Zacks Small-Cap Research

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Medgenics Inc (MDGN-AMEX)

MDGN: neuroFix Acquisition Could Be a Needle-Mover

Current Recommendation	**Buy**
Prior Recommendation	N/A
Date of Last Change	06/08/2014
Current Price (09/11/15)	$7.49
Target Price	**$12.00**

OUTLOOK

With proof-of-concept accomplished, Biopump is being further validated in a recently initiated phase I/II study - preliminary data from which has been very promising.

Rare/orphan disease markets are particularly attractive due to certain incentives and inherent economics. Clinical development may also be accomplished faster, cheaper and with lower risk.

Recent neuroFix acquisition brought high-potential NFC-1 candidate. Ph 1 data looks very encouraging. This could move rapidly through development and be the first commercialized product - could address both ADHD and orphan indications. Add'l positive data, expected in 2016, we think could be a needle-mover to the share price.

SUMMARY DATA

52-Week High	**$9.63**
52-Week Low	**$3.68**
One-Year Return (%)	**27.44**
Beta	**0.38**
Average Daily Volume (sh)	**204,129**
Shares Outstanding (mil)	**25**
Market Capitalization ($mil)	**$187**
Short Interest Ratio (days)	**9.45**
Institutional Ownership (%)	**25**
Insider Ownership (%)	**27**
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 2015 Estimate	**N/A**
P/E using 2016 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Avg.,**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(in '000s of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	0 A	0 A	0 A	0 A	0 A
2015	0 A	0 A	0 E	0 E	0 E
2016					0 E
2017					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	-$0.28 A	-$0.21 A	-$0.16 A	-$0.30 A	-$0.96 A
2015	-$0.36 A	-$0.24 A	-$0.29 E	-$0.28 E	-$1.17 E
2016					-$1.03 E
2017					-$0.86 E

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

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MDGN Acquires CNS Compound

MDGN will acquire neuroFix Therapeutics, LLC and its lead candidate NFC-1, a compound targeting CNS disorders associated with mutations of the metabotropic glutamate receptors (mGluRs). Initial focus will be on Attention Deficit Hyperactivity Disorder (ADHD), where Phase 1 data showed promising results and which a Phase 2/3 study is expected to commence in early 2016, and 22q11.2 Deletion Syndrome, a rare condition also associated with mGluR mutations and one which may offer orphan status opportunities (both specifically for 22q11.2 Deletion Syndrome as well as associated indications).

This is the first opportunity to come from MDGN's relationship with CHOP (management noted on the presentation call that they believe this is just the first of many to come). To be clear, this is an extension of the company's overall focus and MDGN remains highly committed to their $TARGT_{EPO}$ and overall gene therapy programs.

neuroFix was founded by Dr. Hakon Hakonarson, Director of the Center for Applied Genomics at CHOP, in order further develop NFC-1. Prior to MDGN's acquisition, neuroFix licensed certain technology related to ADHD and other neurological and neuropsychological indications from CHOP.

Terms of the deal;

- $2M upfront in cash
- $6M in cash and common stock upon earlier of achievement of a "corporate milestone" (specifics of which were not disclosed) or March 31, 2016
- additional payments of up to $450M upon achievement of certain milestones (development, regulatory and sales) related to an oral formulation of NFC-1 and any new chemical entity (NCE) developed covering the same indication (specifics in terms of exactly what this relates to and what the triggers are were not disclosed)
- sales royalties based on tiered rates ranging from mid-to-high single digits depending on the product or NCE
- $25M for each FDA approved indication beyond the initial indication

Terms of License Agreement between neuroFix and CHOP;

- up to $1.5M in regulatory and sales milestones for each FDA approved indication using IP covering the agreement
- sales royalties based on a fluctuating rate in the low single digits - which adjust downward based on the extent of third party royalties
- $100k or less in annual maintenance fees
- a percentage (ranging from mid-single digits to mid-teens) of any sublicense income (ex-sublicensed sales by a certain party in Japan)
- this license agreement terminates upon the later of the expiration of certain CHOP patent rights and January 1, 2025, at which time neuroFix owns the covered licensed rights

Metabotropic Glutamate Receptors (mGluRs)

The amino acid glutamate is the most prominent excitatory neurotransmitter in the brain. It binds to mGluRs which are involved in the modulation of synaptic transmission and neuronal excitability in the central and peripheral nervous system. Genetic mutations of genes within the mGluR network have been associated with certain conditions including ADHD, anxiety disorders, schizophrenia and other neuropsychiatric disorders.

Research conducted by Dr. Hakonarson and colleagues indicated that mutations in the mGluR gene network are associated with a 10x higher rate of ADHD. They found that disruptions specifically to GRM1 (glutamate receptor, metabotropic 5), GRM3, GRM 7 and GRM8 were associated with ADHD.

NFC-1 GREAT Study

neuroFix, in collaboration with CHOP, conducted a Phase 1, 30-patient, single arm study at Thomas Jefferson University (Philadelphia) assessing NFC-1 in adolescents with ADHD. Inclusion criteria included professionally diagnosed with ADHD and genotyped as having disruptions to the mGluR network. The background of the enrolled population had certain symptoms which could be considered particularly challenging to effectively treat including;

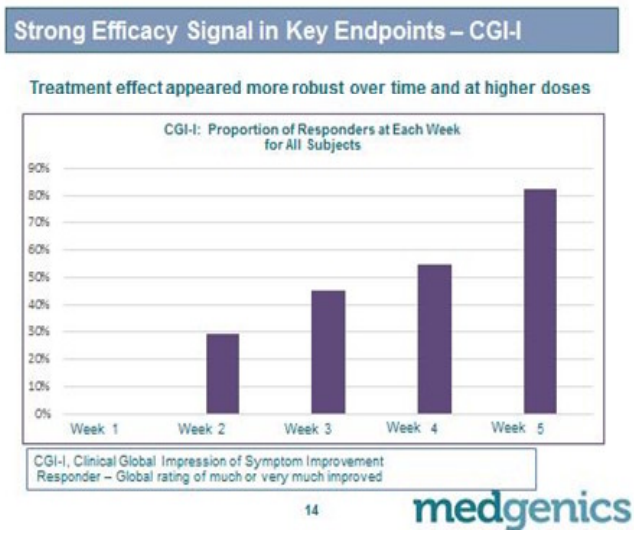
- 73% had severe ADHD (CGI-S>5, on a scale of 1=normal to 7=extremely ill)
- 67% had co-morbid psychiatric conditions such as anxiety, ODD and insomnia

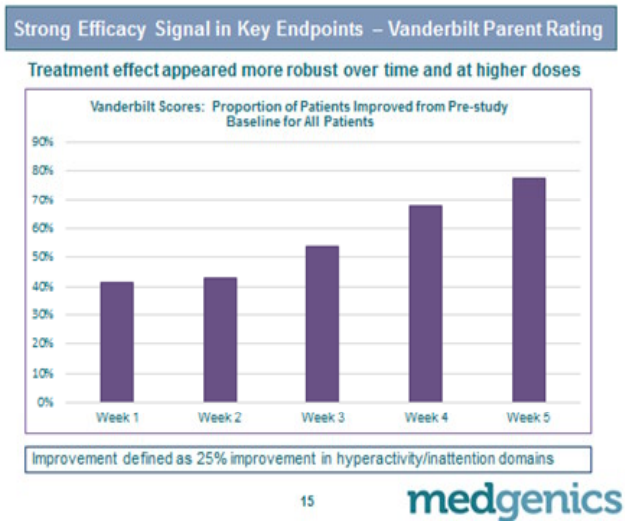
- 30% were on antipsychotics and/or antidepressants
- 70% had been previously treated with ADHD drugs (with presumably little benefit)

One-week run-in on placebo was followed by four weeks of active treatment. Treatment was dose-escalating from 50mg (x2/day) to a maximum of 400mg (x2/day). Dose was escalated weekly. Patients were blinded, clinicians were not. Primary endpoint was safety, secondary endpoint efficacy measures were standard ADHD assessments including Vanderbilt and Clinical Global Impressions (CGI) scores.

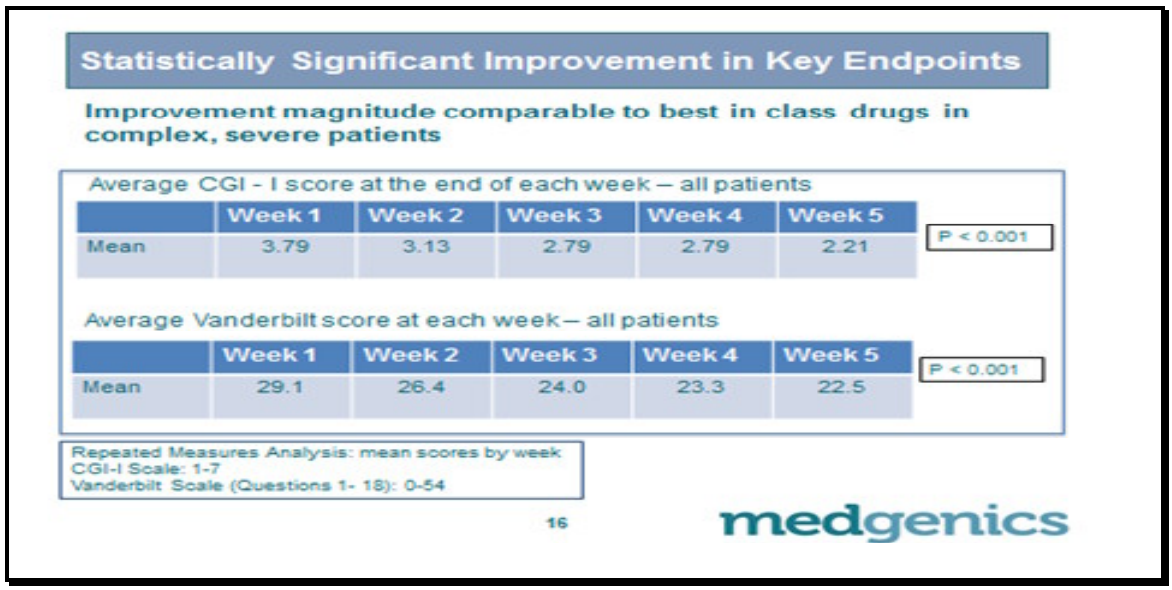
Full results will be presented at AACAP in late October in San Antonio. Management also provided a glimpse of the data on the call announcing the transaction which included;

- dose and time-dependent response on both the CGI-I and Vanderbilt measures
  - over 80% of patients responded to NFC-1 treatment on Vanderbilt measure at week 5
  - just under 80% of patients responded NFC-1 treatment on CGI-I measure at week 5
  - Repeated measure analysis showed statistically significant response on both measures over time and at higher doses
- Mutations to "tier 1" genes (i.e those in the mGluR receptors) and "tier 2" genes (i.e. those that encode proteins that influence mGluR but are not in the receptors) showed much higher response rates compared to "tier 3" genes (more distant from the receptors and therefore likely to show lower response)
- Excellent safety with no treatment related serious adverse events
- 20 of the 30 patients chose to continue to receive NFC-1 therapy in an ongoing long-term safety trial. As management noted in their presentation, this is clearly a positive vote of confidence in the efficacy of NFC-1 given that there's a significant hassle involved in coming to the clinic on a regular basis to receive treatment (i.e. - it's unlikely patients/parents would continue if they experienced no positive effect)





Dose and time dependent response on both the CGI-I and Vanderbilt ADHD measures. CGI-I is a clinician-rated assessment score and standard ADHD measure. Vanderbilt is a parent-rated assessment based on frequency of 47 symptoms.



We note that there is the risk of unintended bias in the CGI-I score given that the clinician was not blinded in this study (management noted that the clinician is highly qualified in ADHD assessment, which we acknowledge is likely a mitigating factor). Risk of bias, however, is not relevant with Vanderbilt which is a parent-rated assessment as the parents were blinded in the study - and both CGI-I and Vanderbilt demonstrated dose and time dependent response, indicating that NFC-1 is effective in ADHD treatment. The planned upcoming Phase 2/3 will be double-blinded and therefore will not be at risk of bias.

Phase 2/3 Study

Given the more pronounced response in tier 1 and tier 2 gene mutations, which are believed to account for approximately 20% of the ADHD population, this will be an inclusion criteria in the Phase 2/3 trial. MDGN is still in process of putting the specific trial design together (hope to meet with FDA in that regard later this year) but expects;

- primary efficacy endpoints to be ADHD RS (parent-assessment) and CGI-I
- is expected to serve as the pivotal trial (although a Phase 3 confirmatory trial is anticipated)
- aiming to initiate in Q1 2016 with initial data in H2 2016

Anticipated enrollment was not provided on the call but certainly expect it to be significantly larger than Phase 1 (n=30). It will be controlled, randomized, double-blind and powered for statistical significance - as such we think the initial data read-out could provide a lot more insight into the efficacy of NFC-1 in ADHD.

ADHD Market Is Attractive: *Positive Phase 2/3 Data Could Be a Needle-Mover to Share Price*

ADHD could be a hugely attractive market for MDGN and a genetic-based therapy including the significant size of the market, ambiguity of diagnosis and unmet need for therapies which are more effective and have less problematic side effect profiles.

- ~6M children (ages 3 - 7) are diagnosed with ADHD in the U.S. This equates to ~10%
- ADHD is the most common neurobehavioral disorder diagnosed in the U.S.
- No definitive test exists to diagnose ADHD - all ADHD diagnoses are arbitrary based on subjective assessment
- Stimulants such as Adderrall (amphetamine and dextroamphetamine), Vyvanse (lisdexamfetamine) and ritalin (methylphenidate) account for over 90% of ADHD prescriptions. These drugs are associated with significant side effects including risk of addiction, irritability and difficulty sleeping, among others. They are highly regulated due to their risk of addiction. These stimulants do not always address all of the underlying symptoms which often can include anxiety and psychotic disorders - mGluR mutations have been associated with other psychiatric conditions which means NFC-1 may be able to address not only ADHD but other of these conditions as well

Unlike stimulants NFC-1 (MDGN has not identified the molecule as additional IP is still being locked down) does address the underlying cause of ADHD. In addition, diagnosis (of mGluR mutations) is genetically-based, not arbitrary. It also (in clinical trials to-date, which includes a 1,000+ patient study in vascular dementia), has

shown an excellent side-effect profile. And 10% - 20% of the entire U.S. ADHD market is ~600k - 1.2M people - which is very significant for a company of MDGN's size, particularly given that the benefits of NFC-1 over stimulants should offer the opportunity for premium pricing. We think it is conceivable that mGluR+ADHD could easily represent a multi-billion dollar market opportunity. As such, if the planned Phase 2/3 study confirms what was demonstrated in Phase 1, **we think this could be a needle-mover to the share price.**

22q11.2 Deletion Syndrome: *Orphan Opportunity for NFC-1 to Address Related Psychological Disorders*

22q11.2 Deletion Syndrome is a relatively rare disease with incidence (per *The International 22q11.2 Foundation Inc*.) estimated at one in every 1,000 live births - which equates to about 4,000 new cases every year in the U.S (~130k worldwide). We have not been able to find an estimate of prevalence rates, although management noted on the call that U.S. prevalence is believed to be approximately 75k - 100k.

22q11.2 Deletion Syndrome is characterized by the deletion on the long arm of one pair of chromosome 22 (region 1, band 1, sub-band 1). The disorder can affect most systems in the body and is associated with serious physical and neuropsychological problems including cardiovascular issues, cleft palate, abnormal facial features, immune disorders and behavioral, psychotic and anxiety disorders (including ADHD). And while many of the physical problems such as heart defects and cleft palate can be addressed by traditional medical intervention such as surgery, there are no current therapies available to address the psychological disorders. It is estimated that about 30% - 40% of individuals with 22q11.2 Deletion Syndrome will eventually progress to schizophrenia.

And mGluR mutations appear to play a roll in 22q11.2 Deletion Syndrome with over 90% of 22q11.2 Deletion Syndrome patients having at least one mGluR network related deletion. In fact two patients in the Phase 1 ADHD study had 22q11.2 mutations (one deletion and one duplication), both of which, per the company's presentation, reported "significant symptom improvement in both CGI-I and Vanderbilt" and both patients continue in the long-term safety trial.

So MDGN will look to capitalize on the potential affect of NFC-1 in 22q11.2 Deletion Syndrome and expects to initiate a Phase 1/2 indication and dose finding study early next year. First steps will be to submit an IND - which they hope to do later this year. The initial study is expected to parse out the first (of potentially other follow-on) indication - which MDGN noted could be related to ADHD, anxiety or mood disorders - and, if all goes well, could have initial read-out around mid-2016.

MDGN thinks a 22q11.2-related indication could be fairly fast-moving and ahead of mGluR+ADHD. Given the rarity of incidence and lack of any effective treatment, it's possible (assuming demonstrated NFC-1 effectiveness) this could be a quick-moving regulatory orphan candidate. While we caution that it's too early to jump on a bandwagon at this point (although positive results from 2 of 2 patients in the GREAT trial is encouraging), if the initial P1/2 study is positive, MDGN thinks they can go directly to a pivotal, regulatory approval-supporting study.

Given the benefits of orphan status (potentially massive pricing power, extended exclusivity, tax credits, fast-track regulatory advantage, etc) and no effective therapies that address the symptoms (much less the underlying cause), this could be a home-run type of candidate for MDGN (although remember, royalties and, potential milestones, will apply). And the beauty is, assuming enrollment in the study(ies) is not a challenge (CHOP is the leader in 22q11.2 research which presumably will facilitate this), evidence of efficacy (or not) may not be a long wait.

Our Take: *Phase 2/3 Data May Be a Catalyst for Share Price…*

MDGN most likely has at least $8 million in this acquisition - which includes $2M upfront and another $6M by 3/31/2016 - and since P2/3 mGluR+ADHD data is not expected until 2H 2016, it's fair to assume $8M is essentially spent - not an unreasonable figure given the strong Ph 1 data, likelihood to move the compound rapidly through development in a range of indications, orphan status potential (in addition to in ADHD) and what could very likely be a captive market given the lack of current effective therapies in these indications.

Terms of the acquisition also include "additional payments of up to $450 million upon the achievement of certain developmental, regulatory and sales milestones related to an oral formulation of NFC-1 (the "*Product*") and any new chemical entity developed by the Company covering the same indication as the Product (an "*NCE*")" as well as royalties on sales of a commercialized product. Specifics in terms of exactly what the 'up to $450M payments' relate to and what the triggers are were not disclosed - although presumably the bulk relates to a

post-approved product. It's a big number but relative to the potential size of the market that NFC-1 may be able to address, including possibly a multi-billion dollar opportunity in mGluR+ADHD alone (and commanding big margins), there could be significant meat left on the bone for MDGN.

While it is still too early for use to model this candidate, we think the Phase 2/3 data, assuming it supports what was seen in Ph 1, could be catalyst for the stock price as this should provide much more insight into the potential of NFC-1 in both ADHD and 22q11.2.

FINANCIAL MODEL

Medgenics, Inc.

	2014 A	Q1A	Q2A	Q3E	Q4E	2015 E	2016 E	2017 E	2018 E
Total Revenues	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
YOY Growth	-	-	-	-	-	-	-	-	-
Cost of Goods Sold	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Gross Income	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Gross Margin	-	-	-	-	-	-	-	-	-
SG&A	$10,686.0	$3,947.0	$3,889.0	$3,940.0	$3,857.0	$15,633.0	$14,655.0	$14,174.0	$13,652.0
% SG&A	-	-	-	-	-	-	-	-	-
R&D, net of grants	$8,253.0	$3,901.0	$3,028.0	$3,365.0	$3,187.0	$13,481.0	$13,421.0	$12,095.0	$10,805.0
% R&D	-	-	-	-	-	-	-	-	-
Operating Income	($18,939.0)	($7,848.0)	($6,917.0)	($7,305.0)	($7,044.0)	($29,114.0)	($28,076.0)	($26,269.0)	($24,457.0)
Operating Margin	-	-	-	-	-	-	-	-	
Financial expense, net	$518.0	($1,073.0)	$835.0	$40.0	$25.0	($173.0)	$47.0	$0.0	$0.0
Total Other Income (Expense)	$518.0	($1,073.0)	$835.0	$40.0	$25.0	($173.0)	$47.0	$0.0	$0.0
Pre-Tax Income	($18,421.0)	($8,921.0)	($6,082.0)	($7,265.0)	($7,019.0)	($29,287.0)	($28,029.0)	($26,269.0)	($24,457.0)
Tax expense (benefit)	$12.0	$1.0	$0.0	$0.0	$0.0	$1.0	$0.0	$0.0	$0.0
Tax Rate	*-0.1%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Net Income	($18,433.0)	($8,922.0)	($6,082.0)	($7,265.0)	($7,019.0)	($29,288.0)	($28,029.0)	($26,269.0)	($24,457.0)
YOY Growth	*24.4%*	*-47.9%*	*13.6%*	*89.2%*	*131.0%*	*58.9%*	*-4.3%*	*-6.3%*	*-6.9%*
Net Margin	-	-	-	-	-	-	-	-	-
EPS	($0.96)	($0.36)	($0.24)	($0.29)	($0.28)	($1.17)	($1.03)	($0.86)	($0.79)
YOY Growth	*-4.9%*	*36.8%*	*24.2%*	*42.9%*	*-2.2%*	*22.5%*	*-11.9%*	*-16.4%*	*-8.7%*
Diluted Shares O/S	19,247	24,844	24,907	25,000	25,080	24,958	27,110	30,400	31,000

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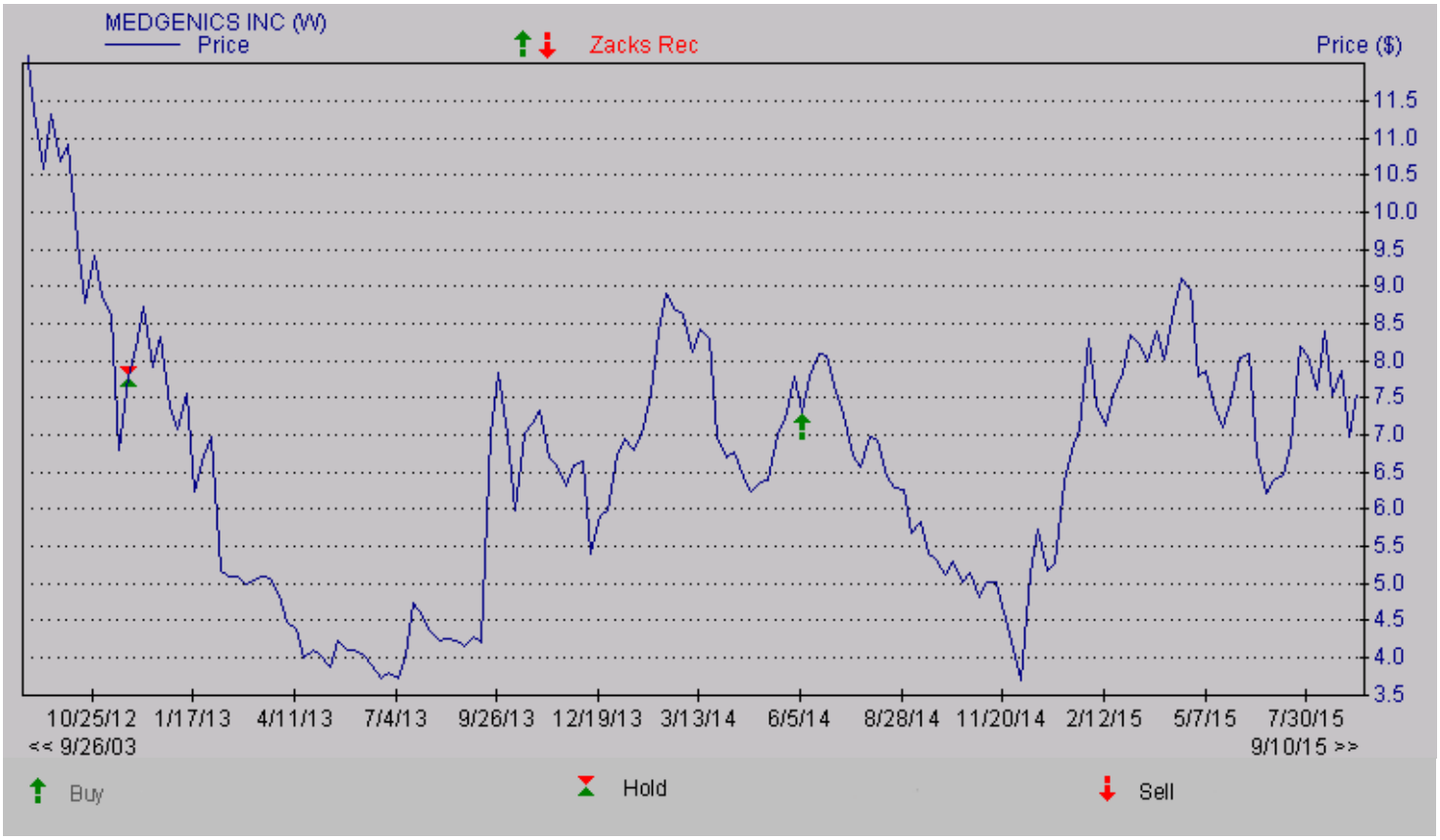

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