Supplementary Information

Endothelial-leukemia interactions modulate drug responses and underline T-ALL vulnerabilities

This file includes:
- Supplementary Methods,
- Supplementary Figures S1-S6,
- Supplementary Figure Legends,
- Supplementary References,
- Supplementary Tables

Supplementary Materials and Methods

PDX generation

To generate patient-derived tumor xenograft (PDX), primary T-ALL cells were injected in 4-6-week-old (male/female ratio: 1:1) NOD.Cg-B2mtm1Unc Prkdcscid Il2rgtm1Wjl/SzJ (NSG B2m) mice via intravenous (iv; 1×10^6, 100 µL of DPBS), intra-bone (2×10^6, 50 µL of DPBS), or subcutaneous (s.c.; 6×10^6, 200 µL DPBS-50% Matrigel) routes. All routes were successful, with intrabone and i.v. displaying similar rapid times of engraftment; s.c. required a longer first engraftment time. In the last stages of tumor growth, distant dissemination to parenchymal and hematopoietic tissues occurred (i.e., spleen, bone marrow etc.). Engraftment was monitored every 2 weeks by total body MRI or multicolor flow cytometry on peripheral blood. Mice were sacrificed when lymphoblastic cells represented ≥50% of the total circulating blood cells. Leukemic cells were harvested from the spleen or femoral bone and then cryopreserved and/or used for *ex-vivo* experiments. Serial passages were obtained by i.v. injection (1×10^6, 100 µL of DPBS) of freshly isolated leukemic cells (from the spleen). The nomenclature used for PDX passaged tumors was T1 (first generation), T2 (second generation) T3 (third generation), etc., corresponding to serial passaging in vivo. All tissues were collected for histology and immunohistochemistry. Animal studies were approved by Weill Cornell Medicine Animal Care and Use Committee (2014-0024).

Histology and Immunohistochemistry (IHC)

Tissues were recovered, fixed in 10% neutral buffered formalin or 4% paraformaldehyde overnight at 4°C, and processed routinely for histology and histochemistry. Immunohistochemical stains were processed using a semi-automated unit (Leica) with the following antibodies: TdT (Leica, SEN28), CD3 (Thermo Scientific, SP7), Notch1, and pSTAT5 (Cell Signaling Technology, 3608 and 9314).

Antibodies for flow cytometry

Flow cytometry was performed as described previously [1] using dedicated instrumentations (BD™ LSR II flow cytometer and BD FACSCelesta™) and high-speed sorting (BD™ Aria). The following antibodies were used: hCD45 (V500C, cat. no: 647450, 2.5 µg/mL), hCD7 (PE, cat. no: 340656, 2.5 µg/mL), hCD3 (PerCP, cat. no: 340663, 2.5 µg/mL), and hCD34 (APC, cat. no: 340667, 2.5 µg/mL) purchased from BD Biosciences; and mCD45 (PECy7, cat. no: 103114, 3 µg/mL), hCD45 (Pacific Blue, cat. no: 368539, 3 µg/mL), mPodoplanin (PE/Cy7, cat. no: 127412; 3 µg/mL), and hCD31 (Pacific Blue, cat. no: 303114; PECy7, cat. no: 303118; 3 µg/mL) from BioLegend and eBioscience (APC, cat. no: 17-0319-42, 3ug/mL). Leukemia cells were identified by flow cytometry after gating on human CD45+ cells, whereas human and mouse ECs were identified using specific antibodies against CD31 antigens. E4-EC or T-ALL cells were labelled with vital dyes (488 Green or 415/516 violet BioTracker) following the manufacturer's instructions (Millipore/Sigma).

Western blotting

T-ALL cell lines were plated at a density of 5 × 10^5/mL and stimulated for 30 min with IL-12 (10 ng/mL), IL-7 (10 ng/mL), IL-15 (25 ng/mL), IL-6 (10 ng/mL), or SDF1α (100 ng/mL). T-ALL cells from the spleens of engrafted mice were cultured in RPMI media supplemented with the cocktail of interleukins and treated for 24 h with 1 μM Ruxolitinib. Total cell lysates were blotted with the following primary antibodies: anti-pSTAT5 (1:1000/1:2000), anti-STAT5 (1:1000/1:5000), anti-phosphoSTAT3 (1:1000/1:2000), anti-STAT3 (1:1000/1:5000), and anti-pJAK2 (1:1000/1:2000). All antibodies were purchased from Cell Signaling Technology.

Isolation of ECs from primary tumors, normal tissue, and mouse embryos
Mouse adult, embryonic, and tumoral tissues were finely dry minced using sterile blades and enzymatically digested using the digestion media as previously described [2].

Isolation of T-ALL cells from the spleen
Human T-ALL cells were collected from engrafted PDX spleens, passed through 100-μm filters, and washed in PBS. Pellets were treated with red blood cell lysis buffer (BD Biosciences), and then human $CD45^+$ cells were isolated using MACS MicroBead Technology (Miltenyi Biotec). Cell suspensions were analyzed by flow cytometry using a panel of monoclonal antibodies.

Isolation of ECs from primary tumors, normal tissue, and mouse embryos
Mouse adult, embryonic, and tumoral tissues were finely dry minced using sterile blades and enzymatically digested using a digestion media [Collagenase A (25 mg/ml) (Roche, 2599323), Dispase II (25 mg/ml) (Sigma- Aldrich, d4993-1G), DNase (250 mg/ml or 500 units) (Roche, 4716728001) in a 140 mM NaCl (Sigma), 5 mM KCl (Sigma), 2 mM $CaCl_2$ (Sigma), 1.3 mM $MgCl_2$ (Sigma), 2.5 mM Phosphate Buffer pH 7.4, 10 mM HEPES (Sigma) medium] reconstituted in RPMI1640 with a 3:1 ratio for 30 minutes at 37°C. Digested tissues were passed through 70-μm nylon filters and cell suspensions were washed twice with PBS. Isolated cells were labelled with fluorescent antibodies, and enriched non-lymphatic ECs (CD31+, CD45-, Podoplanin-) were sorted (BD™ FACSAria cell sorter).

Cell culture, inhibitors, and stimulating factors
Human umbilical vein endothelial cells transduced with E4-ORF1 gene (VeraVec EC; Angiocrine Bioscience), namely E4-ECs, were cultured in *ex vivo* media (composition: 199 Hyclone medium with 50 μg/mL heparin [Sigma], 20 ng/mL FGF-2 [Peprotech], antibiotic-antimycotic [Invitrogen], normocin [InvivoGen], 10 mM HEPES [Invitrogen], Glutamax [Life Technologies]) supplemented with 10% FCS (Lonza) and maintained at 37°C in a humidified 5% CO_2 atmosphere. PDX-derived T-ALL cells were cultured in RPMI with 10% FCS or SS™ (StemCell Technologies) supplemented with 10% knock-out Serum Replacement (KSR; Life Technologies), 100 U/mL penicillin, 100 μg/mL streptomycin, and a cocktail of interleukins (IL2, IL6, IL7, IL12, and IL15) based on the expression of lymphokine receptors of T-ALL PDX. KSR is an FCS-free medium supplement that supports the growth of cultured pluripotent stem cells (PSCs). Human recombinant IL-12 (10 ng/mL), IL-7 (10 ng/mL), IL15 (25 ng/mL), IL-6 (10 ng/mL) SDF1α (100 ng/mL), and Jagged-1 (50 ng/mL) were purchased from R&D Systems.
For the 96- and 384-well drug screening, all compounds were tested at a concentration of 1.0 μM unless differently specified (dose-response experiments). All compounds were purchased from Selleckchem.

High-throughput drug screening
The drug-screening library, composed of 433 targeted-compounds, was purchased from SelleckChem and consists of a subset of SelleckChem's "Targeted Selective inhibitory Library". Drugs were selected based on current clinical applications (FDA-approved), selectivity (target of canonical signaling pathways [JAK/STAT, RAS/ERK, PI3K/AKT, B-catenin., epigenetic, anti-apoptotic etc.]), and redundancy (multiple drugs targeting the same pathways). Collectively, 634 proteins were targeted. Drug screening plates were prepared at a concentration of 1 μM, spanning 2 × 384-well plates using

Tecan Freedom EVO 150 (Tecan, CH) in the High-Throughput and Spectroscopy facility at Rockefeller University. Approximately 33,000 cells derived from PDX models were added per well in a total volume of 50 µL (drug solution + cells) and incubated at 37°C for 72 h. After drug incubation, cell viability was evaluated based on luminescence of CTG-tagged ATP (CellTiter-Glo™ kit; Promega) and assessed using a plate reader (Synergy 4, Biotek); data were processed, analyzed, and plotted using Matlab (Mathworks, MA).

To determine compound activity, each data point was normalized to its corresponding in-plate vehicle control (16 wells of vehicle control per plate) and then linearized to transform the response-matrix (16×33) into a 433×1 drug-response vector. To assess the degree of concordance, sample-replicates were plotted against each other and the correlation, coefficient of variance, and standard error were computed for each compound to determine the reproducibility. To further test reproducibility, we used a representative sample with four replicates and randomized permutation analysis. In this analysis, from a total of four replicates, we computed all possible combinations of 2, 3, or 4 samples. For this method, we computed the overlap in distributions, the average number of active compounds (having <50% viability), and coefficient of variance to determine the degree of concordance; p-values were assessed using one-way ANOVA.

The groupings of the samples' response profiles and drug groupings across all samples were evaluated using unsupervised hierarchical clustering along the axis of maximum variation (ward) of Euclidean distances. Samples and compounds were reordered and illustrated using color-coded heatmaps and dendrogram trees, with the branches delineating groups. Hierarchical clustering analysis was further confirmed using PCA, yielding similar conclusions based on the analyses. Active compounds that reduced viability, as assessed by a reduction in ATP content relative to vehicle controls, were determined in each column within the 433xn matrix and compared among samples. Compounds that induced ≤50% viability among all replicates were considered active and selected for further comparison and analysis. Data shown in the heatmaps denote the average viability across samples.

To evaluate differences in sample responses cultured in the two media types, we computed the differential (viability in condition 1 – viability in condition 2) and deviation scores. Briefly, the standard deviation and mean were computed across the two conditions and the ratio of the standard deviation versus the means was computed. The deviation score is informative since it allows compounds that are different and active to be identified. For example, if a drug induces a viability of 1.5 and 1.2 in two samples and another drug induces a viability of 0.4 and 0.1 in the same two samples, both will yield a differential of 0.3. However, based on the deviation score, one can preferentially highlight the difference in the active drug (with lower viabilities), (i.e., Deviation score = 0.22 vs. 1.2, respectively).

Pathway enrichment analysis in differential drug targets

Differentially active drugs based on underlying genetic profiles were identified based on the deviation score (>3) and differential. From drugs identified as differentially active, 77 drugs were more active in R05/R06 compared with 29 in 3053/3119. The list of drugs in both cases was compiled and the list of targets corresponding to each drug was imported into Cytoscape; ClueGO was used to assess pathway enrichments using GO: biological processes with a significance cutoff of $p \leq 0.05$. Network maps were constructed, with each node (color) representing a sub-pathway within the main pathways and gray lines highlighting the connections among nodes. Note, the length of the connecting links has no significance, and nodes with multiple colors denote shared underlying genes.

Co-culture with ECs

For co-culture experiments under stress conditions, T-ALL cell lines were grown at a density of 2×10^5/mL in serum/cytokine-free media (here referred to as *ex-vivo* media*)*, whereas PDX-derived T-ALL cells were cultured at 5×10^5/mL in RPMI with or without 10% FCS, alone or in co-culture with ECs (8×10^4 per well in a 24-well plate). Cell viability was determined by Trypan blue exclusion count. Cytotoxicity was assessed by flow cytometric evaluation of Annexin V/7AAD staining (PE AnnexinV Apoptosis detection kit I, BD). A total of 20,000 events were acquired by flow cytometry per sample.

Co-culture drug screening
For drug screening in co-culture, the following conditions were applied: ECs were stained with CFSE (1 μM; Invitrogen), plated, and cultured overnight in 96-well plates (13,000 cells/well). On day 0, mice were sacrificed and T-ALL cells were harvested from the spleen. Enriched leukemic cells were stained with Cell Tracer Violet (1 μM, Invitrogen), washed, and plated (83,000 cells/well) in 96-well plates alone or on stromal/E4-EC elements and challenged with the drug library (1□M) in duplicate/triplicate. On selected samples, IGFBP-7 was added to the culture media at a final concentration of 0.5 μg/mL. At 72 hours, cells were collected (using Accutase following the manufacturer's recommendation [Stemcell Technologies]) and stained with propidium iodide (Sigma). E4-EC and T-ALL cell viability was assessed by high-throughput flow cytometry (BD). At least 10,000 events were recorded per well. Flow data were analyzed by FCS Express 6 (De Novo Software) and Prism 8 (GraphPad).

Total RNAseq
Total RNA was extracted from primary and PDX cells using Trizol and a cDNA total library was generated using the TruSeq-Stranded Total RNA Sample Preparation HS protocol (Illumina). The library was sized and quantified using DNA1000 kit (Agilent) on an Agilent 2100 Bioanalyzer according to the manufacturer's instructions. Paired-end RNA-sequencing at read lengths of 100 bp was performed with HiSeq2500 (Illumina). A total of about 268 million paired-end reads were generated, corresponding to ~27 billion bases. All reads were independently aligned with STAR_2.4.0f1 for sequence alignment against the human genome build hg19, downloaded via the UCSC genome browser, and SAMTOOLS v0.1.19 was used for sorting and indexing reads. Cufflinks (2.0.2) was used to obtain the expression values (FPKMS) with Gencode v19 GTF for annotation. Cytoscape_v3.0 software was used to visualize the network hubs and perform connectivity score calculations. For fusion analysis, STAR-fusion (STAR-Fusion_v0.5.1) and Fusioncatcher (v0.99.3e) were used. Fusions with significant support of junction reads and spanning pairs were then selected and reviewed manually. DEseq package in R was used for differential expression analysis. A Wald test was applied for mRNA differential analysis, followed by Benjamini-Hochberg correction for multiple hypothesis testing. Genes with adjusted p-value ≤0.05 were considered statistically significant. For pathway activation, Gene Set Enrichment Analysis (GSEA) [3,4] was used on pre-ranked gene list, with rank defined as the signed p-value (i.e., minus base-10 logarithm of the *p*-value multiplied by the sign of the based-2 logarithm of the FPKM fold-change between two different conditions). Gene sets with $p \leq 0.05$ and FDR ≤ 0.1 were considered significantly enriched. Rnaseqmut was used to detect mutations (https://github.com/davidliwei/rnaseqmut). VAF was calculated based on reference reads and alternate reads from the output generated by rnaseqmut.

Real-time PCR
The primers used for *SMCHD1/JAK2* fusion validation in real-time PCR were the following: forward-TCAGGACTGGGTTTAATTTTTACTG and reverse- CCAGGGCACCTATCCTCATA.

Single-cell RNA-seq, data processing, cell type classification, and clustering
Single cell preparations from freshly isolated leukemic tissue samples (spleen) underwent Ficoll density gradient separation, PBS washes, and cell counts (>90% viable). The standard 10x Genomics Chromium v.2 protocol was carried out according to manufacturer's recommendations (10x Genomics, Pleasanton, CA). A total of 1000–3000 cells per sample were processed using Cell Ranger version 2.1.0 with default parameters. Reads from *in vitro* experiments were aligned to the human reference sequence hg19. Reads from the PDX spleen were additionally aligned to the mouse reference sequence mm10. Downstream analysis was performed using Seurat package (version 3.2.2) in R (Butler et al., 2018). Low-quality cells (i.e., cells with >200 or <5000 unique molecular identifiers (UMIs) per cell and cells with >10% mitochondrial gene percentage) were removed. Doublets were identified using DoubletFinder [5] and removed. Normalization, variance stabilization, and integration were

performed using SCTransform workflow [6]. The, PCA and graph-based clustering were performed. Uniform manifold approximation and projection (UMAP) dimensionality reduction was used to visualize cell clusters. Cells were then annotated using SingleR package [7], which performs reference-based cell annotation. Two cell-type reference datasets from celldex package [7] were utilized for cell annotation: the human primary cell atlas [8] and the Blueprint/ENCODE reference [9]. We further validated cell annotations using known markers for ECs (e.g., VWF) and T-ALL cells (e.g., CD3D).
Cluster markers and differentially expressed genes were identified by a Wilcoxon Rank Sum test in Seurat's method FindMarkers. GSEA was performed to detect enriched gene-sets in cell clusters and educated cells using fgsea package (https://www.biorxiv.org/content/10.1101/060012v2). Pathway activity was evaluated from gene expression data using PROGENy package [10].
Education signature of T-ALL cells was calculated using AddModuleScore method in Seurat based on the most differentially expressed genes in 3119 and RO2 co-cultured samples versus alone. Cellular gene expression heterogeneity (i.e., gene expression entropy) was calculated using SLICE [11] to assess the patterns of expression and level of differentiation for each cell. Cell-cell interactions were evaluated with CellPhoneDB [12] via ligand-receptor combined expression.

***In vivo* treatment**
Mice were injected intravenously with 1 × 10^6 T-ALL cells and engraftment was monitored by flow cytometric analysis of peripheral blood mononuclear cells using antibodies against human T-cells. When human T-cells reached 5% of the total, male and female (ratio 1:1) mice were randomized into untreated (vehicle) and treated arms. Numbers, age and gender of the mice were equally distributed among arms. Compounds were administered as follows: irinotecan (20 mg/kg/day i.p. weekend off, Selleckchem), ruxolitinib (in food, Incyte), tofacitinib (80 mg/kg/day i.p., weekend off, Selleckchem), bortezomib (0.5 mg/kg/day i.p., weekend off, Selleckchem), panobinostat (5 mg/kg/day i.p., weekend off, Selleckchem) daunorubicin (1.2 mg/kg for three consecutive days/week, Selleckchem) and OSI-906 (linsitinib) (50 mg/kg/day oral gavage, weekend off, Selleckchem). Tumor burden was monitored by flow cytometric analysis of peripheral blood or using spleen measurements from total body MRI or measurement of spleen size. Survival curves were estimated using the Kaplan-Meier method. Bodyweight was used as a surrogate for drug toxicity.

Total body MRI
MRI images were acquired on a 1-Tesla Aspect M3 MRI System (Aspect Magnet Technologies Ltd., Netanya, Israel). Mice were anesthetized with isoflurane (Isothesia) and placed in a supine position in a solenoid Tx/Rx coil with an inner diameter of 30 mm. Breath was monitored constantly using a respiratory probe (SAII Instruments, Stony Brook, NY). To assess spleen dimensions, coronal-T2w anatomical images were acquired with a Fast Spin Echo sequence (TR, 6000 s; TE, 40 ms; number of slices, 20; slice thickness, 1 mm; FOV, 90 mm; matrix, 256 × 256; NEX, 4; acquisition time, 3 min 48 sec). The spleen volumes were calculated on T2w-images by drawing a region of interest (ROI) with ITK-SNAP software (http://www.itksnap.org/pmwiki/pmwiki.php) and tabulated using GraphPad Prism 5 (GraphPad Inc).

Mathematical equations
To compute the Shannon entropies, we first computed the fractional cell killing for each of the 39 compounds per PDX line, then used the following equation:

$$S = -\sum_{1}^{39} pi.\ln(pi)$$

Where pi is the fractional cell death per compound for each PDX line, and S is the Shannon entropy.

Figure S1

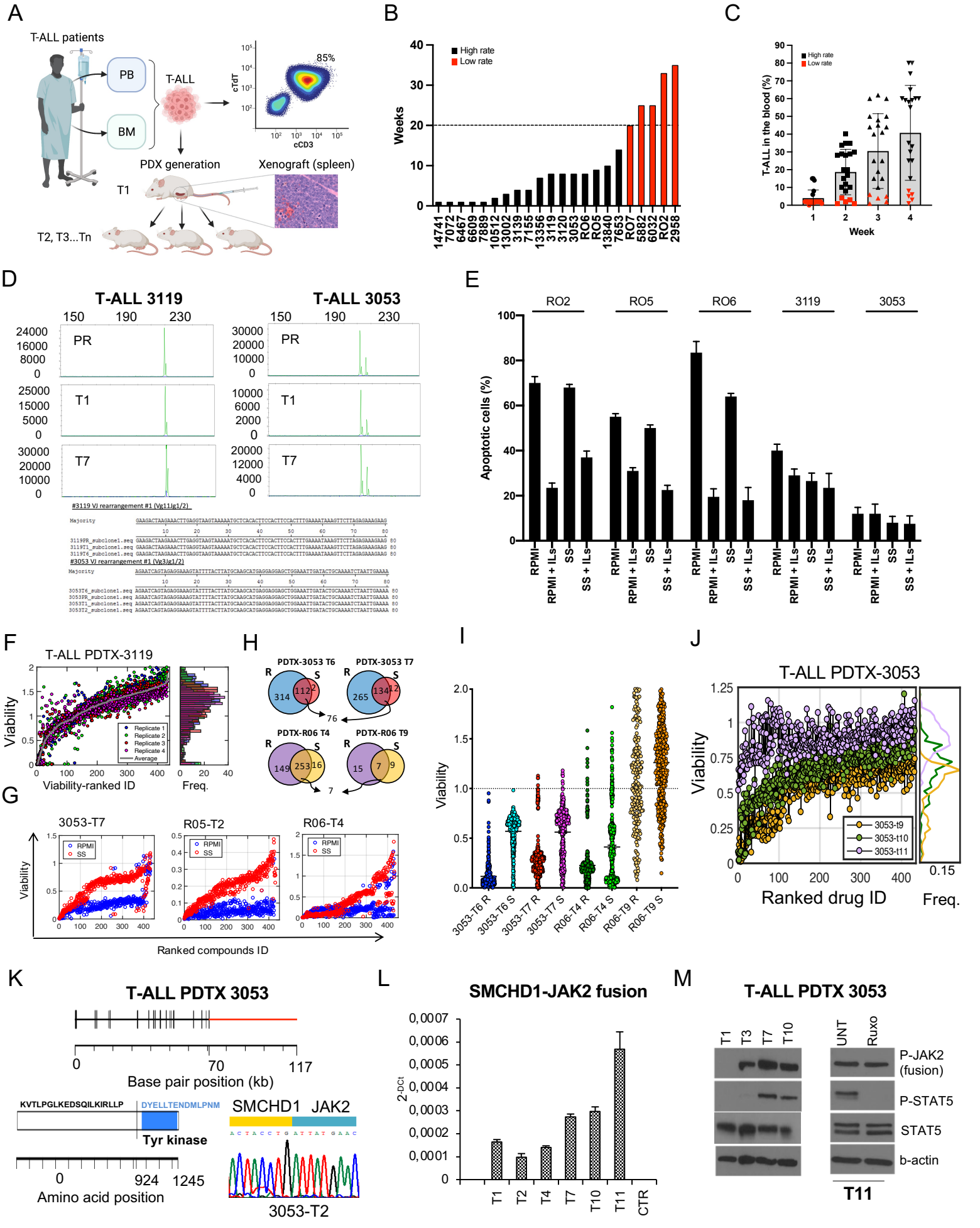
A
T-ALL patients
PB
BM
T-ALL
85%
cTdT
cCD3
PDX generation
Xenograft (spleen)
T1
T2, T3...Tn
B
High rate
Low rate
Weeks
14741
7072
6467
6609
7889
10512
13002
3139
7155
13356
3119
3120
3053
RO6
RO5
13840
7653
RO7
5882
6032
RO2
2958
C
High rate
Low rate
T-ALL in the blood (%)
Week
D
T-ALL 3119
T-ALL 3053
PR
T1
T7
#3119 VJ rearrangement #1 (Vg11Jg1/2)
#3053 VJ rearrangement #1 (Vg3Jg1/2)
E
RO2
RO5
RO6
3119
3053
Apoptotic cells (%)
RPMI
RPMI + ILs
SS
SS + ILs
F
T-ALL PDTX-3119
Viability
Viability-ranked ID
Freq.
Replicate 1
Replicate 2
Replicate 3
Replicate 4
Average
H
PDTX-3053 T6
PDTX-3053 T7
PDTX-R06 T4
PDTX-R06 T9
R
S
I
Viability
3053-T6 R
3053-T6 S
3053-T7 R
3053-T7 S
R06-T4 R
R06-T4 S
R06-T9 R
R06-T9 S
J
T-ALL PDTX-3053
Viability
Ranked drug ID
Freq.
3053-t9
3053-t10
3053-t11
G
3053-T7
R05-T2
R06-T4
RPMI
SS
Viability
Ranked compounds ID
K
T-ALL PDTX 3053
Base pair position (kb)
KVTLPGLKEDSQILKIRLLP
DYELLTENDMLPNM
Tyr kinase
Amino acid position
SMCHD1 JAK2
3053-T2
L
SMCHD1-JAK2 fusion
2-DCt
T1
T2
T4
T7
T10
T11
CTR
M
T-ALL PDTX 3053
T1
T3
T7
T10
UNT
Ruxo
P-JAK2 (fusion)
P-STAT5
STAT5
b-actin
T11

Figure S1

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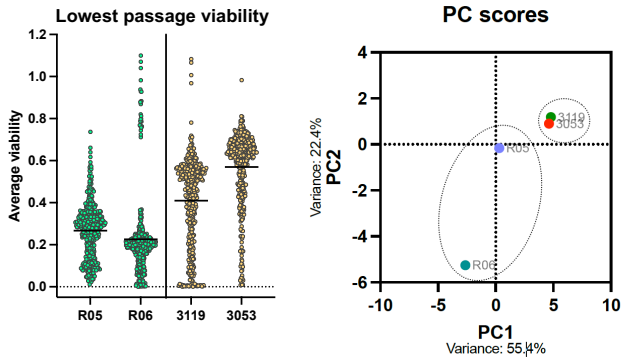

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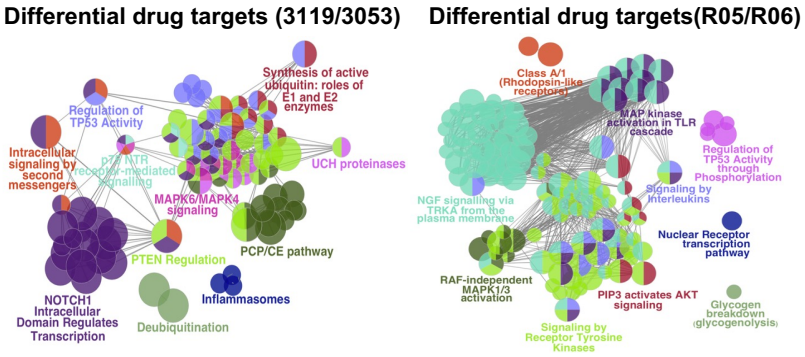

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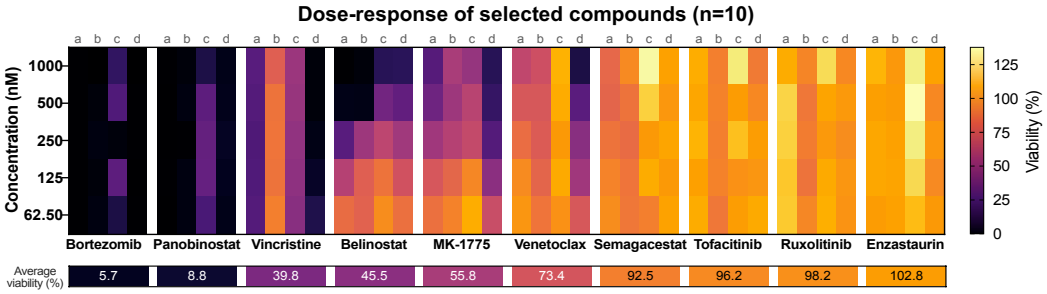

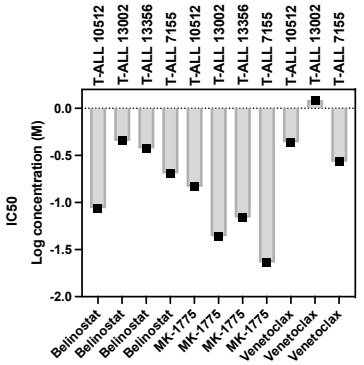

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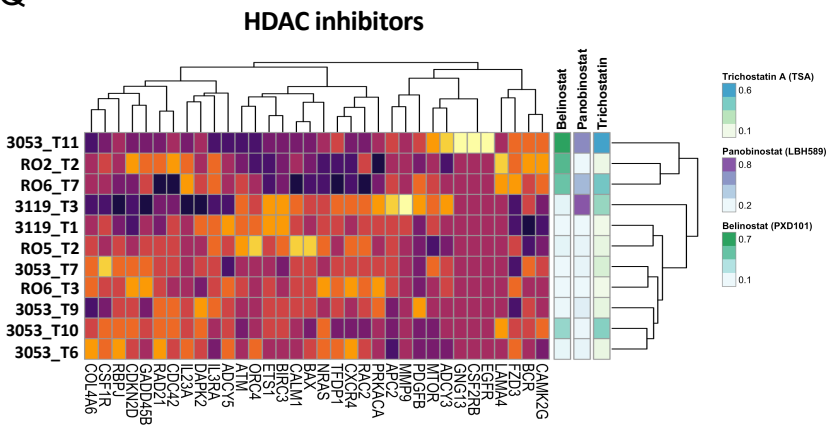

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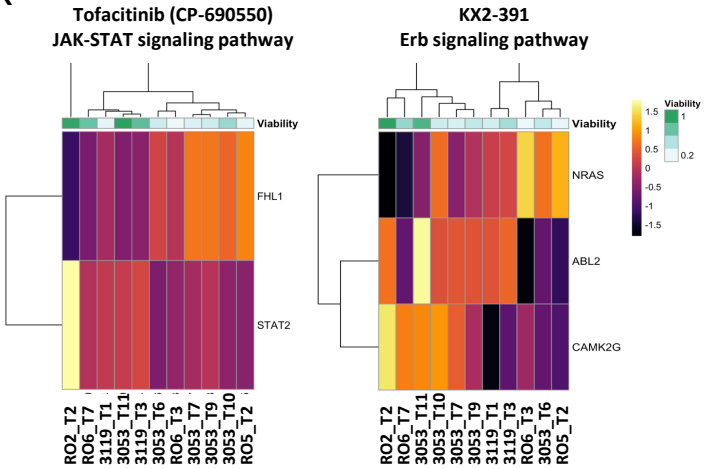


Figure S2

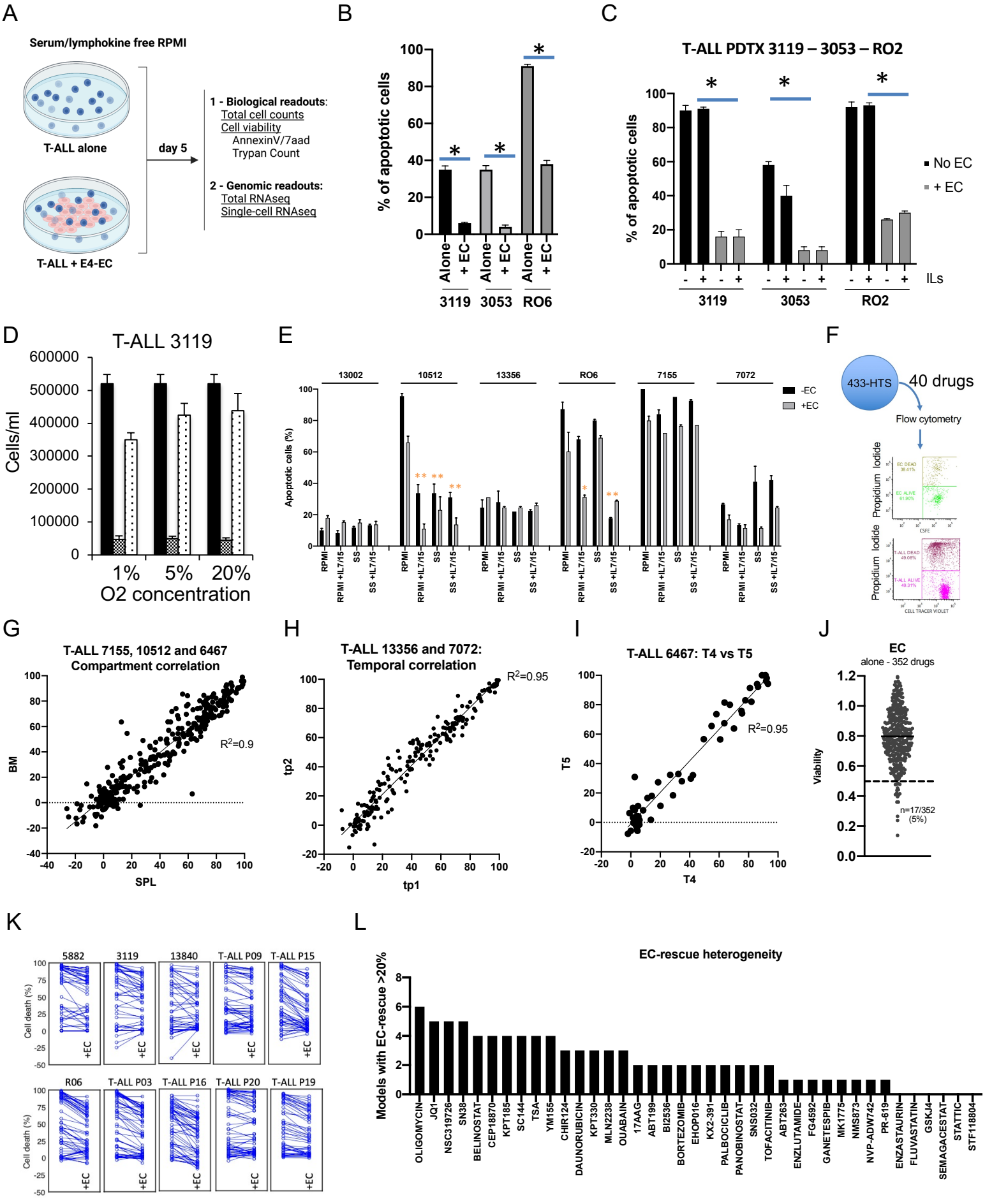
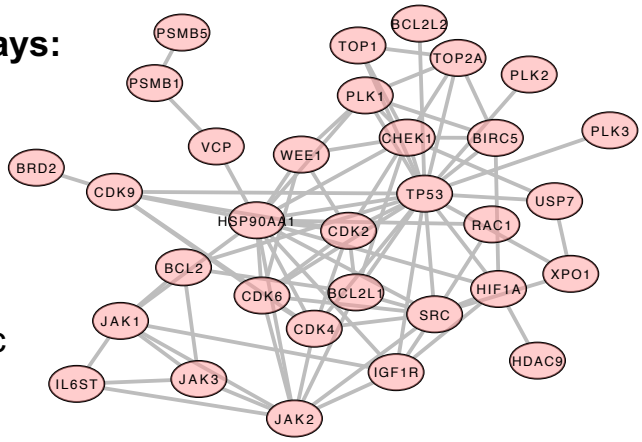

A
Serum/lymphokine free RPMI
T-ALL alone
T-ALL + E4-EC
day 5
1 - Biological readouts:
Total cell counts
Cell viability
AnnexinV/7aad
Trypan Count
2 - Genomic readouts:
Total RNAseq
Single-cell RNAseq
B
% of apoptotic cells
Alone
+ EC
3119
3053
RO6
C
T-ALL PDTX 3119 – 3053 – RO2
% of apoptotic cells
No EC
+ EC
ILs
3119
3053
RO2
D
T-ALL 3119
Cells/ml
1%
5%
20%
O2 concentration
E
13002
10512
13356
RO6
7155
7072
-EC
+EC
Apoptotic cells (%)
RPMI
RPMI +IL7/15
SS
SS +IL7/15
F
433-HTS
40 drugs
Flow cytometry
Propidium Iodide
CSFE
CELL TRACER VIOLET
G
T-ALL 7155, 10512 and 6467
Compartment correlation
BM
SPL
R2=0.9
H
T-ALL 13356 and 7072:
Temporal correlation
tp2
tp1
R2=0.95
I
T-ALL 6467: T4 vs T5
T5
T4
R2=0.95
J
EC
alone - 352 drugs
Viability
n=17/352
(5%)
K
5882
3119
13840
T-ALL P09
T-ALL P15
R06
T-ALL P03
T-ALL P16
T-ALL P20
T-ALL P19
Cell death (%)
+EC
L
EC-rescue heterogeneity
Models with EC-rescue >20%
OLIGOMYCIN
JQ1
NSC319726
SN38
BELINOSTAT
CEP18870
KPT185
SC144
TSA
YM155
CHIR124
DAUNORUBICIN
KPT330
MLN2238
OUABAIN
17AAG
ABT199
BI2536
BORTEZOMIB
EHOP016
KX2-391
PALBOCICLIB
PANOBINOSTAT
SNS032
TOFACITINIB
ABT263
ENZLUTAMIDE
FG4592
GANETESPIB
MK1775
NMS873
NVP-ADW742
PR-619
ENZASTAURIN
FLUVASTATIN
GSKJ4
SEMAGACESTAT
STATTIC
STF118804

Figure S2

M

Rescued drugs enriched pathways:

- PI3K-Akt
- P53
- FoxO
- JAK-STAT
- NOD-like-Rec
- HIF-1



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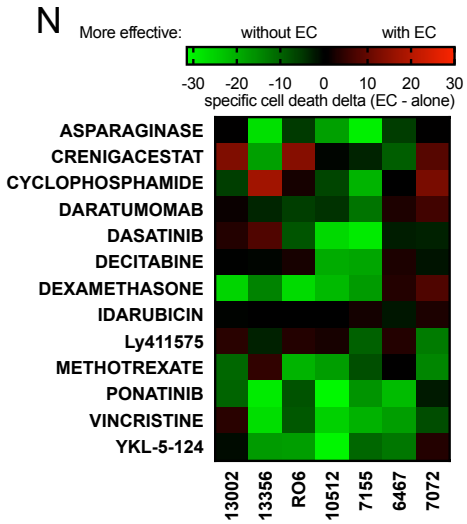

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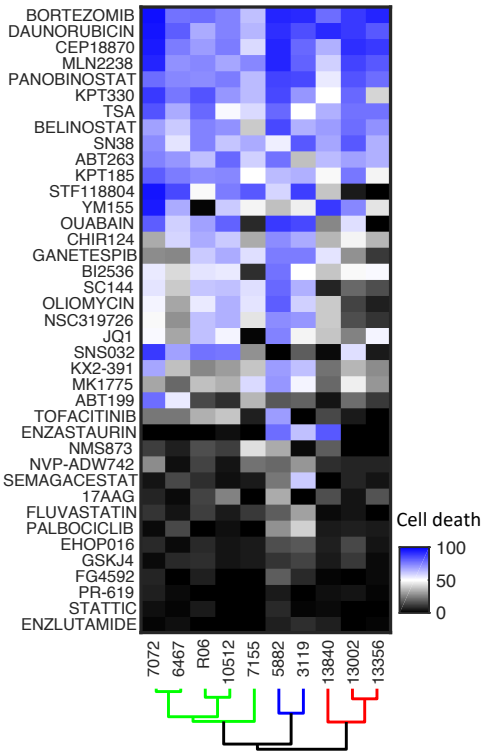

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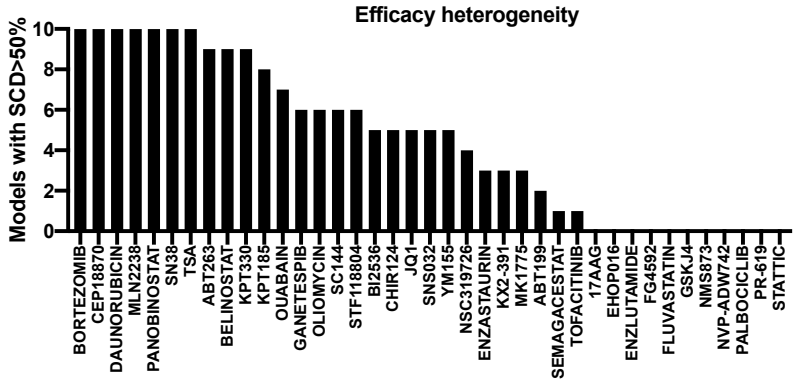

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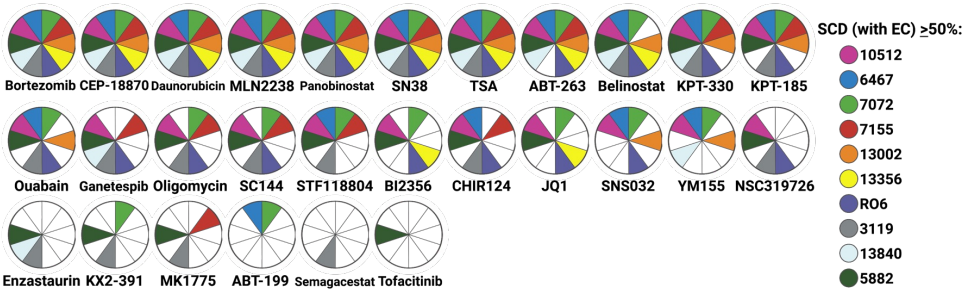
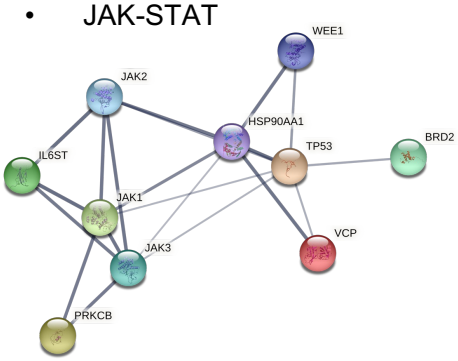


R

ETP-ALL specifically inactive drugs (targeted pathways):

- PI3K-Akt
- JAK-STAT



S

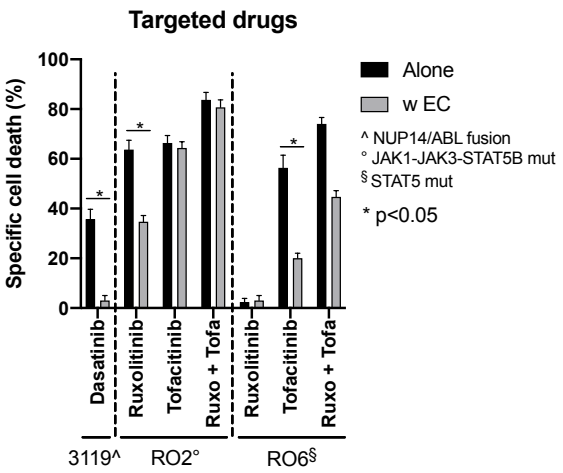


Figure S3

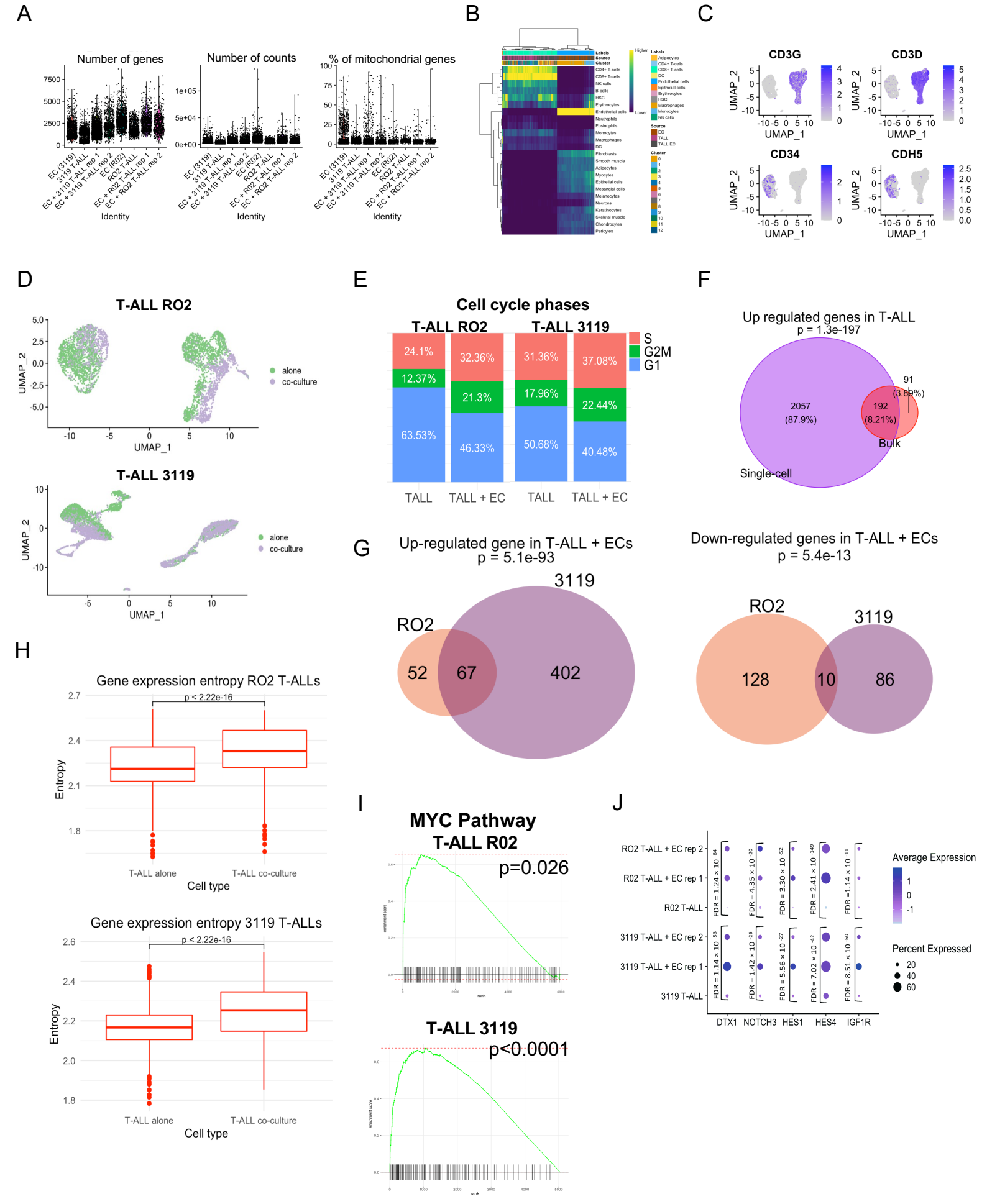

A
Number of genes
Number of counts
% of mitochondrial genes
Identity
B
C
CD3G
CD3D
CD34
CDH5
UMAP_1
UMAP_2
D
T-ALL RO2
T-ALL 3119
alone
co-culture
E
Cell cycle phases
T-ALL RO2
T-ALL 3119
S
G2M
G1
24.1%
12.37%
63.53%
32.36%
21.3%
46.33%
31.36%
17.96%
50.68%
37.08%
22.44%
40.48%
TALL
TALL + EC
F
Up regulated genes in T-ALL
p = 1.3e-197
2057
(87.9%)
192
(8.21%)
91
(3.89%)
Bulk
Single-cell
G
Up-regulated gene in T-ALL + ECs
p = 5.1e-93
RO2
3119
52
67
402
Down-regulated genes in T-ALL + ECs
p = 5.4e-13
RO2
3119
128
10
86
H
Gene expression entropy RO2 T-ALLs
p < 2.22e-16
Entropy
T-ALL alone
T-ALL co-culture
Cell type
Gene expression entropy 3119 T-ALLs
p < 2.22e-16
Entropy
T-ALL alone
T-ALL co-culture
Cell type
I
MYC Pathway
T-ALL R02
p=0.026
T-ALL 3119
p<0.0001
J
RO2 T-ALL + EC rep 2
R02 T-ALL + EC rep 1
R02 T-ALL
3119 T-ALL + EC rep 2
3119 T-ALL + EC rep 1
3119 T-ALL
DTX1
NOTCH3
HES1
HES4
IGF1R
Average Expression
Percent Expressed

Figure S4

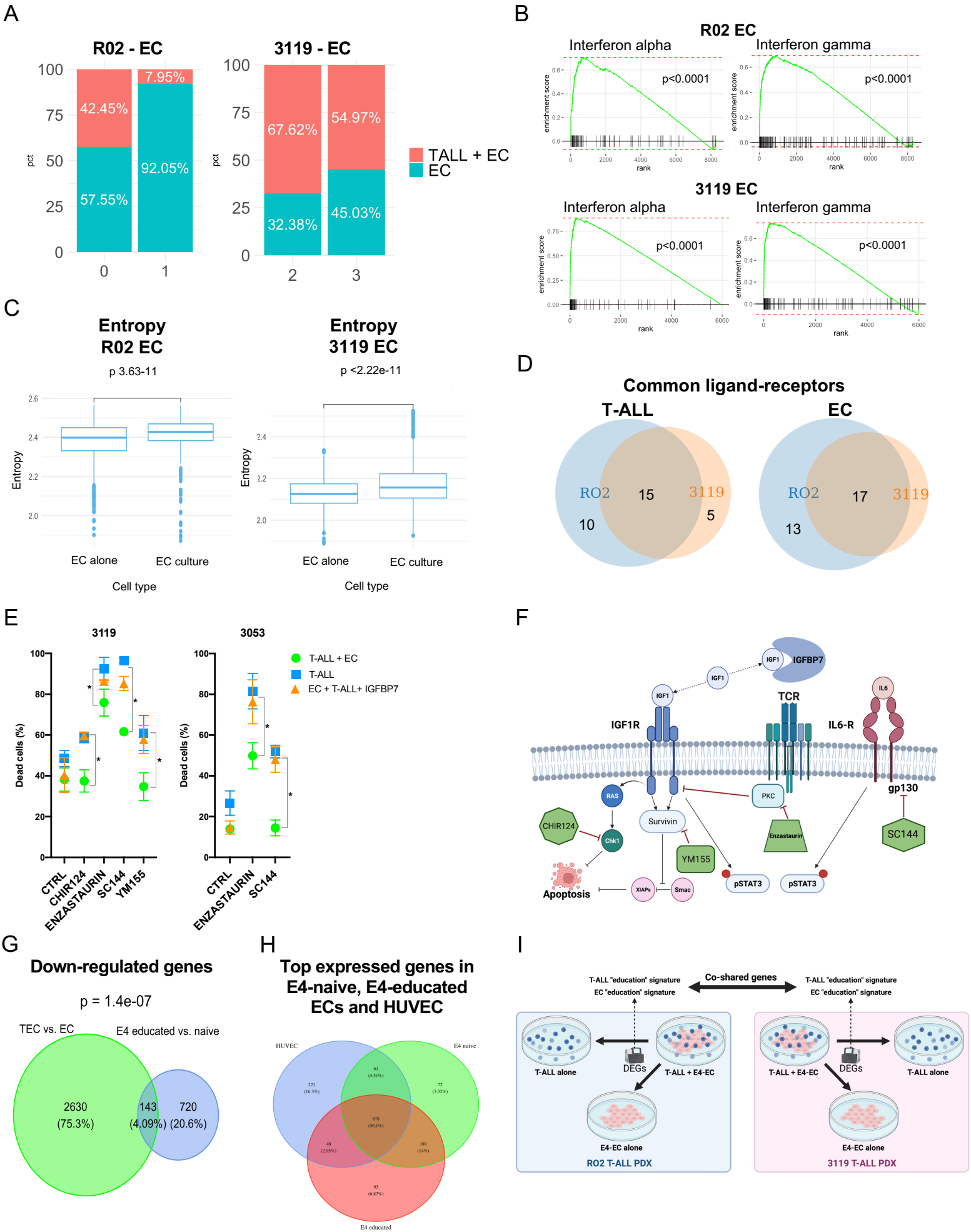

A
R02 - EC
3119 - EC
pct
42.45%
57.55%
7.95%
92.05%
67.62%
32.38%
54.97%
45.03%
TALL + EC
EC
B
R02 EC
Interferon alpha
Interferon gamma
p<0.0001
enrichment score
rank
3119 EC
C
Entropy
R02 EC
p 3.63-11
3119 EC
p <2.22e-11
EC alone
EC culture
Cell type
D
Common ligand-receptors
T-ALL
EC
RO2
3119
15
10
5
17
13
E
3119
3053
Dead cells (%)
T-ALL + EC
T-ALL
EC + T-ALL+ IGFBP7
CTRL
CHIR124
ENZASTAURIN
SC144
YM155
F
IGF1
IGFBP7
IGF1R
TCR
IL6-R
IL6
gp130
RAS
PKC
CHIR124
Chk1
Survivin
Enzastaurin
SC144
YM155
pSTAT3
XIAPs
Smac
Apoptosis
G
Down-regulated genes
p = 1.4e-07
TEC vs. EC
E4 educated vs. naive
2630
(75.3%)
143
(4.09%)
720
(20.6%)
H
Top expressed genes in E4-naive, E4-educated ECs and HUVEC
HUVEC
E4 naive
E4 educated
I
T-ALL "education" signature
EC "education" signature
Co-shared genes
T-ALL alone
DEGs
T-ALL + E4-EC
E4-EC alone
RO2 T-ALL PDX
3119 T-ALL PDX

Figure S5

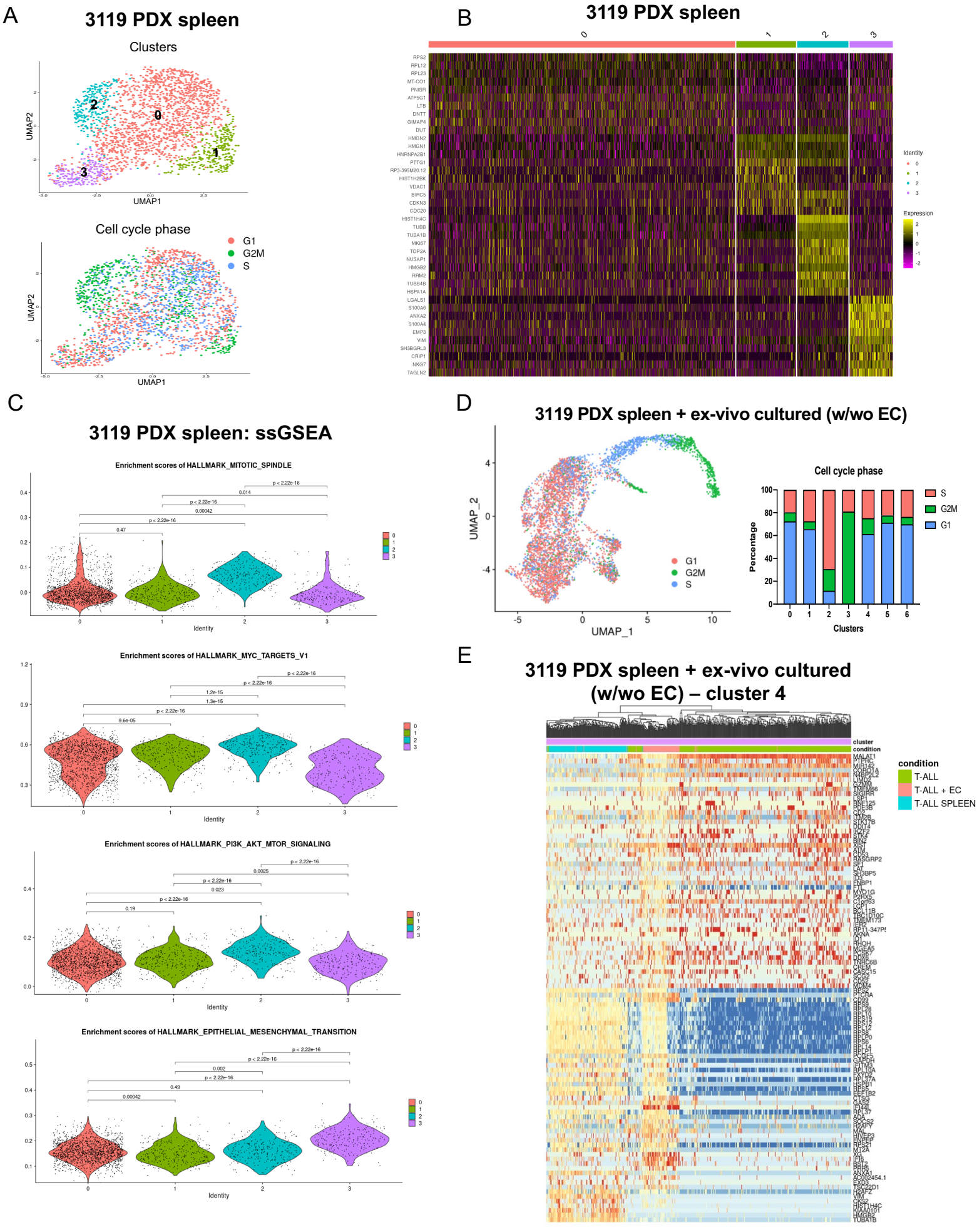
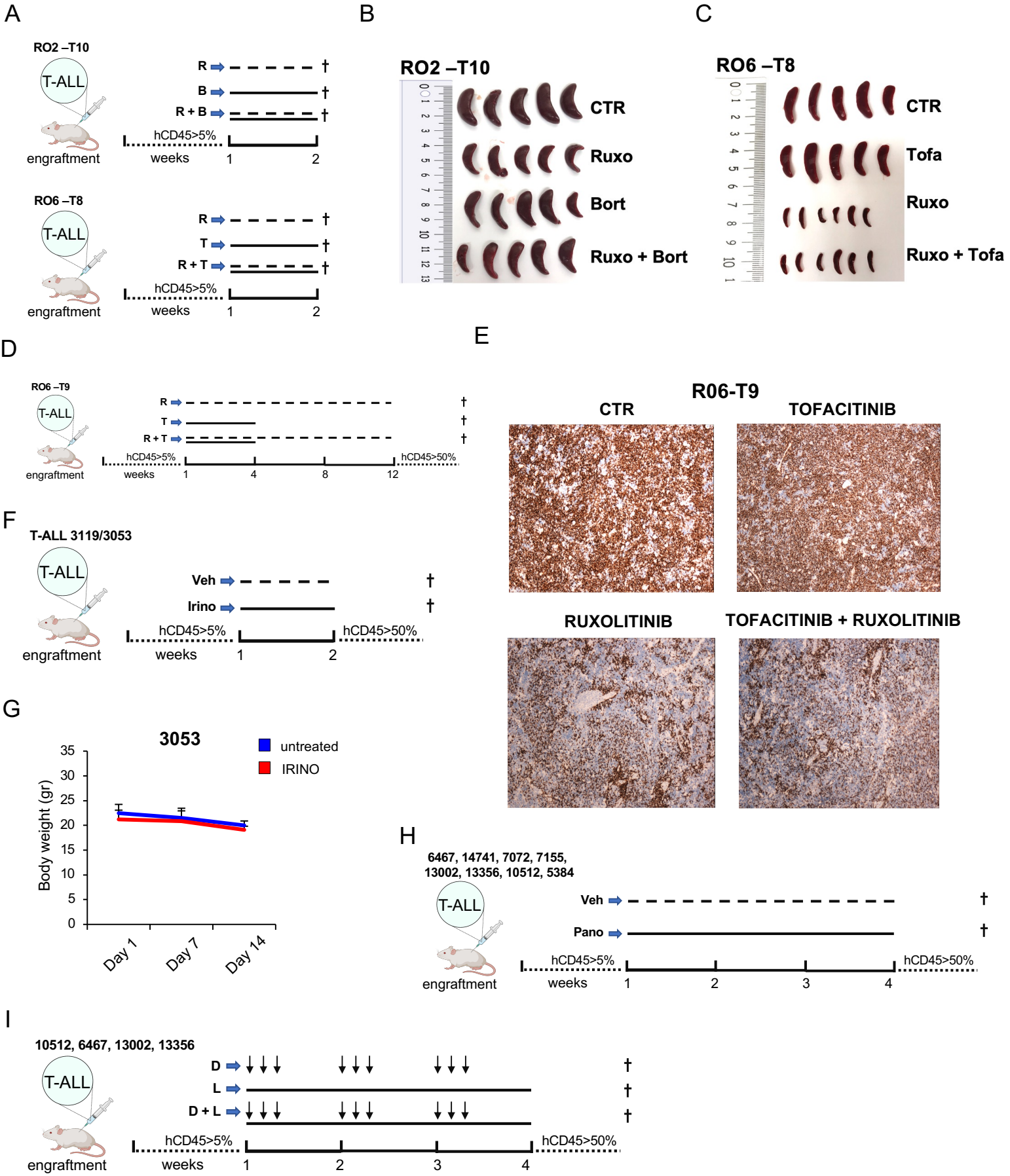

A
3119 PDX spleen
Clusters
UMAP2
UMAP1
0
1
2
3
Cell cycle phase
G1
G2M
S
B
3119 PDX spleen
Identity
Expression
C
3119 PDX spleen: ssGSEA
Enrichment scores of HALLMARK_MITOTIC_SPINDLE
Enrichment scores of HALLMARK_MYC_TARGETS_V1
Enrichment scores of HALLMARK_PI3K_AKT_MTOR_SIGNALING
Enrichment scores of HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION
Identity
D
3119 PDX spleen + ex-vivo cultured (w/wo EC)
UMAP_1
UMAP_2
Cell cycle phase
Percentage
Clusters
E
3119 PDX spleen + ex-vivo cultured (w/wo EC) – cluster 4
cluster
condition
T-ALL
T-ALL + EC
T-ALL SPLEEN

Figure S6


A
RO2 –T10
T-ALL
engraftment
R
B
R + B
hCD45>5%
weeks
1
2
RO6 –T8
T-ALL
engraftment
R
T
R + T
hCD45>5%
weeks
1
2
B
RO2 –T10
CTR
Ruxo
Bort
Ruxo + Bort
C
RO6 –T8
CTR
Tofa
Ruxo
Ruxo + Tofa
D
RO6 –T9
T-ALL
engraftment
R
T
R + T
hCD45>5%
weeks
1
4
8
12
hCD45>50%
E
R06-T9
CTR
TOFACITINIB
RUXOLITINIB
TOFACITINIB + RUXOLITINIB
F
T-ALL 3119/3053
T-ALL
engraftment
Veh
Irino
hCD45>5%
weeks
1
2
hCD45>50%
G
3053
untreated
IRINO
Body weight (gr)
35
30
25
20
15
10
5
0
Day 1
Day 7
Day 14
H
6467, 14741, 7072, 7155,
13002, 13356, 10512, 5384
T-ALL
engraftment
Veh
Pano
hCD45>5%
weeks
1
2
3
4
hCD45>50%
I
10512, 6467, 13002, 13356
T-ALL
engraftment
D
L
D + L
hCD45>5%
weeks
1
2
3
4
hCD45>50%

Supplemental Figures

Figure S1. Patient-derived-tumor-xenograft (PDX) as models of high-risk T-ALL patients (Referred to Figure 1).

(A) Schematic representation of the generation and expansion of T-ALL PDX models. PB: peripheral blood mononuclear cells; BM: bone-marrow aspirate. Representative readout (i.e. flow cytometry and histology) are also reported (created in BioRender.com).

(B) Time required to reach the first engraftment (expressed as the number of weeks from the implant to the 5% of human blood lymphoblasts in the PB).

(C) Rate of tumor growth expressed as the percentage of human blood T-cells along serial passages.

(D) Representative TCR gamma rearrangement analysis of primary (PR) and two serial passages (T1 and T7) of 3119 and 3053 T-ALL PDX models (reported as proof of concept). DNA nucleotide sequences of primary and PDX are reported at the bottom.

(E) T-ALL cells from five different PDX were cultured in RPMI 10% FCS or StemSpan 10% KSR with or without ILs. The percentage of apoptotic cells was determined at day five. Data are represented as means and ± SD of three independent PDX samples.

(F) Dot plot showing reproducibility across four replicates for the 3119 PDX model (as proof of concept).

(G) Ranked compound ID versus viability in RO5, RO6 and 3053 PDX screened in RPMI and StemSpan (SS), showing a decrease in the overall viability for PTDXs screened in RPMI.

(H) Venn diagrams denoting the number of active drugs (viability less than 50%, vehicle control) in each media condition (RPMI vs. SS) for two in vivo passages (3053 and R06). Overlap denotes drugs that are effective in both media.

(I) Dot plot correlating the viabilities of 3053 and RO6 PDX at different passages after 433 drug library exposure for 72hrs, cultured in supplemented- RPMI (R) versus SS media (S).

(J) Activity-ranked drugs versus viability of samples (3053 T-ALL model) as a function of increasing *in vivo* passages. Data show a tendency toward loss of active targets (viabilities <50% of vehicle control) with increasing passages. The plot on the right illustrates the distributions of viabilities per passage, showing a shift in distribution to higher viabilities with the increasing passage.

(K) Schematic representation of the SMCHD1-JAK2 fusion. Intron-exon configuration is depicted: 5' (black) and 3' (red). Transcribed exonic sequences are shown as part of a transcript variant resulting from the fusion.

(L) mRNA expression of the SMCHD1-JAK2 fusion in serial 3053 PDX passages assessed by RTqPCR.

(M) Total protein lysates from 3053 PDX at serial passages (T1, T3, T7, T10) were blotted with indicated antibodies. T-ALL cells from the tenth passage were treated, in conventional RPMI supplemented with 10% FCS, with 1 μM of ruxolitinib (Ruxo) for 24h. Total cell lysates were blotted with indicated antibodies.

(N) Dot plot showing the average viability of the lowest passages of RO5, RO6, 3119, and 3053 PDX T-ALL exposed to the 433-compound library (left panel) and related principal component analysis (right panel).

(O) Pathway enrichment network plot highlighting the interaction of key pathways based on the differential drugs effective in 3119/3053 and R05/R06 T-ALL PDX models. Network plots were generated in Cytoscape with ClueGO, using Reactome: Pathways to determine the links.

(P) Left panel: heatmap showing the dose responses (from 1 μM to 62.5 nM) of four different T-ALL PDX models across 10 selected compounds targeting multiple pathways/target proteins for 72 h. The percentage of viability is depicted with a color scale. The average viability is indicated below. T-ALL PDX models id: a:10512; b: 13002; c: 13356; d:7155. Right panel: barplot depicting IC50 calcuated from the dose-response curves (where applicable). Values are provided on a logarythmic scale.

(Q) Heatmap and unsupervised clustering depicting gene expression within pathways related to a set of HDAC inhibitors. Genes were selected based on a significant correlation between their expression

across samples and the viability of the treated sample. The viability values are indicated in the color bars on the right.
(R) Heatmap and unsupervised clustering depicting gene expression within pathways targeted by the indicated compounds. Genes were selected based on a significant correlation between their expression across the samples and the viability of the treated samples. The viability values are indicated in the upper color bar.

Figure S2. ECs provide pro-tumorigenic signals to PDX cells (Referred to Figure 2).
(A) Schematic representation of stress condition platform in which freshly isolated T-ALL cells from PDX were cultured alone or co-cultured with human E4-ECs(created in BioRender.com).
(B) Pro-survival role of E4-ECs. T-ALL cells from different PDX were cultured in RPMI 10% FCS without interleukins (ILs) (R06 [passages T6]; 3119 [passages T4] and 3053 [passages T6] T-ALL models) in the absence or in the presence of E4-ECs. Left panels: representative histogramas corresponding to Ec and T-ALL recognized by fluorochrome conjugated anti-CD31 or CD45 Abs. Right panels: the percentage of apoptotic cells was determined at day five. Data are represented as means and ± SD of three independent PDX samples. P-value were calculated using student t-test. *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001.
(C) Pro-survival role of E4-ECs with/without ILs. T-ALL cells from different PDX were cultured in RPMI 10% FCS with or without ILs, in the absence or in the presence of E4-ECs. The percentage of apoptotic cells was determined at day five. Data are represented as means and ± SD of three independent PDX samples. P-values were calculated using the student T-test. *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001.
(D) Histograms depicting cell number of 3119 cells cultured for 5 days in SS + 10% KSR at 1%, 5%, or 20% of oxygen.
(E) Pro-survival role of E4-ECs in different media/ILs combinations. T-ALL cells from different PDX were cultured in RPMI 10% FCS or SS with or without ILs, in the absence or in the presence of E4-ECs. The percentage of apoptotic cells was determined at day five. Data are represented as means and ± SD of three independent PDX samples. P-values were calculated using the student T-test. *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001.
(F) Schematics illustrating the second step of the drug screening platform (Co-culture screening), selecting a panel of most-active compounds from the first drug screening (Figure 1F) and challenging them on T-ALL cells with/without E4-ECs. Flow cytometry gating strategy to identify and enumerate E4-ECs and T-ALL cells in the co-culture screening. Viably labeled T-ALL and E4-ECs were harvested after 72h of culture and analyzed by flow-cytomery by an integrated gating strategy.
(G) Overall correlation of drug responses for 7155, 10512, and 6467 T-ALL cells harvested from spleen or bone marrow (compartment correlation) upon exposure to 53 drugs of the library, either in presence or absence of E4-ECs. The linear regression slope and R^2 coefficient are also depicted.
(H) Overall correlation of drug responses for 13356 T-ALL cells harvested from two sibling mice sacrificed one week one from the other (temporal correlation) in presence or absence of E4-ECs. The linear regression slope and R^2 coefficient are also depicted.
(I) Overall correlation of drug responses for 6467 T-ALL cells harvested from two different PDX mice transfer (T4 and T5, passage correlation) in presence or absence of E4-ECs. The linear regression slope and R^2 coefficient are also depicted.
(J) Dotplot depicting the viability of ECs challenged with 352 of the 433 drugs (80%) employed in the screening of T-ALL cells (1uM). Only 17/352 compounds (5%) produced significant toxicity (viability<50%).
(K) Line dot-plots illustrating specific cell death (SCD) of each drug from the drug screening without (left) or with (right) ECs spanning the 10 PDX T-ALL models. A trend towards decreased SCD can be observed in all cases.

(L) Barplot showing the number of models where an EC-rescue>20% is reached for each drug. Some compounds were rescued more efficiently than others, some others were not rescued at all.
(M) Pathway enrichment network plot highlighting the interaction of key pathways targeted by the most rescued drugs (Figure 2D), some common pathways can be observed.
(N) Heatmap showing the differental resposes of drugs per T-ALL PDX line and their proximity through unsupervised clustering (dendrogram at the bottom).
(O) Barplot showing the number of models where the efficacy threshold (SCD≥50%) was reached for each drug (only the +EC conditions were considered). Some compounds were still pan-active regardless of the presence of ECs while others were completely inactive.
(P) Pie charts indicating the drugs having greater than 50% SCD for the 10 T-ALL PDX models.
(Q) Pathway enrichment network plot highlighting the interaction of key pathways targeted by drugs significantly efficient in ETP-ALL vs non-ETP (from Figure 2F).
(R) Heatmap depicting delta SCD (+EC-EC) of 12 extra compounds tested in 7 PDX T-ALL models. Also in this smaller subset, significant rescues and remarkable heterogeneity were observed.
(S) Barplot depicting SCD upon exposure to dasatinib (3119 PDX model) ruxolitinib, tofacitinib or ruxolitinib + tofacitinib (RO2 and RO6 PDX models) in the presence or absence of ECs.

Figure S3. ECs produce transcriptomic changes to T-ALL cells (Referred to Figure 3).
(A) Violin plots describing the number of expressed genes, the number of counts, and the percentage of expressed mitochondrial genes across the samples that were included in the single-cell RNA-sequencing analysis: RO2 and 3119 T-ALL cells and E4-ECs that were cultured alone or together.
(B) Heatmap of annotation scores for single-cell types across all cells. Scores were calculated using SingleR package in R and demonstrated the expression profiles of individual single cells, allowing cell recognition and assignment.
(C) UMAP plots displaying the expression of T-cell marker genes (i.e., CD3G and CD3D) and EC marker genes (i.e., VWF and CDH5).
(D) UMAP plots displaying clusters of T-ALL and ECs in RO2 and 3119 PDX models, color-coded by culture condition (co-cultured vs cultured alone).
(E) Barplot displaying the percentage of cells in G1, S, and G2M phase of the cell cycle in T-ALL alone or co-cultured with ECs of RO2 (left) or 3119 (right) PDX models.
(F) Venn diagram showing overlap of up-regulated genes of bulk (3199, 3139, and 3120 PDX models) and single-cell (3119 PDX model) RNA-seq in T-ALL cells that were cultured together versus T-ALL cells that were cultured alone.
(G) Venn diagrams showing overlap of up- (left) and down- (right) regulated genes in 3119 and RO2 T-ALL cells that were cultured together versus alone. Data were obtained from single-cell RNA-seq.
(H) Gene expression entropy of 3119 and RO2 T-ALL cells calculated using the SLICE tool on single-cell RNA-seq data. T-ALL cells display elevated entropy levels when co-cultured with ECs, implying a higher degree of plasticity than those cultured alone.
(I) Enrichment plots for MYC pathway RO2 and 3119 T-ALL cells that were cultured with E4-ECs versus alone. Gene expression values were obtained from single-cell RNA-sequencing. The adjusted p-values are reported.
(J) Dot-plot displaying expression levels of DTX1, NOTCH3, HES1, HES4, and IGF1R genes in R02 and 3119 T-ALL cells that were cultured alone or co-cultured with E4-ECs. The size of the dot indicates the percentage of cells expressing each gene, and the color denotes the average expression level across all cells. Expression levels were measured using log-normalized counts. Adjusted p-values for the differential expression between the two conditions are reported.

Figure S4. T-ALL interaction modulate the phenotype of ECs (Referred to Figure 4).
(A) Percentage of E4-ECs co-cultured with T-ALL vs cultured alone in the clusters identified by single-cell RNA sequencing in both 3119 and RO2 T-ALL models.

(B) Enrichment plots for interferon-alpha and gamma response pathways E4-ECs cultured with RO2 and 3119 T-ALL cells versus alone. Gene expression values were obtained from single-cell RNA-sequencing. Adjusted p-values are reported.
(C) Gene expression entropy of ECs calculated using the SLICE tool on single-cell RNA-seq data shows that E4-ECs display elevated entropy level when co-cultured with T-ALL elements, implying a higher degree of plasticity compared to those cultured alone.
(D) Venn diagrams depicting overlap of ligand-receptor interactions obtained through CellPhoneDB package on RO2 and 3119 PDX models (both on T-ALL and EC compartments), based on the relative expression level measured by single-cell RNA seq.
(E) Dotplot showing that recombinant IGFBP-7 counteracts the rescue of E4-ECs against selective drugs. Cells from 3119 and 3053 T-ALL models were exposed to the 40 drugs from (A) either alone or in the presence of E4-ECs with and without IGFBP-7 (500 ng/mL). Only drugs with significant rescue abrogation are depicted. The percentage of apoptotic (Propidium-Iodide-PI+) cells is indicated for each compound in relation to the untreated control. Differences were evaluated with T-test and corrected for multiple comparison.
(F) Schematic representation of the IGFR1 signaling pathway and target proteins by the compounds listed in Figure S4E (created with BioRender.com).
(G) Venn diagram showing the comparison of genes down-regulated in TEC vs. normal ECs (green circle) and in educated vs naïve E4-ECs (blue circle). P-value was calculated using a hypergeometric test.
(H) Venn diagram showing the comparison of Top expressed genes in E4-naïve (green circle), E4-educated ECs (red circle) and HUVEC (blue circle). P-value was calculated using a hypergeometric test.
(I) Scheme depicting the identification of "education signatures" on the T-ALL and EC side for both 3119 and RO2 PDX models and the selection of candidates co-shared by the two models (referred to Figure 4G) (created with BioRender.com).

Figure S5. *In vitro* EC-educated T-ALL mirror *in vivo* T-ALL cells (Referred to Figure 5).
(A) UMAP plots (left panel) and cell cycle (right panel) of single-cell RNA-seq of 3119 T-ALL cells harvested from PDX mouse spleen.
(B) Heatmap showing the differentially expressed genes among the four different clusters from the 3119 single-cell RNA-seq analysis. The top 40 up- and down-regulated genes are depicted for each cluster.
(C) Violin plots depicting the GSEA on the 3119 single-cell RNA-seq analysis showing the enrichment of the mitotic spindle hallmarks, Myc targets, and PI3K-AKT-mTOR pathway in the cluster #2, and the enrichment of the epithelial mesenchymal transition hallmarks in the cluster #3.
(D) Single-cell RNA-seq analysis of 3119 T-ALL cells from *in-vitro* experiment (cultured with or without ECs) and *ex-vivo* from the spleen of a 3119 PDX mouse. UMAP plots of single-cell RNA-seq of T-ALL cells color coded by cell cycle (G1, S and G2M phase) (upper panel). Barplots showing the different proportions of cells in G1/S/G2M phase based on cluster identity for both RO2 and 3119 T-ALL PDX models (bottom panel).
(E) Heatmap of the genes from 3119 "education signature" (Figure 3D) applied to cluster 4 (from Figure 5B) containing enough cells of all three compartments (in vitro T-ALL cultured alone vs with ECs and ex-vivo splenic T-ALL). Cell proportions in cluster 4 are found in Figure 5D. T-ALL cells from the spleen are clustered together with EC-co-cultured T-ALL cells based on the expression of the education signature.

Figure S6 Efficacy of positive hits from stepwise drug discovery approach in-vivo (Referred to Figure 6).
(A) Treatment scheme for RO2 and RO6 T-ALL PDX models with ruxolitinib (R), bortezomib (B), tofacitinib (T), or combinations (R+T; R+B). After engraftment (circulating hCD45+ cells>5% in

peripheral blood), mice are randomized in the treatment arms vs vehicle. Mice were treated for 2 weeks and then sacrificed to assess tumor burden and disease dissemination.
(B) Photographs of spleens from RO2 T-ALL PDX models treated with ruxolitinib (ruxo) (clow ab libido), bortezomib (bort) (0.5 mg/kg/day), and combinations (ruxo + bort tofa). The tumor passage was T10.
(C) Photographs of spleens from RO6 T-ALL PDX models treated with ruxolitinib (ruxo) (clow ab libido), tofacitinib (tofa) (80 mg/kg/day) and combinations (ruxo + tofa). The tumor passage was T8.
(D) Treatment scheme for RO6 T-ALL PDX models with ruxolitinib (R), tofacitinib (T), or combination (R+T). After engraftment (circulating hCD45+ cells>5% in peripheral blood), mice are randomized in the treatment arms vs vehicle. Mice were treated for 4 weeks (tofacitinib) or 12 weeks (ruxolitinib) and then followed-up to assess survival and tumor burden. Mice were sacrificed when circulating hCD45+ cells in peripheral blood reached $\geq$50%.
(E) Representative light microscopy of tissue distribution of the neoplastic cells in the spleen treated with the indicated compounds (RO6 PDX model, 20X magnification) as described in (B).
(F) Treatment scheme for 3119 and 3053 T-ALL PDX models with irinotecan (irino) or vehicle (veh). After engraftment (circulating hCD45+ cells>5% in peripheral blood), mice are randomized in the treatment arms vs vehicle. Mice were treated for 2 weeks and then followed-up to assess survival and tumor burden. Mice were sacrificed when circulating hCD45+ cells in peripheral blood reached $\geq$50%.
(G) Mice weight in grams for NSG mice treated with irinotecan or vehicle (3053 T-ALL PDX model).
(H) Treatment scheme for 8 different T-ALL PDX models (6467, 14741, 7072, 7155, 13002, 13356, 10512, 5384) with panobinostat (pano) or vehicle (veh). After engraftment (circulating hCD45+ cells>5% in peripheral blood), mice are randomized in the treatment arms vs vehicle. Mice were treated for 4 weeks and then followed-up to assess survival and tumor burden. Mice were sacrificed when circulating hCD45+ cells in peripheral blood reached $\geq$50%.
(I) Treatment scheme for 4 different T-ALL PDX models (10512, 6467, 13002, 13356) with daunorubicin (D), linsitinib (L), or combination (D+L). After engraftment (circulating hCD45+ cells>5% in peripheral blood), mice are randomized in the treatment arms vs vehicle. Mice were treated for 3 weeks (D) or 4 weeks (L) and then followed-up to assess survival and tumor burden. Mice were sacrificed when circulating hCD45+ cells in peripheral blood reached $\geq$50%.

References

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Tables

Table S1. Patient characteristics.

Patient ID	*Sample type*	*Sex*	*Age*	*Immunophenotype*	*IF*	*Genetic alteration*	*Stratification*	*Therapy*	*Response*	*Survival status*
2958	Diagnosis	M	1	CD1a+/- CD2+ CD4- CD5+ CD7+ CD8+ CD10- CD13+ CD33- CD34+/- CD44- CD45RA- CD99+/- CD117+/- CD123- sCD3- sTCRa/b+/- cCD3+ cTCRa/b+ HLA-Dr- cTDT+	Cortical-T	Karyotype: del(6q) and an add(10q	Canonical	Methotrexate, Vincristine, Daunorubicin, Mercaptopurine, Decadron, Cytoxan, Cytarabine, L-Asparaginase, IT-MTX.	CR	Alive up to 18 years, clinical remmissiom 16 yrs
3053	Diagnosis	M	3	CD1a+/- CD2+ CD4- CD5+ CD7+/-CD8- CD10- CD13+/- CD33- CD34+/- CD44- CD45RA- CD99+ CD117- CD123 -sCD3+/- sTCRa/b+/- cCD3+ cTCRa/b+	Cortical-T	-	Near ETP	no data available	CR	Alive up to 9 years
3119	Diagnosis	F	39	CD1a- CD2+ CD4+ CD5+ CD7+ CD8+ CD10- CD13- CD33- CD44- CD45RA- CD99+ CD117- CD123- cCD3+ cTCRa/b+ HLA-DR- TDT+	Cortical-T	*NUP214/ABL*	Canonical	hyper-CVAD and auto-PBSCT	NA	Deceased
3120*										
3139*	Relapse	F	40	CD2+ CD4+ CD5+ CD7+/- CD8+ CD10- CD13+/- CD34- sCD3- sTCRa/b+/- HLA-DR TDT+	Cortical-T	*NUP214/ABL*	Canonical		NA	Deceased
5882	Diagnosis	F	31	CD1a+ CD2- CD4+/- CD5+ CD7+ CD8- CD10+ CD13+/- CD33- CD34- CD45+ CD117- sCD3+/- cCD3+ HLA-DR- TDT+	Cortical-T	JAK1 L783F**	ETP	hyperCVAD	NA	Lost follow up after 21 months
6032	Diagnosis	F	54	CD2-CD4+/- CD5- CD7+ CD8- CD10- CD11b+ CD13+ CD15+ CD33+ CD34+ CD45- CD56+ CD99+/- CD117- cCD3+ cTDT+	ETP	-	ETP	hyperCVAD with augmented PEG Aspariginase	NA	Deceased 1yr
6467	Diagnosis	M	36	CD2- cCD3+ sCD3+/- CD4- CD5+ CD7+ CD8- CD13- CD33- CD34+/- CD56+/- TdT+/-	Cortical-T	Hyperdiploid karyotype MLL+	Near ETP	CALGB 10403	Relapsed	Deceased 6m
7072	Relapse	M	37	CD2- cCD3+ CD4- CD5+ CD7+ CD8- CD33- CD34- CD38+	Cortical-T	Hyperdiploid karyotype MLL+	Near ETP	HyperCVAD 1B refractory CALGB 10403 BM translant haplocord SCT ⇒neralabine, etoposide, cyclophosphamide	Relapsed	Deceased 1yr
6609	Diagnosis	M	30	CD2+ cCD3+ CD5+ CD4+/- CD7+ CD8 +/- CD13+/- CD33- CD34+ CD38+ CD117- TdT+	Cortical-T	interstitial deletion of 6q (MYB WT)	Canonical	Hyper-CVAD , allogeneic SCT	Refractory	Deceased 1yr
7889	Diagnosis	M	31	CD2+ CD3+ CD4+/- CD8+/- CD5+ CD7+ CD38+ CD34+ CD52+ CD117- CD13+/- CD33- TdT+	Cortical-T	interstitial deletion of 6q (MYB WT)	Canonical	HyperCVAD MTX/Cytarabine, Allogenic SCT ⇒ Cyclophosphamide/Etoposide/nelarabine and Pegasparaginas	Relapsed	Deceased 1yr
7155	Diagnosis	M	14	CD1a- CD2+/- cCD3+/- CD5+/- CD7++ CD4+ CD8- CD34+ CD33- CD13+/- CD38+/- TdT+	ETP	EGR1 (5q31); + D5S23/D5S721 (5p15.2); del 7p13; +8	ETP	COG AALL0434	CR	Alive 8 yrs Clinical remission
7653	Diagnosis	M	5	cCD3+, CD7+, CD2+, CD5+, CD4+ CD8- CD10+/- CD13- CD33- CD117+/- TdT+	Cortical-T	N/A	Canonical	AALL0434 Arm C (HD methotrexate, no nelarabine arm)	CR	Alive 7 yrs remission; 4 yrs off therapy
10512	Diagnosis	M	17	CD1a+/- CD2+ CD5+/- CD7++, CD4+ and CD8+ CD10+ CD38+ CD99+ TdT+	Cortical-T	N/A	Canonical	COG AALL1231 (Arm B)	CR	Alive 5 yrs, 2 yrs off therapy
13002	Diagnosis	M	12	CD45+/- cCD3+ sCD3 +/- CD7+ CD5+ CD34 +/- CD2+ CD4 +/- CD8 +/- CD99+ CD10+/- CD1a +/- CD13+, CD57 +/- TdT+	Cortical-T	N/A	Canonical	AALL0434	CR	Alive 4 yrs
13356	Diagnosis	M	12	cCD3+ sCD3- CD2 +/- CD5+/- CD7++ CD4- CD8+/- CD99+ CD10 +/- CD34+ CD13- CD117- HLA-DR- CD33++ CD11b+/- TdT+	ETP	NOTCH,PHF6 JAK3, SET-NUP214	ETP	AALL0434	CR	Alive 4yrs
14741	Diagnosis	M	9	cCD3+ sCD3 +/- CD7++ CD2+/- CD5+ CD8+ CD4+/- CD10+/- CD99+ CD34+/- CD117+/- TdT+	Cortical-T	Trisomy 8	Canonical	AALL0434	CR	Alive 3 yr
13840	Diagnosis	F	22	CD1a cCD3+ sCD3 +/- CD2+ CD5+ CD4+ CD8+ CD7+ CD10+ CD34- CD56+/- CD117- TdT+	Cortical-T	NA	Canonical	AALL0434	CR	Alive up to 4yrs. 5 months off therapy
R02* **	Diagnosis	F	37	N/A	Cortical-T	JAK1 E897K JAK3 A572V STAT5B S434L NOTCH1 L1585PSTAT5B S434L NOTCH1 +PICALM/ MLLT10	Canonical	GIMEMA LAL2000	Relapse after CR	Lost follow up
R05* **	Diagnosis	M	35	N/A	Cortical-T	IL7R V1381 IL7R V1381	Canonical	GIMEMA LAL2000	NA	Deceased
R06* **	Diagnosis	F	23	CD2+/- CD5+ CD7+CD4+ CD8+/- CD57	Pre-T	STAT5B Y665F STAT5B N642H	Canonical	GIMEMA LAL1308	Relapse after CR	Deceased
R07* **	Diagnosis	M	36	N/A	Cortical-T	H3F3A K28M + *PTEN/FAS* (out of frame)	ETP	NILG 10/07	Refractory	Deceased

* 3119 (peripheral blood at diagnosis), 3120 (bone marrow aspirate sample at diagnosis), and 3139 represent diagnosis and relapse samples from the same patient
** Mutation not confirmed in PDTX
*** Samples provided and previously analyzed by “Sapienza” University of Rome (Gianfelici et al., 2016)
CR = Complete Remission

Table S2. List of compounds and their respective targets used in the 433-drug screening

Index	Compounds	Targets	Description (including IC/EC-50 when available), Source: Selleck Chem
1	FG-4592	EPAS1, EPO	FG-4592 is an oral inhibitor of hypoxia inducible factor (HIF) prolyl hydroxylase currently in clinical development for the treatment of anemia. FG-4592 stabilizes the activities of HIF, a cytosolic transcription factor, leading to activation of the genes associated with erythropoiesis, including erythropoietin and enzymes involved in iron metabolism.
2	Rizatriptan Benzoate	HTR1A	Rizatriptan blocks neurogenic vasodilation via an action on 5-HT(1D) receptors located on perivascular trigeminal nerves to inhibit CGRP release in anesthetized guinea pigs. Rizatriptan evokes a transient reduction in dural blood vessel diameter, which recovered to baseline values within 10 min in anaesthetized guinea pigs. Rizatriptan significantly inhibits dural plasma protein extravasation produced by high intensity electrical stimulation of the trigeminal ganglion. Rizatriptan significantly reduces electrically stimulated dural vasodilation in anesthetised rats. Rizatriptan Benzoate significantly reduced SP mRNA levels in the midbrains of normal and model group rats, indicating that Rizatriptan Benzoate can downregulate SP gene expression in the rat midbrain. Rizatriptan Benzoate significantly reduces midbrain PENK mRNA expression, decreasing the levels of midbrain met-enkephalin and leu-enkephalin, and thereby weakening the analgesic effects of the endogenous pain modulatory system in rat model of migraine. Rizatriptan Benzoate leads to the number of Fos-like immunoreactive neurons decreased in the spinal trigeminal nucleus caudal partand raphe magnus nucleus, increased the number of Fos-like immunoreactive neurons in the periaqueductal gray and remained unchanged in the ventromedial hypothalamic nucleus and mediodorsal thalamus nucleus in conscious rats. Rizatriptan Benzoate markedly reduces the number of head-flicks in the rats. Rizatriptan Benzoate also significantly reduces the duration of grooming behavior by nearly 2-fold when compared with that without treatment.
3	Fulvestrant	ESR	Fulvestrant is an effective inhibitor of the growth of ER-positive MCF-7 (with IC50 of 0.29 nM) but with no effect on the growth of ER-negative BT-20 human breast cancer cells. Fulvestrant causes accumulation of cells in G0/G1 and also reduces the proportion of cells capable of continued DNA synthesis. Fulvestrant competitively inhibits binding of oestradiol to the estrogen receptor. Fulvestrant blocks nuclear localization of the ER through impairing receptor dimerisation, and energy-dependent nucleo-cytoplasmic shuttling. Because of the instability of fulvestrant-ER complex, the binding of Fulvestrant with ER finally results in accelerated degradation of the ER protein. Fulvestrant (10 nM) not only decreases IGF-IR mRNA levels but also decreases the half-life. Treatment with 100 μM Fulvestrant leads to a time dependent increase of TNFR1 and TRADD steady-state mRNA levels in MCF-7 cells. Fulvestrant is capable of down-regulating androgen receptor expression and diminishes androgenic responses in LNCaP human prostate cancer cells. Fulvestrant also significantly attenuates R1881-stimulated growth by 70%. Fulvestrant is able to modulate mitosis and cell death in immature cerebellar neurons via rapid activation of MAPK.
4	Tolfenamic Acid	COX-2	Tolfenamic Acid is a COX-2 inhibitor with IC50 of 0.2 μM.
5	Ramelteon	MTNR1A, MTNR1B	Ramelteon inhibits forskolin-stimulated cAMP production with IC50 of 21.2 pM in CHO cells. Ramelteon has high affinity with recombinant human MT1 and MT2 receptors with pKi of 10.05 and 9.70, respectively. Ramelteon inhibits Xenopus laevis melanophore pigment granule aggregation with pEC50 of 11.48. Ramelteon (1 nM) increases ERK1/2 phosphorylation not only in MT1/MT2 cerebellar granule cells but also in cerebellar granule cells expressing only one of the two melatonin receptors. 4P-PDOT blocks the stimulatory action of Ramelteon (1 nM) in MT1 KO cerebellar granule cells, while luzindole attenuates the action of Ramelteon (1 nM) in MT2 KO cerebellar granule cells. Ramelteon (100 μM) induces any pigment dispersion while melatonin completely disperses aggregated melanophores at 10 μM.
6	Trospium chloride	CHRM1	Trospium chloride (Sanctura) is a competitive muscarinic cholinergic receptor antagonist.
7	Granisetron HCl	HTR3A	Granisetron blocks the delayed rectifier current (IK) of feline isolated ventricular myocytes with a KD of 4.3 mM. Granisetron shows an intrinsic voltage-dependence as the block increases with depolarization. Granisetron blocks from the intracellular side at a binding site located 10% across the transmembrane electrical field. Granisetron (3 mM) prolongs the action potential duration (APD) by about 30% at 0.5 Hz in feline isolated ventricular myocytes. Granisetron but not Ondansetron, could prevent the activation of putative 5-H; autoreceptors, thus leading to a decrease in serotonin release by the enterochromaffin cells.
8	A-769662	PRKAA1	A-769662 stimulates partially purified rat liver AMPK with EC50 with 0.8 μM. A-769662 activates AMPK purified from multiple tissues and species in a dose-responsive manner with modest variations in observed EC50s. EC50s determined for A-769662 using partially purified AMPK extracts from rat heart, rat muscle, or human embryonic kidney cells (HEKs) are 2.2 mM, 1.9 mM, or 1.1 mM, respectively. A 4 hours treatment of primary rat hepatocytes with A-769662 dose-dependently increases ACC phosphorylation, which correlated inhibition of fatty acid synthesis with IC50 of 3.2 μM. A-769662 also inhibits fatty acid sythesis in mouse hepatocytes with IC50 with 3.6 μM A-769662 activates AMPK both allosterically and by inhibiting

			dephosphorylation of AMPK on Thr-172, similar to the effects of AMP. A-769662 inhibits proteasomal function by an AMPK-independent mechanism. A-769662 affects the in-vitro activity of purified 26S proteasomes but not the in-vitro activity of purified 20S proteasomes. A-769662 has toxic effects on MEF cells. A recent research shows A-769662 inhibited cell proliferation and DNA synthesis.
9	Losartan Potassium (DuP 753)	AGTR	Losartan is an angiotensin II receptor antagonist, competes with the binding of angiotensin II to AT1 receptors with IC50 of 20 nM.
10	Tolazoline HCl	ADRA1A	Tolazoline is a pulmonary vasodilator indicated used to decrease pulmonary vascular resistance (PVR) in persistent pulmonary hypertension of the newborn (PPHN). Tolazoline has moderate alpha-adrenergic blocking activity and has histamine agonist activity. Tolazoline usually reduces pulmonary arterial pressure and vascular resistance. Tolazoline is not as broadly effective as SNP against all spasmogens investigated. However, it may be effective in counteracting alpha-adrenoceptor-mediated vasospasm in human radial arteries.
11	Tenofovir Disoproxil Fumarate		Tenofovir disoproxil fumarate belongs to nucleotide analogue reverse transcriptase inhibitors (nRTIs).
12	Ataluren (PTC124)	CFTR	Ataluren (PTC124) selectively induces ribosomal read-through of premature but not normal termination codons, with EC50 of 0.1 μM in HEK293 cells, may provide treatment for genetic disorders caused by nonsense mutations (e.g. CF caused by CFTR nonsense mutation). Phase 3.
13	Candesartan	AGTR	Candesartan is an angiotensin II receptor antagonist with IC50 of 0.26 nM.
14	Belinostat (PXD101)	HDAC	Belinostat inhibits the growth of tumor cells (A2780, HCT116, HT29, WIL, CALU-3, MCF7, PC3 and HS852) with IC50 from 0.2-0.66 μM. PD101 shows low activity in A2780/cp70 and 2780AD cells, which are cisplatin and doxorubicin-resistant derivatives of A2780 cells. Belinostat could induce apoptosis through PARP cleavage and acetylation of histones H3/H4. Belinostat inhibits bladder cancer cell growth, especially in 5637 cells, which shows accumulation of G0-G1 phase, decrease in S phase and increase in G2-M phase. The growth inhibitory activity of belinostat on cell lines is not strongly influenced by the multidrug-resistant phenotype, whereas the activity of docetaxel is clearly affected. Belinostat could enhance the growth inhibitory activity of docetaxel or carboplatin in OVCAR-3 and A2780 cells. Belinostat also shows enhanced tubulin acetylation in ovarian cancer cell lines. A recent study shows that Belinostat activates protein kinase A in a TGF-β signaling-dependent mechanism and decreases survivin mRNA.
15	Semagacestat (LY450139)	APP, NOTCH	Semagacestat reduces the secretion of Aβ42, Aβ40 and Aβ38 from H4 human glioma cells stably overexpressing human wild-type APP into the culture medium, with IC50 of 10.9 nM, 12.1 nM and 12.0 nM, respectively, without affecting cell viability. Semagacestat also increases β-CTF in cell lysates with ECmax of 16.0 nM, and the increase can be unexpectedly attenuated at high concentrations. Semagacestat inhibits Notch signaling with IC50 of 14.1 nM, and shows minimal Notch-sparing selectivity with Notch IC50/Aβ42 IC50 only 1.3. Semagacestat causes a concentration-dependent decrease in Aβ40 secreted into the medium with IC50 of 111 nM from murine CTX expressing endogenous murine APP, but murine Aβ42 formation in CTX is roughly 12-fold less than Aβ40 in accordance with data for neurons from wild type mice.
16	NVP-ADW742	IGF1R	NVP-ADW742 exhibits a 6-fold greater selectivity for IGF-1R versus InsR with IC50 of 2.8 μM; minimal inhibitory activity against c-Kit, HER1, PDGFR, VEGFR2, or Bcr-Abl p210 with IC50 greater than 5 μM. NVP-ADW742 significantly inhibits the serum-stimulated cell proliferation in a variety of tumor cell lines in dose-dependent manner, with IC50 values of 0.1-0.5 μM for the multiple myeloma (MM) cell lines, and the antitumor effects on MM cells can not be overcome by the co-culture with BMSCs. NVP-ADW742 also abrogates the responsiveness of tumor cells to IL-6 in the presence of serum. In addition, NVP-ADW742 is active against MM cell lines with resistance to conventional (cytotoxic chemotherapy, dexamethasone) or investigational (thalidomide, CC-5013, TRAIL/Apo2L, PS-341) anticancer agents, as well as primary tumor cells from MM patients with multi-drug-resistant disease. NVP-ADW742 decreases the production of VEGF by tumor cells and bone marrow stromal cells, and suppresses the IGF-1-induced secretion of VEGF by various tumor types such as thyroid cancer cells or MM cells. IGF-1R inhibition by NVP-ADW742 (0.75 μM) sensitizes MM cells or prostate cancer cells to other anticancer agents such as doxorubicin, melphalan, dexamethasone, TRAIL/Apo2L, or PS-341. [1]
17	NSC 319726	TP53 (R175)	NSC319726 is a p53(R175) mutant reactivator, exhibits growth inhibition in cells expressing mutant p53, with IC50 of 8 nM for p53(R175) mutant, shows no inhibition for p53 wild-type cells, shows 10- to 100-fold selectivity over the other hotspot p53 mutants. NSC319276 induces p53(R175)-mutant-dependent apoptosis. NSC319726 treatment induces a WT-like conformational change in the p53(R175) mutant protein that restores sequence-specific p53 transcription. The activity of NSC319726 depends on the zinc ion chelating properties of the compound as well as redox changes. [1]
18	Icotinib	EGFR	Icotinib inhibits EGFR activity in a dose-dependent manner, with an IC50 value of 5 nM and complete inhibition at 62.5 nM. Icotinib selectively solely inhibits the EGFR members including the wild type and mutants with inhibition efficacies of 61-99%. Icotinib blocks EGFR-mediated intracellular tyrosine phosphorylation in human epidermoid carcinoma A431 cells in a dose-dependent manner. Meanwhile, in our proliferation assay performed on A431, BGC-823, A549, H460, HCT8, KB and Bel-7402 cell lines, we found that the relative sensitivity of cell lines to Icotinib is A431 >

			BGC-823 > A549 > H460 > KB > HCT8 and Bel-7402. Icotinib exhibits a broad spectrum of antitumor activity and it is especially effective against tumors expressing higher levels of EGFR. [1]
19	Ilomastat (GM6001, Galardin)	MMP1, MMP2, MMP3, MMP7, MMP8, MMP9, MMP12, MMP14, MMP26	Ilomastat (GM6001, Galardin) is a broad spectrum matrix metalloprotease (MMP) inhibitor for MMP-1, MMP-2, MMP-3, MMP-7, MMP-8, MMP-9, MMP-12, MMP-14, and MMP-26 with Ki of 0.4 nM, 0.5 nM, 27 nM, 3.7 nM, 0.1 nM, 0.2 nM, 3.6 nM, 13.4 nM, 0.36 nM, respectively.
20	Rivaroxaban	F10	Rivaroxaban is an oral, direct inhibitor of Factor Xa (FXa), being developed for the prevention and treatment of arterial and venous thrombosis with a Ki of 0.4 nM. Rivaroxaban also inhibits prothrombinase activity with IC50 of 2.1 nM. Rivaroxaban also shows a similar affinity to purified human and rabbit FXa (IC50 0.7 nM and 0.8 nM, respectively), but a lesser potency against purified rat FXa (IC50 3.4 nM). Endogenous human and rabbit FXa in plasma is inhibited to a similar extent by Rivaroxaban (IC50 21 nM and 21 nM, respectively), while 14-fold higher concentrations are required in rat plasma (IC50 290 nM). Rivaroxaban exhibits high permeability and polarized transport across Caco-2 cells as a substrate of the P-gp, but exhibits no inhibitory effect on P-gp-mediated drug transport up to concentrations of 100 μM in-vitro.
21	STF-118804	NAMPT	STF-118804 reduces the viability of B-ALL cell lines containing MLL chromosomal translations, with IC50 values in the low nanomolar range. In addition, leukemic samples from five pediatric ALL patients are also sensitive to STF-118804 in the low nanomolar range. STF-118804 induces leukemia MV411 cell apoptosis without antecedent cell cycle arrest.
22	Rimonabant	CNR1	Rimonabant dose-dependently reduces ACAT activity in Raw264.7macrophages with IC50 of 2.9 μM and isolated peritoneal macrophages. Rimonabant inhibits ACATactivity in intact CHO-ACAT1 and CHO-ACAT2 cells and in cell-free assays with approximately equal efficiency with IC50 of 1.5 μM and 2.2 μM for CHO-ACAT1 and CHO-ACAT2, respectively. Consistent with ACAT inhibition, Rimonabant treatment blocks ACAT dependent processes in macrophages, oxysterol-induced apoptosis and acetylated-LDL induced foam cell formation. Rimonabant antagonizes the inhibitory effects of cannabinoid receptor agonists on both mouse vas deferens contractions and adenylyl cyclase activity in rat brain membranes in a concentration-dependent manner. Rimonabant significantly reduces cell growth and induces cell death of human colorectal cancer cells (DLD-1, CaCo-2 and SW620). Rimonabant is able to alter cell cycle distribution in all the cell lines tested. Particularly, Rimonabant produces a G2/M cell cycle arrest in DLD-1 cells without inducing apoptosis or necrosis.
23	FLI-06		FLI-06 is a novel inhibitor of Notch signaling with EC50 of 2.3 μM.
24	Sitaxentan sodium	EDNRA	Sitaxentan sodium is a selective endothelin A receptor (ETA) antagonist with IC50 and Ki of 1.4 nM and 0.43 nM, respectively, exhibits 7000-fold selectivity over ETB. Phase 3.
25	ABT-263 (Navitoclax)	BCL2, BCL2L1, BCL2L2	ABT-263 is structurally related to ABT-737; it is a disruptor of Bcl-2/Bcl-xL interactions with pro-apoptotic proteins. Overexpression of the prosurvival Bcl-2 family members is commonly associated with tumor maintenance, progression, and chemoresistance. ABT-263 displays the protection afforded by overexpression of Bcl-2 or Bcl-xL with EC50 values of 60 nM and 20 nM, respectively. A wide range of cellular activity is observed with ABT-263 having a 50% growth inhibition (EC50) of 110 nM against the most sensitive line (H146), whereas its activity in the least sensitive line (H82) results in an EC50 at 22 μM. All four cell lines with EC50 values of <400 nM (H146, H889, H1963, and H1417) are also highly sensitive to ABT-737, and the two most resistant lines (H1048 and H82) are similarly resistant to ABT-263.
26	Brinzolamide	CA2	Brinzolamide is a potent carbonic anhydrase II inhibitor with IC50 of 3.19 nM.
27	Nilotinib (AMN-107)	ABL1	Nilotinib inhibits proliferation, migration, and actin filament formation, as well as the expression of α-SMA and collagen in activated HSCs. Nilotinib induces apoptosis of HSCs, which is correlated with reduced bcl-2 expression, increases p53 expression, cleavage of PARP, as well as increases expression of PPARγ and TRAIL-R. Nilotinib also induces cell cycle arrest, accompanied by increased expression of p27 and downregulation of cyclin D1. Interestingly, Nilotinib not only inhibits activation of PDGFR, but also TGFRII through Src. Nilotinib significantly inhibits PDGF and TGFβ-simulated phosphorylation of ERK and Akt. Furthermore, PDGF- and TGFβ-activated phosphorylated form(s) of Abl in human HSCs are inhibited by Nilotinib. Nilotinib inhibits most imatinib-resistant Bcr-Abl mutations, except for T315I. Nilotinib inhibits PDGF-DD-mediated ERK1/2 activation, basal and PDGF-DD-mediated activation of PDGFRβ and Akt, and schwannoma proliferation. Nilotinib is more potent than imatinib, exerting its maximal inhibitory effect at concentrations lower than steady-state trough plasma levels. Nilotinib also significantly reduces the expression levels of the genes for TGF-β1 and platelet-derived growth factor (PDGF). Nilotinib treatment also significantly inhibits the PDGF-induced proliferation of lung fibroblasts. Nilotinib inhibits the proliferation of Ba/F3 cells expressing p210- and p190-Bcr-Abl, or K562 and Ku-812F cells with IC50 values ≤12 nM.
28	Tranylcypromine (2-PCPA) HCl	MAO, CYP2A6	R-(+)-Tranylcypromine, (±)-Tranylcypromine, and S-(−)-Tranylcypromine competitively inhibits CYP2A6-mediated metabolism of nicotine with apparent Ki values of 0.05 μM, 0.08 μM, and 2.0 μM, respectively, in human liver microsomes. Tranylcypromine (500 μg/mL) severely inhibits bradykinin-stimulated arachidonic acid

			release in calf aortic endothelial cells. Tranylcypromine inhibits CYP2A6 and CYP2E1 activity with IC50 of 0.42 μM and 3 μM, respectively, in human liver microsomes. Tranylcypromine induces type II and cyclopropylbenzene type I difference spectrum in human liver microsomes.
29	Tandutinib (MLN518)	FLT3, PDGFR KIT	Tandutinib has little activity against EGFR, FGFR, KDR, InsR, Src, Abl, PKC, PKA and MAPKs. Tandutinib inhibits IL-3-independent cell growth and FLT3-ITD autophosphorylation with an IC50 of 10-100 nM. Tandutinib also inhibits the proliferation of human leukemia Ba/F3 cells containing FLT3-ITD mutations with IC50 values of 10-30 nM, and the FLT3-ITD-positive Molm-13 and Molm-14 cells with an IC50 of 10 nM. In FLT3-ITD-positive Molm-14 cells but not the FLT3-ITD-negative THP-1 cells, Tandutinib treatment leads to significant apoptosis by 51% and 78% at 24 and 96 hours, respectively, due to specific FLT3 inhibition. Tandutinib preferentially inhibits the growth of blast colonies from FLT3 ITD-positive compared with ITD-negative patients with AML, without affecting colony formation by normal human progenitor cells.
30	Zebularine	DNMT1, DNMT3A, DNMT3B	Zebularine is a cytidine analogue containing a 2-(1H)-pyrimidinone ring, originally synthesized as a cytidine deaminase inhibitor. Zebularine is shown to form a tight, covalent complex with bacterial methyltransferases. In N. crassa, zebularine inhibits DNA methylation and reactivates a gene previously silenced by methylation. Zebularine is a global inhibitor of DNA methylation, similar to 5-Aza-CR, rather than a selective inhibitor. Zebularine induces the myogenic phenotype in 10T1/2 cells, which is a phenomenon unique to DNA methylation inhibitors. Zebularine reactivates a silenced p16 gene and demethylates its promoter region in T24 bladder carcinoma cells. Zebularine is only slightly cytotoxic to T24 cells. Zebularine is preferentially incorporated into DNA and exhibits greater cell growth inhibition and gene expression in cancer cell lines compared to normal fibroblasts. In addition, zebularine preferentially depletes DNA methyltransferase 1 (DNMT1) and induces expression of cancer-related antigen genes in cancer cells relative to normal fibroblasts.
31	MLN8054	AURKA	MLN8054 is an ATP-competitive, reversible inhibitor of recombinant Aurora A kinase with an IC50 of 4 nM, which shows >40-fold more selective inhibitory activity for Aurora A compared with Aurora B. In-vitro, MLN8054 exhibits the activity of growth inhibition across various cell lines from diverse tissue origins with IC50 values ranging from 0.11 μM to 1.43 μM. In addition, MLN8054 selectively inhibits Aurora A over Aurora B in cultured cells, and inhibits cell proliferation by promoting G2/M accumulation and spindle defects in multiple cultured human tumor cells lines. A recent study shows that MLN8054 sensitizes androgen-resistant prostate cancer to radiation by inhibiting Aurora A kinase, which is associated with sustained DNA double-strand breaks.
32	PR-619	ATXN7L3, BAP1, OTUB1, OTUD1, OTUD6A, OTUDB7A, UBB, UCHL3, USP1, USP2, USP4, USP5, USP7, USP8, USP14, USP15, USP17, USP26, USP30, USP36, YOD1	PR-619 is a cell-permeable pyridinamine class broad-spectrum DUB inhibitor whose known targets include ATXN3, BAP1, JOSD2, OTUD5, UCH-L1, UCH-L3, UCH-L5/UCH37, USP1, 2, 4, 5, 7, 8, 9X, 10, 14, 15, 16, 19, 20, 22, 24, 28, 47, 48, VCIP135, YOD1, as well as deISGylase PLpro, deNEDDylase DEN1, and deSUMOlyase SENP6. PR-619 are shown to increase overall protein polyubiquitination in HEK293T cells in a dose- and time-dependent manner (20 to 150 μM, 0.5 to 20 h). PR619 treatment results in upregulation of both K 48 - and K63-linked polyUb chains. PR-619 induces HCT116 cell death with EC50 values of 6.3 μM.[1]
33	Roxatidine Acetate HCl	HRH2	Roxatidine Acetate HCl is a specific and competitive histamin H2-receptor antagonist, with IC50 of 3.2 μM, inhibits gastric acid secretion and ulcer formation.
34	GSK1904529A	IGF1R, INSR	GSK1904529A is a reversible, ATP-competitive inhibitor and has enzyme-inhibitor binding values against IGF-1R and IR with Ki of 1.6 nM and 1.3 nM, respectively. GSK1904529A potently inhibits the ligand-induced phosphorylation of IGF-1R and IR at concentrations above 0.01 μM, followed by blocking downstream signaling (AKT, IRS-1, and ERK). GSK1904529A potently inhibits NIH-3T3/LISN, TC-71, SK-N-MC, SK-ES RD-ES cells with IC50 of 60 nM, 35 nM, 43 nM, 61 nM and 62 nM, respectively. GSK1904529A also inhibits other multiple myeloma and Ewing's sarcoma cell lines including NCI-H929, MOLP-8, LP-1 and KMS-12-BM etc. GSK1904529A induces cell cycle arrest at the G1 phase in cell lines COLO 205, MCF-7, and NCI-H929, which are sensitive to GK1904529A.
35	Atorvastatin Calcium	HMGCR	Atorvastatin inhibits pre-proET-1 mRNA expression in a concentration- and time-dependent fashion (60-70% maximum inhibition) and reduces immunoreactive ET-1 levels (25-50%), this inhibitory effect is maintained in the presence of oxidized LDL (1-50 mg/mL). Atorvastatin significantly reduces angiotensin II-induced and epidermal growth factor-induced ROS production in VSMCs. Atorvastatin downregulates mRNA expression of the NAD(P)H oxidase subunit nox1 in VSMCs, whereas p22phox mRNA expression is not significantly altered. Atorvastatin inhibits membrane translocation of rac1 GTPase, which is required for the activation of NAD(P)H oxidase. Atorvastatin (0.1 μM) significantly diminishes NF-κB activation induced by Ang II and TNF-α in mononuclear cells and VSMC. Atorvastatin (1 μM) diminishes MCP-1 expression induced by Ang II, TNF-α and is reversed by Mevalonate only in

			Ang II-stimulated cells. Atorvastatin (1 μM) diminishes IP-10 expression induced by Ang II and by TNF-α in VSMC, and this reduction is partially reversed by Mevalonate. Atorvastatin and Gemfibrozil metabolites, but not the parent drugs, are potent antioxidants against lipoprotein oxidation.
36	SNS-032 (BMS-387032)	CDK2	SNS-032 has low sensitivity to CDK1 and CDK4 with IC50 of 480 nM and 925 nM, respectively. SNS-032 effectively kills chronic lymphocytic leukemia cells in-vitro regardless of prognostic indicators and treatment history. Compared with flavopiridol and roscovitine, SNS-032 is more potent, both in inhibition of RNA synthesis and at induction of apoptosis. SNS-032 activity is readily reversible; removal of SNS-032 reactivates RNA polymerase II, which led to resynthesis of Mcl-1 and cell survival. SNS-032 inhibits three dimensional capillary network formations of endothelial cells. SNS-032 completely prevents U87MG cell–mediated capillary formation of HUVECs. In addition, SNS-032 significantly prevents the production of VEGF in both cell lines, SNS-032 prevents in-vitro angiogenesis, and this action is attributable to blocking of VEGF. Preclinical studies have shown that SNS-032 induces cell cycle arrest and apoptosis across multiple cell lines. SNS-032 blocks the cell cycle via inhibition of CDKs 2 and 7, and transcription via inhibition of CDKs 7 and 9. SNS-032 activity is unaffected by human serum. SNS-032 induces a dose-dependent increase in annexin V staining and caspase-3 activation. At the molecular level, SNS-032 induces a marked dephosphorylation of serine 2 and 5 of RNA polymerase (RNA Pol) II and inhibits the expression of CDK2 and CDK9 and dephosphorylated CDK7.
37	Naltrexone HCl	OPRK1, OPRM1, OPRD1	Naltrexone (0.32 mg/kg) reduces ethanol-reinforced responding at the concentration that maintained the most responding (1% or 2%) in rhesus monkeys. Naltrexone (0.1 mg/kg) reduces ethanol-reinforced responding, both at a low ethanol concentration (0.25%) that produced little ethanol intake (g/kg), and at a higher concentration (4%) with an appreciable intake. Naltrexone (1-3 mg/kg) potently and dose-dependently inhibits reinstatement of ethanol-seeking produced by non-contingent deliveries of the liquid dipper filled with 8% ethanol. Naltrexone elicits optimal enhancement of morphine's antinociceptive potency in mice when co-administered (i.p.) at about 100 ng/kg together with morphine (3 mg/kg). Naltrexone (10 ng/kg i.p.) augments the antinociception produced by an acute submaximal dose of intrathecal (5 mg) or systemic (7.5 mg/kg i.p.) morphine in the tail-flick test in rats. Naltrexone combined with Morphine inhibits the decline in morphine antinociception and prevented the loss of morphine potency in rats. Naltrexone significantly suppresses ethanol self-administration and prevents ethanol-induced increases in dialysate dopamine levels. Naltrexone completely prevents the reduction in anogenital distance in prenatally stressed (PS) males and restores the growth rate of both sexes. Naltrexone also decreases the anxiety of PS rats in the plus-maze, increases the opioid component of exploration to control levels, but increases anxiety in control males.
38	Ganetespib (STA-9090)	HSP90	The 50% inhibitory concentrations (IC50) for Ganetespib against malignant mast cell lines are 10-50 times lower than that for 17-AAG, indicating that triazolone class of HSP90 inhibitors likely exhibits greater potency than geldanamycin based inhibitors. Ganetespib inhibits MG63 cell lines with IC50 of 43 nM. Ganetespib binds to the ATP-binding domain at the N-terminus of Hsp90 and serves as a potent Hsp90 inhibitor by causing degradation of multiple oncogenic Hsp90 client proteins including HER2/neu, mutated EGFR, Akt, c-Kit, IGF-1R, PDGFRα, Jak1, Jak2, STAT3, STAT5, HIF-1α, CDC2 and c-Met as well as Wilms' tumor 1. Ganetespib, at low nanomolar concentrations, potently arrests cell proliferation and induces apoptosis in a wide variety of human cancer cell lines, including many receptor tyrosine kinase inhibitor- and tanespimycin-resistant cell lines. Ganetespib exhibits potent cytotoxicity in a range of solid and hematologic tumor cell lines, including those that express mutated kinases that confer resistance to small-molecule tyrosine kinase inhibitors. Ganetespib treatment rapidly caused the degradation of known Hsp90 client proteins, exhibits superior potency to the ansamycin inhibitor 17-AAG, and shows sustained activity even with short exposure times. In anohter study, Ganetespib induces apoptosis of malignant canine mast cell lines. Ganetespib is active at significantly lower concentrations for C2 and BR canine malignant mast cells with IC50 of 19 and 4 nM, respectively, while 17-AAG inhibits C2 and BR canine malignant mast cells with IC50 of 958 and 44 nM, respectively. Both the expression of WT and mutant Kit are downregulated by 100 nM Ganetespib after 24 hours in all lines treated including C2 and BMCMCs cells. However, no effects on PI3K or HSP90 expression are observed following treatment with Ganetespib.
39	CGS 21680 HCl	ADORA2A	CGS 21680 HCl is an adenosine A2 receptor agonist with IC50 of 22 nM, exhibits 140-fold over A1 receptor. In an isolated perfused working rat heart model, CGS 21680C effectively increases coronary flow with an ED25 value of 1.8 nM. CGS 21680 binds adenosine A2 receptor with high affinity (Kd = 15.5 nM) and limited capacity (apparent Bmax = 375 fmol/mg of protein) to a single dass of recognition sites. In hippocampal slices, CGS 21680 apis weak agonist on pre- and postsynaptic measures of electrophysiologicaJ activity (putative Al receptor mediated events) and is ineffective at stimulating the formation of cAMP (a putative A2 mediated response). In striatal slices, CGS 21680 potently stimulates the formation of cAMP with an EC50 of 110 nM but is ineffective at inhibiting electrically stimulated dopamine release. CGS 21680A is the hydrochloride salt, while CGS 21680C is the sodium salt of CGS 21680.
40	Vemurafenib (PLX4032, RG7204)	BRAF (V600E)	PLX4032 inhibits B-RAFV600E, C-RAF, as well as wildtype B-RAF, with IC50 of 31 nM, 48 nM and 100 nM, respectively. PLX4032 also inhibits several non-RAF kinases, including ACK1, KHS1, and SRMS, with IC50 of 18 nM to 51 nM. In melanoma cell

			lines, the inhibitory effect by PLX4032 depends on B-RAF mutational status, because PLX4032 potently inhibits those harboring B-RAF V600 mutants, including V600E, V600D, V600K, and V600R, but not wildtype or other mutants. The IC50 values of PLX4032 on these cells, including MALME-3M, Colo829, Colo38, A375, SK-MEL28, and A2058, ranges from 20 nM to 1 μM. In these cells, PLX4032 (0.1 μM to 30 μM) also inhibits the phosphorylation of both MEK1/2 and ERK1/2. PLX4032 is highly effective in the treatment of melanoma, for its ability of inhibiting B-RAFV600E. However, PLX4032 displays limited effect in colon cancer patients that also carrying B-RAFV600E oncoprotein. The reason for this is that, in colon cancer cells, B-RAFV600E inhibition by PLX4032 results in a rapid feedback EGFR activation, which compensates for the PLX4032-inhibited cell proliferation.
41	Pancuronium dibromide		Pancuronium results in open channel block of embryonic-type nicotinic acetylcholine receptor channels after coapplication of blocker and acetylcholine, characterized by decrease of the time constant of current decay. Pancuronium also results in competitive block of embryonic-type nicotinic acetylcholine receptor channels. Pancuronium increases heart rate, vecuronium and rocuronium produces positive inotropic effects, and vecuronium shortens refractoriness in isolated rat atria. Pancuronium (0.5 mM) induces a complete fade of the tetanic contraction while leaving the twitch unaffected in the extensor digitorum longus muscle of the rat. Pancuronium decreases the amplitude and increases the tetanic rundown of trains of endplate potentials (e.p.ps) evoked in the frequency of 50 Hz in the extensor digitorum longus muscle of the rat.
42	Loratadine	HRH1	Loratadine is identified as a selective inhibitor of B(0)AT2 with an IC50 of 4 μM while being less active or inactive against several other members of the SLC6 family. Loratadine concentration-dependently inhibits the release of histamine and LTC4 when preincubating before Der p 1 antigen or anti-Fc epsilon RI challenge in human Fc epsilon RI+ cells. Loratadine (0.1 mM) also inhibits (10-40%) histamine, LTC4, and PGD2 release from purified HLMC (16-68%) activated by anti-Fc epsilon RI. Loratadine causes concentration-dependent inhibition (10-40%) of histamine, tryptase, LTC4, and PGD2 release from purified HSMC (24-72%) immunologically challenged with anti-Fc epsilon RI. Loratadine inhibits significantly IL-6 and IL-8 secretion induced by histamine with a more powerful efficiency of the active metabolite in human umbilical vein endothelial cells (HUVEC). Loratadine blocks hKv1.5 channels in a concentration-, voltage-, time- and use-dependent manner but only at concentrations much higher than therapeutic plasma levels in man in Ltk- cells transfected with the gene encoding hKv1.5 channels. Loratadine inhibits rhinovirus-induced ICAM-1 upregulation in both primary bronchial or transformed (A549) respiratory epithelial cells. Loratadine also inhibits ICAM-1 mRNA induction caused by rhinovirus infection in a dose-dependent manner, and they completely inhibits rhinovirus-induced ICAM-1 promoter activation.
43	PNU-120596		PNU-120596 increases agonist (Ach)-evoked calcium flux mediated by an engineered variant of the human α7 nAChR. PNU-120596 increases agonists (choline and ACh)-evoked currents mediated by wild-type receptors and also demonstrates a pronounced prolongation of the evoked response in the continued presence of agonist in Xenopus oocytes. PNU-120596 increases the channel mean open time ofα7 nAChRs but has no effect on ion selectivity and relatively little, if any, effect on unitary conductance. When applied to acute hippocampal slices, PNU-120596 increases the frequency of ACh-evoked GABAergic postsynaptic currents measured in pyramidal neurons; this effect is suppressed by TTX, suggesting that PNU-120596 modulates the function of α7 nAChRs located on the somatodendritic membrane of hippocampal interneurons. Besides the positive modulation to α7 nAChR, PNU-120596 induces a profound retardation of the kinetics of desensitization, raising the potential of Ca2+-induced toxicity through excessive stimulation of α7 nAChR. PNU-120596 causes changes in cysteine accessibility at the inner beta sheet, transition zone and agonist binding site while binding to α7 nAChR. Binding sites for PNU-120596 are not in the agonist-binding sites and PNU-120596 enhances agonist-evoked gating of nicotinic receptors by eliciting conformational effects that are similar but nonidentical to the gating conformations promoted by Ach.
44	Ruxolitinib (INCB018424)	JAK1, JAK2	INCB018424 potently and selectively inhibits JAK2V617F-mediated signaling and proliferation in Ba/F3 cells and HEL cells. INCB018424 markedly increases apoptosis in a dose dependent manner in Ba/F3 cells. INCB018424 (64 nM) results in a doubling of cells with depolarized mitochondria in Ba/F3 cells. INCB018424 inhibits proliferating of erythroid progenitors from normal donors and polycythemia vera patients with IC50 of 407 nM and 223 nM, respectively. INCB018424 demonstrates remarkable potency against erythroid colony formation with IC50 of 67nM.
45	GW3965 HCl	NR1H3, NR1H2	GW3965 recruits the steroid receptor coactivator 1 to human LXRα with EC50 of 125 nM in a cell-free ligand-sensing assay. GW3965 shows a potent antagonistic activity against hLXRα and hLXRβ in cell-based assays with EC50 of 190 nM and 30 nM, respectively. Besides, GW3965 also sows excellent selectivity over other nuclear receptors. In human islets, GW3965 (1 μM) reduces expression of selected pro-inflammatory cytokines including IL-8, monocyte chemotactic protein-1 and tissue factor.
46	AZD6482	PIK3CB	AZD6482 also inhibits PI3Kα, γ, and δ, with IC50 of 80 nM to 1.09 μM, which are significantly lower than its (+)-enantiomer (S-form). AZD6482 is an antiplatelet agent; it blocks platelet activation adhesion/aggregation and promotes platelet disaggregation in assay of washed platelet aggregation (WPA), with an IC50 value of

			6 nM. Furthermore, by targeting PI3Kβ, AZD6482 specifically inhibits thrombosis without interfering with normal haemostasis. Therefore, AZD6482 is used as an anti-thrombotic drug for the prophylaxis of thrombotic disorders.
47	SB705498	TRPV1	SB705498 (0.3 nM-1 μM) potently inhibits capsaicin-induced activation of human TRPV1 expressed in 1321N1 cells or HEK293 cells with apparent pKi of 7.5 or 7.6, respectively. Coapplication of 100 nM SB705498 rapidly, completely and reversibly inhibits hTRPV1 expressed in HEK293 cells. SB705498 has no significant effect on endogenous [Ca2+] responses in HEK293 cells produced by muscarinic acetylcholine receptor activation with carbachol or store-operated channel-mediated Ca2+ entry after depletion of intracellular stores with the Ca2+ pump inhibitor thapsigargin. SB705498 (10 pM-1 μM) also has no significant antagonist effect versus the close TRPV1 receptor paralog TRPV4 transiently expressed in HEK293 cells and activated using the synthetic ligand 4α-phorbol-12,13-didecanoate (10 μM). SB705498 reveals good antagonist potency against both the rat and guinea pig TRPV1. SB705498 antagonizes rat and guinea pig TRPV1 with pKi of 7.5 and 7.3, respectively. Coapplication of 100 nM to 10 μM SB705498 to the steady state of a maintained capsaicin response leads to rapid and complete inhibition of hTRPV1 at -70 mV. SB705498 inhibits capsaicin-mediated activation of hTRPV1 with IC50 of 3 nM and 17 nM at positive and negative holding potentials (-70 mV and + 70 mV), respectively. Coapplication of 1 μM SB705498 to the plateau period of the response produces complete and reversible inhibition of the TRPV1-mediated conductance. SB705498 shows approximately equal activity versus multiple and diverse chemical and physical modes of TRPV1 receptor activation. SB705498 shows little or no activity versus a wide range of ion channels, receptors and enzymes. SB705498 produces full blockade of heat as well as pH activation of hTRPV1.
48	Safinamide Mesylate	MAOB, MAOA	Safinamide is a highly selective MAO-B inhibitor in rat brain mitochondria, with an IC50 of 98 nM. safinamide inhibits MAO-B in human brain with an IC50 of 9 nM. Safinamide has high affinity for the Na+ channel-binding site II in rat cortical membranes, with an IC50 of 8 μM. Safinamide inhibits the fast Na+ currents in a concentration- and state-dependent manner in rat cortical neurons. Safinamide blocks N-Type Ca2+ currents in rat cortical neurons with IC50 of 23 μM. Safinamide inhibits glutamate release induced by depolarizing conditions in rat hippocampal synaptosomes with IC50 of 9 μM. Safinamide incubated 1 hour before veratridine reduces the neuron damage with an IC50 1.4 μM through blockade of opening voltage-dependent Na+ and Ca2+ channels in rat primary cortical neurons. Safinamide binds to human MAO B with a Ki of 0.5 μM. Safinamide binds to human MAO B in an extended conformation occupying both flavin and entrance cavity.
49	Tenofovir		Tenofovir reduces the viral cytopathic effect of HIV-1(IIIB), HIV-2(ROD) and HIV(EHO) with EC50 of 1.15 μg/mL, 1.12 μg/mL and 1.05 μg/mL in MT-4 cells. Tenofovir also reduces the viral cytopathic effect of SIV(mac251) , SIV(B670) ,SHIV(89.6) and SHIV(RTSHIV). Tenofovir is uniquely active against multinucleoside-resistant HIV expressing the Q151M mutation, but shows reduced susceptibility to the T69S insertion mutations. Tenofovir inhibits hepatitis B virus (HBV) activity in HepG2 2.2.15, HepAD38 and HepAD79 cells. Tenofovir (4 μM) completely inhibits the growth of HIVIIIB in MT-2 cells. Tenofovir inhibits synthesis of negative strand strong-stop DNA with IC50 of 9 μM for wild-type RT, 6 μM for M184V RT and 50 μM for K65R RT.
50	P22077	USP7, USP47	P22077 is an analog of the recently discovered USP7 inhibitor P5091. P22077 has negligible activity versus DEN1 and SENP2core over the concentration range tested, but inhibits USP7 with an IC50 of 8 μM. The inhibitory activities of P22077 in-vitro against a panel of DUBs, cysteine proteases, and other families of proteolytic enzymes demonstrate that P22077 inhibits USP7 and the closely related DUB USP47. P22077 inhibits a smaller subset of DUBs at a concentration of 15–45 mM in cell lysates. P22077 induces (tumor) cell death with EC50 values in the low micromolar range. P22077 inhibition exhibited changes in ubiquitylated protein levels that are distinct from the broad specificity inhibitor. P22077 treatment of U2OS cells during release from G1/S arrest induces with hydroxyurea resulted in a dose-dependent loss of claspin protein and a concomitant decrease in phospho Serine 317 Chk1. Furthermore, quantitative MS suggestes the E3 ubiquitin ligase components RBX1, DCAF7, DCAF11, and the DNA damage binding protein 1 (DDB1) to be reduced upon cellular treatment with P22077.
51	Aloxistatin		Aloxistatin can enter the intact platelet and inhibit proteolysis by inhibiting calpain. Aloxistatin blunts Parathyroid hormone (PTH)-induced cell proliferation and inhibits differentiation osteoblasts in-vitro.
52	NSC697923	UBE2	NSC697923 selectively inhibits PMA-induced NF-κB activation, and also inhibits IκBα phosphorylation by both RANKL and LPS. NSC697923 impedes the formation of the Ubc13 and ubiquitin thioester conjugate and suppresses constitutive NF-κB activity in ABC-DLBCL cells. In addition, NSC697923 inhibits the proliferation and survival of ABC-DLBCL cells and GCB-DLBCL cells, and also induces apoptosis of primary DLBCL cells. In neuroblastoma (NB) cell lines, NSC697923 shows cytotoxic effect, and inhibits both anchorage-dependent and -independent colony formation.
53	Apixaban	F10	Apixaban exhibits a high degree of potency, selectivity, and efficacy on Factor Xa with Ki of 0.08 nM and 0.17 nM for Human Factor Xa and Rabbit Factor Xa, respectively. In-vitro, Apixaban prolongs the clotting times of normal human plasma with the concentrations (EC2x) of 3.6 μM, 0.37 μM, 7.4 μM, and 0.4 μM, which are required respectively to double the prothrombin time (PT), modified prothrombin time

			(mPT), activated partial thromboplastin time (APTT) and HepTest. Besides, Apixaban shows the highest potency in human and rabbit plasma, but less potency in rat and dog plasma in both the PT and APTT assays.
54	ML347	ACVR1, ACVRL1	ML347 is a selective BMP receptor inhibitor with IC50 of 32 nM for ALK2, >300-fold selectivity over ALK3. Also inhibits ALK1 activity with IC50 of 46 nM.
55	Irinotecan HCl Trihydrate	TOP1	Irinotecan is activated to SN-38 by carboxylesterases to become able to interact with its target, topoisomerase I. Irinotecan induces similar amounts of cleavable complexes at its IC50 in LoVo cells and HT-29 cell lines. SN-38 induces a concentration-dependent formation of cleavable complexes, which is not significantly different in LoVo cells and HT-29 cell lines. Cell accumulation of Irinotecan is markedly different, reaching consistently higher levels in HT-29 cells than in LoVo cells. The lactone E-ring of Irinotecan and SN-38 hydrolyses reversibly in aqueous solutions, and the interconversion between the lactone and carboxylate forms is dependent on pH and temperature. Liver is primarily responsible for the activation of Irinotecan to SN-38. At equal concentrations of Irinotecan and SN-38 glucuronide, the rate of beta-glucuronidase-mediated SN-38 production is higher than that formed from Irinotecan in both tumour and normal tissue. Irinotecan is also converted to SN-38 in intestines, plasma and tumor tissues. Irinotecan is significantly more active in SCLC than in NSCLC cell lines, whereas no significant difference between histological types is observed with SN-38.
56	SSR128129E	FGFR1	SSR128129E is an orally-active and allosteric FGFR1 inhibitor with IC50 of 1.9 μM, while not affecting other related RTKs.
57	VX-765	CASP1	VX-765 is a potent and selective inhibitor of caspase-1 with Ki of 0.8 nM.
58	Ferrostatin-1 (Fer-1)	VDAC	Ferrostatin-1 (Fer-1) is a potent and selective inhibitor of ferroptosis with EC50 of 60 nM.
59	Rotundine	DRD1	Rotundine (L-tetrahydropalmatine, L-THP) is a selective dopamine D1 receptor antagonist with IC50 of 166 nM.
60	MM-102	KANSL1	MM-102 is a high-affinity peptidomimetic MLL1 inhibitor with IC50 of 0.4 μM.
61	PF-3845	FAAH	PF-3845 is a potent, selective and irreversible FAAH inhibitor with Ki of 230 nM, showing negligible activity against FAAH2.
62	OTX015	BRD2, BRD3, BRD4	OTX015 is a potent BET bromodomain inhibitor with EC50 ranging from 10 to 19 nM for BRD2, BRD3, and BRD4. Phase 1.
63	Ibrutinib (PCI-32765)	BTK	Ibrutinib is a potent and highly selective Btk inhibitor with IC50 of 0.5 nM, modestly potent to Bmx, CSK, FGR, BRK, HCK, less potent to EGFR, Yes, ErbB2, JAK3, etc.
64	4E1RCat	EIF4E	4E1RCat is a dual inhibitor of eIF4E:eIF4G and eIF4E:4E-BP1 interaction, and inhibits the binding of eIF4G to eIF4E with IC50 of 3.2 μM.
65	Tofacitinib (CP-690550,Tasocitinib)	JAK3	Tofacitinib is a novel inhibitor of JAK3 with IC50 of 1 nM, 20- to 100-fold less potent against JAK2 and JAK1.
66	PHA-793887	CDK2, CDK5, CDK7	PHA-793887 is a novel and potent inhibitor of CDK2, CDK5 and CDK7 with IC50 of 8 nM, 5 nM and 10 nM. It is greater than 6-fold more selective for CDK2, 5, and 7 than CDK1, 4, and 9. Phase 1.
67	WZ811	CXCR4	WZ811 is a highly potent competitive CXCR4 antagonist with EC50 of 0.3 nM.
68	Allopurinol	HCRTR1, HCRTR2	Allopurinol (Zyloprim) is a xanthine oxidase inhibitor with an IC50 of 7.82±0.12 μM.
69	HC-030031	TRPA1	HC-030031 is a selective TRPA1 channel blocker that antagonizes AITC- and formalin-evoked calcium influx with IC50 of 6.2 μM and 5.3 μM respectively.
70	Telmisartan	AGTR	Telmisartan (Micardis) is an angiotensin II receptor antagonist (ARB) used in the management of hypertension.
71	Mozavaptan	AVPR1, AVPR2	Mozavaptan is a novel competitive vasopressin receptor antagonist for both V1 and V2 receptors with IC50 of 1.2 μM and 14 nM, respectively.
72	Cyproterone Acetate	AR	Cyproterone acetate is an androgen receptor (AR) antagonist with IC50 of 7.1 nM, as well as a weak progesterone receptor agonist with weak pro-gestational and glucocorticoid activity.
73	Sodium 4-Aminosalicylate	NFKB	Sodium 4-Aminosalicylate is an antibiotic used to treat tuberculosis via NF-κB inhibition and free radical scavenging.
74	GSK1292263	GPR119	GSK1292263 is a novel GPR119 agonist, showing potential for the treatment of type 2 diabetes. Phase 2.
75	SGC 0946	DOT1L	SGC 0946 is a highly potent and selective DOT1L methyltransferase inhibitor with IC50 of 0.3 nM, is inactive against a panel of 12 PMTs and DNMT1.
76	LY2157299	TGFBR1	LY2157299 is a potent TGFβ receptor I (TβRI) inhibitor with IC50 of 56 nM. Phase 2.
77	IPA-3	PAK1	IPA-3 is a selective non-ATP competitive Pak1 inhibitor with IC50 of 2.5 μM, no inhibition to group II PAKs (PAKs 4-6).
78	Esomeprazole Sodium	ATP4A	Esomeprazole sodium (Nexium) is a sodium salt of esomeprazole that is a potent proton pump inhibitor with an IC50 of 0.076 mg/kg.
79	DMH1	ACVR1	DMH1 is a selective BMP receptor inhibitor with IC50 of 107.9 nM for ALK2, exhibiting no inhibition on AMPK, ALK5, KDR (VEGFR-2) or PDGFR.
80	Ozagrel	TBXA2R	Ozagrel is a potent and selective thromboxane A2 synthetase inhibitor with an IC50 of 4 nM.
81	AZD4547	FGFR1, FGFR2, FGFR3	AZD4547 is a novel selective FGFR inhibitor targeting FGFR1/2/3 with IC50 of 0.2 nM/2.5 nM/1.8 nM, weaker activity against FGFR4, VEGFR2(KDR), and little activity observed against IGFR, CDK2, and p38. Phase 1/2.
82	GW9508	FFAR1, FFAR4	GW9508 is a potent and selective agonist for FFA1 (GPR40) with pEC50 of 7.32, 100-fold selective against GPR120, stimulates insulin secretion in a glucose-sensitive manner.

83	VE-821	ATR	VE-821 is a potent and selective ATP competitive inhibitor of ATR with Ki/IC50 of 13 nM/26 nM, shows inhibition of H2AX phosphorylation, minimal activity against PIKKs ATM, DNA-PK, mTOR and PI3Kγ.
84	NSC 405020	MMP14	NSC 405020 is a noncatalytic inhibitor of MT1-MMP, directly interacts with PEX domain of MT1-MMP, affects PEX homodimerization but not catalytic activity of MT1-MMP.
85	GNF-2	ABL1	GNF-2 is a highly selective non-ATP competitive inhibitor of Bcr-Abl, shows no activity to Flt3-ITD, Tel-PDGFR, TPR-MET and Tel-JAK1 transformed tumor cells.
86	TPCA-1	IKBKB	TPCA-1 is an inhibitor of IKK-2 with IC50 of 17.9 nM, inhibits NF-κB pathway, exhibits 22-fold selectivity over IKK-1.
87	T0901317	NR1H3, NR1H2, NR1H4	T0901317 is a potent and selective agonist for both LXR and FXR, with EC50 of ~50 nM and 5 μM, respectively.
88	PD0325901	MAP2K1, MAP2K2	PD0325901 (PD325901) is selective and non ATP-competitive MEK inhibitor with IC50 of 0.33 nM, roughly 500-fold more potent than CI-1040 on phosphorylation of ERK1 and ERK2. Phase 1/2.
89	PYR-41	UBA1	PYR-41 is the first cell-permeable inhibitor of ubiquitin-activating enzyme E1, with no activity at E2.
90	U0126-EtOH	MAP2K1, MAP2K2	U0126-EtOH is a highly selective inhibitor of MEK1/2 with IC50 of 0.07 μM/0.06 μM, 100-fold higher affinity for ΔN3-S218E/S222D MEK than PD098059.
91	LDN-212854	ACVR1, ACVRL1	LDN-212854 is a potent and selective BMP receptor inhibitor with IC50 of 1.3 nM for ALK2, about 2-, 66-, 1641-, and 7135-fold selectivity over ALK1, ALK3, ALK4, and ALK5, respectively.
92	Ki16425	LPAR1, LPAR2, LPAR3	Ki16425 is a competitive, potent and reversible antagonist to LPA1, LPA2 and LPA3 with Ki of 0.34 μM, 6.5 μM and 0.93 μM, respectively, shows no activity at LPA4, LPA5, LPA6.
93	C646	EP300	C646 is an inhibitor for histone acetyltransferase, and inhibits p300 with a Ki of 400 nM. Preferentially selective for p300 versus other acetyltransferases.
94	Oxcarbazepine	SCN	Oxcarbazepine inhibits the binding of [3H]BTX to sodium channels with IC50 of 160 μM and also inhibits the influx of 22Na+ into rat brain synaptosomes with IC50 about 100 μM.
95	Mdivi-1	DRP1, DNM1	Mdivi-1 is a selective cell-permeable inhibitor of mitochondrial division DRP1 (dynamin-related GTPase) and mitochondrial division Dynamin I (Dnm1) with IC50 of 1-10 μM.
96	MRS 2578	P2RY6	MRS2578 is a potent P2Y6 receptor antagonist with IC50 of 37 nM, exhibits insignificant activity at P2Y1, P2Y2, P2Y4,and P2Y11 receptors.
97	AGI-5198	IDH1	AGI-5198 is the first highly potent and selective inhibitor of IDH1 R132H/R132C mutants with IC50 of 0.07 μM/0.16 μM.
98	LY2603618	CHEK1	LY2603618 is a selective Chk1 inhibitor with potential anti-tumor activity.
99	BTB06584	ATP5A1	BTB06584 is an IF1-dependent, selective inhibitor of the mitochondrial F1 Fo-ATPase.
100	NPS-2143	CASR	NPS 2143 is a novel potent and selective antagonist of Ca(2+) receptor with IC50 of 43 nM.
101	Veliparib (ABT-888)	PARP1, PARP2	Veliparib (ABT-888) is a potent inhibitor of PARP1 and PARP2 with Ki of 5.2 nM and 2.9 nM, respectively. It is inactive to SIRT2. Phase 1/2.
102	Dalcetrapib (JTT-705, RO4607381)	CETP	Dalcetrapib (JTT-705) is a rhCETP inhibitor with IC50 of 0.2 μM that increases the plasma HDL cholesterol. Phase 3.
103	Vandetanib (ZD6474)	KDR	Vandetanib (ZD6474) is a potent inhibitor of VEGFR2 with IC50 of 40 nM.
104	Istradefylline	ADORA2A	Istradefylline is a selective adenosine A2A receptor (A2AR) antagonist with Ki of 2.2 nM.
105	Iniparib (BSI-201)	PARP1	BSI-201 (Iniparib, SAR240550) is a PARP1 inhibitor with demonstrated effectiveness in triple-negative breast cancer (TNBC). Phase 3.
106	Dabrafenib (GSK2118436)	BRAF (V600)	Dabrafenib (GSK2118436) is a mutant BRAFV600 specific inhibitor with IC50 of 0.8 nM, with 4- and 6-fold less potency against B-Raf(wt) and c-Raf, respectively. Phase 3.
107	Finasteride	SRD5A2	Finasteride is an inhibitor of steroid Type II 5α-reductase.
108	Tyrphostin AG 879	ERBB2	Tyrphostin AG 879 potently inhibits HER2/ErbB2 with IC50 of 1 μM, 100- and 500-fold higher selective to ErbB2 than PDGFR and EGFR.
109	Cilomilast	PDE4	Cilomilast is a potent PDE4 inhibitor with IC50 of about 110 nM, has anti-inflammatory activity and low central nervous system activity.
110	TAE226 (NVP-TAE226)	PTK2, PTK2B	NVP-TAE226 is a potent FAK inhibitor with IC50 of 5.5 nM and modestly potent to Pyk2, ~10- to 100-fold less potent against InsR, IGF-1R, ALK, and c-Met.
111	Ozagrel HCl	TBXAS1	Ozagrel HCl is a selective thromboxane A2 synthetase enzyme inhibitors with IC50 of 11 nM, used as antiasthmatic agent.
112	Vildagliptin (LAF-237)	DPP4	Vildagliptin (LAF-237) inhibits DPP−4 with IC50 of 2.3 nM.
113	Dynasore	DNM1, DNM2	Dynasore is a cell-permeable, reversible non-competitive dynamin inhibitor of GTPase activity of dynamin 1/2, with IC50 of 15 μM, also inhibits the mitochondrial dynamin Drp1, with no effect against other small GTPase.
114	Piceatannol	SYK	Piceatannol, a natural stilbene, is a selective Syk inhibitor and ~10-fold selectivity versus Lyn.
115	Quizartinib (AC220)	FLT3	Quizartinib (AC220) is a second-generation FLT3 inhibitor for Flt3(ITD/WT) with IC50 of 1.1 nM/4.2 nM, 10-fold more selective for Flt3 than KIT, PDGFRα, PDGFRβ, RET, and CSF-1R. Phase 1/2.

116	Tenovin-6	TP53, SIRT2, SIRT1, SIRT3	Tenovin-6 is a small molecule activator of p53 transcriptional activity.
117	Enzastaurin (LY317615)	PRKCB, PRKCA, PRKCG, PRKCE	Enzastaurin (LY317615) is a potent PKCβ selective inhibitor with IC50 of 6 nM, 6- to 20-fold selectivity against PKCα, PKCγ and PKCε. Phase 3.
118	CGP 57380	MKNK1	CGP 57380 is potent MNK1 inhibitor with IC50 of 2.2 μM, exhibiting no inhibitory activity on p38, JNK1, ERK1 and -2, PKC, or c-Src-like kinases.
119	Bisoprolol fumarate	ADRB1	Bisoprolol is a selective type β1 adrenergic receptor blocker.
120	Bosutinib (SKI-606)	SRC, ABL1	Bosutinib (SKI-606) is a novel, dual Src/Abl inhibitor with IC50 of 1.2 nM and 1 nM, respectively.
121	S3I-201	STAT3	S3I-201 shows potent inhibition of STAT3 DNA-binding activity with IC50 of 86 μM, and low activity towards STAT1 and STAT5.
122	HA14-1	BCL2	HA14-1 is a non-peptidic ligand of a Bcl-2 surface pocket with IC50 of ~9 μM.
123	TG100-115	PIK3CG, PIK3CD	TG100115 is a PI3Kγ/δ inhibitor with IC50 of 83 nM/235 nM, with little effect on PI3Kα/β. Phase 1/2.
124	ADL5859 HCl	OPRK1, OPRM1	ADL5859 HCl is a δ-opioid receptor agonist with Ki of 0.8 nM, selectivity against opioid receptor κ, μ, and weak inhibitory activity at the hERG channel. Phase 2.
125	Voriconazole	CYP51A1	Voriconazole is a new triazole derivative similar to fluconazole and itraconazole that acts by inhibiting fungal cytochrome P-450-dependent, 14-alpha-sterol demethylase-mediated synthesis of ergosterol.
126	BIBR 1532	TERT	BIBR 1532 is a potent, selective, non-competitive telomerase inhibitor with IC50 of 100 nM.
127	Thiazovivin	ROCK1, ROCK2	Thiazovivin (Tzv) is a novel ROCK inhibitor with IC50 of 0.5 μM, promotes hESC survival after single-cell dissociation.
128	Anastrozole	CYP19A1	Anastrozole is a third-generation nonsteroidal selective aromatase inhibitor.
129	SB743921		SB743921 is a kinesin spindle protein (KSP) inhibitor with Ki of 0.1 nM, almost no affinity to MKLP1, Kin2, Kif1A, Kif15, KHC, Kif4 and CENP-E. Phase 1/2.
130	EUK 134	SOD1	EUK 134, a synthetic superoxide dismutase (SOD)/catalase mimetic, exhibits potent antioxidant activities, and inhibits the formation of β-amyloid and related amyloid fibril.
131	Bergenin		Bergenin is trihydroxybenzoic acid glycoside and the C-glycoside of 4-O-methyl gallic acid.
132	SN-38	TOP1	SN-38 is an active metabolite of CPT-11, inhibits DNA topoisomerase I, DNA synthesis and causes frequent DNA single-strand breaks.
133	CP-91149	PYGL, PYGM, PYGB	CP-91149 is a selective glycogen phosphorylase (GP) inhibitor with IC50 of 0.13 μM in the presence of glucose, 5- to 10-fold less potent in the absence of glucose.
134	Wnt-C59 (C59)	WNT3A	Wnt-C59 (C59) is a PORCN inhibitor for Wnt3A-mediated activation of a multimerized TCF-binding site driving luciferase with IC50 of 74 pM.
135	NU7026	PRKDC	NU7026 is a potent DNA-PK inhibitor with IC50 of 0.23 μM, 60-fold selective for DNA-PK than PI3K and inactive against both ATM and ATR.
136	BAM7	BAX	BAM 7 is a direct and selective activator of proapoptotic Bax with EC50 of 3.3 μM.
137	ZM 306416	FLT1	ZM 306416 is a VEGFR (Flt and KDR) inhibitor for VEGFR1 with IC50 of 0.33 μM, but also found to inhibit EGFR with IC50 of <10 nM.
138	(+)-JQ1	BRD4	(+)-JQ1 is a BET bromodomain inhibitor, with IC50 of 77 nM/33 nM for BRD4(1/2), binding to all bromodomains of the BET family, but not to bromodomains outside the BET family.
139	GW9662	PPARG	GW9662 is a selective PPAR antagonist for PPARγ with IC50 of 3.3 nM, with at least 100 to 1000-fold functional selectivity in cells with PPARγversus PPARα and PPARδ.
140	KPT-185	XPO1	KPT-185 is a selective CRM1 inhibitor.
141	Pifithrin-μ	TP53, HSPBP1	Pifithrin-μ is a specific p53 inhibitor by reducing its affinity to Bcl-xL and Bcl-2, and also inhibits HSP70 function and autophagy.
142	Batimastat (BB-94)	MMP1, MMP2, MMP3, MMP7, MMP9	Batimastat (BB-94) is a potent, broad spectrum matrix metalloprotease (MMP) inhibitor for MMP-1, MMP-2, MMP-9, MMP-7 and MMP-3 with IC50 of 3 nM, 4 nM, 4 nM, 6 nM and 20 nM, respectively.
143	Sertraline HCl		Sertraline HCl is a 5-HT antagonist with Ki of 13 nM.
144	OG-L002	KDM1A	OG-L002 is a potent and specific LSD1 inhibitor with IC50 of 20 nM, exhibiting 36- and 69-fold selectivity over MAO-B and MAO-A, respectively.
145	MK-1775	WEE1	MK-1775 is a potent and selective Wee1 inhibitor with IC50 of 5.2 nM; hinders G2 DNA damage checkpoint. Phase 2.
146	Costunolide	TERT	Costunolide, a natural sesquiterpene compound with multiple biological activities; inhibits FPTase with IC50 of 20 μM, also inhibits telomerase with IC50 of 65-90 μM.
147	AT101	BCL2, BCL2L1, MCL1	AT101, the R-(-) enantiomer of Gossypol acetic acid, binds with Bcl-2, Bcl-xL and Mcl-1 with Ki of 0.32 μM, 0.48 μM and 0.18 μM; does not inhibit BIR3 domain and BID. Phase 1/2.
148	GSK690693	AKT1, AKT2, AKT3	GSK690693 is a pan-Akt inhibitor targeting Akt1/2/3 with IC50 of 2 nM/13 nM/9 nM, also sensitive to the AGC kinase family: PKA, PrkX and PKC isozymes. Phase 1.
149	Tropicamide	CHRM4	Tropicamide is an anticholinergic and a muscarinic receptor subtype M4-preferring antagonist with IC50 of 8.0 nM.
150	BMS-707035		BMS-707035 is a specific HIV-I integrase (IN) inhibitor with IC50 of 15 nM. Phase 2.
151	Raltegravir (MK-0518)		Raltegravir (MK-0518) is a potent integrase (IN) inhibitor for WT and S217Q PFV IN with IC50 of 90 nM and 40 nM, respectively.
152	EX 527 (Selisistat)	SIRT1	EX 527 is a potent and selective SIRT1 inhibitor with IC50 of 38 nM, exhibits >200-fold selectivity against SIRT2 and SIRT3.

153	CCT128930	AKT2	CCT128930 is a potent, ATP-competitive and selective inhibitor of Akt2 with IC50 of 6 nM, 28-fold greater selectivity for Akt2 than the closely related PKA kinase.
154	Pomalidomide	TNF	Pomalidomide inhibits LPS-induced TNF-α release with IC50 of 13 nM.
155	AS-252424	PIK3CG	AS-252424 is a novel, potent PI3Kγ inhibitor with IC50 of 30 nM with 30-fold selectivity for PI3Kγ than PI3Kα, and low inhibitory activity towards PI3Kδ/β.
156	Tie2 kinase inhibitor	TEK	Tie2 kinase inhibitor is an optimized compound of SB-203580, selective to Tie2 with IC50 of 0.25 μM, 200-fold more potent than p38.
157	Ouabain	ATP1B	Ouabain is a selective Na+/K+, -ATPase inhibitor, binds to α2 /α3 subunit with Ki of 41 nM/15 nM.
158	Ranitidine	HRH2	Ranitidine is a histamine H2-receptor antagonist with IC50 of 3.3 ± 1.4 μM.
159	SKI II	S1PR	SKI II is a highly selective and non ATP-competitive S1P receptor inhibitor with IC50 of 0.5 μM, while exhibits no inhibitory on other kinases including PI3K, PKCα and ERK2.
160	Fluvastatin Sodium	HMGCR	Fluvastatin Sodium inhibits HMG-CoA reductase activity with IC50 of 8 nM.
161	Propranolol HCl	ADRB1	Propranolol HCl is a competitive non-selective beta-adrenergic receptors inhibitor with IC50 of 12 nM.
162	Erastin	VDAC	Erastin is a ferroptosis activator by acting on mitochondrial VDAC, exhibiting selectivity for tumor cells bearing oncogenic RAS.
163	Ifenprodil Tartrate	GRIN	Ifenprodil is an atypical noncompetitive antagonist at the NMDA receptor, it interacts with high affinity at a homogeneous population of NMDA receptors in neonatal rat forebrain with IC50 of 0.3 μM.
164	KPT-276	XPO1	KPT-276 is an orally bioavailable selective CRM1 inhibitor.
165	AZD2461	PARP	AZD2461 is a novel PARP inhibitor with low affinity for Pgp than Olaparib. Phase 1.
166	KPT-330	XPO1	KPT-330 is an orally bioavailable selective CRM1 inhibitor.
167	AGI-6780	IDH2	AGI-6780 is a potent and selective inhibitor of IDH2 R140Q mutant with IC50 of 23 nM.
168	SGI-1027	DNMT1, DNMT3A, DNMT3B	SGI-1027 is a DNMT inhibitor with IC50 of 6, 8, 7.5 μM for DNMT1, DNMT3A, and DNMT3B
169	Atglistatin	PNPLA2	Atglistatin is a highly potent, and selective inhibitor of adipose triglyceride lipase (ATGL) with IC50 of 0.7 μM, high selectivity over other key metabolic lipases.
170	Suvorexant (MK-4305)	HCRTR1, HCRTR2	Suvorexant (MK-4305) is a potent dual OX receptor antagonist with Ki of 0.55 nM and 0.35 nM for OX1 receptor and OX2 receptor, respectively. Phase 3.
171	SRT1720	SIRT1	SRT1720 is a selective SIRT1 activator with EC50 of 0.16 μM, but is >230-fold less potent for SIRT2 and SIRT3.
172	4EGI-1	EIF4E	4EGI-1 is a competitive eIF4E/eIF4G interaction inhibitor by binding to eIF4E with KD of 25 μM.
173	Exemestane	CYP19A1	Exemestane is an aromatase inhibitor, inhibits human placental and rat ovarian aromatase with IC50 of 30 nM and 40 nM, respectively.
174	NSC 23766	RAC	NSC 23766 is an inhibitor of Rac GTPase targeting Rac activation by guanine nucleotide exchange factors (GEFs) with IC50 of ~50 μM; does not inhibit the closely related targets, Cdc42 or RhoA.
175	2-Methoxyestradiol (2-MeOE2)	HIF1A	2-Methoxyestradiol depolymerizes microtubules and blocks HIF-1α nuclear accumulation and HIF-transcriptional activity. Phase 2.
176	Palbociclib (PD-0332991) HCl	CDK4, CDK6	PD0332991 is a highly selective inhibitor of CDK4/6 with IC50 of 11 nM/16 nM. It shows no activity against CDK1/2/5, EGFR, FGFR, PDGFR, InsR, etc. Phase 2/3.
177	EHop-016	RAC1, RAC3	EHop-016 is a specific Rac GTPase inhibitor with IC50 of 1.1 μM for Rac1, equally potent inhibition for Rac3.
178	PF-573228	PTK2	PF-573228 is an ATP-competitive inhibitor of FAK with IC50 of 4 nM, ~50- to 250-fold selective for FAK than Pyk2, CDK1/7 and GSK-3β.
179	ABT-199 (GDC-0199)	BCL2	ABT-199 (GDC-0199) is a Bcl-2-selective inhibitor with Ki of <0.01 nM, >4800-fold more selective versus Bcl-xL and Bcl-w, and no activity to Mcl-1. Phase 2.
180	Memantine HCl	CYP2B6	Memantine hydrochloride (Namenda) is a CYP2B6 and CYP2D6 inhibitor for recombinant CYP2B6 and CYP2D6 with Ki of 0.51 nM and 94.9 μM, respectively.
181	PTC-209	BMI1	PTC-209 is a potent and selective BMI-1 inhibitor with IC50 of 0.5 μM, and results in irreversible reduction of cancer-initiating cells (CICs).
182	Trimebutine	OPRK1, OPRM1, OPRD1	Trimebutine is an agonist of peripheral mu, kappa and delta opiate receptors, used as spasmolytic agent for treatment of both acute and chronic abdominal pain.
183	CK-636	ARPC2, ARPC3	CK-636 is an Arp2/3 complex inhibitor with IC50 of 4 μM, 24 μM and 32 μM for inhibition of actin polymerization induced by human, fission yeast and bovine Arp2/3 complex, respectively.
184	SGI-1776 free base	PIM1, FLT3, GSG2	SGI-1776 is a novel ATP competitive inhibitor of Pim1 with IC50 of 7 nM, 50- and 10-fold selective versus Pim2 and Pim3, also potent to Flt3 and haspin. Phase 1.
185	AZD7545	PDK1, PDK2	AZD7545 is a potent PDHK inhibitor with IC50 of 36.8 nM and 6.4 nM for PDHK1 and PDHK2, respectively.
186	URB597	FAAH	URB597 is a potent, orally bioavailable FAAH inhibitor with IC50 of 4.6 nM, with no activity on other cannabinoid-related targets.
187	GW0742	PPARD	GW0742 is a potent and highly selective PPARβ/δ agonist, with IC50 of 1 nM, with 1000-fold selectivity over hPPARα and hPPARγ.
188	TAK-875	FFAR1	TAK-875 is a selective GPR40 agonist with EC50 of 14 nM, 400-fold more potent than oleic acid.
189	Pacritinib (SB1518)	JAK2, FLT3	Pacritinib (SB1518) is a potent and selective inhibitor of Janus Kinase 2 (JAK2) and Fms-Like Tyrosine Kinase-3 (FLT3) with IC50s of 23 and 22 nM, respectively.

190	KX2-391	SRC	KX2-391 (KX01), the first clinical Src inhibitor (peptidomimetic class) that targets the peptide substrate site of Src, with GI50 of 9-60 nM in cancer cell lines. Phase 1/2.
191	PluriSIn #1 (NSC 14613)	SCD	PluriSIn #1 is an inhibitor of the stearoyl-coA desaturase 1 (SCD1), which is able to selectively eliminate hPSCs.
192	Crenolanib (CP-868596)	PDGFRA, PDGFRB, FLT3 (D842V)	Crenolanib (CP-868596) is a potent and selective inhibitor of PDGFRα/β with Kd of 2.1 nM/3.2 nM, also potently inhibits FLT3, sensitive to D842V mutation not V561D mutation, >100-fold more selective for PDGFR than c-Kit, VEGFR-2, TIE-2, FGFR-2, EGFR, erbB2, and Src.
193	Enzalutamide (MDV3100)	AR	Enzalutamide (MDV3100) is an androgen-receptor (AR) antagonist with IC50 of 36 nM.
194	PFI-1 (PF-6405761)	BRD4	PFI-1 is a selective BET (bromodomain-containing protein) inhibitor for BRD4 with IC50 of 0.22 μM.
195	Dapagliflozin	SLC5A2	Dapagliflozin is a potent and selective hSGLT2 inhibitor with EC50 of 1.1 nM, exhibiting 1200-fold selectivity over hSGLT1. Phase 3.
196	Maraviroc	CCR5	Maraviroc is a CCR5 antagonist for MIP-1α, MIP-1β and RANTES with IC50 of 3.3 nM, 7.2 nM and 5.2 nM, respectively.
197	Nebivolol	ADRB1	Nebivolol selectively inhibits β1-adrenoceptor with IC50 of 0.8 nM.
198	I-BET151 (GSK1210151A)	BRD2, BRD3, BRD4	I-BET151 (GSK1210151A) is a novel selective BET inhibitor for BRD2, BRD3 and BRD4 with IC50 of 0.5 μM, 0.25 μM, and 0.79 μM, respectively.
199	VX-809 (Lumacaftor)	CFTR	VX-809 acts to correct CFTR mutations common in cystic fibrosis by increasing mutant CFTR (F508del-CFTR) maturation,EC50 of 0.1 μM. Phase 3.
200	Apoptosis Activator 2	CASP3	Apoptosis Activator 2 strongly induces caspase-3 activation, PARP cleavage, and DNA fragmentation which leads to the destruction of cells (Apaf-1 dependent) with IC50 of ~4 μM, inactive to HMEC, PREC, or MCF-10A cells.
201	Naproxen	PTGS1, PTGS2	Naproxen is a COX inhibitor for COX-1 and COX-2 with IC50 of 8.7 μM and 5.2 μM, respectively.
202	Bosentan Hydrate	EDNRA, EDNRB	Bosentan is an endothelin (ET) receptors antagonist for ET-A and ET-B with Ki of 4.7 nM and 95 nM, respectively.
203	Acadesine	PRKAA1	Acadesine results in accumulation of ZMP, which mimics the stimulating effect of AMP on AMPK and AMPK kinase. Phase 3.
204	E-64	CTSK	E-64 is an irreversible and selective cysteine protease inhibitor with IC50 of 9 nM for papain.
205	Captopril	ACE	Captopril is an angiotensin-converting enzyme (ACE) inhibitor with IC50 of 6 nM.
206	Selumetinib (AZD6244)	MAP2K1, MAPK3, MAPK1	Selumetinib (AZD6244) is a potent, highly selective MEK1 inhibitor with IC50 of 14 nM, also inhibits ERK1/2 phosphorylation with IC50 of 10 nM, no inhibition to p38α, MKK6, EGFR, ErbB2, ERK2, B-Raf, etc. Phase 1/2.
207	Tolvaptan	AVPR2	Tolvaptan is a selective, competitive arginine vasopressin receptor 2 antagonist with an IC50 of 1.28μM for the inhibition of AVP-induced platelet aggregation.
208	PD184352 (CI-1040)	MAP2K1, MAP2K2	CI-1040 (PD 184352) is an ATP non-competitive MEK1/2 inhibitor with IC50 of 17 nM, 100-fold more selective for MEK1/2 than MEK5. Phase 2.
209	OSI-906 (Linsitinib)	IGF1R, INSR	OSI-906 (Linsitinib) is a selective inhibitor of IGF-1R with IC50 of 35 nM; modestly potent to InsR with IC50 of 75 nM, and no activity towards Abl, ALK, BTK, EGFR, FGFR1/2, PKA etc. Phase 3.
210	Canagliflozin	SLC5A2	Canagliflozin is a highly potent and selective SGLT2 inhibitor for hSGLT2 with IC50 of 2.2 nM, exhibits 413-fold selectivity over hSGLT1.
211	CP-673451	PDGFRA, PDGFRB	CP 673451 is a selective inhibitor of PDGFRα/β with IC50 of 10 nM/1 nM, exhibits >450-fold selectivity over other angiogenic receptors, has antiangiogenic and antitumor activity.
212	Sirtinol	SIRT1, SIRT2	Sirtinol is a specific SIRT1 and SIRT2 inhibitor with IC50 of 131 μM and 38 μM, respectively.
213	Methotrexate	DHFR	Methotrexate is an antimetabolite and antifolate drug, which acts by inhibiting the metabolism of folic acid.
214	SAR131675	FLT4	SAR131675 is a VEGFR3 inhibitor with IC50/Ki of 23 nM/12 nM, about 50- and 10-fold more selective for VEGFR3 than VEGFR1/2, little activity against Akt1, CDKs, PLK1, EGFR, IGF-1R, c-Met, Flt2 etc.
215	Pralatrexate	DHFR	Pralatrexate(Folotyn) is an antifolate, and structurally a folate analog. Its IC50 is < 300 nM in some cell lines.
216	BML-190	CNR2	BML-190 is a selective cannabinoid CB2 receptor inverse agonist with Ki of 435 nM, with 50-fold selectivity over CB1 receptor.
217	TWS119	GSK3B	TWS119 is a GSK-3β inhibitor with IC50 of 30 nM; capable of inducing neuronal differentiation and may be useful to stem cell biology.
218	IKK-16 (IKK Inhibitor VII)	IKBKB, CHUK	IKK 16 is a selective IκB kinase (IKK) inhibitor for IKK-2, IKK complex and IKK-1 with IC50 of 40 nM, 70 nM and 200 nM, respectively.
219	Enalaprilat Dihydrate	ACE	Enalaprilat is an angiotensin-converting enzyme (ACE) inhibitor with IC50 of 1.94 nM.
220	Triamterene	SCN	Triamterene blocks epithelial Na+ channel (ENaC) in a voltage-dependent manner with IC50 of 4.5 μM.
221	Clemastine Fumarate	HRH1	Clemastine Fumarate (Clemastine) is a selective histamine H1 receptor antagonist with IC50 of 3 nM.
222	Fingolimod (FTY720) HCl	S1PR	Fingolimod (FTY720) is a S1P antagonist with IC50 of 0.033 nM.
223	Amlodipine	CACNA1C	Amlodipine(Norvasc) is a long-acting calcium channel blocker with an IC50 of 1.9 nM.
224	PP2	SRC	PP2 is Src family kinase inhibitor, potently inhibits Lck/Fyn with IC50 of 4 nM/5 nM, ~100-fold less potent to EGFR, inactive for ZAP-70, JAK2 and PKA.

225	CHIR-124	CHEK1	CHIR-124 is a novel and potent Chk1 inhibitor with IC50 of 0.3 nM. It shows 2,000-fold selectivity against Chk2, 500- to 5,000-fold less activity against CDK2/4 and Cdc2.
226	Temsirolimus (CCI-779, NSC 683864)	MTOR	Temsirolimus (CCI-779) is a specific mTOR inhibitor with IC50 of 1.76 μM.
227	YO-01027	APP, APPL1, NOTCH	YO-01027 (Dibenzazepine, DBZ) is a dipeptidic γ-secretase inhibitor with IC50 of 2.6 nM and 2.9 nM for APPL and Notch cleavage, respectively.
228	Trichostatin A (TSA)	ALL HDACS (Except HDAC8)	Trichostatin A (TSA) is an HDAC inhibitor with IC50 of ~1.8 nM – HDAC8 is the only known member of the HDAC-family that is not affected by TSA. Phase 3.
229	PAC-1	CASP3	PAC-1 is a potent procaspase-3 activator with EC50 of 0.22 μM and the first small molecule known to directly activate procaspase-3 to caspase-3.
230	PHA-665752	MET	PHA-665752 is a potent, selective and ATP-competitive c-Met inhibitor with IC50 of 9 nM, >50-fold selectivity for c-Met than RTKs or STKs.
231	VE-822	ATR	VE-822 is an ATR inhibitor with IC50 of 19 nM.
232	SB203580	MAPK11, MAPK12, MAPK13, MAPK14	SB203580 is a p38 MAPK inhibitor with IC50 of 0.3-0.5 μM, 10-fold less sensitive to SAPK3(106T) and SAPK4(106T) and blocks PKB phosphorylation with IC50 of 3-5 μM.
233	EPZ-6438	EZH2	EPZ-6438 is a potent, and selective EZH2 inhibitor with Ki and IC50 of 2.5 nM and 11 nM, exhibiting a 35-fold selectivity versus EZH1 and >4,500-fold selectivity relative to 14 other HMTs.
234	KU-55933 (ATM Kinase Inhibitor)	ATM	KU-55933 is a potent and specific ATM inhibitor with IC50/Ki of 12.9 nM/2.2 nM, and is highly selective for ATM as compared to DNA-PK, PI3K/PI4K, ATR and mTOR.
235	CGK 733	ATM, ATR	CGK 733 is a potent and selective inhibitor of ATM/ATR with IC50 of ~200 nM.
236	WZ4002	EGFR	WZ4002 is a novel, mutant-selective EGFR inhibitor for EGFR(L858R)/(T790M) with IC50 of 2 nM/8 nM; does not inhibit ERBB2 phosphorylation (T798I).
237	WZ4003	NUAK1, NUAK2	WZ4003 is a highly specific NUAK kinase inhibitor with IC50 of 20 nM and 100 nM for NUAK1 and NUAK2, respectively, without significant inhibition on 139 other kinases.
238	TAK-700 (Orteronel)	CYP17A1	TAK-700 (Orteronel) is a potent and highly selective human 17,20-lyase inhibitor with IC50 of 38 nM, exhibits >1000-fold selectivity over other CYPs (e.g. 11-hydroxylase and CYP3A4). Phase 3.
239	Loxistatin Acid (E-64C)		Loxistatin Acid (E-64C), a derivative of E-64, is an irreversible and membrane-permeant cysteine protease inhibitor.
240	Zibotentan (ZD4054)	EDNRA	Zibotentan (ZD4054) is a specific Endothelin (ET)A antagonist with IC50 of 21 nM, exhibiting no activity at ETB. Phase 3.
241	Pyrimethamine	DHFR	Pyrimethamine is a dihydrofolate reductase(DHFR) inhibitor with an IC50 of 15.4 nM.
242	RKI-1447	ROCK1, ROCK2	RKI-1447 is a potent inhibitor of ROCK1 and ROCK2, with IC50 of 14.5 nM and 6.2 nM, respectively, has anti-invasive and antitumor activities.
243	UNC2250	MERTK	UNC2250 is a potent and selective Mer inhibitor with IC50 of 1.7 nM, about 160- and 60-fold selectivity over the closely related kinases Axl/Tyro3.
244	SMI-4a	PIM1	SMI-4a is a potent inhibitor of Pim1 with IC50 of 17 nM, modest potent to Pim-2, does not significantly inhibit other serine/threonine- or tyrosine-kinases.
245	SB415286	GSK3A	SB415286 is a potent GSK3α inhibitor with IC50/Ki of 78 nM/31 nM with equally effective inhibition of GSK-3β.
246	PRT062607 (P505-15, BIIB057) HCl	SYK	PRT062607 (P505-15) HCl is a novel, highly selective Syk inhibitor with IC50 of 1 nM, >80-fold selective for Syk than Fgr, Lyn, FAK, Pyk2 and Zap70.
247	Torcetrapib	CETP	Torcetrapib is a CETP inhibitor with IC50 of 37 nM, elevates HDL-C and reduces nonHDL-C in plasma. Phase 3.
248	MK-2206 2HCl	AKT1, AKT2, AKT3	MK-2206 2HCl is a highly selective inhibitor of Akt1/2/3 with IC50 of 8 nM/12 nM/65 nM, respectively; no inhibitory activities against 250 other protein kinases observed. Phase 2.
249	ML130 (Nodinitib-1)	NOD1	ML130 is a potent and selective inhibitor of NOD1 with IC50 of 0.56 μM, inhibits NF-κB activation, exhibits 36-fold selectivity over NOD2.
250	PF-04217903	MET	PF-04217903 is a selective ATP-competitive c-Met inhibitor with IC50 of 4.8 nM, susceptible to oncogenic mutations (no activity to Y1230C mutant). Phase 1.
251	GW441756	NTRK1	GW441756 is a potent, selective inhibitor of TrkA with IC50 of 2 nM, with very little activity to c-Raf1 and CDK2.
252	Varespladib (LY315920)	PLA2G2A	LY315920 (Varespladib) is a potent and selective human non-pancreatic secretory phospholipase A2 (hnsPLA) inhibitor with IC50 of 7 nM. Phase 3.
253	ML161	PARP1	ML-161 is an allosteric inhibitor of PAR1 with IC50 of 0.26 μM.
254	MK-2866 (GTx-024)	AR	MK-2866 (GTx-024) is a selective androgen receptor modulator (SARM) with Ki of 3.8 nM, and is tissue-selective for anabolic organs. Phase 3.
255	Ticagrelor	P2RY12	Ticagrelor is the first reversibly binding oral P2Y12 receptor antagonist, also inhibits CYP2C9 and 4-hydroxylation with IC50 of 10.5 μM and 8.2 μM respectively.
256	Letrozole	CYP19A1	Letrozole is a third generation inhibitor of aromatase with IC50 of 0.07-20 nM.
257	GW2580	CSF1R	GW2580 is a selective CSF-1R inhibitor for c-FMS with IC50 of 30 nM, 150- to 500-fold selective compared to b-Raf, CDK4, c-KIT, c-SRC, EGFR, ERBB2/4, ERK2, FLT-3, GSK3, ITK, JAK2 etc.
258	Zosuquidar (LY335979) 3HCl	ABCB1	Zosuquidar (LY335979) is a potent modulator of P-glycoprotein-mediated multi-drug resistance with Ki of 60 nM. Phase 3.
259	KU-60019	ATM	KU-60019 is an improved analogue of KU-55933, with IC50 of 6.3 nM for ATM, 270- and 1600-fold more selective for ATM than DNA-PK and ATR,and is a highly effective radiosensitizer.

260	LY2228820	MAPK11, MAPK12, MAPK13, MAPK14	LY2228820 is a novel and potent inhibitor of p38 MAPK with IC50 of 7 nM, does not alter p38 MAPK activation. Phase 1/2.
261	MLN2238	PSMC1	MLN2238 inhibits the chymotrypsin-like proteolytic (β5) site of the 20S proteasome with IC50 and Ki of 3.4 nM and 0.93 nM, respectively, also inhibits the caspase-like (β1) and trypsin-like (β2) proteolytic sites, with IC50 of 31 and 3500 nM.
262	Org 27569	CNR1	Org 27569 is an allosteric modulator of cannabinoid CB1 receptor, induces a CB1 receptor state that is characterized by enhanced agonist affinity and decreased inverse agonist affinity.
263	Oxymetazoline HCl	ADRA1A	Oxymetazoline hydrochloride is an α1 and α2 adrenergic receptor agonist.
264	DMXAA (Vadimezan)	NQ01	DMXAA (Vadimezan) is a vascular disrupting agents (VDA) and competitive inhibitor of DT-diaphorase with Ki of 20 μM and IC50 of 62.5 μM, respectively. Phase 3.
265	Anacetrapib (MK-0859)	CETP	Anacetrapib (MK0859) is a potent, selective, reversible rhCETP and mutant CETP(C13S) inhibitor with IC50 of 7.9 nM and 11.8 nM, increases HDL-C and decreases LDL-C, does not increase aldosterone or blood pressure. Phase 3.
266	AM1241	CNR2	AM-1241 is a selective cannabinoid CB2 receptor agonist with Ki of 3.4 nM, exhibits 82-fold selectivity over CB1 receptor.
267	Embelin	XIAP	Embelin, a quinone isolated from the Japanese Ardisia herb, is an inhibitor of X-linked inhibitor of apoptosis (XIAP) with IC50 of 4.1 μM.
268	Toremifene Citrate	ESR	Toremifene Citrate is an oral selective estrogen receptor modulator (SERM) which helps oppose the actions of estrogen in the body.
269	GSK2656157	EIF2AK3	GSK2656157 is an ATP-competitive and highly selective inhibitor of PERK with IC50 of 0.9 nM, 500-fold greater against a panel of 300 kinases.
270	Felodipine	CACNA1C	Felodipine is a selective L-type Ca2+ channel blocker with IC50 of 0.15 nM.
271	(+)-Bicuculline	GABR, KCNMA1	(+)-Bicuculline is a competitive antagonist of GABAA receptors with IC50 of 2 μM, also blocks Ca(2+)-activated potassium channels.
272	Ticlopidine HCl	P2RY	Ticlopidine HCl is an P2 receptor inhibitor against ADP-induced platelet aggregation with IC50 of ~2 μM.
273	SANT-1	SMO	SANT-1 directly binds to Smoothened (Smo) receptor with Kd of 1.2 nM and inhibits Smo agonist effects with IC50 of 20 nM.
274	Ispinesib (SB-715992)		Ispinesib (SB-715992, CK0238273) is a potent, specific and reversible inhibitor of kinesin spindle protein (KSP) with Ki app of 1.7 nM, no inhibition to CENP-E, RabK6, MCAK, MKLP1, KHC or Kif1A. Phase 1/2.
275	BTZ043 Racemate		BTZ043 racemate is a decaprenylphosphoryl-β-D-ribose 2'-epimerase (DprE1) inhibitor acting as a new antimycobacterial agent that kill Mycobacterium tuberculosis.
276	AZD7762	CHEK1, CHEK2	AZD7762 is a potent and selective inhibitor of Chk1 with IC50 of 5 nM. It is equally potent against Chk2 and less potent against CAM, Yes, Fyn, Lyn, Hck and Lck. Phase 1.
277	AVL-292	BTK	AVL-292 is a covalent, orally active, and highly selective BTK inhibitor with IC50 of <0.5 nM, displaying at least 1400-fold selectivity over the other kinases assayed. Phase 1.
278	Pimobendan	PDE3	Pimobendan is a selective inhibitor of PDE3 with IC50 of 0.32 μM.
279	DBeQ	VCP	DBeQ is a selective, potent, reversible, and ATP-competitive p97 inhibitor with IC50 of 1.5 μM.
280	Formoterol Hemifumarate	ADRB2	Formoterol hemifumarate is a potent, selective and long-acting β2-adrenoceptor agonist to β2 and β1 receptors with pKd of 8.12 and 5.58, respectively.
281	CNX-774	BTK	CNX-774 is an irreversible, orally active, and highly selective BTK inhibitor with IC50 of <1 nM.
282	Lovastatin	HMGCR	Lovastatin is an inhibitor of HMG-CoA reductase with IC50 of 3.4 nM, used for lowering cholesterol (hypolipidemic agent).
283	4μ8C	ERN1	4μ8C is a potent and selective IRE1 Rnase inhibitor with IC50 of 76 nM.
284	Lafutidine	HRH2	Lafutidine, a newly developed histamine H(2)-receptor antagonist, inhibits gastric acid secretion.
285	AZ191	DYRK1B	AZ191 is a potent and selective DYRK1B inhibitor with IC50 of 17 nM, about 5- and 110-fold selectivity over DYRK1A and DYRK2, respectively.
286	(-)-Parthenolide	MDM2, P53	(-)-Parthenolide is a sesquiterpene lactone which occurs naturally in the plant feverfew (Tanacetum parthenium) and also promotes the ubiquitination of MDM2 and activates p53 cellular functions.
287	JSH-23	NFKB	JSH-23 is an inhibitor of NF-κB transcriptional activity with IC50 of 7.1 μM.
288	Pramipexole	DRD2S,DRD2L, DRD3, DRD4	Pramipexole is a partial/full D2S, D2L, D3, D4 receptor agonist with a Ki of 3.9, 2.2, 0.5 and 5.1 nM for D2S, D2L, D3, D4 receptor, respectively.
289	RepSox	TGFBR1	RepSox is a potent and selective inhibitor of the TGFβR-1/ALK5 with IC50 of 23 nM and 4 nM for ATP binding to ALK5 and ALK5 autophosphorylation, respectively.
290	Bazedoxifene HCl	ESR1, ESR2	Bazedoxifene HCl is a novel, non-steroidal, indole-based estrogen receptor modulator (SERM) binding to both ERα and ERβ with IC50 of 23 nM and 89 nM.
291	Golgicide A	GBF1	Golgicide A is a potent and rapidly reversible GBF1 inhibitor.
292	LDE225 (NVP-LDE225,Erismodegib)	SMO	LDE225 (NVP-LDE225) is a Smoothened (Smo) antagonist, inhibiting Hedgehog (Hh) signaling with IC50 of 1.3 nM (mouse) and 2.5 nM (human), respectively. Phase 3.
293	Ridaforolimus (Deforolimus, MK-8669)	MTOR	Ridaforolimus (Deforolimus) is a selective mTOR inhibitor with IC50 of 0.2 nM; while not classified as a prodrug, mTOR inhibition and FKBP12 binding is similar to rapamycin.

294	LY2784544	JAK2	LY2784544 is a potent JAK2 inhibitor with IC50 of 3 nM, effective in JAK2V617F, 8- and 20-fold selective versus JAK1 and JAK3. Phase 2.
295	SNS-314 Mesylate	AURKA, AURKB, AURKC	SNS-314 Mesylate is a potent and selective inhibitor of Aurora A, Aurora B and Aurora C with IC50 of 9 nM, 31 nM, and 3 nM, respectively. It is less potent to Trk A/B, Flt4, Fms, Axl, c-Raf and DDR2. Phase 1.
296	BGJ398 (NVP-BGJ398)	FGFR1, FGFR2, FGFR3	BGJ398 (NVP-BGJ398) is a potent and selective FGFR inhibitor for FGFR1/2/3 with IC50 of 0.9 nM/1.4 nM/1 nM, >40-fold selective for FGFR versus FGFR4 and VEGFR2, and little activity to Abl, Fyn, Kit, Lck, Lyn and Yes. Phase 2.
297	Irinotecan	TOP1	Irinotecan is a topoisomerase I inhibitor for LoVo cells and HT-29 cells with IC50 of 15.8 μM and 5.17 μM, respectively.
298	OSI-420	EGFR	OSI-420 is the active metabolite of Erlotinib (EGFR inhibitor with IC50 of 2 nM).
299	Dutasteride	SRD5A2, SRD5A1	Dutasteride is a dual 5-α reductase inhibitor that inhibits conversion of testosterone to dihydrotestosterone (DHT).
300	Apigenin	CYP2C9	Apigenin is a potent P450 inhibitor for CYP2C9 with IC50 of 23 pM.
301	Rigosertib (ON-01910)	PLK1, PLK2	Rigosertib (ON-01910) is a non-ATP-competitive inhibitor of PLK1 with IC50 of 9 nM. It shows 30-fold greater selectivity against Plk2 and no activity to Plk3. Phase 3.
302	Forskolin	ADCY4	Forskolin is a ubiquitous activator of eukaryotic adenylyl cyclase (AC), commonly used to raise levels of cAMP in the study and research of cell physiology.
303	Rolipram	PDE4	Rolipram is a PDE4-inhibitor and an anti-inflammatory agent.Phase 1.
304	Bupivacaine HCl	ADCY4	Bupivacaine hydrochloride(Marcain) is a more potent cAMP production inhibitor with an IC50 of 2.3 μM
305	UNC669	L3MBTL1	UNC669 is a potent and selective MBT (malignant brain tumor) inhibitor with IC50 of 6 μM for L3MBTL1, 5- and 11-fold selective over L3MBTL3 and L3MBTL4.
306	Tioxolone	CA1	Tioxolone is a metalloenzyme carbonic anhydrase I inhibitor with a Ki of 91 nM.
307	PF-4708671	RPS6KB1	PF-4708671 is a cell-permeable inhibitor of p70 ribosomal S6 kinase (S6K1 isoform) with Ki/IC50 of 20 nM/160 nM, 400-fold greater selectivity for S6K1 than S6K2, and 4- and >20-fold selectivity for S6K1 than MSK1 and RSK1/2, respectively. First S6K1-specific inhibitor to be reported.
308	5-hydroxymethyl Tolterodine (PNU 200577, 5-HMT, 5-HM)	CHRM1	5-hydroxymethyl tolterodine (PNU 200577) is a new muscarinic receptor antagonist with Kb of 0.84 nM.
309	XAV-939	WNT	XAV-939 selectively inhibits Wnt/β-catenin-mediated transcription through tankyrase1/2 inhibition with IC50 of 11 nM/4 nM, regulates axin levels and does not affect CRE, NF-κB or TGF-β.
310	SB742457	HTR6	SB742457 is a highly selective 5-HT6 receptor antagonist with pKi of 9.63, exhibits >100-fold selectivity over other receptors. Phase 2.
311	Cinacalcet HCl	CASR	AMG-073 represents a new class of compounds for the treatment of hyperparathyroidism.
312	Linagliptin	DPP4	Linagliptin is a highly potent, selective DPP-4 inhibitor with IC50 of 1 nM.
313	Etomidate	GABR	Etomidate is a GABAA receptors agonist at GABAA receptors.
314	Entacapone	COMT	Entacapone inhibits catechol-O-methyltransferase(COMT) with IC50 of 151 nM.
315	AG-14361	PARP1	AG14361 is a potent inhibitor of PARP1 with Ki of <5 nM. It is at least 1000-fold more potent than the benzamides.
316	Moclobemide (Ro 111163)	MAOA	Moclobemide is MAO-A (5-HT) inhibitor with IC50 of 6.1 μM.
317	LY411575	APP, NOTCH	LY411575 is a potent γ-secretase inhibitor with IC50 of 0.078 nM/0.082 nM (membrane/cell-based), also inhibits Notch clevage with withIC50 of 0.39 nM.
318	GDC-0152	XIAP, BIRC7, AP1, AP2	GDC-0152 is a potent antagonist of XIAP-BIR3, ML-IAP-BIR3, cIAP1-BIR3 and cIAP2-BIR3 with Ki of 28 nM, 14 nM, 17 nM and 43 nM, respectively; less affinity shown to cIAP1-BIR2 and cIAP2-BIR2. Phase 1.
319	OC000459	PTGDR2	OC000459 is a potent and selective D prostanoid receptor 2 (DP2) antagonist with IC50 of 13 nM.
320	NLG919	IDO1	NLG919 is a potent IDO (indoleamine-(2,3)-dioxygenase) pathway inhibitor with Ki/EC50 of 7 nM/75 nM.
321	Levosulpiride	DRD2	Levosulpiride is a selective antagonist for D2 dopamine receptors used as an antipsychotic and prokinetic agent.
322	Imatinib (STI571)	ABL1, KIT, PDGFR	Imatinib is a multi-target inhibitor of v-Abl, c-Kit and PDGFR with IC50 of 0.6 μM, 0.1 μM and 0.1 μM, respectively.
323	DCC-2036 (Rebastinib)	ABL1, SRC, LYN, FGR, HCK, KDR, FLT3	DCC-2036 is a conformational control Bcr-Abl inhibitor for Abl1(WT) and Abl1(T315I) with IC50 of 0.8 nM and 4 nM, also inhibits SRC, LYN, FGR, HCK, KDR, FLT3, and Tie-2, and low activity to seen towards c-Kit. Phase 1/2.
324	XL335	NR1H4	XL335 is a potent, selective FXR agonist with EC50 of 4 nM, highly selective versus other nuclear receptors, such as LXR, PPAR, ER and etc. Phase 1.
325	Nilvadipine	CACNA1C	Nilvadipine is a potent calcium channel blocker with an IC50 of 0.03 nM.
326	CHIR-98014	GSK3A, GSK3B	CHIR-98014 is a potent GSK-3α/β inhibitor with IC50 of 0.65 nM/0.58 nM, with the ability to distinguish GSK-3 from its closest homologs Cdc2 and ERK2.
327	GW4064	NR1H4	GW4064 is an agonist of farnesoid X receptor (FXR) with EC50 of 65 nM.
328	PF-5274857	SMO	PF-5274857 is a potent and selective Smoothened (Smo) antagonist, inhibits Hedgehog (Hh) signaling with IC50 and Ki of 5.8 nM and 4.6 nM, respectively, and can penetrate the blood–brain barrier.
329	GDC-0068	AKT1, AKT2, AKT3	GDC-0068 is a highly selective pan-Akt inhibitor targeting Akt1/2/3 with IC50 of 5 nM/18 nM/8 nM, 620-fold selectivity over PKA. Phase 2.

330	JNJ-1661010	FAAH	JNJ-1661010 is a potent and selective FAAH inhibitor with IC50 of 10 nM (rat) and 12 nM (human), exhibits >100-fold selectivity for FAAH-1 when compared to FAAH-2.
331	VU 0364770	GRM4	VU 0364770 is a positive allosteric modulator(PAM) of mGlu4 with EC50 of 1.1 μM, exhibits insignificant activity at 68 other receptors, including other mGlu subtypes.
332	U-104	CA12	U-104 is a potent carbonic anhydrase (CA) inhibitor for CA IX and CA XII with Ki of 45.1 nM and 4.5 nM, respectively, very low inhibition for CA I and CA II.
333	Daunorubicin HCl	TOP2	Daunorubicin HCl inhibits both DNA and RNA synthesis and inhibits DNA synthesis with Ki of 0.02 μM.
334	PF-562271	PTK2	PF-562271 is a potent, ATP-competitive, reversible inhibitor of FAK with IC50 of 1.5 nM, ~10-fold less potent for Pyk2 than FAK and >100-fold selectivity against other protein kinases, except for some CDKs.
335	AZD3463	ALK, IGF1R	AZD3463 is a novel orally bioavailable ALK inhibitor with Ki of 0.75 nM, which also inhibits IGF1R with equivalent potency.
336	IOX2	EGLN1	IOX2 is a potent inhibitor of HIF-1α prolyl hydroxylase-2 (PHD2) with IC50 of 21 nM, >100-fold selectivity over JMJD2A, JMJD2C, JMJD2E, JMJD3, or the 2OG oxygenase FIH.
337	IMD 0354	IKBKB, CHUK	IMD-0354 is an IKKβ inhibitor and blocks IκBα phosphorylation in NF-κB pathway.
338	CRT0044876	APE1	CRT0044876 is a potent and selective APE1 inhibitor with IC50 of ~3 μM.
339	TCID	UCHL3	TCID is a DUB inhibitor for ubiquitin C-terminal hydrolase L3 with IC50 of 0.6 μM, 125-fold selective to L1.
340	LB42708	FNTA	LB42708 is an orally active farnesyltransferase (FTase) inhibitor with IC50 of 0.8, 1.2, and 2.0 nM toward H-ras, N-ras, and K-ras, respectively.
341	Necrostatin-1	RIPK1	Necrostatin-1 is a specific RIP1 inhibitor and inhibits TNF-α-induced necroptosis with EC50 of 490 nM.
342	Empagliflozin (BI 10773)	SLC5A2	Empagliflozin (BI-10773) is a potent and selective SGLT-2 inhibitor with IC50 of 3.1 nM, exhibits >300-fold selectivity over SGLT-1, 4, 5 and 6. Phase 3.
343	SU11274	MET	SU11274 is a selective Met inhibitor with IC50 of 10 nM, no effects on PGDFRβ, EGFR or Tie2.
344	Bortezomib (PS-341)	PSMC1	Bortezomib (PS-341) is a potent 20S proteasome inhibitor with Ki of 0.6 nM.
345	YM155 (Sepantronium Bromide)	BIRC5	YM155 is a potent survivin suppressant by inhibiting Survivin promoter activity with IC50 of 0.54 nM; does not significantly inhibit SV40 promoter activity, but is observed to slightly inhibit the interaction of Survivin with XIAP. Phase 1/2.
346	Lenalidomide (CC-5013)	TNF	Lenalidomide (CC-5013) is a TNF-α secretion inhibitor with IC50 of 13 nM.
347	Ivacaftor (VX-770)	CFTR	Ivacaftor (VX-770) is a potentiator of CFTR targeting G551D-CFTR and F508del-CFTR with EC50 of 100 nM and 25 nM, respectively.
348	AUY922 (NVP-AUY922)	HSP90A, HSP90B	AUY922 (NVP-AUY922) is a highly potent HSP90 inhibitor for HSP90α/β with IC50 of 13 nM /21 nM, weaker potency against the HSP90 family members GRP94 and TRAP-1, exhibits the tightest binding of any small-molecule HSP90 ligand. Phase 1/2.
349	Agomelatine	HTR2C	Agomelatine is classified as a norepinephrine-dopamine disinhibitor (NDDI) due to its antagonism of the 5-HT2C receptor.
350	17-AAG (Tanespimycin)	HSP90	17-AAG is a potent HSP90 inhibitor with IC50 of 5 nM, having a 100-fold higher binding affinity for HSP90 derived from tumour cells than HSP90 from normal cells.
351	SP600125	JKAMP, MAPK9, MAPK10; MAP2K4; MAP2K3, MAP2K6, AKT1, PRKC; MAPK1, MAPK14, CHEK1, EGFR	SP600125 is a broad-spectrum JNK inhibitor for JNK1, JNK2 and JNK3 with IC50 of 40 nM, 40 nM and 90 nM, respectively; 10-fold greater selectivity against MKK4, 25-fold greater selectivity against MKK3, MKK6, PKB, and PKCα, and 100-fold selectivity against ERK2, p38, Chk1, EGFR etc.
352	CEP-18770 (Delanzomib)	PSMC1	CEP-18770 is an orally active inhibitor of the chymotrypsin-like activity of proteasome with IC50 of 3.8 nM, with only marginal inhibition of the tryptic and peptidylglutamyl activities of the proteosome. Phase 1/2.
353	Aprepitant	TACR1	Aprepitant is a potent and selective neurokinin-1 receptor antagonist.
354	Fluvoxamine maleate		Fluvoxamine maleate is a selective serotonin (5-HT) reuptake inhibitor (SSRI).
355	Oligomycin A	ATPAF1	Oligomycin A is an inhibitor of ATP synthase, inhibits oxidative phosphorylation and all the ATP-dependent processes occurring on the coupling membrane of mitochondria.
356	Ginkgolide A	GABR	Ginkgolide A is an extract from in Ginkgo biloba and a g-aminobutyric acid (GABA) antagonist with a Ki of 14.5 μM.
357	Cryptotanshinone	STAT3	Cryptotanshinone (CPT) is a STAT3 inhibitor with IC50 of 4.6 μM, strongly inhibits phosphorylation of STAT3 Tyr705, with a small effect on STAT3 Ser727, but none against STAT1 nor STAT5.
358	ICG-001	WNT	ICG-001 antagonizes Wnt/β-catenin/TCF-mediated transcription and specifically binds to element-binding protein (CBP) with IC50 of 3 μM, but is not the related transcriptional coactivator p300.
359	Stattic	STAT3	Stattic, the first nonpeptidic small molecule, potently inhibits STAT3 activation and nuclear translocation with IC50 of 5.1 μM, highly selectivity over STAT1.
360	SC144	IL6ST	SC144 is an orally active small-molecule gp130 inhibitor.
361	SRPIN340	SRPK1	SRPIN340 is a selective SRPK inhibitor with Ki of 0.89 μM for SRPK1, showing no significant inhibitory activity against more than 140 other kinases.

362	Trelagliptin	DPP4	Trelagliptin is a highly selective, long-acting DPP-4 inhibitor. Phase 3.
363	Panobinostat (LBH589)	HDAC	Panobinostat (LBH589) is a novel broad-spectrum HDAC inhibitor with IC50 of 5 nM. Phase 3.
364	VX-680 (Tozasertib, MK-0457)	AURKA	VX-680 (Tozasertib, MK-0457) is a pan-Aurora inhibitor, mostly against Aurora A with Kiapp of 0.6 nM, less potent towards Aurora B/Aurora C and 100-fold more selective for Aurora A than 55 other kinases. Phase 2.
365	GDC-0941	PIK3CA, PIK3CD	GDC-0941 is a potent inhibitor of PI3Kα/δ with IC50 of 3 nM, with modest selectivity against p110β (11-fold) and p110γ (25-fold).
366	OSU-03012 (AR-12)	PDK1	OSU-03012 is a potent inhibitor of recombinant PDK-1 with IC50 of 5 μM and 2-fold increase in potency over OSU-02067.
367		Akt1, PKCη, PKCθ, PrkX, Akt3, Akt2, PKCδ, PKCβ, PKCε, PKA, PKG1β	GSK690693 is a pan-Akt inhibitor targeting Akt1/2/3 with IC50 of 2 nM/13 nM/9 nM in cell-free assays, also sensitive to the AGC kinase family: PKA, PrkX and PKC isozymes. Phase 1.
368	Everolimus (RAD001)	MTOR	Everolimus (RAD001) is an mTOR inhibitor of FKBP12 with IC50 of 1.6-2.4 nM.
369	MK-8245	SCD	MK-8245 is a liver-targeting inhibitor of stearoyl-CoA desaturase (SCD) with IC50 of 1 nM for human SCD1 and 3 nM for both rat SCD1 and mouse SCD1, with anti-diabetic and anti-dyslipidemic efficacy. Phase 2.
370	Aniracetam	GRIA1,	Aniracetam is a nootropics and neuroprotective drug.
371	Doxazosin Mesylate	ADRA1A	Doxazosin mesylate is an alpha-1 adrenergic receptor blocker.
372	Ginkgolide B	PTAFR	Ginkgolide B is a PAFR antagonist with IC50 of 3.6 μM.
373	Tosedostat (CHR2797)	LAP3, NPEPPS, ANPEP	CHR-2797 is an aminopeptidase inhibitor for LAP, PuSA and Aminopeptidase N with IC50 of 100 nM, 150 nM and 220 nM, respectively, and does not effectively inhibit either PILSAP, MetAP-2, LTA4 hydrolase, or MetAP-2. Phase 2.
374	Rebamipide	CCKAR	Rebamipide is a cholecystokinin type 1 (CCK1) receptor inhibitor for inhibiting [125I]BH-CCK-8S with IC50 of 37.7 μM.
375	Rasagiline Mesylate	MAOB	Rasagiline Mesylate is a new MAO-B inhibitor for the treatment of idiopathic Parkinson's disease.
376	PD128907 HCl	DDR3	PD 128907 HCl is a potent and selective dopamine D3 receptor agonist, with EC50 of 0.64 nM, exhibits 53-fold selectivity over dopamine D2 receptor.
377	Apatinib	KDR	Apatinib is an orally bioavailable, selective VEGFR2 inhibitor with IC50 of 1 nM.
378	ADX-47273	GRM5	ADX47273 is a potent and specific mGlu5 positive allosteric modulator(PAM) with EC50 of 0.17 μM, showing no activity at other mGlu subtypes.
379	AZ 3146	TTK, CENPE	AZ3146 is a selective Mps1 inhibitor with IC50 of ~35 nM, contributes to recruitment of CENP-E (kinesin-related motor protein), less potent to FAK, JNK1, JNK2, and Kit.
380	VU 0357121	GRM5	VU0357121 is a novel positive allosteric modulator (PAM) of mGlu5 with EC50 of 33 nM, is inactive or very weakly antagonizing at other mGlu receptor subtypes.
381	(-)-MK 801 Maleate	GRIN	MK-801 is a potent, selective and non-competitive NMDA receptor antagonist with Kd of 37.2 nM in rat brain membranes.
382	Mirabegron	ADRB3	Mirabegron is a selective β3-adrenoceptor agonist with EC50 of 22.4 nM.
383	AP26113	ALK	AP26113 is a potent ALK inhibitor with IC50 of 0.62 nM, demonstrated ability overcome Crizotinib resistance mediated by a L1196M mutation. Phase 1/2.
384	Birinapant	DIABLO (AP1)	Birinapant is a SMAC mimetic antagonist, mostly to cIAP1 with Kd of <1 nM, less potent to XIAP. Phase 1/2.
385	AZD1981	PTGDR2	AZD1981 is a potent, selective CRTh2 (DP2) receptor antagonist with IC50 of 4 nM, showing >1000-fold selectivity over more than 340 other enzymes and receptors, including DP1.
386	LDK378	ALK	LDK378 is potent inhibitor against ALK with IC50 of 0.2 nM, shows 40- and 35-fold selectivity against IGF-1R and InsR, respectively. Phase 2.
387	(S)-crizotinib	NUDT1	(S)-crizotinib, the (S)-enantiomer of crizotinib, is a potent MTH1 (NUDT1) inhibitor with IC50 of 72 nM.
388	ZM 447439	AURKA, AURKB	ZM 447439 is a selective and ATP-competitive inhibitor for Aurora A and Aurora B with IC50 of 110 nM and 130 nM, respectively. It is more than 8-fold selective for Aurora A/B than MEK1, Src, Lck and has little effect againstCDK1/2/4, Plk1, Chk1, etc.
389	BX-912	PDK1	BX912 is a potent and specific PDK1 inhibitor with IC50 of 12 nM, 9- and 105- fold greater selectivity for PDK1 than PKA and PKC, respectively. In comparison to GSK3β, selectivity for PDK1 is 600-fold.
390	Tadalafil	PDE5	Tadalafil is a PDE-5 inhibitor with IC50 of 1.8 nM.
391	Elvitegravir (GS-9137, JTK-303)		Elvitegravir (EVG, JTK-303/GS-9137) is an HIV integrase inhibitor for HIV-1 IIIB, HIV-2 EHO and HIV-2 ROD with IC50 of 0.7 nM, 2.8 nM and 1.4 nM, respectively.
392	Fostamatinib (R788)	SYK	Fostamatinib (R788), a prodrug of the active metabolite R406, is a Syk inhibitor with IC50 of 41 nM, strongly inhibits Syk but not Lyn, 5-fold less potent to Flt3. Phase 2.
393	GSK J4 HCl	KDM6A, KDM6B	GSK J4 HCl is a cell permeable prodrug of GSK J1, which is the first selective inhibitor of the H3K27 histone demethylase JMJD3 and UTX with IC50 of 60 nM and inactive against a panel of demethylases of the JMJ family.
394	TCS 359	FLT3	TCS 359 is a potent FLT3 inhibitor with IC50 of 42 nM.
395	Carvedilol	ADRB1	Carvedilol is a non-selective beta blocker/alpha-1 blocker with an IC50 of 3.8 μM for inhibition of LDL oxidation.
396	Naftopidil	ADRA1A	Naftopidil (Flivas) is a selective α1-adrenergic receptor antagonist or alpha blocker with a Ki of 58.3 nM.

397	ML133 HCl	KCNJ2	ML133 is a selective potassium channel inhibitor for Kir2.1 with IC50 of 1.8 μM (pH 7.4) and 290 nM (pH 8.5), has no effect on Kir1.1 and weak activity for Kir4.1 and Kir7.1.
398	T0070907	PPARG	T0070907 is a potent and selective PPARγ inhibitor with IC50 of 1 nM, with a >800-fold selectivity over PPARα and PPARδ.
399	Gliquidone	KCNJ	Gliquidone is an ATP-sensitive K+ channel antagonist with IC50 of 27.2 nM.
400	SC-514	IKBKB	SC-514 is an orally active, ATP-competitive IKK-2 inhibitor with IC50 of 3-12 μM, blocks NF-κB-dependent gene expression, does not inhibit other IKK isoforms or other serine-threonine and tyrosine kinases.
401	ZCL278	CDC42	ZCL278 is a selective Cdc42 GTPase inhibitor with Kd of 11.4 μM.
402	Caffeic Acid Phenethyl Ester	NFKB	Caffeic acid phenethyl ester is a potent and specific inhibitor of NF-κB activation, and also displays antioxidant, immunomodulatory and antiinflammatory activities.
403	VU 0364439	GRM4	VU 0364439 is a mGlu4 positive allosteric modulator (PAM), with EC50 of 19.8 nM.
404	SB431542	TGFBR1	SB431542 is a potent and selective inhibitor of ALK5 with IC50 of 94 nM, 100-fold more selective for ALK5 than p38 MAPK and other kinases.
405	Odanacatib (MK-0822)	CTSK	Odanacatib (MK 0822) is a potent, selective, and neutral inhibitor of cathepsin K (human/rabbit) with IC50 of 0.2 nM/1 nM, and demonstrated high selectivity versus off-target cathepsin B, L, S. Phase 3.
406	Celecoxib	PTGS2	Celecoxib is a selective COX-2 inhibitor with IC50 of 40 nM.
407	Etodolac	PTGS1	Etodolac (Lodine) is a COX inhibitor with an IC50 of 53.5 nM.
408	Isotretinoin		It was developed to be used as a chemotherapy medication for the treatment of brain cancer, pancreatic cancer and more.
409	Stavudine (d4T)		Stavudine is a nucleoside analog reverse transcriptase inhibitor (NARTI) active against HIV.
410	VX-745	MAPK14	VX-745 is a potent and selective inhibitor of p38α with IC50 of 10 nM, 22-fold greater selectivity versus p38β and no inhibition to p38γ.
411	GSK429286A	ROCK1, ROCK2	GSK429286A is a selective inhibitor of ROCK1 and ROCK2 with IC50 of 14 nM and 63 nM, respectively.
412	SB408124	HCRTR1	SB408124 (Tocris-1963) is a non-peptide antagonist for OX1 receptor with Ki of 57 nM and27 nM in both whole cell and membrane, respectively, exhibits 50-fold selectivity over OX2 receptor.
413	H 89 2HCl	PRKAC	H 89 2HCl is a potent PKA inhibitor with Ki of 48 nM, 10-fold selective for PKA than PKG, greater than 500-fold selectivity than PKC, MLCK, calmodulin kinase II and casein kinase I/II.
414	Mubritinib (TAK 165)	ERBB2	Mubritinib (TAK-165) is a potent inhibitor of HER2/ErbB2 with IC50 of 6 nM; no activity to EGFR, FGFR, PDGFR, JAK1, Src and Blk.
415	BMS-378806	CD4	BMS-378806 selectively inhibits the binding of HIV-1 gp120 to the CD4receptor with EC50 of 0.85-26.5 nM in virus.
416	Ki16198	LPAR1, LPAR3	Ki16198 is the methyl ester of Ki16425, which is a LPA antagonist and inhibits LPA1- and LPA3-induced inositol phosphate production with Ki of 0.34 μM and 0.93 μM, respectively, shows weaker inhibition for LPA2, no activity at LPA4, LPA5, LPA6.
417	AZ20	ATR	AZ20 is a novel potent and selective inhibitor of ATR kinase with IC50 of 5 nM, 8-fold selectivity over mTOR.
418	AMG-517	TRPV1	AMG 517 is a potent and selective TRPV1 antagonist, antagonizes capsaicin, proton, and heat activation of TRPV1 with IC50 of 0.76 nM, 0.62 nM and 1.3 nM.
419	NMS-873	VCP	NMS-873 is an allosteric and specific p97 inhibitor with IC50 of 30 nM.
420	Sorafenib	RAF1, BRAF, KDR	Sorafenib is a multikinase inhibitor of Raf-1, B-Raf and VEGFR-2 with IC50 of 6 nM, 22 nM and 90 nM, respectively.
421	NH125	EEF2K, PRKC, PRKA, CAMK2, Histidine Kinase	NH125 is a selective eEF-2 kinase inhibitor with IC50 of 60 nM, >125-fold selectivity over PKC, PKA, and CaMKII, and also a potent histidine kinase inhibitor.
422	Sal003	EIF2A	Sal003 is a potent and cell-permeable eIF-2α phosphatase inhibitor.
423	Tariquidar	ABCB1	Tariquidar (XR9576) is a potent and selective noncompetitive inhibitor of P-glycoprotein with Kd of 5.1 nM, reverses drug resistance in MDR cell Lines. Phase 3.
424	Lomeguatrib	MGMT	Lomeguatrib is a potent inhibitor of O6-alkylguanine-DNA-alkyltransferase with IC50 of 5 nM.
425	BI 2536	PLK1, PLK2, PLK3	BI2536 is a potent Plk1 inhibitor with IC50 of 0.83 nM. It shows 4- and 11-fold greater selectivity against Plk2 and Plk3. Phase 2.
426	Imidapril HCl	ACE	Imidapril HCl is a angiotensin-converting enzyme (ACE) inhibitor with IC50 of 2.6 nM, used for the treatment of hypertension.
427	GSK461364	PLK1, PLK2, PLK3	GSK461364 inhibits purified Plk1 with Ki of 2.2 nM. It is more than 1000-fold selective against Plk2/3. Phase 1.
428	Gliclazide	KCNJ	Gliclazide (Diamicron) is a whole-cell beta-cell ATP-sensitive potassium currents blocker with an IC50 of 184 ± 30 nM.
429	Sotrastaurin	PRKC (especially PRKCQ; inactive to PRKCZ)	Sotrastaurin is a potent and selective pan-PKC inhibitor, mostly for PKCθ with Ki of 0.22 nM; inactive to PKCζ. Phase 1/2.
430	BI-D1870	RPS6KA1, RPS6KA2,	BI-D1870 is an ATP-competitive inhibitor of S6 ribosome for RSK1/2/3/4 with IC50 of 31 nM/24 nM/18 nM/15 nM, respectively; 10- to 100-fold selectivity for RSK than MST2, GSK-3β, MARK3, CK1 and Aurora B.

		RPS6KA3, RPS6KA4	
431	Go 6983	PRKCA, PRKCB, PRKCG, PRKCD	Go 6983 is a pan-PKC inhibitor against for PKCα, PKCβ, PKCγ and PKCδ with IC50 of 7 nM, 7 nM, 6 nM and 10 nM, respectively; less potent to PKCζ and inactive to PKCμ.
432	MNS (3,4-Methylenedioxy-β-nitrostyrene, MDBN)	SYK, SRC, VCP	MNS is a tyrosine kinases inhibitor, inhibits Syk, Src, p97 with IC50 of 2.5 μM, 29.3 μM and 1.7 μM, respectively.
433	THZ1	CDK7	THZ1 uses a unique mechanism, combining ATP-site and allosteric covalent binding, as a means of attaining potency and selectivity for CDK7. THZ1 irreversibly inhibits RNAPII CTD phosphorylation by covalently targeting a unique cysteine located outside the kinase domain of CDK7. THZ1, but not THZ1-R, completely inhibits the phosphorylation of the established intracellular CDK7 substrate RNAPII CTD at Ser 5 and Ser 7, with concurrent loss of Ser 2 phosphorylation at 250 nM in Jurkat cells. THZ1 exhibits strong antiproliferative effects across a broad range of cancer cell lines from various cancer types. In Jurkat cells, low-dose THZ1 has a profound effect on a small subset of genes, including the key regulator RUNX1, thus contributing to subsequent loss of the greater gene expression program and cell death. THZ1 causes defects in Pol II(polymerase II) phosphorylation, co-transcriptional capping, promoter proximal pausing, and productive elongation.

Table S3. Compounds killing >50% of 2 representative T-ALL PDTX cells in RPMI or StemSpan (SS) media supplemented with interleukins.

PDTX 3053-T7

RPMI		**SS**	
398 compounds		**145 compounds**	
Compound	**Target**	**Compound**	**Target**
FG-4592	EPAS1, EPO	FG-4592	EPAS1, EPO
Tolfenamic Acid	PTGS2	Rizatriptan Benzoate	HTR1A
Ramelteon	MTNR1A, MTNR1B	Fulvestrant	ESR
Trospium chloride	CHRM1	Tolfenamic Acid	PTGS2
A-769662	PRKAA1	Ramelteon	MTNR1A, MTNR1B
Losartan Potassium (DuP 753)	AGTR	Trospium chloride	CHRM1
Tolazoline HCl	ADRA1A	Granisetron HCl	HTR3A
Tenofovir Disoproxil Fumarate	0	A-769662	PRKAA1
Ataluren (PTC124)	CFTR	Losartan Potassium (DuP 753)	AGTR
Candesartan	AGTR	Tolazoline HCl	ADRA1A
Belinostat (PXD101)	HDAC	Tenofovir Disoproxil Fumarate	0
Semagacestat (LY450139)	APP, NOTCH	Ataluren (PTC124)	CFTR
NVP-ADW742	IGFR1	Candesartan	AGTR
NSC 319726	TP53 (R175)	Belinostat (PXD101)	HDAC
STF-118804	NAMPT	Semagacestat (LY450139)	APP, NOTCH
Rimonabant	CNR1	NVP-ADW742	IGFR1
FLI-06	NOTCH	NSC 319726	TP53 (R175)
Sitaxentan sodium	EDNRA	Icotinib	EGFR
ABT-263 (Navitoclax)	BCL2, BCL2L1, BCL2L2	Ilomastat (GM6001, Galardin)	MMP1, MMP2, MMP3, MMP7, MMP8, MMP9, MMP12, MMP14, MMP26
Brinzolamide	CA2	Rivaroxaban	F10
Nilotinib (AMN-107)	ABL1	STF-118804	NAMPT
Tranylcypromine (2-PCPA) HCl	MAO, CYP2A6	Rimonabant	CNR1
Tandutinib (MLN518)	FLT3, PDGFR KIT	FLI-06	NOTCH
Zebularine	DNMT1, DNMT3A, DNMT3B	Sitaxentan sodium	EDNRA
MLN8054	AURKA	ABT-263 (Navitoclax)	BCL2, BCL2L1, BCL2L2
PR-619	ATXN7L3, BAP1, OTUB1,OTUD1, OTUD6A, OTUDB7A, UBB, UCHL3, USP1-2-4-5-7-8-14-15-17-26-30-366, YOD1	Brinzolamide	CA2
Roxatidine Acetate HCl	HRH2	Tandutinib (MLN518)	FLT3, PDGFR KIT
GSK1904529A	IGFR1, INSR	MLN8054	AURKA
Atorvastatin Calcium	HMGCR	PR-619	ATXN7L3, BAP1, OTUB1, OTUD1, OTUD6A, OTUDB7A, UBB, UCHL3, USP1, USP2, USP4, USP5, USP7, USP8, USP14,

			USP15, USP17, USP26, USP30, USP36, YOD1
SNS-032 (BMS-387032)	CDK2	Roxatidine Acetate HCl	HRH2
Naltrexone HCl	OPRK1, OPRM1, OPRD1	GSK1904529A	IGFR1, INSR
Ganetespib (STA-9090)	HSP90	Atorvastatin Calcium	HMGCR
CGS 21680 HCl	ADORA2A	SNS-032 (BMS-387032)	CDK2
Vemurafenib (PLX4032, RG7204)	BRAF (V600E)	Vemurafenib (PLX4032, RG7204)	BRAF (V600E)
Pancuronium dibromide	0	Pancuronium dibromide	0
Loratadine	HRH1	Loratadine	HRH1
PNU-120596	0	PNU-120596	0
Ruxolitinib (INCB018424)	JAK1, JAK2	AZD6482	PIK3CB
GW3965 HCl	NR1H3, NR1H2	Safinamide Mesylate	MAOB, MAOA
AZD6482	PIK3CB	Tenofovir	0
SB705498	TRPV1	P22077	USP7, USP47
Safinamide Mesylate	MAOB, MAOA	Aloxistatin	0
Tenofovir	0	Irinotecan HCl Trihydrate	TOP1
P22077	USP7, USP47	Ferrostatin-1 (Fer-1)	VDAC
Aloxistatin	0	OTX015	BRD2, BRD3, BRD4
NSC697923	UBE2	Ibrutinib (PCI-32765)	BTK
Apixaban	F10	4E1RCat	EIF4E
ML347	ACVR1, ACVRL1	Tofacitinib (CP-690550,Tasocitinib)	JAK3
Irinotecan HCl Trihydrate	TOP1	PHA-793887	CDK2, CDK5, CDK7
SSR128129E	FGFR1	WZ811	CXCR4
VX-765	CASP1	HC-030031	TRPA1
Ferrostatin-1 (Fer-1)	VDAC	Telmisartan	AGTR
Rotundine	DRD1	Cyproterone Acetate	AR
MM-102	KANSL1	Sodium 4-Aminosalicylate	NFKB
PF-3845	FAAH	GSK1292263	GPR119
OTX015	BRD2, BRD3, BRD4	SGC 0946	DOT1L
Ibrutinib (PCI-32765)	BTK	LY2157299	TGFBR1
4E1RCat	EIF4E	IPA-3	PAK1
Tofacitinib (CP-690550,Tasocitinib)	JAK3	Esomeprazole Sodium	ATP4A
PHA-793887	CDK2, CDK5, CDK7	Ozagrel	TBXA2R
WZ811	CXCR4	AZD4547	FGFR1, FGFR2, FGFR3
Allopurinol	HCRTR1, HCRTR2	GNF-2	ABL1
HC-030031	TRPA1	TPCA-1	IKBKB
Telmisartan	AGTR	T0901317	NR1H3, NR1H2, NR1H4
Mozavaptan	AVPR1, AVPR2	PYR-41	UBA1
Cyproterone Acetate	AR	LDN-212854	ACVR1, ACVRL1
Sodium 4-Aminosalicylate	NFKB	Ki16425	LPAR1, LPAR2, LPAR3
GSK1292263	GPR119	Oxcarbazepine	SCN
SGC 0946	DOT1L	MRS 2578	P2RY6

LY2157299	TGFBR1	AGI-5198	IDH1
IPA-3	PAK1	BTB06584	ATP5A1
Esomeprazole Sodium	ATP4A	Dalcetrapib (JTT-705, RO4607381)	CETP
DMH1	ACVR1	Iniparib (BSI-201)	PARP1
Ozagrel	TBXA2R	Vildagliptin (LAF-237)	DPP4
AZD4547	FGFR1, FGFR2, FGFR3	Dynasore	DNM1, DNM2
GW9508	FFAR1, FFAR4	Piceatannol	SYK
VE-821	ATR	Quizartinib (AC220)	FLT3
NSC 405020	MMP14	Enzastaurin (LY317615)	PRKCB, PRKCA, PRKCG, PRKCE
GNF-2	ABL1	Anastrozole	CYP19A1
TPCA-1	IKBKB	SB743921	0
T0901317	NR1H3, NR1H2, NR1H4	SN-38	TOP1
PD0325901	MAP2K1, MAP2K2	Wnt-C59 (C59)	WNT3A
PYR-41	UBA1	BAM7	BAX
U0126-EtOH	MAP2K1, MAP2K2	(+)-JQ1	BRD4
LDN-212854	ACVR1, ACVRL1	KPT-185	XPO1
Ki16425	LPAR1, LPAR2, LPAR3	OG-L002	KDM1A
C646	EP300	MK-1775	WEE1
Oxcarbazepine	SCN	AT101	BCL2, BCL2L1, MCL1
Mdivi-1	DRP1, DNM1	BMS-707035	0
MRS 2578	P2RY6	Ouabain	ATP1B
AGI-5198	IDH1	Fluvastatin Sodium	HMGCR
LY2603618	CHEK1	Propranolol HCl	ADRB1
BTB06584	ATP5A1	KPT-276	XPO1
NPS-2143	CASR	KPT-330	XPO1
Veliparib (ABT-888)	PARP1, PARP2	Exemestane	CYP19A1
Dalcetrapib (JTT-705, RO4607381)	CETP	Palbociclib (PD-0332991) HCl	CDK4, CDK6
Vandetanib (ZD6474)	KDR	EHop-016	RAC1, RAC3
Istradefylline	ADORA2A	SGI-1776 free base	PIM1, FLT3, GSG2
Iniparib (BSI-201)	PARP1	KX2-391	SRC
Dabrafenib (GSK2118436)	BRAF (V600)	Enzalutamide (MDV3100)	AR
Finasteride	SRD5A2	PD184352 (CI-1040)	MAP2K1, MAP2K2
Tyrphostin AG 879	ERBB2	OSI-906 (Linsitinib)	IGFR1, INSR
Cilomilast	PDE4	Methotrexate	DHFR
TAE226 (NVP-TAE226)	PTK2, PTK2B	Pralatrexate	DHFR
Ozagrel HCl	TBXAS1	Enalaprilat Dihydrate	ACE
Vildagliptin (LAF-237)	DPP4	Trichostatin A (TSA)	ALL HDACS (Except HDAC8)
Dynasore	DNM1, DNM2	WZ4003	NUAK1, NUAK2
Piceatannol	SYK	MLN2238	PSMC1
Quizartinib (AC220)	FLT3	Ispinesib (SB-715992)	0
Tenovin-6	TP53, SIRT2, SIRT1, SIRT3	SNS-314 Mesylate	AURKA, AURKB, AURKC
Enzastaurin (LY317615)	PRKCB, PRKCA, PRKCG, PRKCE	Irinotecan	TOP1
CGP 57380	MKNK1	Rigosertib (ON-01910)	PLK1, PLK2

Bisoprolol fumarate	ADRB1	Rolipram	PDE4
Bosutinib (SKI-606)	SRC, ABL1	Bupivacaine HCl	ADCY4
S3I-201	STAT3	UNC669	L3MBTL1
HA14-1	BCL2	Entacapone	COMT
TG100-115	PIK3CG, PIK3CD	AG-14361	PARP1
ADL5859 HCl	OPRK1, OPRM1	NLG919	IDO1
Voriconazole	CYP51A1	Levosulpiride	DRD2
BIBR 1532	TERT	Daunorubicin HCl	TOP2
Thiazovivin	ROCK1, ROCK2	IMD 0354	IKBKB, CHUK
Anastrozole	CYP19A1	CRT0044876	APE1
EUK 134	SOD1	TCID	UCHL3
Bergenin	0	LB42708	FNTA
SN-38	TOP1	Bortezomib (PS-341)	PSMC1
CP-91149	PYGL, PYGM, PYGB	YM155 (Sepantronium Bromide)	BIRC5
Wnt-C59 (C59)	WNT3A	Agomelatine	HTR2C
NU7026	PRKDC	CEP-18770 (Delanzomib)	PSMC1
BAM7	BAX	Oligomycin A	ATPAF1
ZM 306416	FLT1	ICG-001	WNT
(+)-JQ1	BRD4	Stattic	STAT3
GW9662	PPARG	SC144	IL6ST
KPT-185	XPO1	Panobinostat (LBH589)	HDAC
Pifithrin-μ	TP53, HSPBP1	VX-680 (Tozasertib, MK-0457)	AURKA
Batimastat (BB-94)	MMP1, MMP2, MMP3, MMP7, MMP9	Birinapant	DIABLO (AP1)
Sertraline HCl	0	Tadalafil	PDE5
OG-L002	KDM1A	GSK J4 HCl	KDM6A, KDM6B
MK-1775	WEE1	ZCL278	CDC42
Costunolide	TERT	Stavudine (d4T)	0
AT101	BCL2, BCL2L1, MCL1	Mubritinib (TAK 165)	ERBB2
GSK690693	AKT1, AKT2, AKT3	AZ20	ATR
Tropicamide	CHRM4	NMS-873	VCP
BMS-707035	0	NH125	EEF2K, PRKC, PRKA, CAMK2, Histidine Kinase
Raltegravir (MK-0518)	0	BI 2536	PLK1, PLK2, PLK3
EX 527 (Selisistat)	SIRT1	GSK461364	PLK1, PLK2, PLK3
CCT128930	AKT2		
Pomalidomide	TNF		
AS-252424	PIK3CG		
Tie2 kinase inhibitor	TEK		
Ouabain	ATP1B		
Ranitidine	HRH2		
SKI II	S1PR		
Fluvastatin Sodium	HMGCR		
Propranolol HCl	ADRB1		
Erastin	VDAC		

Ifenprodil Tartrate	GRIN	
KPT-276	XPO1	
AZD2461	PARP	
KPT-330	XPO1	
AGI-6780	IDH2	
SGI-1027	DNMT1, DNMT3A, DNMT3B	
Atglistatin	PNPLA2	
Suvorexant (MK-4305)	HCRTR1, HCRTR2	
SRT1720	SIRT1	
4EGI-1	EIF4E	
Exemestane	CYP19A1	
NSC 23766	RAC	
2-Methoxyestradiol (2-MeOE2)	HIF1A	
Palbociclib (PD-0332991) HCl	CDK4, CDK6	
EHop-016	RAC1, RAC3	
PF-573228	PTK2	
ABT-199 (GDC-0199)	BCL2	
Memantine HCl	CYP2B6	
PTC-209	BMI1	
Trimebutine	OPRK1, OPRM1, OPRD1	
CK-636	ARPC2, ARPC3	
SGI-1776 free base	PIM1, FLT3, GSG2	
AZD7545	PDK1, PDK2	
URB597	FAAH	
GW0742	PPARD	
TAK-875	FFAR1	
Pacritinib (SB1518)	JAK2, FLT3	
KX2-391	SRC	
PluriSIn #1 (NSC 14613)	SCD	
Crenolanib (CP-868596)	PDGFRA, PDGFRB, FLT3 (D842V)	
Enzalutamide (MDV3100)	AR	
PFI-1 (PF-6405761)	BRD4	
Dapagliflozin	SLC5A2	
Maraviroc	CCR5	
Nebivolol	ADRB1	
I-BET151 (GSK1210151A)	BRD2, BRD3, BRD4	
VX-809 (Lumacaftor)	CFTR	
Apoptosis Activator 2	CASP3	
Naproxen	PTGS1, PTGS2	
Bosentan Hydrate	EDNRA, EDNRB	
Acadesine	PRKAA1	
E-64	CTSK	
Captopril	ACE	
Selumetinib (AZD6244)	MAP2K1, MAPK3, MAPK1	

Tolvaptan	AVPR2	
PD184352 (CI-1040)	MAP2K1, MAP2K2	
OSI-906 (Linsitinib)	IGFR1, INSR	
Canagliflozin	SLC5A2	
CP-673451	PDGFRA, PDGFRB	
Sirtinol	SIRT1, SIRT2	
Methotrexate	DHFR	
SAR131675	FLT4	
Pralatrexate	DHFR	
BML-190	CNR2	
TWS119	GSK3B	
IKK-16 (IKK Inhibitor VII)	IKBKB, CHUK	
Enalaprilat Dihydrate	ACE	
Triamterene	SCN	
Clemastine Fumarate	HRH1	
Fingolimod (FTY720) HCl	S1PR	
Amlodipine	CACNA1C	
PP2	SRC	
CHIR-124	CHEK1	
Temsirolimus (CCI-779, NSC 683864)	MTOR	
YO-01027	APP, APPL1, NOTCH	
Trichostatin A (TSA)	ALL HDACS (Except HDAC8)	
PAC-1	CASP3	
PHA-665752	MET	
VE-822	ATR	
SB203580	MAPK11, MAPK12, MAPK13, MAPK14	
EPZ-6438	EZH2	
KU-55933 (ATM Kinase Inhibitor)	ATM	
CGK 733	ATM, ATR	
WZ4002	EGFR	
WZ4003	NUAK1, NUAK2	
TAK-700 (Orteronel)	CYP17A1	
Loxistatin Acid (E-64C)	0	
Zibotentan (ZD4054)	EDNRA	
Pyrimethamine	DHFR	
RKI-1447	ROCK1, ROCK2	
UNC2250	MERTK	
SMI-4a	PIM1	
SB415286	GSK3A	
PRT062607 (P505-15, BIIB057) HCl	SYK	
Torcetrapib	CETP	
MK-2206 2HCl	AKT1, AKT2, AKT3	
ML130 (Nodinitib-1)	NOD1	
PF-04217903	MET	

GW441756	NTRK1	
Varespladib (LY315920)	PLA2G2A	
ML161	PARP1	
MK-2866 (GTx-024)	AR	
Ticagrelor	P2RY12	
Letrozole	CYP19A1	
GW2580	CSF1R	
Zosuquidar (LY335979) 3HCl	ABCB1	
KU-60019	ATM	
LY2228820	MAPK11, MAPK12, MAPK13, MAPK14	
MLN2238	PSMC1	
Org 27569	CNR1	
Oxymetazoline HCl	ADRA1A	
DMXAA (Vadimezan)	NQ01	
Anacetrapib (MK-0859)	CETP	
AM1241	CNR2	
Embelin	XIAP	
Toremifene Citrate	ESR	
GSK2656157	EIF2AK3	
Felodipine	CACNA1C	
(+)-Bicuculline	GABR, KCNMA1	
Ticlopidine HCl	P2RY	
SANT-1	SMO	
Ispinesib (SB-715992)	0	
BTZ043 Racemate	0	
AZD7762	CHEK1, CHEK2	
AVL-292	BTK	
Pimobendan	PDE3	
DBeQ	VCP	
Formoterol Hemifumarate	ADRB2	
CNX-774	BTK	
Lovastatin	HMGCR	
4μ8C	ERN1	
Lafutidine	HRH2	
AZ191	DYRK1B	
(-)-Parthenolide	MDM2, P53	
JSH-23	NFKB	
Pramipexole	DRD2S,DRD2L, DRD3, DRD4	
RepSox	TGFBR1	
Bazedoxifene HCl	ESR1, ESR2	
Golgicide A	GBF1	
LDE225 (NVP-LDE225,Erismodegib)	SMO	
Ridaforolimus (Deforolimus, MK-8669)	MTOR	

LY2784544	JAK2	
SNS-314 Mesylate	AURKA, AURKB, AURKC	
BGJ398 (NVP-BGJ398)	FGFR1, FGFR2, FGFR3	
Irinotecan	TOP1	
OSI-420	EGFR	
Dutasteride	SRD5A2, SRD5A1	
Apigenin	CYP2C9	
Rigosertib (ON-01910)	PLK1, PLK2	
Forskolin	ADCY4	
Rolipram	PDE4	
Bupivacaine HCl	ADCY4	
UNC669	L3MBTL1	
Tioxolone	CA1	
PF-4708671	RPS6KB1	
5-hydroxymethyl Tolterodine (PNU 200577, 5-HMT, 5-HM)	CHRM1	
XAV-939	WNT	
SB742457	HTR6	
Cinacalcet HCl	CASR	
Linagliptin	DPP4	
Etomidate	GABR	
Entacapone	COMT	
AG-14361	PARP1	
Moclobemide (Ro 111163)	MAOA	
LY411575	APP, NOTCH	
GDC-0152	XIAP, BIRC7, AP1, AP2	
OC000459	PTGDR2	
NLG919	IDO1	
Levosulpiride	DRD2	
Imatinib (STI571)	ABL1, KIT, PDGFR	
DCC-2036 (Rebastinib)	ABL1, SRC, LYN, FGR, HCK, KDR, FLT3	
XL335	NR1H4	
Nilvadipine	CACNA1C	
CHIR-98014	GSK3A, GSK3B	
GW4064	NR1H4	
PF-5274857	SMO	
GDC-0068	AKT1, AKT2, AKT3	
JNJ-1661010	FAAH	
VU 0364770	GRM4	
U-104	CA12	
Daunorubicin HCl	TOP2	
PF-562271	PTK2	
AZD3463	ALK, IGFR1	
IOX2	EGLN1	
IMD 0354	IKBKB, CHUK	

CRT0044876	APE1	
TCID	UCHL3	
LB42708	FNTA	
Necrostatin-1	RIPK1	
Empagliflozin (BI 10773)	SLC5A2	
SU11274	MET	
Bortezomib (PS-341)	PSMC1	
YM155 (Sepantronium Bromide)	BIRC5	
Lenalidomide (CC-5013)	TNF	
Ivacaftor (VX-770)	CFTR	
Agomelatine	HTR2C	
17-AAG (Tanespimycin)	HSP90	
SP600125	JKAMP, MAPK9, MAPK10; MAP2K4; MAP2K3, MAP2K6, AKT1, PRKC; MAPK1, MAPK14, CHEK1, EGFR	
CEP-18770 (Delanzomib)	PSMC1	
Aprepitant	TACR1	
Oligomycin A	ATPAF1	
Ginkgolide A	GABR	
Stattic	STAT3	
SC144	IL6ST	
Panobinostat (LBH589)	HDAC	
VX-680 (Tozasertib, MK-0457)	AURKA	
GDC-0941	PIK3CA, PIK3CD	
Everolimus (RAD001)	MTOR	
Rebamipide	CCKAR	
Rasagiline Mesylate	MAOB	
PD128907 HCl	DDR3	
ADX-47273	GRM5	
AP26113	ALK	
Birinapant	DIABLO (AP1)	
LDK378	ALK	
ZM 447439	AURKA, AURKB	
BX-912	PDK1	
Elvitegravir (GS-9137, JTK-303)	0	
Fostamatinib (R788)	SYK	
TCS 359	FLT3	
Carvedilol	ADRB1	
Naftopidil	ADRA1A	
T0070907	PPARG	
Gliquidone	KCNJ	
SC-514	IKBKB	
ZCL278	CDC42	
VU 0364439	GRM4	

SB431542	TGFBR1	
Odanacatib (MK-0822)	CTSK	
Celecoxib	PTGS2	
Etodolac	PTGS1	
VX-745	MAPK14	
GSK429286A	ROCK1, ROCK2	
SB408124	HCRTR1	
H 89 2HCl	PRKAC	
Mubritinib (TAK 165)	ERBB2	
BMS-378806	CD4	
Ki16198	LPAR1, LPAR3	
AZ20	ATR	
AMG-517	TRPV1	
NMS-873	VCP	
Sorafenib	RAF1, BRAF, KDR	
NH125	EEF2K, PRKC, PRKA, CAMK2, Histidine Kinase	
Sal003	EIF2A	
Tariquidar	ABCB1	
Lomeguatrib	MGMT	
BI 2536	PLK1, PLK2, PLK3	
Imidapril HCl	ACE	
Gliclazide	KCNJ	
Sotrastaurin	PRKC (especially PRKCQ; inactive to PRKCZ)	
BI-D1870	RPS6KA1, RPS6KA2, RPS6KA3, RPS6KA4	
Go 6983	PRKCA, PRKCB, PRKCG, PRKCD	
MNS (3,4-Methylenedioxy-β-nitrostyrene, MDBN)	SYK, SRC, VCP	

PDTX R06-T4

RPMI		**SS**	
402 compounds		**269 compounds**	
Compound	**Target**	**Compound**	**Target**
FG-4592	EPAS1, EPO	Rizatriptan Benzoate	HTR1A
Rizatriptan Benzoate	HTR1A	Tolfenamic Acid	PTGS2
Fulvestrant	ESR	Ramelteon	MTNR1A, MTNR1B
Tolfenamic Acid	PTGS2	Belinostat (PXD101)	HDAC
Ramelteon	MTNR1A, MTNR1B	Rivaroxaban	F10
Trospium chloride	CHRM1	Rimonabant	CNR1
Granisetron HCl	HTR3A	FLI-06	NOTCH
A-769662	PRKAA1	Sitaxentan sodium	EDNRA
Losartan Potassium (DuP 753)	AGTR	Brinzolamide	CA2
Tolazoline HCl	ADRA1A	Zebularine	DNMT1, DNMT3A, DNMT3B
Tenofovir Disoproxil Fumarate	0	MLN8054	AURKA
Ataluren (PTC124)	CFTR	PR-619	ATXN7L3, BAP1, OTUB1, OTUD1, OTUD6A, OTUDB7A, UBB, UCHL3, USP1, USP2, USP4, USP5, USP7, USP8, USP14, USP15, USP17, USP26, USP30, USP36, YOD1
Candesartan	AGTR	Naltrexone HCl	OPRK1, OPRM1, OPRD1
Belinostat (PXD101)	HDAC	Ganetespib (STA-9090)	HSP90
Semagacestat (LY450139)	APP, NOTCH	Vemurafenib (PLX4032, RG7204)	BRAF (V600E)
NVP-ADW742	IGFR1	Pancuronium dibromide	0
NSC 319726	TP53 (R175)	Loratadine	HRH1
Icotinib	EGFR	PNU-120596	0
Ilomastat (GM6001, Galardin)	MMP1, MMP2, MMP3, MMP7, MMP8, MMP9, MMP12, MMP14, MMP26	GW3965 HCl	NR1H3, NR1H2
Rivaroxaban	F10	AZD6482	PIK3CB
STF-118804	NAMPT	SB705498	TRPV1
Rimonabant	CNR1	Safinamide Mesylate	MAOB, MAOA
FLI-06	NOTCH	Tenofovir	0
Sitaxentan sodium	EDNRA	Apixaban	F10
ABT-263 (Navitoclax)	BCL2, BCL2L1, BCL2L2	ML347	ACVR1, ACVRL1
Brinzolamide	CA2	Ferrostatin-1 (Fer-1)	VDAC
Nilotinib (AMN-107)	ABL1	Rotundine	DRD1
Tranylcypromine (2-PCPA) HCl	MAO, CYP2A6	MM-102	KANSL1
Tandutinib (MLN518)	FLT3, PDGFR KIT	OTX015	BRD2, BRD3, BRD4
Zebularine	DNMT1, DNMT3A, DNMT3B	Tofacitinib (CP-690550,Tasocitinib)	JAK3

MLN8054	AURKA	PHA-793887	CDK2, CDK5, CDK7
PR-619	ATXN7L3, BAP1, OTUB1, OTUD1, OTUD6A, OTUDB7A, UBB, UCHL3, USP1, USP2, USP4, USP5, USP7, USP8, USP14, USP15, USP17, USP26, USP30, USP36, YOD1	Allopurinol	HCRTR1, HCRTR2
Roxatidine Acetate HCl	HRH2	HC-030031	TRPA1
GSK1904529A	IGFR1, INSR	Telmisartan	AGTR
Atorvastatin Calcium	HMGCR	Cyproterone Acetate	AR
SNS-032 (BMS-387032)	CDK2	Sodium 4-Aminosalicylate	NFKB
Naltrexone HCl	OPRK1, OPRM1, OPRD1	GSK1292263	GPR119
Ganetespib (STA-9090)	HSP90	SGC 0946	DOT1L
CGS 21680 HCl	ADORA2A	LY2157299	TGFBR1
Vemurafenib (PLX4032, RG7204)	BRAF (V600E)	IPA-3	PAK1
Pancuronium dibromide	0	Esomeprazole Sodium	ATP4A
Loratadine	HRH1	DMH1	ACVR1
PNU-120596	0	Ozagrel	TBXA2R
Ruxolitinib (INCB018424)	JAK1, JAK2	GW9508	FFAR1, FFAR4
GW3965 HCl	NR1H3, NR1H2	NSC 405020	MMP14
AZD6482	PIK3CB	TPCA-1	IKBKB
SB705498	TRPV1	PYR-41	UBA1
Safinamide Mesylate	MAOB, MAOA	U0126-EtOH	MAP2K1, MAP2K2
Tenofovir	0	LDN-212854	ACVR1, ACVRL1
P22077	USP7, USP47	Ki16425	LPAR1, LPAR2, LPAR3
Aloxistatin	0	Mdivi-1	DRP1, DNM1
NSC697923	UBE2	MRS 2578	P2RY6
Apixaban	F10	LY2603618	CHEK1
ML347	ACVR1, ACVRL1	BTB06584	ATP5A1
Irinotecan HCl Trihydrate	TOP1	NPS-2143	CASR
SSR128129E	FGFR1	Veliparib (ABT-888)	PARP1, PARP2
VX-765	CASP1	Dalcetrapib (JTT-705, RO4607381)	CETP
Ferrostatin-1 (Fer-1)	VDAC	Istradefylline	ADORA2A
Rotundine	DRD1	Iniparib (BSI-201)	PARP1
MM-102	KANSL1	Dabrafenib (GSK2118436)	BRAF (V600)
PF-3845	FAAH	Tyrphostin AG 879	ERBB2
OTX015	BRD2, BRD3, BRD4	Cilomilast	PDE4
Ibrutinib (PCI-32765)	BTK	TAE226 (NVP-TAE226)	PTK2, PTK2B
4E1RCat	EIF4E	Vildagliptin (LAF-237)	DPP4
Tofacitinib (CP-690550,Tasocitinib)	JAK3	Dynasore	DNM1, DNM2
PHA-793887	CDK2, CDK5, CDK7	Piceatannol	SYK

WZ811	CXCR4	Quizartinib (AC220)	FLT3
Allopurinol	HCRTR1, HCRTR2	Enzastaurin (LY317615)	PRKCB, PRKCA, PRKCG, PRKCE
HC-030031	TRPA1	HA14-1	BCL2
Telmisartan	AGTR	TG100-115	PIK3CG, PIK3CD
Mozavaptan	AVPR1, AVPR2	BIBR 1532	TERT
Cyproterone Acetate	AR	Anastrozole	CYP19A1
Sodium 4-Aminosalicylate	NFKB	SB743921	0
GSK1292263	GPR119	EUK 134	SOD1
SGC 0946	DOT1L	Bergenin	0
LY2157299	TGFBR1	CP-91149	PYGL, PYGM, PYGB
IPA-3	PAK1	Wnt-C59 (C59)	WNT3A
Esomeprazole Sodium	ATP4A	NU7026	PRKDC
DMH1	ACVR1	BAM7	BAX
Ozagrel	TBXA2R	(+)-JQ1	BRD4
AZD4547	FGFR1, FGFR2, FGFR3	GW9662	PPARG
GW9508	FFAR1, FFAR4	KPT-185	XPO1
VE-821	ATR	Pifithrin-μ	TP53, HSPBP1
NSC 405020	MMP14	Batimastat (BB-94)	MMP1, MMP2, MMP3, MMP7, MMP9
GNF-2	ABL1	Sertraline HCl	0
TPCA-1	IKBKB	OG-L002	KDM1A
T0901317	NR1H3, NR1H2, NR1H4	MK-1775	WEE1
PD0325901	MAP2K1, MAP2K2	AT101	BCL2, BCL2L1, MCL1
PYR-41	UBA1	Tropicamide	CHRM4
U0126-EtOH	MAP2K1, MAP2K2	BMS-707035	0
LDN-212854	ACVR1, ACVRL1	Raltegravir (MK-0518)	0
Ki16425	LPAR1, LPAR2, LPAR3	AS-252424	PIK3CG
C646	EP300	Tie2 kinase inhibitor	TEK
Oxcarbazepine	SCN	Ouabain	ATP1B
Mdivi-1	DRP1, DNM1	Ranitidine	HRH2
MRS 2578	P2RY6	Fluvastatin Sodium	HMGCR
AGI-5198	IDH1	Propranolol HCl	ADRB1
LY2603618	CHEK1	Erastin	VDAC
BTB06584	ATP5A1	Ifenprodil Tartrate	GRIN
NPS-2143	CASR	KPT-276	XPO1
Veliparib (ABT-888)	PARP1, PARP2	AZD2461	PARP
Dalcetrapib (JTT-705, RO4607381)	CETP	KPT-330	XPO1
Vandetanib (ZD6474)	KDR	AGI-6780	IDH2
Istradefylline	ADORA2A	SGI-1027	DNMT1, DNMT3A, DNMT3B
Iniparib (BSI-201)	PARP1	Atglistatin	PNPLA2

Dabrafenib (GSK2118436)	BRAF (V600)	Suvorexant (MK-4305)	HCRTR1, HCRTR2
Finasteride	SRD5A2	SRT1720	SIRT1
Tyrphostin AG 879	ERBB2	Exemestane	CYP19A1
Cilomilast	PDE4	NSC 23766	RAC
TAE226 (NVP-TAE226)	PTK2, PTK2B	EHop-016	RAC1, RAC3
Ozagrel HCl	TBXAS1	PF-573228	PTK2
Vildagliptin (LAF-237)	DPP4	ABT-199 (GDC-0199)	BCL2
Dynasore	DNM1, DNM2	Memantine HCl	CYP2B6
Piceatannol	SYK	Trimebutine	OPRK1, OPRM1, OPRD1
Quizartinib (AC220)	FLT3	AZD7545	PDK1, PDK2
Tenovin-6	TP53, SIRT2, SIRT1, SIRT3	URB597	FAAH
Enzastaurin (LY317615)	PRKCB, PRKCA, PRKCG, PRKCE	GW0742	PPARD
CGP 57380	MKNK1	Pacritinib (SB1518)	JAK2, FLT3
Bisoprolol fumarate	ADRB1	KX2-391	SRC
Bosutinib (SKI-606)	SRC, ABL1	Crenolanib (CP-868596)	PDGFRA, PDGFRB, FLT3 (D842V)
S3I-201	STAT3	PFI-1 (PF-6405761)	BRD4
HA14-1	BCL2	Dapagliflozin	SLC5A2
TG100-115	PIK3CG, PIK3CD	Maraviroc	CCR5
ADL5859 HCl	OPRK1, OPRM1	Nebivolol	ADRB1
Voriconazole	CYP51A1	E-64	CTSK
BIBR 1532	TERT	OSI-906 (Linsitinib)	IGFR1, INSR
Thiazovivin	ROCK1, ROCK2	Canagliflozin	SLC5A2
Anastrozole	CYP19A1	Sirtinol	SIRT1, SIRT2
SB743921	0	Methotrexate	DHFR
EUK 134	SOD1	SAR131675	FLT4
Bergenin	0	Pralatrexate	DHFR
SN-38	TOP1	TWS119	GSK3B
CP-91149	PYGL, PYGM, PYGB	IKK-16 (IKK Inhibitor VII)	IKBKB, CHUK
Wnt-C59 (C59)	WNT3A	Enalaprilat Dihydrate	ACE
NU7026	PRKDC	Triamterene	SCN
BAM7	BAX	Clemastine Fumarate	HRH1
ZM 306416	FLT1	Fingolimod (FTY720) HCl	S1PR
(+)-JQ1	BRD4	PP2	SRC
GW9662	PPARG	CHIR-124	CHEK1
KPT-185	XPO1	Temsirolimus (CCI-779, NSC 683864)	MTOR
Pifithrin-μ	TP53, HSPBP1	Trichostatin A (TSA)	ALL HDACS (Except HDAC8)
Batimastat (BB-94)	MMP1, MMP2, MMP3, MMP7, MMP9	PHA-665752	MET
Sertraline HCl	0	CGK 733	ATM, ATR
OG-L002	KDM1A	WZ4002	EGFR

MK-1775	WEE1	TAK-700 (Orteronel)	CYP17A1
Costunolide	TERT	Loxistatin Acid (E-64C)	0
AT101	BCL2, BCL2L1, MCL1	Zibotentan (ZD4054)	EDNRA
GSK690693	AKT1, AKT2, AKT3	Pyrimethamine	DHFR
Tropicamide	CHRM4	RKI-1447	ROCK1, ROCK2
BMS-707035	0	SMI-4a	PIM1
Raltegravir (MK-0518)	0	SB415286	GSK3A
EX 527 (Selisistat)	SIRT1	Torcetrapib	CETP
CCT128930	AKT2	MK-2206 2HCl	AKT1, AKT2, AKT3
Pomalidomide	TNF	PF-04217903	MET
AS-252424	PIK3CG	GW441756	NTRK1
Tie2 kinase inhibitor	TEK	Varespladib (LY315920)	PLA2G2A
Ouabain	ATP1B	Ticagrelor	P2RY12
Ranitidine	HRH2	Letrozole	CYP19A1
SKI II	S1PR	GW2580	CSF1R
Fluvastatin Sodium	HMGCR	Zosuquidar (LY335979) 3HCl	ABCB1
Propranolol HCl	ADRB1	KU-60019	ATM
Erastin	VDAC	LY2228820	MAPK11, MAPK12, MAPK13, MAPK14
Ifenprodil Tartrate	GRIN	Oxymetazoline HCl	ADRA1A
KPT-276	XPO1	DMXAA (Vadimezan)	NQ01
AZD2461	PARP	Embelin	XIAP
KPT-330	XPO1	Toremifene Citrate	ESR
AGI-6780	IDH2	GSK2656157	EIF2AK3
SGI-1027	DNMT1, DNMT3A, DNMT3B	Ticlopidine HCl	P2RY
Atglistatin	PNPLA2	SANT-1	SMO
Suvorexant (MK-4305)	HCRTR1, HCRTR2	Ispinesib (SB-715992)	0
SRT1720	SIRT1	BTZ043 Racemate	0
4EGI-1	EIF4E	AZD7762	CHEK1, CHEK2
Exemestane	CYP19A1	AVL-292	BTK
NSC 23766	RAC	Pimobendan	PDE3
2-Methoxyestradiol (2-MeOE2)	HIF1A	DBeQ	VCP
Palbociclib (PD-0332991) HCl	CDK4, CDK6	Formoterol Hemifumarate	ADRB2
EHop-016	RAC1, RAC3	Lovastatin	HMGCR
PF-573228	PTK2	Pramipexole	DRD2S,DRD2L, DRD3, DRD4
ABT-199 (GDC-0199)	BCL2	RepSox	TGFBR1
Memantine HCl	CYP2B6	Bazedoxifene HCl	ESR1, ESR2
PTC-209	BMI1	Golgicide A	GBF1
Trimebutine	OPRK1, OPRM1, OPRD1	LDE225 (NVP-LDE225,Erismodegib)	SMO

CK-636	ARPC2, ARPC3	Ridaforolimus (Deforolimus, MK-8669)	MTOR
SGI-1776 free base	PIM1, FLT3, GSG2	LY2784544	JAK2
AZD7545	PDK1, PDK2	SNS-314 Mesylate	AURKA, AURKB, AURKC
URB597	FAAH	Irinotecan	TOP1
GW0742	PPARD	Dutasteride	SRD5A2, SRD5A1
TAK-875	FFAR1	Apigenin	CYP2C9
Pacritinib (SB1518)	JAK2, FLT3	Forskolin	ADCY4
KX2-391	SRC	Rolipram	PDE4
PluriSIn #1 (NSC 14613)	SCD	Bupivacaine HCl	ADCY4
Crenolanib (CP-868596)	PDGFRA, PDGFRB, FLT3 (D842V)	UNC669	L3MBTL1
Enzalutamide (MDV3100)	AR	Tioxolone	CA1
PFI-1 (PF-6405761)	BRD4	PF-4708671	RPS6KB1
Dapagliflozin	SLC5A2	5-hydroxymethyl Tolterodine (PNU 200577, 5-HMT, 5-HM)	CHRM1
Maraviroc	CCR5	XAV-939	WNT
Nebivolol	ADRB1	SB742457	HTR6
I-BET151 (GSK1210151A)	BRD2, BRD3, BRD4	Cinacalcet HCl	CASR
VX-809 (Lumacaftor)	CFTR	Linagliptin	DPP4
Apoptosis Activator 2	CASP3	Etomidate	GABR
Naproxen	PTGS1, PTGS2	Entacapone	COMT
Bosentan Hydrate	EDNRA, EDNRB	LY411575	APP, NOTCH
Acadesine	PRKAA1	OC000459	PTGDR2
E-64	CTSK	NLG919	IDO1
Captopril	ACE	Levosulpiride	DRD2
Selumetinib (AZD6244)	MAP2K1, MAPK3, MAPK1	Imatinib (STI571)	ABL1, KIT, PDGFR
Tolvaptan	AVPR2	DCC-2036 (Rebastinib)	ABL1, SRC, LYN, FGR, HCK, KDR, FLT3
PD184352 (CI-1040)	MAP2K1, MAP2K2	XL335	NR1H4
OSI-906 (Linsitinib)	IGFR1, INSR	Nilvadipine	CACNA1C
Canagliflozin	SLC5A2	CHIR-98014	GSK3A, GSK3B
CP-673451	PDGFRA, PDGFRB	GW4064	NR1H4
Sirtinol	SIRT1, SIRT2	PF-5274857	SMO
Methotrexate	DHFR	GDC-0068	AKT1, AKT2, AKT3
SAR131675	FLT4	VU 0364770	GRM4
Pralatrexate	DHFR	Daunorubicin HCl	TOP2
BML-190	CNR2	PF-562271	PTK2
TWS119	GSK3B	AZD3463	ALK, IGFR1
IKK-16 (IKK Inhibitor VII)	IKBKB, CHUK	IOX2	EGLN1
Enalaprilat Dihydrate	ACE	IMD 0354	IKBKB, CHUK

Triamterene	SCN	CRT0044876	APE1
Clemastine Fumarate	HRH1	TCID	UCHL3
Fingolimod (FTY720) HCl	S1PR	Necrostatin-1	RIPK1
Amlodipine	CACNA1C	Empagliflozin (BI 10773)	SLC5A2
PP2	SRC	SU11274	MET
CHIR-124	CHEK1	Bortezomib (PS-341)	PSMC1
Temsirolimus (CCI-779, NSC 683864)	MTOR	YM155 (Sepantronium Bromide)	BIRC5
YO-01027	APP, APPL1, NOTCH	Lenalidomide (CC-5013)	TNF
Trichostatin A (TSA)	ALL HDACS (Except HDAC8)	AUY922 (NVP-AUY922)	HSP90A, HSP90B
PAC-1	CASP3	Agomelatine	HTR2C
PHA-665752	MET	17-AAG (Tanespimycin)	HSP90
VE-822	ATR	SP600125	JKAMP, MAPK9, MAPK10; MAP2K4; MAP2K3, MAP2K6, AKT1, PRKC; MAPK1, MAPK14, CHEK1, EGFR
SB203580	MAPK11, MAPK12, MAPK13, MAPK14	CEP-18770 (Delanzomib)	PSMC1
EPZ-6438	EZH2	Aprepitant	TACR1
KU-55933 (ATM Kinase Inhibitor)	ATM	Fluvoxamine maleate	0
CGK 733	ATM, ATR	Oligomycin A	ATPAF1
WZ4002	EGFR	Ginkgolide A	GABR
WZ4003	NUAK1, NUAK2	Cryptotanshinone	STAT3
TAK-700 (Orteronel)	CYP17A1	ICG-001	WNT
Loxistatin Acid (E-64C)	0	SC144	IL6ST
Zibotentan (ZD4054)	EDNRA	SRPIN340	SRPK1
Pyrimethamine	DHFR	Panobinostat (LBH589)	HDAC
RKI-1447	ROCK1, ROCK2	VX-680 (Tozasertib, MK-0457)	AURKA
UNC2250	MERTK	Everolimus (RAD001)	MTOR
SMI-4a	PIM1	MK-8245	SCD
SB415286	GSK3A	Aniracetam	GRIA1,
PRT062607 (P505-15, BIIB057) HCl	SYK	PD128907 HCl	DDR3
Torcetrapib	CETP	AP26113	ALK
MK-2206 2HCl	AKT1, AKT2, AKT3	Birinapant	DIABLO (AP1)
ML130 (Nodinitib-1)	NOD1	BX-912	PDK1
PF-04217903	MET	Tadalafil	PDE5
GW441756	NTRK1	Fostamatinib (R788)	SYK
Varespladib (LY315920)	PLA2G2A	GSK J4 HCl	KDM6A, KDM6B
ML161	PARP1	Carvedilol	ADRB1
MK-2866 (GTx-024)	AR	SC-514	IKBKB

Ticagrelor	P2RY12	ZCL278	CDC42
Letrozole	CYP19A1	Isotretinoin	0
GW2580	CSF1R	VX-745	MAPK14
Zosuquidar (LY335979) 3HCl	ABCB1	GSK429286A	ROCK1, ROCK2
KU-60019	ATM	Mubritinib (TAK 165)	ERBB2
LY2228820	MAPK11, MAPK12, MAPK13, MAPK14	BMS-378806	CD4
MLN2238	PSMC1	Ki16198	LPAR1, LPAR3
Org 27569	CNR1	AZ20	ATR
Oxymetazoline HCl	ADRA1A	AMG-517	TRPV1
DMXAA (Vadimezan)	NQ01	NMS-873	VCP
Anacetrapib (MK-0859)	CETP	Sorafenib	RAF1, BRAF, KDR
AM1241	CNR2	NH125	EEF2K, PRKC, PRKA, CAMK2, Histidine Kinase
Embelin	XIAP	BI 2536	PLK1, PLK2, PLK3
Toremifene Citrate	ESR	GSK461364	PLK1, PLK2, PLK3
GSK2656157	EIF2AK3	BI-D1870	RPS6KA1, RPS6KA2, RPS6KA3, RPS6KA4
Felodipine	CACNA1C		
(+)-Bicuculline	GABR, KCNMA1		
Ticlopidine HCl	P2RY		
SANT-1	SMO		
Ispinesib (SB-715992)	0		
BTZ043 Racemate	0		
AZD7762	CHEK1, CHEK2		
AVL-292	BTK		
Pimobendan	PDE3		
DBeQ	VCP		
Formoterol Hemifumarate	ADRB2		
CNX-774	BTK		
Lovastatin	HMGCR		
4μ8C	ERN1		
Lafutidine	HRH2		
AZ191	DYRK1B		
(-)-Parthenolide	MDM2, P53		
JSH-23	NFKB		
Pramipexole	DRD2S,DRD2L, DRD3, DRD4		
RepSox	TGFBR1		
Bazedoxifene HCl	ESR1, ESR2		
Golgicide A	GBF1		
LDE225 (NVP-LDE225,Erismodegib)	SMO		

Ridaforolimus (Deforolimus, MK-8669)	MTOR	
LY2784544	JAK2	
SNS-314 Mesylate	AURKA, AURKB, AURKC	
BGJ398 (NVP-BGJ398)	FGFR1, FGFR2, FGFR3	
Irinotecan	TOP1	
OSI-420	EGFR	
Dutasteride	SRD5A2, SRD5A1	
Apigenin	CYP2C9	
Rigosertib (ON-01910)	PLK1, PLK2	
Forskolin	ADCY4	
Rolipram	PDE4	
Bupivacaine HCl	ADCY4	
UNC669	L3MBTL1	
Tioxolone	CA1	
PF-4708671	RPS6KB1	
5-hydroxymethyl Tolterodine (PNU 200577, 5-HMT, 5-HM)	CHRM1	
XAV-939	WNT	
SB742457	HTR6	
Cinacalcet HCl	CASR	
Linagliptin	DPP4	
Etomidate	GABR	
Entacapone	COMT	
AG-14361	PARP1	
Moclobemide (Ro 111163)	MAOA	
LY411575	APP, NOTCH	
GDC-0152	XIAP, BIRC7, AP1, AP2	
OC000459	PTGDR2	
NLG919	IDO1	
Levosulpiride	DRD2	
Imatinib (STI571)	ABL1, KIT, PDGFR	
DCC-2036 (Rebastinib)	ABL1, SRC, LYN, FGR, HCK, KDR, FLT3	
XL335	NR1H4	
Nilvadipine	CACNA1C	
CHIR-98014	GSK3A, GSK3B	
GW4064	NR1H4	
PF-5274857	SMO	
GDC-0068	AKT1, AKT2, AKT3	
JNJ-1661010	FAAH	

VU 0364770	GRM4	
U-104	CA12	
Daunorubicin HCl	TOP2	
PF-562271	PTK2	
AZD3463	ALK, IGFR1	
IOX2	EGLN1	
IMD 0354	IKBKB, CHUK	
CRT0044876	APE1	
TCID	UCHL3	
LB42708	FNTA	
Necrostatin-1	RIPK1	
Empagliflozin (BI 10773)	SLC5A2	
SU11274	MET	
Bortezomib (PS-341)	PSMC1	
YM155 (Sepantronium Bromide)	BIRC5	
Lenalidomide (CC-5013)	TNF	
Ivacaftor (VX-770)	CFTR	
AUY922 (NVP-AUY922)	HSP90A, HSP90B	
Agomelatine	HTR2C	
17-AAG (Tanespimycin)	HSP90	
SP600125	JKAMP, MAPK9, MAPK10; MAP2K4; MAP2K3, MAP2K6, AKT1, PRKC; MAPK1, MAPK14, CHEK1, EGFR	
CEP-18770 (Delanzomib)	PSMC1	
Oligomycin A	ATPAF1	
ICG-001	WNT	
Stattic	STAT3	
SC144	IL6ST	
Panobinostat (LBH589)	HDAC	
VX-680 (Tozasertib, MK-0457)	AURKA	
OSU-03012 (AR-12)	PDK1	
0	Akt1, PKCη, PKCθ, PrkX, Akt3, Akt2, PKCδ, PKCβ, PKCε, PKA, PKG1β	
Everolimus (RAD001)	MTOR	
Aniracetam	GRIA1,	
Doxazosin Mesylate	ADRA1A	
Tosedostat (CHR2797)	LAP3, NPEPPS, ANPEP	
Rebamipide	CCKAR	
Rasagiline Mesylate	MAOB	

PD128907 HCl	DDR3	
ADX-47273	GRM5	
AZ 3146	TTK, CENPE	
VU 0357121	GRM5	
(-)-MK 801 Maleate	GRIN	
Mirabegron	ADRB3	
AP26113	ALK	
Birinapant	DIABLO (AP1)	
LDK378	ALK	
(S)-crizotinib	NUDT1	
ZM 447439	AURKA, AURKB	
BX-912	PDK1	
Tadalafil	PDE5	
Elvitegravir (GS-9137, JTK-303)	0	
Fostamatinib (R788)	SYK	
GSK J4 HCl	KDM6A, KDM6B	
TCS 359	FLT3	
ML133 HCl	KCNJ2	
T0070907	PPARG	
Gliquidone	KCNJ	
SC-514	IKBKB	
Caffeic Acid Phenethyl Ester	NFKB	
SB431542	TGFBR1	
Odanacatib (MK-0822)	CTSK	
Isotretinoin	0	
VX-745	MAPK14	
GSK429286A	ROCK1, ROCK2	
SB408124	HCRTR1	
NMS-873	VCP	
Sorafenib	RAF1, BRAF, KDR	
Sal003	EIF2A	
Lomeguatrib	MGMT	
Imidapril HCl	ACE	
Gliclazide	KCNJ	
Sotrastaurin	PRKC (especially PRKCQ; inactive to PRKCZ)	
BI-D1870	RPS6KA1, RPS6KA2, RPS6KA3, RPS6KA4	

Table S4. Compounds killing >50% of 4 representative T-ALL PDTX cells derived from different transfers (T) challenged in interleukin supplemented StemSpan (SS) media.

PDTX 3053
(P.S. zero compounds killing at T11)

T7		**T8**		**T9**	
145 compounds		**129 compounds**		**75 compounds**	
Compound	**Target**	**Compound**	**Target**	**Compound**	**Target**
FG-4592	EPAS1, EPO	FG-4592	EPAS1, EPO	FG-4592	EPAS1, EPO
Rizatriptan Benzoate	HTR1A	Rizatriptan Benzoate	HTR1A	Rizatriptan Benzoate	HTR1A
Fulvestrant	ESR	Fulvestrant	ESR	Trospium chloride	CHRM1
Tolfenamic Acid	PTGS2	Tolfenamic Acid	PTGS2	Granisetron HCl	HTR3A
Ramelteon	MTNR1A, MTNR1B	Ramelteon	MTNR1A, MTNR1B	A-769662	PRKAA1
Trospium chloride	CHRM1	Trospium chloride	CHRM1	Losartan Potassium (DuP 753)	AGTR
Granisetron HCl	HTR3A	Granisetron HCl	HTR3A	Tolazoline HCl	ADRA1A
A-769662	PRKAA1	A-769662	PRKAA1	Tenofovir Disoproxil Fumarate	0
Losartan Potassium (DuP 753)	AGTR	Losartan Potassium (DuP 753)	AGTR	Ataluren (PTC124)	CFTR
Tolazoline HCl	ADRA1A	Tolazoline HCl	ADRA1A	Candesartan	AGTR
Tenofovir Disoproxil Fumarate	0	Tenofovir Disoproxil Fumarate	0	Belinostat (PXD101)	HDAC
Ataluren (PTC124)	CFTR	Ataluren (PTC124)	CFTR	Semagacestat (LY450139)	APP, NOTCH
Candesartan	AGTR	Candesartan	AGTR	NVP-ADW742	IGFR1
Belinostat (PXD101)	HDAC	Belinostat (PXD101)	HDAC	NSC 319726	TP53 (R175)
Semagacestat (LY450139)	APP, NOTCH	Semagacestat (LY450139)	APP, NOTCH	ABT-263 (Navitoclax)	BCL2, BCL2L1, BCL2L2
NVP-ADW742	IGFR1	NVP-ADW742	IGFR1	MLN8054	AURKA
NSC 319726	TP53 (R175)	NSC 319726	TP53 (R175)	PR-619	ATXN7L3, BAP1, OTUB1, OTUD1, OTUD6A, OTUDB7A, UBB, UCHL3, USP1, USP2, USP4, USP5, USP7, USP8, USP14, USP15, USP17, USP26, USP30, USP36, YOD1
Icotinib	EGFR	STF-118804	NAMPT	Safinamide Mesylate	MAOB, MAOA
Ilomastat (GM6001, Galardin)	MMP1, MMP2, MMP3, MMP7, MMP8, MMP9,	ABT-263 (Navitoclax)	BCL2, BCL2L1, BCL2L2	4E1RCat	EIF4E

	MMP12, MMP14, MMP26				
Rivaroxaban	F10	MLN8054	AURKA	Tofacitinib (CP-690550,Tasocitinib)	JAK3
STF-118804	NAMPT	PR-619	ATXN7L3, BAP1, OTUB1, OTUD1, OTUD6A, OTUDB7A, UBB, UCHL3, USP1, USP2, USP4, USP5, USP7, USP8, USP14, USP15, USP17, USP26, USP30, USP36, YOD1	Ozagrel	TBXA2R
Rimonabant	CNR1	Roxatidine Acetate HCl	HRH2	MRS 2578	P2RY6
FLI-06	NOTCH	Atorvastatin Calcium	HMGCR	Vildagliptin (LAF-237)	DPP4
Sitaxentan sodium	EDNRA	SNS-032 (BMS-387032)	CDK2	Enzastaurin (LY317615)	PRKCB, PRKCA, PRKCG, PRKCE
ABT-263 (Navitoclax)	BCL2, BCL2L1, BCL2L2	SB705498	TRPV1	Anastrozole	CYP19A1
Brinzolamide	CA2	Safinamide Mesylate	MAOB, MAOA	SB743921	0
Tandutinib (MLN518)	FLT3, PDGFR KIT	Tenofovir	0	SN-38	TOP1
MLN8054	AURKA	Irinotecan HCl Trihydrate	TOP1	KPT-185	XPO1
PR-619	ATXN7L3, BAP1, OTUB1, OTUD1, OTUD6A, OTUDB7A, UBB, UCHL3, USP1, USP2, USP4, USP5, USP7, USP8, USP14, USP15, USP17, USP26, USP30, USP36, YOD1	4E1RCat	EIF4E	OG-L002	KDM1A
Roxatidine Acetate HCl	HRH2	Tofacitinib (CP-690550,Tasocitinib)	JAK3	MK-1775	WEE1
GSK1904529A	IGFR1, INSR	Ozagrel	TBXA2R	Ouabain	ATP1B
Atorvastatin Calcium	HMGCR	AZD4547	FGFR1, FGFR2, FGFR3	Fluvastatin Sodium	HMGCR

SNS-032 (BMS-387032)	CDK2	GW9508	FFAR1, FFAR4	Propranolol HCl	ADRB1
Vemurafenib (PLX4032, RG7204)	BRAF (V600E)	MRS 2578	P2RY6	KPT-276	XPO1
Pancuronium dibromide	0	AGI-5198	IDH1	KPT-330	XPO1
Loratadine	HRH1	Vildagliptin (LAF-237)	DPP4	Palbociclib (PD-0332991) HCl	CDK4, CDK6
PNU-120596	0	Dynasore	DNM1, DNM2	EHop-016	RAC1, RAC3
AZD6482	PIK3CB	Piceatannol	SYK	KX2-391	SRC
Safinamide Mesylate	MAOB, MAOA	Quizartinib (AC220)	FLT3	Crenolanib (CP-868596)	PDGFRA, PDGFRB, FLT3 (D842V)
Tenofovir	0	Enzastaurin (LY317615)	PRKCB, PRKCA, PRKCG, PRKCE	Enzalutamide (MDV3100)	AR
P22077	USP7, USP47	Anastrozole	CYP19A1	PD184352 (CI-1040)	MAP2K1, MAP2K2
Aloxistatin	0	SB743921	0	PP2	SRC
Irinotecan HCl Trihydrate	TOP1	SN-38	TOP1	Trichostatin A (TSA)	ALL HDACS (Except HDAC8)
Ferrostatin-1 (Fer-1)	VDAC	(+)-JQ1	BRD4	Ispinesib (SB-715992)	0
OTX015	BRD2, BRD3, BRD4	KPT-185	XPO1	RepSox	TGFBR1
Ibrutinib (PCI-32765)	BTK	OG-L002	KDM1A	Levosulpiride	DRD2
4E1RCat	EIF4E	MK-1775	WEE1	Daunorubicin HCl	TOP2
Tofacitinib (CP-690550,Tasocitinib)	JAK3	BMS-707035	0	AZD3463	ALK, IGFR1
PHA-793887	CDK2, CDK5, CDK7	Ouabain	ATP1B	IMD 0354	IKBKB, CHUK
WZ811	CXCR4	Fluvastatin Sodium	HMGCR	Bortezomib (PS-341)	PSMC1
HC-030031	TRPA1	Propranolol HCl	ADRB1	YM155 (Sepantronium Bromide)	BIRC5
Telmisartan	AGTR	KPT-276	XPO1	CEP-18770 (Delanzomib)	PSMC1
Cyproterone Acetate	AR	KPT-330	XPO1	Aprepitant	TACR1
Sodium 4-Aminosalicylate	NFKB	NSC 23766	RAC	Fluvoxamine maleate	0
GSK1292263	GPR119	Palbociclib (PD-0332991) HCl	CDK4, CDK6	Oligomycin A	ATPAF1
SGC 0946	DOT1L	EHop-016	RAC1, RAC3	Ginkgolide A	GABR
LY2157299	TGFBR1	KX2-391	SRC	Cryptotanshinone	STAT3
IPA-3	PAK1	Crenolanib (CP-868596)	PDGFRA, PDGFRB, FLT3 (D842V)	ICG-001	WNT
Esomeprazole Sodium	ATP4A	Enzalutamide (MDV3100)	AR	Stattic	STAT3
Ozagrel	TBXA2R	PD184352 (CI-1040)	MAP2K1, MAP2K2	SC144	IL6ST

AZD4547	FGFR1, FGFR2, FGFR3	OSI-906 (Linsitinib)	IGFR1, INSR	SRPIN340	SRPK1
GNF-2	ABL1	Pralatrexate	DHFR	Panobinostat (LBH589)	HDAC
TPCA-1	IKBKB	PP2	SRC	MK-8245	SCD
T0901317	NR1H3, NR1H2, NR1H4	CHIR-124	CHEK1	Apatinib	KDR
PYR-41	UBA1	Trichostatin A (TSA)	ALL HDACS (Except HDAC8)	Birinapant	DIABLO (AP1)
LDN-212854	ACVR1, ACVRL1	Loxistatin Acid (E-64C)	0	AZD1981	PTGDR2
Ki16425	LPAR1, LPAR2, LPAR3	Zibotentan (ZD4054)	EDNRA	GSK J4 HCl	KDM6A, KDM6B
Oxcarbazepine	SCN	Pyrimethamine	DHFR	ZCL278	CDC42
MRS 2578	P2RY6	RKI-1447	ROCK1, ROCK2	Odanacatib (MK-0822)	CTSK
AGI-5198	IDH1	Letrozole	CYP19A1	Stavudine (d4T)	0
BTB06584	ATP5A1	GW2580	CSF1R	Mubritinib (TAK 165)	ERBB2
Dalcetrapib (JTT-705, RO4607381)	CETP	MLN2238	PSMC1	AZ20	ATR
Iniparib (BSI-201)	PARP1	Ticlopidine HCl	P2RY	NH125	EEF2K, PRKC, PRKA, CAMK2, Histidine Kinase
Vildagliptin (LAF-237)	DPP4	SANT-1	SMO	BI 2536	PLK1, PLK2, PLK3
Dynasore	DNM1, DNM2	Ispinesib (SB-715992)	0		
Piceatannol	SYK	JSH-23	NFKB		
Quizartinib (AC220)	FLT3	Pramipexole	DRD2S,DRD2L, DRD3, DRD4		
Enzastaurin (LY317615)	PRKCB, PRKCA, PRKCG, PRKCE	RepSox	TGFBR1		
Anastrozole	CYP19A1	SNS-314 Mesylate	AURKA, AURKB, AURKC		
SB743921	0	BGJ398 (NVP-BGJ398)	FGFR1, FGFR2, FGFR3		
SN-38	TOP1	Irinotecan	TOP1		
Wnt-C59 (C59)	WNT3A	Bupivacaine HCl	ADCY4		
BAM7	BAX	UNC669	L3MBTL1		
(+)-JQ1	BRD4	AG-14361	PARP1		
KPT-185	XPO1	LY411575	APP, NOTCH		
OG-L002	KDM1A	NLG919	IDO1		
MK-1775	WEE1	Levosulpiride	DRD2		
AT101	BCL2, BCL2L1, MCL1	Imatinib (STI571)	ABL1, KIT, PDGFR		
BMS-707035	0	DCC-2036 (Rebastinib)	ABL1, SRC, LYN, FGR,		

			HCK, KDR, FLT3	
Ouabain	ATP1B	Daunorubicin HCl	TOP2	
Fluvastatin Sodium	HMGCR	AZD3463	ALK, IGFR1	
Propranolol HCl	ADRB1	IOX2	EGLN1	
KPT-276	XPO1	IMD 0354	IKBKB, CHUK	
KPT-330	XPO1	CRT0044876	APE1	
Exemestane	CYP19A1	LB42708	FNTA	
Palbociclib (PD-0332991) HCl	CDK4, CDK6	Bortezomib (PS-341)	PSMC1	
EHop-016	RAC1, RAC3	YM155 (Sepantronium Bromide)	BIRC5	
SGI-1776 free base	PIM1, FLT3, GSG2	17-AAG (Tanespimycin)	HSP90	
KX2-391	SRC	SP600125	JKAMP, MAPK9, MAPK10; MAP2K4; MAP2K3, MAP2K6, AKT1, PRKC; MAPK1, MAPK14, CHEK1, EGFR	
Enzalutamide (MDV3100)	AR	CEP-18770 (Delanzomib)	PSMC1	
PD184352 (CI-1040)	MAP2K1, MAP2K2	Aprepitant	TACR1	
OSI-906 (Linsitinib)	IGFR1, INSR	Fluvoxamine maleate	0	
Methotrexate	DHFR	Oligomycin A	ATPAF1	
Pralatrexate	DHFR	Ginkgolide A	GABR	
Enalaprilat Dihydrate	ACE	Cryptotanshinone	STAT3	
Trichostatin A (TSA)	ALL HDACS (Except HDAC8)	ICG-001	WNT	
WZ4003	NUAK1, NUAK2	Stattic	STAT3	
MLN2238	PSMC1	SC144	IL6ST	
Ispinesib (SB-715992)	0	SRPIN340	SRPK1	
SNS-314 Mesylate	AURKA, AURKB, AURKC	Panobinostat (LBH589)	HDAC	
Irinotecan	TOP1	VX-680 (Tozasertib, MK-0457)	AURKA	
Rigosertib (ON-01910)	PLK1, PLK2	MK-8245	SCD	
Rolipram	PDE4	Doxazosin Mesylate	ADRA1A	
Bupivacaine HCl	ADCY4	Ginkgolide B	PTAFR	
UNC669	L3MBTL1	Apatinib	KDR	
Entacapone	COMT	AZD1981	PTGDR2	

AG-14361	PARP1	Tadalafil	PDE5	
NLG919	IDO1	GSK J4 HCl	KDM6A, KDM6B	
Levosulpiride	DRD2	ZCL278	CDC42	
Daunorubicin HCl	TOP2	Caffeic Acid Phenethyl Ester	NFKB	
IMD 0354	IKBKB, CHUK	Stavudine (d4T)	0	
CRT0044876	APE1	Mubritinib (TAK 165)	ERBB2	
TCID	UCHL3	BMS-378806	CD4	
LB42708	FNTA	AZ20	ATR	
Bortezomib (PS-341)	PSMC1	NMS-873	VCP	
YM155 (Sepantronium Bromide)	BIRC5	NH125	EEF2K, PRKC, PRKA, CAMK2, Histidine Kinase	
Agomelatine	HTR2C	BI 2536	PLK1, PLK2, PLK3	
CEP-18770 (Delanzomib)	PSMC1	GSK461364	PLK1, PLK2, PLK3	
Oligomycin A	ATPAF1			
ICG-001	WNT			
Stattic	STAT3			
SC144	IL6ST			
Panobinostat (LBH589)	HDAC			
VX-680 (Tozasertib, MK-0457)	AURKA			
Birinapant	DIABLO (AP1)			
Tadalafil	PDE5			
GSK J4 HCl	KDM6A, KDM6B			
ZCL278	CDC42			
Stavudine (d4T)	0			
Mubritinib (TAK 165)	ERBB2			
AZ20	ATR			
NMS-873	VCP			
NH125	EEF2K, PRKC, PRKA, CAMK2, Histidine Kinase			
BI 2536	PLK1, PLK2, PLK3			
GSK461364	PLK1, PLK2, PLK3			

PDTX 3119

T2 **235 compounds**		**T4** **26 compounds**	
Compound	**Target**	**Compound**	**Target**
FG-4592	EPAS1, EPO	Tenofovir Disoproxil Fumarate	0
Rizatriptan Benzoate	HTR1A	Belinostat (PXD101)	HDAC
Fulvestrant	ESR	NSC 319726	TP53 (R175)
Tolfenamic Acid	PTGS2	STF-118804	NAMPT
Ramelteon	MTNR1A, MTNR1B	ABT-263 (Navitoclax)	BCL2, BCL2L1, BCL2L2
Trospium chloride	CHRM1	Ganetespib (STA-9090)	HSP90
Granisetron HCl	HTR3A	Ruxolitinib (INCB018424)	JAK1, JAK2
A-769662	PRKAA1	Tofacitinib (CP-690550,Tasocitinib)	JAK3
Losartan Potassium (DuP 753)	AGTR	PHA-793887	CDK2, CDK5, CDK7
Tolazoline HCl	ADRA1A	KPT-185	XPO1
Tenofovir Disoproxil Fumarate	0	MK-1775	WEE1
Ataluren (PTC124)	CFTR	Ouabain	ATP1B
Candesartan	AGTR	KX2-391	SRC
Belinostat (PXD101)	HDAC	Crenolanib (CP-868596)	PDGFRA, PDGFRB, FLT3 (D842V)
Semagacestat (LY450139)	APP, NOTCH	CHIR-124	CHEK1
NVP-ADW742	IGFR1	Trichostatin A (TSA)	ALL HDACS (Except HDAC8)
NSC 319726	TP53 (R175)	AZD7762	CHEK1, CHEK2
Icotinib	EGFR	DBeQ	VCP
Ilomastat (GM6001, Galardin)	MMP1, MMP2, MMP3, MMP7, MMP8, MMP9, MMP12, MMP14, MMP26	Bortezomib (PS-341)	PSMC1
Rivaroxaban	F10	YM155 (Sepantronium Bromide)	BIRC5
STF-118804	NAMPT	AUY922 (NVP-AUY922)	HSP90A, HSP90B
Rimonabant	CNR1	17-AAG (Tanespimycin)	HSP90
FLI-06	NOTCH	CEP-18770 (Delanzomib)	PSMC1
Sitaxentan sodium	EDNRA	Oligomycin A	ATPAF1
ABT-263 (Navitoclax)	BCL2, BCL2L1, BCL2L2	Stattic	STAT3
Brinzolamide	CA2	SC144	IL6ST
Tandutinib (MLN518)	FLT3, PDGFR KIT	Rasagiline Mesylate	MAOB
Zebularine	DNMT1, DNMT3A, DNMT3B	(S)-crizotinib	NUDT1
MLN8054	AURKA	GSK J4 HCl	KDM6A, KDM6B
PR-619	ATXN7L3, BAP1, OTUB1, OTUD1, OTUD6A, OTUDB7A, UBB, UCHL3, USP1, USP2, USP4, USP5, USP7, USP8, USP14, USP15, USP17,	Caffeic Acid Phenethyl Ester	NFKB

	USP26, USP30, USP36, YOD1		
Roxatidine Acetate HCl	HRH2	AZ20	ATR
GSK1904529A	IGFR1, INSR	NMS-873	VCP
Atorvastatin Calcium	HMGCR	GSK461364	PLK1, PLK2, PLK3
SNS-032 (BMS-387032)	CDK2	Sotrastaurin	PRKC (especially PRKCQ; inactive to PRKCZ)
Naltrexone HCl	OPRK1, OPRM1, OPRD1	BI-D1870	RPS6KA1, RPS6KA2, RPS6KA3, RPS6KA4
Ganetespib (STA-9090)	HSP90		
CGS 21680 HCl	ADORA2A		
Pancuronium dibromide	0		
Loratadine	HRH1		
PNU-120596	0		
Ruxolitinib (INCB018424)	JAK1, JAK2		
GW3965 HCl	NR1H3, NR1H2		
AZD6482	PIK3CB		
SB705498	TRPV1		
Safinamide Mesylate	MAOB, MAOA		
Tenofovir	0		
P22077	USP7, USP47		
Aloxistatin	0		
NSC697923	UBE2		
Apixaban	F10		
ML347	ACVR1, ACVRL1		
Irinotecan HCl Trihydrate	TOP1		
SSR128129E	FGFR1		
VX-765	CASP1		
Ferrostatin-1 (Fer-1)	VDAC		
PF-3845	FAAH		
OTX015	BRD2, BRD3, BRD4		
Ibrutinib (PCI-32765)	BTK		
4E1RCat	EIF4E		
Tofacitinib (CP-690550,Tasocitinib)	JAK3		
PHA-793887	CDK2, CDK5, CDK7		
WZ811	CXCR4		
Allopurinol	HCRTR1, HCRTR2		
HC-030031	TRPA1		
Telmisartan	AGTR		
Mozavaptan	AVPR1, AVPR2		
Cyproterone Acetate	AR		
Sodium 4-Aminosalicylate	NFKB		

GSK1292263	GPR119	
SGC 0946	DOT1L	
LY2157299	TGFBR1	
IPA-3	PAK1	
Esomeprazole Sodium	ATP4A	
DMH1	ACVR1	
Ozagrel	TBXA2R	
AZD4547	FGFR1, FGFR2, FGFR3	
GW9508	FFAR1, FFAR4	
VE-821	ATR	
NSC 405020	MMP14	
GNF-2	ABL1	
TPCA-1	IKBKB	
T0901317	NR1H3, NR1H2, NR1H4	
PD0325901	MAP2K1, MAP2K2	
PYR-41	UBA1	
U0126-EtOH	MAP2K1, MAP2K2	
C646	EP300	
Oxcarbazepine	SCN	
Mdivi-1	DRP1, DNM1	
MRS 2578	P2RY6	
AGI-5198	IDH1	
LY2603618	CHEK1	
BTB06584	ATP5A1	
NPS-2143	CASR	
Veliparib (ABT-888)	PARP1, PARP2	
Dalcetrapib (JTT-705, RO4607381)	CETP	
Vandetanib (ZD6474)	KDR	
Istradefylline	ADORA2A	
Iniparib (BSI-201)	PARP1	
Dabrafenib (GSK2118436)	BRAF (V600)	
Finasteride	SRD5A2	
Tyrphostin AG 879	ERBB2	
Cilomilast	PDE4	
TAE226 (NVP-TAE226)	PTK2, PTK2B	
Ozagrel HCl	TBXAS1	
Vildagliptin (LAF-237)	DPP4	
Dynasore	DNM1, DNM2	
Piceatannol	SYK	
Quizartinib (AC220)	FLT3	
Tenovin-6	TP53, SIRT2, SIRT1, SIRT3	

Enzastaurin (LY317615)	PRKCB, PRKCA, PRKCG, PRKCE	
CGP 57380	MKNK1	
Bisoprolol fumarate	ADRB1	
Bosutinib (SKI-606)	SRC, ABL1	
S3I-201	STAT3	
HA14-1	BCL2	
ADL5859 HCl	OPRK1, OPRM1	
Voriconazole	CYP51A1	
BIBR 1532	TERT	
Thiazovivin	ROCK1, ROCK2	
Anastrozole	CYP19A1	
SB743921	0	
EUK 134	SOD1	
Bergenin	0	
SN-38	TOP1	
CP-91149	PYGL, PYGM, PYGB	
Wnt-C59 (C59)	WNT3A	
NU7026	PRKDC	
BAM7	BAX	
ZM 306416	FLT1	
(+)-JQ1	BRD4	
GW9662	PPARG	
KPT-185	XPO1	
Pifithrin-μ	TP53, HSPBP1	
Batimastat (BB-94)	MMP1, MMP2, MMP3, MMP7, MMP9	
Sertraline HCl	0	
OG-L002	KDM1A	
MK-1775	WEE1	
Costunolide	TERT	
AT101	BCL2, BCL2L1, MCL1	
GSK690693	AKT1, AKT2, AKT3	
Tropicamide	CHRM4	
BMS-707035	0	
Raltegravir (MK-0518)	0	
EX 527 (Selisistat)	SIRT1	
CCT128930	AKT2	
Pomalidomide	TNF	
Tie2 kinase inhibitor	TEK	
Ouabain	ATP1B	
Ranitidine	HRH2	
SKI II	S1PR	

Fluvastatin Sodium	HMGCR	
Propranolol HCl	ADRB1	
Erastin	VDAC	
Ifenprodil Tartrate	GRIN	
KPT-276	XPO1	
AZD2461	PARP	
KPT-330	XPO1	
AGI-6780	IDH2	
SGI-1027	DNMT1, DNMT3A, DNMT3B	
Atglistatin	PNPLA2	
Suvorexant (MK-4305)	HCRTR1, HCRTR2	
SRT1720	SIRT1	
4EGI-1	EIF4E	
Exemestane	CYP19A1	
NSC 23766	RAC	
2-Methoxyestradiol (2-MeOE2)	HIF1A	
Palbociclib (PD-0332991) HCl	CDK4, CDK6	
EHop-016	RAC1, RAC3	
PF-573228	PTK2	
ABT-199 (GDC-0199)	BCL2	
PTC-209	BMI1	
Trimebutine	OPRK1, OPRM1, OPRD1	
CK-636	ARPC2, ARPC3	
SGI-1776 free base	PIM1, FLT3, GSG2	
AZD7545	PDK1, PDK2	
URB597	FAAH	
Pacritinib (SB1518)	JAK2, FLT3	
KX2-391	SRC	
PluriSIn #1 (NSC 14613)	SCD	
Crenolanib (CP-868596)	PDGFRA, PDGFRB, FLT3 (D842V)	
Enzalutamide (MDV3100)	AR	
PFI-1 (PF-6405761)	BRD4	
Dapagliflozin	SLC5A2	
Maraviroc	CCR5	
Nebivolol	ADRB1	
I-BET151 (GSK1210151A)	BRD2, BRD3, BRD4	
Apoptosis Activator 2	CASP3	
Naproxen	PTGS1, PTGS2	
Bosentan Hydrate	EDNRA, EDNRB	
Acadesine	PRKAA1	

E-64	CTSK	
Captopril	ACE	
Selumetinib (AZD6244)	MAP2K1, MAPK3, MAPK1	
Tolvaptan	AVPR2	
PD184352 (CI-1040)	MAP2K1, MAP2K2	
OSI-906 (Linsitinib)	IGFR1, INSR	
Canagliflozin	SLC5A2	
CP-673451	PDGFRA, PDGFRB	
Sirtinol	SIRT1, SIRT2	
Methotrexate	DHFR	
SAR131675	FLT4	
Pralatrexate	DHFR	
BML-190	CNR2	
TWS119	GSK3B	
IKK-16 (IKK Inhibitor VII)	IKBKB, CHUK	
Triamterene	SCN	
Clemastine Fumarate	HRH1	
Fingolimod (FTY720) HCl	S1PR	
Amlodipine	CACNA1C	
PP2	SRC	
CHIR-124	CHEK1	
Temsirolimus (CCI-779, NSC 683864)	MTOR	
YO-01027	APP, APPL1, NOTCH	
Trichostatin A (TSA)	ALL HDACS (Except HDAC8)	
PAC-1	CASP3	
PHA-665752	MET	
VE-822	ATR	
SB203580	MAPK11, MAPK12, MAPK13, MAPK14	
EPZ-6438	EZH2	
KU-55933 (ATM Kinase Inhibitor)	ATM	
CGK 733	ATM, ATR	
WZ4002	EGFR	
WZ4003	NUAK1, NUAK2	
TAK-700 (Orteronel)	CYP17A1	
Loxistatin Acid (E-64C)	0	
Zibotentan (ZD4054)	EDNRA	
Pyrimethamine	DHFR	
RKI-1447	ROCK1, ROCK2	
UNC2250	MERTK	
SMI-4a	PIM1	

SB415286	GSK3A	
PRT062607 (P505-15, BIIB057) HCl	SYK	
Torcetrapib	CETP	
MK-2206 2HCl	AKT1, AKT2, AKT3	
ML130 (Nodinitib-1)	NOD1	
PF-04217903	MET	
Varespladib (LY315920)	PLA2G2A	
ML161	PARP1	
MK-2866 (GTx-024)	AR	
Ticagrelor	P2RY12	
Letrozole	CYP19A1	
GW2580	CSF1R	
Zosuquidar (LY335979) 3HCl	ABCB1	
KU-60019	ATM	
LY2228820	MAPK11, MAPK12, MAPK13, MAPK14	
MLN2238	PSMC1	
Org 27569	CNR1	
Oxymetazoline HCl	ADRA1A	
DMXAA (Vadimezan)	NQ01	
Anacetrapib (MK-0859)	CETP	
AM1241	CNR2	
Embelin	XIAP	
Toremifene Citrate	ESR	
GSK2656157	EIF2AK3	
Felodipine	CACNA1C	
(+)-Bicuculline	GABR, KCNMA1	
Ticlopidine HCl	P2RY	
SANT-1	SMO	
Ispinesib (SB-715992)	0	
BTZ043 Racemate	0	
AZD7762	CHEK1, CHEK2	
AVL-292	BTK	
Pimobendan	PDE3	
DBeQ	VCP	
Formoterol Hemifumarate	ADRB2	
CNX-774	BTK	
Lovastatin	HMGCR	
Lafutidine	HRH2	
AZ191	DYRK1B	
JSH-23	NFKB	

Pramipexole	DRD2S,DRD2L, DRD3, DRD4	
RepSox	TGFBR1	
Bazedoxifene HCl	ESR1, ESR2	
Golgicide A	GBF1	
LDE225 (NVP-LDE225,Erismodegib)	SMO	
Ridaforolimus (Deforolimus, MK-8669)	MTOR	
LY2784544	JAK2	
SNS-314 Mesylate	AURKA, AURKB, AURKC	
BGJ398 (NVP-BGJ398)	FGFR1, FGFR2, FGFR3	
Irinotecan	TOP1	
OSI-420	EGFR	
Dutasteride	SRD5A2, SRD5A1	
Apigenin	CYP2C9	
Rigosertib (ON-01910)	PLK1, PLK2	
Forskolin	ADCY4	
Rolipram	PDE4	
Bupivacaine HCl	ADCY4	
UNC669	L3MBTL1	
Tioxolone	CA1	
PF-4708671	RPS6KB1	
5-hydroxymethyl Tolterodine (PNU 200577, 5-HMT, 5-HM)	CHRM1	
XAV-939	WNT	
SB742457	HTR6	
Cinacalcet HCl	CASR	
Linagliptin	DPP4	
Etomidate	GABR	
Entacapone	COMT	
Moclobemide (Ro 111163)	MAOA	
LY411575	APP, NOTCH	
GDC-0152	XIAP, BIRC7, AP1, AP2	
OC000459	PTGDR2	
NLG919	IDO1	
Levosulpiride	DRD2	
Imatinib (STI571)	ABL1, KIT, PDGFR	
DCC-2036 (Rebastinib)	ABL1, SRC, LYN, FGR, HCK, KDR, FLT3	
XL335	NR1H4	
Nilvadipine	CACNA1C	
CHIR-98014	GSK3A, GSK3B	
GW4064	NR1H4	
PF-5274857	SMO	

GDC-0068	AKT1, AKT2, AKT3	
JNJ-1661010	FAAH	
VU 0364770	GRM4	
U-104	CA12	
Daunorubicin HCl	TOP2	
PF-562271	PTK2	
AZD3463	ALK, IGFR1	
IOX2	EGLN1	
IMD 0354	IKBKB, CHUK	
CRT0044876	APE1	
TCID	UCHL3	
LB42708	FNTA	
Necrostatin-1	RIPK1	
Empagliflozin (BI 10773)	SLC5A2	
SU11274	MET	
Bortezomib (PS-341)	PSMC1	
YM155 (Sepantronium Bromide)	BIRC5	
Lenalidomide (CC-5013)	TNF	
AUY922 (NVP-AUY922)	HSP90A, HSP90B	
Agomelatine	HTR2C	
17-AAG (Tanespimycin)	HSP90	
SP600125	JKAMP, MAPK9, MAPK10; MAP2K4; MAP2K3, MAP2K6, AKT1, PRKC; MAPK1, MAPK14, CHEK1, EGFR	
CEP-18770 (Delanzomib)	PSMC1	
Aprepitant	TACR1	
Fluvoxamine maleate	0	
Oligomycin A	ATPAF1	
Ginkgolide A	GABR	
Cryptotanshinone	STAT3	
ICG-001	WNT	
Stattic	STAT3	
SC144	IL6ST	
SRPIN340	SRPK1	
Trelagliptin	DPP4	
Panobinostat (LBH589)	HDAC	
VX-680 (Tozasertib, MK-0457)	AURKA	
GDC-0941	PIK3CA, PIK3CD	
OSU-03012 (AR-12)	PDK1	
0	Akt1, PKCη, PKCθ, PrkX, Akt3, Akt2, PKCδ, PKCβ, PKCε, PKA, PKG1β	

Everolimus (RAD001)	MTOR	
MK-8245	SCD	
Aniracetam	GRIA1,	
Doxazosin Mesylate	ADRA1A	
Ginkgolide B	PTAFR	
Tosedostat (CHR2797)	LAP3, NPEPPS, ANPEP	
Rebamipide	CCKAR	
Rasagiline Mesylate	MAOB	
PD128907 HCl	DDR3	
Apatinib	KDR	
ADX-47273	GRM5	
AZ 3146	TTK, CENPE	
VU 0357121	GRM5	
(-)-MK 801 Maleate	GRIN	
Mirabegron	ADRB3	
AP26113	ALK	
Birinapant	DIABLO (AP1)	
AZD1981	PTGDR2	
LDK378	ALK	
(S)-crizotinib	NUDT1	
ZM 447439	AURKA, AURKB	
BX-912	PDK1	
Tadalafil	PDE5	
Elvitegravir (GS-9137, JTK-303)	0	
Fostamatinib (R788)	SYK	
GSK J4 HCl	KDM6A, KDM6B	
TCS 359	FLT3	
Carvedilol	ADRB1	
Naftopidil	ADRA1A	
ML133 HCl	KCNJ2	
T0070907	PPARG	
Gliquidone	KCNJ	
SC-514	IKBKB	
ZCL278	CDC42	
Caffeic Acid Phenethyl Ester	NFKB	
VU 0364439	GRM4	
SB431542	TGFBR1	
Odanacatib (MK-0822)	CTSK	
Celecoxib	PTGS2	
Etodolac	PTGS1	
Isotretinoin	0	

Stavudine (d4T)	0	
VX-745	MAPK14	
GSK429286A	ROCK1, ROCK2	
SB408124	HCRTR1	
H 89 2HCl	PRKAC	
Mubritinib (TAK 165)	ERBB2	
BMS-378806	CD4	
Ki16198	LPAR1, LPAR3	
AZ20	ATR	
AMG-517	TRPV1	
NMS-873	VCP	
Sorafenib	RAF1, BRAF, KDR	
NH125	EEF2K, PRKC, PRKA, CAMK2, Histidine Kinase	
Sal003	EIF2A	
Tariquidar	ABCB1	
Lomeguatrib	MGMT	
BI 2536	PLK1, PLK2, PLK3	
Imidapril HCl	ACE	
GSK461364	PLK1, PLK2, PLK3	
Gliclazide	KCNJ	
Sotrastaurin	PRKC (especially PRKCQ; inactive to PRKCZ)	
BI-D1870	RPS6KA1, RPS6KA2, RPS6KA3, RPS6KA4	
Go 6983	PRKCA, PRKCB, PRKCG, PRKCD	
MNS (3,4-Methylenedioxy-β-nitrostyrene, MDBN)	SYK, SRC, VCP	

PDTX R05

T2 **414 compounds** **Compound**	**Target**	**T6** **35 compounds** **Compound**	**Target**
FG-4592	EPAS1, EPO	Tenofovir Disoproxil Fumarate	0
Rizatriptan Benzoate	HTR1A	Belinostat (PXD101)	HDAC
Fulvestrant	ESR	NSC 319726	TP53 (R175)
Tolfenamic Acid	PTGS2	STF-118804	NAMPT
Ramelteon	MTNR1A, MTNR1B	ABT-263 (Navitoclax)	BCL2, BCL2L1, BCL2L2
Trospium chloride	CHRM1	Ganetespib (STA-9090)	HSP90
Granisetron HCl	HTR3A	Ruxolitinib (INCB018424)	JAK1, JAK2
A-769662	PRKAA1	Tofacitinib (CP-690550,Tasocitinib)	JAK3
Losartan Potassium (DuP 753)	AGTR	PHA-793887	CDK2, CDK5, CDK7
Tolazoline HCl	ADRA1A	KPT-185	XPO1
Tenofovir Disoproxil Fumarate	0	MK-1775	WEE1
Ataluren (PTC124)	CFTR	Ouabain	ATP1B
Candesartan	AGTR	KX2-391	SRC
Belinostat (PXD101)	HDAC	Crenolanib (CP-868596)	PDGFRA, PDGFRB, FLT3 (D842V)
Semagacestat (LY450139)	APP, NOTCH	CHIR-124	CHEK1
NVP-ADW742	IGFR1	Trichostatin A (TSA)	ALL HDACS (Except HDAC8)
NSC 319726	TP53 (R175)	AZD7762	CHEK1, CHEK2
Icotinib	EGFR	DBeQ	VCP
Ilomastat (GM6001, Galardin)	MMP1, MMP2, MMP3, MMP7, MMP8, MMP9, MMP12, MMP14, MMP26	Bortezomib (PS-341)	PSMC1
Rivaroxaban	F10	YM155 (Sepantronium Bromide)	BIRC5
STF-118804	NAMPT	AUY922 (NVP-AUY922)	HSP90A, HSP90B
Rimonabant	CNR1	17-AAG (Tanespimycin)	HSP90
FLI-06	NOTCH	CEP-18770 (Delanzomib)	PSMC1
Sitaxentan sodium	EDNRA	Oligomycin A	ATPAF1
ABT-263 (Navitoclax)	BCL2, BCL2L1, BCL2L2	Stattic	STAT3
Brinzolamide	CA2	SC144	IL6ST
Tandutinib (MLN518)	FLT3, PDGFR KIT	Rasagiline Mesylate	MAOB
Zebularine	DNMT1, DNMT3A, DNMT3B	(S)-crizotinib	NUDT1
MLN8054	AURKA	GSK J4 HCl	KDM6A, KDM6B
PR-619	ATXN7L3, BAP1, OTUB1, OTUD1, OTUD6A, OTUDB7A, UBB, UCHL3, USP1, USP2, USP4, USP5, USP7, USP8, USP14, USP15, USP17,	Caffeic Acid Phenethyl Ester	NFKB

	USP26, USP30, USP36, YOD1		
Roxatidine Acetate HCl	HRH2	AZ20	ATR
GSK1904529A	IGFR1, INSR	NMS-873	VCP
Atorvastatin Calcium	HMGCR	GSK461364	PLK1, PLK2, PLK3
SNS-032 (BMS-387032)	CDK2	Sotrastaurin	PRKC (especially PRKCQ; inactive to PRKCZ)
Naltrexone HCl	OPRK1, OPRM1, OPRD1	BI-D1870	RPS6KA1, RPS6KA2, RPS6KA3, RPS6KA4
Ganetespib (STA-9090)	HSP90		
CGS 21680 HCl	ADORA2A		
Pancuronium dibromide	0		
Loratadine	HRH1		
PNU-120596	0		
Ruxolitinib (INCB018424)	JAK1, JAK2		
GW3965 HCl	NR1H3, NR1H2		
AZD6482	PIK3CB		
SB705498	TRPV1		
Safinamide Mesylate	MAOB, MAOA		
Tenofovir	0		
P22077	USP7, USP47		
Aloxistatin	0		
NSC697923	UBE2		
Apixaban	F10		
ML347	ACVR1, ACVRL1		
Irinotecan HCl Trihydrate	TOP1		
SSR128129E	FGFR1		
VX-765	CASP1		
Ferrostatin-1 (Fer-1)	VDAC		
PF-3845	FAAH		
OTX015	BRD2, BRD3, BRD4		
Ibrutinib (PCI-32765)	BTK		
4E1RCat	EIF4E		
Tofacitinib (CP-690550,Tasocitinib)	JAK3		
PHA-793887	CDK2, CDK5, CDK7		
WZ811	CXCR4		
Allopurinol	HCRTR1, HCRTR2		
HC-030031	TRPA1		
Telmisartan	AGTR		
Mozavaptan	AVPR1, AVPR2		
Cyproterone Acetate	AR		
Sodium 4-Aminosalicylate	NFKB		

GSK1292263	GPR119	
SGC 0946	DOT1L	
LY2157299	TGFBR1	
IPA-3	PAK1	
Esomeprazole Sodium	ATP4A	
DMH1	ACVR1	
Ozagrel	TBXA2R	
AZD4547	FGFR1, FGFR2, FGFR3	
GW9508	FFAR1, FFAR4	
VE-821	ATR	
NSC 405020	MMP14	
GNF-2	ABL1	
TPCA-1	IKBKB	
T0901317	NR1H3, NR1H2, NR1H4	
PD0325901	MAP2K1, MAP2K2	
PYR-41	UBA1	
U0126-EtOH	MAP2K1, MAP2K2	
C646	EP300	
Oxcarbazepine	SCN	
Mdivi-1	DRP1, DNM1	
MRS 2578	P2RY6	
AGI-5198	IDH1	
LY2603618	CHEK1	
BTB06584	ATP5A1	
NPS-2143	CASR	
Veliparib (ABT-888)	PARP1, PARP2	
Dalcetrapib (JTT-705, RO4607381)	CETP	
Vandetanib (ZD6474)	KDR	
Istradefylline	ADORA2A	
Iniparib (BSI-201)	PARP1	
Dabrafenib (GSK2118436)	BRAF (V600)	
Finasteride	SRD5A2	
Tyrphostin AG 879	ERBB2	
Cilomilast	PDE4	
TAE226 (NVP-TAE226)	PTK2, PTK2B	
Ozagrel HCl	TBXAS1	
Vildagliptin (LAF-237)	DPP4	
Dynasore	DNM1, DNM2	
Piceatannol	SYK	
Quizartinib (AC220)	FLT3	
Tenovin-6	TP53, SIRT2, SIRT1, SIRT3	

Enzastaurin (LY317615)	PRKCB, PRKCA, PRKCG, PRKCE	
CGP 57380	MKNK1	
Bisoprolol fumarate	ADRB1	
Bosutinib (SKI-606)	SRC, ABL1	
S3I-201	STAT3	
HA14-1	BCL2	
ADL5859 HCl	OPRK1, OPRM1	
Voriconazole	CYP51A1	
BIBR 1532	TERT	
Thiazovivin	ROCK1, ROCK2	
Anastrozole	CYP19A1	
SB743921	0	
EUK 134	SOD1	
Bergenin	0	
SN-38	TOP1	
CP-91149	PYGL, PYGM, PYGB	
Wnt-C59 (C59)	WNT3A	
NU7026	PRKDC	
BAM7	BAX	
ZM 306416	FLT1	
(+)-JQ1	BRD4	
GW9662	PPARG	
KPT-185	XPO1	
Pifithrin-μ	TP53, HSPBP1	
Batimastat (BB-94)	MMP1, MMP2, MMP3, MMP7, MMP9	
Sertraline HCl	0	
OG-L002	KDM1A	
MK-1775	WEE1	
Costunolide	TERT	
AT101	BCL2, BCL2L1, MCL1	
GSK690693	AKT1, AKT2, AKT3	
Tropicamide	CHRM4	
BMS-707035	0	
Raltegravir (MK-0518)	0	
EX 527 (Selisistat)	SIRT1	
CCT128930	AKT2	
Pomalidomide	TNF	
Tie2 kinase inhibitor	TEK	
Ouabain	ATP1B	
Ranitidine	HRH2	
SKI II	S1PR	

Fluvastatin Sodium	HMGCR	
Propranolol HCl	ADRB1	
Erastin	VDAC	
Ifenprodil Tartrate	GRIN	
KPT-276	XPO1	
AZD2461	PARP	
KPT-330	XPO1	
AGI-6780	IDH2	
SGI-1027	DNMT1, DNMT3A, DNMT3B	
Atglistatin	PNPLA2	
Suvorexant (MK-4305)	HCRTR1, HCRTR2	
SRT1720	SIRT1	
4EGI-1	EIF4E	
Exemestane	CYP19A1	
NSC 23766	RAC	
2-Methoxyestradiol (2-MeOE2)	HIF1A	
Palbociclib (PD-0332991) HCl	CDK4, CDK6	
EHop-016	RAC1, RAC3	
PF-573228	PTK2	
ABT-199 (GDC-0199)	BCL2	
PTC-209	BMI1	
Trimebutine	OPRK1, OPRM1, OPRD1	
CK-636	ARPC2, ARPC3	
SGI-1776 free base	PIM1, FLT3, GSG2	
AZD7545	PDK1, PDK2	
URB597	FAAH	
Pacritinib (SB1518)	JAK2, FLT3	
KX2-391	SRC	
PluriSIn #1 (NSC 14613)	SCD	
Crenolanib (CP-868596)	PDGFRA, PDGFRB, FLT3 (D842V)	
Enzalutamide (MDV3100)	AR	
PFI-1 (PF-6405761)	BRD4	
Dapagliflozin	SLC5A2	
Maraviroc	CCR5	
Nebivolol	ADRB1	
I-BET151 (GSK1210151A)	BRD2, BRD3, BRD4	
Apoptosis Activator 2	CASP3	
Naproxen	PTGS1, PTGS2	
Bosentan Hydrate	EDNRA, EDNRB	
Acadesine	PRKAA1	

E-64	CTSK	
Captopril	ACE	
Selumetinib (AZD6244)	MAP2K1, MAPK3, MAPK1	
Tolvaptan	AVPR2	
PD184352 (CI-1040)	MAP2K1, MAP2K2	
OSI-906 (Linsitinib)	IGFR1, INSR	
Canagliflozin	SLC5A2	
CP-673451	PDGFRA, PDGFRB	
Sirtinol	SIRT1, SIRT2	
Methotrexate	DHFR	
SAR131675	FLT4	
Pralatrexate	DHFR	
BML-190	CNR2	
TWS119	GSK3B	
IKK-16 (IKK Inhibitor VII)	IKBKB, CHUK	
Triamterene	SCN	
Clemastine Fumarate	HRH1	
Fingolimod (FTY720) HCl	S1PR	
Amlodipine	CACNA1C	
PP2	SRC	
CHIR-124	CHEK1	
Temsirolimus (CCI-779, NSC 683864)	MTOR	
YO-01027	APP, APPL1, NOTCH	
Trichostatin A (TSA)	ALL HDACS (Except HDAC8)	
PAC-1	CASP3	
PHA-665752	MET	
VE-822	ATR	
SB203580	MAPK11, MAPK12, MAPK13, MAPK14	
EPZ-6438	EZH2	
KU-55933 (ATM Kinase Inhibitor)	ATM	
CGK 733	ATM, ATR	
WZ4002	EGFR	
WZ4003	NUAK1, NUAK2	
TAK-700 (Orteronel)	CYP17A1	
Loxistatin Acid (E-64C)	0	
Zibotentan (ZD4054)	EDNRA	
Pyrimethamine	DHFR	
RKI-1447	ROCK1, ROCK2	
UNC2250	MERTK	
SMI-4a	PIM1	

SB415286	GSK3A	
PRT062607 (P505-15, BIIB057) HCl	SYK	
Torcetrapib	CETP	
MK-2206 2HCl	AKT1, AKT2, AKT3	
ML130 (Nodinitib-1)	NOD1	
PF-04217903	MET	
Varespladib (LY315920)	PLA2G2A	
ML161	PARP1	
MK-2866 (GTx-024)	AR	
Ticagrelor	P2RY12	
Letrozole	CYP19A1	
GW2580	CSF1R	
Zosuquidar (LY335979) 3HCl	ABCB1	
KU-60019	ATM	
LY2228820	MAPK11, MAPK12, MAPK13, MAPK14	
MLN2238	PSMC1	
Org 27569	CNR1	
Oxymetazoline HCl	ADRA1A	
DMXAA (Vadimezan)	NQ01	
Anacetrapib (MK-0859)	CETP	
AM1241	CNR2	
Embelin	XIAP	
Toremifene Citrate	ESR	
GSK2656157	EIF2AK3	
Felodipine	CACNA1C	
(+)-Bicuculline	GABR, KCNMA1	
Ticlopidine HCl	P2RY	
SANT-1	SMO	
Ispinesib (SB-715992)	0	
BTZ043 Racemate	0	
AZD7762	CHEK1, CHEK2	
AVL-292	BTK	
Pimobendan	PDE3	
DBeQ	VCP	
Formoterol Hemifumarate	ADRB2	
CNX-774	BTK	
Lovastatin	HMGCR	
Lafutidine	HRH2	
AZ191	DYRK1B	
JSH-23	NFKB	

Pramipexole	DRD2S,DRD2L, DRD3, DRD4	
RepSox	TGFBR1	
Bazedoxifene HCl	ESR1, ESR2	
Golgicide A	GBF1	
LDE225 (NVP-LDE225,Erismodegib)	SMO	
Ridaforolimus (Deforolimus, MK-8669)	MTOR	
LY2784544	JAK2	
SNS-314 Mesylate	AURKA, AURKB, AURKC	
BGJ398 (NVP-BGJ398)	FGFR1, FGFR2, FGFR3	
Irinotecan	TOP1	
OSI-420	EGFR	
Dutasteride	SRD5A2, SRD5A1	
Apigenin	CYP2C9	
Rigosertib (ON-01910)	PLK1, PLK2	
Forskolin	ADCY4	
Rolipram	PDE4	
Bupivacaine HCl	ADCY4	
UNC669	L3MBTL1	
Tioxolone	CA1	
PF-4708671	RPS6KB1	
5-hydroxymethyl Tolterodine (PNU 200577, 5-HMT, 5-HM)	CHRM1	
XAV-939	WNT	
SB742457	HTR6	
Cinacalcet HCl	CASR	
Linagliptin	DPP4	
Etomidate	GABR	
Entacapone	COMT	
Moclobemide (Ro 111163)	MAOA	
LY411575	APP, NOTCH	
GDC-0152	XIAP, BIRC7, AP1, AP2	
OC000459	PTGDR2	
NLG919	IDO1	
Levosulpiride	DRD2	
Imatinib (STI571)	ABL1, KIT, PDGFR	
DCC-2036 (Rebastinib)	ABL1, SRC, LYN, FGR, HCK, KDR, FLT3	
XL335	NR1H4	
Nilvadipine	CACNA1C	
CHIR-98014	GSK3A, GSK3B	
GW4064	NR1H4	
PF-5274857	SMO	

GDC-0068	AKT1, AKT2, AKT3	
JNJ-1661010	FAAH	
VU 0364770	GRM4	
U-104	CA12	
Daunorubicin HCl	TOP2	
PF-562271	PTK2	
AZD3463	ALK, IGFR1	
IOX2	EGLN1	
IMD 0354	IKBKB, CHUK	
CRT0044876	APE1	
TCID	UCHL3	
LB42708	FNTA	
Necrostatin-1	RIPK1	
Empagliflozin (BI 10773)	SLC5A2	
SU11274	MET	
Bortezomib (PS-341)	PSMC1	
YM155 (Sepantronium Bromide)	BIRC5	
Lenalidomide (CC-5013)	TNF	
AUY922 (NVP-AUY922)	HSP90A, HSP90B	
Agomelatine	HTR2C	
17-AAG (Tanespimycin)	HSP90	
SP600125	JKAMP, MAPK9, MAPK10; MAP2K4; MAP2K3, MAP2K6, AKT1, PRKC; MAPK1, MAPK14, CHEK1, EGFR	
CEP-18770 (Delanzomib)	PSMC1	
Aprepitant	TACR1	
Fluvoxamine maleate	0	
Oligomycin A	ATPAF1	
Ginkgolide A	GABR	
Cryptotanshinone	STAT3	
ICG-001	WNT	
Stattic	STAT3	
SC144	IL6ST	
SRPIN340	SRPK1	
Trelagliptin	DPP4	
Panobinostat (LBH589)	HDAC	
VX-680 (Tozasertib, MK-0457)	AURKA	
GDC-0941	PIK3CA, PIK3CD	
OSU-03012 (AR-12)	PDK1	
0	Akt1, PKCη, PKCθ, PrkX, Akt3, Akt2, PKCδ, PKCβ, PKCε, PKA, PKG1β	

Everolimus (RAD001)	MTOR	
MK-8245	SCD	
Aniracetam	GRIA1,	
Doxazosin Mesylate	ADRA1A	
Ginkgolide B	PTAFR	
Tosedostat (CHR2797)	LAP3, NPEPPS, ANPEP	
Rebamipide	CCKAR	
Rasagiline Mesylate	MAOB	
PD128907 HCl	DDR3	
Apatinib	KDR	
ADX-47273	GRM5	
AZ 3146	TTK, CENPE	
VU 0357121	GRM5	
(-)-MK 801 Maleate	GRIN	
Mirabegron	ADRB3	
AP26113	ALK	
Birinapant	DIABLO (AP1)	
AZD1981	PTGDR2	
LDK378	ALK	
(S)-crizotinib	NUDT1	
ZM 447439	AURKA, AURKB	
BX-912	PDK1	
Tadalafil	PDE5	
Elvitegravir (GS-9137, JTK-303)	0	
Fostamatinib (R788)	SYK	
GSK J4 HCl	KDM6A, KDM6B	
TCS 359	FLT3	
Carvedilol	ADRB1	
Naftopidil	ADRA1A	
ML133 HCl	KCNJ2	
T0070907	PPARG	
Gliquidone	KCNJ	
SC-514	IKBKB	
ZCL278	CDC42	
Caffeic Acid Phenethyl Ester	NFKB	
VU 0364439	GRM4	
SB431542	TGFBR1	
Odanacatib (MK-0822)	CTSK	
Celecoxib	PTGS2	
Etodolac	PTGS1	
Isotretinoin	0	

Stavudine (d4T)	0	
VX-745	MAPK14	
GSK429286A	ROCK1, ROCK2	
SB408124	HCRTR1	
H 89 2HCl	PRKAC	
Mubritinib (TAK 165)	ERBB2	
BMS-378806	CD4	
Ki16198	LPAR1, LPAR3	
AZ20	ATR	
AMG-517	TRPV1	
NMS-873	VCP	
Sorafenib	RAF1, BRAF, KDR	
NH125	EEF2K, PRKC, PRKA, CAMK2, Histidine Kinase	
Sal003	EIF2A	
Tariquidar	ABCB1	
Lomeguatrib	MGMT	
BI 2536	PLK1, PLK2, PLK3	
Imidapril HCl	ACE	
GSK461364	PLK1, PLK2, PLK3	
Gliclazide	KCNJ	
Sotrastaurin	PRKC (especially PRKCQ; inactive to PRKCZ)	
BI-D1870	RPS6KA1, RPS6KA2, RPS6KA3, RPS6KA4	
Go 6983	PRKCA, PRKCB, PRKCG, PRKCD	

PDTX R06

T4		**T7**	
269 compounds		**25 compounds**	
Compound	**Target**	**Compound**	**Target**
Rizatriptan Benzoate	HTR1A	Belinostat (PXD101)	HDAC
Tolfenamic Acid	PTGS2	NSC 319726	TP53 (R175)
Ramelteon	MTNR1A, MTNR1B	STF-118804	NAMPT
Belinostat (PXD101)	HDAC	ABT-263 (Navitoclax)	BCL2, BCL2L1, BCL2L2
Rivaroxaban	F10	Ganetespib (STA-9090)	HSP90
Rimonabant	CNR1	Ruxolitinib (INCB018424)	JAK1, JAK2
FLI-06	NOTCH	Tofacitinib (CP-690550,Tasocitinib)	JAK3
Sitaxentan sodium	EDNRA	PHA-793887	CDK2, CDK5, CDK7
Brinzolamide	CA2	KPT-185	XPO1
Zebularine	DNMT1, DNMT3A, DNMT3B	MK-1775	WEE1
MLN8054	AURKA	Ouabain	ATP1B

PR-619	ATXN7L3, BAP1, OTUB1, OTUD1, OTUD6A, OTUDB7A, UBB, UCHL3, USP1, USP2, USP4, USP5, USP7, USP8, USP14, USP15, USP17, USP26, USP30, USP36, YOD1	KX2-391	SRC
Naltrexone HCl	OPRK1, OPRM1, OPRD1	Crenolanib (CP-868596)	PDGFRA, PDGFRB, FLT3 (D842V)
Ganetespib (STA-9090)	HSP90	CHIR-124	CHEK1
Vemurafenib (PLX4032, RG7204)	BRAF (V600E)	Trichostatin A (TSA)	ALL HDACS (Except HDAC8)
Pancuronium dibromide	0	AZD7762	CHEK1, CHEK2
Loratadine	HRH1	DBeQ	VCP
PNU-120596	0	Bortezomib (PS-341)	PSMC1
GW3965 HCl	NR1H3, NR1H2	YM155 (Sepantronium Bromide)	BIRC5
AZD6482	PIK3CB	AUY922 (NVP-AUY922)	HSP90A, HSP90B
SB705498	TRPV1	17-AAG (Tanespimycin)	HSP90
Safinamide Mesylate	MAOB, MAOA	CEP-18770 (Delanzomib)	PSMC1
Tenofovir	0	Oligomycin A	ATPAF1
Apixaban	F10	Stattic	STAT3
ML347	ACVR1, ACVRL1	SC144	IL6ST
Ferrostatin-1 (Fer-1)	VDAC	Rasagiline Mesylate	MAOB
Rotundine	DRD1	(S)-crizotinib	NUDT1
MM-102	KANSL1	GSK J4 HCl	KDM6A, KDM6B
OTX015	BRD2, BRD3, BRD4	Caffeic Acid Phenethyl Ester	NFKB
Tofacitinib (CP-690550,Tasocitinib)	JAK3	AZ20	ATR
PHA-793887	CDK2, CDK5, CDK7	NMS-873	VCP
Allopurinol	HCRTR1, HCRTR2	GSK461364	PLK1, PLK2, PLK3
HC-030031	TRPA1	Sotrastaurin	PRKC (especially PRKCQ; inactive to PRKCZ)
Telmisartan	AGTR	BI-D1870	RPS6KA1, RPS6KA2, RPS6KA3, RPS6KA4
Cyproterone Acetate	AR		
Sodium 4-Aminosalicylate	NFKB		
GSK1292263	GPR119		
SGC 0946	DOT1L		
LY2157299	TGFBR1		
IPA-3	PAK1		
Esomeprazole Sodium	ATP4A		
DMH1	ACVR1		
Ozagrel	TBXA2R		
GW9508	FFAR1, FFAR4		
NSC 405020	MMP14		

TPCA-1	IKBKB	
PYR-41	UBA1	
U0126-EtOH	MAP2K1, MAP2K2	
LDN-212854	ACVR1, ACVRL1	
Ki16425	LPAR1, LPAR2, LPAR3	
Mdivi-1	DRP1, DNM1	
MRS 2578	P2RY6	
LY2603618	CHEK1	
BTB06584	ATP5A1	
NPS-2143	CASR	
Veliparib (ABT-888)	PARP1, PARP2	
Dalcetrapib (JTT-705, RO4607381)	CETP	
Istradefylline	ADORA2A	
Iniparib (BSI-201)	PARP1	
Dabrafenib (GSK2118436)	BRAF (V600)	
Tyrphostin AG 879	ERBB2	
Cilomilast	PDE4	
TAE226 (NVP-TAE226)	PTK2, PTK2B	
Vildagliptin (LAF-237)	DPP4	
Dynasore	DNM1, DNM2	
Piceatannol	SYK	
Quizartinib (AC220)	FLT3	
Enzastaurin (LY317615)	PRKCB, PRKCA, PRKCG, PRKCE	
HA14-1	BCL2	
TG100-115	PIK3CG, PIK3CD	
BIBR 1532	TERT	
Anastrozole	CYP19A1	
SB743921	0	
EUK 134	SOD1	
Bergenin	0	
CP-91149	PYGL, PYGM, PYGB	
Wnt-C59 (C59)	WNT3A	
NU7026	PRKDC	
BAM7	BAX	
(+)-JQ1	BRD4	
GW9662	PPARG	
KPT-185	XPO1	
Pifithrin-μ	TP53, HSPBP1	
Batimastat (BB-94)	MMP1, MMP2, MMP3, MMP7, MMP9	
Sertraline HCl	0	
OG-L002	KDM1A	

MK-1775	WEE1	
AT101	BCL2, BCL2L1, MCL1	
Tropicamide	CHRM4	
BMS-707035	0	
Raltegravir (MK-0518)	0	
AS-252424	PIK3CG	
Tie2 kinase inhibitor	TEK	
Ouabain	ATP1B	
Ranitidine	HRH2	
Fluvastatin Sodium	HMGCR	
Propranolol HCl	ADRB1	
Erastin	VDAC	
Ifenprodil Tartrate	GRIN	
KPT-276	XPO1	
AZD2461	PARP	
KPT-330	XPO1	
AGI-6780	IDH2	
SGI-1027	DNMT1, DNMT3A, DNMT3B	
Atglistatin	PNPLA2	
Suvorexant (MK-4305)	HCRTR1, HCRTR2	
SRT1720	SIRT1	
Exemestane	CYP19A1	
NSC 23766	RAC	
EHop-016	RAC1, RAC3	
PF-573228	PTK2	
ABT-199 (GDC-0199)	BCL2	
Memantine HCl	CYP2B6	
Trimebutine	OPRK1, OPRM1, OPRD1	
AZD7545	PDK1, PDK2	
URB597	FAAH	
GW0742	PPARD	
Pacritinib (SB1518)	JAK2, FLT3	
KX2-391	SRC	
Crenolanib (CP-868596)	PDGFRA, PDGFRB, FLT3 (D842V)	
PFI-1 (PF-6405761)	BRD4	
Dapagliflozin	SLC5A2	
Maraviroc	CCR5	
Nebivolol	ADRB1	
E-64	CTSK	
OSI-906 (Linsitinib)	IGFR1, INSR	
Canagliflozin	SLC5A2	

Sirtinol	SIRT1, SIRT2	
Methotrexate	DHFR	
SAR131675	FLT4	
Pralatrexate	DHFR	
TWS119	GSK3B	
IKK-16 (IKK Inhibitor VII)	IKBKB, CHUK	
Enalaprilat Dihydrate	ACE	
Triamterene	SCN	
Clemastine Fumarate	HRH1	
Fingolimod (FTY720) HCl	S1PR	
PP2	SRC	
CHIR-124	CHEK1	
Temsirolimus (CCI-779, NSC 683864)	MTOR	
Trichostatin A (TSA)	ALL HDACS (Except HDAC8)	
PHA-665752	MET	
CGK 733	ATM, ATR	
WZ4002	EGFR	
TAK-700 (Orteronel)	CYP17A1	
Loxistatin Acid (E-64C)	0	
Zibotentan (ZD4054)	EDNRA	
Pyrimethamine	DHFR	
RKI-1447	ROCK1, ROCK2	
SMI-4a	PIM1	
SB415286	GSK3A	
Torcetrapib	CETP	
MK-2206 2HCl	AKT1, AKT2, AKT3	
PF-04217903	MET	
GW441756	NTRK1	
Varespladib (LY315920)	PLA2G2A	
Ticagrelor	P2RY12	
Letrozole	CYP19A1	
GW2580	CSF1R	
Zosuquidar (LY335979) 3HCl	ABCB1	
KU-60019	ATM	
LY2228820	MAPK11, MAPK12, MAPK13, MAPK14	
Oxymetazoline HCl	ADRA1A	
DMXAA (Vadimezan)	NQ01	
Embelin	XIAP	
Toremifene Citrate	ESR	
GSK2656157	EIF2AK3	

Ticlopidine HCl	P2RY	
SANT-1	SMO	
Ispinesib (SB-715992)	0	
BTZ043 Racemate	0	
AZD7762	CHEK1, CHEK2	
AVL-292	BTK	
Pimobendan	PDE3	
DBeQ	VCP	
Formoterol Hemifumarate	ADRB2	
Lovastatin	HMGCR	
Pramipexole	DRD2S,DRD2L, DRD3, DRD4	
RepSox	TGFBR1	
Bazedoxifene HCl	ESR1, ESR2	
Golgicide A	GBF1	
LDE225 (NVP-LDE225,Erismodegib)	SMO	
Ridaforolimus (Deforolimus, MK-8669)	MTOR	
LY2784544	JAK2	
SNS-314 Mesylate	AURKA, AURKB, AURKC	
Irinotecan	TOP1	
Dutasteride	SRD5A2, SRD5A1	
Apigenin	CYP2C9	
Forskolin	ADCY4	
Rolipram	PDE4	
Bupivacaine HCl	ADCY4	
UNC669	L3MBTL1	
Tioxolone	CA1	
PF-4708671	RPS6KB1	
5-hydroxymethyl Tolterodine (PNU 200577, 5-HMT, 5-HM)	CHRM1	
XAV-939	WNT	
SB742457	HTR6	
Cinacalcet HCl	CASR	
Linagliptin	DPP4	
Etomidate	GABR	
Entacapone	COMT	
LY411575	APP, NOTCH	
OC000459	PTGDR2	
NLG919	IDO1	
Levosulpiride	DRD2	
Imatinib (STI571)	ABL1, KIT, PDGFR	
DCC-2036 (Rebastinib)	ABL1, SRC, LYN, FGR, HCK, KDR, FLT3	

XL335	NR1H4	
Nilvadipine	CACNA1C	
CHIR-98014	GSK3A, GSK3B	
GW4064	NR1H4	
PF-5274857	SMO	
GDC-0068	AKT1, AKT2, AKT3	
VU 0364770	GRM4	
Daunorubicin HCl	TOP2	
PF-562271	PTK2	
AZD3463	ALK, IGFR1	
IOX2	EGLN1	
IMD 0354	IKBKB, CHUK	
CRT0044876	APE1	
TCID	UCHL3	
Necrostatin-1	RIPK1	
Empagliflozin (BI 10773)	SLC5A2	
SU11274	MET	
Bortezomib (PS-341)	PSMC1	
YM155 (Sepantronium Bromide)	BIRC5	
Lenalidomide (CC-5013)	TNF	
AUY922 (NVP-AUY922)	HSP90A, HSP90B	
Agomelatine	HTR2C	
17-AAG (Tanespimycin)	HSP90	
SP600125	JKAMP, MAPK9, MAPK10; MAP2K4; MAP2K3, MAP2K6, AKT1, PRKC; MAPK1, MAPK14, CHEK1, EGFR	
CEP-18770 (Delanzomib)	PSMC1	
Aprepitant	TACR1	
Fluvoxamine maleate	0	
Oligomycin A	ATPAF1	
Ginkgolide A	GABR	
Cryptotanshinone	STAT3	
ICG-001	WNT	
SC144	IL6ST	
SRPIN340	SRPK1	
Panobinostat (LBH589)	HDAC	
VX-680 (Tozasertib, MK-0457)	AURKA	
Everolimus (RAD001)	MTOR	
MK-8245	SCD	
Aniracetam	GRIA1,	
PD128907 HCl	DDR3	

AP26113	ALK	
Birinapant	DIABLO (AP1)	
BX-912	PDK1	
Tadalafil	PDE5	
Fostamatinib (R788)	SYK	
GSK J4 HCl	KDM6A, KDM6B	
Carvedilol	ADRB1	
SC-514	IKBKB	
ZCL278	CDC42	
Isotretinoin	0	
VX-745	MAPK14	
GSK429286A	ROCK1, ROCK2	
Mubritinib (TAK 165)	ERBB2	
BMS-378806	CD4	
Ki16198	LPAR1, LPAR3	
AZ20	ATR	
AMG-517	TRPV1	
NMS-873	VCP	
Sorafenib	RAF1, BRAF, KDR	
NH125	EEF2K, PRKC, PRKA, CAMK2, Histidine Kinase	
BI 2536	PLK1, PLK2, PLK3	
GSK461364	PLK1, PLK2, PLK3	
BI-D1870	RPS6KA1, RPS6KA2, RPS6KA3, RPS6KA4	

Table S5. Viability of E4-ECs across the 433-drugs library.

Sample number	Compound ID	Target	Viability
345	*YM155 (Sepantronium Bromide)*	*Survivin*	*0.012*
348	*AUY922 (NVP-AUY922)*	*HSP (e.g. HSP90)*	*0.227*
350	*17-AAG (Tanespimycin)*	*HSP (e.g. HSP90)*	*0.257*
38	*Ganetespib (STA-9090)*	*HSP (e.g. HSP90)*	*0.29*
157	*Ouabain*	*Sodium Channel*	*0.293*
352	*CEP-18770 (Delanzomib)*	*Proteasome*	*0.346*
36	*SNS-032 (BMS-387032)*	*CDK*	*0.381*
344	*Bortezomib (PS-341)*	*Proteasome*	*0.382*
14	*Belinostat (PXD101)*	*HDAC*	*0.456*
160	*Fluvastatin Sodium*	*HMG-CoA Reductase*	*0.46*
88	*PD0325901*	*MEK*	*0.499*
191	*PluriSIn #1 (NSC 14613)*	*Dehydrogenase*	*0.503*
110	*TAE226 (NVP-TAE226)*	*FAK*	*0.515*
163	*Ifenprodil Tartrate*	*GluR*	*0.542*
394	*TCS 359*	*FLT3*	*0.542*
190	*KX2-391*	*Src*	*0.549*
185	*AZD7545*	*PDHK*	*0.579*
12	*Ataluren (PTC124)*	*CFTR*	*0.593*
150	*BMS-707035*	*Integrase*	*0.594*
111	*Ozagrel HCl*	*Others*	*0.605*
384	*Birinapant*	*IAP*	*0.605*
62	*OTX015*	*BET*	*0.607*
43	*PNU-120596*	*AChR*	*0.612*
366	*OSU-03012 (AR-12)*	*PDK-1*	*0.612*
189	*Pacritinib (SB1518)*	*JAK*	*0.613*
63	*Ibrutinib (PCI-32765)*	*BTK*	*0.632*
171	*SRT1720*	*Sirtuin*	*0.634*
398	*T0070907*	*PPAR*	*0.634*

91	*LDN-212854*	*BMP*	*0.656*
318	*GDC-0152*	*IAP*	*0.657*
81	*AZD4547*	*FGFR*	*0.658*
334	*PF-562271*	*FAK*	*0.669*
87	*T0901317*	*Liver X Receptor*	*0.681*
242	*RKI-1447*	*ROCK*	*0.681*
198	*I-BET151 (GSK1210151A)*	*Epigenetic Reader Domain*	*0.682*
93	*C646*	*Histone Acetyltransferase*	*0.695*
159	*SKI II*	*S1P Receptor*	*0.695*
181	*PTC-209*	*BMI*	*0.696*
175	*2-Methoxyestradiol (2-MeOE2)*	*HIF*	*0.698*
400	*SC-514*	*IκB/IKK*	*0.698*
59	*Rotundine*	*Dopamine Receptor*	*0.707*
158	*Ranitidine*	*Histamine Receptor*	*0.709*
11	*Tenofovir Disoproxil Fumarate*	*Reverse Transcriptase*	*0.71*
138	*(+)-JQ1*	*Epigenetic Reader Domain*	*0.71*
358	*ICG-001*	*Wnt/beta-catenin*	*0.71*
337	*IMD 0354*	*IκB/IKK*	*0.713*
25	*ABT-263 (Navitoclax)*	*Bcl-2*	*0.714*
277	*AVL-292*	*BTK*	*0.715*
168	*SGI-1027*	*DNA Methyltransferase*	*0.716*
26	*Brinzolamide*	*Carbonic Anhydrase*	*0.718*
24	*Sitaxentan sodium*	*Endothelin Receptor*	*0.722*
47	*SB705498*	*TRPV*	*0.722*
368	*Everolimus (RAD001)*	*mTOR*	*0.722*
261	*MLN2238*	*Proteasome*	*0.723*
419	*NMS-873*	*p97*	*0.723*
282	*Lovastatin*	*HMG-CoA Reductase*	*0.728*
15	*Semagacestat (LY450139)*	*Gamma-secretase*	*0.729*
360	*SC144*	*Others*	*0.729*
252	*Varespladib (LY315920)*	*Phospholipase (e.g. PLA)*	*0.731*

172	*4EGI-1*	*ELF4*	*0.737*
147	*AT101*	*Bcl-2*	*0.74*
206	*Selumetinib (AZD6244)*	*MEK*	*0.742*
61	*PF-3845*	*FAAH*	*0.749*
200	*Apoptosis Activator 2*	*Caspase*	*0.753*
139	*GW9662*	*PPAR*	*0.754*
390	*Tadalafil*	*PDE*	*0.754*
67	*WZ811*	*CXCR*	*0.758*
370	*Aniracetam*	*AMPA Receptor-kainate Receptor-NMDA Receptor*	*0.758*
194	*PFI-1 (PF-6405761)*	*Epigenetic Reader Domain*	*0.759*
28	*Tranylcypromine (2-PCPA) HCl*	*Histone demethylases*	*0.76*
142	*Batimastat (BB-94)*	*MMP*	*0.76*
215	*Pralatrexate*	*DHFR*	*0.76*
7	*Granisetron HCl*	*5-HT Receptor*	*0.761*
356	*Ginkgolide A*	*GABA Receptor*	*0.761*
274	*Ispinesib (SB-715992)*	*Kinesin*	*0.769*
212	*Sirtinol*	*Sirtuin*	*0.77*
326	*CHIR-98014*	*GSK-3*	*0.771*
22	*Rimonabant*	*Cannabinoid Receptor*	*0.772*
64	*4E1RCat*	*ELF4*	*0.772*
341	*Necrostatin-1*	*TNF-alpha*	*0.773*
55	*Irinotecan HCl Trihydrate*	*Topoisomerase*	*0.774*
174	*NSC 23766*	*Rac*	*0.776*
76	*LY2157299*	*TGF-beta/Smad*	*0.778*
126	*BIBR 1532*	*Telomerase*	*0.779*
314	*Entacapone*	*Histone Methyltransferase*	*0.779*
133	*CP-91149*	*Phosphorylase*	*0.782*
387	*(S)-crizotinib*	*MTH*	*0.782*
296	*BGJ398 (NVP-BGJ398)*	*FGFR*	*0.785*
127	*Thiazovivin*	*ROCK*	*0.787*
153	*CCT128930*	*Akt*	*0.787*

51	*Aloxistatin*	*Cysteine protease*	*0.793*
146	*Costunolide*	*Telomerase*	*0.794*
145	*MK-1775*	*Wee1*	*0.797*
208	*PD184352 (CI-1040)*	*MEK*	*0.797*
280	*Formoterol Hemifumarate*	*Adrenergic Receptor*	*0.797*
29	*Tandutinib (MLN518)*	*FLT3*	*0.803*
298	*OSI-420*	*EGFR*	*0.805*
312	*Linagliptin*	*DPP-4*	*0.807*
207	*Tolvaptan*	*Vasopressin Receptor*	*0.808*
408	*Isotretinoin*	*Hydroxylase*	*0.808*
108	*Tyrphostin AG 879*	*HER2*	*0.813*
125	*Voriconazole*	*P450 (e.g. CYP17)*	*0.814*
173	*Exemestane*	*Aromatase*	*0.814*
399	*Gliquidone*	*Potassium Channel*	*0.814*
58	*Ferrostatin-1 (Fer-1)*	*Ferroptosis*	*0.815*
254	*MK-2866 (GTx-024)*	*Androgen Receptor*	*0.817*
77	*IPA-3*	*PAK*	*0.821*
375	*Rasagiline Mesylate*	*MAO*	*0.821*
154	*Pomalidomide*	*TNF-alpha*	*0.827*
95	*Mdivi-1*	*Dynamin*	*0.829*
56	*SSR128129E*	*FGFR*	*0.833*
186	*URB597*	*FAAH*	*0.833*
187	*GW0742*	*PPAR*	*0.839*
315	*AG-14361*	*PARP*	*0.839*
195	*Dapagliflozin*	*SGLT*	*0.841*
402	*Caffeic Acid Phenethyl Ester*	*NF-κB*	*0.841*
306	*Tioxolone*	*Carbonic Anhydrase*	*0.842*
245	*SB415286*	*GSK-3*	*0.845*
27	*Nilotinib (AMN-107)*	*Bcr-Abl*	*0.846*
155	*AS-252424*	*PI3K*	*0.847*
262	*Org 27569*	*Cannabinoid Receptor*	*0.849*

156	*Tie2 kinase inhibitor*	*Tie-2*	*0.851*
220	*Triamterene*	*Sodium Channel*	*0.853*
176	*Palbociclib (PD-0332991) HCl*	*CDK*	*0.857*
335	*AZD3463*	*ALK*	*0.863*
339	*TCID*	*DUB*	*0.865*
60	*MM-102*	*Histone Methyltransferase*	*0.869*
285	*AZ191*	*Others*	*0.869*
293	*Ridaforolimus (Deforolimus, MK-8669)*	*mTOR*	*0.869*
349	*Agomelatine*	*5-HT Receptor*	*0.869*
427	*GSK461364*	*PLK*	*0.869*
37	*Naltrexone HCl*	*Opioid Receptor*	*0.871*
363	*Panobinostat (LBH589)*	*HDAC*	*0.871*
57	*VX-765*	*Caspase*	*0.872*
276	*AZD7762*	*Chk*	*0.872*
119	*Bisoprolol fumarate*	*Adrenergic Receptor*	*0.877*
169	*Atglistatin*	*ATGL*	*0.877*
397	*ML133 HCl*	*Potassium Channel*	*0.877*
78	*Esomeprazole Sodium*	*ATPase*	*0.879*
114	*Piceatannol*	*Syk*	*0.879*
219	*Enalaprilat Dihydrate*	*RAAS*	*0.88*
250	*PF-04217903*	*c-Met*	*0.882*
178	*PF-573228*	*FAK*	*0.883*
16	*NVP-ADW742*	*IGF-1R*	*0.884*
23	*FLI-06*	*Notch*	*0.885*
101	*Veliparib (ABT-888)*	*PARP*	*0.887*
379	*AZ 3146*	*Kinesin*	*0.887*
19	*Ilomastat (GM6001, Galardin)*	*MMP*	*0.888*
46	*AZD6482*	*PI3K*	*0.894*
270	*Felodipine*	*Calcium Channel*	*0.894*
286	*(-)-Parthenolide*	*E3 Ligase*	*0.897*
92	*Ki16425*	*LPA Receptor*	*0.898*

123	*TG100-115*	*PI3K*	*0.899*
224	*PP2*	*Src*	*0.904*
44	*Ruxolitinib (INCB018424)*	*JAK*	*0.908*
331	*VU 0364770*	*GluR*	*0.908*
317	*LY411575*	*Gamma-secretase*	*0.916*
184	*SGI-1776 free base*	*Pim*	*0.918*
271	*(+)-Bicuculline*	*GABA Receptor*	*0.918*
424	*Lomeguatrib*	*DNA Methyltransferase*	*0.918*
322	*Imatinib (STI571)*	*PDGFR*	*0.919*
10	*Tolazoline HCl*	*Adrenergic Receptor*	*0.92*
140	*KPT-185*	*CRM1*	*0.922*
222	*Fingolimod (FTY720) HCl*	*S1P Receptor*	*0.922*
351	*SP600125*	*JNK*	*0.923*
143	*Sertraline HCl*	*5-HT Receptor*	*0.925*
392	*Fostamatinib (R788)*	*Syk*	*0.925*
247	*Torcetrapib*	*CETP*	*0.931*
327	*GW4064*	*FXR*	*0.936*
120	*Bosutinib (SKI-606)*	*Src*	*0.937*
112	*Vildagliptin (LAF-237)*	*DPP-4*	*0.941*
302	*Forskolin*	*cAMP*	*0.941*
96	*MRS 2578*	*P2 Receptor*	*0.945*
9	*Losartan Potassium (DuP 753)*	*RAAS*	*0.947*
357	*Cryptotanshinone*	*STAT*	*0.947*
295	*SNS-314 Mesylate*	*Aurora Kinase*	*0.948*
428	*Gliclazide*	*Potassium Channel*	*0.948*
148	*GSK690693*	*Akt*	*0.949*
90	*U0126-EtOH*	*MEK*	*0.95*
294	*LY2784544*	*JAK*	*0.951*
319	*OC000459*	*GPR*	*0.954*
246	*PRT062607 (P505-15, BIIB057) HCl*	*Syk*	*0.955*
284	*Lafutidine*	*Histamine Receptor*	*0.958*

35	*Atorvastatin Calcium*	*HMG-CoA Reductase*	*0.959*
214	*SAR131675*	*VEGFR*	*0.959*
362	*Trelagliptin*	*DPP-4*	*0.959*
45	*GW3965 HCl*	*Liver X Receptor*	*0.96*
367	*GSK690693*	*AKT*	*0.96*
188	*TAK-875*	*GPR*	*0.963*
8	*A-769662*	*AMPK*	*0.964*
290	*Bazedoxifene HCl*	*Estrogen/progestogen Receptor*	*0.975*
227	*YO-01027*	*Gamma-secretase*	*0.976*
410	*VX-745*	*p38 MAPK*	*0.976*
42	*Loratadine*	*Histamine Receptor*	*0.977*
121	*S3I-201*	*STAT*	*0.977*
232	*SB203580*	*p38 MAPK*	*0.977*
234	*KU-55933 (ATM Kinase Inhibitor)*	*ATM/ATR*	*0.977*
99	*BTB06584*	*Fo-ATPase*	*0.979*
216	*BML-190*	*Cannabinoid Receptor*	*0.979*
378	*ADX-47273*	*GluR*	*0.979*
217	*TWS119*	*GSK-3*	*0.981*
3	*Fulvestrant*	*Estrogen/progestogen Receptor*	*0.982*
354	*Fluvoxamine maleate*	*5-HT Receptor*	*0.982*
2	*Rizatriptan Benzoate*	*5-HT Receptor*	*0.983*
31	*MLN8054*	*Aurora Kinase*	*0.983*
238	*TAK-700 (Orteronel)*	*P450 (e.g. CYP17)*	*0.984*
205	*Captopril*	*RAAS*	*0.99*
300	*Apigenin*	*P450 (e.g. CYP17)*	*0.99*
407	*Etodolac*	*COX*	*0.99*
72	*Cyproterone Acetate*	*Androgen Receptor*	*0.991*
321	*Levosulpiride*	*Dopamine Receptor*	*0.994*
113	*Dynasore*	*Dynamin*	*0.995*
5	*Ramelteon*	*MT Receptor*	*1.004*
355	*Oligomycin A*	*ATPase*	*1.004*

278	*Pimobendan*	*PDE*	*1.011*
98	*LY2603618*	*Chk*	*1.015*
53	*Apixaban*	*Factor Xa*	*1.016*
301	*Rigosertib (ON-01910)*	*PLK*	*1.017*
431	*Go 6983*	*PKC*	*1.017*
316	*Moclobemide (Ro 111163)*	*MAO*	*1.019*
6	*Trospium chloride*	*AChR*	*1.02*
149	*Tropicamide*	*AChR*	*1.022*
249	*ML130 (Nodinitib-1)*	*NOD1*	*1.023*
141	*Pifithrin-μ*	*p53*	*1.024*
267	*Embelin*	*IAP*	*1.024*
391	*Elvitegravir (GS-9137, JTK-303)*	*Integrase*	*1.024*
422	*Sal003*	*ELF2*	*1.024*
328	*PF-5274857*	*Hedgehog/Smoothened*	*1.032*
279	*DBeQ*	*p97*	*1.034*
116	*Tenovin-6*	*p53*	*1.035*
167	*AGI-6780*	*IDH2*	*1.038*
396	*Naftopidil*	*Adrenergic Receptor*	*1.038*
48	*Safinamide Mesylate*	*MAO*	*1.039*
304	*Bupivacaine HCl*	*cAMP*	*1.039*
221	*Clemastine Fumarate*	*Histamine Receptor*	*1.043*
52	*NSC697923*	*E2*	*1.049*
248	*MK-2206 2HCl*	*Akt*	*1.049*
30	*Zebularine*	*DNA Methyltransferase*	*1.05*
107	*Finasteride*	*5-alpha Reductase*	*1.051*
269	*GSK2656157*	*PERK*	*1.051*
382	*Mirabegron*	*Adrenergic Receptor*	*1.051*
423	*Tariquidar*	*P-gp*	*1.051*
50	*P22077*	*DUB*	*1.052*
204	*E-64*	*Cathepsin K*	*1.054*
239	*Loxistatin Acid (E-64C)*	*Cysteine protease*	*1.054*

416	*Ki16198*	*LPA Receptor*	*1.054*
259	*KU-60019*	*ATM/ATR*	*1.056*
418	*AMG-517*	*TRPV*	*1.056*
109	*Cilomilast*	*PDE*	*1.057*
383	*AP26113*	*ALK*	*1.057*
13	*Candesartan*	*RAAS*	*1.059*
79	*DMH1*	*BMP*	*1.059*
80	*Ozagrel*	*Factor Xa*	*1.059*
131	*Bergenin*	*Others*	*1.059*
291	*Golgicide A*	*ATPase*	*1.059*
359	*Stattic*	*STAT*	*1.059*
376	*PD128907 HCl*	*Dopamine Receptor*	*1.059*
386	*LDK378*	*ALK*	*1.059*
426	*Imidapril HCl*	*RAAS*	*1.059*
130	*EUK 134*	*Beta Amyloid*	*1.06*
203	*Acadesine*	*AMPK*	*1.062*
406	*Celecoxib*	*COX*	*1.062*
164	*KPT-276*	*CRM1*	*1.067*
287	*JSH-23*	*NF-κB*	*1.071*
122	*HA14-1*	*Bcl-2*	*1.082*
152	*EX 527 (Selisistat)*	*Sirtuin*	*1.082*
202	*Bosentan Hydrate*	*Endothelin Receptor*	*1.083*
307	*PF-4708671*	*S6 Kinase*	*1.085*
134	*Wnt-C59 (C59)*	*Wnt/beta-catenin*	*1.086*
74	*GSK1292263*	*GPR*	*1.088*
105	*Iniparib (BSI-201)*	*PARP*	*1.088*
381	*(-)-MK 801 Maleate*	*GluR*	*1.088*
20	*Rivaroxaban*	*Factor Xa*	*1.09*
102	*Dalcetrapib (JTT-705, RO4607381)*	*CETP*	*1.091*
54	*ML347*	*BMP*	*1.092*
162	*Erastin*	*Ferroptosis*	*1.093*

253	*ML161*	*Others*	*1.093*
258	*Zosuquidar (LY335979) 3HCl*	*P-gp*	*1.094*
264	*DMXAA (Vadimezan)*	*VDA*	*1.099*
340	*LB42708*	*Ftase*	*1.099*
342	*Empagliflozin (BI 10773)*	*SGLT*	*1.1*
177	*EHop-016*	*Rac*	*1.103*
343	*SU11274*	*c-Met*	*1.105*
235	*CGK 733*	*ATM/ATR*	*1.106*
414	*Mubritinib (TAK 165)*	*HER2*	*1.106*
346	*Lenalidomide (CC-5013)*	*TNF-alpha*	*1.107*
180	*Memantine HCl*	*AMPA Receptor-kainate Receptor-NMDA Receptor*	*1.109*
333	*Daunorubicin HCl*	*Toposiomerase II*	*1.112*
94	*Oxcarbazepine*	*Sodium Channel*	*1.114*
75	*SGC 0946*	*Histone Methyltransferase*	*1.116*
374	*Rebamipide*	*Others*	*1.116*
213	*Abitrexate (Methotrexate)*	*DHFR*	*1.119*
199	*VX-809 (Lumacaftor)*	*CFTR*	*1.121*
404	*SB431542*	*TGF-beta/Smad*	*1.121*
4	*Tolfenamic Acid*	*COX*	*1.123*
323	*DCC-2036 (Rebastinib)*	*Bcr-Abl*	*1.125*
100	*NPS-2143*	*CaSR*	*1.129*
183	*CK-636*	*Arp2/3*	*1.13*
89	*PYR-41*	*E1 Activating*	*1.135*
210	*Canagliflozin*	*SGLT*	*1.135*
299	*Dutasteride*	*5-alpha Reductase*	*1.139*
430	*BI-D1870*	*S6 Kinase*	*1.139*
41	*Pancuronium dibromide*	*AChR*	*1.14*
209	*OSI-906 (Linsitinib)*	*IGF-1R*	*1.14*
313	*Etomidate*	*GABA Receptor*	*1.14*
365	*GDC-0941*	*PI3K*	*1.14*
255	*Ticagrelor*	*P2 Receptor*	*1.143*

166	*KPT-330*	*CRM1*	*1.145*
308	*5-hydroxymethyl Tolterodine (PNU 200577, 5-HMT, 5-HM)*	*AChR*	*1.146*
320	*NLG919*	*IDO*	*1.148*
240	*Zibotentan (ZD4054)*	*Endothelin Receptor*	*1.149*
32	*PR-619*	*DUB*	*1.151*
305	*UNC669*	*MBT*	*1.153*
283	*4μ8C*	*Others*	*1.155*
179	*ABT-199 (GDC-0199)*	*Bcl-2*	*1.158*
197	*Nebivolol*	*Adrenergic Receptor*	*1.16*
403	*VU 0364439*	*GluR*	*1.16*
336	*IOX2*	*HIF*	*1.161*
1	*FG-4592*	*HIF*	*1.165*
303	*Rolipram*	*PDE*	*1.165*
353	*Aprepitant*	*Substance P*	*1.165*
432	*MNS (3,4-Methylenedioxy-β-nitrostyrene, MDBN)*	*p97*	*1.165*
124	*ADL5859 HCl*	*Opioid Receptor*	*1.166*
347	*Ivacaftor (VX-770)*	*CFTR*	*1.166*
136	*BAM7*	*Bcl-2*	*1.168*
332	*U-104*	*Carbonic Anhydrase*	*1.168*
311	*Cinacalcet HCl*	*CaSR*	*1.17*
17	*NSC 319726*	*p53*	*1.173*
144	*OG-L002*	*Histone demethylases*	*1.175*
71	*Mozavaptan*	*Vasopressin Receptor*	*1.183*
372	*Ginkgolide B*	*PAFR*	*1.183*
244	*SMI-4a*	*Pim*	*1.188*
18	*Icotinib*	*EGFR*	*1.19*
218	*IKK-16 (IKK Inhibitor VII)*	*IκB/IKK*	*1.195*
135	*NU7026*	*DNA-PK*	*1.2*
388	*ZM 447439*	*Aurora Kinase*	*1.2*
268	*Toremifene Citrate*	*Estrogen/progestogen Receptor*	*1.201*
231	*VE-822*	*ATM/ATR*	*1.202*

412	SB408124	OX Receptor	1.202
165	AZD2461	PARP	1.203
395	Carvedilol	Adrenergic Receptor	1.203
40	Vemurafenib (PLX4032, RG7204)	Raf	1.208
196	Maraviroc	CCR	1.212
251	GW441756	Trk receptor	1.214
338	CRT0044876	APE	1.215
309	XAV-939	Wnt/beta-catenin	1.222
115	Quizartinib (AC220)	FLT3	1.227
128	Anastrozole	Aromatase	1.229
192	Crenolanib (CP-868596)	PDGFR	1.229
310	SB742457	5-HT Receptor	1.23
82	GW9508	GPR	1.231
325	Nilvadipine	Calcium Channel	1.233
223	Amlodipine	Calcium Channel	1.241
21	STF-118804	Others	1.245
226	Temsirolimus (CCI-779, NSC 683864)	mTOR	1.249
256	Letrozole	Aromatase	1.249
129	SB743921	Kinesin	1.253
385	AZD1981	GPR	1.253
151	Raltegravir (MK-0518)	Integrase	1.259
39	CGS 21680 HCl	Adenosine A2	1.265
364	VX-680 (Tozasertib, MK-0457)	Aurora Kinase	1.265
132	SN-38	Topoisomerase	1.272
330	JNJ-1661010	FAAH	1.273
97	AGI-5198	Dehydrogenase	1.277
377	Apatinib	VEGFR	1.277
65	Tofacitinib (CP-690550,Tasocitinib)	JAK	1.278
369	MK-8245	Dehydrogenase	1.278
117	Enzastaurin (LY317615)	PKC	1.283
85	GNF-2	Bcr-Abl	1.29

170	*Suvorexant (MK-4305)*	*OX Receptor*	*1.293*
266	*AM1241*	*Cannabinoid Receptor*	*1.3*
233	*EPZ-6438*	*Histone Methyltransferase*	*1.308*
413	*H 89 2HCl*	*PKA*	*1.308*
229	*PAC-1*	*Caspase*	*1.315*
411	*GSK429286A*	*ROCK*	*1.315*
236	*WZ4002*	*EGFR*	*1.316*
288	*Pramipexole*	*Dopamine Receptor*	*1.319*
243	*UNC2250*	*Others*	*1.322*
182	*Trimebutine*	*Opioid Receptor*	*1.324*
193	*Enzalutamide (MDV3100)*	*Androgen Receptor*	*1.325*
201	*Naproxen*	*COX*	*1.325*
401	*ZCL278*	*Rac*	*1.325*
405	*Odanacatib (MK-0822)*	*Cathepsin K*	*1.325*
104	*Istradefylline*	*Others*	*1.333*
66	*PHA-793887*	*CDK*	*1.337*
260	*LY2228820*	*p38 MAPK*	*1.342*
34	*GSK1904529A*	*IGF-1R*	*1.346*
86	*TPCA-1*	*IκB/IKK*	*1.348*
137	*ZM 306416*	*VEGFR*	*1.352*
389	*BX-912*	*PDK-1*	*1.352*
225	*CHIR-124*	*Chk*	*1.353*
409	*Stavudine (d4T)*	*Reverse Transcriptase*	*1.353*
297	*Irinotecan*	*Topoisomerase*	*1.363*
429	*Sotrastaurin*	*PKC*	*1.363*
289	*RepSox*	*TGF-beta/Smad*	*1.367*
425	*BI 2536*	*PLK*	*1.367*
273	*SANT-1*	*Hedgehog/Smoothened*	*1.37*
83	*VE-821*	*ATM/ATR*	*1.372*
272	*Ticlopidine HCl*	*P2 Receptor*	*1.372*
329	*GDC-0068*	*Akt*	*1.372*

161	*Propranolol HCl*	*Adrenergic Receptor*	*1.374*
393	*GSK J4 HCl*	*Histone demethylases*	*1.374*
281	*CNX-774*	*BTK*	*1.375*
106	*Dabrafenib (GSK2118436)*	*Raf*	*1.38*
228	*Trichostatin A (TSA)*	*HDAC*	*1.388*
49	*Tenofovir*	*Reverse Transcriptase*	*1.405*
324	*XL335*	*FXR*	*1.416*
263	*Oxymetazoline HCl*	*Adrenergic Receptor*	*1.454*
420	*Sorafenib*	*Raf*	*1.454*
257	*GW2580*	*CSF-1R*	*1.458*
417	*AZ20*	*ATM/ATR*	*1.458*
241	*Pyrimethamine*	*DHFR*	*1.462*
68	*Allopurinol*	*OX Receptor*	*1.463*
265	*Anacetrapib (MK-0859)*	*CETP*	*1.466*
421	*NH125*	*ELF2*	*1.466*
275	*BTZ043 Racemate*	*Others*	*1.482*
69	*HC-030031*	*Others*	*1.488*
371	*Doxazosin Mesylate*	*Adrenergic Receptor*	*1.488*
73	*Sodium 4-Aminosalicylate*	*NF-κB*	*1.518*
373	*Tosedostat (CHR2797)*	*Aminopeptidase*	*1.518*
103	*Vandetanib (ZD6474)*	*VEGFR*	*1.526*
380	*VU 0357121*	*GluR*	*1.526*
118	*CGP 57380*	*MNK*	*1.53*
292	*LDE225 (NVP-LDE225,Erismodegib)*	*Hedgehog/Smoothened*	*1.54*
84	*NSC 405020*	*MMP*	*1.559*
33	*Roxatidine Acetate HCl*	*Histamine Receptor*	*1.561*
361	*SRPIN340*	*Others*	*1.561*
237	*WZ4003*	*AMPK*	*1.562*
415	*BMS-378806*	*gp120/CD4*	*1.562*
70	*Telmisartan*	*RAAS*	*1.586*
230	*PHA-665752*	*c-Met*	*1.606*

211	*CP-673451*	*PDGFR*	*1.649*

Table S6. Gene set enrichment analysis (GSEA) of T-ALL alone and T-ALL co-cultured with E4-ECs by scRNAseq

Pathway	pval	padj	NES	Cluster
TGF BETA SIGNALING	0.00332226	0.04152824	-2.0737188	EC+3119
DNA REPAIR	0.0210396	0.11688669	1.67919792	EC+3119
G2M CHECKPOINT	0.00112486	0.01874766	2.16885049	EC+3119
APOPTOSIS	0.04483188	0.1867995	1.5808908	EC+3119
ESTROGEN RESPONSE EARLY	0.01357466	0.09696186	-1.8175447	EC+3119
APICAL SURFACE	0.02800659	0.14003295	1.53024848	EC+3119
E2F TARGETS	0.00107875	0.01874766	2.32648618	EC+3119
MYC TARGETS V1	0.00106383	0.01874766	2.52322544	EC+3119
OXIDATIVE PHOSPHORYLATION	0.01651982	0.1032489	1.61324151	EC+3119
REACTIVE OXIGEN SPECIES PATHWAY	0.0443686	0.1867995	-1.5920027	EC+3119
ALLOGRAFT REJECTION	0.01219512	0.09696186	-1.748738	EC+3119
KRAS SIGNALING UP	0.00816327	0.08163265	-1.8670345	EC+3119
IL6 JAK STAT3 SIGNALING	0.00712589	0.08726003	-1.995715	EC+RO2
G2M CHECKPOINT	0.00143678	0.03591954	2.25327382	EC+RO2
NOTCH SIGNALING	0.008726	0.08726003	1.72428132	EC+RO2
ADIPOGENESIS	0.01736973	0.14005602	-1.7416187	EC+RO2
E2F TARGETS	0.00142045	0.03591954	2.22940136	EC+RO2
MYC TARGETS V1	0.00285307	0.04755112	1.85739035	EC+RO2
INFLAMMATORY RESPONSE	0.03739837	0.20776874	1.63676435	EC+RO2
REACTIVE OXIGEN SPECIES PATHWAY	0.01960784	0.14005602	-1.7312182	EC+RO2
HEME METABOLISM	0.0257732	0.16108247	-1.6383136	EC+RO2

Table S7. Gene set enrichment analysis (GSEA) of E4-EC alone and E4-EC co-cultured with T-ALL by scRNAseq.

Pathway	pval	padj	NES	cluster
TNFA SIGNALING VIA NFKB	0.0019802	0.0255102	2.73776348	EC+RO2
TGF BETA SIGNALING	0.01972387	0.07586102	1.77431491	EC+RO2
DNA REPAIR	0.00992063	0.05544467	-1.8530979	EC+RO2
G2M CHECKPOINT	0.04417671	0.12993149	1.60936981	EC+RO2
ADIPOGENESIS	0.002	0.0255102	-2.1843099	EC+RO2
ESTROGEN RESPONSE EARLY	0.04125737	0.12892927	1.64845607	EC+RO2
INTERFERON ALPHA RESPONSE	0.00592885	0.04940711	2.24543835	EC+RO2
INTERFERON GAMMA RESPONSE	0.00197628	0.0255102	2.74300968	EC+RO2
APICAL JUNCTION	0.01581028	0.06587615	1.62006251	EC+RO2
MYC TARGETS V1	0.01394422	0.06338283	-1.7404282	EC+RO2
EPITHELIAL MESENCHYMAL TRANSITION	0.03571429	0.11904762	-1.6097033	EC+RO2
INFLAMMATORY RESPONSE	0.00813008	0.05544467	2.24231977	EC+RO2
OXIDATIVE PHOSPHORYLATION	0.00204082	0.0255102	-4.0045232	EC+RO2
REACTIVE OXIGEN SPECIES PATHWAY	0.00404858	0.04048583	-1.9158732	EC+RO2
UV RESPONSE UP	0.01209677	0.06048387	1.80350298	EC+RO2
IL2 STAT5 SIGNALING	0.00998004	0.05544467	1.79608545	EC+RO2
PANCREAS BETA CELLS	0.0240481	0.08588606	-1.6509889	EC+RO2
HYPOXIA	0.01688555	0.12357581	-1.8388679	EC+3119
G2M CHECKPOINT	0.02892562	0.16993802	-1.7451539	EC+3119
ESTROGEN RESPONSE LATE	0.01840491	0.12357581	-1.7927604	EC+3119
INTERFERON ALPHA RESPONSE	0.00212314	0.03398409	2.35592365	EC+3119
INTERFERON GAMMA RESPONSE	0.0021692	0.03398409	1.99100382	EC+3119
UNFOLDED PROTEIN RESPONSE	0.0392562	0.18450413	-1.6724766	EC+3119
XENOBIOTIC METABOLISM	0.00806452	0.07580645	-1.8763453	EC+3119
UV RESPONSE DN	0.03653846	0.18450413	-1.6976005	EC+3119
COAGULATION	0.00578035	0.06791908	-1.991888	EC+3119
BILE ACID METABOLISM	0.00189753	0.03398409	1.63361852	EC+3119

Table S8. Enriched pathways TEC vs E4-ECs.

Up regulated pathways TEC vs. EC	Down regulated pathways TEC vs. EC	Up regulated pathways E4 educated vs. naïve	Down regulated pathways E4 educated vs. naïve
MYC_TARGETS_V1	PEROXISOME	ALLOGRAFT_REJECTION	MYC_TARGETS_V1
E2F_TARGETS	BILE_ACID_METABOLISM	INFLAMMATORY_RESPONSE	REACTIVE_OXIGEN_SPECIES_ PATHWAY
G2M_CHECKPOINT	FATTY_ACID_METABOLISM	TNFA_SIGNALING_VIA_NFKB	PROTEIN_SECRETION
EPITHELIAL_MESENCHYMAL_ TRANSITION	XENOBIOTIC_METABOLISM	INTERFERON_GAMMA_ RESPONSE	ADIPOGENESIS
GLYCOLYSIS		HEDGEHOG_SIGNALING	PEROXISOME
MITOTIC_SPINDLE		WNT_BETA_CATENIN_ SIGNALING	FATTY_ACID_METABOLISM
HYPOXIA		KRAS_SIGNALING_UP	
MTORC1_SIGNALING		IL6_JAK_STAT3_SIGNALING	
MYC_TARGETS_V2		G2M_CHECKPOINT	
INFLAMMATORY_ RESPONSE		E2F_TARGETS	
ALLOGRAFT_REJECTION		COMPLEMENT	
		PI3K_AKT_MTOR_SIGNALING	
		SPERMATOGENESIS	
		HEME_METABOLISM	
		MITOTIC_SPINDLE	
		ESTROGEN_RESPONSE_ EARLY	
		IL2_STAT5_SIGNALING	