## Methods

IC<sub>50</sub> Dose Determination for GO in AML Cell Lines. Cell lines were incubated with the range of concentration (0.01, 0.1, 1, 10, 100, 1000, 10,000 ng/mL) of GO for 72h followed by flow-based cytotoxicity assay. IC<sub>50</sub> values were calculated by non-linear regression analysis of dose versus response of a logarithm-transformed data. IC<sub>50</sub> values were calculated based on 50% cytotoxicity.

Flow Cytometry-Based Drug Efflux Assay. Cell-based multi drug resistance (MDR) direct dye efflux assay (ECM910, Millipore) was performed to determine whether BATs primed GO resistant HL60/VCR cell line (vincristine resistant HL60 cells) can become chemo-responsive as described<sup>34</sup>. In this assay, the efflux activity of ABC transporters is optimal at 37°C and ineffective at 4°C. HL60/VCR and HL60 cells are preloaded with MDR1 fluorescent substrates retain dye and exhibit high fluorescence when incubated at 4°C while cells incubated at 37 °C will efflux the dye and show reduced fluorescence. The persistent intracellular accumulation of Rhodamine 123 and DiOC<sub>2</sub> in HL60/VCR and HL60 shows resistance by rapid efflux whereas delayed efflux shows impaired MDR pump function at 37°C. Flow data was acquired by NovoCyte flow cytometer and analyzed using NovoExpress software.

Cytokines/Chemokines Profile in the Supernatant of Target and Effector Cells Co-cultures. CD33GO BATs, CD123 BATs, or unarmed ATC were co-cultured overnight in the presence of AML targets and the cell-free supernatants were quantitated for 45-panel (R&D Systems) cytokines, chemokines and growth factors using a Bio-Plex 200 system (BIO-RAD, Hercules, CA). The values are reported in pg/mL of culture supernatants, effector cells and target cells alone served as controls.

Cell Type	Specific Phenotype Markers	<b>Common Phenotype Markers</b>
AML Blasts	CD34 <sup>+</sup> /CD38 <sup>-</sup>	CD33/CD123
AML Leukemic Stem cells (LSC)	CD34 <sup>+</sup> CD38 <sup>-</sup> /CD90 <sup>-</sup> /TIM3 <sup>+</sup>	CD33/CD123
Hematopoietic Stem cells (HSC)	CD34 <sup>+</sup> CD38 <sup>-</sup> /CD90 <sup>+</sup> /TIM3 <sup>-</sup>	CD33/CD123

Table S1. Specific and common surface biomarkers to identify normal and leukemic cell populations.

## **Figure Legends**

**Figure S1. A)** Shows the expression of CD33 and CD123 on KG1, EOL1, NoMo1, TF1, HL60 and HL60/VCR (*right dotplots*). Left plots show proportions CD34+/CD38-, CD34+/CD38+ and CD34<sup>-</sup>/CD38<sup>+</sup> cells in all cell lines. **B)** Shows the bar plot of subpopulations gated on CD33, CD123, CD34 and CD38 phenotype in all six cell lines.

**Figure S2. Drug Efflux Assay.** Vincristine and GO resistant HL-60/VCR AML cell lines primed with BATs show high cellular uptake and retention of Rhodamine 123 compared to control unprimed HL-60/VCR cells. High fluorescence (elevated MFI) after priming with BATs suggest decreased activities of efflux transporters, MRD1 and MRP1 pumps.

Figure S3. Engraftment of AML cells NSG Mice. NOD *scid* gamma ([NSG] NOD.Cg-*Prkdc<sup>scid</sup> Il2rg<sup>tm1Wjl</sup>*/SzJ) mice 6-8-week-old were irradiated with 250 Rads, after 24h of irradiation mice were intravenously injected with  $10x10^{6}$  KG1 cells to establish human AML graft. The AML engraftment was monitored by staining for human CD45<sup>+</sup> cells in the flushed bone marrow (BM) on days 7, 14, and 21, treatment was started once ~15% human CD45<sup>+</sup> cells were engrafted. Flow cytometry plots show engraftment of human CD33<sup>+</sup> CD123<sup>+</sup> CD45<sup>+</sup> cells on day 21.



## A. Co-Expression of CD33 and CD123 and Proportions of Blast in Cell lines

## **B.** Phenotype of AML Cell Lines







**Drug Efflux Assay** 

