In the Phase 2 Study CMX001-201 was a placebo-controlled, double-blind, clinical trial to evaluate the safety and efficacy of CMX001 in subjects with BKV infection. Subjects were randomized to receive either placebo or oral CMX001, in doses ranging from 40 mg weekly (QW) to 200 mg twice weekly (BIW). Subjects post-DHCT were enrolled at the time of enrollment and replaced if BKV infection was confirmed in CMX001 or placebo (3 to 1 ratio) and received blinded therapy until approximately Day 100 post-transplantation. CMX001 doses were 40 mg QW, 100 mg QW, 200 mg QW, 200 mg BIW, and 100 mg QW. Exclusion of the next dose was decided by the Data Monitoring Committee (DMC) according to the safety data from the previous cohort. Subjects who developed CMV disease or CMV infection requiring pre-emptive therapy with local standard of care were discontinued from blinded therapy and followed for 4 weeks. Subjects with completed treatment with blinded therapy were followed for 8 weeks after therapy. Subjects were monitored weekly by plasma CMV PCR and urine BKV PCR; plasma was tested by BKV PCR if the urine sample was positive. As part of routine laboratory testing, hematuria and serum creatinine were monitored during the study at the end of treatment phase.

The primary endpoint of the trial was prevention of CMV reactivation. The results have been presented elsewhere and showed that doses of CMX001 of 100 mg QW and higher had anti-CMV activity.6 There was dose limiting at 200 mg, while lower doses of CMX001 were generally well tolerated with no indication of myelotoxicity or nephrotoxicity.

One key secondary study endpoint was to assess the incidence of other dsDNA virus infections. Results of analyses conducted retrospectively with respect to BKV and its end-organ complications are presented below.

Study Design

CMX001 has broad spectrum in vitro antiviral activity against all dsDNA viruses of importance to immunocompromised patients, including multiple BKV isolates, adenovirus (AdV), Epstein–Barr virus (EBV), human herpesvirus 6 (HHV-6), and low levels of human herpesvirus 8 (HHV-8), assessed in cell culture experiments, is presented in Table 1.

There were 126/230 (55%) subjects had measurable BKV in urine samples at some time during treatment. Of these, 101/126 (80%) were separately in some of the analyses as this dose has been selected for further development of CMX001 in Phase 3 trials.

BKV infection is associated with HC in approximately 30% (5 to 60%) of HSCT recipients; the risk of HC is increased after myeloablative conditioning, male gender, and Cyclophosphamide use as part of the conditioning regimen and male gender appear to be associated with BKV reactivation post HSCT.5 Hematuria and renal dysfunction are rare in HSCT subjects without BKV reactivation and were not different between CMX001 and placebo groups due to the limited sample sizes within individual groups. This approach is conservative since the 40 mg QW dose had no antiviral effect against CMV in the primary analysis. Data from the largest study cohort (CMX001 100 mg BIW) are presented here and allow a more adequate sample size to evaluate BKV reactivation, renal dysfunction, and HC.

The impact of CMX001 therapy on BKV induced end-organ disease appears to be related to attenuation of the viral load increases that were associated with emergence of infection in the placebo recipients over this 8-20 week timeframe.