

Chimerix, Inc.

Second-Quarter Financials Non-Event; AdV Study 202 Demonstrates Trends; Dosing in SUPPRESS Imminent

On Wednesday, August 14, before markets opened, Chimerix reported second quarter 2013 financial results (exhibit 1, on page 5). The company ended the second quarter with \$123 million in cash; we estimate the current cash should sustain operations through the data release from SUPPRESS expected during first half 2015. Net loss for the quarter (pretax) was \$12.5 million, with a per share loss of \$0.91 versus our estimates of \$10.9 million and \$0.43, respectively. We updated our model as illustrated in exhibit 1.

The most incremental news on the earnings call was the top-line data from Study 202 in which brincidofovir (formerly CMX001) was evaluated in adenovirus-infected hematopoietic stem cell transplantation (HSCT) patients. Other issues include: 1) SUPPRESS is on track for dosing the first patient during the third quarter; 2) the BARDA contract has been extended for a year and \$5 million funding was granted; and 3) competitors Astellas and Vical (VICL \$1.51) initiated the Phase III study of their CMV vaccine. We discuss each issue in detail below.

Chimerix announced top-line data from Study 202; brincidofovir (formerly CMX001) demonstrated numerical trends in reducing adenovirus (AdV) viremia, AdV-related disease, and all-cause mortality in hematopoietic stem cell transplantation (HSCT) patients. Detailed data will be presented as an oral late-breaker presentation at the upcoming ICAAC (Interscience Conference on Antimicrobial Agents and Chemotherapy) annual meeting (Denver, September 10-13).

- **Study 202 design.** Study 202 is a multicenter, randomized, placebo-controlled study evaluating brincidofovir in 12 adult and 36 pediatric HSCT recipients. A total of 735 HSCT patients in 29 centers were screened for AdV viremia, and patients with asymptomatic AdV viremia were enrolled and randomized to receive brincidofovir 100 mg BIW (twice weekly), 200 mg QW (once weekly), or placebo for 12 weeks as preemptive therapy, followed by a four-week follow-up period. The primary endpoint is treatment failure rate, a composite of 1) progression to symptomatic AdV disease, or 2) 10-fold increase of AdV levels in the blood. Secondary endpoints include the incidence and time to mortality, and the proportion of patients with undetectable plasma AdV.
- **Trends in reduction of risk on all endpoints.** The study demonstrated that the brincidofovir 100 mg BIW dose led to decreased levels of AdV viremia and showed numerical benefit in reducing both progression to AdV disease and all-cause mortality, as compared with the 200 mg QW and placebo arms.
- **But not meeting statistical significance.** Study 202 assumed 50% progression to AdV-related disease for the placebo arm. It is unclear whether the study population was too small and/or the assumption was off, as there have been few prior studies that could provide solid historical data on progression.

Chimerix, Inc., a biopharmaceutical company based in Durham, North Carolina, focuses its research-and-development efforts on antiviral therapies.

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Please consult the last page of this report for all disclosures.

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August 15, 2013

Stock Rating: **Outperform**
Company Profile: **Aggressive Growth**
Price Target: \$28.00

Symbol: CMRX (NASDAQ)
Price: \$17.56 (52-Wk.: \$15-\$27)
Market Value (mil.): \$453
Fiscal Year End: December
Long-Term EPS Growth Rate:
Dividend/Yield: None

	2012A	2013E	2014E
Estimates			
EPS Q1	NA	A\$-22.58	NA
Q2	NA	A\$-0.91	NA
Q3	NA	\$-0.41	NA
Q4	NA	\$-0.45	NA
FY	\$-5.71	\$-4.08	\$-1.91
CY		\$-4.08	\$-1.91
Sales (mil.)	NA	5	3
Valuation			
FY P/E	NM	NM	NM
CY P/E		NM	NM

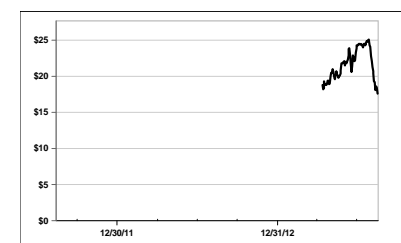
Trading Data (FactSet)

Shares Outstanding (mil.)	2
Float (mil.)	12
Average Daily Volume	122,798

Financial Data (FactSet)

Long-Term Debt/Total Capital (MRQ)	0.1
Book Value Per Share (MRQ)	-88.1
Enterprise Value (mil.)	294.7
EBITDA (TTM)	0.0
Enterprise Value/EBITDA (TTM)	0.0x
Return on Equity (TTM)	-7.5

Two-Year Price Performance Chart



Sources: FactSet, William Blair & Company estimates

- **No new safety issues were identified with brincidofovir 100 mg BIW in the study**, and no changes were deemed necessary to the Phase III SUPPRESS protocol for the prevention of cytomegalovirus (CMV) infection. We note that 100 mg BIW is the chosen dose for SUPPRESS.
- **Chimerix intends to review the Phase II AdV study with the Food and Drug Administration (FDA) during fourth quarter 2013.** Management plans to discuss the results of the study with the agency and the implications on how it could support further development of brincidofovir in pediatric and high-risk patients. We note that since AdV infection is much less frequent than CMV, a prevention study design similar to Phase III SUPPRESS is not practical because it would require an excessive number of patients.

Dosing in the Phase III SUPPRESS study is expected to begin during the third quarter, as previously guided. Management believes three main points could increase chance for success.

- **Earlier dosing following transplant.** Chimerix believes dosing earlier in the post-transplant period allows patients to achieve an earlier, effective steady state level of CMX001 coinciding with the period with the greatest risk of CMV reactivation. Second, early dosing has potential to prevent earlier CMV events in the treatment arm while capturing earlier events in the placebo arm, potentially allowing for greater separation between the two arms.
- **Inclusion of a single-dose cohort.** The company is moving forward with a single 100 mg BIW dose cohort instead of multiple dose groups. Chimerix believes that 100 mg BIW dose will have sufficient efficacy to demonstrate a significant difference versus placebo. In addition, moving to fewer dosing arms will allow for greater power to the study.
- **Based on a Phase I food effect study, SUPPRESS will evaluate brincidofovir at 100 mg BIW with a low fat meal against placebo.** Management believes that the concomitant administration of brincidofovir with a low fat meal should decrease the potential for patient discontinuation in the study because of gastrointestinal (GI) side effects, on top of the safety monitoring and management plan (SMMP) to be implemented in the study.

Positive SUPPRESS Phase III results should lead to accelerated approval in the United States of brincidofovir in late 2015 or early 2016; full approval could come with a pediatric or SOT study, which must have a clinical endpoint. The first indication to pursue for brincidofovir is prevention of CMV infection in the HSCT setting, with potential approval and launch in late 2015 or early 2016. Chimerix intends to use the single pivotal SUPPRESS study to obtain conditional approval followed by a supplemental new drug application (sNDA) with either a pediatric HSCT or solid-organ transplant (SOT) study to obtain full approval; the second study has to have a clinical endpoint. Chimerix is also negotiating with European regulatory authorities to elucidate a clear pathway to approval on the continent based on the Phase III SUPPRESS study.

Chance of Success of SUPPRESS Based on Phase II Data: We Estimate 80%

In the Phase II study (Study 201) for CMV prevention in HSCT patients, 10% of brincidofovir -treated patients experienced prevention failure, versus 37% from placebo, which demonstrates a relative 73% reduction in CMV disease and risk for infection ($p=0.002$). When the inclusion criteria and protocol of the Phase III SUPPRESS study were applied to the Study 201 patients, the analysis yielded a relative reduction of 52% in prevention failure for the brincidofovir -treated group versus placebo, in the most conservative scenario.

Further, in the SUPPRESS study, the initiation of prevention therapy is much earlier (within the first two weeks following transplant) than that in Study 201 (on day 24 post-transplantation), which could lead to more favorable outcomes, as earlier initiation of prevention therapy might result in more effective suppression of CMV reactivation. Lastly, the duration of therapy in SUPPRESS is also longer (14 weeks) than that in Study 201 (9-13 weeks), which is also in favor of SUPPRESS.

- **We compare and contrast similarities and differences between Study 201 and SUPPRESS in exhibit 3, on page 7.** We note the SUPPRESS study will enroll similar patients as in the brincidofovir Study 201; however, several notable differences between the studies exist. The major difference lies in the definition of when to initiate preemptive therapy. In SUPPRESS, initiation of preemptive therapy with another antiviral in the study will occur when a patient has CMV DNA over 1,000 copies per mL or if the patient meets certain specified criteria in the protocol, such as being at high risk, and has CMV DNA higher than 150 copies per mL; the threshold on initiating preemptive therapy in Study 201 was 200 copies per mL. In addition, in SUPPRESS, initiation of therapy is expected to occur within two weeks from transplant for 90% of patients, as compared with Study 201, where therapy typically began on day 24. Also, in SUPPRESS, duration of therapy

with brincidofovir will be uniform at 14 weeks, while in Study 201, the duration ranged between 9 and 13 weeks. We believe standardizing the definition of initiation of preemptive therapy, the time to initiation, and duration of brincidofovir therapy should translate into a greater likelihood of success of the SUPPRESS study.

- **Phase III SUPPRESS study design.** SUPPRESS plans to enroll and randomize 450 allogeneic hematopoietic stem cell transplantation (HSCT) patients who are cytomegalovirus (CMV) seropositive (R+) 2-to-1 to brincidofovir at 100 mg BIW and placebo. The primary endpoint is 1) CMV disease or 2) initiation of preemptive therapy triggered by a positive test for CMV in the blood; secondary endpoints of the study include overall and nonrelapse mortality as well as proportion of patients with graft failure. The study is powered at 85%, with one-sided p-value of 0.025 in the superiority design, to detect 50% reduction in treatment failure for brincidofovir versus placebo. The design assumes the prevention failure rate for the placebo arm is 30%. It also assumes that 16% of enrolled patients will drop out, become lost to follow-up, or die from non-CMV-related causes. The double-blind, placebo-controlled study will be conducted at 40 sites in the United States and Canada, with significant site overlap with the Phase II brincidofovir Study 201.

Chimerix extends its contract with Biomedical Advanced Research and Development Authority (BARDA) to continue the smallpox project. In June, Chimerix announced a contract extension with BARDA for an additional 12 months and would receive a total of \$5 million in funding from June 1, 2013, to May 31, 2014, for continuing development of CMX001 in smallpox. The company is conducting preclinical studies to comply with the agency's Animal Rule, which requires testing in two animal models. On the call, management noted that studies in mice are underway and studies in rabbits are close to completion. Results from the rabbit study demonstrated statistical significance at doses comparable to those used in the SUPPRESS study. We note that successful demonstration in the animal models, supplemented by the large safety database of brincidofovir to date, could lead to brincidofovir approval as a countermeasure against smallpox.

In June, competitors Astellas and Vical announced the initiation of the Phase III ASP0113 (formerly TransVax) study, which will evaluate the therapeutic CMV vaccine in HSCT patients. Importantly, the primary endpoint of the Phase III ASP0113 study is overall survival (OS), a key secondary endpoint of Chimerix's SUPPRESS study. We believe that the rationale for selecting OS as the primary endpoint of the Phase III ASP0113 by Astellas and Vical is primarily based on literature connecting the impact of CMV serostatus with mortality, in particular a 20% to 30% survival disadvantage for CMV seropositive HSCT recipients. In addition, we believe that inclusion of an overall mortality endpoint in the study, if successfully met, provides the companies with the ability to avoid conducting a second confirmatory study of the therapeutic vaccine. We note that with initiation of the study, ASP0113 becomes the first investigational therapeutic CMV vaccine to enter Phase III development. We provide additional details of the ASP0113 program on the following page.

In contrast, Chimerix has adopted a different strategy. The primary endpoint in the Phase III SUPPRESS study is CMV disease or initiation of preemptive therapy triggered by a positive test for CMV in the blood, and secondary objectives of the study include all-cause mortality and nonrelapse mortality. As the primary endpoint of SUPPRESS is not a clinical endpoint, a second confirmatory study with clinical endpoints needs to be conducted for full approval.

In our opinion, if CMV infection is truly partly responsible for all-cause mortality and nonrelapse mortality in HSCT recipients, then an agent such as brincidofovir could demonstrate an OS benefit as well, at a probability that is similar to or higher than ASP0113—albeit OS is not a primary endpoint in SUPPRESS. We note that ASP0113 is specific for CMV, while brincidofovir is much broader in spectrum coverage of double-stranded DNA viruses, such as AdV, BK virus, and HHV6 virus, which causes additional mortality and morbidity as well.

We maintain our Outperform rating and \$28 price target (exhibit 2, on page 6). In our probability-adjusted NPV model, we expect brincidofovir to reach the market by early 2016 and become the market leader in the prevention setting. We assume brincidofovir achieves peak sales of roughly \$530 million in the United States and \$410 million in Europe; for Europe, we project that Chimerix will license out the commercial rights to brincidofovir to a partner and receive 30% royalties on EU sales. We assign an 80% probability of success to brincidofovir in the HSCT setting. Chimerix's second asset, CMX157, has been licensed to Merck (MRK \$48.57) for development of novel HIV combo therapies that could have certain advantages over Gilead's (GILD \$58.17; Outperform) industry-leading regimens. We assign \$4 per share to the program, which is in Phase I development. We estimate a 35% probability for the CMX157-containing combo to reach the market in 2019, \$1.1 billion in peak worldwide sales, and 15% royalties to Chimerix. Adding net cash of about \$2 per share to our valuation of brincidofovir and CMX157, we derive our 12-month price target of \$28 per share.

Key risks to our Outperform rating and price target include: 1) failure of brincidofovir to meet primary or second endpoints in the SUPPRESS study, 2) a worse-than-expected tolerability profile for brincidofovir, 3) failure of CMX157 to advance in Merck's HIV pipeline, 4) other clinical and business-development setbacks, and 5) financing risks.

Additional Details of ASP0113 Phase III Study

In 2011, Vical and Astellas entered an exclusive worldwide license agreement to develop and commercialize ASP0113. ASP0113 is a DNA plasmid-based vaccine encoding two specific antigens of CMV—glycoprotein B (gB) and phosphoprotein 65 (pp65)—co-formulated with a proprietary delivery system. We review the Phase III study design of ASP0113 and offer our thoughts on the studies as well as the competitive landscape for prevention of CMV herein.

- **Phase III ASP0113 study design.** Astellas plans to enroll and randomize approximately 500 allogeneic CMV seropositive (R+) HSCT patients one-to-one to receive a series of intramuscular injections of either ASP0113 or placebo; patients will be stratified based on donor-recipient relatedness and donor CMV serostatus. The adaptive study will comprise two segments: segment 1 will enroll roughly 100 patients with a primary endpoint of overall survival (OS); segment 2 will enroll about 400 patients with a primary endpoint of either OS at one year or a composite endpoint including OS and other variables at one year, based on the statistical analysis of segment 1 results. Enrollment will continue uninterrupted through both segments of the study, and the segment 2 endpoint is expected to be determined by full enrollment. Secondary objectives include time to first assessment of CMV disease (defined as CMV DNA over 1,000 copies per mL), and time to first preemptive CMV therapy. Treatment and follow-up of each patient will continue for one year following enrollment. The study design has been reviewed by regulatory agencies in the United States, Europe, and Japan.
- **Key differences in Phase III study designs from our viewpoint relate to inclusion criteria and primary endpoints.** We note that the ASP0113 study will enroll similar patients as SUPPRESS; however, the study will exclude patients undergoing cord blood transplantation (banked stem cells from newborns' placentas). Cord blood recipients are typically considered to be a higher-risk patient population, and we believe the inclusion of such patients in the SUPPRESS Phase III study may benefit brincidofovir in the long run because cord blood transplants are growing at a faster pace, whereas bone marrow use has been decreasing over the past few years.

With respect to the differences in the primary endpoints between the two studies, we believe that Vical's and Astellas's selection of OS for the ASP0113 study, based on data in the literature showing that a survival disadvantage persists for R+ patients compared with R- patients, is a significant departure from the ASP0113 Phase II study objectives, whose primary endpoint of occurrence rate of clinically significant CMV viremia. However, with the OS primary endpoint, only one study is needed for full approval, and a potential OS benefit in the label would be powerful as well.

- **Partners Astellas and Vical also announced plans to initiate a separate Phase II study evaluating ASP0113 in solid-organ transplant (SOT) by year end 2013.**

Exhibit 1
Chimerix, Inc.
Income Statement
(dollars in thousands)

	2011A	2012A	2013					2014E	2015E
			Q1A	Q2A	Q3E	Q4E	FY:13E		
Revenues									
Brincidofovir U.S. revenue	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Brincidofovir EU royalties	-	-	-	-	-	-	-	-	-
CMX157 royalties	-	-	-	-	-	-	-	-	-
Collaboration and licensing revenue	55	17,445	-	-	-	-	-	-	-
Contract and grant revenue	12,046	16,275	1,771	808	1,250	1,250	5,079	2,500	-
Total Revenues	12,101	33,720	1,771	808	1,250	1,250	5,079	2,500	0
Expenses									
COGS	-	-	-	-	-	-	-	-	-
R&D expense	27,695	27,821	6,498	6,276	8,638	9,502	30,915	39,748	46,092
SG&A expense	9,398	8,682	1,821	2,188	2,513	2,638	9,160	10,765	12,300
Total Operating Expenses	37,093	36,503	8,319	8,464	11,151	12,141	40,075	50,513	58,393
Operating income	(24,992)	(2,783)	(6,548)	(7,656)	(9,901)	(10,891)	(34,996)	(48,013)	(58,393)
Interest expense, net	(212)	(776)	(356)	(415)	(415)	(415)	(1,601)	(749)	(375)
Fair value adjustments to warrant liability	(385)	(847)	(2,203)	(4,388)	(250)	(240)	(7,081)	(720)	(720)
Other income/(expense)	-	-	-	-	-	-	-	-	-
Pretax income/(loss)	(25,589)	(4,406)	(9,107)	(12,459)	(10,566)	(11,546)	(43,678)	(49,483)	(59,487)
Other comprehensive gain/(loss)	(4)	2	(1)	-	-	-	(1)	-	-
Accretion of redeemable convertible preferred stock	(9,565)	(4,357)	(25,525)	(8,582)	-	-	(34,107)	-	-
Provision for income taxes/(income)	-	-	-	-	-	-	-	-	-
Net Income/(Loss)	(\$35,154)	(\$8,763)	(\$34,632)	(\$21,041)	(\$10,566)	(\$11,546)	(\$77,785)	(\$49,483)	(\$59,487)
GAAP EPS	(\$23.17)	(\$5.71)	(\$22.58)	(\$0.91)	(\$0.41)	(\$0.45)	(\$4.08)	(\$1.91)	(\$2.30)
Weighted average shares outstanding, diluted	1,517	1,534	1,534	23,067	25,810	25,820	19,058	25,845	25,885

Sources: Chimerix, Inc. and William Blair & Company, L.L.C. estimates

Exhibit 2
Chimerix, Inc.
Sum-of-the-Parts Fair Value
(dollars in thousands)

Drug Candidate	Peak Sales	Stage of Development	Estimated Launch Date	Probability of Commercialization	Percentage of Sales to Company	Probability-Adjusted NPV	Value Per Share	Percentage of Fair Value
Brincidofovir—United States	\$526,017	Phase III start mid-2013	H1:2016	80%	100%	\$445,114	\$17.23	60.7%
Brincidofovir—European Union	\$413,065	Phase III start mid-2013	H1:2017	80%	30%	\$114,102	\$4.42	15.6%
CMX157—HIV	\$1,074,060	Phase I	H1:2019	35%	15%	\$112,361	\$4.35	15.3%
Subtotal						\$671,576	\$25.99	91.6%
Net Cash at mid-2014						\$73,279	\$2.84	10.0%
Net Present Value of additional Gain (Loss)*						(\$11,364)	(\$0.44)	(1.5%)
Sum-of-Parts Fair Value						\$733,492	\$28.39	100.0%

*Includes costs not directly related to programs above
Sources: Company reports and William Blair & Company, L.L.C. estimates

Exhibit 3
Chimerix, Inc.
Comparison of Study 201 and SUPPRESS

	Study 201 Phase II	SUPPRESS Phase III
<i>Inclusion criteria</i>	R+ HSCT adult, including high-risk patients (10% cord blood transplant, 25% mismatched donors); also included a few PCR+ patients	R+ HSCT adult, including high-risk patients; but with no PCR+ patients at baseline
<i>Dosage</i>	Dose escalation to 100 mg BIW and 200 mg QW and placebo; found 100 mg BIW as the optimal dose. About 25-50 patients per dose arm.	n=450, 2:1 to 100 mg BIW and placebo. Dosing with low fat meal.
<i>Timing of dose initiation</i>	Average initiation was day 24 after transplant; timing of initiation was varied; initiation of required demonstration of engraftment.	50% of patients could start dosing at day 7, and 90% of patients should start dosing within 2 weeks. Earlier dosing might increase efficacy of prevention.
<i>Treatment duration</i>	9-13 weeks, then 8 weeks followup	14 weeks, then follow-up until week 24
<i>Primary endpoint/ Definition of prevention failure</i>	1) CMV disease or 2) initiation of preemptive therapy	1) CMV disease or 2) initiation of preemptive therapy
<i>When to initiate preemptive treatment</i>	When CMV DNA exceeded 200 copies/mL; or at physician discretion	Strict protocol to follow: CMV DNA exceeds 1,000 copies/mL in any patient, or over 150 copies/mL in high-risk patients
<i>Efficacy on primary endpoint</i>	10% for 100 mg BIW vs. 37% placebo, p=0.002, relative 73% reduction in prevention failure	Powered 85% to detect 50% reduction in prevention failure
<i>Efficacy: Study 201 data based on SUPPRESS inclusion criteria</i>	22% for 100 mg BIW vs. 46% placebo, relative 52% reduction in prevention failure. This models the "worst-case scenario."	---
<i>Safety</i>	Diarrhea is the major AE; 10% of 100 mg BIW arm, 60% of 200 mg BIW arm dropped out due to GI AE, versus 3% for placebo	Management program to reduce GI dropout

Sources: Chimerix, Inc., ClinicalTrials.gov, and William Blair & Company, L.L.C.

Exhibit 4
Chimerix, Inc.
Clinical Development Timeline and Milestones

Drug	brincidofovir (CMX001)			CMX157
Indication	Prevention of CMV Infection in HSCT	Preemption of AdV Infection in Adult and Pediatric HSCT	Smallpox Under Animal Efficacy Rule	HIV
Class	Lipid-conjugated cidofovir (Vistide)			Lipid-conjugated tenofovir (Viread)
Partner				Merck
Q3:12				Licensed worldwide rights to Merck (July)
Q4:12				
Q1:13		Type C meeting with the FDA		
Q2:13	Finalized Phase III SUPPRESS adult study design in April; dosing mid-year (Study 301, n=450)		BARDA contract renewal	
Q3:13	Initiate dosing in Phase III SUPPRESS	Phase II pediatric study data release (Study 202)		
Q4:13	Initiate Phase III pediatric study (Study 311)	FDA meeting		
Q1:14		Potential NDA submission		
Q2:14				
Q3:14	Completion of enrollment of SUPPRESS			
Q4:14		Potential approval and launch		
H1:15	Data release from SUPPRESS			Merck starts Phase II study; Chimerix collects milestone
H2:15	Submit NDA and MAA			
H1:16	Approval and launch; data from pediatric study			
H2:16				

Coral highlight: events likely to affect the stock price

Sources: Company reports and William Blair & Company, L.L.C. estimates

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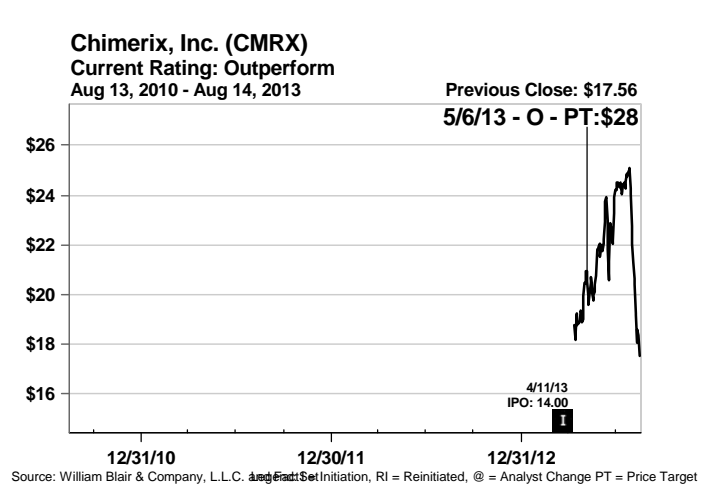
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DOW JONES: 15,337.66

S&P 500: 1,685.39

NASDAQ: 3,669.27



Current Rating Distribution (as of 07/31/13)

Coverage Universe	Percent	Inv. Banking Relationships*	Percent
Outperform (Buy)	63	Outperform (Buy)	10
Market Perform (Hold)	33	Market Perform (Hold)	1
Underperform (Sell)	1	Underperform (Sell)	0

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