

Chimerix

Initiating With Outperform (1)

May 6, 2013

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Stopping Viruses Before They Get Started

Conclusion: Chimerix's lead candidate CMX001 is a phospholipid derivative of GILD's cidofovir that can potentially kill a wide range of dsDNA viruses. It has successfully completed a Phase II trial for the prophylaxis against CMV reactivation in hematopoietic stem cell transplant (HSCT) patients. A Phase III trial is expected to begin in mid-2013, supporting a U.S. launch by 2016. Our consultants think CMX001 is safe, well tolerated, and potent, and is therefore likely to succeed in its Phase III SUPPRESS trial. Moreover, they think there is a need for a prophylactic to prevent infection with CMV and other dsDNA viral infections in transplant patients, and expect CMX001 to be widely adopted once available. Based on our analysis we believe that Chimerix is undervalued based solely on CMX001's potential as a CMV prophylactic in HSCT patients, with no contribution from other indications or other pipeline programs. We are initiating coverage with an Outperform rating.

- **Phase II Data Provide Strong Proof Of Concept For CMX001 In CMV Prophylaxis.** At its Phase III dose CMX001 reduced the risk of CMV reactivation by 72% (10% for CMX001 100mg BIW, compared to 37% for placebo, $p = 0.002$).
- **Consultants Think Phase III Has Good Chance Of Success...** Our consultants think that the Study 201 data provide strong proof of concept and are quite optimistic for the success of the Phase III. With the Phase III of very similar design to the Phase II, they think the Phase II results strongly predict that CMX001 should be able to hit the Phase III endpoint.
- **...And That CMX001 Will Be Widely Adopted As A Prophylactic In HSCT.** Our consultants think there is a need for a CMV prophylactic given the high risk of CMV reactivation in most HSCT patients. Based on its profile, they think CMX001 could be used in the majority of high-risk patients. We project \$330MM in 2019 worldwide sales in HSCT alone.

CMRX (05/03)	\$20.95	Revenue \$MM							
Mkt cap	534.2MM	FY	2012	2013E		2014E		2015E	
Dil shares out	25.5MM	Dec	Actual	Prior	Current	Prior	Current	Prior	Current
Avg daily vol	23.6K	Q1	0.0	—	0.0	—	—	—	—
52-wk range	\$15.1-21.5	Q2	0.0	—	0.0	—	—	—	—
Dividend	Nil	Q3	0.0	—	0.0	—	—	—	—
Dividend yield	Nil	Q4	0.0	—	0.0	—	—	—	—
BV/sh	\$3.92	Year	33.7	—	0.0	—	5.0	—	15.5
Net cash/sh	\$3.92	EV/S	—	—	—	—	85.0x	—	27.4x
Debt/cap	NA								
ROIC (LTM)	NA								
5-yr fwd EPS growth (Norm)	NA	EPS \$							
		FY	2012	2013E		2014E		2015E	
		Dec	Actual	Prior	Current	Prior	Current	Prior	Current
		Q1	0.00	—	(1.76)	—	—	—	—
		Q2	0.00	—	(0.42)	—	—	—	—
		Q3	0.00	—	(0.43)	—	—	—	—
S&P 500	1614.4	Q4	0.00	—	(0.45)	—	—	—	—
		Year	(1.62)	—	(2.10)	—	(1.55)	—	(1.20)
		P/E	—	—	—	—	—	—	—

Investment Summary

Chimerix is a biopharmaceutical company focused on the discovery and development of novel antivirals. Chimerix has a propriety lipid technology that has been shown to improve the potency of antivirals, and has produced two clinical stage candidates. Lead candidate CMX001 is a phospholipid derivative of GILD's cidofovir that can potently kill a wide range of dsDNA viruses. It has successfully completed a Phase II trial for the prophylaxis against CMV reactivation in hematopoietic stem cell transplant (HSCT) patients. A Phase III trial is expected to begin in mid-2013, supporting an U.S. launch by 2016. Our consultants think CMX001 is safe, well tolerated, and potent, and is consequently likely to succeed in its Phase III SUPPRESS trial. Moreover, they think there is a need for a prophylactic to prevent infection with CMV and other dsDNA viral infections in transplant patients, and therefore expect CMX001 to be widely adopted once available. We project that CMX001 will achieve worldwide sales of \$330MM in HSCT alone by 2019, with Chimerix achieving profitability in 2017. CMX001 is also in development for the prevention of viral infection in solid organ transplant patients, and as a bioterrorism measure to prevent smallpox. Behind CMX001 is CMX157, a phospholipid derivative of GILD's tenofovir that partner Merck is developing for the treatment of HIV. Based on our analysis, we believe that Chimerix is undervalued based just on CMX001's potential as a CMV prophylactic in HSCT patients, with no contribution from other indications or other pipeline programs. We are initiating coverage with an Outperform rating.

CMX001 Is A Potent Antiviral That Has Produced Strong Phase II Data

CMX001 is a phospholipid derivative of GILD's cidofovir that can potently kill a wide range of dsDNA viruses including herpesviruses, adenoviruses, polyomaviruses, orthopoxviruses, and papillomaviruses. It has been most extensively tested as a prophylactic against CMV infection in patients who have received a hematopoietic stem cell transplant. In the Phase II CMX001 reduced the risk of CMV reactivation by 72% (10% for CMX001 100mg BIW, compared to 37% for placebo, $p = 0.002$) at its Phase III dose. Chimerix had predefined as a subgroup those patients who were CMV negative at baseline and in this group CMX001's efficacy was even more striking. None of the 41 patients on 100mg BIW CMX001 developed CMV PCR of $>1,000$ copies/mL during the dosing period, compared to 15 of the 47 (32%) of patients in the placebo cohort, $p < 0.001$. CMX001 100mg BIW was safe and well tolerated in the trial, with the frequency of adverse events being similar to placebo. Importantly, there was no myelosuppression observed for CMX001. This is a side effect produced by currently available CMV antivirals that can be particularly problematic for HSCT patients.

CMX001 To Begin Phase III In Mid-2013

Chimerix will initiate dosing in the Phase III SUPPRESS pivotal study of CMX001 in CMV prophylaxis in mid-2013. SUPPRESS will enroll 450 CMV seropositive adult patients and randomize them 2:1 to 100mg BIW CMX001 or placebo for 14 weeks. The primary endpoint of the study is failure to prevent CMV reactivation through week 24. The trial is powered to detect a 50% decrease in CMV reactivation in CMX001 vs. placebo. A single measure of CMV in the blood greater than or equal to 1,000 copies/mL (by Roche TAQMAN real-time PCR) will be considered of a failure of CMV prevention. In addition, subjects at risk for rapid progression to CMV disease

(recipients of umbilical cord blood stem cells, for example) will have a lower threshold of 150 copies/mL (the lower limit of quantification of the assay) for the initiation of pre-emptive therapy. Data from the SUPPRESS trial are expected in 2015.

Our Consultants Expect CMX001's Phase III To Succeed, And Think It Will Be Broadly Adopted

Our physician consultants have experience with CMX001 through Study 201 as well as emergency INDs to treat patients with intractable viral infections. They are universally impressed with it. They think its most advantageous attributes include its ability to potentially kill a broad spectrum of double stranded DNA viruses, its oral delivery, and its relatively benign side effect profile. On use as a prophylactic in HSCT itself, they think that the Study 201 data provide strong proof of concept. The physicians are therefore quite optimistic for the success of CMX001's Phase III trial. With the Phase III of very similar design to the Phase II, they think the statistically significant improvement in prevention of CMV reactivation produced by the 100mg BIW arm in the Phase II strongly predicts that CMX001 should be able to hit the primary endpoint of the Phase III.

Our consultants think CMX001 will be broadly adopted as a prophylactic agent to prevent CMV reactivation in HSCT patients. They note that the HSCT field wants to move toward CMV prophylaxis if an active, oral, nontoxic agent can be developed. They think there is little doubt that the 40-70% of patients at high risk for CMV reactivation could benefit from a prophylactic therapy. One-third to one-half will need preemptive therapy against CMV if not prophylaxed. They think that prophylaxis is the best way to manage high risk patients, as it would prevent the patients from having to deal with the risks and burdens associated with CMV reactivation, such as a higher incidence of graft failure. Valganciclovir, the currently marketed CMV preemptive therapy, is too toxic to be used as a prophylactic as it has a high rate of myelotoxicity and nephrotoxicity. Therefore, should the Phase III data replicate the Phase II, our consultants think CMX001 would be widely adopted.

Chimerix Is Undervalued Based On The Potential Of CMX001 In HSCT Alone

Our model assumes that by 2019 about 60% of adult high risk HSCT patients in the U.S. will be prophylaxed with CMX001, and that about 45% of pediatric high risk patients in the U.S. will be prophylaxed with it. We believe these penetration estimates are consistent with our consultant checks. Our 2019 U.S. CMX001 estimate is \$220MM. Similarly, our model assumes that by 2019 about 30% of adult high risk HSCT patients in the EU will be prophylaxed with CMX001, and that about 20% of pediatric high risk patients in the EU will be prophylaxed. Our 2019 EU CMX001 estimate is \$110MM, and our 2019 worldwide CMX001 estimate is \$330MM. Based on our CMX001 estimates we project that Chimerix will break into profitability in 2017, and will achieve over \$5 of EPS in 2019.

We have incorporated our revenue and profitability assumptions into a DCF. We assume that CMX001's revenue will fall to zero after 2025 when its IP (with expected extensions) expires. We employ a 10% discount rate, and attribute no terminal value to the CMX001 franchise. Despite these relatively conservative assumptions, our analysis suggests that Chimerix is significantly undervalued based on CMX001's opportunity as a prophylactic in HSCT alone.

Upcoming Chimerix Milestones

Event	Timing
Initiate Phase III SUPPRESS trial of CMX001 as prophylactic against CMV in adult HSCT	Mid:2013
Data from Phase II Study 202 of CMX001 as preemptive therapy for adenoviral disease in HSCT	H2:13
Define pediatric development plan for CMX001	H2:13
Data from Study 350 of CMX001 in transplant patients with severe, life threatening dsDNA infections	2013
Negotiation with BARDA over continued funding of CMX001's smallpox program	2013

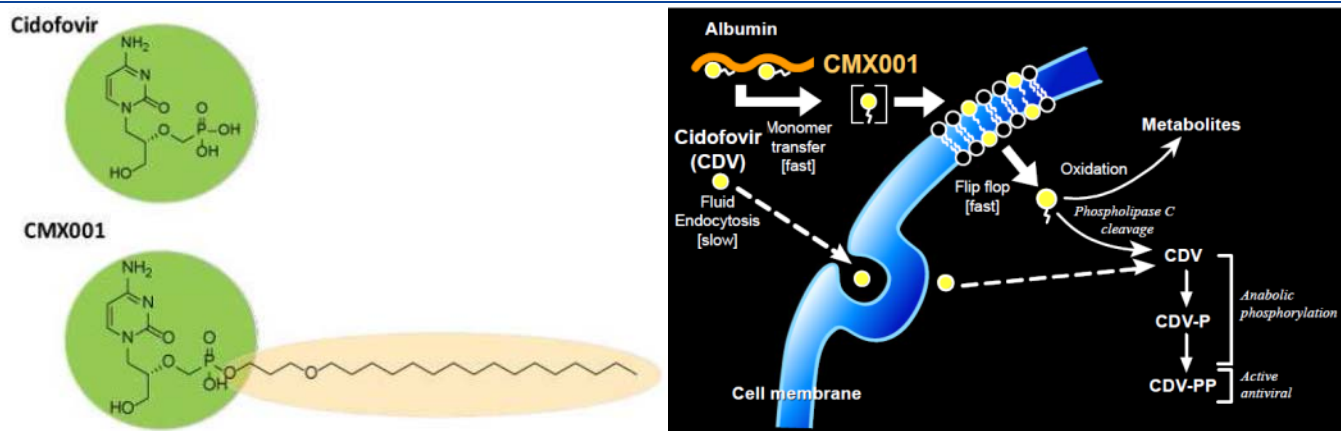
Source: Cowen and Company

CMX001: A Superior Composition, A Superior Drug

Chimerix's lead drug candidate, CMX001, is a proprietary lipid-conjugated derivative of cidofovir. CMX001 has Fast Track designation for cytomegalovirus (CMV), adenovirus (AdV), and smallpox. It has completed Phase II clinical development for the prevention of cytomegalovirus (CMV) in patients who receive hematopoietic stem cell transplant, and is expected to begin Phase III in mid-2013.

Cidofovir, or 1-[(S)-3-hydroxy-2-(phosphonomethoxy)propyl]cytosine dihydrate (HPMPC), is a nucleoside analogue that suppresses double-stranded DNA (dsDNA) replication by acting as an alternative substrate for viral DNA polymerase. Within cells, CMX001 undergoes Phospholipase C-mediated cleavage into the potent antiviral compound, cidofovir-diphosphate (CDV-PP). The advantage of CMX001 compared to cidofovir is that its lipid formulation technology allows much higher intracellular concentrations to be delivered intracellularly at lower doses. Thus, treatment with CMX001 results in lower plasma concentrations of drug and decreased risk of nephrotoxicity, which is one of the main limitations of cidofovir. Another benefit of CMX001's lipid-conjugated formulation is that it may allow for fewer pills and more convenient dosing for patients, due to the long duration of detectable CDV-PP in cells following dosing. CMX001 can be orally dosed in tablet or liquid form, while the approved form of cidofovir, Vistide (marketed by Gilead Sciences), is administered intravenously.

CMX001 Lipid Technology Allows For Enhanced Cellular Uptake



Source: Chimerix

Preclinical Studies Support CMX001's Enhanced Profile

Numerous preclinical studies, as well as several in-human clinical trials, support the superior characteristics of CMX001. Preclinically, CMX001 has demonstrated broad activity against all families of dsDNA viruses including herpesviruses (e.g., CMV, herpes simplex virus, varicella zoster, and Epstein-Barr virus), adenoviruses (over 50 subspecies), polyomaviruses (e.g., BKV and JCV), papillomaviruses, and poxviruses (vaccinia, monkeypox, and smallpox). Of note, CMV, AdV, and BKV are the three dsDNA viruses responsible for the majority of viral infections that are of concern for human illnesses.

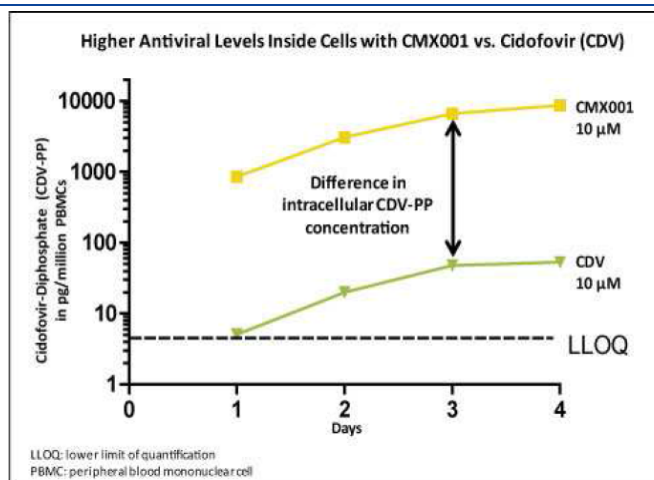
Five Families Of dsDNA Viruses That Cause Human Illness

Viral Class	Virus Abbreviation	Virus Name
Adenovirus	AdV	Adenovirus
Herpes	CMV	Cytomegalovirus
	EBV	Epstein-Barr virus
	HHV-6	Human herpesvirus 6
	HSV	Herpes simplex virus
	VZV	Varicella zoster virus
Papilloma	HPV	Human papilloma virus
Polyoma	BKV	BK virus
	JCV	JC virus
Pox	Variola major	Variola major
	Vaccinia	Vaccinia

Source: Chimerix

CMX001's lipid tail results in around a 100-fold greater intracellular concentration of CDV-PP compared to the same exposure of cells to cidofovir. Consistent with this observation, *in vitro* experiments have shown that CMX001 has around a 50- to 100-fold greater potency against dsDNA viruses. Specifically, in cell culture assays, much lower concentrations of CMX001 are required to reduce viral replication by 50% (known as effective concentration EC₅₀, where smaller EC₅₀ values correspond with greater potency). The EC₅₀ for CMX001 against CMV, AdV, and BKV is 0.001 μM, 0.02 μM, and 0.13 μM, respectively, while the EC₅₀ for cidofovir against these viruses is 0.38 μM, 1.3 μM, and 115.1 μM, respectively. This translates into a 422-fold, 65-fold, and 885-fold greater potency for CMX001 compared to cidofovir against these viruses, respectively. CMX001 has also demonstrated superior *in vitro* potency compared to other common antivirals. For example, the EC₅₀ for ganciclovir, foscarnet, acyclovir, and maribavir against CMV is 3.8 μM, 50-800 μM, >200 μM, and 0.31 μM, respectively.

This increase in potency has allowed CMX001 to be used in indications for which cidofovir and other antivirals are not potent or safe enough to tackle. Of note, preclinical studies have found that CMX001 has a high barrier to viral resistance. The CMX001-resistant strain of CMV that developed *in vitro* has reduced fitness due to a specific mutation, and is slow to evolve. In Chimerix's Phase II Study 201, no resistant mutations emerged. CMX001's preclinical characterization is further supported by 41 Absorption, Distribution, Metabolism and Excretion (ADME) studies, a 39-week chronic toxicology study in non-human primates, and 26 other *in vivo* studies in non-human primates, dogs, rabbits, rats, and mice.

CMX001: More Inside The Cell And More Active Vs. Cidofovir

Viral Class	Virus	CMX001 EC ₅₀ (μM)	Cidofovir EC ₅₀ (μM)	Enhanced Activity (in vitro)
Herpes	CMV	0.0009	0.38	422
	EBV	0.04	>170	>4250
	HHV 6	0.004	0.2	50
	HSV 1	0.06	15	250
	VZV	0.0004	0.5	1250
Adenovirus	AdV 5	0.02	1.3	65
Polyoma	BK	0.13	115.1	885
	JC	0.02	0.38	19
Pox	Variola major	0.1	27.3	271
	Vaccinia	0.8	46	57
Papilloma	HPV 11	17	716	42

Source: Chimerix

The Basics On Bone Marrow Transplantation

Bone marrow transplants (also known as hematopoietic stem cell transplants or HSCTs) are used to replace damaged or defective bone marrow cells with healthy bone marrow cells. There are numerous ways in which healthy bone marrow cells can become compromised including malignancy (e.g., leukemia or Non-Hodgkin's lymphoma), bone marrow failure (e.g., severe aplastic anemia or viral takeover), genetic and immune system disorders (e.g., systemic lupus erythematosus or thalassemia), and chemotherapy-induced destruction. Since bone marrow stem cells are responsible for producing the various components of blood, patients who are bone marrow compromised may suffer from anemia due to lack of red blood cell production, risk of infections due to lack of white blood cell production, or increased bleeding due to lack of platelet production.

Bone marrow transplants are classified by (1) stem cell donor (autologous or allogeneic); (2) stem cell source (umbilical cord, bone marrow, or peripheral blood); or (3) pre-transplantation conditioning regimen (myeloablative or reduced intensity). When myeloablation is used to suppress patient immune systems (thereby minimizing the risk of transplant rejection), patients are susceptible to reactivation of dormant viruses such as CMV. Allogeneic transplants and autologous transplants are differentiated by whether donor cells are taken from non-self or self. In the case of allogeneic transplants, cells are taken from a family member or an unrelated donor who has the best human leukocyte antigen (HLA) match possible. HLAs are cell surface proteins that define a person's tissue type and play a key role in immunity and self/non-self-recognition. The more dissimilar the HLA type, the higher the chances for graft-versus-host disease (GvHD), and the greater the need for immunosuppression which can increase the risk of infections. Despite the associated risks, allogeneic transplants have been successfully used to treat numerous disorders ranging from leukemias, radiation injury, hemoglobinopathies, aplastic anemias, inborn errors of metabolism, autoimmune diseases, lymphomas, and myelodysplastic syndrome.

Autologous marrow transplantations, where cells are removed prior to high-dose radiation or chemotherapy and administered after treatment, have been used in patients with hematologic and solid malignancies, amyloidosis, and autoimmune

conditions. In addition to GvHD, some complications that can occur following bone marrow transplantation include serious infections (especially during the beginning stages of the transplant), anemia, internal bleeding, cataracts, gastrointestinal complications (diarrhea, vomiting, nausea), and inflammation.

Conditions Commonly Treated With Hematopoietic Stem Cell Transplants (HSCT)

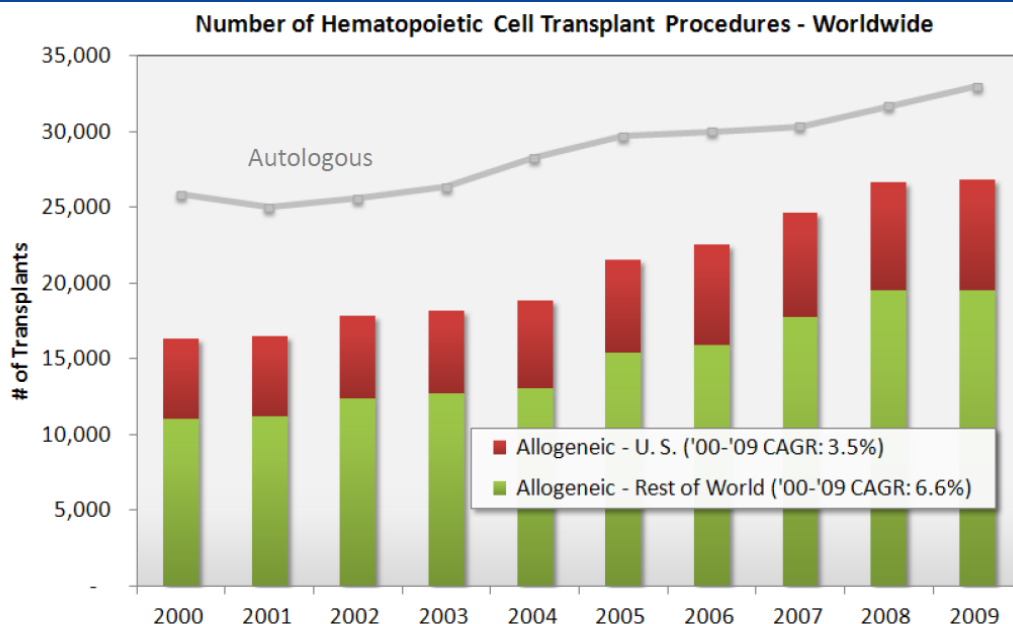
Autologous Transplantation		Allogeneic Transplantation	
Malignant	Non-Malignant	Malignant	Non-Malignant
Neuroblastoma	Autoimmune disorders	Acute myeloid leukemia	Aplastic anemia
Non-Hodgkin lymphoma	Amyloidosis	Non-Hodgkin lymphoma	Fanconi anemia
Hodgkins lymphoma		Hodgkin disease	Sevre combined
Acute myeloid leukemia		Acute lymphoblastic	immunodeficiency
Medulloblastoma		leukemia	Thalassemia major
Germ-cell tumors		Chronic myeloid leukemia	Diamond-Blackfan anemia
Multiple myeloma		Myelodysplastic syndromes	Sickle cell anemia
		Myeloid leukemia	Wiskott-Aldrich Syndrome
		Chronic lymphocytic	Osteopetrosis
		leukemia	Inborn errors of metabolism
			Autoimmune disorders

Source: Cowen and Company, Adapted from Copelan, *N Engl J Med*, 2006

Bone Marrow Transplants Are Increasingly Common...

According to some estimates, more than 240K bone marrow transplantations have been provided worldwide since 1955. These have occurred in around 50 countries, at 450 centers, and for more than 50 different lethal conditions. Autologous transplants are somewhat more common, with around 25-35K per year compared to approximately 15K allogeneic transplants per year. In the U.S. there are around 200 centers that perform transplants, 75% of which specifically perform HSCTs.

The Center for International Blood and Marrow Transplant Research estimates that around 20K HSCTs are performed annually in the U.S., and the European Group for Blood and Marrow Transplantation estimates a similar number in the E.U. Stem cell transplants have grown considerably over time (approximately 4% annually in the U.S. since 2000), given that they are the only way to treat certain conditions such as leukemias, lymphomas, and other cancers of the immune system. Within allogeneic transplants, the subset with unrelated donors has grown at a faster rate than other subsets within HSCT, which may suggest a greater role for antivirals as they are needed to suppress viruses when greater immunosuppression is utilized.

HSCT Growth In The Past Decade

Source: Center for International Blood and Marrow Transplant Research (CIBMTR).

...And CMV Reactivation Remains An Important Risk

Prior to transplantation, patients' immune systems are ablated to help ensure successful engraftment. This is done to prevent their "original" immune systems from attacking the new donor cells. Engraftment usually occurs within the first month after transplantation, and during this time patients have few immune cells to help fight off infection. As a result, they are susceptible to serious and life-threatening infections such as pneumonia. While engraftment occurs during the first month, the first 100 days post-transplantation are considered "high risk" since during this time dsDNA viral infections may cause co-infection with other pathogens and significant morbidity.

The most common infectious pathogen in HSCT is CMV. CMV is a beta herpes virus that has a 230 kbp, double-stranded linear DNA genome contained within an icosahedral nucleocapsid. The virus is latent and infects between 50-80% of the general population. Normally, the immune systems of healthy CMV-infected individuals maintain a fine balance of co-existence with CMV as long as reactivations remain asymptomatic. However, in immunocompromised patients, this delicate balance is not maintained, and uncontrolled CMV replication and dissemination can result in pneumonitis, gastroenteritis, retinitis, hepatitis, encephalitis, and ultimately death.

Over 65% of HSCT patients are seropositive and are thus susceptible to CMV infection. Of CMV seropositive patients who receive allogeneic transplants, around 80% develop detectable CMV in the blood, which correlates with disease progression and mortality when left untreated. This compares to 30% risk of CMV infection for patients who are seronegative but have seropositive donors, and less than 5% risk for patients who are seronegative with seronegative donors.

Risk Of CMV Reactivation In HSCT

Type	CMV Serostatus ⁽¹⁾	Risk of CMV Infection ⁽²⁾	Non-Relapse Mortality ⁽³⁾
Allogeneic	R+	80%	21%
	D-/R-	<5%	17%
	D+/R-	30%	18%
Autologous	R+	40%	27%

Source: Chimerix; R+, R-, D+, and D- refer to recipient seropositive, recipient seronegative, donor seropositive, and donor seronegative for CMV, respectively

The Current Standard Of Care For Managing CMV In HSCT Patients Is Far From Ideal

Given that the complications associated with CMV reactivation can lead to mortality, it is crucial for physicians to address it when performing HSCT. Unfortunately, current treatment options are limited and far from ideal. There are three general approaches for addressing CMV in HSCT patients: prevention, preemption, and treatment. Prevention involves administering a drug to seropositive patients who are at risk of CMV viral reactivation. Preventative treatment seeks to keep CMV “at bay” so that it does not become an issue in the first place. This approach obviates the need to frequently check for virus in the blood and is the preferred option when available. Examples of viral indications for which prevention is used include palizumivab for the prevention of respiratory syncytial virus and valganciclovir for the prevention of herpes simplex virus. However, despite the fact that prevention is the preferred approach to address CMV in HSCT, no anti-CMV drugs are approved in this setting due to their serious renal and hematological side effects. For example, although ganciclovir has been tested for prevention of CMV, its tendency to cause neutropenia has limited its use for prevention.

Preemption is the second approach for CMV management in HSCT and is the current standard of care used in around 30-40% of HSCT recipients. Preemptive treatment involves administering drug only after virus is detected in the blood above a certain threshold in order to stop progression to symptomatic disease. This requires careful monitoring. The most commonly used drug is ganciclovir, and although it is associated with toxicities, its side effects are somewhat more acceptable given that the risk of mortality is increased at this stage. Nonetheless, the toxicities associated with ganciclovir and other drugs currently used preemptively (e.g., valganciclovir, foscarnet, or intravenous cidofovir) are highly undesirable and include cytopenia, leukopenia, neutropenia, nephrotoxicity, and myelosuppression.

Moreover, preemptive CMV therapy has other significant drawbacks including increased hospitalizations, higher susceptibility to secondary infections, and emergence of CMV resistance.

Significant Toxicities Associated With Approved CMV Antivirals

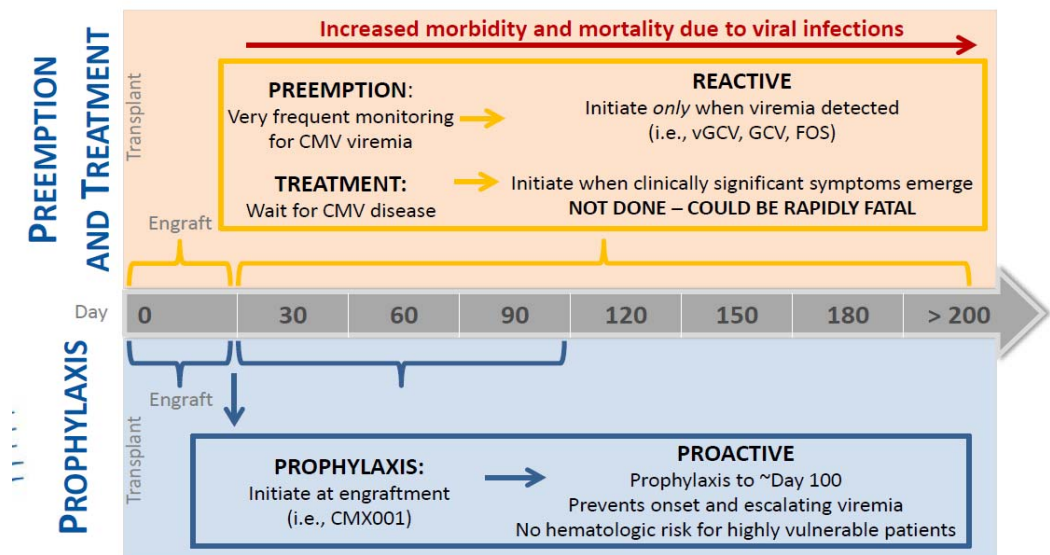
Drug	Major Pros	Major Cons
Valcyte valganciclovir HCl tablets	<ul style="list-style-type: none"> Standard of care for CMV prevention post-SOT Label in CMV prevention post adult and pediatric kidney and heart transplant Oral 	<ul style="list-style-type: none"> Cytopenia, leukopenia, neutropenia, some nephrotoxicity Too myelosuppressive for use in HSCT Need for regular laboratory monitoring Contraindicated in liver Resistance
Cytovene®-IV ganciclovir sodium for injection	<ul style="list-style-type: none"> Label for CMV prevention post HSCT/SOT Less myelotoxic than Valcyte 	<ul style="list-style-type: none"> IV administration Cytopenia, leukopenia, neutropenia, some nephrotoxicity Myelosuppressive Need for regular laboratory monitoring Resistance
Foscavir® (Foscarnet Sodium)	<ul style="list-style-type: none"> Different toxicity profile vs. GCV Low myelotoxicity/use before engraftment Activity against GCV resistant CMV Activity against all known herpes viruses 	<ul style="list-style-type: none"> IV administration Nephrotoxicity and seizures Need for regular laboratory monitoring Chronic supply shortage
Vistide® cidofovir injection	<ul style="list-style-type: none"> Broad spectrum efficacy for dsDNA viruses Off label standard of care for BK/AdV Infrequent administration (1-2x week) 	<ul style="list-style-type: none"> IV administration Highly nephrotoxic, regular monitoring needed Limited controlled data/no label in transplant
ZOVIRAX acyclovir	<ul style="list-style-type: none"> Gold standard for prevention of HSV/VZV Strong safety profile Oral and inexpensive 	<ul style="list-style-type: none"> Pill burden/frequency of dosing GCV cross-resistance HSV resistance due to non-compliance

Source: Chimerix

The third strategy for managing CMV in HSCT is a careful “watch and wait” approach where treatment is given only after symptoms begin to manifest or the virus is detected in organs. However, given that treatment after the onset of symptoms has very limited impact, this approach is not preferred.

Given the limitations of the preemptive and post-symptomatic treatment approaches, there is a great need for safe and effective antivirals that can be used in the prevention setting.

Why Prophylaxis Should Become The Standard Of Care For HSCT



Source: Chimerix

Study 201 Provided Proof Of Concept For CMX001 In CMV Prophylaxis

Chimerix conducted Study 201 to provide proof-of-concept that CMX001 can be used as a CMV prophylactic in stem cell transplant patients.

Study 201 was a randomized, placebo-controlled dose-escalation study in 230 CMV seropositive allogeneic HSCT recipients. The trial included a wide range of HSCT patients, including cordblood and mismatched recipients, but all patients had to have evidence of stem cell engraftment before dosing could be initiated. Patients were randomized to placebo or one of five CMX001 doses (40mg QW, 100mg QW, 200mg QW, 200mg BIW, 100mg BIW). The primary endpoint was a composite of (1) The incidence of CMV disease at any time during therapy and (2) a CMV polymerase chain reaction (PCR) of > 200 copies/mL at the time of the last dose of study drug.

All CMX001 doses except the lowest showed at least a trend in reducing CMV events compared to placebo, and statistical significance was reached for the 100mg BIW dose. The proportion of subjects who developed CMV disease or a CMV PCR positive result at the end of the dosing period was 10% for the 100mg BIW group, compared to 37% for placebo-treated patients, $p=0.002$. The fact that the higher 200mg BIW dose did not hit statistical significance has caused some controversy among investors, as some are uncomfortable with the “inverse” dose response. However, our consultants note that the lack of statistical significance was due simply to the fact that many patients on 200mg BIW discontinued therapy due to side effects, and that all of the CMV events occurred after patients had discontinued CMX001. Therefore the diarrhea-related dropouts obscured the efficacy of the 200mg BIW dose.

CMX001 Study 201 Primary Endpoint Data

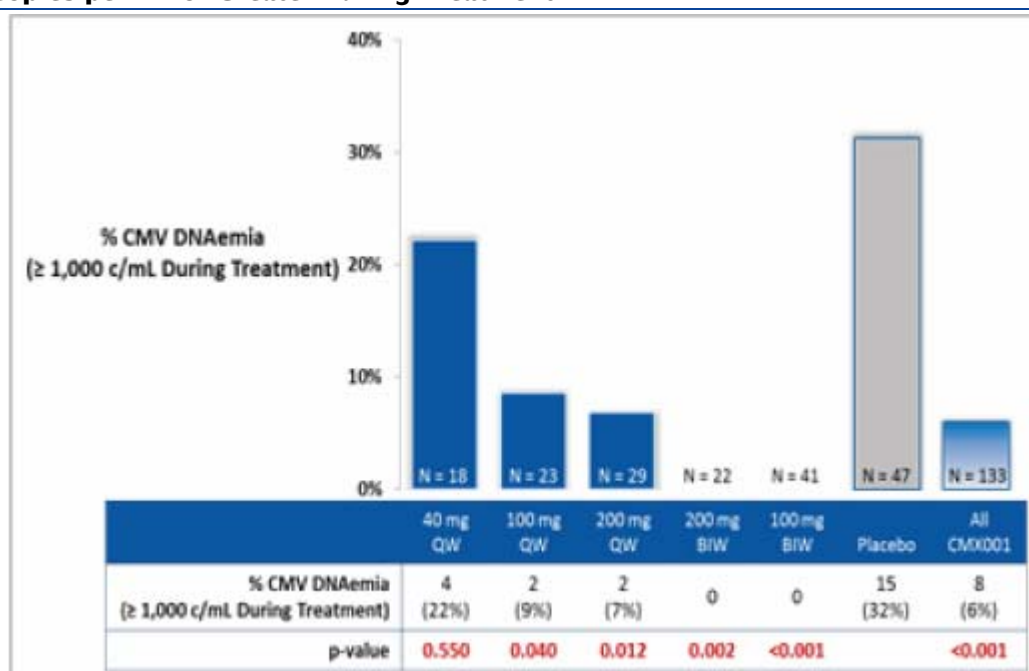
	Patients With CMV Events	
	n(%)	p-value
Placebo	22 (37%)	
40mg weekly	13 (52%)	NS
100mg weekly	6 (22%)	0.218
200mg weekly	12 (31%)	0.525
200mg BIW	7 (23%)	0.235
100mg BIW	5 (10%)	0.002

Source: Chimerix, Cowen and Company

Chimerix had predefined as a subgroup those patients who were CMV negative at baseline. In this group of 133 patients, CMX001's efficacy was even more striking. None of the 41 patients on 100mg BIW CMX001 developed CMV PCR of >1,000 copies/mL during the dosing period, compared to 15 of the 47 (32%) of patients in the placebo cohort, $p<0.001$. Additionally, none of the patients on 200mg BIW CMX001 had CMV DNAemia >1,000 c/mL during treatment, either, further corroborating the fact that the miss of statistical significance for this arm on the primary outcome measure was likely due to CMV viremia following discontinuation

of therapy. CMV DNAemia of >1,000 c/mL while on therapy was the criteria for the initiation of pre-emptive CMV therapy in the trial.

Percent of Subjects CMV Negative At Baseline Who Developed CMV PCR of 1,000 Copies per mL or Greater During Treatment



Source: Chimerix, Cowen and Company

Study 201 helped Chimerix better understand CMX001's safety and tolerability, and identified the 100mg BIW dose as the most appropriate for Phase III. The 100mg BIW dose was well tolerated, with a similar frequency of adverse events compared to the placebo group.

CMX001 Study 201: 100mg BIW Adverse Event Data

Adverse Event	100mg BIW	Placebo
>1 Adverse Event	100%	98%
Grade 3 AE	38%	42%
Grade 4 AE	14%	7%
Grade 5 AE	10%	9%
Adverse events leading to withdrawal	36%	46%
Drop Out Rates Due To:		
Blood and Lymphatic	2%	3%
Gastrointestinal	10%	3%
General and Administration site	0	2%
Hepatobiliary	0	0
Immune System	6%	2%
Infections and infestations (including CMV)	14%	31%

Source: Chimerix, Cowen and Company

The most common adverse events associated with CMX001 were gastrointestinal-associated events, and elevated ALT levels.

There was a dose-related, transient increase in ALT in Study 201. At the 100mg BIW dose, approximately 30% of subjects experienced ALT increases greater than three times the upper limit of normal, compared to 16% of placebo patients. However, the proportion of patients experiencing >5x, >10x, or >20x ULN was not significantly different between 100mg BIW and placebo. Additionally, CMX001 was not associated with increases in aspartate aminotransferase or bilirubin, and there were no signs of liver injury or hepatic necrosis in any patient. With little clinical consequence from the elevations, our consultants have been unconcerned by CMX001's impact on ALT levels, and say that in the Phase II it was of only minor concern.

CMX001 Study 201: ALT Elevations

ALT Levels	100mg BIW	Placebo
>3x ULN - 5x ULN	10 (20%)	4 (7%)
>5x ULN - 10x ULN	4 (8%)	4 (7%)
>10x ULN - 20x ULN	1 (2%)	1 (2%)
>20x ULN	1 (2%)	0

Source: Chimerix, Cowen and Company

CMX001's dose-limiting toxicity is gastrointestinal, and diarrhea in particular. The incidence and severity of GI adverse events was not particularly bad for the 100mg BIW dose, with 10% of CMX001 patients discontinuing due to GI adverse events, compared to 3% of placebo patients.

The incidence and severity of diarrhea was unacceptably high at the 200mg BIW dose, so much so in fact that the FDA requested that doses of CMX001 be limited to a total weekly dose of 200mg or less. In response to high rate of diarrhea seen at the 200mg BIW dose, Chimerix implemented a safety monitoring and management plan (SMMP) that codified how physicians should deal with diarrhea and other gastrointestinal adverse events. The plan includes interruption of CMX001 for patients who experience a Grade 3 or higher GI adverse event, and monitoring of serum albumin as a decrease in serum albumin from baseline is a marker of drug-related diarrhea (as opposed to diarrhea of other etiologies, including infections and other complications of the transplant). Following the introduction of the management plan, fewer than 10% of patients discontinued CMX001 due to diarrhea and other gastrointestinal side effects.

Our consultants think that the rate and severity of diarrhea is acceptable at the 100mg BIW dose, particularly in light of the management plan. They don't think the diarrhea will prevent either the approval of CMX001, or the adoption of CMX001 in the prophylactic setting.

Phase III SUPPRESS Trial To Begin Mid-2013

Chimerix will initiate dosing in the Phase III SUPPRESS pivotal study of CMX001 in CMV prophylaxis in mid-2013.

SUPPRESS will enroll 450 CMV seropositive adult patients and randomize them 2:1 to 100mg BIW CMX001 or placebo. Dosing with CMX001 will begin shortly after patients receive allogeneic hematopoietic stem cell transplants, and does not require

evidence of stem cell engraftment (in contrast to the Phase II trial). Patients will receive CMX001 or placebo through week 14, and will continue to be monitored through week 24 for evidence of CMV disease or CMV in the blood at levels high enough to require pre-emptive therapy. A single measure of CMV in the blood greater than or equal to 1,000 copies/mL (by Roche TAQMAN real-time PCR) will be considered of a failure of CMV prevention. In addition, subjects at risk for rapid progression to CMV disease (recipients of umbilical cord blood stem cells, for example) will have a lower threshold of 150 copies/mL (the lower limit of quantification of the assay) for the initiation of pre-emptive therapy.

The primary endpoint of the study is failure to prevent CMV reactivation through week 24. The trial is powered to detect a 50% decrease in CMV reactivation in CMX001 vs. placebo with greater than 85% power. We believe that the trial assumes a 30% failure rate in the placebo arm, and a 15% in the CMX001 arm, with a 16% drop out rate in both arms.

Data from the SUPPRESS trial are expected in 2015.

Chimerix has performed an analysis of the '201 data based on the statistics and endpoint of the SUPPRESS trial. In this analysis, 37% of placebo patients had CMV reactivation, compared to 10% of 100mg BIW CMX001 patients, a reduction of 73%. In our opinion these data bode well for the success of the Phase III trial.

Consultants Are Optimistic For Success Of SUPPRESS, And Adoption of CMX001 As Prophylactic In HSCT

Our physician consultants have experience with CMX001 through Study 201 as well as emergency INDs to treat patients with intractable viral infections. They are universally impressed with it. They think its most advantageous attributes include its ability to potentially kill a broad spectrum of double stranded DNA viruses, its oral delivery, and its relatively benign side effect profile (particularly at low dose). They think it will be a welcome addition to their antiviral armamentarium.

On use as a prophylactic in HSCT itself, they think that the Study 201 data provide strong proof of concept for CMX001 as a prophylactic agent. The large reduction in the proportion of patients with CMV reactivation convinces them that CMX001 is a very active drug with “amazing” antiviral activity. They also think at the 100mg BIW dose its adverse event profile is quite manageable. Although in their experience the incidence and severity of diarrhea at higher doses is unworkable, at the 100mg BIW dose they find it acceptable, particularly in light of the management plan. They think it unlikely that diarrhea will meaningfully impact the conduct of the Phase III, or CMX001's ultimate adoption. The physicians were similarly unconcerned by CMX001's other side effects. One of our consultants had a patient with an ALT elevation during the Phase II trial. However, the physician said it was “minor” and resolved without consequences. Our consultants are particularly encouraged by the fact that CMX001 does not suppress a patients' bone marrow, as this is a particularly unattractive side effect in post-transplant patients.

The physicians are quite optimistic for the success of CMX001's Phase III trial. With the Phase III of very similar design to the Phase II, they think the statistically significant improvement in prevention of CMV reactivation produced by the 100mg BIW arm in the Phase II strongly predicts that CMX001 should be able to hit the primary endpoint of the Phase III. Moreover, their experience with CMX001 in its compassionate use program has further solidified their belief that CMX001 is very

potent at killing the CMV virus. In light of the Phase II data and CMX001's potency, they note that the design of the Phase III is reasonable, and that its assumptions (50% reduction in risk, 16% dropout rate) are sound.

Assuming that CMX001 succeeds in its Phase III, our consultants think it will be broadly adopted as a prophylactic agent to prevent CMV reactivation in HSCT patients. They note that the HSCT field wants to move toward CMV prophylaxis if an active, oral, nontoxic agent can be developed. They think there is little doubt that the 70% of patients at high risk for CMV reactivation could benefit from a prophylactic therapy, as one-third to one-half will need preemptive therapy against CMV if not prophylaxed. They think that prophylaxis is the best way to manage high risk patients, as it would prevent the patients from having to deal with the risks and burdens associated with CMV reactivation, such as a higher incidence of graft failure. Valganciclovir, the currently marketed CMV preemptive therapy, is too toxic to be used as a prophylactic as it has a high rate of myelotoxicity and nephrotoxicity. Therefore, should the Phase III data replicate the Phase II, our consultants think CMX001 would be widely adopted as a prophylactic.

Our consultants think that a 50% reduction in the risk of CMV reactivation, with no neutropenia, will be sufficiently persuasive to cause the field to switch to CMX001 prophylaxis. Although they note that an elevated rate of diarrhea would dull their enthusiasm for CMX001, they suggest that the diarrhea in the Phase III would need to be much of much greater severity than that seen in the Phase II to prevent CMX001's adoption. They think that even if 20% of patients in the Phase III discontinued due to diarrhea, CMX001 would likely still be adopted as a prophylactic, as 20-30% of valganciclovir patients must switch therapy because of side effects. It would seem unlikely that CMX001 will produce diarrhea at these levels, as in the Phase II following the introduction of the management plan, fewer than 10% of patients discontinued CMX001 due to diarrhea and other gastrointestinal side effects.

Competition: CMX001 Is The Leader Of The Pack

Merck/AiCuris' Letermovir: During 2012 Merck licensed letermovir (AIC246) from AiCuris. Letermovir is a viral terminase inhibitor that specifically kills the CMV virus. Results from a Phase II trial of letermovir for CMV prevention in HSCT patients were released in February 2012. The Phase II enrolled 133 CMV-positive allogeneic human blood precursor cell patients and they were randomized to receive placebo, letermovir 240 mg/day or letermovir 120 mg/day for 84 days. The trial excluded mismatched or cord blood recipients, as well as patients with graft versus host disease or with impaired liver or renal function. The primary efficacy endpoint was incidence and time to onset of CMV prophylaxis failure, as defined by the development of systematic detectable CMV replication (viral load above the assay threshold of 42 DNA copies/mL) or CMV end organ disease.

The incidence of failure was reduced by both letermovir doses: it was experienced by 29.4% and 32.3% of 240mg/day and 120mg/day patients, respectively, compared to 63.6% of placebo patients ($p=0.007$ for the comparison of 240mg/day vs. placebo and $p=0.014$ for 120 mg/day vs. placebo). The incidence of CMV prophylaxis failure among patients receiving treatment for at least 7 days prior to CMV reactivation was none for letermovir 240mg ($p=0.004$ vs. placebo) and only 2 patients for letermovir 120mg ($p=0.109$ vs. placebo). The high letermovir dose also hit the endpoint of time to prophylaxis failure ($p=0.02$) compared to patients receiving placebo, while the low dose missed statistical significance. Letermovir appeared safe and well tolerated, with fewer patients on letermovir having either one treatment emergent

AE (17.3% for letermovir vs. 33.3% of placebo) or an AE-prompted discontinuation (25.5% on letermovir vs. 57.6% for placebo).

Based on these data AiCuris expects partner Merck will begin a Phase III trial for letermovir. However, clinicaltrials.gov lists no currently active or planned trials.

Although our consultants think that letermovir is a viable CMV prophylactic, they think CMX001 is more promising. While letermovir antiviral activity is specific to CMV (it does not kill other viruses), CMX001 is effective against a very wide range of double stranded DNA viruses. As HSCT patients are at risk for infections from many dsDNA viruses, our consultants would prefer to use the more broad-spectrum agent, providing patients with more comprehensive protection. In fact, some of our consultants had the option of participating in either the CMX001 or letermovir clinical studies, and chose the CMX001 trials. Therefore they expect that if letermovir and CMX001 are both on the market, CMX001 will take majority share.

ViroPharma's Maribavir:

Maribavir is an oral anti-CMV drug which targets viral DNA/capsid assembly and may have less toxicity than valganciclovir. Maribavir was previously tested in a Phase III program aimed at prevention of CMV disease in transplant patients, which was not successful. However, in June 2012, ViroPharma announced the initiation of a Phase II program that is instead testing higher doses of Maribavir for the treatment of CMV infection. ViroPharma's confidence in this program is bolstered by data from a handful of patients suggesting that Maribavir is effective at reducing CMV viremia in HSCT and organ transplant patients, including those with known resistance to valganciclovir.

Maribavir's Preliminary Data In CMV

	US Emergency-IND (E-IND) ^a	EU Name Patient Program (NPP) ^b
Population studied	Resistant / Refractory CMV	
Number with data	6	9
SCT / SOT	1 / 5	3 / 6
Known resistance mutations to GCV or FOS	4 (67%)	6 (67%)
Virologic response	CMV Undetectable: 4 (67%)	CMV ↓ ≥1.5 log or undetectable: 4 / 8* (50%)

* 1 EU patient received MBV as secondary prophylaxis,
so is not included in treatment response

a) Avery et al., Transplant Infect Dis 2010; 12: 489-96
b) Alain et al., 24th Intl. Congress of The Transplantation Society 2012

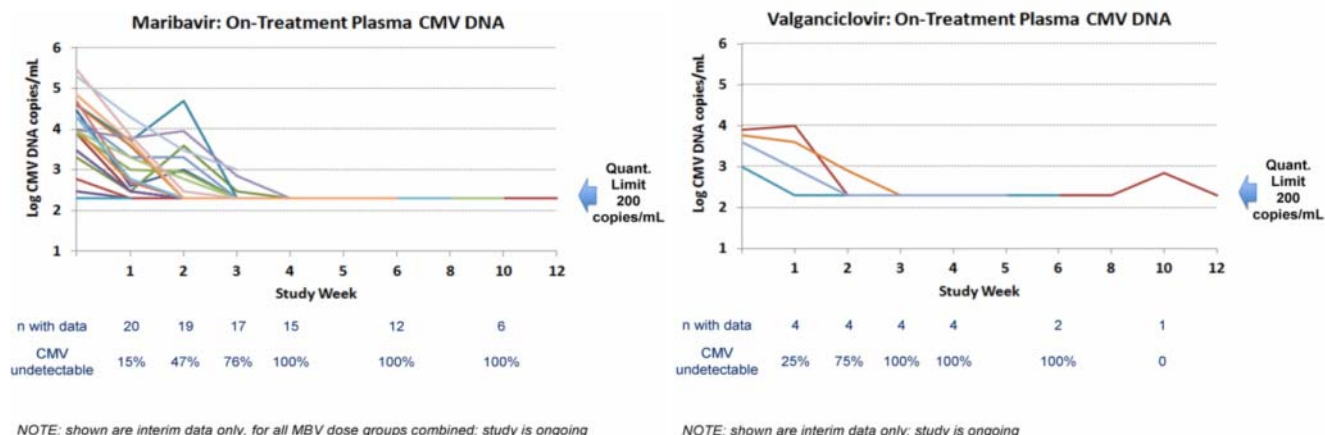
Source: ViroPharma 2012 Analyst Day

There are two ongoing trials, one for asymptomatic, first-line CMV viremia, and one for CMV that has failed other anti-viral agents. The first-line study is enrolling 160 transplant patients in Europe who have CMV viremia but not CMV organ disease. Patients will be randomized to either one of three doses of Maribavir (400mg, 800mg, or 1200mg BID), or valganciclovir, and treated for up to 12 weeks with blood levels of CMV DNA monitored. The "resistant/refractory" study is enrolling 120 U.S. patients with CMV viremia, with or without CMV organ disease. All patients must have failed at least one of ganciclovir, valganciclovir, or foscarnet. Patients will be

randomized to one of three doses of Maribavir for up to 24 weeks, with blood CMV DNA monitored.

The most recent interim data from the EU first line trial were presented on ViroPharma's Q1 earnings call on May 1, 2013. The data are encouraging, with 26/28 patients achieving undetectable CMV viremia by week 4 of the study, including all 26 evaluable patients. This is comparable to the valganciclovir comparator for which 5 of 8 patients, and 5 of 5 evaluable patients, achieved undetectable. 1 patient on maribavir had their viral loads rebound while on drug.

Maribavir's Interim E.U. Phase II Data



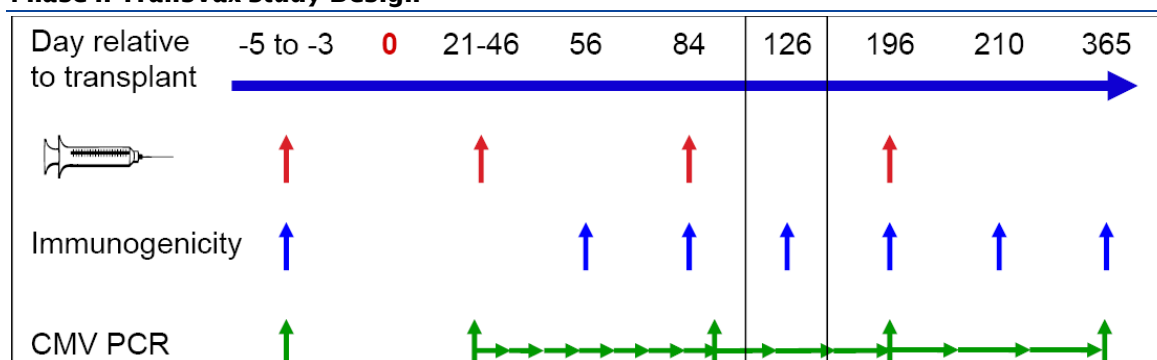
Source: ViroPharma

The U.S. Phase II resistant/refractory trial has enrolled 13 patients, of whom 12 are evaluable and all 12 achieved undetectable. 3 of the maribavir patients rebounded while on therapy.

Maribavir appeared safe and well tolerated in both Phase IIs, with no myelosuppression and only taste disturbance as the most prominent AE.

ViroPharma has not committed to advancing maribavir into Phase III for CMV. It is important to note that while maribavir does appear effective, it will not compete directly against CMX001 as maribavir's trials are testing it as a preemptive therapy, and a treatment for CMV viremia. Therefore patients will have failed CMX001 before getting maribavir.

Vical and Astellas' TransVax: Vical/Astellas' TransVax, a DNA-based prophylactic vaccine for CMV reactivation in immunocompromised patients, has also produced proof-of-concept data. Vical initiated Phase I trials with bivalent and trivalent (three-plasmid) developmental candidates, each formulated with a poloxamer that enhances cellular uptake and expression. While data from these trials indicated that both formulations were safe, the bivalent vaccine (a.k.a. TransVax) induced higher levels of antibody and T-cell responses, and was selected for future studies. TransVax contains two plasmid encoded antigens, pp65 and gB, formulated with a poloxamer designed to stimulate T-cell responses. Vical has partnered TransVax to Astellas, which has plans to begin a Phase III trial in H1:13.

Phase II TransVax Study Design

Source: Vical

A randomized, double-blind, placebo-controlled Phase II trial on TransVax began enrolling patients in 2006, and sought to recruit approximately 80 bone marrow transplant donor/recipient pairs and 80 stem cell transplant recipients (only) from unrelated donors at 15-20 centers. Individuals enrolled in the trial were vaccinated twice prior to donation (four weeks and two weeks) and once after donation (four-to-six weeks). The primary endpoint is safety, with the occurrence rate of clinically significant CMV levels being the secondary endpoint.

Phase II TransVax Clinical Efficacy Results

Per Protocol Population (to 1 yr)		TransVax™ (N=40)	Placebo (N=34)	% Change	p-value
*Occurrence of CMV reactivation (≥ 500 copies/mL)		13 (32%)	21 (62%)	-48%	0.008 ^a
Time to initial CMV reactivation (days)	Median	>365	109.5	NA	0.003 ^b
Number of CMV reactivation episodes	0	27 (68%)	13 (38%)	NA	0.017 ^c
	1	8 (20%)	14 (41%)		
	2	4 (10%)	3 (9%)		
	3	1 (3%)	3 (9%)		
	≥ 4	0	1 (3%)		
Duration of viremia (days)	Mean	10.6 (0-68)	19.5 (0-181)	-46%	0.069 ^c
Normalized (as a % of time on study)	Mean	4.9 (0-63)	7.7 (0-49)	-36%	0.042 ^c
*Occurrence of initiating CMV-specific antiviral therapy		19 (48%)	21 (62%)	-23%	0.145 ^a
Cumulative CMV-specific antiviral therapy (days)	Mean	30.4 (0-323)	39.8 (0-212)	-24%	0.266 ^c
CMV-associated disease (GI and/or pneumonia)		3 (8%)	4 (12%)	-33%	0.696 ^d

*Note that viral load endpoints were obtained from the central lab, whereas local lab results and site-specific algorithms were primarily used for treatment decisions.
p-value was computed by ^aCMH test stratified by site, ^blog rank test, ^cWilcoxon rank sum, or ^dFisher's exact test.

Source: Vical

Twelve-month data from 74 evaluable (80 total) patients indicated vaccination was associated with reductions in the incidence of CMV viremia (-48%, $p=0.008$) and duration of viremia (-36%, $p=0.04$), and an increase in the time to viremia (>365 days vs. 110 days, $p=0.003$) relative to placebo. The TransVax arm also exhibited favorable trends toward reducing antiviral therapy. CMV disease was detected in 8% of TransVax patients vs. 12% of placebo patients.

Phase II TransVax Safety Data

- No safety concerns
- No significant difference between groups in SAEs

Adverse Events (ITT Population)	TransVax™ (N=42)	Placebo (N=38)
Subjects with at least one AE	42 (100%)	38 (100%)
Subjects with related AEs	16 (38%)	17 (45%)
Subjects with at least one SAE	33 (79%)	29 (76%)
Subjects with possibly related SAEs	2 ^a (5%)	1 ^b (3%)
Subjects who died during the study	8 (19%)	12 (32%)

^aAngioedema (1 hr) and subarachnoid hemorrhage from a known aneurysm (3 mo) after receiving the investigational product.

^bCMV colitis 6 mo after last dose.

Source: Vical

Trial data also showed favorable immunogenicity data for the vaccine patients. Despite the immunosuppressed status of these blood cancer patients, T-cell response to pp65 protein challenge was significantly higher in the TransVax group ($p=0.003$) and T-cell and antibody response to glycoprotein B challenge showed an increasing trend. There were no differences in SAEs between TransVax and placebo.

In April 2012, Vical announced that the partners have finalized Phase III design. Though precise details have not been disclosed, Vical has said that, based on FDA and EMA guidance, CMV disease will not be the primary endpoint. A viremia-based endpoint should allow a much smaller trial (Vical has expressed hope for less than 300 patients) than a disease endpoint. Vical and Astellas have stated that they plan to begin enrollment in a Phase III trial for HSCT recipients in H1:13, and also plan to begin a Phase II trial in solid organ transplant recipients in H1:13.

CMX001 Has Potential In Other Indications, Too

Although CMX001's first Phase III trial is in adult HSCT, its broad activity against a range of dsDNA viruses suggests it could be useful in other populations too.

Chimerix is developing CMX001 in pediatric patients as well as adult patients, and targets an end of Phase II meeting with the FDA to define a pediatric plan during H2:2013. Chimerix is completing Study 202, with data expected during H2:2013. Study 202 is a randomized, placebo-controlled study of CMX001 as a preemptive therapy for adenovirus infection in HSCT patients. Chimerix estimates that 5-7% of patients have adenovirus viremia during the first 100 days post-transplant based on its screening data. While less frequent than CMV viremia, adenovirus viremia can be just as serious, with the medical literature estimating that disseminated adenovirus infection can have a mortality rate as high as 80%. Study 202 is evaluating QW and BIW regimens of CMX001 versus placebo for the preemptive management of asymptomatic adenovirus viremia in 48 pediatric and adult HSCT recipients.

Patients were randomized to receive 12 weeks of preemptive therapy with CMX001 or placebo, and patients were followed for an additional 4 weeks post-therapy. Adults or children weighing 50kg or greater receive CMX001 tablets at doses of 100mg BIW or 200mg QW, while pediatric patients receive CMX001 as a liquid formulation at doses of 2mg/kg BIW or 4mg/kg QW. The primary endpoint of Study 202 is treatment failure, which is a composite endpoint of progression to probable

or definite adenovirus disease, or increasing adenovirus viremia during randomized therapy that requires discontinuation from randomized therapy. Patients who are classified as failures during the blinded portion of the trial are offered open-label CMX001 as a treatment. Secondary endpoints of the trial include incidence and time to mortality, the percentage of subjects on randomized therapy with undetectable plasma AdV PCR, and the percentage of subjects with the emergence of CMV, EBV or Bk virus viremia or disease.

Chimerix has made CMX001 available to transplant centers worldwide through emergency INDs and a formal open-label expanded access study, Study 350. Over 230 patients have been treated with CMX001 under EINDs, and 142 adult and 68 pediatric patients have been enrolled in Study 350. CMX001 has been used to treat life-threatening infections of CMV, AdV, BKV, EBV, JCV, HHV-6, HHV-8, HSV-1, HSV-2, VZV, HPV, molluscum, and vaccinia.

Based on the compassionate use/EIND data, Chimerix has confidence in the ability of CMX001 to manage a wide range of dsDNA infections. Safety data from the program has not produced any worrisome safety signals, which is notable given the complicated health status of these highly compromised patients.

Based on the accumulated data, Chimerix thinks that CMX001 could also have promise in the prevention of BKV disease in HSCT and solid organ transplant patients, and is contemplating development.

CMX001 Under Contract With BARDA As Medical Countermeasure Against Smallpox

CMX001 has shown potency at inhibiting the variola virus, the dsDNA virus that causes smallpox. Efficacy has been demonstrated against variola in cultured cells, and CMX001 has shown activity against related viruses in animal models of smallpox including ectromelia in mice, rabbitpox, monkeypox.

In February 2011 Chimerix received a contract from BARDA to fund development of CMX001 for the treatment of smallpox in the event of a smallpox outbreak. The funding from the February 2011 contract will be exhausted during H1:2013.

Chimerix is working with FDA to define a program to develop CMX001 under the animal efficacy rule. Preliminary feedback from the FDA is that Chimerix can use the mouse ectromelia and rabbit rabbitpox models for CMX001. Future BARDA funding will depend on Chimerix successfully negotiating a path with the FDA. Our model assumes no BARDA funding after H1:13.

We Project CMX001 Will Achieve \$330MM In WW HSCT Revenue By 2019

According to the Center for International Blood & Marrow Transplant Research (CIBMTR), there were 8,860 allogeneic hematopoietic stem cell transplants and 9,026 autologous hematopoietic stem cell transplants in the United States during 2010. Of those, approximately one-quarter were pediatric patients, while three-quarters were adults. Our consultants estimate that 70% of allogeneic recipients, and 40% of autologous recipients, are at high risk for CMV reactivation and therefore would be appropriate for prophylactic therapy.

For CMV prophylaxis in adult HSCT we project a U.S. launch in 2016, and an EU launch in 2017. We project a launch in pediatric HSCT in 2017 in the U.S. and 2018 in the EU. We assume that CMX 001 will be priced at 2,500/week, and that patients will receive 14 weeks of therapy.

Our model assumes that by 2019 about 60% of adult high risk HSCT patients in the U.S. will be prophylaxed, and that about 45% of pediatric high risk patients in the U.S. will be prophylaxed. We believe these penetration estimates are consistent with our consultant checks. Our 2019 U.S. CMX001 estimate is \$220MM.

Similarly, our model assumes that by 2019 about 30% of adult high risk HSCT patients in the EU will be prophylaxed, and that about 20% of pediatric high risk patients in the EU will be prophylaxed. Our 2019 EU CMX001 estimate is \$110MM, and our 2019 worldwide CMX001 estimate is \$330MM.

CMX001 Revenue Model (\$MM)

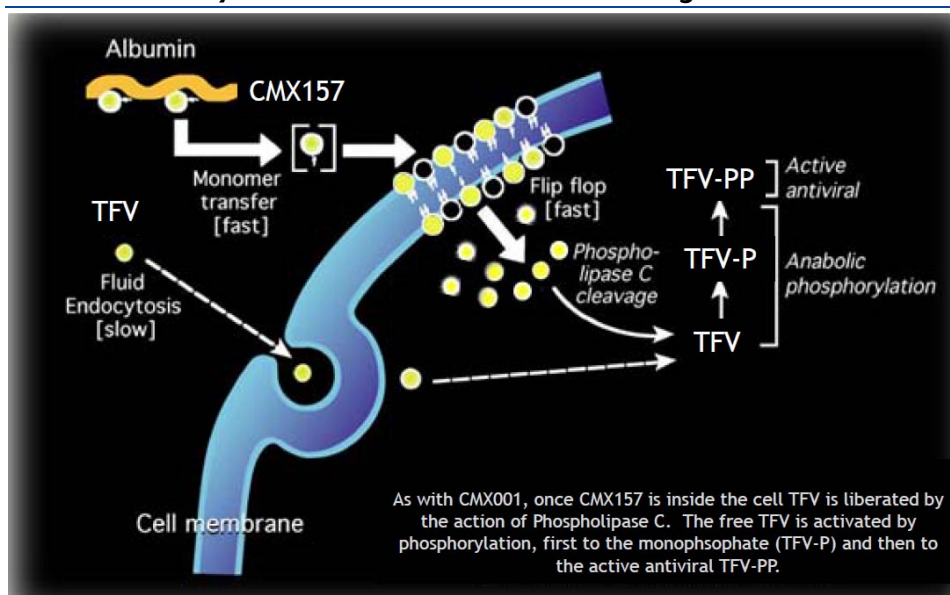
	2012A	2013E	2014E	2015E	2016E	2017E	2018E	2019E	Assumptions/Notes
U.S. Transplant Market									
Adult HSCT									
Number of Adult Allogeneic Transplants in The U.S.	6645	6778	6913	7052	7193	7337	7483	7633	From Center for International Blood and Marrow Donor Program Consultants' estimate
% At Risk For CMV Reactivation or Other dsDNA Infection	70%	70%	70%	70%	70%	70%	70%	70%	
Number High Risk Adult Allogeneic Transplants	4652	4745	4839	4936	5035	5136	5238	5343	
% Who Receive CMX-001 Prophylaxis	0%	0%	0%	0%	17%	31%	49%	59%	
Number On CMX-001	0	0	0	0	857	1571	2571	3143	
Average Cost per Patient (\$000)	35	35	35	35	35	35	35	35	Assume \$2,500/week, for 14 weeks
CMX-001 Revenue From Adult Allogeneic (\$MM)	0.0	0.0	0.0	0.0	30.0	55.0	90.0	110.0	
Number of Adult Autologous Transplants in The U.S.	6770	6905	7043	7184	7328	7474	7624	7776	From Center for International Blood and Marrow Donor Program Consultants' estimate
% At Risk For CMV Reactivation or Other dsDNA Infection	40%	40%	40%	40%	40%	40%	40%	40%	
Number High Risk Adult Autologous Transplants	2708	2762	2817	2874	2931	2990	3049	3110	
% Who Receive CMX-001 Prophylaxis	0%	0%	0%	0%	15%	33%	47%	60%	
Number On CMX-001	0	0	0	0	429	1000	1429	1857	
Average Cost per Patient (\$000)	35	35	35	35	35	35	35	35	Assume \$2,500/week, for 14 weeks
CMX-001 Revenue From Adult Autologous (\$MM)	0.0	0.0	0.0	0.0	15.0	35.0	50.0	65.0	
Total CMX001 Revenue From U.S. Adult HSCT (\$MM)	0.0	0.0	0.0	0.0	45.0	90.0	140.0	175.0	
Pediatric HSCT									
Number of Pediatric Allogeneic Transplants in The U.S.	2215	2259	2304	2351	2398	2446	2494	2544	From Center for International Blood and Marrow Donor Program
% At Risk For CMV Reactivation or Other dsDNA Infection	70%	70%	70%	70%	70%	70%	70%	70%	
Number High Risk Pediatric Allogeneic Transplants	1551	1582	1613	1645	1678	1712	1746	1781	
% Who Receive CMX-001 Prophylaxis	0%	0%	0%	0%	0%	15%	33%	47%	
Number On CMX-001	0	0	0	0	0	257	571	829	
Average Cost per Patient (\$000)	35	35	35	35	35	35	35	35	
CMX-001 Revenue From Pediatric Patients (\$MM)	0.0	0.0	0.0	0.0	0.0	9.0	20.0	29.0	
Number of Pediatric Autologous Transplants in The U.S.	2257	2302	2348	2395	2443	2491	2541	2592	
% At Risk For CMV Reactivation or Other dsDNA Infection	40%	40%	40%	40%	40%	40%	40%	40%	
Number High Risk Pediatric Autologous Transplants	903	921	939	958	977	997	1016	1037	
% Who Receive CMX-001 Prophylaxis	0%	0%	0%	0%	0%	17%	28%	44%	
Number On CMX-001	0	0	0	0	0	171	286	457	
Average Cost per Patient (\$000)	35	35	35	35	35	35	35	35	
CMX-001 Revenue From Pediatric Autologous (\$MM)	0.0	0.0	0.0	0.0	0.0	6.0	10.0	16.0	
Total CMX001 Revenue From U.S. Pediatric HSCT (\$MM)	0.0	0.0	0.0	0.0	0.0	15.0	30.0	45.0	
CMX-001 U.S. Revenue (\$MM)	0.0	0.0	0.0	0.0	45.0	105.0	170.0	220.0	
EU Transplant Market									
Adult HSCT									
Number of Adult Allogeneic Transplants in The EU	6645	6778	6913	7052	7193	7337	7483	7633	Approximately same number of transplants as US
% At Risk For CMV Reactivation or Other dsDNA Infection	70%	70%	70%	70%	70%	70%	70%	70%	
Number High Risk Adult Allogeneic Transplants	4652	4745	4839	4936	5035	5136	5238	5343	
% Who Receive CMX-001 Prophylaxis	0%	0%	0%	0%	0%	11%	21%	30%	
Number On CMX-001	0	0	0	0	0	571	1114	1600	
Average Cost per Patient (\$000)	35	35	35	35	35	35	35	35	Assume parity pricing with U.S.
CMX-001 Revenue From EU Adult Allogeneic (\$MM)	0.0	0.0	0.0	0.0	0.0	20.0	39.0	56.0	
Number of Adult Autologous Transplants in The EU	6770	6905	7043	7184	7328	7474	7624	7776	
% At Risk For CMV Reactivation or Other dsDNA Infection	40%	40%	40%	40%	40%	40%	40%	40%	
Number High Risk Adult Autologous Transplants	2708	2762	2817	2874	2931	2990	3049	3110	
% Who Receive CMX-001 Prophylaxis	0%	0%	0%	0%	0%	10%	20%	31%	
Number On CMX-001	0	0	0	0	0	286	600	971	
Average Cost per Patient (\$000)	35	35	35	35	35	35	35	35	
CMX-001 Revenue From EU Adult Autologous (\$MM)	0.0	0.0	0.0	0.0	0.0	10.0	21.0	34.0	
Total CMX001 Revenue From EU Adult HSCT (\$MM)	0.0	0.0	0.0	0.0	0.0	30.0	60.0	90.0	
Pediatric HSCT									
Number of Pediatric Allogeneic Transplants in The EU	2215	2259	2304	2351	2398	2446	2494	2544	
% At Risk For CMV Reactivation or Other dsDNA Infection	70%	70%	70%	70%	70%	70%	70%	70%	
Number High Risk Pediatric Allogeneic Transplants	1551	1582	1613	1645	1678	1712	1746	1781	
% Who Receive CMX-001 Prophylaxis	0%	0%	0%	0%	0%	0%	10%	21%	
Number On CMX-001	0	0	0	0	0	0	171	371	
Average Cost per Patient (\$000)	35	35	35	35	35	35	35	35	
CMX-001 Revenue From EU Pediatric Allogeneic Patients (\$M)	0.0	0.0	0.0	0.0	0.0	0.0	6.0	13.0	
Number of Pediatric Autologous Transplants in The EU	2257	2302	2348	2395	2443	2491	2541	2592	
% At Risk For CMV Reactivation or Other dsDNA Infection	40%	40%	40%	40%	40%	40%	40%	40%	
Number High Risk Pediatric Autologous Transplants	903	921	939	958	977	997	1016	1037	
% Who Receive CMX-001 Prophylaxis	0%	0%	0%	0%	0%	0%	11%	19%	
Number On CMX-001	0	0	0	0	0	0	114	200	
Average Cost per Patient (\$000)	35	35	35	35	35	35	35	35	
CMX-001 Revenue From EU Pediatric Autologous Patients (\$M)	0.0	0.0	0.0	0.0	0.0	0.0	4.0	7.0	
Total CMX001 Revenue From EU Pediatric HSCT (\$MM)	0.0	0.0	0.0	0.0	0.0	0.0	10.0	20.0	
CMX-001 EU Revenue (\$MM)	0.0	0.0	0.0	0.0	0.0	30.0	70.0	110.0	
Worldwide CMX-001 Revenue	0.0	0.0	0.0	0.0	45.0	135.0	240.0	330.0	

Source: Cowen and Company

CMX157 Being Developed For HIV

Chimerix's second drug candidate CMX157 is in Phase I development for HIV infection. CMX157 is a lipid conjugated form of tenofovir, the most widely used nucleotide reverse transcriptase inhibitor (NRTI) for HIV. Similar to CMX001, CMX157's lipid technology allows for enhanced delivery into cells. Once inside the cell, CMX157 is cleaved into TFV by Phospholipase C and undergoes anabolic phosphorylation into the active antiviral TVF-PP.

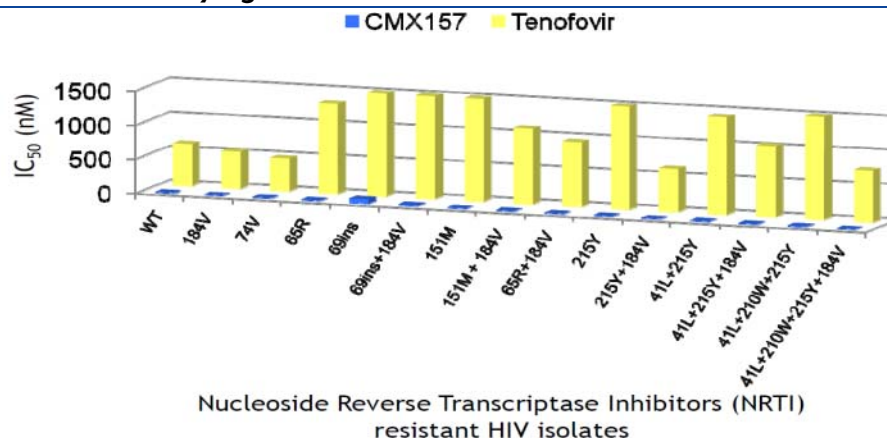
CMX157 Delivery Into Cells And Activation Into Drug



Source: Chimerix

Chimerix has preclinical data to suggest that CMX157 has superior properties versus tenofovir including the potential to deliver higher intracellular concentrations of active drug, improved safety, and lower dosing frequency. *In vitro* data suggest that CMX157 is 200-fold more potent than tenofovir against the major resistant HIV subtypes.

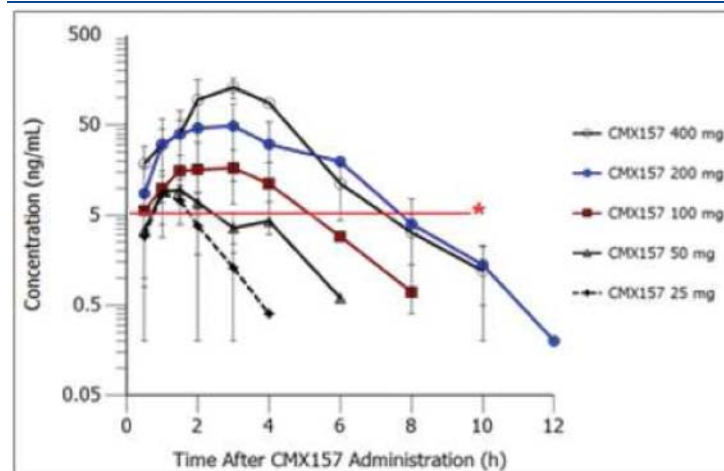
CMX157 Activity Against NRTI Resistant HIV Isolates



Source: Chimerix

Additionally, CMX157's structure may allow for less renal toxicity due to reduced systemic exposure. In a pre-Merck deal Phase I study in healthy individuals, CMX157 was safe and well-tolerated and demonstrated long-lived plasma levels that may support less frequent dosing compared to tenofovir.

Plasma Concentrations After CMX157 Oral Dosing



*Concentration that equaled TFV-PP level produced by TFV peak concentration *in vitro*

Source: Chimerix

In 2012 Chimerix granted Merck an exclusive worldwide license to develop and commercialize CMX157 for all human indications. The deal included a \$17.5MM upfront payment from Merck, \$151MM of potential milestone payments, and a tiered royalty on net sales ranging from high single digits to low double digits. Based on its potentially superior properties compared to tenofovir, Chimerix believes the drug has the potential to displace tenofovir in fixed-dose combinations.

Superior Properties Of CMX157 Vs. Tenofovir

	<i>In vitro</i> HIV Activity	Cleaved in Plasma	Binds directly to HIV	Dosing	Fixed-Dose Combinations
Viread	Micromolar IC ₅₀ s	Yes; active secretion into kidney via hOATs	No	Once daily	300mg
CMX157	Nanomolar IC ₅₀ s; active against TFV resistant HIV ✓	No; CMX157 not a substrate for hOATs ✓	Yes; CMX157 "hitchhikes" on HIV ✓	Once weekly? monthly? ✓	Anticipate 25 - 100 mg ✓

Source: Chimerix

Chimerix's Intellectual Property Robust

Chimerix's intellectual property position is robust and includes both issued patents (including exclusive licenses from The Regents of the University of California) and patent applications. There do not appear to be any patents from third parties that encompass CMX001 or CMX157. In addition to its issued patents detailed below, the company is actively engaged in expanding its IP by filing patents on methods of treatment, different dosage forms, and identification of more nucleotide derivatives and compounds.

CMX001 has issued U.S. composition of matter patents (# 6,716,825; #7,034,014; #7,094,772; # 7,790,703) and issued U.S. method of use patents (#6,716,825; #7,452,898; #7,790,703) that are expected to expire in 2020. Chimerix is eligible for a five year extension under the Hatch-Waxman Act which should extend CMX001's protection to 2025. Additionally, Chimerix has patent applications that could extend CMX001's protection out to 2031 if issued.

CMX157 is protected by issued U.S. composition of matter patents (#6,716,825; #7,034,014; #7,094,772; and #7,790,703) and method of use patents (#6,716,825; #7,790,703; and #7,687,480) that expire in 2020. Similar to the patents covering CMX001, these patents should be eligible for an extension out to 2025. Patent applications covering CMX157 could extend protection out to 2031 if issued.

Our Analysis Suggests Chimerix Is Undervalued

Based on our CMX001 estimates we project that Chimerix will break into profitability in 2017, and will achieve over \$5 of EPS in 2019. Our model assumes that Chimerix markets CMX001 worldwide through a specialty sales force targeting transplant centers, and that in 2019 Chimerix will have an operating margin of 59%.

We have incorporated our revenue and profitability assumptions into a DCF. We assume that CMX001's revenue will fall to zero after 2025 when its IP (with expected extensions) expires. We employ a 10% discount rate, and attribute no terminal value to the CMX001 franchise. Despite these relatively conservative assumptions, our analysis suggests that Chimerix is significantly undervalued.

Chimerix Quarterly P&L (\$MM)

	2012A	Q1:13E	Q2:13E	Q3:13E	Q4:13E	2013E	2014E
CMX-001		-					
CMX-157 Royalty		-					
Collaboration and Licensing Revenue	17.4	-	-	-	-	-	5.0
Contract And Grant Revenue	16.3						
Total Revenue	33.7	-	-	-	-	-	5.0
COGS		-	-	-	-	-	0.5
<i>Gross Margin</i>							
R&D	27.8	7.0	7.2	7.8	8.3	30.3	34.5
SG&A	8.7	2.5	2.8	3.0	3.1	11.4	12.0
Other							
Operating Expenses	36.5	9.5	10.0	10.8	11.4	41.7	47.0
Operating Income / (Loss)	(2.8)	(9.5)	(10.0)	(10.8)	(11.4)	(41.7)	(42.0)
Interest Income, net	(0.8)	(0.2)	(0.2)	(0.2)	(0.2)	(0.8)	0.5
Other Income	(0.8)						
Pretax net income	(4.4)	(9.7)	(10.2)	(11.0)	(11.6)	(42.5)	(41.5)
Accretion of redeemable convertible preferred stock	(4.4)						
Taxes		-	-	-	-	-	-
<i>Tax Rate</i>		0%	0%	0%	0%	0%	0%
GAAP Net Income	(8.8)	(9.7)	(10.2)	(11.0)	(11.6)	(42.5)	(41.5)
GAAP EPS	\$(1.62)	\$(1.76)	\$(0.42)	\$(0.43)	\$(0.45)	\$(2.10)	\$(1.55)
Diluted Shares Outstanding (MM)	5.4	5.5	24.3	25.5	25.7	20.2	26.8

Source: Cowen and Company

Chimerix Annual P&L (\$MM)

	2012A	2013E	2014E	2015E	2016E	2017E	2018E	2019E
CMX-001	-	-	-	-	45.0	135.0	240.0	330.0
CMX-157 Royalty	-	-	-	-	-	-	-	-
Collaboration and Licensing Revenue	17.4	-	5.0	15.5	20.0	20.0	20.0	20.0
Contract And Grant Revenue	16.3	-	-	-	-	-	-	-
Total Revenue	33.7	-	5.0	15.5	65.0	155.0	260.0	350.0
COGS	-	-	0.5	1.6	3.6	10.8	19.2	26.4
<i>Gross Margin</i>		0%	0%	0%	0%	0%	0%	0%
R&D	27.8	30.3	34.5	38.0	45.0	55.0	65.0	75.0
SG&A	8.7	11.4	12.0	13.0	28.0	34.0	40.0	45.0
Other	-	-	-	-	-	-	-	-
Operating Expenses	36.5	41.7	47.0	52.6	76.6	99.8	124.2	146.4
Operating Income / (Loss)	(2.8)	(41.7)	(42.0)	(37.1)	(11.6)	55.2	135.8	203.6
Interest Income, net	(0.8)	(0.8)	0.5	1.0	1.0	2.0	6.0	6.0
Other Income								
Pretax net income	(4.4)	(42.5)	(41.5)	(36.1)	(10.6)	57.2	141.8	209.6
Accretion of redeemable convertible preferred stock								
Taxes	-	-	-	-	-	-	-	-
<i>Tax Rate</i>	-	0%	0%	0%	0%	0%	0%	0%
GAAP Net Income	(8.8)	(42.5)	(41.5)	(36.1)	(10.6)	57.2	141.8	209.6
GAAP EPS	(1.62)	(2.10)	(1.55)	(1.20)	(0.35)	1.65	3.95	5.65
Diluted Shares Outstanding (MM)	5.4	20.2	26.8	30.0	30.5	34.8	35.9	37.1

Source: Cowen and Company

Chimerix DCF Analysis

Financial Year End	12/31/2012
Valuation Date	5/1/2013
Discount Rate	10.0%
Terminal Growth Rate	-20.0%

Chimerix: DCF Valuation														
SMM	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	
CMX-001	0	0	0	45	135	240	330	347	364	382	401	421	442	
Growth (%)					20%	10%	5%	5%	5%	5%	5%	5%	5%	
CMX-157 Royalty	0	0	0	0	0	0	0	0	0	0	0	0	0	
Growth (%)														
Collaboration and Licensing Revenue	0	5	16	20	20	20	20	20	20	20	20	20	20	
Growth (%)														
Contract And Grant Revenue	0	0	0	0	0	0	0	0	0	0	0	0	0	
Growth (%)														
Total Revenues	0	5	16	65	155	260	350	367	384	402	421	441	462	
Growth (%)					138%	68%	35%	5%	5%	5%	5%	5%	5%	
COGS	0	1	2	4	11	19	26	30	31	33	34	36	37	
COGS as a % of sales				8%	8%	8%	8%	9%	9%	9%	8%	8%	8%	
R&D	30	35	38	45	55	65	75	55	50	44	46	44	46	
R&D as a % of Revenues				69%	35%	25%	21%	15%	13%	11%	11%	10%	10%	
SG&A	11	12	13	28	34	40	45	51	54	48	51	53	55	
SG&A as a % of Revenues				43%	22%	15%	13%	14%	14%	12%	12%	12%	12%	
Operating Income	-42	-42	-37	-12	55	136	204	230	249	277	290	308	323	
Tax	0	0	0	0	0	0	0	69	75	83	87	93	97	
Tax rate	0%	0%	0%	0%	0%	0%	0%	30%	30%	30%	30%	30%	30%	
NOL/ Tax Assets Utilized														
Tax rate														
Taxes Paid	0	0	0	0	0	0	0	69	75	83	87	93	97	
Approx Free Cash Flow	(42)	(42)	(37)	(12)	55	136	204	161	174	194	203	216	226	
Years	0.67	1.66	2.66	3.67	4.67	5.66	6.66	7.67	8.67	9.66	10.66	11.66	12.66	
Discount Factor	0.94	0.85	0.78	0.71	0.64	0.58	0.53	0.48	0.44	0.40	0.36	0.33	0.30	
NPV of Cash flows	(39)	(36)	(29)	(8)	35	79	108	78	76	77	74	71	68	

Terminal Value Calculation	
Final year FCF	0
Perpetual Growth Rate	-20.0%
Terminal Value	0
Discount Factor	0
Present Value of Terminal Value	0
Present Value of Cash Flows	554
Enterprise Value	554
Add: Net cash	100
Market Value	654
Fully Diluted Shares Outstanding	25.5
Value per Fully Diluted Share	\$25.65

Source: Cowen and Company

Addendum

STOCKS MENTIONED IN IMPORTANT DISCLOSURES

Ticker	Company Name
ACT	Actavis
CMRX	Chimerix
FOLD	Amicus Therapeutics
GILD	Gilead Sciences
VIVO	Meridian Bioscience

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Outperform (1)	Stock expected to outperform the S&P 500
Neutral (2)	Stock expected to perform in line with the S&P 500
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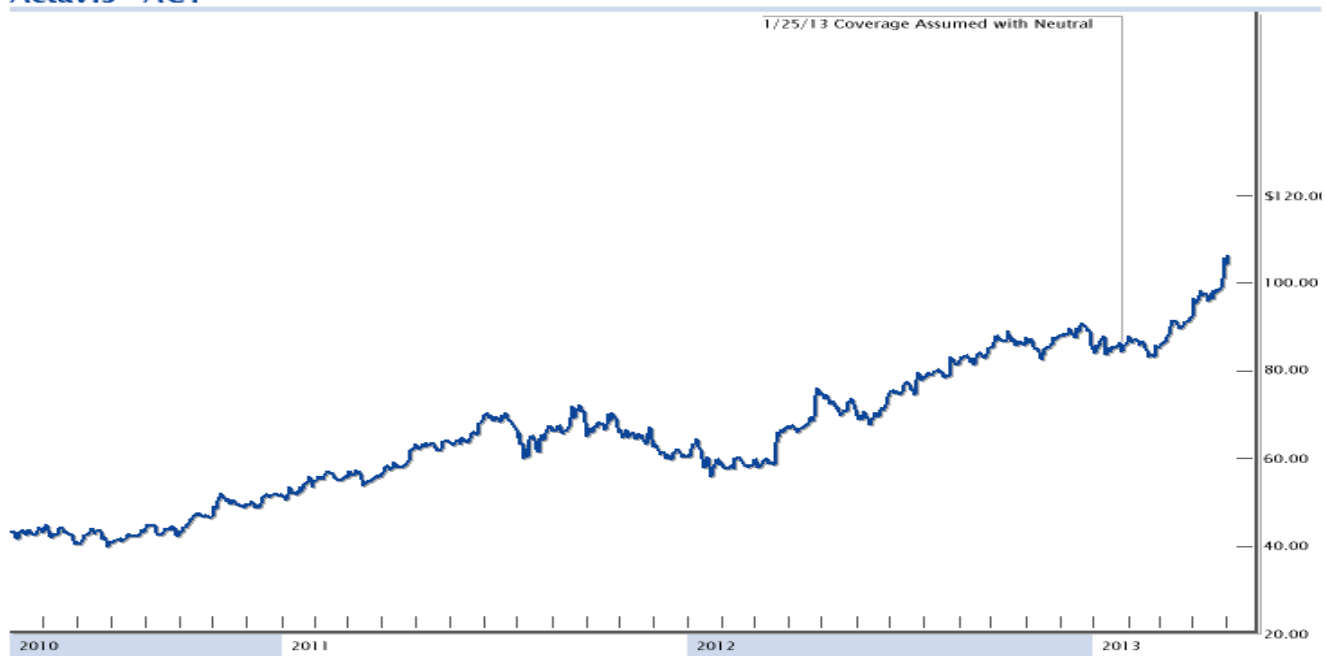
(a) Assumptions: Time horizon is 12 months; S&P 500 is flat over forecast period.

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Rating	Pct of companies under coverage with this rating	Pct for which Investment Banking services have been provided within the past 12 months
Buy (b)	53.3%	9.3%
Hold (c)	43.0%	0.5%
Sell (d)	3.4%	0.0%

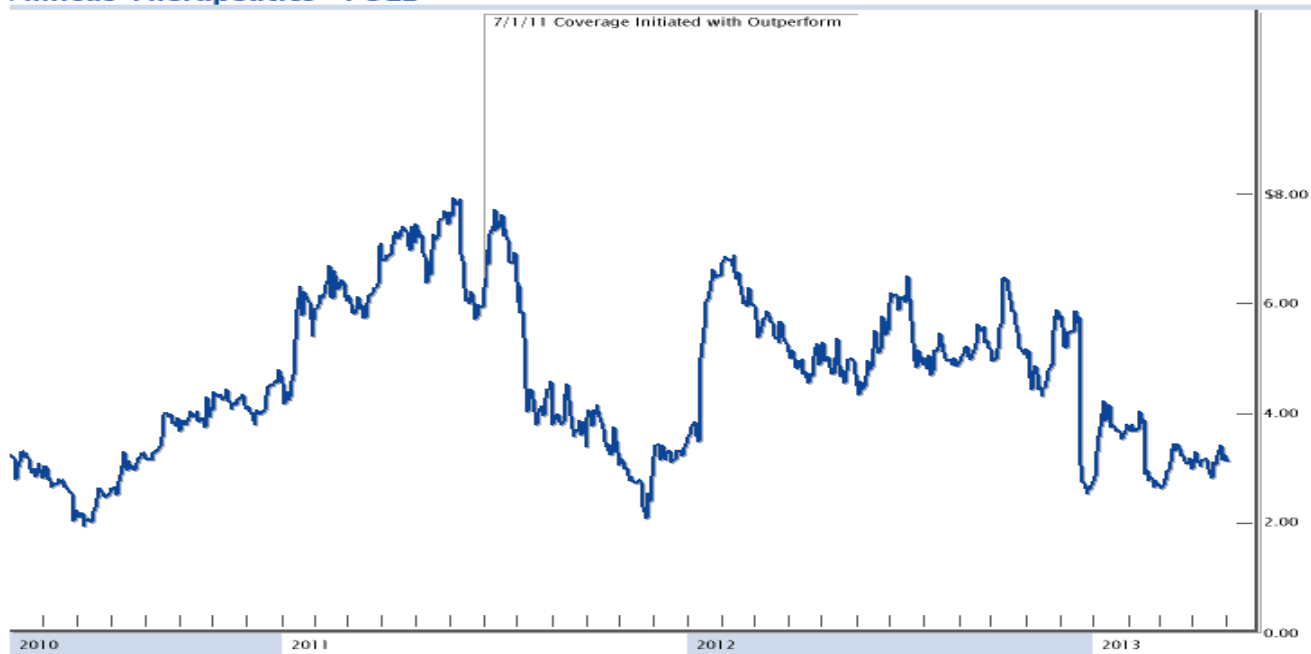
(a) As of 03/31/2013. (b) Corresponds to "Outperform" rated stocks as defined in Cowen and Company, LLC's rating definitions (see above). (c) Corresponds to "Neutral" as defined in Cowen and Company, LLC's ratings definitions (see above). (d) Corresponds to "Underperform" as defined in Cowen and Company, LLC's ratings definitions (see above). Note: "Buy," "Hold" and "Sell" are not terms that Cowen and Company, LLC uses in its ratings system and should not be construed as investment options. Rather, these ratings terms are used illustratively to comply with NASD and NYSE regulations.

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Actavis - ACT

Pricing data provided by Reuters America. Chart as of 5/3/13 in USD.

Cowen and Company Price and Ratings History

Amicus Therapeutics - FOLD

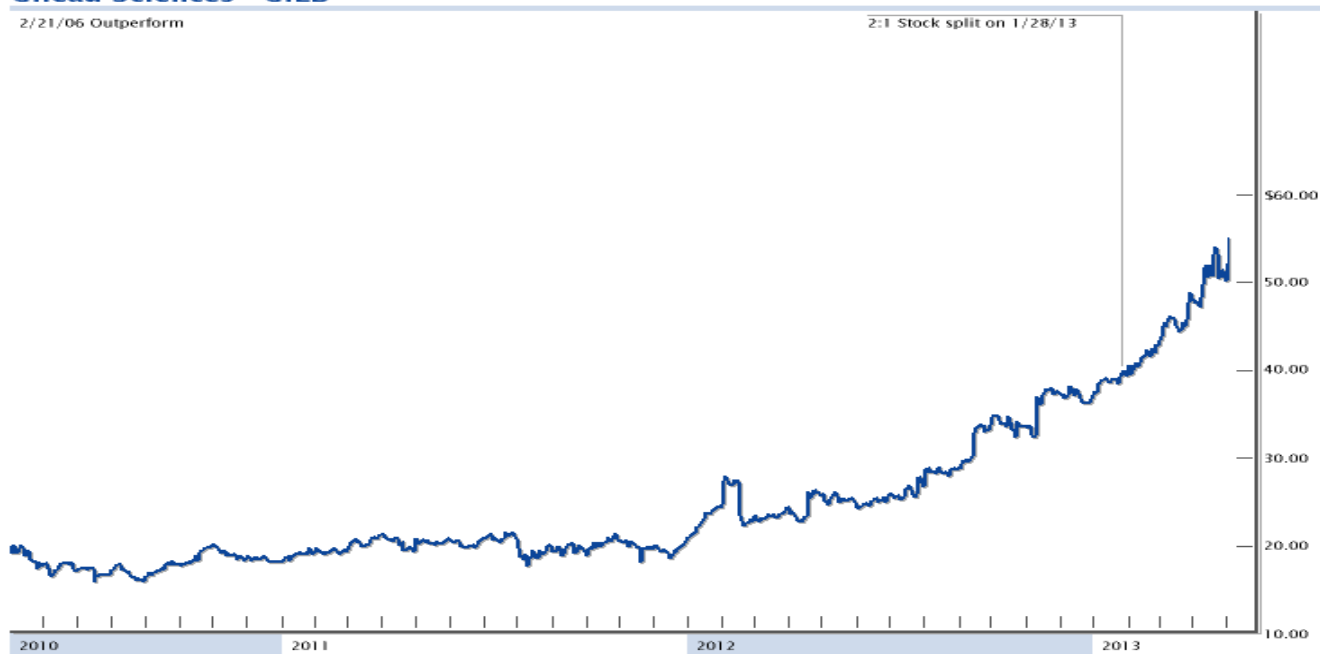
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Cowen and Company Price and Ratings History

Gilead Sciences - GILD

2/21/06 Outperform

2:1 Stock split on 1/28/13

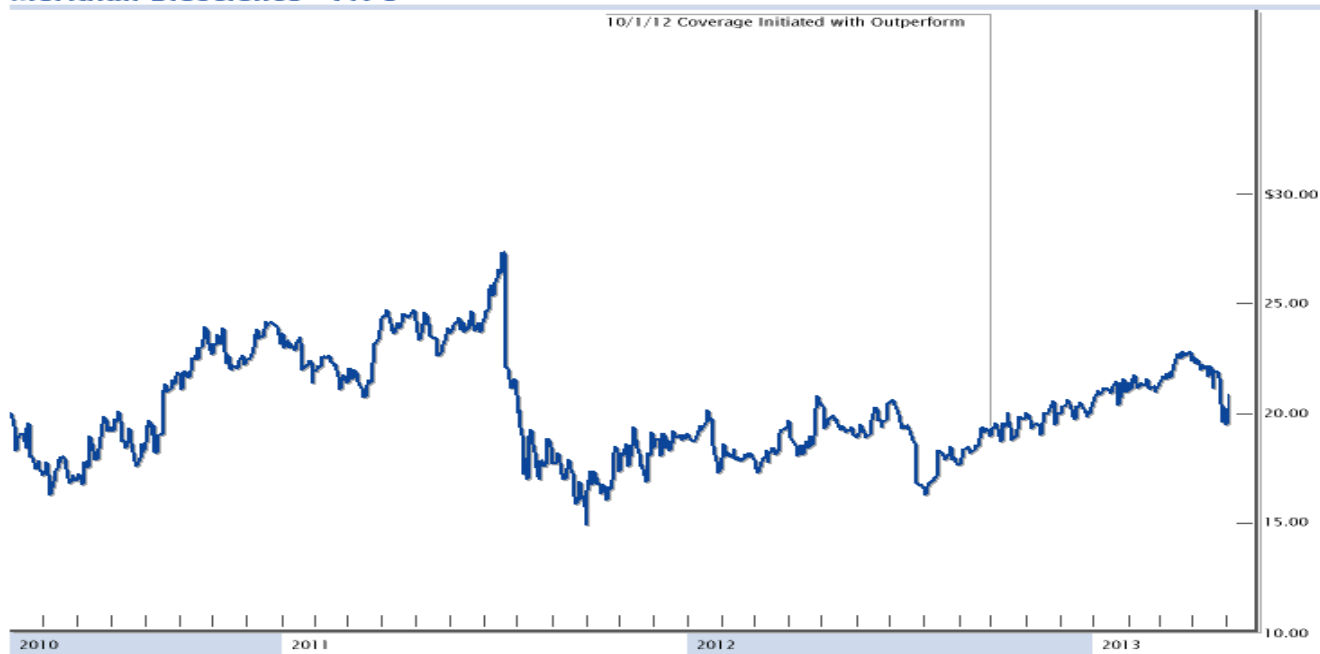


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Cowen and Company Price and Ratings History

Meridian Bioscience - VIVO

10/1/12 Coverage Initiated with Outperform



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