Supplementary Methods and Materials:

Cell culture: The SKBR-3, MDA-MB-231 cell lines were kindly provided by Dr. Angelika Burger from Wayne State University, Michigan. They were authenticated by Dr. Burger's laboratory by western blotting and DNA fingerprinting. MCF-7 and MCF10A cells were purchased from American Type Culture Collection- ATCC (Rockville, MD, USA). They were authenticated by ATCC by DNA fingerprinting and karyotyping. Cells were not passaged/maintained for more than 6 months after resuscitation. Cells were maintained in ATCC recommended culture media with 10% fetal bovine serum (FBS) (Atlanta Biologicals, Lawrenceville, GA, USA) and 1% penicillin/streptomycin (Invitrogen). Cells were grown as a monolayer in T75 or T150 tissue culture flasks in a humidified incubator (5% CO_2, 95% air) at 37 ^{o}C.

Cell growth inhibition (MTT colorimetric assay):MTT (Sigma Aldrich) assay was performed as previously described. For time course study of VN/12-1 experiment, cells were treated with the VN/12-1 for indicated time points; media was replaced with new media without the drug. MTT assay was performed at the end of the experiment (96 hours). Calculations of combination indices were done using the Calcusyn program (Biosoft, Cambridge, United Kingdom).

Western blot analysis: For immunoblot detection of various proteins, SKBR-3 cells were cultured as described above in T75 flasks. Cells were treated with VN/12-1 or chloroquine and whole cell lysates were prepared using RIPA lysis buffer (Sigma Aldrich) and protease and phosphatase inhibitors (Sigma Aldrich). All of the antibodies were ordered from cell signaling technology. SDS PAGE was performed and protein expression was normalized to β-actin and densitometry was carried out using Image J or ImageQuant 5.0 (Molecular Dynamics, Sunnyvale, CA, USA). For tumor lysates, tumor tissue was homogenized using T-PER tissue

protein extraction reagent (Pierce protein research product), lysates were made and subjected to SDS-PAGE as described above.

Annexin FITC assay: Cells were treated with indicated concentrations of the compounds and assessed for their apoptotic potential by Annexin FITC assay as per protocols in the BD biosciences apoptosis kit I.

Immunofluorescence experiment: SKBR-3 cells were grown and treated with various agents for 24 h. After fixing with 4% paraformaldehyde, cells were stained with LC3B antibody (Cell signaling technology) overnight. Images were obtained using a Leica DMI 6000 microscope after staining with Alexafluor 488 (Invitrogen).

Electron microscopy: Cells were grown to monolayer in plastic flasks and fixed in half-strength Karnovsky fixative (2% paraformaldehyde, 2.5% glutaraldehyde, 0.025% $CaCl_2 \bullet 2H_2O$, and 0.1 M sodium cacodylate buffer, pH 7.4). Cells were postfixed with 1% OsO_4 and 1% $K_4Ru(II)(CN)$ 6 or 1.5% $K_3Fe(CN)_6$, dehydrated in ethanol, and embedded in epon. Ultrathin sections were stained with uranyl acetate and lead citrate. All EM sections were examined with amicroscope (1200EX or 1010; Jeol). autophagic vesicles, i.e., autophagosomes, amphisomes, and autolysosomes were exclusively identified by morphology.

Si-RNA experiment: For siRNA transfection, cells at a concentration of 2.5 or 5 x 10^4 cells/ml were incubated for 24 hours in six-well plates in culture medium. The cells were then transfected with 100 nM Beclin-1 and scrambled siRNA (SignalSilence® Beclin-1 siRNA II and SignalSilence® Control siRNA -cell signaling technology) for 72 hours in the presence of Oligofectamine (Invitrogen) and Beclin-1 silencing was confirmed by immunoblot. For

cytotoxicity analysis, tumor cells transfected with 100 nM Beclin-1 or scrambled siRNA for 24 hours were treated with vehicle alone or VN/12-1 for 96 hours for the MTT assay.

In vivo tumor growth

Cells were suspended in matrigel (10 mg/ml) at 1 x 10^7 cells/ml and 100 µl of cell suspension was injected subcutaneously at one site on one flank. Tumors were synchronized to be approximately 150-300 mm^3 at the start of treatment (day 0), and were measured every 4 days during the course of 4 weeks. Tumors were measured twice a week with calipers and tumor volume calculated. At the end of the experiment, tumors were excised and weighed.

Statistical analysis

All experiments were carried out in at least triplicates and are expressed as mean ± S.E. where applicable. Treatments were compared to controls using the Student's t-test with either GraphPad Prism or Sigma Plot. P-values less than 0.05 were considered to be statistically significant. For xenograft studies, Mixed-effects regression was used for the main analyses of tumor growth. This approach does not depend on an arbitrary endpoint target tumor size, yields generalizable parameters of interest (e.g., average daily tumor growth rate and tumor doubling time), and can investigate treatment interactions. It is also quite powerful since it utilizes the repeated tumor size measurements obtained over the entire study period, while it appropriate handles unbalanced data and the correlation of each animal's measurements over time.