Supplementary Materials and methods

Cell culture and reagents. All of cell lines were all purchased from the American Type Culture Collection (ATCC) and cultured as recommended by the manufacturer. All experiments were carried out using cells harvested at low (<20) passages. The anti-COVID-19 drugs, Remdesivir and Molnupiravir were purchased from Selleck Chemicals. All the other chemicals if not indicated specifically were purchased from Sigma-Aldrich.

Cytotoxicity assay. The cytotoxicity was measured using the WST-1 cell proliferation assays (Roche). Briefly, after the period of treatment of cells, 10 μL/well of cell proliferation reagent, WST-1 (4-[3-(4-Iodophenyl)-2-(4-nitro-phenyl)-2H-5-tetrazolio]-1,3-benzene disulfonate), was added and incubated for 3 h at 37°C in 5% CO_2. The absorbance of samples was measured by using a microplate reader at 490 nm. Data was normalized as the inhibition ration to the vehicle control.

qPCR and qRT-PCR. Total RNA was isolated using the RNeasy Mini kit (Qiagen), and cDNA was synthesized using a SuperScript III First-Strand Synthesis SuperMix Kit (Invitrogen). Primers used for amplification of target genes were listed in Supplementary Table 1. Amplification was carried out using an iCycler IQ Real-Time PCR Detection System, and cycle threshold (Ct) values were tabulated in duplicate for each gene of interest in each experiment. "No template" (water) controls were used to ensure minimal background contamination. Using mean Ct values tabulated for each gene, and paired Ct values for *β-actin* as a loading control, fold changes for experimental groups relative to assigned controls were calculated using automated iQ5 2.0 software (Bio-rad).

Western blot. Total cell lysates (20 μg) were resolved by 10% SDS-PAGE, transferred to nitrocellulose membranes, and immunoblotted with antibodies to KSHV-ORF26 (Novus), ORF45 (Abbiotec), phosphor (p)-STAT3 (Tyr705)/total (t)-STAT3, p-p38 (Thr180/Tyr182)/t-p38, p-AMPK (Thr172)/t-AMPK, and Tubulin or GAPDH as loading controls (Cell Signaling). Immunoreactive bands were identifies using an enhanced chemiluminescence reaction (Perkin-Elmer), and visualized by autoradiography.

Statistical analysis. Significant differences between experimental and control groups were determined using the two-tailed Student's *t*-test. The 50% Cytotoxicity Concentrations (CC_{50}) were calculated by using Graphpad Prism 5.0.

Supplementary Table 1. Primer sequences used for qPCR and qRT-PCR

	Gene	Forward primers	Reverse primers
qPCR	LANA	5'-TCCCTCTACACTAAACCCAATA-3'	5'-TTGCTAATCTCGTTGTCCC-3'
	GAPDH	5'-GCTCCCTCTTTCTTTGCAGCAAT-3'	5'-TACCATGAGTCCTTCCACGATAC-3'
qRT-PCR	RTA	5’-CACAAAAATGGCGCAAGATGA-3’	5’-TGGTAGAGTTGGGCCTTCAGTT-3’
	PF	5’-CGAGTCTTCGCAAAAGGTTC-3’	5’-AAGGGACCAACTGGTGTGAG-3’
	ORF26	5’-GCTCGAATCCAACGGATTTG -3’	5’- AATAGCGTGCCCCAGTTGC-3’
	BHRF1	5'-GGAGATACTGTTAGCCCTG-3’	5'-GTGTGTTATAAATCTGTTCCAAG-3’
	BZLF1	5'-AAATTTAAGAGATCCTCGTGTAAAACATC-3’	5'-CGCCTCCTGTTGAAGCAGAT-3’
	β-actin	5’-ATCGTGCGTGACATTAAGGAG-3’	5’-GGAAGGAAGGCTGGAAGAGT-3’