**Supplementary Figure 1. Decitabine and MUC1-C inhibitor combination increases hydrogen peroxide (H2O2) levels, which is abrogated by addition of NAC and is not synergistic in inducing cytotoxicity in MUC1-C low/negative CTCL cell lines.** A–B, Representative FACS histograms of H9 and HuT-78 cells; untreated, treated with 3 μM GO-203 each day for 3 days, single dose of 25 nM or 40 nM Decitabine or the combination followed by measurement of fluorescence of oxidized DCF at 96 hours are shown. The combination treated cells were also incubated in the presence of 5 mM NAC for the last 2 days. C-D,SeAx and HH cells were left untreated, treated with GO-203 (3 uM) each day for 3 days, single dose of Dac (40 nM) or the combination. Cell Titer Glo was added and viability was measured at 96 hours. The results are expressed as relative percentage viability (mean ± SD of 3 determinations) compared to the control. E-F, Amino acid sequence and chemical structure of the MUC1-C inhibitor, GO-203 are presented.

**Supplementary Figure 2. Decitabine and MUC1-C inhibitor combination increases hydrogen peroxide (H2O2) levels and is cytotoxic in Myla cells.** A-B, Myla cells were left untreated, treated with 3 μM GO-203 each day for 3 days, single dose of 40 nM Decitabine (Dac) or the combination. The combination treated cells were also incubated in the presence of 5 mM NAC for the last 2 days (combination plus NAC). At 96 hours harvested cells were incubated with c-H2DCFDA for 30 minutes. Fluorescence of oxidized DCF was measured by flow cytometry. The results are expressed as the relative hydrogen peroxide levels in live cells (mean ± SD of 3 determinations) compared with that obtained for control cells. C-D, Myla cells were left untreated, treated with varying concentrations of GO-203 (GO or G; 1.5-2.5 uM) each day for 3 days, single dose of Dac (Dac or D; 40 nM) or the combination. Cell Titer Glo was added and viability was measured at 96 hours. The results are expressed as relative percentage viability (mean ± SD of 3 determinations) compared to the control. Excess over Bliss independence Model was used to calculate synergy co-efficients reported in adjoining tables. Values greater than 10 signify synergy. Combination Index (CI) was used to confirm synergy and is reported. Values <1 represent synergy.

**Supplementary Figure 3.** A schema of the various CpG locations that were analyzed in the Nox4 promoter of the gene is presented.

**Supplementary Figure 4.** A schema of the various CpG locations that were analyzed in the Duox2 promoter of the gene is presented.

**Supplementary Figure 5. Decitabine and** **GO-203 combination increases Nox4 and Duox2 mRNA levels.** A-B**,** H9 cells were left untreated, treated with GO-203 3 uM each day for 3 days, single dose of decitabine (Dac) 40 nM or the combination. Real-time qPCR was performed with primers amplifying cDNA fragments specific for human Nox4, Duox2 or GAPDH. Quantification was performed by ∆CT calculation. C-D, Similar conditions were used for analysis of Nox4 and Duox2 mRNA levelsinHuT-78 cells.

**Supplementary Figure 6.** **Decitabine and** **GO-203 combination induces apoptosis in CTCL cells.** A-B, H9 and HuT-78 cells were left untreated, treated with GO-203 3 uM each day for 3 days, single dose of decitabine (Dac) 40 nM or the combination. Cells were exposed to N-acetyl cysteine (NAC) 5 mM for the last 2 days. Cells were incubated with PI and annexin V, and analyzed by flow cytometry at 96 hours. The results are expressed as percentage of cells with early, late apoptosis and necrosis (mean ± SD of 3 determinations). C-D, Representative flow plots of H9 and HuT-78 cells untreated, treated with 3 μM GO-203 each day for 3 days, single dose of decitabine (Dac 25 nM or 40 nM) or the combination followed by measurement of Annexin/PI stained cells at 96 hours are shown. The combination treated cells were also incubated in the presence of 5 mM NAC for the last 2 days.

**Supplementary Figure 7. Decitabine and** **GO-203 combination is synergistically cytotoxic in CTCL cells.** A-B,H9 and HuT-78 cells were left untreated, treated with varying concentrations of GO-203 (GO or G; 1.5-3 uM) each day for 3 days, single dose of Dac (Dac or D; 10-40 nM) or the combination. Cell Titer Glo was added and viability was measured at 96 hours. The results are expressed as relative percentage viability (mean ± SD of 3 determinations) compared to the control. C-D, Excess over Bliss independence Model was used to calculate synergy co-efficients reported in adjoining tables. Values greater than 10 signify synergy. Combination Index (CI) was used to confirm synergy and is reported. Values <1 represent synergy.

**Supplementary Figure 8. Decitabine and MUC1-C inhibitor combination increases hydrogen peroxide (H2O2) levels, which is abrogated by addition of NAC in primary CTCL cells.** A-B**,** Double positive, TCR Vβ and MUC1-N primary CTCL cells from 2 patients were left untreated, treated with 3 μM GO-203 each day for 3 days, single dose of 40 nM Decitabine (Dac) or the combination. The combination treated cells were also incubated in the presence of 5 mM NAC for the last 2 days (combination plus NAC). At 96 hours harvested cells were incubated with c-H2DCFDA for 30 minutes. Fluorescence of oxidized DCF was measured by flow cytometry. The results are expressed as the relative hydrogen peroxide levels in live cells compared with that obtained for control cells. C-D, Representative FACS histograms are presented.