Zacks Small-Cap Research

February 28, 2011
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Nile Therapeutics, Inc. (NLTX-NASDAQ)

NLTX: Medtronic On Board For Phase 1 Study In New Post-Acute Indication.

Current Recommendation	**Outperform**
Prior Recommendation	N/A
Date of Last Change	01/26/2010
Current Price (02/28/10)	$0.52
Target Price	**$2.00**

UPDATE

This morning Nile Therapeutics announced it would seek a new indication for cenderitide (formerly CD-NP). Nile will study the effects of cenderitide administered via a continuous infusion pump for out-patient care following discharge from the hospital. Medtronic, make of the MiniMed Paradigm Infusion Pump, will fund a phase 1 pk/pd study to begin in the second quarter 2011. Nile believes that cenderitide may qualify for FDA “Fast Track” status in this new “post-acute” indication. Management continues its plans to partner cenderitide for the acute (in-hospital) indication. We are expecting that a deal will get done to fund the phase 2b program later this year. If all goes well, Nile could be in position to have 2 phase 2 programs with cenderitide ongoing in 2012. We reiterate our ‘Outperform’ rating and $2 target.

SUMMARY DATA

52-Week High	**$1.20**
52-Week Low	**$0.30**
One-Year Return (%)	**-52.54**
Beta	**1.88**
Average Daily Volume (sh)	**85,257**
Shares Outstanding (mil)	**35**
Market Capitalization ($mil)	**$19**
Short Interest Ratio (days)	**0.07**
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 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					0 E
2012					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					-$0.16 E
2012					-$0.17 E

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

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WHAT'S NEW

New Post-Acute Indication

On February 28, 2011, Nile Therapeutics announced it will seek development of cenderitide (formerly CD-NP) in a new indication, seeking to treat patients with acutely decompensated heart failure (ADHF) on an outpatient basis for up to 90 days after discharge from the hospital. Nile plans to file a new Investigational New Drug (IND) application for this "post-acute" indication within the next few weeks. We remind investors that management met with the U.S. FDA on the future development plans for cenderitide in ADHF earlier this year. Following that meeting, management believes that cenderitide could qualify for FDA "Fast Track" status development status. We expect an application in this regard here before the end of the second quarter 2011.

...Medtronic To Fund Phase I Study…

In a separate announcement this morning, Nile also noted that it has teamed up with medical device maker, Medtronic, for a phase 1 pharmacokinetic (pk) / pharmacodynamic (pd) study testing cenderitide delivered through Medtronic's MiniMed Paradigm Insulin Pump. In the planned clinical trial, cenderitide will be delivered to heart failure patients for up to 24 hours through continuous subcutaneous infusion following discharge from the hospital. We expect this program will enroll in the area of 40-50 patients, looking to determine what subcutaneous dose of this new formulation of cenderitide will match plasma levels that management previously determined to be safe and effective in the company's phase 2a program under continuous 72-hour infusion. Financial terms were not disclosed, but we estimate this program, along with some manufacturing work, will cost roughly $2 million. We expect this study will get underway in the second quarter 2011 and offer data early next year.

If the phase 1 pk / pd study is successful, we expect Nile to seek a development partner, which may or may not be Medtronic, for a phase 2a double-blind, placebo-controlled, dose-ranging study to start during the second quarter of 2012. We would expect this program to include endpoints in cardiac remodeling, renal function, re-hospitalization, and mortality. Previous data with cenderitide is supportive of the potential here. Cenderitide was designed to provide cardiac unloading while maintaining renal function. Nile believes that the continuous and extended infusion of cenderitide through a subcutaneous pump will provide patients with sustained symptomatic relief in the outpatient setting that could contribute to a reduction in post-acute hospitalizations and persistent improvement in outcomes.

We remind investors that in November 2010, the company released encouraging data from a phase 2a (n=77) trial testing cenderitide in an "acute" (in-hospital) 72-hour continuous infusion. The data show favorable effects on renal function compared to placebo, and favorable trends in several biomarkers correlated with kidney function, including creatinine and cystatin-c. A full analysis from this trial will be available shortly, and may be presented at the American College of Cardiology meeting in April 2011.

…Potential Blockbuster Indication…

We believe this new "post-acute" indication could be a blockbuster opportunity for cenderitide. In the U.S., approximately 5.5 million people (~2% of the population) suffer from heart failure (HF). 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 15 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. Mortality at 1-year is over 10%.

Nile and Medtronic are looking at the potential to administer cenderitide continuously for 90-day using Medtronic's MiniMed Paradigm pump currently used for continuous infusion of insulin. If Nile can capture only 10% of these patients, at a cost of $5,000 per treatment, sales would be $600 million. We think the opportunity exists to charge even more for this therapy given the high burden and unmet medical need.

The potential to use cenderitide in a post-acute indication is very exciting in our view. There are currently no approved heart failure drugs targeting cardio-renal improvement in an outpatient setting. Management will seek a development partner for this indication following the phase 1 pk / pd data. The logical partner here would be Medtronic, keeping cenderitide and the MiniMed Paradigm together. However, other potential partners could be interested, and the ideal situation for Nile shareholders would be a bidding war.

Talks Continue For Hospital Indication

Management is also continuing discussions with potential partners on the acute setting for cenderitide. Talks include the potential for Ex-U.S. rights to cenderitide as well. The next steps for an acute indication would be to initiate a double-blind, placebo controlled phase 2b study. We expect this trial to test two doses of cenderitide 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 trial could run upwards to $20 million, so Nile clearly needs a partner here.

…A Wide Open Market…

The rise and fall of Natrecor (nesiritide) sent physicians back almost a decade in treating ADHF. Natrecor was headed towards blockbuster sales before the “Dear Doctor” letter ended its 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	✓	✓	✗	✓	-

Based on preclinical, phase 1, and phase 2a data, cenderitide looks to possess all the characteristics of an ideal drug for ADHF.

OVERVIEW

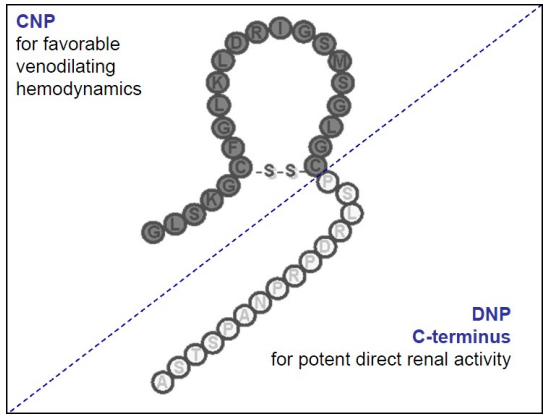
Cenderitide

Nile Therapeutics is developing cenderitide, a chimeric natriuretic peptide currently in phase II clinical studies for the treatment of ADHF. Cenderitide was rationally designed by scientists at the Mayo Clinic's cardio-renal research labs. The candidate 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.



…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 cenderitide 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 in November 2010 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 3 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 3 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 3 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 1 and Phase 2a 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. Amgen and Cytokinetics plan a phase 2b program for later in 2011. Cytokinetics can earn an additional $525 million in future development and commercialization milestones from Amgen.

It is clear that a post phase 2 candidate in this space is worth in the area of $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 done when CK-1827452 was only in phase 1 trials. Amgen came back three years later with another $600 million to secure the compound after phase 2a. Over the past year we seeing 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 cenderitide, the more money they will command on the open market. This is what is particularly exciting about the phase 1 deal for the post-acute indication with Medtronic. Nile gets the potential to test its drug in a new, blockbuster, indication and Medtronic is paying for the whole thing. Positive phase 2 data with the acute or post-acute trial puts the value of the candidate at $80 to 100 million in our view. Not bad considering the current market capitalization is only $20 million. If Nile can get cenderitide ready for phase 3 trials, the value may be even higher.

RISKS

Nile faces two key risks. The first is that partnership talks around cenderitide will drag into 2012, and the company will need to raise cash to fund operations in the fourth quarter 2011. We estimate that Nile would seek to raise $4-5 million, or around a 20% dilution at today's capitalization. The second risk is that the full data analysis from the phase 2a program with cenderitide in underwhelms, or the phase 1 pk / pd study being conducted with Medtronic fails to establish a safe and effective dose. Under this scenario, Nile may struggle to ever partner cenderitide.

RECOMMENDATION

We remain optimistic on Nile Therapeutics and the potential for cenderitide. We are excited to see the company team up with Medtronic to explore a potential new indication for the drug. We have previously stated that with positive phase 2b data in hand, Nile is worth an estimated $80 to $100 million. This is how we arrive at our $2 price target. However, Nile now has potentially two chances to generate this data, one in the acute (in hospital indication) and another in the post-acute (out-patient) setting. The post-acute indication has the potential to receive U.S. FDA "Fast Track" development status. With a current market capitalization of only $20 million, Nile Therapeutics looks bafflingly under-valued.

Based on our financial model, Nile exited 2010 with an estimated $3.1 million in cash. We think this is enough cash to fund operations into the fourth quarter 2011. We remind investors that Medtronic is paying for the planned phase 1 pk / pd study in the post-acute indication. We do not expect Nile to conduct any additional studies in the acute indication without a development partner. Management has reported being in discussion with several interested parties around cenderitide. We remind investors that Nile met with the U.S. FDA earlier this year, and plans to provide additional information around these discussions and full data from the recently completed phase 2a program shortly. Partners are most likely waiting to see this data and hear how the meeting with the FDA went.

Accordingly, we expect management to strike a deal later this year, and would be buyers of the stock ahead of this major upside potential. We view Nile has a high risk / high reward speculative play, where at $0.52 the stock is trading like a call option. Our target is $2 / 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
cenderitide (U.S. Sales)	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-	-
cenderitide (Row Sales)	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-	-
cenderitide (Royalties)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-	-	-
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-	-	-
R&D	$4.5	$1.3	$1.1	$1.1	$0.7	$4.2	$4.5	$5.0	$5.0	$5.0
% R&D	-	-	-	-	-	-	-	-	-	-
SG&A	$3.4	$0.6	$0.4	$0.7	$0.6	$2.3	$2.5	$3.0	$3.0	$3.0
% SG&A	-	-	-	-	-	-	-	-	-	-
Operating Income	($7.9)	($1.9)	($1.5)	($1.8)	($1.3)	($6.6)	($7.0)	($8.0)	($8.0)	($8.0)
Operating Margin	*0%*	-	-	-	-	*0%*	*0%*	*0%*	*0%*	*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)	($6.9)	($7.7)	($7.6)	($7.6)
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)	($6.9)	($7.7)	($7.6)	($7.6)
Net Margin	*0%*	-	-	-	-	*0%*	*0%*	*0%*	*0%*	*0%*
Reported EPS	**($0.31)**	**($0.07)**	**($0.05)**	**($0.05)**	**($0.04)**	**($0.20)**	**($0.19)**	**($0.21)**	**($0.20)**	**($0.19)**
YOY Growth	-	-	-	-	-	*-34.9%*	*-5.7%*	*8.6%*	*-3.9%*	*-2.6%*
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*

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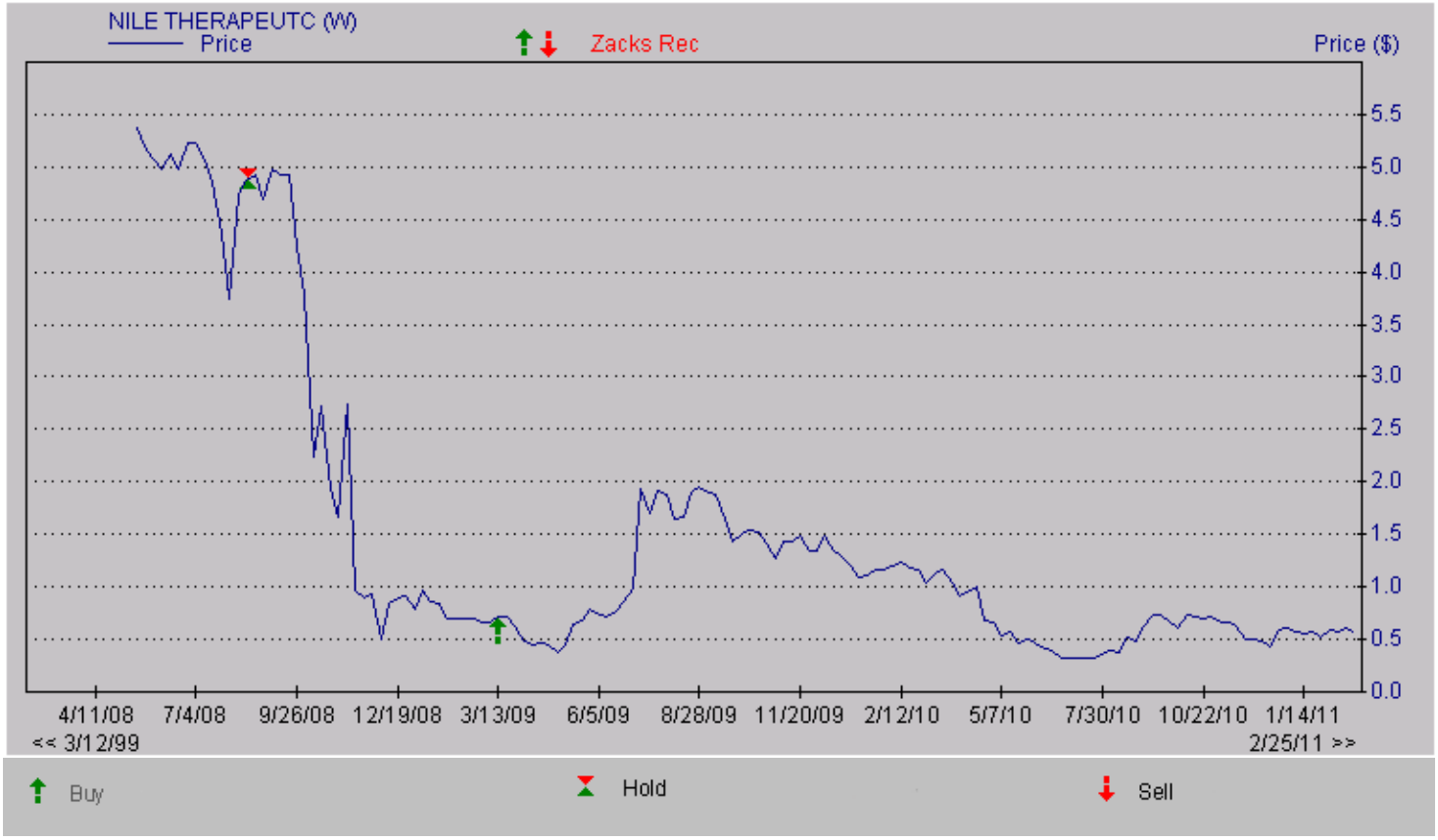
HISTORICAL ZACKS RECOMMENDATIONS



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The current distribution of Zacks Ratings is as follows on the 1018 companies covered: Buy/Outperform- 15.4%, Hold/Neutral- 77.6%, Sell/Underperform – 6.1%. Data is as of midnight on the business day immediately prior to this publication.

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