Zacks Small-Cap Research

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Medgenics Inc (MDGN-AMEX)

MDGN: Q3 Results, neuroFix Program Could Be Fast-Moving

Current Recommendation	**Buy**
Prior Recommendation	N/A
Date of Last Change	06/08/2014
Current Price (10/23/15)	$6.79
Target Price	**$11.00**

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	**$9.96**
52-Week Low	**$3.70**
One-Year Return (%)	**35.53**
Beta	**0.40**
Average Daily Volume (sh)	**252,479**
Shares Outstanding (mil)	**31**
Market Capitalization ($mil)	**$211**
Short Interest Ratio (days)	**12.46**
Institutional Ownership (%)	**20**
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 A	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	-$0.66 A	-$0.25 E	-$1.48 E
2016					-$1.20 E
2017					-$1.11 E

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

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Q3 Results, Operational Update

Medgenics reported third quarter financial results and provided a brief operational update. The majority of the two most recent conference calls have been focused on the newly acquired NFC-1 compound, although the MDGN-201 TARGT therapy study also remains ongoing. Relative to MDGN-201 the low-dose cohort is fully enrolled. Five of the six patients maintained hemoglobin levels within the targeted range for at least five months. One of the six patients still remains in the study and has been stable 16 months after implantation. The mid-dose cohort has enrolled four of an expected six total patients with three of the four stable and still in the study, including one through 7 months.

Relative to the Israel-based peritoneal dialysis (PD) study, two patients have been enrolled, one of which required rescue rEPO approximately 5 months following implantation and the other patient remains stable. In Q2 MDGN received clearance from FDA to proceed with their IND application – the company has since commenced a U.S.-based PD study – the first patient was enrolled at the end of Q2. The patient required one rEPO injection two months following implantation but remains in the study.

We discuss the neuroFix Therapeutics/NFC-1 acquisition in greater detail below.

Q3 operating expenses were $15.7M, which includes $8.2M worth of non-recurring R&D expense related to the neuroFix acquisition ($2M upfront pymnt + $6M in milestones). Excluding the acquisition-related expenses, OpEx of $7.6M was largely inline with our $7.3M estimate. Net loss and EPS, excluding the one-time expenses and non-cash revaluation of derivative liabilities, were approximately $7.2M and ($0.33), compared to our $7.3M and ($0.29) estimates.

Cash used in operating activities was $16.9M through the first nine months of the year. Excluding changes in working capital, this was $22.4M. In mid-October MDGN raised $43M, net (7.1M shares @ $6.50 less offering costs), via a secondary public-placed equity offering. Pro forma for the raise, MDGN had approximately $61M in cash and equivalents at the end of Q3.

Management estimates the cash balance will be sufficient to fund the company at least through mid-2017 – which includes financing the upcoming NFC-1 trials in ADHD (phase 2/3) and 22.q11.2 Deletion Syndrome (phase 1/2). Read-out of both of these studies could come next year and has the potential to be highly insightful into NFC-1 and important operational milestones for MDGN. If the data confirms what was seen in the phase 1 GREAT study, we think this sets the stage for an additional financing on even more favorable terms (i.e. – higher valuation) in order to extend development to (hopefully) eventual commercialization of NFC-1 in the first of potentially one or more indications.

MDGN Acquires CNS Compound

In September MDGN acquired 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. The acquisition was consummated with neuroFix, CHOP, Philip Harper and Hakon Hakonarson.

Terms of the deal;

- $2M upfront in cash
- $6M in cash ($2.8M) and common stock ($3.2M worth) upon earlier of achievement of a "corporate milestone" or March 31, 2016 – this was paid/issued in October

- 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;

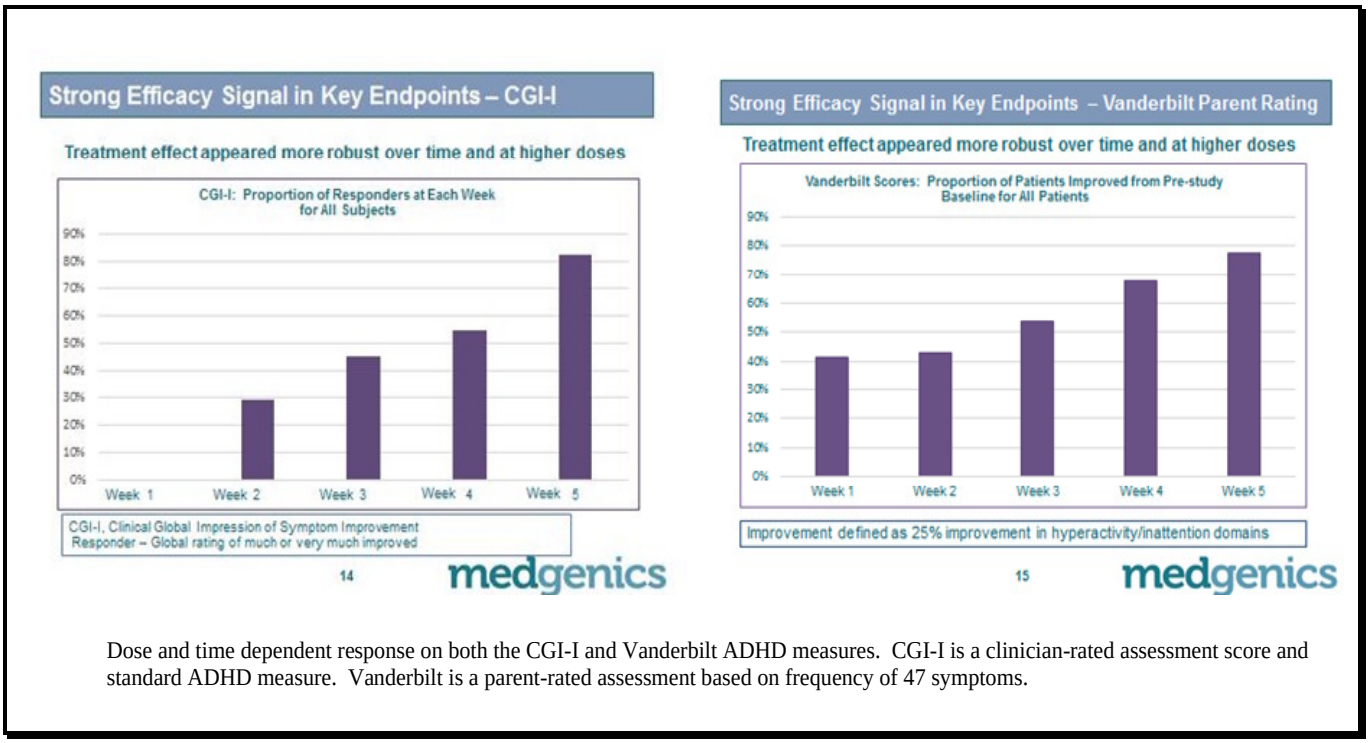
- 73% had severe ADHD (CGI-S>5, on a scale of 1=normal to 7=extremely ill)
- 67% had co-morbid psychiatric conditions such as anxiety, ODD and insomnia
- 30% were on antipsychotics and/or antidepressants
- 70% had been previously treated with ADHD drugs (with presumably little benefit)

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.

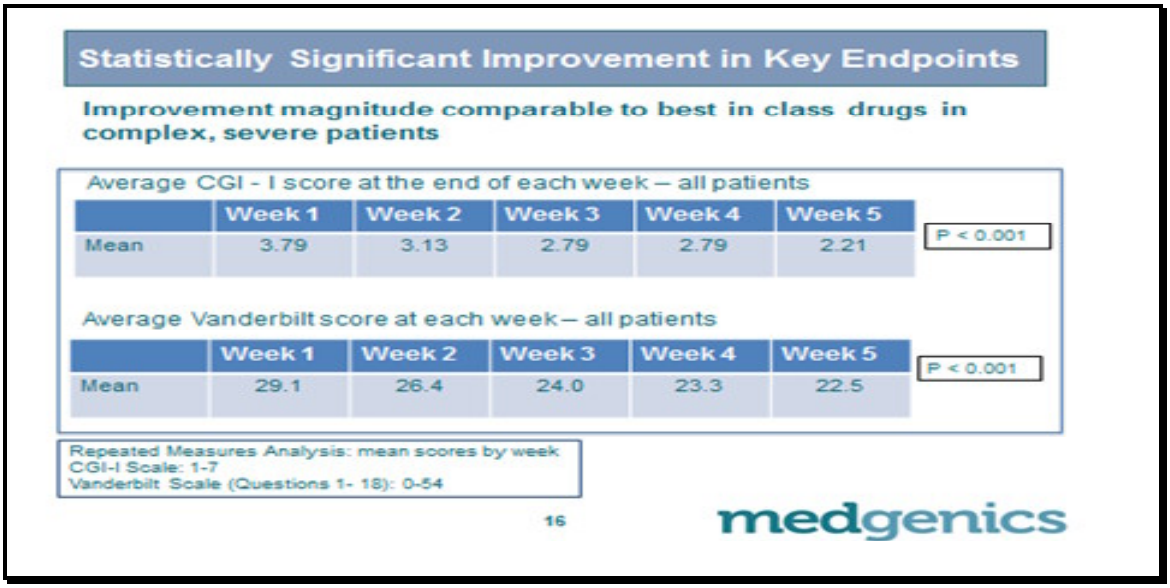
Full results will be presented at AACAP in late October in San Antonio. Management also provided a glimpse of the data on the call announcing the transaction which included;

- 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 has at least $8 million in this acquisition - which includes $2M upfront and another $6M paid in cash and stock shortly following the close of the transaction - 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.

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.

TARGT Therapy Update

While the company provided only a limited update on MDGN-201 in the Q3 10-Q, they did note that one patient remains stable in the low-dose cohort and three of the four patients enrolled in the mid-dose cohort are stable and remain in the study.

- **Low dose**
  - o enrollment completed
  - o five of the six patients maintained hgb in targeted range for at least five months
  - o all six showed positive response to TARGT$_{EPO}$ therapy at ~100x lower Cmax (exposure) than recombinant EPO
  - o one patient remains stable which is now in the 17 month following implantation
  - o no treatment related serious events in either the low or mid-dose groups

- **Mid dose**
  - o four patients enrolled
  - o one patient was removed from the study as he showed poor response and required rescue rEPO
  - o the three other patients remain stable, with one through approximately 7 months
  - o noteworthy is that one of these three remaining patients had Hb above 13 (i.e. – just above the target range) and had one of the implanted TARGT biopumps excised – following which he experienced a decrease in both EPO and Hb, with Hb coming down into the targeted range. This indicates that not only is TARGT eliciting a EPO and Hb response, but also that TARGT biopumps can be efficiently and effectively removed when conditions require
  - o enrollment continues

Update on Other EPO-Related Programs: *PD Initiated in Israel and U.S, Other Renal Indications to Initiate*

As a reminder, last October MDGN announced that they expected to pursue several indications related to TARGT$_{EPO}$. Those being (also see chart below):

- ESRD patients that are hypo-responsive to ESAs - a U.S. population that the company estimates at approximately 40k - 70k
- Beta Thalassemia, a rare blood disorder associated with anemia (i.e. - low hemoglobin) and low levels of EPO. The company estimates that there are ~16k people in the U.S. and Europe combined that suffer from Beta Thalassemia.
- anemic CKD patients which are candidates for transplant - a population MDGN estimates at about 10k in the U.S.
- peritoneal dialysis patients estimated at about 20k people in the U.S.
- myelodysplastic syndrome about 60k people in the U.S.

Potential Orphan Indications for TARGT$_{EPO}$

INDICATION	PATIENT / PAYOR NEED	CLINICAL RATIONALE	ESTIMATED PREVALENCE
PERITONEAL DIALYSIS (PD)	PD provides 20% cost reduction vs hemodialysis	Improved compliance will boost outcomes and reduce costs for PD patients	20,000 (US)[5]
ANEMIC CKD TRANSPLANT CANDIDATES	Heightened immunogenic profile due to repeat transfusions	Reduced transfusions will prevent increased immunogenicity, shorten wait times and improve transplant outcomes	10,000 (US)[5]
HYPO-RESPONDERS TO rHuEPO	Unable to manage anemia on high doses of rHuEPO; often leading to hypertension	Continuous, physiologic levels of eEPO will stimulate bone marrow more effectively and safely than intermittent IV dosing[5]	40,000 – 70,000 (US)[5]
MYELODYSPLATIC SYNDROMES (MDS)	20-55% of MDS patients respond to rHuEPO but use limited due to safety concerns[3]	Reduced need for transfusions would limit iron overload	60,000 (US)[4]
BETA THALASSEMIA INTERMEDIA	Requires frequent transfusions (up to 12 per annum)	rHuEPO shown ability to raise Hb in beta thalassemia[1]; safety concerns limit use	15,000 (US/EU)[2]

MDGN has already made meaningful progress towards moving these programs along. This includes the recent initiation of a peritoneal dialysis (PD) clinical study in both Israel and the U.S. called **MG-EP-RF-04**.

Goal of the phase II MG-EP-RF-04 open label study is to maintain hemoglobin levels within the targeted range of 9-12 g/dl in peritoneal dialysis patients. It will enroll two cohorts targeting two dose levels; one at 18-25 IU/Kg/day and the other at (35-45 IU/Kg/day). Safety and biological activity, including TARGT$_{EPO}$ secretion measured as EPO levels above baseline, will be assessed.

To-date two patients have been enrolled in Israel, one of which required rescue rEPO approximately 5 months following implantation and the other patient remains stable. In Q2 MDGN received clearance from FDA to proceed with their IND application – the company has since commenced a U.S.-based PD study – the first patient was enrolled at the end of Q2. The patient required one rEPO injection two months following implantation but remains in the study. The IND will cover PD, anemic transplant patients and hypo-responders.

On the Q1 call management noted that an Israeli-based myelodysplatic syndrome (MDS) clinical study, previously expected to commence in Q2, had been pushed back to the second half of this year as MDGN locks down regulatory approval to start the study. The company did not provide an update on the proposed MDS study in the Q2 or Q3 earnings release. Beta thalassemia is the last of the already announced EPO-related programs which is expected to begin (pre-clinical) following a meeting with Israeli regulators.

While the company has not provided an update to the specific additional renal programs since the Q1 call, they did note in the Q2 earnings release that they expect to initiate small proof-of-concept studies in other renal indications in 2H 2015.

GLP Program: *Progress Continues, NPS Pharma May Be Interested*
Management has recently spent only limited time talking about their GLP-2 program. On the Q1 call they noted that they were making progress and, interestingly, that they had been in discussions with NPS Pharmaceuticals (NPSP) which, apparently may have interest in MDGN s GLP-2 program.

The short half lives of small endogenous peptides provides therapeutic challenges when administered externally - including the need to use high doses and short effect. Since TARGT would produce the peptide naturally and provide a continuous flow (at the "correct" concentration), these challenges could potentially be overcome.

The company's initial focus will be on glucagon-like peptide-2 (GLP-2), which is produced naturally by the intestinal endocrine L cell and certain neurons. It promotes intestinal growth and enhances intestinal function. It's half life is approximately only 5 - 7 minutes. In addition to GLP-2, MDGN expects to pursue several other peptides.

MDGN expects to target short bowel syndrome, an orphan indication with TARGT$_{GLP-2}$. Short bowel syndrome (SBS) is typically the result of surgical removal of part of the small intestine as a result of a variety of disorders. SBS patients often suffer from malabsorption and may require intravenous nutrition. It is estimated that there are approximately 3k - 5k SBS patients in the U.S.

Gattex (teduglutide), marketed by NPS Pharma, is a GLP-2 analog that has orphan designation for SBS and was approved by FDA in late 2012. Gattex promotes intestinal absorption and is dosed once per day via subcutaneous injection. NPS has priced the therapy at approximately $295k per person per year. It is estimated that there are approximately 3k - 5k SBS patients in the U.S. As such the calculated potential market for Gattex is $1B+.

Gattex suffers from certain drawbacks however. Such as being associated with nausea/vomiting, which may be a result of the rapid peak from the bolus injection which is characteristic of injected peptides. TARGT$_{GLP-2}$ could potentially eliminate or reduce peaks and troughs and potential related health risks associated with bolus injections. Development of TARGT$_{GLP-2}$ is in preclinical stage and has been used in mice which showed secretion of GLP-2 for a term of 100 days.

At the January 2015 Biotech Showcase presentation MDGN announced SCID mouse data of GLP-2 following 100 days after implantation which indicated the micro-organ has been able to produce GLP-2 through 100 days with only a slight peak through about the first two weeks. Also presented was SCID mouse data versus sham control which demonstrated a biological effect of the GLP-2 micro organ (data was through two weeks).

VALUATION

Given the early stage of the company along with various uncertainties that are inherent of most development stage companies, valuation is less than straightforward. We think the most reasonable methodologies are to look at a pure-play development stage orphan drug company and DCF valuation based on annual revenue of an "average" orphan drug.

Comparable Methodology Values TARGT at ~ $300M Market Value
Synageva BioPharma (GEVA) is developing sebelipase alfa (SBC-102), an orphan-designated compound for lysosomal acid lipase deficiency. The market for SBC-102 has been estimated at approximately $600M per year. The company went public in 2011 with the stock commencing trading in July 2011. In December 2011 GEVA completed enrollment of their phase I/II study for SBC-102 - at that time the company had an approximate $310M market value. GEVA's current market cap is $8.9B.

We think it is reasonable to equate TARGT's current product development status with that of GEVA's when enrollment had completed for SBC-102 and when the company traded at a market value of ~$300M. While MDGN has yet to commence enrollment for a specific orphan designated clinical trial, we think their development status is comparable for several reasons. TARGT$_{EPO}$ has demonstrated efficacy (with no safety concerns) in phase I/II trials. Preliminary clinical data from MDGN-201, including one patient treated with EPO

micro-organ for 16 months, is highly encouraging. And while TARGT$_{EPO}$ is not yet orphan-designated, the TARGT technology had already received orphan designation for INFRADURE - as such, it is conceivable it could receive orphan designation for other targets.

Incremental Value From NFC-1

Initial clinical results in the phase 1 GREAT showed promising results of NFC-1 in individuals with ADHD and mutations of the metabotropic glutamate receptors. While initial focus will be in ADHD and 22.q11.2 Deletion Syndrome, NFC-1 could have potential utility in several other CNS disorders associated with mGluR mutations.

Both the ADHD and 22.q11.2 Deletion Syndrome clinical development programs could be fairly fast moving with a deep glimpse into utility in one or both indications coming as early mid-2016 – which is likely to be more near-term than equally substantive data coming from the TARGT programs.

Valuing NFC-1 is a challenge, however, particularly given that MDGN is subject to potentially significant development and commercialization milestones including the $450M ("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*")") – specifics of which were not disclosed. But, as noted earlier, we think the mGluR+ADHD market alone could be in the billions of dollars and presumably the bulk of any applicable milestones would relate to a post-approved product. 22.q11.2 Deletion Syndrome offers a possible near-term orphan indication.

MDGN bought NFC-1 for about $8M, which is insignificant compared to the markets that the compound could address and potentially dominate. So, we view this as a situation when neuroFix, et al. essentially outsourced development when they sold NFC-1 to MDGN (but, to be clear, CHOP will still be intimately involved in development-related activities) with the sellers maintaining upside in a more fully developed and/or commercialized compound. We do not know how much of the share of the upside each party "owns" based on the unknowns surrounding the milestones and, of course, ultimately how much, if any, revenue NFC-1 eventually generates or how much the market would value the compound with additional positive supporting clinical data.

As a placeholder for now we assign incremental value of $50M related to NFC-1. However, we think the phase 2/3 data, assuming it supports what was seen in ph 1, could be catalyst for additional valuation premium as it should provide much more insight into the potential of NFC-1 in both ADHD and 22q11.2.

Value MDGN at $350M, Maintain Buy Recommendation

We value the company at $350M or approximately $11/share. Our valuation moved up from $300M since our last update but price target has moved down from $12/share as a result of the additional shares from the recent equity raise. Further successful progression through the development pathway should provide for additional de-risking and potential upside to our current $11/share target price.

FINANCIAL MODEL

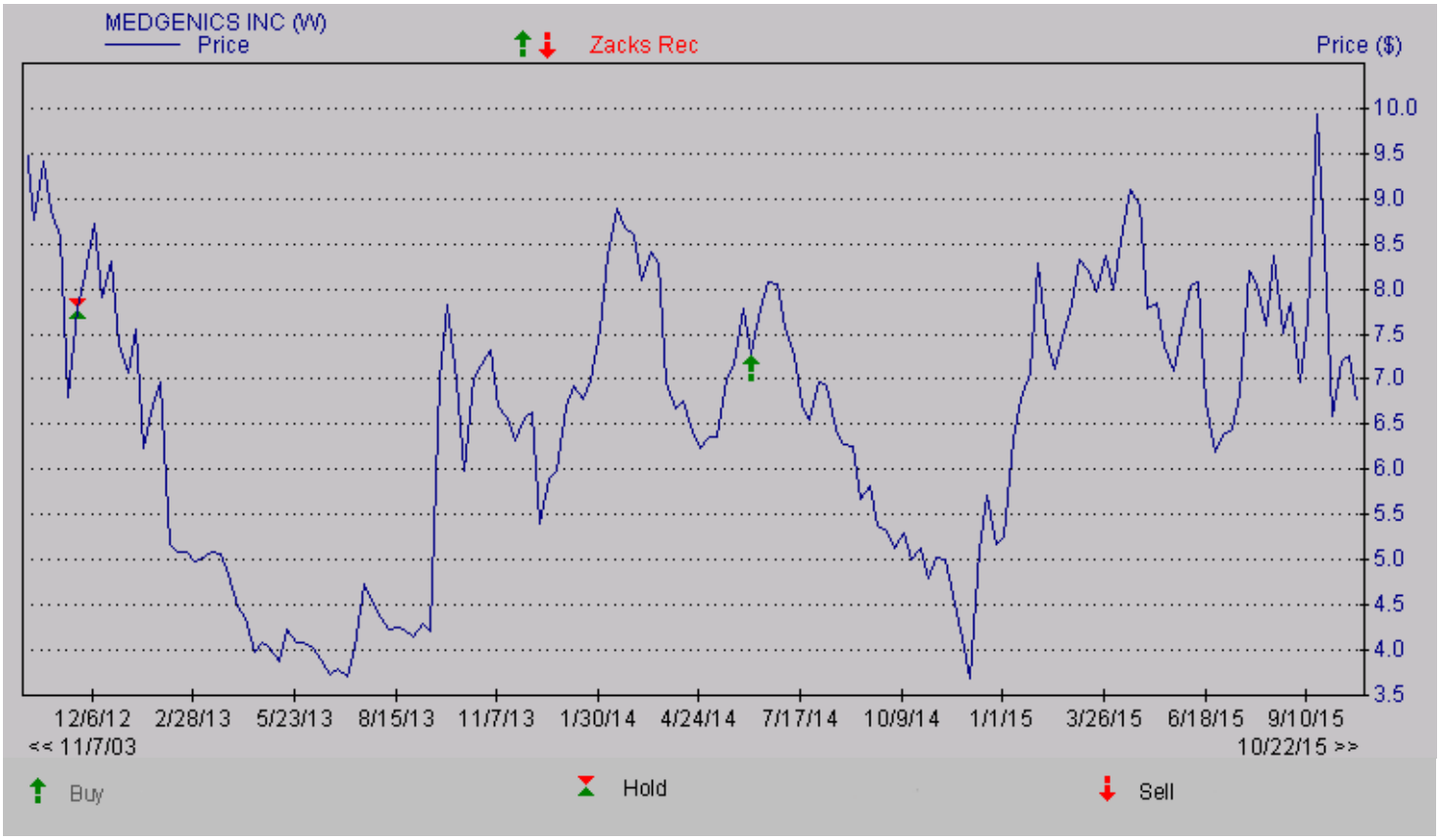
Medgenics, Inc.

	2014 A	Q1A	Q2A	Q3A	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	$2,996.0	$3,857.0	$14,689.0	$14,981.0	$15,444.0	$15,925.0
% SG&A	-	-	-	-	-	-	-	-	-
R&D, net of grants	$8,253.0	$3,901.0	$3,028.0	$12,371.0	$3,989.0	$23,289.0	$25,242.0	$26,687.0	$24,661.0
% R&D	-	-	-	-	-	-	-	-	-
Operating Income	($18,939.0)	($7,848.0)	($6,917.0)	($15,367.0)	($7,846.0)	($37,978.0)	($40,223.0)	($42,131.0)	($40,586.0)
Operating Margin	-	-	-	-	-	-	-	-	
Financial expense, net	$518.0	($1,073.0)	$835.0	($1,148.0)	$25.0	($1,361.0)	$47.0	$0.0	$0.0
Total Other Income (Expense)	$518.0	($1,073.0)	$835.0	($1,148.0)	$25.0	($1,361.0)	$47.0	$0.0	$0.0
Pre-Tax Income	($18,421.0)	($8,921.0)	($6,082.0)	($16,515.0)	($7,821.0)	($39,339.0)	($40,176.0)	($42,131.0)	($40,586.0)
Tax expense (benefit)	$12.0	$1.0	$0.0	$6.0	$0.0	$7.0	$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)	($16,521.0)	($7,821.0)	($39,346.0)	($40,176.0)	($42,131.0)	($40,586.0)
YOY Growth	*24.4%*	*-47.9%*	*13.6%*	*330.2%*	*157.4%*	*113.5%*	*2.1%*	*4.9%*	*-3.7%*
Net Margin	-	-	-	-	-	-	-	-	-
EPS	($0.96)	($0.36)	($0.24)	($0.66)	($0.25)	($1.48)	($1.20)	($1.11)	($0.97)
YOY Growth	*-4.9%*	*36.8%*	*24.2%*	*165.9%*	*-5.6%*	*54.6%*	*-19.0%*	*-7.6%*	*-12.4%*
Diluted Shares O/S	19,247	24,844	24,907	24,983	31,540	26,568	33,512	38,016	41,800

Brian Marckx, CFA

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