**OUTPERFORM** 

Reason for report:

**PROPRIETARY INSIGHTS** 

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## HEALTHCARE EQUITY RESEARCH

#### **Kev Stats:** (OTC Un:MGNX)

S&P 600 Health Care Index: 1.264.96 Price: \$21.82 Price Target: \$34.00 Methodology: Sum-of-parts DCF analysis 52 Week High: \$30.25 52 Week Low: \$21.50 Shares Outstanding (mil): 25.0 Market Capitalization (mil): \$545.5 Book Value/Share: \$0.00 Cash Per Share: \$2 61 Dividend (ann): \$0.00 Dividend Yield: 0.0%

# Cash Per Share: based on '14E

# 1 Year Price History/Ave. Daily Vol. (mil) for MGNX 27 24 2014 0.45 0.3 0.15 Created by BlueMatri

# MACROGENICS, INC.

#### Cancer Stem Cell Targeting Profile of MGD006 Is Compelling, **Based on KOL Checks**

- Bottom Line: Following checks with MEDACorp specialists, we believe MGD006 is a promising new agent in the area of cancer stem cell targeting therapeutics. MGD006 is MGNX's most advanced preclinical pipeline candidate with Phase I trials expected to start in 1H:14. The drug is a dual affinity antibody construct (DART) targeting CD123 (IL-3R), which is expressed on leukemic stem cells, and CD3, which is expressed on effector T-cells. We believe MGD006 addresses a clinically validated target and is differentiated from other CD123-targeting agents in that it induces a T-cell mediated response which could potentially lead to a more durable treatment effect. Reiterate OP rating and \$34 price target.
- · MGD006 targets CD123 (IL-3R), an attractive target, according to MEDACorp acute myeloid leukemia (AML) specialists. Leukemic stem cells have high levels of CD123 expression, which is not present in the hematopoietic stem cell population in normal human bone marrow. Based on specialist feedback, we believe the ability to target leukemic stem cells while sparing normal cells is highly attractive.
- MGD006 is differentiated from other CD123-targeting agents. According to MEDACorp specialists, MGD006-based therapy may result in additional sensitization of the immune system to allow for prolonged responses in patients. Preclinical data in this regard in primates have been "dramatic," noted MGNX mgmt. MGD006 may also potentially lack transaminase and creatine kinase elevations typically seen with diphtheria toxin conjugates, making it combinable with other drugs.
- Positive single-agent data from STML's SL-401 validate CD123 as a target, in our view. Based on feedback from MEDACorp AML specialists, we believe SL-401 has activity in selectively killing AML blasts and tumor bulk without severe depression of hematopoiesis. SL-401 is a recombinant protein comprised of IL-3 (ligand of CD123) conjugated to a truncated diphtheria toxin, which is a potent inhibitor of protein synthesis. Data presented at ASCO 2013 showed that 2/59 complete responses (CRs) and 5/59 partial responses (PRs) were seen in 59 patients with relapsed/refractory AML. To date, STML also saw 4/6 CRs in patients with BPDCN, an ultra-orphan disease.
- MGD006 Phase I data possibly in late '14 is a meaningful catalyst, in our view. Bispecific antibodies have been highly active in acute lymphoblastic leukemia (ALL), with some limitations. A cleaner safety profile in Phase I could thus be a significant catalyst for MGNX, in our view. MGNX has retained U.S. rights to MGD006, as part of its partnership with Servier. Recall, Servier has the option to license ex-U.S. rights for MGD006. MGNX qualifies for a \$5MM payment when the IND is accepted, likely in 1Q:14, and a \$15MM licensing payment when Servier exercises its license option, potentially in 1H:14.

Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	
2012A					\$63.8					\$7.72	NM
2013E	\$10.6A	\$12.3A	\$20.2A	\$19.1	\$62.2	(\$2.80)A	(\$0.29)A	\$0.14A	\$0.00	\$0.43	NM
2014E					\$44.0					(\$1.52)	NM
2015E					\$48.0					(\$2.20)	NM

Source: Company Information and Leerink Swann LLC Research

Revenues in \$MM; GAAP EPS



#### **INVESTMENT THESIS**

We rate MGNX with an Outperform and \$34 price target. MacroGenics is a leader in the area of immune-modulation and is a fully integrated R&D driven biotechnology company. The company is focused on developing new antibody-based therapeutics for cancer and autoimmune diseases and is based on a suite of platform technologies that allow generation of therapeutic antibodies with superior properties. MGNX has applied its antibody discovery and engineering platform to generate a proprietary product pipeline and to enter into strategic collaborations that provide the company with funding and leverage the additional expertise of partners.

Lead product candidate Margetuximab is an Fc-enhanced anti-Her2 antibody in Phase IIa trials for treatment of metastatic breast cancer patients with moderate Her2 over expression and who are not eligible for Herceptin or Kadcyla therapy. We believe positive Phase IIa data in late 2014 would significantly derisk this program and preclinical and Phase I data support activity of the therapeutic antibody, which could significantly expand the addressable market of Herceptin (Roche). We model an addressable market opportunity of \$590MM in the U.S. in metastatic breast and gastric cancer.

The second clinical stage pipeline product, MGA271, is a first-in-class, Fc-enhanced monoclonal antibody that targets B7-H3, currently in Phase Ib trials for a wide range of solid tumors. B7-H3 is a tumor-specific antigen and a novel member of the B7 family of immune regulators. We believe MGA271 addresses a promising new target in immuno-oncology that could be active in a wide array of solid tumor indications, based on preclinical data. Positive Phase I expansion phase data in 2014 will be a key catalyst for this program for which partner Servier has an option to license European rights. Based on our due-diligence we believe MGA271 has potentially two mechanisms by which it could exert its anti-cancer activity: (1) tumor cell-killing via antibody-dependent cellular cytotoxicity (ADCC), and (2) enhancement of anti-tumor immunity by blockade of T-cell inhibition.

Partnerships with Gilead, Boehringer Ingelheim, Pfizer, and Servier validate MGNX's leading bispecific antibody ("DART") platform, in our view. We believe MGNX's technology has potential advantages over other bi-specific mAb technologies including BiTEs (AMGN [MP]), since it can generate highly stable DARTs that are more active. Existing partnerships validate the DART (Dual Affinity Re-Targeting) platform, in our view, and additional partnerships could be sources of upside. The company currently theoretically qualifies for an impressive \$5Bn in total potential milestone payments from existing partners. MGNX received over \$100MM in milestone payments over the last three years, and we believe there is a high likelihood that it will receive at least \$100MM until 2015E as preclinical programs advance.

MGD006 is MGNX's first DART molecule to enter clinical trials in 1H:14. MGD006 is MGNX's most advanced dual affinity re-targeting (DART) molecule and is expected to enter the clinic in 1H:14 for patients with relapsed or refractory AML or in patients with untreated AML who are not candidates for standard induction chemotherapy. The molecule is currently in late preclinical development for acute myeloid leukemia (AML).

MGD006 targets CD123 (IL-3R), an attractive target, according to MEDACorp specialists. Leukemic stem cells have high levels of CD123 expression, which is not present in the hematopoietic stem cell population in normal human bone marrow. Based on feedback from MEDACorp specialists, we believe the prospect of being able to target cancer stem cells while sparing normal cells is highly attractive. AML is believed to result from a population of leukemic stem cells which are resistant to conventional chemotherapy.

DARTs are capable of targeting two antigens and have the ability to recruit effector T-cells in a patient's body to destroy targeted cancer stem cells. MGD006 can recognize both CD123 expressed on leukemic cells and CD3 expressed on effector T-cells. Hence, MGD006's primary mechanism of action is to induce T-cell mediated killing of leukemic stem cells.

Positive single-agent data from STML's SL-401 validate CD123 as a target in AML, in our view. SL-401 is a recombinant protein comprised of IL-3 (ligand of CD123) conjugated to a truncated diphtheria toxin, which is a potent inhibitor of protein synthesis. SL-401 is in Phase 1/2 development for AML and ultra-orphan indication blastic plasmacytoid dendritic cell neoplasm (BPDCN).



Based on feedback from MEDACorp AML specialists, we believe SL-401 is active in selectively killing cancer stem cells and tumor bulk vs. normal hematopoietic cells. Data presented at ASCO 2013 showed that complete responses (CRs) were seen in 2/59 patients and partial responses (PRs) were seen in 5/59 patients with relapsed/refractory AML. STML also saw 4/6 CRs in patients with BPDCN (ASH 2013 abstract).

MEDACorp KOLs were also encouraged, given that CD123-targeted therapy was not associated with severe depression of hematopoiesis, indicating good selectivity of the agent which further validates this approach, in our view. Our checks also indicated that liver toxicity has been within an acceptable level when used as single agent, but based on the level of efficacy seen in AML MEDACorp specialists believed SL-401 combination therapy might be warranted to get a higher response rate. Recall the overall response rate (ORR) with Mylotarg (CD-33 ADC) was 30% in 2nd line r/rAML patients (16% CRs). The ability to combine SL-401 with other agents however may be limited due to potential liver toxicity issues, which are likely off-target effects of the drug, according to specialists.

Based on MEDACorp KOL feedback, we believe MGD006 is differentiated from other CD123 targeting modalities. Given that MGD006 is not conjugated to a cytotoxin, it might potentially lack transaminase and creatine kinase elevations seen with SL-401. One specialist noted that toxicity seen with molecules conjugated to diphtheria toxin (SL-401, Ontak (Eisai)) may be due to low-level de-conjugation of the toxin, where free toxin may be taken up by hepatocytes via pinocytosis. The absence of a toxin may potentially makes MGD006 more attractive for use in conjunction with chemotherapy agents.

MGD006 also recruits T-cells via its affinity for CD3 which could produce more durable responses. The specialist compared the CD3 recognition component of MGD006 to chimeric antigen receptor (CAR) T cells, which have shown long-term persistence. In addition, AMGN's blinatumomab has been highly active in ALL, validating the approach. Theoretical MGD006 issues to be watched in the clinic include central nervous system (CNS) toxicities seen with blinatumomab and cytokine release syndrome. According to MEDACorp KOLs, the CNS toxicities were surprising and it is not clear to date how they relate to blinatumomab. Cytokine release syndrome may be managed with tocilizumab (Actemra).

We believe positive clinical data for MGD006 would further validate MGNX's DART platform with implications for MGD007 and other T-cell recruiting DART molecules. MGNX is eligible to receive up to \$1Bn in license grant fees and milestone payments if Servier exercises all three DART options and successfully commercializes all three DARTs. MGNX and Servier will share Phase II and III development costs in markets where MGNX has rights.

#### **VALUATION**

We estimate a \$34 fair value for MGNX shares in 12 months, based on a discounted cash flow (DCF) sum-of-parts analysis. We use a 12% discount rate for probability of success-weighted margetuximab (25%) and MGA271 (12%) sales. Based on our DCF analysis, we attribute \$8/ share to margetuximab, \$9/share to MGA271, and \$14/share to the preclinical pipeline and platform and the remainder to expected cash in one year.

#### RISKS TO VALUATION

Developmental pipeline agents face clinical and regulatory development risk, as well as commercial risks. MGNX also faces execution risk and financial risk. We estimate that MGNX current cash will be sufficient to fund operations through the end of 2015, and the company may have additional financing needs before turning cash flow positive.

MGNX P&L	2011A	2012A	1Q13A	2Q13A	3Q13A	4Q13E	2013E	2014E	2015E
Collaborative research revenue	47.1	59.6	10.1	11.8	20.1	19.0	61.0	43.0	48.0
Grant revenue	10.2	4.2	0.5	0.5	0.1	0.1	1.2	1.0	-
Royalties	_	-	-	-	-	-	-	_	-
Product sales	_	-	-	-	-	-	-	_	-
Total Revenue	57.2	63.8	10.6	12.3	20.2	19.1	62.2	44.0	48.0
cogs	_	_	-	_	-	-	-	-	-
R&D	41.1	45.4	10.1	11.1	11.1	13.0	45.2	62.0	78.0
SG&A	10.9	10.2	3.8	1.5	2.0	6.0	13.3	20.0	25.0
Operating expenses	52.0	55.6	13.9	12.6	13.1	19.0	58.6	82.0	103.0
Operating income (expense)	5.2	8.2	(3.3)	(0.3)	7.2	0.1	3.7	(38.0)	(55.0)
Total Other income (expense)	1.5	0.2	(0.0)	(0.0)	(0.6)	-	(0.6)	-	-
ЕВТ	6.7	8.4	(3.3)	(0.3)	6.6	0.1	3.1	(38.0)	(55.0)
Tax expense (income)	-	-	-	-	-	-	-	-	-
Net income	6.7	8.4	(3.3)	(0.3)	6.6	0.1	3.1	(38.0)	(55.0)
GAAP EPS	6.55	7.72	(2.80)	(0.29)	0.14	0.00	0.43	(1.52)	(2.20)
Common shares outstanding	1.0	1.1	1.2	1.2	1.2	25.0	7.1	25.0	25.0
BS & CFS	2011A	2012A	1Q13A	2Q13A	3Q13A	4Q13E	2013E	2014E	2015E
Cash & equivalents	55.2	47.7	43.5	33.8	33.6	97.7	97.7	65.3	17.5
Debt	-	-	-	-	-	-	-	-	-
Change in Cash	18.3	(7.5)	(4.2)	(9.7)	(0.2)	63.9	49.7	(32.4)	(47.8)
Cash from operations	6.8	(6.6)	(3.8)	(9.9)	0.8	(18.1)	(31.1)	(30.4)	(45.8)
Net income (loss)	6.7	8.4	(3.3)	(0.3)	6.6	0.1	3.1	(38.0)	(55.0)
Share based comp	2.3	0.8	0.1	0.1	0.1	0.5	0.9	6.6	8.2
D&A	1.1	1.0	0.3	0.3	0.3	0.3	1.1	1.0	1.0
Other (Change in WC)	(3.5)	(16.7)	(0.9)	(10.0)	(6.3)	(19.0)	(36.2)	-	-
Cash from investing	(0.5)	(0.9)	(0.4)	(0.5)	(1.2)	(0.5)	(2.5)	(2.0)	(2.0)
CapEx	(0.5)	(0.9)	(0.4)	(0.5)	(1.2)	(0.5)	(2.5)	(2.0)	(2.0)
Acquisitions	-	-	-	-	-	-	-	-	-
Other	-	-	-	-	-	-	-	-	-
Cash from financing	12.1	0.0	0.1	0.7	0.1	82.5	83.4	-	-
Equity issue (buyback)	12.1	0.0	0.1	0.7	0.1	82.5	83.4	-	-
Debt issue (principal payment)	-	-	-	-	-	-	-	-	-
Other	-	-	-	-	-	-	-	-	_

Source: Leerink Swann Estimates and Company Filings

Program	Target	Platform	Partner	Indication	Current Status	Next milestone	Timing
Margetuximab	Her2	Fc	proprietary	Breast cancer (Her2 IHC2+)	Phase IIa	Phase IIa data	late 2014
						Initiate Phase IIb/III	2015
				3rd line Gastric cancer	Phase I	Initiate Phase III	2H14
						Phase III data	2018
				Other cancers (bladder)	Phase I	Initiate Phase II	2015
MGA271	B7-H3	Fc, CSLC	Servier (EU rights)	Solid tumors	Phase Ib	Phase la DE data	mid-2014
						Servier opt-in	1H14
						Phase Ib expansion data	2H14
						Initiation, Phase II	1Q15
MGD006	CD123 x CD3	DART	Servier (EU rights)	AML	Preclinical	Preclinical data at ASH	4Q13
						IND accepted	1Q14
						Servier opt-in	2014
						Initiate Phase I	1H14
MGD007	gpA33 x CD3	DART, CSLC	Servier (EU rights)	Colorectal cancer	Preclinical	IND accepted	mid-14
						Initiate Phase I	2H14
						Servier opt-in	2015
MGD010	CD32B x CD79B	DART	proprietary	Autoimmune (SLE, RA)	Preclinical	IND prep	2014
						IND accepted	2015
Teplizumab	CD3	Fc	proprietary	Type 1 Diabetes	Investigator-Sponsored Study	Partnership	n/a

Source: SEC Filings, Leerink Swann Estimates



# **Disclosures Appendix Analyst Certification**

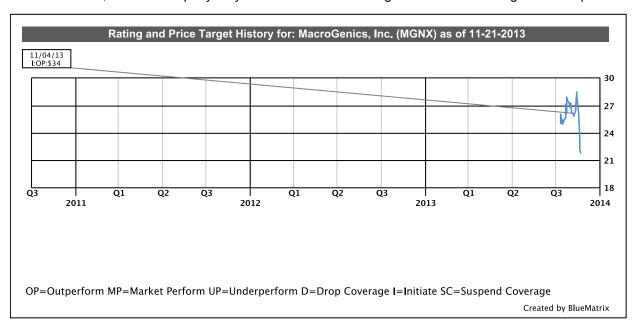
I, Michael Schmidt, Ph.D., certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

#### **Valuation**

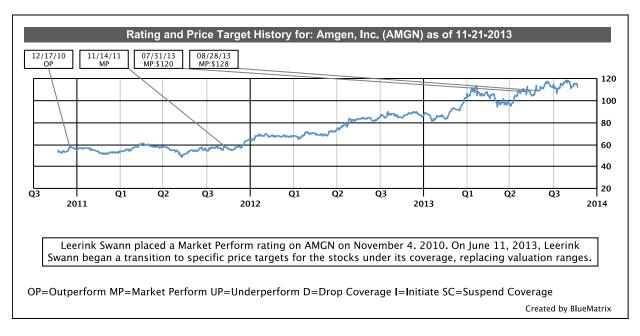
We estimate a \$34 fair value for MGNX shares in 12 months, based on a discounted cash flow (DCF) sum-of-parts analysis. We use a 12% discount rate for probability of success-weighted margetuximab (25%) and MGA271 (12%) sales. Based on our DCF analysis, we attribute \$8/share to margetuximab, \$9/share to MGA271, and \$14/share to the preclinical pipeline and platform and the remainder to expected cash in one year.

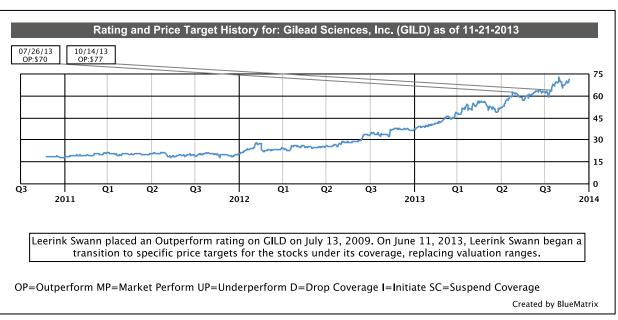
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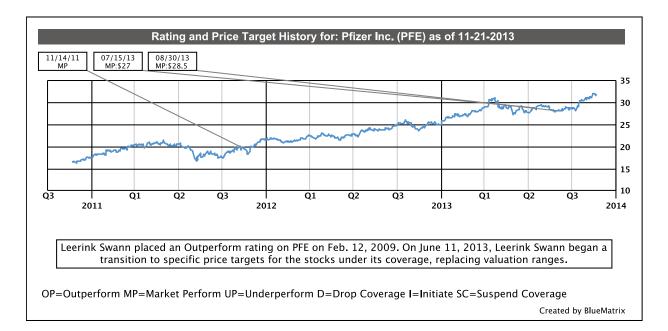














Distribu	Distribution of Ratings/Investment Banking Services (IB) as of 09/30/13 IB Serv./Pa						
Rating	Count	Percent	Count	Percent			
BUY [OP] HOLD [MP]	111 60	64.90 35.10	27 0	24.00 0.00			
SELL [UP]	0	0.00	0	0.00			

# **Explanation of Ratings**

Outperform (Buy): We expect this stock to outperform its benchmark over the next 12 months.

<u>Market Perform (Hold/Neutral)</u>: We expect this stock to perform in line with its benchmark over the next 12 months.

<u>Underperform (Sell):</u> We expect this stock to underperform its benchmark over the next 12 months. The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company.

For the purposes of these definitions the relevant benchmark will be the S&P 600® Health Care Index for issuers with a market capitalization of less than \$2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over \$2 billion.



### **Important Disclosures**

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In the past 12 months, the Firm has received compensation for providing investment banking services to MacroGenics, Inc.

Leerink Swann LLC makes a market in MacroGenics, Inc., Amgen, Inc. and Gilead Sciences, Inc.

Leerink Swann LLC is willing to sell to, or buy from, clients the common stock of Pfizer Inc. on a principal basis. In the past 12 months, an affiliate of the Firm, Leerink Swann Consulting LLC, has received compensation for providing non-securities services to: Amgen, Inc. and Pfizer Inc.

Leerink Swann LLC has acted as a co-manager for a public offering of MacroGenics, Inc. in the past 12 months.

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