Chimerix

CMRX : NASDAQ : US$20.80

Buy | US$34.00 Target

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NEW COMPASSIONATE USE IND UNDERSCORES ADV UNMET NEED, SETS THE STAGE FOR EXPANDED ADV PIVOTAL TRIAL

Investment recommendation

Reiterating BUY, $34 target: We see the new open-label pilot trial as underscoring brincidofovir/CMX001's promise as well the unmet need in AdV. We think brincidofovir could greatly improve post-transplant care for patients at risk for CMV and other double-stranded DNA viral infections like AdV and BKV. We think the Ph3 SUPPRESS trial for CMV prevention has a high chance of success, and of supporting US and EU approval. Further, given the drug's therapeutic profile, including lack of bone marrow suppression and kidney toxicity as well as activity against AdV and BKV, we think brincidofovir could become standard of care for bone marrow and select solid organ transplants.

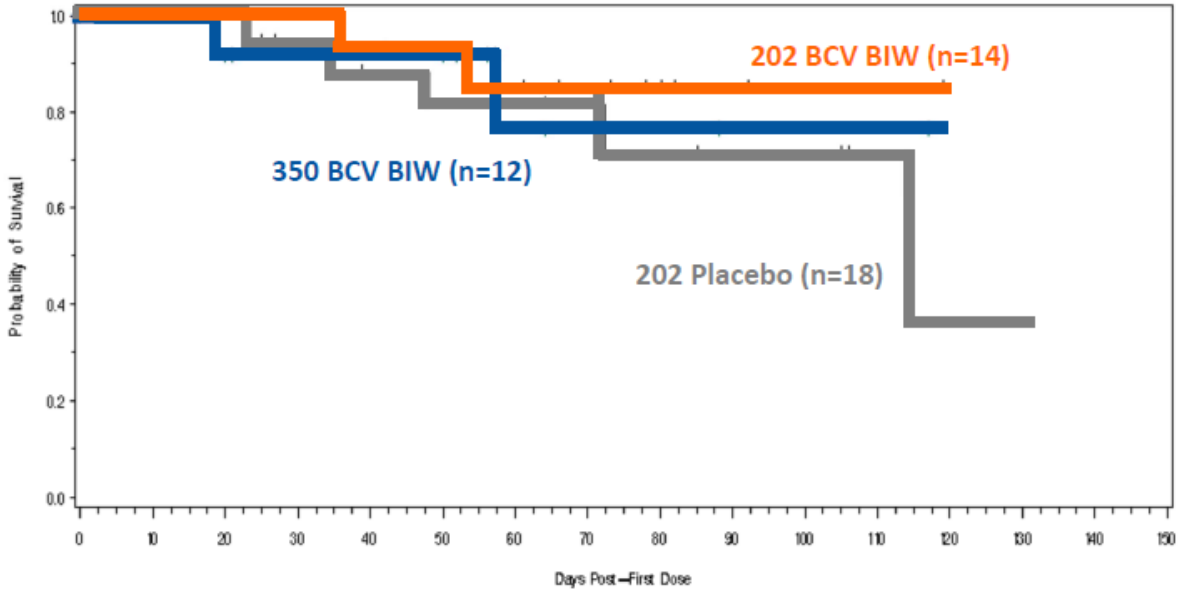
Investment highlights

- **CMRX announced last night the start of an open-label pilot trial of CMX001 for the treatment of adenovirus (AdV) infections in immunocompromised patients**. This development follows increasing media reports of appeals to CMRX for compassionate use of the drug in select cases. CMRX had run an emergency IND protocol as well as a compassionate use protocol (trial 350). However, those protocols ended H2/13 when CMRX started preparations for the now ongoing Phase 3 SUPPRESS for CMV disease prophylaxis post-transplant.

- **While CMRX had previously not had fixed plans for further AdV-specific clinical development due to the difficulties of AdV trial design, there may now be a path forward and we anticipate further detail shortly.** CMRX's statement indicated that "FDA has committed to work expeditiously with Chimerix on the design of a pivotal Phase 3 study that would be a continuation of this [20-patient open-label] pilot study." We look forward to more details on a potential pivotal design and how it might address shortcoming in the current technology around timely virus detection (in the blood, GI or lung) and sensitivity of viral load quantification.

- **New AdV analysis presented at BMT/Tandem 2014 strongly suggests benefit of post-transplant CMX001 for AdV (see our March 4 note); other data underscored the unmet need in the disease.** While investors were disappointed with the final AdV Ph2 "trial 202" data last year, we continue to see very strong trends suggesting clinical benefit of CMX001 in prevention of morbidity and mortality from AdV. BMT subanalysis of non-relapse related mortality (i.e. mortality not related to the diseases necessitating BMT) illustrates what we think is meaningfully reduced risk. Discussions with KOLs at BMT underscored perceived benefit of CMX001, but that the approach to treatment would need to be very different. Current standard viremia measures couldn't be relied upon: more sensitive measures relying on either GI tract or lung fluid would likely be more indicative of viral burden. Further, other conference data underscored the need for better pediatric AdV treatments. One oral presentation by Rustia et al. looked at incidence and risk factors for CMV, EBV and AdV. The incidence of peri-transplant, early and late viremia for the viruses was CMV: 5%, 22.2% and 6.6%; EBV: 1%, 9.1% and 1.1%; AdV: 5%, 10.1%, and 6.6%, respectively. However, the vast majority of the infection-related mortality in this pediatric group was attributable to AdV.

Figure 1: Study 202 Non-relapse mortality



Source: Grimley et al. oral presentation BMT/TANDEM 2014

Figure 2: Study 202 Non-relapse causes of death

Combined BCV BIW 4/26 (15%)	Baseline AdV Viremia (copies/mL)	Minimum AdV Viremia (copies/mL)	Last AdV Viremia (copies/mL)
Intracranial hemorrhage secondary to HHV-6 meningitis and fungal meningitis	$7.7x10^4$	$5.1x10^4$	$1.7x10^6$
Coagulase-negative Staphylococcus pneumonia	Undetectable	Undetectable	Undetectable
Pseudomonas aeruginosa septic shock	Not done	Undetectable	$3.6x10^4$
Toxoplasmosis and Aspergillus infection	$3.9x10^5$	$3.2x10^5$	$3.2x10^5$

202 Placebo 5/18 (28%)	Baseline AdV Viremia (copies/mL)	Minimum AdV Viremia (copies/mL)	Last AdV Viremia (copies/mL)
Grade 4 aGvHD, HHV-6 encephalitis	$2.4x10^5$	Undetectable	Undetectable
Multiple organ failure secondary to septic shock (AdV and liver microabcesses)*	$6.1x10^4$	$6.9x10^5$	$6.9x10^5$
Aspiration pneumonia	3500	Undetectable	Undetectable
Multiple organ failure secondary to graft failure and Enterococcus sepsis*	100	Undetectable	700
Respiratory failure of unknown origin, with proven AdV enteritis*	7100	5700	$3.4x10^6$

Source: Grimley et al. oral presentation BMT/TANDEM 2014

Figure 3: Side effect analysis in study 350

System Organ Class[1] Preferred Term[2]	Recommended or Lower BCV Doses: ≤ 200 mg/wk or 4 mg/kg/wk (n=36)	Higher than Recommended BCV Doses: > 200 mg/wk or 4 mg/kg/wk (n=41)
No. of subjects with ≥ 1 event	**14 (38.9%)**	**22 (53.7%)**
Gastrointestinal Disorders		
Abdominal pain	1 (2.8%)	3 (7.3%)
Diarrhea	6 (16.7%)	14 (34.1%)
Nausea	2 (5.6%)	3 (7.3%)
Vomiting	1 (2.8%)	4 (9.8%)
Investigations		
ALT increased	2 (5.6%)	2 (4.9%)
Bilirubin increased	0	2 (4.9%)
Metabolism and Nutrition Disorders		
Decreased appetite	0	4 (9.8%)
Dehydration	0	2 (4.9%)

	Recommended or Lower BCV Doses: ≤ 200 mg/wk or 4 mg/kg/wk (n=36)	Higher than Recommended BCV Doses: > 200 mg/wk or 4 mg/kg/wk (n=41)
No. of subj. with ≥ 1 event	**8 (22.2%)**	**7 (17.1%)**
Gastrointestinal		
Diarrhea	0	1 (2.4%)
Ileus	1 (2.8%)	1 (2.4%)
Lower GI hemorrhage	2 (5.6%)	0
Pancreatitis	0	2 (4.9%)
Hepatobiliary		
ALT increased	1 (2.8%)	0
AST increased	1 (2.8%)	0
Hepatic failure	0	1 (2.4%)
Immune System		
Acute GvHD	1 (2.8%)	1 (2.4%)
Renal and Urinary		
Renal failure acute	1 (2.8%)	0

Source:Prasad et al. oral presentation BMT/TANDEM 2014

Figure 4: Drug-related Grade 3-5 SAEs of particular interest in Study 202 (pediatric subjects)

System Organ Class[1] Preferred Term[2]	Randomized Phase			Open-label
	BCV 2 mg/kg BIW (n=11)	BCV 4 mg/kg QW (n=12)	Placebo (n=12)	BCV 2 mg/kg BIW (n=8)
Gastrointestinal Disorders				
Diarrhea	0	1 (8.3%)	1 (8.3%)	2 (25.0%)
Investigations				
Neutrophil count decreased	0	2 (16.7%)	0	1 (12.5%)
Immune System Disorders				
Acute GvHD	0	0	1 (8.3%)	0

Source: Prasad et al. oral presentation BMT/TANDEM 2014

Valuation

Our $34.00 price target is based on a probability-weighted NPV model of peak sales.

Investment risks

Clinical risk -- Chimerix's Phase 3 SUPPRESS trial may not be successful. While we view the SUPPRESS trial as well designed and powered for success based on the Phase 2 data, there is inherent risk to any clinical trial.

Clinical risk -- The SUPPRESS trial and other clinical may show brincidofovir to have an unacceptable safety and/or tolerability profile. While brincidofovir has not shown the immunosuppression and nephrotoxicity that is common with other CMV and AdV therapies, it has its own unique side-effect profile.

Clinical risk -- Chimerix may fail to generate additional positive supportive data for brincidofovir in AdV and BK, adversely impacting brincidofovir's ultimate commercial potential.

Regulatory risk -- FDA may change its mind on the appropriateness of conditional approval on a surrogate endpoint for brincidofovir. Chimerix plans to file for conditional approval for brincidofovir using viremia as a surrogate endpoint

Clinical/regulatory risk -- Chimerix may not be successful in meeting the post-approval data requirements required as part of a potential conditional approval.

Commercial risk -- Chimerix faces competition from cheap, generic well-established therapies as well as potential new therapies. Chimerix's operating results will suffer if they fail to successfully compete with the other biotech and pharma companies (Vical/Astellas, Merck, and Viropharma) that are also creating drugs for CMV and AdV.

Commercial risk -- Chimerix plans to hire its own small, specialized sales force. Chimerix currently does not have an organization for sales, marketing, and distribution of pharmaceutical products; the cost of establishing and maintaining such an organization may exceed the cost-effectiveness doing so.

Financing risk -- Chimerix has sufficient cash to reach SUPPRESS data but not enough to secure final US approval of the drug.

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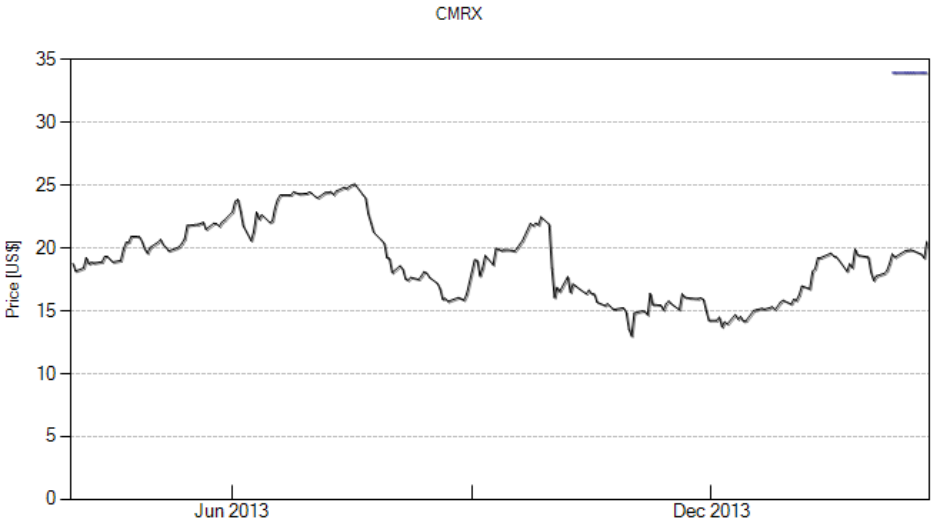
Site Visit: An analyst has visited Chimerix' material operations in Durham, NC. No payment or reimbursement was received from the issuer for the related travel costs.

Price Chart:*



Date	Analyst	Rating	Target Price	Date	Analyst	Rating	Target Price
1) 02/13/2014	Baral	Buy	34.00				

*Price charts assume event 1 indicates initiation of coverage or the beginning of the measurement period.

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	990*	100.0%	

*Total includes stocks that are Under Review

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Chimerix	5, 7

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