Zacks Equity Research

www.zacks.com

November 12, 2010
Jason Napodano, CFA
312-265-9421
jnapodano@zacks.com

111 North Canal Street, Chicago, IL 60606

Nile Therapeutics, Inc. (NLTX-NASDAQ)

NLTX: Encouraging Phase II Data Allows Nile To Push Forward With CN-NP.

Current Recommendation	**Outperform**
Prior Recommendation	N/A
Date of Last Change	01/26/2010
Current Price (11/12/10)	$0.68
Target Price	**$2.00**

UPDATE

On November 2, 2010, Nile Therapeutics announced that CD-NP had successfully completed the phase II study in patients with acute decompensated heart failure (ADHF) and mild to moderate renal insufficiency. The goal of the program was to characterize the dose-response and risk of hypotension. Based on the data, CD-NP infusion at 1.25, 2.5 and 3.75 ng/kg/min appeared to be well tolerated.

We believe with positive data from the phase II program in hand the company is worth at least $80 to 100 million. Taking the mid-range at $90 million, and then backing out the $20 million most likely required to fund the phase IIb program, we arrive at a value of $70 million for Nile Therapeutics. This equates to a price of $2.00 per share.

SUMMARY DATA

52-Week High	**$1.60**
52-Week Low	**$0.30**
One-Year Return (%)	**-53.28**
Beta	**2.01**
Average Daily Volume (sh)	**50,008**
Shares Outstanding (mil)	**35**
Market Capitalization ($mil)	**$23**
Short Interest Ratio (days)	**0.36**
Institutional Ownership (%)	**18**
Insider Ownership (%)	**24**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2009 Estimate	**N/A**
P/E using 2010 Estimate	**N/A**
Zacks Rank	**2**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**
Zacks Rank in Industry	**46 of 141**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2009	0 A	0 A	0 A	0 A	0 A
2010	0 A	0 A	0 A	0 E	0 E
2011					10.0 E
2012					20.0 E

Earnings per Share
(EPS is operating earnings before non-recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2009	-$0.07 A	-$0.10 A	-$0.08 A	-$0.06 A	-$0.31 A
2010	-$0.07 A	-$0.05 A	-$0.05 A	-$0.04 E	-$0.20 E
2011					-$0.21 E
2012					$0.06 E

Zacks Projected EPS Growth Rate - Next 4 Years % **N/A**

© Copyright 2010, Zacks Investment Research. All Rights Reserved.

WHAT'S NEW

CD-NP Update

…Positive Top-Line Phase IIa Data…

On November 2, 2010, Nile Therapeutics announced that CD-NP had successfully completed the phase II study in patients with acute decompensated heart failure (ADHF) and mild to moderate renal insufficiency. As a reminder, in July 2010, Nile Therapeutics announced it had completed enrollment in this phase II program at 77 patients. The trial, NIL-CDNP-CT005, was an open-label, single-blind, placebo-controlled study designed to assess the safety and tolerability of 4 doses of CD-NP (1.25, 2.5, 3.75, and 5.0ng/kg/min) when infused for up to 72 hours in patients with ADHF and mild to moderate renal insufficiency. Patients were followed for 30 days after infusion. The trial enrolled patients in the U.S. (~1/3rd), and Israel and Germany (~2/3^{rds}).

The goal of the program was to characterize the dose-response and risk of hypotension. Based on the data, CD-NP infusion at 1.25, 2.5 and 3.75 ng/kg/min appeared to be well tolerated. A dose-dependent effect on blood pressure was observed, with minimal or mild blood pressure reduction at 1.25 and 2.5 ng/kg/min, and moderate blood pressure reduction at 3.75 ng/kg/min. Dose escalation was limited by significant blood pressure reduction at 5 ng/kg/min.

Secondary efficacy endpoints were also evaluated during the trial. The data show favorable effects of CD-NP on renal function, particularly at the 1.25 and 2.5 ng/kg/min doses, with respect to preservation or enhancement of renal function compared to placebo, as evidenced by favorable trends in several biomarkers correlated with kidney function, including creatinine and cystatin-c. However, given the small size of the trial at only 77 patients, we do not expect these results to be statistically significant. Management may make additional data available early next year; however, we expect the full analysis to be presented at the American College of Cardiology meeting in April 2011.

…Next Up, Phase IIb In 2011…

The next steps for Nile is to finalize the design of a double-blind, placebo controlled phase IIb study and to discuss that trial design with the FDA and other regulatory authorities. Management's goal is to have this discussion with the U.S. FDA in early 2011. We expect this program to test 2 doses of CD-NP and enroll roughly 300-400 patients, with endpoints to include relief of symptomatic dyspnea, as well as analysis of biomarkers for kidney function and ischemia, as well as safety assessments including risk of hypotension, renal function, cardiovascular events, and mortality. The cost of this planned phase IIb program is estimated to be between $15 and $20 million.

Third Quarter Financials

On November 12, 2010, Nile released financial results for the third quarter ended September 30, 2010. The company did not report any revenues for the third quarter. This was expected. Net loss was $1.8 million, or 5 cents per share. This was also in-line with our expectations. Nile exited the third quarter with $4.4 million in cash and investments. With positive phase IIa data now in hand, we expect that management will seek to raise funds in the next few months to fund the planned phase IIb program. Funds required for the phase IIb program are, at a minimum, $15 million. We believe Nile requires at least $20 million in new funding in order to have enough cash to support the planned phase IIb program and fund operations through competition and data presentation.

OVERVIEW

Heart Failure

Heart Failure (HF) can be a chronic or acute condition in which the structure of function of the heart impairs its ability to supply sufficient blood flow to meet the body's needs. The most common manifestation of the disease is low cardiac output (known as congestive heart failure). HF is most commonly caused by an acute myocardial infarction (heart attack), ischemic heart disease, hypertension, valvular heart disease, or cardiomyopathy. These can cause impairment to the contractility (systolic heart failure) or impairment to relaxation and ventricular filling (diastolic heart failure). The most common cause of heart failure is left ventricular systolic dysfunction. Dysfunction is defined as an ejection fraction of 50% or less, or a categorical assessment of moderately or severely impaired.

According to data from the National Health and Nutrition Examination Survey (NHANES I), a 19-year, 13,000 patient retrospective analysis, risk of developing HF is associated with the following underlying conditions:

Underlying Condition	Risk of HF
…Ischaemic Heart Disease	62%
…Cigarette Smoking	16%
…Hypertension	10%
…Obesity	8%
…Diabetes	3%
…Valvular Disease	2%

According to the Acute Decompensated Heart Failure National Registry (ADHERE), a 10-year observational registry of the management of 200,000 patients treated in 280 hospitals for HF, common co-morbid conditions that must be considered during treatment include:

Co-Morbid Condition	Frequency
…Hypertension	73%
…Coronary Artery Disease	57%
…Diabetes	44%
…Atrial Fibrillation	31%
…Asthma / COPD	31%
…Chronic Renal Insufficiency	30%

Acute decompensated heart failure (ADHF) is the sudden onset of heart failure, and can lead to severe consequences, including acute respiratory distress. Symptoms include shortness of breath (dyspnea), coughing, ankle swelling, and reduced exercise capacity. The dyspnea is generally associated with rapid accumulation of fluid within the lung's interstitial and alveolar spaces, which is the result of acutely elevated cardiac filling pressures (cardiogenic pulmonary edema). Heart failure is also associated with significantly reduced physical and mental health, resulting in a markedly decreased quality of life. Renal insufficiency (kidney failure) is also often common in patients with ADHF. In fact, over the past several years, it has become apparent that the interaction between the heart and the kidneys plays a critical role in the progression of heart failure. Generally speaking, worsening stages of chronic kidney disease (CKD) are associated with longer hospital stays and higher mortality rates in patients with acute heart failure.

…Epidemiology…

In the U.S., approximately 5.5 million people (~2% of the population) suffer from heart failure. The incidence is even higher for patients above the age of 65, where approximately 6% to 10% of the population is at risk. There are an estimated 650,000 new cases diagnosed annually.

Treatment of heart failure generates annual costs of approximately $35 billion, of which approximately $3 billion is spent on drugs and $19 billion is spent in the acute hospital setting. HF patients frequently suffer acute episodes of decompensated heart failure (ADHF) which require hospitalization. Each year, HF is responsible for over 1.2 million hospitalizations. For Americans over the age of 65, ADHF is the most frequent cause of hospital admission, and the incidence has doubled in the past 25 years. The average length of hospital stay is 4.3 days. Subsequent to a discharge for ADHF, the average time to re-admission is 3 months and mortality is high. In fact, 50% of patients discharged with a primary or secondary code of ADHF will require re-hospitalization during the following 9 months.

Period Following Hospitalization	Mortality Rate
…1 Month	12%
…12 Months	33%
…5 Years	50%

According to the ADHERE Registry, mortality rates are higher for patients with elevated blood urea nitrogen (BUN), low systolic blood pressure (SBP), and high serum creatinine (SCr). Data from the ADHERE study demonstrates that elevated BUN is the single strongest predictor of in-hospital mortality in patients admitted with ADHF. The BUN test is a measure of the amount of nitrogen in the blood in the form of urea, and a measurement of kidney function. Urea is a substance secreted by the liver, and removed from the blood by the kidneys.

Vital Signs		Mortality Rate
…Blood Urea Nitrogen (BUN)	≥ 43mg/dL	▼
	≤ 43mg/dL	▲
…Serum Creatinine Levels (SCr)	≥ 2.75 mg/dL	▲
	≤ 2.75 mg/dL	▼
…Systolic Blood Pressure (SBP)	≥ 115 mm Hg	▲
	≤ 115 mm Hg	▼

Chronic kidney disease (CKD) is identified by a blood test for creatinine and BUN. Creatinine, normally produced by the body at a fairly constant rate, is a break-down waste product of creatine phosphate in muscle. It is chiefly filtered out of the blood by the kidneys, though a small amount is actively secreted by the kidneys into the urine. Therefore, if the filtering of the kidney is deficient, e.g. in kidney failure, blood levels for both urea and creatinine rise. Glomerular filtration rate (GFR) describes the flow rate of filtered fluid through the kidney. Lower GFR indicates a failing kidney with decreased capability to excrete waste products. Creatinine levels may be normal in the early stages of CKD, but increase in time as the disease worsens. As such, creatinine clearance, reflected by the GFR, is a clinically important measurement of renal function.

Prevalence and severity of renal dysfunction in patients with ADHF, along with mortality rate, demonstrates the relationship between worsening kidney function and heart failure:

CKD Severity	Prevalence	In-Hospital Mortality Rate
Stage I *(GFR > 90)*	Male = 11%	1.9%
	Female = 8%	
Stage II *(GFR 60 - 90)*	Male = 30%	2.3%
	Female = 25%	
Stage III *(GFR 30 - 60)*	Male = 41%	3.9%
	Female = 46%	
Stage IV *(GFR 15 - 30)*	Male = 12%	7.6%
	Female = 15%	
Stage V *(GFR < 15)*	Male = 7%	6.5%
	Female = 7%	

Source: Journal of Cardiac Failure Vol. 13 No. 6 August 2007

It is clear that patients with worsening renal function during hospitalization for heart failure are associated with higher unfavorable outcomes. As noted above, and confirmed by Haywood et al in the Journal of Cardiac Failure (Vol. 13 No. 6 August 2007), BUN is the single strongest predictor of inpatient mortality. However, GFR provides a more accurate estimation of renal function and better quantifies the degree of renal impairment. Therefore, calculating both GFR and BUN provides complementary information that can be used as a prognostic tool for predicting patient outcomes during hospitalization with ADHF. Accordingly, when looking for an ideal treatment option for a patient presenting to the hospital with ADHF, the following characteristics should be considered:

Characteristics	Clinical Endpoints
Diuretic & Natriuretic	Improvement in dyspnea
Preserve / Enhance Renal Function	Reduce end-organ damage
Reduce Cardiac Filling Pressure	Rapid improvement in dyspnea
Low Risk of Hypotension	Safety

…Treatment Options…

Treatment of HF includes a combination of vasodilators, diuretics, and non-invasive positive pressure ventilation (NIPPV). Other treatment options also include a mixture of pharmaceutical products, including ACE inhibitors, angiotensin receptor blockers (ARBs), Beta-blockers, inotropic agents, and surgery.

- Vasodilators: Vasodilation refers to the widening of blood vessels resulting from relaxation of smooth muscle cells within the vessel walls, particularly in the large arteries, smaller arterioles and large veins. When vessels dilate, the flow of blood is increased due to a decrease in vascular resistance. The resulting dilation leads to a decrease in blood pressure. Vasodilators include nitrates such as nitroglycerin and nitroprusside. The body converts the nitroglycerin into nitric oxide, a messenger molecule that tells the smooth muscles of the surrounding blood vessels to relax. Nitro comes in sublingual tablets and sprays for short-acting (acute) heart failure, or patches for long-acting (chronic) heart failure. Physicians have been using nitro efficacy for the treatment of angina and heart attack for over 100 years. However, these drugs do very little to preserve renal function and patients must be monitored while on the drug for risk of hypotension (low blood pressure). Side effects include severe headaches, dizziness, and tachycardia. The body also develops a tolerance to nitro, leading to a resistance to its vasodilating effects. The body can also experience withdrawal symptoms following long-term use. This makes the drug a rather poor choice for patients with chronic heart failure.

- Diuretics: A diuretic is any drug that elevates the rate of urination and provides a means for reducing fluid retention. Commonly used diuretics include furosemide and metolazone. Furosemide (sold branded by Sanofi-Aventis as Lasix) is a loop diuretic. The drug acts by inhibiting the body's ability to reabsorb sodium at the ascending loop in the kidney. This leads to retention of water in the urine. The effects of Lasix are roughly six hours ("last-six"). Overuse can cause dehydration, electrolyte imbalance, metabolic alkalosis, seizures, and renal damage. Metolazone is a thiazide diuretic that indirectly decreases the amount of water reabsorbed into the bloodstream by the kidney, so that blood volume decreases and urine volume increases. It his lowers blood pressure and prevents excess fluid accumulation in heart failure. Metolazone is commonly used in combination with furosemide. This causes effective diuresis, but can often lead to significant electrolyte abnormalities, hyponatremia (low sodium), hypokalemia (low potassium), hypercalcemia (high calcium), and hyperuricemia (high uric acid). Side effects include dizziness, headache, and heart palpitations.

- Inotropes: Inotropic agents alter the force of energy of muscular contractions by manipulating calcium levels in the cytoplasm. There are two types of inotropic agents, negative agents that weaken muscle contraction by decreasing calcium and positive agents that strengthen muscle contraction by increasing calcium. The choice largely depends on specific pharmacological effects of individual agents with respect to the condition. Positive inotropic agents increase myocardial contractility, and are used to support cardiac function in conditions such as ADHF, myocardial infarction, and cardiomyopathy. Commonly used positive inotropic agents for the treatment of heart failure include milrinone, dobutamine, and levosimedan. Milrinone is a phosphodiesterase III inhibitor that increases the effects of cyclic adenosine monophosphate (cAMP) and enhances relaxation of the left ventricle by increasing calcium uptake. It is primarily used with when vasodilating and diuretic agents are insufficient. However, ventricular arrhythmia is a potential serious side effect and limits more widespread use. Levosimendan is a calcium sensitizer that increased the sensitivity of the heart to calcium and facilitates cardiac contractility without actually having to intracellular calcium levels. The drug also has mild vasodilating properties. Unfortunately, the drug is contraindicated in patients with moderate-to-severe renal impairment, and thus not a good option for broad-scale use. Dobutamine is a direct-acting agent that stimulates the beta-1-adrenoceptors of the heart, thus increasing contractility and cardiac output. Both dobutamine and levosimedan are associated with tachycardia and hypertension.

- VAD: A ventricular assist device ("VAD") is a mechanical circulatory device that is used to partially or completely replace the function of a failing heart. They can be used over the short-term when patients are recovering from a heart attack or heart surgery, or can be implanted for long-term use in patients with congestive heart failure (that require a transplant). VADs are divided into two main categories: pulsatile pumps, that mimic the natural pulsing action of the heart, and continuous flow pumps. Retrospective analysis demonstrates that use of left ventricular VAD result in improved cardiac and metabolic function, less renal failure, and significant higher event-free survival rates that inotropic agents. However, because the devices generally result in blood flowing over a non biologic surface, predisposing the blood to clotting, there is need for continuous anticoagulation measures.

…Along Comes Natrecor…

In August 2001, a small biotechnology company, Scios Inc., received approval for what, at the time, was considered to be a major breakthrough for the treatment of ADHF with Natrecor (nesiritide). Nesiritide is the recombinant form of the 32 amino acid human B-type natriuretic peptide (BNP), which is normally produced by the ventricular myocardium. Nesiritide works to facilitate cardiovascular fluid homeostasis through counter-regulation of the renin-angiotensin-aldoesterone system, stimulating cyclic guanosine monophosphate, leading to smooth muscle cell relaxation. The product was believed to provide all of the vasodilating characteristics of nitroglycerine, with the diuretic and natriuretic properties of furosemide, while also reducing cardiac filling pressure. This was virtually a homerun in terms of treating patients with ADHF, as long as the risk of hypotension (low blood pressure) could be effectively managed. Scios was later acquired by large-cap pharmaceutical company, Johnson & Johnson, in 2003 for $2.4 billion in cash. At the time the deal valued Scios at over 50x Natrecor's revenue.

Natrecor sales were annualizing over $400 million in 2004 and were on schedule to be the billion-dollar blockbuster J&J had anticipated. Unfortunately, in 2005, a meta-analysis of patient outcomes on Natrecor painted a very different profile than the drugs proposed mechanism. Use of Natrecor was identified with increased mortality and increased renal dysfunction compared to the standard of care. Natrecor was thought to increase GFR by causing dilation of the afferent renal arterioles and constriction of the efferent renal arterioles. BNP stimulation also leads to relaxation of renal mesangial cells, increasing the surface area for filtration, thus further increasing GFR. Unfortunately, there were significant indirect effects that actually lead to a decrease in GFR (worsening in renal function) in the real world setting. BNP, a rather potent vasodilator, lowers systemic blood pressure (SBP), decreasing renal blood flow and hence decreasing GFR. In addition, BNP inhibits angiotensin II production. Angiotensin II normally causes constriction of the efferent renal arterioles (increasing GFR). Inhibition of angiotensin II results in a decreased GFR.

In June 2005, the U.S. FDA and J&J issued a "Dear Doctor" letter reminding physicians that, "Nesiritide should be strictly limited to patients presenting to the hospital with acutely decompensated heart failure who have dyspnea at rest." The warning also urged physicians to consider the possible risks of the drug, and the availability of alternate therapies to relieve the symptoms of congestive heart failure. The warning finally notes that nesiritide should not be used for intermittent outpatient infusion, for scheduled repetitive use, to improve renal function, or to enhance diuresis. This was a significant blow to the sales prospect of the drug. Some even lobbied for the drugs withdrawal from the market. Sales of Natrecor in 2008 were only $64 million.

…A Wide Open Market…

The rise and fall of Natrecor sent physicians back almost a decade in treating ADHF. Natrecor's was headed towards blockbuster sales before the meta-analysis ended the run. Nitroglycerin and furosemide returned as the standards of care despite significant limitations. In our view, the market for an effective product is wide open. The objectives are simple, increase cardiac output while offloading fluid and preserving renal function. An effective product with the target profile listed below is sure to offer blockbuster potential.

Clinical Profile	Ideal Drug	Lasix	Nitro	Inotropes	Natrecor
Diuretic & Natriuretic	✓	✓	-	-	-
Preserve / Enhance Renal Function	✓	✗	-	✗	✗
Reduce Cardiac Filling Pressure	✓	✓	✓	✓	✓
Low Risk of Hypotension	✓	✓	✗	✓	-

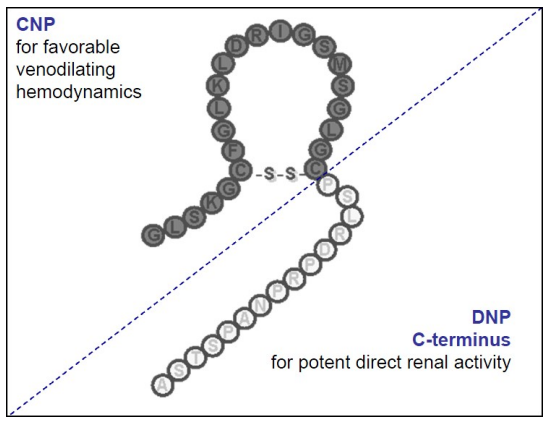
CD-NP

Nile Therapeutics is developing CD-NP, a chimeric natriuretic peptide currently in phase II clinical studies for the treatment of ADHF. CD-NP was rationally designed by scientists at the Mayo Clinic's cardio-renal research labs. CD-NP was designed to preserve the favorable effects of current therapies while eliminating or attenuating the hypotensive response, and enhancing or preserving renal function. Natriuretic peptides are naturally occurring proteins produced in the heart and blood vessels that cause natriuresis (the removal of sodium and water from the blood).

There are four naturally produced natriuretic peptides: atria "A-type" natriuretic peptide (ANP), brain "B-type" natriuretic peptide (BNP), cell "C-type" natriuretic peptide, (CNP), and dendroaspis "D-type" natriuretic peptide (DNP). These peptides possess potent natriuretic, diuretic, and vasodilating activities and are implicated in body fluid homeostasis and blood pressure control. Unlike ANP, BNP and DNP, CNP does not have direct natriuretic activity. This is because CNP is a selective agonist for the B-type natriuretic receptor (NPR_B) whereas ANP, BNP and DNP are selective for NPR_A. ANP, BNP and DNP have potent arteriodilation effects, whereas CNP has venodilation effects. ANP and BNP have direct renal effects offset by reduced renal perfusion. DNP, on the other hand is potent direct renal activator. CNP has no known renal effects.

Natriuretic Peptides	Receptor Target	Hemodynamic Effects	Renal Effects
ANP 	NPR_A	Arteriodilation	Renal Effects Offset by Reduce Perfusion
BNP 	NPR_A	Arteriodilation	Renal Effects Offset by Reduce Perfusion
CNP 	NPR_B	Venodilation	None
DNP 	NPR_A	Arteriodilation	Potent Direct Renal Activator

Niles' CD-NP is a combination of two natriuretic peptides, CNP and DNP. The scientists at the Mayo Clinic developed the drug combining the n-terminus of the CNP molecule, preserving the favorable venodilating and hemodynamic properties of the molecule, with the c-terminus of the DNP molecule, preserving the potent direct renal activity. Preclinical data demonstrates the drug has both natriuretic and diuretic properties. Animal studies yielded very encouraging data with respect to improvement in GFR (improvement in renal function) and less risk of hypotension as compared to BNP. Preclinical data on the mechanism of action was published in the Journal of the American College of Cardiology (ACC), Vol. 52, No. 1, 2008.

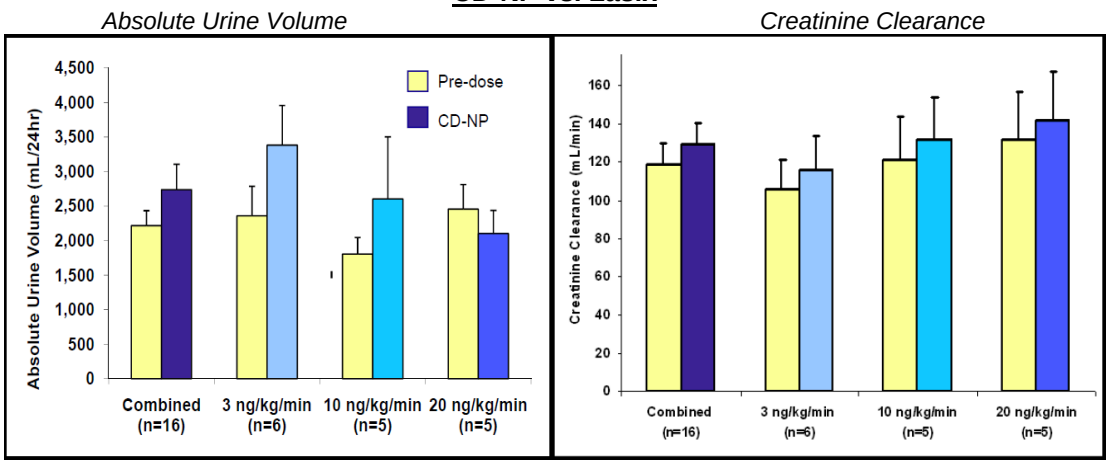


…Phase I & II Data…

In 2007, Nile conducted a phase Ia program in 22 healthy volunteers with a 4 hour IV infusion of CD-NP. The trial included an open-label dose-escalation cohort (10, 17.5, 25 ng/kg/min) and a double-blind cohort vs. placebo at the 17.5 ng/kg/min dose. Results demonstrated safety, as well as natriuretic and diuretic actions with preservation of GFR and minimal hypotension risk. Nile then conducted a phase Ib open-label dose escalating program in 20 patients with heart failure and evidence of intravascular volume (fluid) overload. The program assessed the pharmacodynamic, hemodynamic, and renal effects of a 24-hour IV infusion of CD-NP. Results demonstrated:

- ✓ CD-NP was well tolerated at doses up to 20 ng/kg/min
- ✓ A statistically significant reduction in serum creatinine
- ✓ A statistically significant increase in creatinine clearance
- ✓ Diuresis similar to Lasix
- ✓ Blood pressure effects were dose dependent and well characterized.

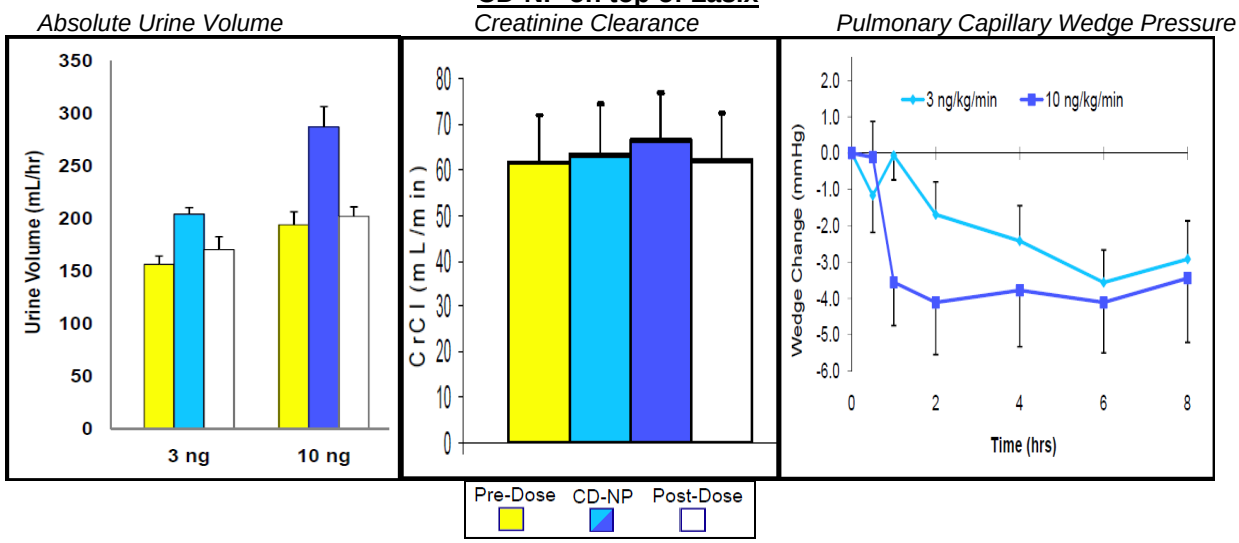
CD-NP vs. Lasix



The encouraging phase Ib data was follow-up by a phase IIa program initiated in July 2008 testing the proof-of-concept in 23 patients with "stabilized" acute heart failure. The trial was designed to assess the hemodynamic effects of CD-NP on patients with stabilized AHF in an open-label, dose escalating format. Patients received two 8 hour IV infusions of CD-NP, separated by a 14 hour washout period, on top of existing Lasix therapy. Preliminary top-line results were released demonstrated:

- ✓ A reduction in pulmonary capillary wedge pressure (PCWP)
- ✓ An increase in diuresis
- ✓ No symptomatic hypotension
- ✓ No observed change in renal function
- ✓ Dose response from the 3 to 10 ng/kg/min level

CD-NP on top of Lasix



There were no drug-related serious adverse events in the phase Ib or phase IIa program. In our view, the clinical program so far has been very astutely designed to assess the clinical effects of the drug. The phase Ia program studied the drug in healthy patients. The phase Ib moved dosing into patients with acute heart failure that has been stable for at least the past six months. In the phase IIa program, management tested CD-NP in patients with acute heart failure that have been stable for at least the past 24 hours. All the while the safety, pharmacokinetics and pharmacodynamics of the drug were being analyzed to plan for the larger phase II program.

…Phase II…

In June 2009, Nile initiated a phase II (NIL-CDNP-CT005) open-label, single-blind, placebo-controlled study designed to assess the safety and tolerability of 4 doses of CD-NP (1.25, 2.5, 3.75, and 5.0ng/kg/min) when infused for up to 72 hours in patients in the acute (presenting to the hospital) setting in combination with the standard of care (furosemide + vasoactive or inotropic agents) and mild to moderate renal insufficiency. Patients were followed for 30 days after infusion. The trial enrolled patients in the U.S. (~1/3rd), and Israel and Germany (~2/3^{rds}). In July 2010, Nile Therapeutics announced it had completed enrollment at 77 patients. The goal of the program was to characterize the dose-response and risk of hypotension.

On November 2, 2010, Nile Therapeutics announced that CD-NP had successfully completed the phase II study. Based on the data, CD-NP infusion at 1.25, 2.5 and 3.75 ng/kg/min appeared to be well tolerated. A dose-dependent effect on blood pressure was observed, with minimal or mild blood pressure reduction at 1.25 and 2.5 ng/kg/min, and moderate blood pressure reduction at 3.75 ng/kg/min. Dose escalation was limited by significant blood pressure reduction at 5 ng/kg/min.

Secondary efficacy endpoints were also evaluated during the trial. The data show favorable effects of CD-NP on renal function, particularly at the 1.25 and 2.5 ng/kg/min doses, with respect to preservation or enhancement of renal function compared to placebo, as evidenced by favorable trends in several biomarkers correlated with kidney function, including creatinine and cystatin-c. However, given the small size of the trial at only 77 patients, we do not expect these results to be statistically significant. Management may make additional data available early next year; however, we expect the full analysis to be presented at the American College of Cardiology meeting in April 2011.

…Next Up, Phase IIb In 2011…

The next steps for Nile is to finalize the design of a double-blind, placebo controlled phase IIb study and to discuss that trial design with the FDA and other regulatory authorities. Management's goal is to have this discussion with the U.S. FDA in early 2011. We expect this program to test 2 doses of CD-NP and enroll roughly 300-400 patients, with endpoints to include relief of symptomatic dyspnea, as well as analysis of biomarkers for kidney function and ischemia, as well as safety assessments including risk of hypotension, renal function, cardiovascular events, and mortality. The cost of this planned phase IIb program is estimated to be between $15 and $20 million.

…Commercialization Plans…

Following the successful completion of the phase II program discussed above, we believe the company will look to secure a development partnership for the next wave of clinical programs. This may or may not include the phase IIb program. We expect that management will seek to meet with the U.S. FDA to finalize the endpoints following the analysis of the current phase II trial. If management cannot secure a partnership on the above phase II data alone, we may see an interim cash raise coming soon. The cost of the phase IIb program is estimated at around $15 to 20 million. Nile, along with its partner, will need to conduct two phase III programs, one focusing on efficacy (dyspnea, kidney function biomarkers, cardiac output) and another focusing on safety (risk of hypotension, cardiovascular events, mortality). If these trials are completed on schedule, the duo should be in position to file a new drug application (NDA) around the middle of 2013, putting U.S. FDA action on CD-NP in 2014.

As noted above, there is a significant market opportunity for CD-NP. There are an estimated 1.2 million hospitalizations each year in the U.S. with the primary admission cause of acute decompensated heart failure (ADHF). Nearly three-quarters of these patients also have stage II or stage III chronic kidney disease (CKD). The majority (~75%) present with a systolic blood pressure (SBP) above 120 mmHg and would be eligible for treatment with a vasodilator. A product specifically indicated for the treatment of patients with ADHF with mild to moderate CKD, which is safe to use on top of Lasix, could have significant sales potential. The target profile is clear: improve dyspnea, remove excess fluid volume, and preserve kidney function. Do this, and there are at least 650k patients each year that could use the drug. The opportunity outside the U.S. is equally as attractive. We think that makes CD-NP a potential $500 million + product within a few years after launch.

In addition to Nile's current clinical program in ADHF, the mechanism of CD-NP presents an opportunity to develop the molecule in other indications, including preservation of cardiac function subsequent to acute myocardial infarction (AMI), and preservation of renal damage subsequent to cardiac surgery.

…Taking a Stab at Partnership Terms…

There are four deals we are using as a basis for predicting what a potential partnership between Nile Therapeutics and a larger or specialty pharmaceutical company on CD-NP could look like:

- J&J acquires Scios for $2.4 billion in February 2003. J&J paid a very hefty premium for Scios and Natrecor back in 2003. At the time of the deal close, Natrecor had trailing twelve-month sales of only $50 million. However, the trajectory was straight up, and J&J had hopes that Natrecor was going to be a blockbuster. We note that J&J has not given up on Natrecor however. The company is current conducting a massive, 10,000 patient outcome study over a four year period with Natrecor called ASCEND-HF (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure). ASCEND-HF is a testing lower doses of Natrecor with the goal to show reduced mortality. It began in September 2006 and is expected to offer data on November 14th at the American Heart Association (AHA) meeting in Chicago.

- Merck acquires NovaCardia for $350 million in July 2007: Valuing Merck's purchase of NovaCardia is a little difficult because the company was privately-held at the time of the deal. NovaCardia's lead product candidate, rolofylline (MK-7418), was an adenosine A1 receptor antagonist in phase III clinical trials in patients with acute congestive heart failure (CHF). KW-3902 was believed to block adenosine-mediated constriction of blood flow to the kidneys and inhibit reabsorption of salt and water by the kidney, thereby increasing urine volume and maintaining renal function in patients with CHF. Merck believed they would be first to market with a vasodilator that demonstrated that helps preserve renal function. Unfortunately for Merck, the drug failed its phase III program (PROTECT-1 and PROTECT-2) and future development is on hold.

- Novartis acquires Corthera for $120 million in December 2009: Novartis scooped up Corthera, and its phase III candidate, relaxin, for the potential treatment of acute decompensated heart failure (ADHF) in late 2009. Relaxin, a naturally occurring hormone, is a potent vasodilator, which has shown in previous clinical trials to increase cardiac output after a 48-hour infusion post hospitalization for ADHF. The $120 million seems like a steal for Novartis until you factor in the potential $500 million in future milestones the company could still owe to Corthera shareholders upon successful commercialization of the drug.

- Amgen licenses CK-1827452 from Cytokinetics for up to $675 million in May 2009: CK-1827452 is a novel cardiac myosin activator that has been the subject of a clinical trials program comprised of multiple Phase I and Phase IIa trials. In December 2006, Amgen paid Cytokinetics $75 million through a $42 million technology access fee and a $33 million equity investment to commence the development plan for CK-1827452. In May 2009, Amgen exercised an option, paying Cytokinetics $50 million, to take over development. Cytokinetics can earn an additional $525 million in future development and commercialization milestones from Amgen.

It is clear that a post phase II candidate in this space is worth at least $350 million. However, given the failures of the Merck deal, and what happened with Natrecor at J&J, we are not surprised at all to see Novartis acquire Corthera with a heavily back-end loaded milestone format. Amgen did the same thing with Cytokinetics. The first $75 million upfront was staggered between a technology fee and equity investment. The initial deal was doen when CK-1827452 was only in phase I trials. Amgen came back three years later with another $600 million to secure the compound after phase IIa data showed encouraging results. Over the past year we are starting to see more and more pharma-biotech deals taking this upfront + future cash format. If management at Nile is looking to sell the entire company, we expect a similar type deal.

The question is when Nile looks to sell or partner. Obviously the farther along the development timeline management can take CD-NP the more money they will command on the open market. Positive phase II results in the current ongoing trial probably puts the value of the program at $80 to 100 million. Not bad considering the current market capitalization is only $30 million. Positive phase IIb results in the next 330 patient program means Nile can probably sell for $300 million or higher. However, management will need to bridge that financing gap between the current phase II program and the completion of a large-scale phase IIb. The company may need to raise as much as $20 million to conduct this trial on its own.

…Preclinical Pipeline…

Besides CD-NP, Nile Therapeutics also licensed CU-NP from the Mayo Clinical. Similarly to CD-NP, CU-NP arose from the cardio-renal research labs in an attempt to create the ideal pharmaceutical candidate for the treatment of heart failure. CU-NP was designed to combine the favorable hemodynamic venodilating effects of CNP generated via NPR_B receptor agonism, with the beneficial renal effects of Urodilatin (URO) generated via NPR_A receptor agonism. In animal models, CU-NP was shown to increase natriuresis, diuresis, and glomerular filtration (GFR) rate in a dose dependent manner, decrease cardiac filling pressure, and inhibit the renin-angiotensin system without inducing significant hypotension. The company is currently working on preclinical pharmacological studies to evaluate formulations and dose levels of CU-NP for chronic administration. If feasible, Nile plans to initiate pre-clinical toxicology and manufacturing activities in 2010.

RECOMMENDATION

We see a significant market opportunity for CD-NP. There are an estimated 1.2 million hospitalizations each year in the U.S. with the primary admission cause of acute decompensated heart failure (ADHF). Nearly three-quarters of these patients also have stage II or stage III chronic kidney disease (CKD). The majority (~75%) present with a systolic blood pressure (SBP) above 120 mmHg and would be eligible for treatment with a vasodilator. A product specifically indicated for the treatment of patients with ADHF with mild to moderate CKD, which is safe to use on top of Lasix, could have significant sales potential. The target profile is clear: improve dyspnea, remove excess fluid volume, and preserve kidney function. Do this, and there are at least 650,000 patients each year that could use the drug. The opportunity outside the U.S. is equally as attractive.

Natrecor (nesiritide), a recombinant form of the 32 amino acid human B-type natriuretic peptide (BNP), entered the market in 2001. By 2004 the drug was annualizing over $400 million in revenues and on its way to $1 billion. J&J acquired Natrecor's developer, Scios, for $2.4 billion in February 2003. Natrecor was priced aggressively – roughly $10,000 for a 72-hour treatment. Generic alternatives including nitroglycerine and furosemide cost virtually nothing in comparison. At this point, estimating a price on CD-NP is a difficult task. We have yet to see the phase II data. However, phase I data and the mechanism of action are extremely promising. Even assuming a price for the drug half that of the flawed Natrecor gets us to peak sales at $500 million. And in addition to Nile's current clinical program in ADHF, the mechanism presents an opportunity to develop the molecule in other indications, including preservation of cardiac function subsequent to acute myocardial infarction (AMI), and preservation of renal damage subsequent to cardiac surgery.

We think if CD-NP can demonstrate effectiveness in the planned phase IIb, Nile can fetch at least $300 million on a takeover in 2011 or 2012. However, shareholders may not have to wait that long to reap their rewards. Our expectation is that management will look to secure funding from a partner after the phase II data comes out around the middle of this year. We could be looking at an upfront payment plus potential takeover milestones in 2011. Or management could look for an equity investment from a potential partner to conduct the phase IIb program. What is clear to us is that with a market capitalization of only $20 million, Nile Therapeutics shares are bafflingly under-valued. We believe with positive data in hand, the company is worth at least $80 to 100 million. Taking the mid-range at $90 million, and then backing out the $20 million most likely required to fund the phase IIb program, we arrive at a value of $70 million for Nile Therapeutics. This equates to a price of $2.00 per share.

PROJECTED FINANCIALS

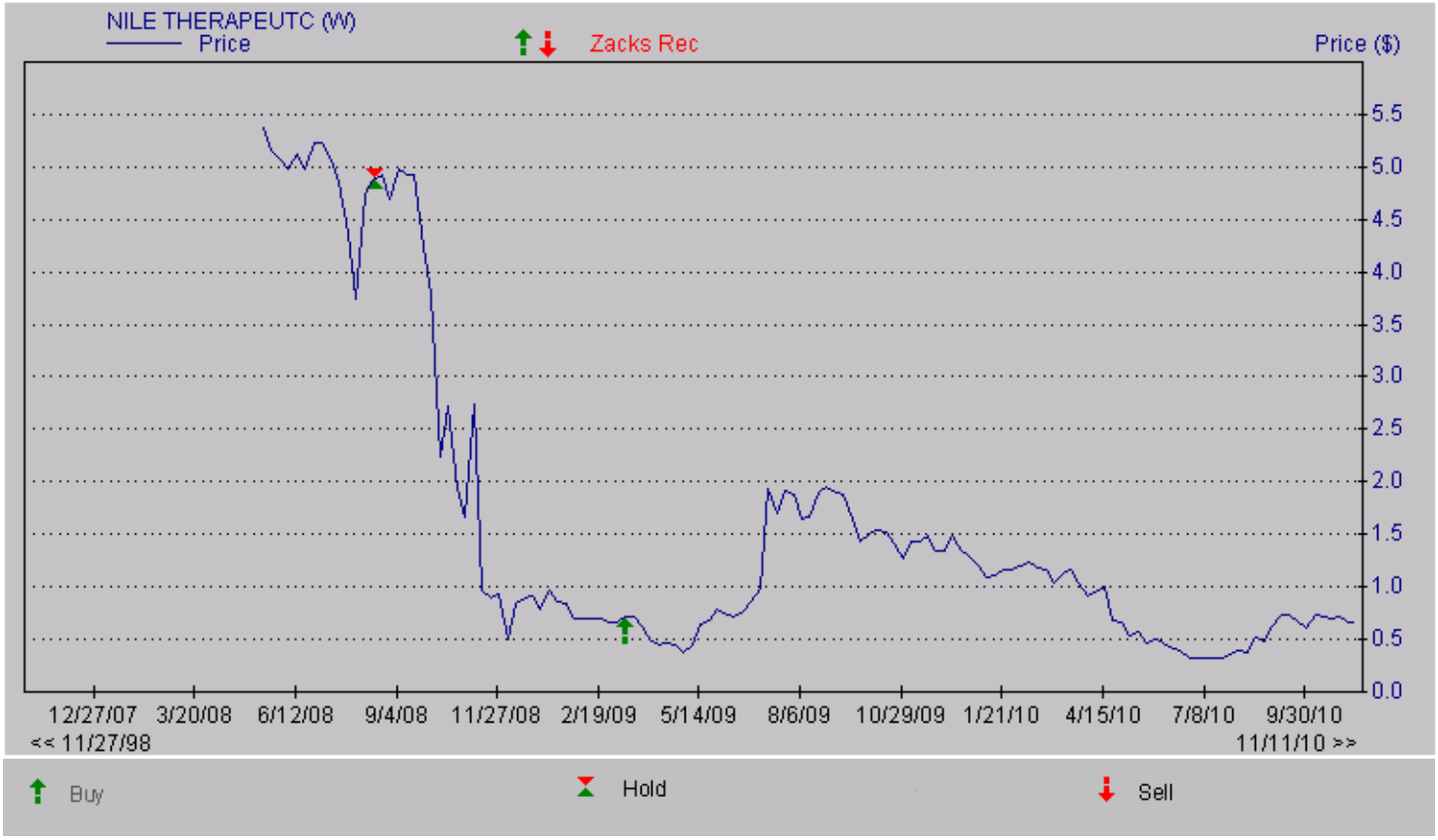
Nile Therapeutics, Inc.
Income Statement

	2009 A	Q1 A	Q2 A	Q3 A	Q4 E	2010 E	2011 E	2012 E	2013 E	2014 E
CD-NP (U.S. Sales)	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-	-
CD-NP (Row Sales)	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-	-
CD-NP (Royalties)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-	-	-
Grants, Licenses & Milestones	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$10.0**	**$20.0**	**$25.0**	**$25.0**
YOY Growth	-	-	-	-	-	-	*100.0%*	*100.0%*	*25.0%*	*0.0%*
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$10.0**	**$20.0**	**$25.0**	**$25.0**
YOY Growth	-	-	-	-	-	-	*100.0%*	*100.0%*	*25.0%*	*0.0%*
CoGS	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	*0%*	-	-	-	-	*0.0%*	*0%*	*0%*	*0%*	*0%*
R&D	$4.5	$1.3	$1.1	$1.1	$0.7	$4.2	$15.0	$15.0	$10.0	$5.0
% R&D	-	-	-	-	-	-	*150.0%*	*75.0%*	*40.0%*	*20.0%*
SG&A	$3.4	$0.6	$0.4	$0.7	$0.6	$2.3	$2.5	$3.0	$4.0	$5.0
% SG&A	-	-	-	-	-	-	*25.0%*	*15.0%*	*16.0%*	*20.0%*
Operating Income	($7.9)	($1.9)	($1.5)	($1.8)	($1.3)	($6.6)	($7.5)	$2.0	$11.0	$15.0
Operating Margin	*0%*	-	-	-	-	*0.0%*	*-75.0%*	*10.0%*	*44.0%*	*60.0%*
Interest & Other Income	($0.1)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.1	$0.3	$0.4	$0.4
Pre-Tax Income	($7.9)	($1.9)	($1.5)	($1.8)	($1.3)	($6.5)	($7.4)	$2.3	$11.4	$15.4
Taxes	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($7.9)	($1.9)	($1.5)	($1.8)	($1.3)	($6.5)	($7.4)	$2.3	$11.4	$15.4
Net Margin	*0%*	-	-	-	-	*0.0%*	*-74.0%*	*11.5%*	*45.6%*	*61.6%*
Reported EPS	**($0.31)**	**($0.07)**	**($0.05)**	**($0.05)**	**($0.04)**	**($0.20)**	**($0.21)**	**$0.06**	**$0.30**	**$0.39**
YOY Growth	-	-	-	-	-	*-34.9%*	*1.1%*	*-130.2%*	*382.6%*	*31.6%*
FAS-123R Expense	$2.2	$0.4	$0.2	$0.4	$0.3	$1.3	$1.8	$2.0	$2.5	$3.0
EPS Impact of FAS-123R	*($0.09)*	*($0.02)*	*($0.01)*	*($0.01)*	*($0.01)*	*($0.04)*	*($0.05)*	*($0.05)*	*($0.07)*	*($0.08)*
Weighted Ave. Shares Out	25.5	27.1	32.3	34.6	34.7	32.2	36.0	37.0	38.0	39.0

Source: Zacks Investment Research, Inc. *Jason Napodano, CFA*

© Copyright 2010, Zacks Investment Research. All Rights Reserved.

HISTORICAL ZACKS RECOMMENDATIONS



DISCLOSURES

The analysts contributing to this report do not hold any shares of NLTX.

Zacks Investment Research may have, or seeks to have, a business relationship with the companies listed in this report. Additionally, the analysts contributing to this report certify that the views expressed herein accurately reflect the analysts' personal views as to the subject securities and issuers. Zacks certifies that no part of the analysts' compensation was, is, or will be, directly or indirectly, related to the specific recommendation or views expressed by the analyst in the report. Additional information on the securities mentioned in this report is available upon request. This report is based on data obtained from sources we believe to be reliable, but is not guaranteed as to accuracy and does not purport to be complete. Because of individual objectives, the report should not be construed as advice designed to meet the particular investment needs of any investor. Any opinions expressed herein are subject to change. This report is not to be construed as an offer or the solicitation of an offer to buy or sell the securities herein mentioned. Zacks or its officers, employees or customers may have a position long or short in the securities mentioned and buy or sell the securities from time to time. Zacks uses the following rating system for the securities it covers. **Outperform**- Zacks expects that the subject company will outperform the broader U.S. equity market over the next one to two quarters. **Neutral**- Zacks expects that the company will perform in line with the broader U.S. equity market over the next one to two quarters. **Underperform**- Zacks expects the company will under perform the broader U.S. Equity market over the next one to two quarters. The current distribution of Zacks Ratings is as follows on the 1007 companies covered: Outperform- 13.2%, Neutral- 80.0%, Underperform – 6.3%. Data is as of midnight on the business day immediately prior to this publication.

© Copyright 2010, Zacks Investment Research. All Rights Reserved.