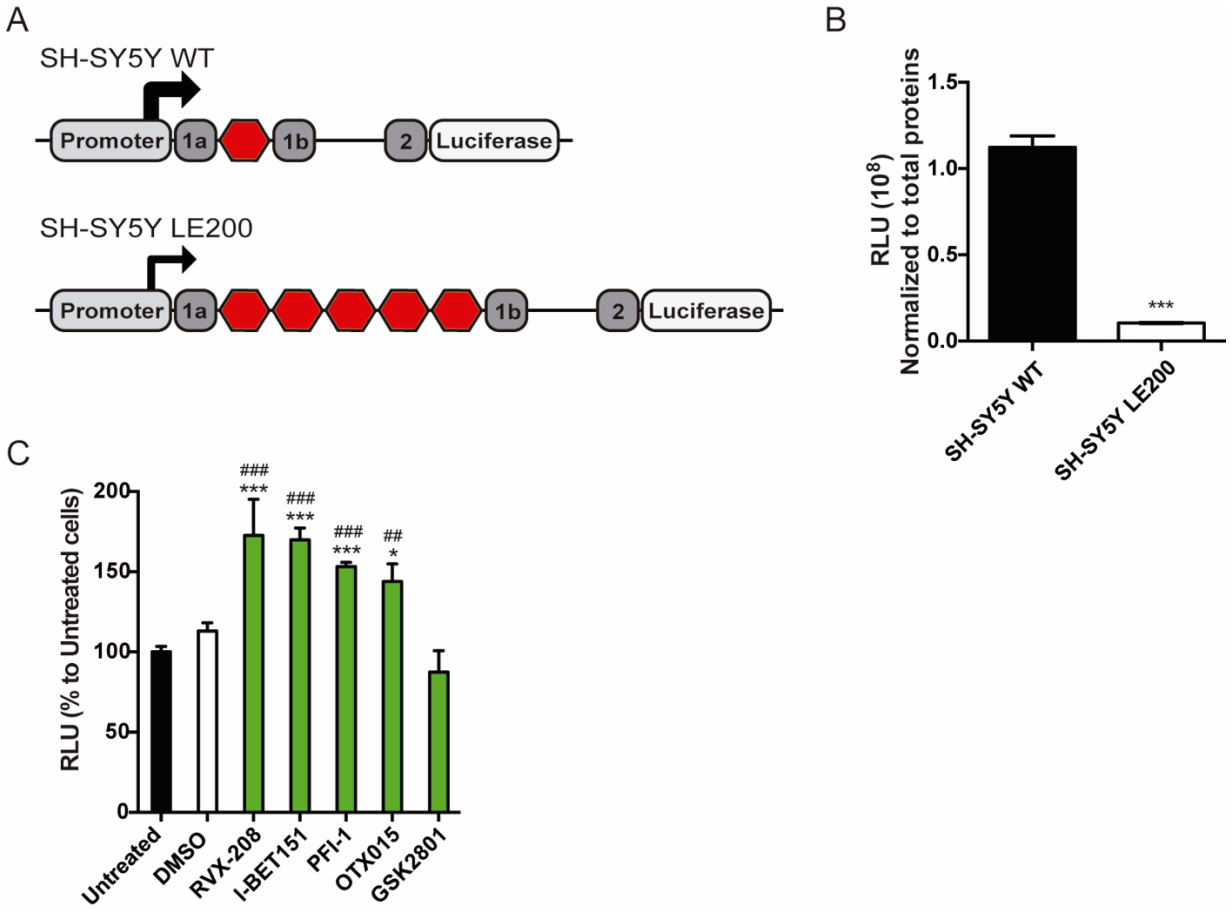
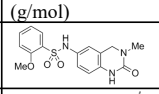
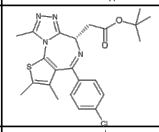
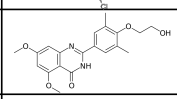
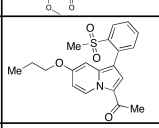
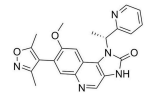
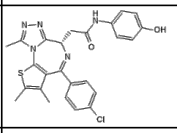
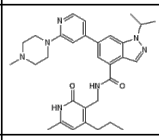
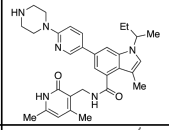
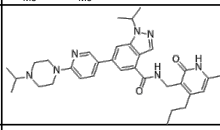
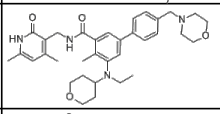
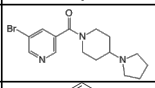
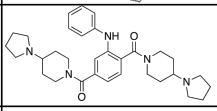
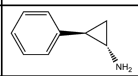
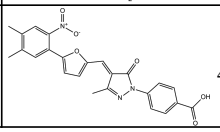


Supplementary Figure 1: Bromodomain inhibitors enhance *C9ORFF72* gene promoter-driven expression in SH-SY5Y LE200 G4C2 reporter cell lines.

(A) Schematic representation of two SH-SY5Y cell lines stably expressing a segment of the human *C9ORF72* gene, including the promoter region and exons 1a through 2, driving the expression of a luciferase reporter gene. Between exons 1a and 1b, increasing G4C2 hexanucleotide repeat expansions (red hexagons) were inserted: 8 (SH-SY5Y WT) or 200 (SH-SY5Y LE200). (**B**) Quantification of the basal luciferase activity in each cell line. Values were normalized to total protein concentration and displayed as relative luciferase unit (RLU). Bars represent mean±S.E.M. ***P<0.001 relative to SH-SY5Y WT cells, unpaired Student's t-test (n=3 independent experiments). (**C**) Quantification of luciferase activity at the SH-SY5Y LE200 cells following an incubation for 24 h with 5 selective small molecule inhibitors targeting bromodomains (green bars). As a control, SH-SY5Y LE200 cells were also treated with 0.05% (v/v) DMSO (white bar), the same concentration used as the vehicle for most of the epidrugs. Luciferase activity in the treated SH-SY5Y LE200 cells was normalized to untreated SH-SY5Y LE200 cells (black bar). Bars represent mean±S.E.M. *P<0.05 and ***P<0.001 relative to DMSO, or ##P<0.01 and ###P<0.001 relative to Untreated, one-way ANOVA (n=3 independent experiments).

Table 1. Epidrugs used in screening							
Epidrug	Concentration	Company/ Cat #	Reference	Target protein	IC50	logP	Molecular structure and weight (g/mol)
PFI-1	5μM	BioVision 2203-1	Picaud et al., *Cancer Res.*, 2013	BRD4(BD1)	220nM	1.3	 347.1
(+)-JQ1	5μM	Tocris 4499	Filippakopoulos et al., *Nature*, 2010	BRD4(BD1)	77nM	4.0	 456.1
RVX-208	25μM	MedChem HY-16652	Picaud et al., *Proc Natl Acad Sci*, 2013	BRD4(BD2)	510nM ± 41nM	2.3	 370.4
GSK2801	5μM	Sigma SML0768	Chen et al., *J. Med. Chem.*, 2016	BAZ2A, BAZ2B	260nM 140nM	3.5	 371.5
I-BET151	5μM	BioVision 2220-1	Dawson et al., *Nature*, 2011	BRD2 BRD3 BRD4	500nM 250nM 790nM	2.7	 415.4
OTX015	2,5μM	Sigma SML1605	Noel et al., *Mol. Cancer Ther.*, 2013	BRD2 BRD3 BRD4	99–112nM	4.5	 491.1
GSK343	0,5μM	BioVision 2281-1	Verma et al., *ACS Med. Chem. Lett.*, 2012	EZH2	4nM	3.23	 541.3
GSK126	5μM	BioVision 2282-1	McCabe et al., *Nature*, 2012	EZH2	9.9nM	3.9	 526.7
UNC1999	5μM	BioVision 2449-5	Xu et al., *Blood*, 2015	EZH2	2nM	4.01	 569.7
EPZ-6438	5μM	BioVision 2383-5	Knutson et al., *Proc Natl Acad Sci*, 2013	EZH2	11nM	4.2	 572.7
UNC669	5μM	BioVision 2620-5	Herold et al., *J. Med. Chem.*, 2011	L3MBTL1	6μM	-	 338.2
UNC1215	5μM	BioVision 2252-1	James et al., *Nat. Chem. Biol.*, 2013	L3MBTL3	40nM	4.17	 529.3
TCP	5μM	R&D 3852/10	Lee et al., *Chem. Biol.*, 2006	LSD1	200nM	1.5	 133.1
C646	5μM	BioVision 1948-1	Bowers et al., *Chem. Biol.*, 2010	P300/CBP	1μM	4.2	 445.4

Supplementary Table 2: TaqMan probes information.

TaqMan probe	Type of assay	Sequence	Primers	Assay code
V1	Commercial assay	AGATGACGCTTGATATCTCCGGAGC	Not shown	Hs00331877_m1, Thermo Fisher Scientific
V2	Custom assay	CGACTCTTTGCCCACCG	F:AGGCGGTGGCGAGTGGATA R:TTGGAGCCCAAATGTGCCTTA	Thermo Fisher Scientific
V3	Custom assay	CCACCGCCATCTC	F:GCGGGGTCTAGCAAGAGCAG R:TTGGAGCCCAAATGTGCCTTA	Thermo Fisher Scientific
Vall	Commercial assay	AGAATATGGATGCATAAGGAAAGAC	Not shown	Hs00376619_m1
HPRT	Commercial assay	Not shown	Not shown	Mm01545399_m1