AlloVir Announces Positive Final Results from Randomized, Double-Blind, Placebo-Controlled Phase 2 Study of Posoleucel in Kidney Transplant Recipients with BK Viremia

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Repeat administration of posoleucel was generally well tolerated, with balanced safety across posoleucel dosing groups and placebo

In Week 24 efficacy analysis, 39% (15/38) of patients who received posoleucel experienced a ≥1-log viral load reduction, more than double the placebo rate (14%; 2/14)

Posoleucel dose response was observed, with a ≥1-log viral load reduction in the biweekly dosing group of 50% (10/20) vs. 28% (5/18) in the monthly dosing group and 14% (2/14) in the placebo group

In the high viral load stratum (≥10,000 copies/mL), 69% (11/16) of patients who received posoleucel overall and 75% (6/8) of patients in the biweekly dosing group, achieved a ≥1-log viral load reduction vs. 25% (1/4) of patients in the placebo group

First demonstration of therapeutic potential of posoleucel for solid organ transplant patients

Company to host investor webcast at 9:00 a.m. EST today including Anil K. Chandraker, M.D., Director of Renal Transplant Medicine, Brigham & Women's Hospital

WALTHAM, Mass.--(BUSINESS WIRE)--Feb. 15, 2023-- AlloVir, Inc. (Nasdaq: ALVR), a late-clinical stage allogeneic T cell immunotherapy company, today announced positive final results from a Phase 2 study of posoleucel, an investigational, allogeneic, off-the-shelf, multi-virus-specific T cell (VST) therapy, being studied for the treatment of BK viremia (BKV) in adult kidney transplant recipients. The data support the safety and antiviral activity of posoleucel in this population, which has no effective BKV treatment options. In the randomized, double-blind, placebo-controlled study, posoleucel was shown to be generally well tolerated, with balanced safety across the two posoleucel dosing groups and placebo. Patients who received posoleucel achieved a clinically meaningful greater decline in BK viral load compared with those receiving placebo. The study results showed an even greater antiviral effect with posoleucel in patients with BK viral load ≥10,000 copies/mL at screening and in the biweekly posoleucel dosing group, identifying a dosing regimen and patient population to advance into a future trial.

"BKV is one of the most feared transplant-associated viral infections, due to the lack of available effective antiviral therapies and its profoundly negative impact on transplant outcomes," said Anil K. Chandraker, M.D., Director of Renal Transplant Medicine, Brigham and Women's Hospital, and principal investigator of the posoleucel BKV treatment study. "The safety profile of posoleucel and its antiviral activity, which is amplified in high viral load patients who have the greatest unmet need, suggest it could potentially offer a transformative treatment option for kidney transplant patients with BK viremia."

"This study is the first to evaluate a virus-specific T cell therapy in solid organ transplant patients, with the primary goal of exploring the safety of posoleucel treatment for BK viremia in kidney transplant patients. We are pleased with the consistency of posoleucel's safety profile across solid and stem cell transplant patient populations and with the important antiviral efficacy results in kidney transplant patients at highest risk for BKV-associated graft loss observed in this study," said Diana Brainard, M.D., CEO, AlloVir. "We believe today's results are an important and compelling milestone not just for AlloVir but for the entire kidney transplant community."

Dr. Brainard continued, "These safety and efficacy data in solid organ transplant patients provide important insights into the potential of posoleucel, which is also being studied in our three ongoing Phase 3 registrational trials in allo-HCT patients. We look forward to working with regulatory authorities and transplant specialists on our forward-looking clinical development strategy in kidney transplant patients, and potentially other solid organ transplant recipients."

This Phase 2 study evaluated the safety and efficacy of posoleucel to treat BK viremia in adult kidney transplant recipients with BK viral load between 350-10,000,000 copies/mL (stratified by low (<10,000 copies/mL) or high (≥10,000 copies/mL) viral load at study screening). Sixty-one patients were randomized 1:1:1 to receive one of two dosing regimens of posoleucel – weekly administration of posoleucel for three weeks, then every two weeks, or weekly administration of posoleucel for three weeks, then once a month – or placebo over 12 weeks. Following this dosing period, patients were followed through Week 24. Of the 61 enrolled patients, 58 patients completed the study through Week 24; two patients were lost to follow-up and one patient withdrew consent.

The primary endpoint of the study was safety and tolerability of posoleucel versus placebo. Across all patients who received at least a single dose of study drug, posoleucel was well tolerated. The incidence and severity of adverse events were consistent with the underlying patient population and background immunosuppression. Low rates of infusion reactions were observed in patients receiving posoleucel (2%) and those receiving placebo (5%). There were no deaths or reports of graft versus host disease or cytokine release syndrome. Emergence of donor-specific antibodies was uncommon and occurred with similar frequency in patients receiving posoleucel (7%) or placebo (5%). Three patients who received posoleucel were reported to have acute rejection per biopsy report by a central reader: one who was clinically diagnosed with, and successfully treated for, renal tuberculosis, one who had rejection on a biopsy prior to posoleucel dosing during the screening window, and one who developed rejection at Week 22 of the trial. None of these cases were assessed by the investigator as related to study drug.

The key secondary endpoint of the study was the change in BK viral load in patients receiving posoleucel versus those receiving placebo. The efficacy analysis excluded six patients in whom significant reductions in immunosuppression were made immediately prior to study entry. Posoleucel achieved

greater viral load reductions versus placebo consistently across multiple BK viral load measures. This clinically meaningful treatment effect was strongest among patients receiving posoleucel every two weeks and among those with high viral loads. Antiviral responses among posoleucel patients increased over time, with maximal responses observed at Week 24. Renal function in this group remained stable throughout the study, with a median change in estimated glomerular filtration rate from baseline to Week 24 of 0 mL/min/1.73m^2 in the overall posoleucel group and 0 mL/min/1.73m^2 in the placebo group.

Summary of Week 24 Virologic Changes Among Patients With Stable Immunosuppression Prior to Randomization*

	Overall (N=52)				High VL Stratum (N=20)			
	PSL Biweekly (N=20)	PSL Monthly$^+$ (N=18)	PSL Overall (N=38)	PBO (N=14)$^\pm$	PSL Biweekly (N=8)	PSL Monthly (N=8)	PSL Overall (N=16)	PBO (N=4)
% Patients with ≥1 $\log_{10}$ copies/mL reduction	50	28	39	14	75	63	69	25
BK VL change median $\log_{10}$ BKV DNA copies/mL (min, max)	-0.9 (-2.1, 0.1)	-0.45 (-1.8, 0.5)	-0.6 (-2.1, 0.5)	-0.15 (-2.1, 0.3)	-1.4 (-2.1, 0.1)	-1.5 (-1.8, -0.2)	-1.4 (-2.1, 0.1)	-0.4 (-2.1, -0.01)
% Patients with ≥50% VL copies/mL reduction	85	56	71	43	88	88	88	50

*PSL = posoleucel; PBO = placebo; VL = viral load

$^+$Excludes two patients who discontinued study

$^\pm$Excludes one patient who discontinued study

The company plans to present comprehensive results from the BKV Phase 2 study at a scientific congress later this year, and will work with regulatory authorities and transplant specialists to inform next steps for this program and AlloVir's broader solid organ transplant strategy.

Investor Webcast Details

The company will host an investor webcast today at 9:00 a.m. EST to discuss the study findings and the potential clinical impact of using posoleucel to treat viral infections in the solid organ transplant setting. The webcast will feature remarks from Dr. Brainard and Dr. Chandraker.

A live audio webcast of the presentation will be available on the Investors & Press section of the AlloVir website at https://ir.allovir.com/events-and-presentations. An archived replay of the presentation will be available on the website for 30 days following the event.

About BK Viremia in Kidney Transplant Recipients

Due to the long-term immunosuppression required to prevent graft rejection, solid organ transplant recipients are at high risk for reactivating common viruses that are typically controlled by the body's natural immune system. Uncontrolled, these viruses can have devastating consequences.

BK viral infection poses a significant threat to kidney graft survival. Approximately 80,000 kidney transplants are performed each year globally, and the virus reactivates in up to 20% of these patients. In patients who have reactivated BKV, a substantial portion will develop high-level viremia, and approximately half of those will develop BKV-associated nephropathy (BKVAN), which can lead to decreased kidney survival and a return to end-stage renal disease and dialysis. Consensus groups including the American Society of Nephrology and the American Society of Transplantation consider BK viral load of greater than or equal to 10,000 copies/mL to be presumptive BKVAN.[i]

There are no approved or effective antiviral treatments for BK viremia. The only approach to managing BK viremia is a reduction in immunosuppression to allow the body's immune system to fight the virus; this is typically triggered by a BK viral load of greater than or equal to 10,000 copies/mL. However, this reduction in immunosuppression can also lead to graft rejection and the development of donor-specific antibodies, putting the success of the kidney transplant at risk.

Data suggest that VST therapy may play a role in managing BK viremia and BKVAN. Kidney transplant recipients who do not develop BKVAN have been shown to have approximately 10-fold higher BKV-specific T-cell responses versus those with BKVAN. Kidney transplant recipients with BK viremia who develop robust BKV-specific T-cell responses have also been shown to clear the virus, while those who progressed to BKVAN required interventions such as a reduction in immunosuppression.

About Posoleucel

AlloVir's lead product, posoleucel, is in late-stage clinical development as an allogeneic, off-the-shelf, multi-virus specific T-cell therapy targeting six viral pathogens in immunocompromised individuals: adenovirus (AdV), BK virus (BKV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), human herpesvirus-6 (HHV-6) and JC virus (JCV). In the positive Phase 2 proof-of-concept CHARMS study, more than 90% of patients who failed conventional treatment and received posoleucel demonstrated a complete or partial clinical response based on predefined criteria, most with complete elimination of detectable virus in the blood and resolution of major clinical symptoms.

Based on the strength of the posoleucel Phase 2 data for both treatment and prevention, the FDA has granted posoleucel Regenerative Medicine Advanced Therapy (RMAT) designation for each of the three indications being evaluated in Phase 3 clinical trials – for the treatment of hemorrhagic cystitis (HC) caused by BKV, for the treatment of AdV infection in adults and children following allo-HCT, and for the prevention of clinically significant infections and disease caused by posoleucel's six target viruses. The FDA also granted posoleucel Orphan Drug Designation for the treatment of virus-associated HC. The European Medicines Agency has granted posoleucel PRIority MEdicines (PRIME) designation for the treatment of serious infections with AdV, BKV, CMV, EBV and HHV-6, and Orphan Medicinal Product designation as a potential treatment of viral diseases and infections in patients undergoing HCT.

About AlloVir

AlloVir is a leading late clinical-stage allogeneic T cell immunotherapy company with a focus on restoring natural immunity against life-threatening viral diseases in pediatric and adult patients with weakened immune systems. The company's innovative and proprietary technology platforms leverage off-the-shelf, allogeneic, single- and multi-virus-specific T cells for patients with T cell deficiencies who are at risk from the life-threatening consequences of viral diseases. AlloVir's technology and manufacturing process enable the potential for the treatment and prevention of a spectrum of devastating viruses with each single allogeneic cell therapy. The company is advancing multiple mid- and late-stage clinical trials across its product portfolio. For more information, visit www.allovir.com or follow us on Twitter or LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding the potential efficacy of posoleucel as a treatment for BK viremia, AlloVir's development plans and the regulatory status of AlloVir's product candidates, the planned conduct of its preclinical studies, and clinical trials and its prospects for success in those studies and trials, and its strategy, business plans and focus. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties, and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, those related to the potential of posoleucel as a treatment for BKV, the potential of posoleucel as a transformative treatment option for kidney transplant patients with BK viremia, AlloVir's financial results, the timing for the initiation and successful completion of AlloVir's clinical trials of its product candidates, whether and when, if at all, AlloVir's product candidates will receive approval from the U.S. Food and Drug Administration, or FDA, or other foreign regulatory authorities, competition from other biopharmaceutical companies, the impact of the COVID-19 pandemic on AlloVir's product development plans, supply chain, and business operations and other risks identified in AlloVir's SEC filings, including but not limited to the risks discussed in AlloVir's Annual Report on Form 10-K for the year ended December 31, 2021, and in our other filings with the SEC. AlloVir cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. AlloVir disclaims any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions, or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this press release represent AlloVir's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date.

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[i] Imlay et al. CID 2022.

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