The AdVance Study: a Landmark Natural History Study of Adenovirus in Allogeneic Hematopoietic Cell Transplant Shows Strong Correlation Between Disease Burden and Mortality Risk

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European, multi-center study reinforces need for effective therapies for adenovirus in immunocompromised patients

DURHAM, N.C., March 19, 2018 (GLOBE NEWSWIRE) -- Chimerix (NASDAQ:CMRX), a biopharmaceutical company developing novel antivirals to address unmet medical needs, today announced data from AdVance, the first large, multi-center study of adenovirus (AdV) incidence, natural history, management and clinical outcomes in allogeneic hematopoietic cell transplant (allo-HCT) recipients. These data will be presented at the 44th Annual Meeting of the European Society of Blood and Marrow Transplantation held March 18–21 in Lisbon, Portugal.

Prior to the AdVance study, data and evidence regarding AdV epidemiology after allo-HCT has been generally limited to single-center studies. As Chimerix advances its brincidofovir development program in serious adenovirus infections, the Company undertook the AdVance study to better characterize the real-world incidence and outcomes of these infections.

“The AdVance study is the first of its kind to evaluate the impact of adenovirus infection in the transplant setting,” said M. Michelle Berrey, MD, MPH, President and Chief Executive Officer of Chimerix. “This groundbreaking study provides further evidence of the tremendous unmet need for an effective treatment for adenovirus, given an infection rate upwards of 32 percent in pediatric allo-HCT recipients and a strong correlation between adenovirus viral burden and mortality in the first year post-transplant. These results further strengthen our commitment to advance brincidofovir as the first potential treatment for serious adenovirus infections.”

The multi-center, multinational study, conducted in 2017, examined the incidence, practice patterns, hospitalization and clinical outcomes of 4,276 (1,738 pediatric, 2,538 adults) allo-HCT recipients. The population of this study included allo-HCT performed at 50 centers in Europe from January 2013 to September 2015. The study also assessed AdV plasma viral burden, measured by time-averaged area under the curve (AAUC), and its correlation with overall and non-relapse-related mortality.

“The robust findings of the AdVance study are extremely important for transplant clinicians, as we seek to better understand the rates and clinical outcomes of adenovirus infection and assess ways to evaluate antiviral therapies,” said Marco Zecca, MD, pediatric hematologist and oncologist at Fondazione IRCCS Policlinico San Matteo and an investigator in the AdVance study. “Among pediatric allo-HCT recipients in the study, the highest mortality was observed in those with the greatest adenovirus burden, with 52 percent mortality in the quartile of highest adenovirus AAUC, compared to 3 percent mortality reported in the quartile of lowest AAUC. These data suggest that AdV AAUC is an appropriate endpoint to assess the potential benefits of antiviral therapies for the treatment of adenovirus.”

One in Three Pediatric Allo-HCT Recipients Impacted by Adenovirus

- In the AdVance study, 32 percent of pediatric allo-HCT recipients developed an AdV infection in the first six months following allo-HCT.
    - Among pediatric allo-HCT recipients, 23 percent developed detectable AdV viremia (virus in the blood) and 14 percent developed greater than 1,000 copies/mL, a level previously associated with negative clinical outcomes.
    - In adults, a much lower rate of 6 percent of transplant recipients were found to have AdV viremia, but only 36 percent of adult transplant centers employed regular screening protocols compared with 100 percent of pediatric centers. Thus, AdV infections in adult HCT may be under-diagnosed and underreported.

Greater than Ten-Fold Risk of Mortality with Highest AdV Burden

Among pediatric allo-HCT recipients:

- In patients with AdV viremia over 1,000 copies/mL in the first six months after transplant, there was an 18 percent mortality rate of any cause within 6 months.
- In a multivariate analysis, each 10-fold increase in AdV AAUC (total viral burden) was associated with almost a doubling (1.9 times) of the mortality risk.
    - A patient with AdV level in the highest AdV AAUC quartile had a 12 times greater risk of dying than a patient with AdV in the lowest AAUC quartile.
- The highest mortality was observed in those with the greatest adenovirus burden, as measured by AdV AAUC. The highest AdV AAUC quartile had 52 percent 6-month mortality compared to 3 percent mortality in the quartile of lowest AdV AAUC.
- These data suggest that AdV AAUC is an appropriate endpoint to assess the potential benefits of antiviral therapies for the treatment of adenovirus.
- Adenovirus infection in pediatric allo-HCT recipients was also associated with significantly longer hospital stays.

Chimerix will share additional findings from the AdVance study in four presentations on Tuesday, March 20, 2018 at EBMT:

- *Incidence of Adenovirus Infections in Pediatric and Adult Allogeneic Hematopoietic Cell Transplant Recipients in Europe*; Sebastian Voigt, OS-9: Infectious Complications, 18:00 WET, Auditorium VIII
- *Adenovirus Viral Burden is Associated with Mortality in Pediatric Allogeneic Hematopoietic Cell Transplant Recipients: Results from the Advance Study*; Marco Zecca, OS-9: Infectious Complications, 18:10 WET, Auditorium VIII
- *Adenovirus Viremia is Associated with Substantially Prolonged Hospitalization in Pediatric Allogeneic Hematopoietic Cell Transplant Recipients*; Antonio Pèrez-Martinez, B073, Infectious Complications poster session, 9:00 WET, Poster Area / Pavilion 1
- *Screening, Monitoring, and Treatment of Adenovirus Infections in Pediatric and Adult Recipients of Allogeneic Hematopoietic Cell Transplants: Multicenter Survey of European Transplant Centers*; Kanchan Rao, B043, Hematopoietic Stem Cells poster session, 9:00 WET, Poster Area / Pavilion 1

About Brincidofovir

Chimerix's lead product candidate, brincidofovir, is a nucleotide analog that has antiviral activity against all five families of DNA viruses that affect humans, including the herpesviruses and adenoviruses. Brincidofovir has a high barrier to resistance, no myelosuppression and a low risk of nephrotoxicity. Brincidofovir has received Fast Track designation from the FDA for adenovirus, CMV and smallpox. Brincidofovir has also received Orphan Medicinal Product Designation from the European Commission for the treatment of adenovirus, for the prevention of CMV disease, and for the treatment of smallpox.

About Chimerix

Chimerix is a biopharmaceutical company dedicated to discovering, developing and commercializing medicines that improve outcomes for immunocompromised patients. Chimerix's proprietary lipid conjugate technology and compound library have produced brincidofovir (BCV, CMX001); CMX157, which was licensed to ContraVir Pharmaceuticals; and a new clinical candidate, CMX521, the first clinical stage direct-acting antiviral for the treatment and prevention of norovirus. For further information, please visit Chimerix's website, www.chimerix.com.

Forward-Looking Statements

This press release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks, uncertainties and other factors, including the possibility that there may not be a viable continued development path for brincidofovir, that FDA and other regulatory authorities may not approve brincidofovir or brincidofovir-based regimens, and that marketing approvals, if granted, may have significant limitations on their use. As a result, brincidofovir may never be successfully commercialized. In addition, Chimerix may be unable to file for regulatory approval for brincidofovir with other regulatory authorities. These risks, uncertainties and other factors could cause actual results to differ materially from those expressed or implied by such forward-looking statements. Risks are described more fully in the Company's filings with the Securities and Exchange Commission, including without limitation the Company's most recent Annual Report on Form 10-K and other documents subsequently filed with or furnished to the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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