 4Q14. We believe these data can further our understanding of the relationship ALT/AST decline and fibrosis.

FIGURE 26. Change in ALT/AST Levels in PBC Patients



Source: Company reports

- **GR-MD-02**. Galectin Therapeutics is developing complex carbohydrate-based drugs. dGR-MD-02 is an IV administered compound from the galacto-hramnogalturonate class. The compound has been shown to reverse cirrhosis in a rat model and is in Phase 1development in NASH. The primary endpoint will be safety and the company will assess various biomarkers as well.

- **FG-3019**. FibroGen is developing human monoclonal antibodies to block connective tissue growth factor (CTGF) activity. FG-3019 has potential applications in a wide range of diseases, including chronic kidney disease (CKD), metastatic cancers, and fibrotic diseases, such as idiopathic pulmonary disease. FibroGen is currently recruiting for its first major clinical trial in liver fibrosis. This placebo-controlled, Phase 2 study will focus on patients with chronic HBV infection. In addition to FG-3019, patients will receive the antiviral entecavir and the primary efficacy endpoint will be the impact on fibrosis, as measured by Ishak score.

New HCV antivirals could reduce the available patient population. We anticipate approval of two new all-oral HCV regimens in 2014 that could cure most chronically infected patients, reducing the number of patients with HCV-related liver fibrosis. We think this could decrease the overall size of the patient pool for emricasan by ~25% in ACLF and CLF and potentially even more in HCV-POLT. We believe HCV DAA regimens will likely be the first-line therapy in the HCV-POLT population because they may be curative. Those refractory to therapy may then be treated with another agent such as emricasan, or these therapies may be used in combination.

MARKET OPPORTUNITY FOR EMRICASAN

ALCF

Of the three indications, ACLF is the largest, with 150,000 patients in the U.S. and EU combined. The ACLF population is comprised of patients with various causes of liver disease. We estimate that about one-third of these cases are derived from chronic HCV infection in the U.S. and EU (in Asia HBV is more prevalent and plays a larger role), a market we expect to contract significantly as the vast majority of patients are cured over the next five to ten years. This contraction may be partially offset by the aging of baby boomers and increased obesity rates, leading to increases in liver fibrosis caused by alcoholism and NASH, respectively.

In terms of disease severity, ACLF patients are stratified into moderate (30%), severe (50%), and critical (20%). Based on our discussions with physicians, we believe there should be rapid uptake into the severe and critical segments of market, a population of about 56,000 in the U.S. and 80,000 in the EU.

Due to the unmet medical need and no competition, we currently estimate a high level of penetration of 50% into the U.S. and EU markets, about five years after a 2018 launch in the U.S. and 2019 launch in the EU. We anticipate expansion into the moderate patient population, depending upon the safety profile and relative risk-benefit profile, as physicians become familiar with emricasan, which would be upside to our estimates. We assume a launch price of $8,000 per month for three months; however, we note that the duration of therapy and pricing will also be largely determined by the outcome of the Phase 3 study. Assuming annual 5% price increases, 80% compliance, and 20% in gross-net adjustments, we arrive at peak sales of $389M in 2024 in the U.S. In Europe, we estimate a price of $5,000 a month, a discount to the U.S. price, and we do not include any price increases. With these assumptions, and assuming 80% compliance, we derive peak sales of $363M for emricasan in 2024 in the E.U.

CLF

CLF is a smaller opportunity that encompasses about 5% of patients with liver failure, or about 5,000 and 6,500 patients in the U.S. and EU, respectively. We keep our assumptions on duration of therapy, penetration, compliance, price, and adjustments consistent with ACLF. Emricasan could be approved in CLF, a year ahead of ACLF, should the data from a single study be sufficiently convincing. At this juncture, we assume a 2017 U.S. launch and EU launch in 2018. Our U.S. peak revenue is $32M and EU peak revenue projection is $30M in 2024.

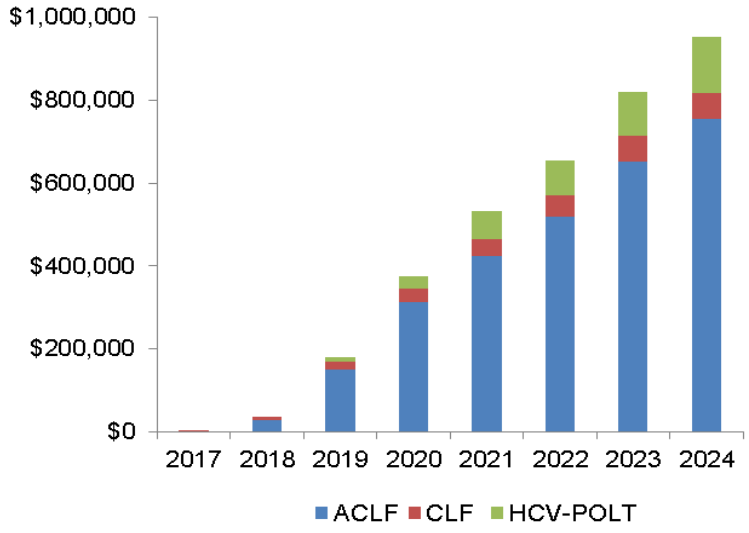
HCV-POLT

There are about 50,000 HCV patients in need of transplants with the gating factor the number of transplants per year, about 6,000 in the U.S. and 9,000 in the EU, half of which go to HCV patients. We expect high cure rates with the HCV therapy will dramatically reduce the demand for transplants however, given the limited supply and expectation that not all patients will be cured, we anticipate the number of transplants to remain stable. That being said, cure of HCV in the post-transplant setting is likely to vastly increased, which we anticipate will reduce the eligible patient population.

Thus, we model emricasan as a therapy in HCV-POLT for patients who fail to achieve cure with HCV anti-virals or about 50% of the population, ahead of data indicating cure rates. We believe that this year, there are about 5,800 (U.S. and EU) patients who would be targeted for emricasan therapy, dropping to ~4,700 patients by 2024. We assume rapid uptake into this small segment of the population – 50% in the U.S. and EU in the 2023-24 timeframe, three years following U.S. and EU launches in 2019 and 2020, respectively.

We maintain monthly pricing consistent with the ACLF/CLF patients, although this is a chronic therapy, making the cost per patient per year significantly higher at $100,800 at time of launch (discounted to $60,000 in the EU). In our view, the small population treated can justify this price. We estimate 80% compliance as this will be positioned as a chronic therapy, with 20% gross to net adjustments; we arrive at peak U.S. and EU revenue of $67M and $68 in 2024, respectively.

FIGURE 27. JMP Estimated Revenue Build per Indication



Source: JMP Securities LLC Estimates

MANAGEMENT TEAM

Conatus' management team has many members from Idun, the company that initially developed emricasan before the acquisition by Pfizer. The team is widely regarded as leaders in caspase therapy by physicians in the field.

FIGURE 28. Management Team

Name	Position	Previous Company
Steven Mento, PhD	CEO	Idun
Alfred Spada, PhD	CSO	Idun
Gary Burgess, MB, ChB MMed	CMO	Pfizer
Charles Cashion	CFO	Idun

Source: Company reports

FIGURE 29. Board of Directors

Name	Since	Affiliation
David Hale	2006	Hale BioPharma Ventures
Paul Klingenstein	2005	Aberdare Ventures
Louis Lacasse	2011	AgeChem, GeneChem
Shahzad Malik MD	2009	Advent Venture Partners
Steven Mento, PhD	2005	CEO Canatus
Marc Perret	2006	Gilde Healthcare Partners
Jim Scopa JD, MBA	2011	MPM Capital
Harold Van Wart PhD	2007	Metabolex

Source: Company reports

FIGURE 30. JMP Projected Income Statement for Conatus

	FY11A	FY012A	Mar-13A	Jun-13E	Sep-13E	Dec-13E	FY013E	FY014E	FY015E	FY016E	FY017E	FY018E	FY019E	FY20E	FY21E	FY22E	FY23E	FY24E
Revenues:																		
ALCF		0	0	0	0	0	0	0	0	0	0	25,770	149,462	310,694	422,344	517,097	650,846	752,155
CLF							0	0	0	0	942	7,722	18,011	33,910	41,071	51,994	60,231	62,680
HCV-POLT			0	0	0	0	0	0	0	0	0	0	9,746	29,664	67,325	83,608	106,825	135,365
Total product revenue	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**942**	**33,491**	**177,219**	**374,268**	**530,740**	**652,698**	**817,902**	**950,199**
Total revenue	**-**	**-**	**-**	**-**	**-**	**-**	**0**	**-**	**-**	**-**	**942**	**33,491**	**177,219**	**374,268**	**530,740**	**652,698**	**817,902**	**950,200**
Operating expenses:																		
COGS	0	0	-	-	-	-	-	-	-	-	-	3,349	14,178	29,941	26,537	32,635	40,895	47,510
R&D	9487	5,528	200	500	1500	2500	4,700	20,000	40,000	50,000	40,000	25,000	20,000	20,000	20,000	20,000	20,000	20,000
SG&A	2875	3,086	1500	1500	1800	2000	6,800	6,936	7,075	12,000	20,000	26,000	33,800	43,940	57,122	71,403	78,543	82,470
Total operating expenses	**12361**	**8615**	**1700**	**2,000**	**3,300**	**4,500**	**11,500**	**26,936**	**47,075**	**62,000**	**60,000**	**54,349**	**67,978**	**93,881**	**103,659**	**124,037**	**139,438**	**149,980**
Loss from operations	**(12,361)**	**(8,615)**	**(1,700)**	**(2,000)**	**(3,300)**	**(4,500)**	**(11,500)**	**(26,936)**	**(47,075)**	**(62,000)**	**(59,058)**	**(20,858)**	**109,242**	**280,387**	**427,081**	**528,661**	**678,464**	**800,221**
Interest expense	(114)	(70)	(18)	(18)	(18)	(18)	(70)	(70)	(70)	(70)	(70)	(70)	(70)	(70)	0	0	0	0
Other, net	450	(90)	(18)	(18)	(18)	(18)	(70)											
Total other income (expense)	**365**	**(135)**	**(35)**	**(34)**	**(30)**	**(32)**	(131)	**(53)**	**18**	**(7)**	**52**	**166**	**385**	**806**	**1689**	**3256**	**6275**	**12096**
							0											
Net loss	**$ (12,001)**	**$ (8,744)**	**$ (1,735)**	**$ (2,034)**	**$ (3,330)**	**$ (4,532)**	**$ (11,631)**	**$ (26,989)**	**$ (47,056)**	**$ (62,007)**	**$ (59,006)**	**$ (20,692)**	**$ 104,145**	**$ 239,014**	**$ 300,139**	**$ 345,746**	**$ 445,081**	**$ 528,006**
Loss per Share basic	**$ (1.44)**	**$ (1.04)**	**$ (0.20)**	**$ (0.22)**	**$ (0.24)**	**$ (0.28)**	**$ (0.93)**	**$ (1.36)**	**$ (2.32)**	**$ (2.40)**	**$ (2.01)**	**$ (0.69)**	**$ 3.44**	**$ 7.76**	**$ 9.59**	**$ 10.88**	**$ 13.78**	**$ 16.10**
Shares outstanding, basic	8,346	8,390	8,890	9,390	13,990	16,290	12,140	19,790	20,290	25,790	29,290	29,790	30,290	30,790	31,290	31,790	32,290	32,791

Source: Company reports, JMP Securities LLC

Company Description

Conatus Pharmaceuticals is a San Diego-based biopharmaceutical company focused on the development of emricasan, a pan-caspase inhibitor with potential to be used to treat liver fibrosis, particularly in areas of large unmet need, including cirrhosis-induced liver failure and graft fibrosis in transplant patients.

Investment Risks

Clinical Risk. Emricasan has not yet been evaluated in clinical trials longer than 12 weeks. Longer trials may result in unanticipated safety concerns, which could cause emricasan to underperform in clinical trials. Although successful in the regulation of biomarkers, emricasan may not impact clinical outcomes.

Regulatory Risk. Conatus hopes to use the Ishak Fibrosis Score as a primary clinical end-point for HCV-POLT; however, endpoints for fibrosis are still under discussion with the FDA. Failure to establish Ishak could slow development in this indication.

Intellectual Property Risk. The composition of matter patent for emricasan expires in 2017 and has not yet received a Hatch Waxman extension. As such, Conatus may have to rely on a polymorph composition and method patent, which expires in 2027, for long-term market exclusivity. If Conatus does not receive orphan exclusivity for emricasan, protection may also be limited.

Commercial Risk. As a small company, Conatus may have difficulty educating healthcare payers and providers on the benefits of a novel drug. As such, emricasan adoption may be slowed.

Sector Risk. Valuation of biopharmaceutical stocks is subject to both investor assessments of the prospects of the underlying companies, as well as tolerance for risk and level of confidence in the prospects of pharmaceutical stocks as a group. Therefore, Conatus' stock price may fall even while the company meets or exceeds investor expectations.

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JMP Securities Disclosures:

JMP Securities currently makes a market in the securities of Conatus Pharmaceuticals Inc. and Raptor Pharmaceuticals Corp.

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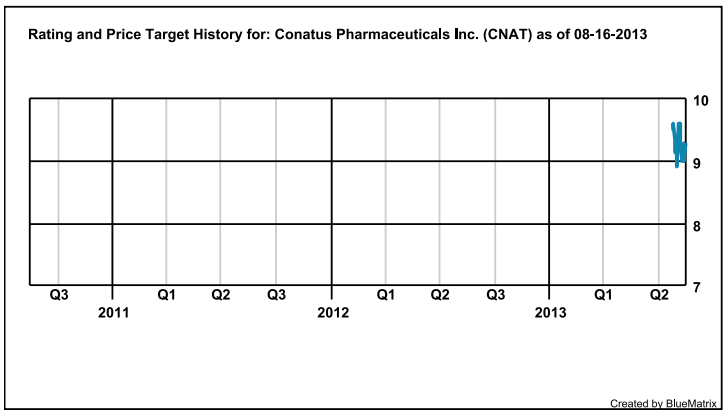
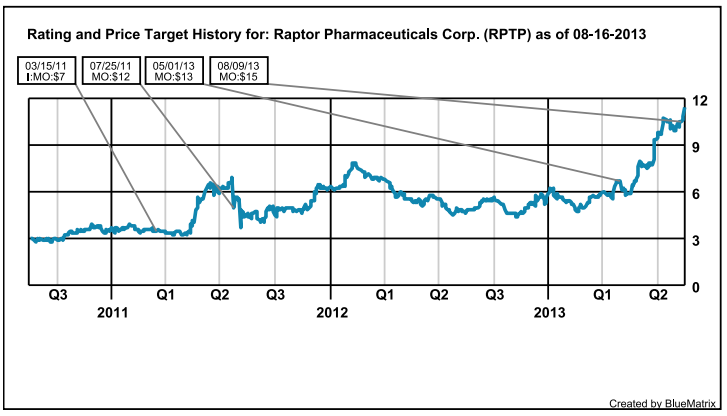
JMP Rating	Regulatory Equivalent	# Co's Under Coverage	% *of Total*	Regulatory Equivalent	# Co's Under Coverage	% *of Total*	# Co's Receiving IB Services in Past 12 Months	*% of Co's With This Rating*
MARKET OUTPERFORM	Buy	239	*60.97%*	Buy	239	*60.97%*	76	*31.80%*
MARKET PERFORM	Hold	147	*37.50%*	Hold	147	*37.50%*	21	*14.29%*
MARKET UNDERPERFORM	Sell	6	*1.53%*	Sell	6	*1.53%*	0	*0%*
TOTAL:		392	*100%*		392	*100%*	97	*24.74%*

Stock Price Chart of Rating and Target Price Changes:

Note: First annotation denotes initiation of coverage or 3 years, whichever is shorter. If no target price is listed, then the target price is N/A. In accordance with NASD Rule 2711, the chart(s) below reflect(s) price range and any changes to the rating or price target as of the end of the most recent calendar quarter. The action reflected in this note is not annotated in the stock price chart. Source: JMP Securities.





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