Supplementary Table 1: Characteristics of leukemia subjects used in this study

Subject	Age	Cytogenetics	History	In vitro	Xenograft
MD1	59	46,XY,t(9;22)(q34;q11.2),der(9)	New	+	+
MD4	9	46,XY,t(9;22)(q34;q11.2),t(1;4)(q22;p15.3),del(2)(p14),add(2)(q37),add(7)(q36)	Relapse	+	+
MD9	54	t(9;22)(q34;q11.2)	Relapse		+
MD11	53	t(9;22)(q34;q11.2)	Relapse		+
UCI-2	63	t(9;22)(q34;q11.2),der(7;12)	Relapse	+	
UCI-5	42	t(9;22)(q34;q11.2)	New	+	
UCI-K	23	Multiple hyperdiploid anomalies	Relapse		+
MS-1	Adult	46,XX	New	+	
MS-2	16	46,XX	New	+	
MS-3	55	dic(9;20)(p11;q11.2),+r	New	+	
MS-4	28	der(4)t(4;11)(q21;q23),der(8)t(8;11)(q24.1;q13)t(4;11),der(11)t(8;11)	New	+	
CV-5	Adult	Multiple hyperdiploid anomalies	Relapse	+	+
CV-7	Adult	Multiple hyperdiploid anomalies	Relapse	+	
CV-10	Adult	Multiple hyperdiploid anomalies	New		+
CV-19	Adult	Multiple hyperdiploid anomalies	New	+	
CHOC-1	3	46XY	New	+	+
CHOC-2	2	54XX,+21q22abnl,+chromX,4,6,10,14,17,18,21[cp7]	New	+	
CHOC-3	7	46XY,del(6)(q23),-11,+mar[4]	New	+	
CHOC-4	4	46XX	New	+	+
CHOC-5	10	XY,+17,+multiple21	New	+	
CHOC-6	4	46XY	New	+	+
CHOC-10	14	44-45XX,del(6)(q15q21), 9, add(17)(p11.2) +mar[cp12]	New	+	
CHOC-11	5	55-58XY,+4,+5,+6,+10,+16,+17,+18,+21[6]	New	+	
CHOC-23	6	XY,+4,+10,+17	New		+

Supplementary Figure 1: MLN0128 inhibits mTOR activity more completely than rapamycin in p190 BCR-ABL transformed mouse bone marrow progenitor B cells. (A-B) p190 cells were treated for 3 hours with indicated inhibitors and concentration (nM). Lysates were prepared and analyzed by western blotting.

Supplementary Figure 2: Efficacy of MLN0128 alone or in combination with dasatinib in primary Ph+ xenografts. (A-B) Sample MD9 and MD4 were treated for 3 or 1.5 weeks respectively as indicated with DA (5 mg/kg/day, p.o.), MLN0128 (0.75 mg/kg/day, p.o.), or DA in combination with MLN0128. Normal mouse $CD45^+$ BM is not depicted for mice engrafted with sample MD4 because of the excessive leukemic burden of human $CD34^+CD19^+$ cells.

Supplementary Figure 3: Efficacy of MLN0128 alone in CHOC1 and CHOC23 xenografts treated early after engraftment. Mice bearing (A) CHOC1 and (B) CHO23 xenografts were treated starting 7-10 days after human cell injection and analyzed 2 weeks later for % leukemia in the bone marrow. The engraftment percentages were lower in these cohorts than in the CHOC6 cohort (Figure 5E) but the results were similar. The effect of MLN0128 was statistically significant for CHOC1 and there was a similar trend ($p = 0.13$) for CHOC23.

Supplementary Figure 4: MLN0128 suppresses leukemic proliferation in the spleen but not the bone marrow in established xenograft CHOC4. Single cell suspensions from bone marrow (BM) and spleen of mice bearing established CHOC4 xenografts were analyzed for proliferation by EdU incorporation (A) and stained for human CD34 and CD19 to quantitate leukemic burden (B). n.s. = not significant.