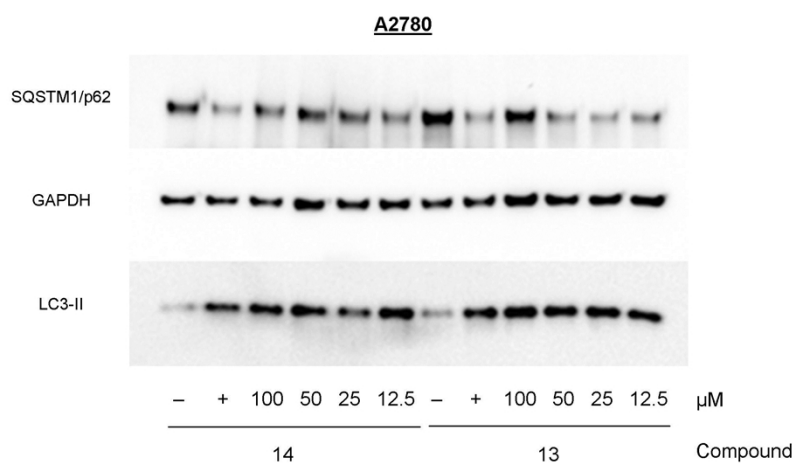


## Supplementary Information

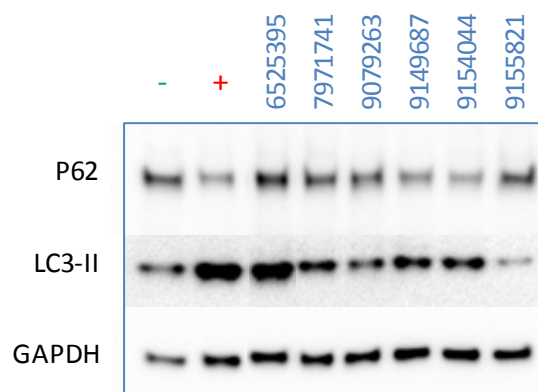
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**Figure S3.** Repeat of the dose response immunoblotting experiment for ligands **13** and **14**.



**Figure S4.** Western blot for compounds **43** (6525395), **53** (7971741), **58** (9079263), **61** (9154044) and **62** (9155821).

## NCI's 60-cell line panel growth inhibition assay

The NCI's human 60-cell lines were grown in RPMI 1640 medium containing 5% FBS and 2mM L-glutamine. Cells were inoculated into 96-well plates at plating densities 5000–40 000 cells per well, based on the doubling time of individual cell lines. Plates were then incubated at 37 °C, 5% CO<sub>2</sub>, 95% air and 100% relative humidity for 24 h prior to addition of tested compounds. After 24 h, two plates of each cell line were fixed *in situ* with trichloroacetic acid (TCA), to represent a measurement of the cell population for each cell line at the time of tested compound addition. Tested compounds were solubilized in DMSO at a concentration 400 times that of the desired final maximum test concentration and stored frozen prior to use. An aliquot of each frozen tested concentrate was thawed and diluted to twice the desired final maximum test concentration with complete medium containing 50 µg mL<sup>-1</sup> gentamicin. 100 µL aliquot of the tested drug diluted solution was added to appropriate wells containing 100 µL of medium, resulting in the required final drug doses. Following tested compound addition, plates were incubated for additional 48 h. The assay was terminated by the addition of cold TCA for adherent cells. Cells were fixed *in situ* by addition of 50 µL of cold 50% (w/v) TCA (final concentration, 10% TCA) and incubated for 60 min at 4 °C. The supernatant was discarded, and plates were washed 5 times with water and air dried. Sulforhodamine B (SRB) solution (100 µL), 0.4%(w/v) in 1% acetic acid was added to each well, and plates were incubated for 10 min at rt. After staining, the unbound dye was removed by washing five times with 1% acetic acid and plates were air dried. The bound stain was subsequently solubilized with 10 mM Trizma base, and the absorbance was measured on a plate reader at 515 nm. For suspension cells, the methodology was identical except the assay termination by fixing settled cells at the bottom of each well by adding 50 µL of 80%TCA (final concentration, 16% TCA).

Taken from: K. A. El Sayed, A. I. Foudah, A. M. S. Mayer, A. M. Crider and D. Song, *Med. Chem. Comm.*, 2013, 4, 1231-1238.

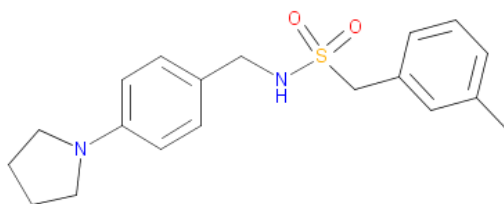
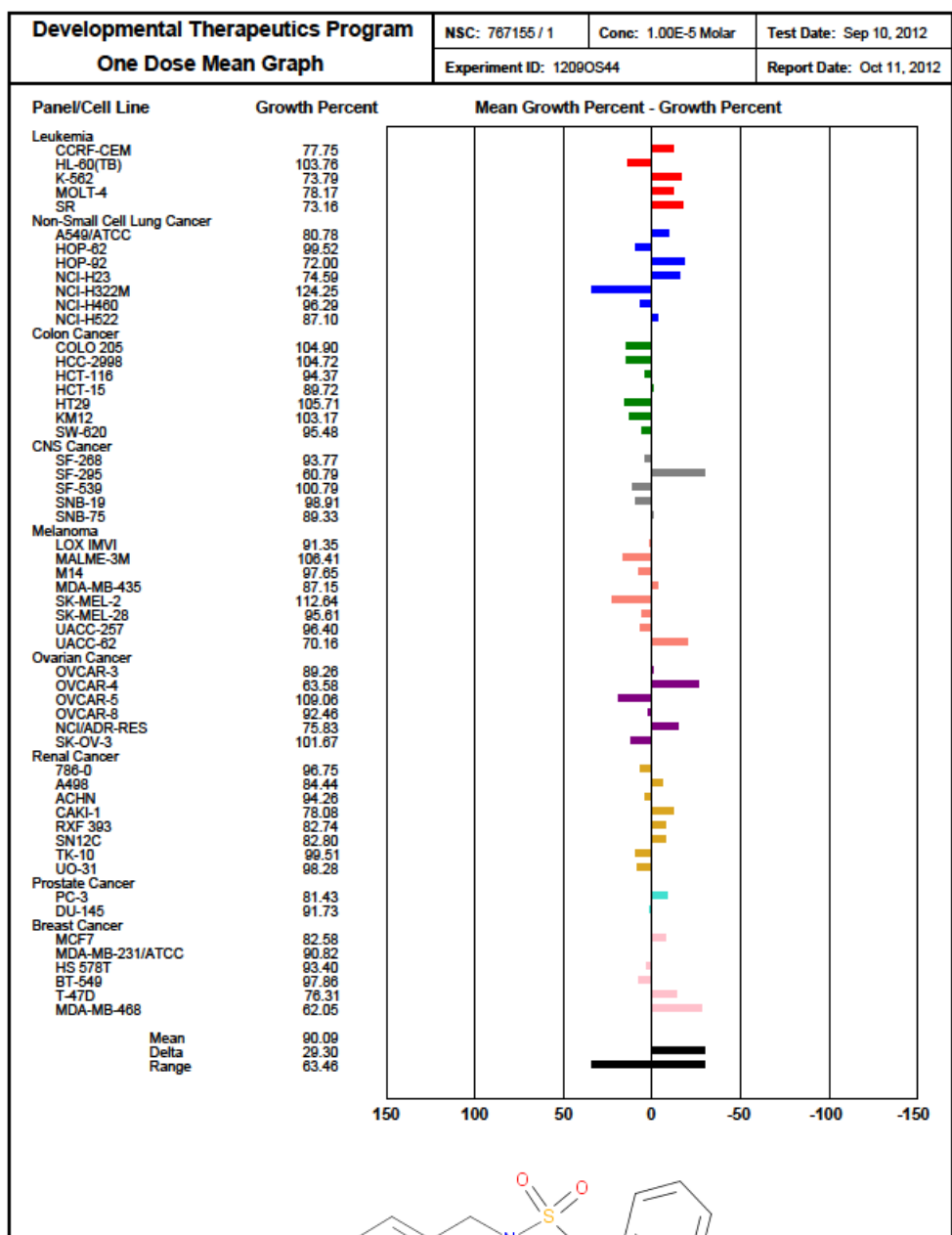
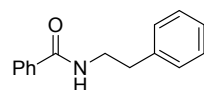


Figure S5. NCI60 screening results for ligand 62.

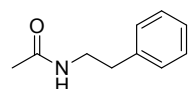
**Table S1.** They key to the ChemBridge codes. Compounds **32 – 40** were synthesised in house.

<b>Number</b>	<b>Code</b>	<b>Number</b>	<b>Code</b>
1	5106372	28	6115259
2	5139189	29	5274150
3	5146538	30	5349520
4	5162907	31	5378129
5	5229998	41	6045327
6	5236623	42	6067284
7	5529858	43	6525395
8	5542582	44	7643458
9	5555211	45	7661021
10	4012455	46	7668219
11	4013951	47	7669739
12	5217339	48	7680448
13	5329246	49	7685637
14	5330932	50	7689756
15	5334325	51	7755811
16	5337355	52	7804934
17	5361579	53	7971741
18	5528440	54	7981744
19	7226051	55	9008875
20	7260078	56	9017025
21	7264596	57	9038873
22	5328083	58	9079263
23	5328241	59	9138062
24	5334050	60	9149687
25	5334466	61	9154044
26	5335716	62	9155821
27	5557287		

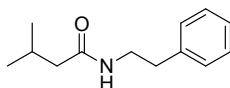
## Synthetic Chemistry



**3-Methyl-N-Phenylethylbutanamide (32)**: To a solution of phenethylamine hydrochloride (2.50 g, 15.9 mmol) in dichloromethane (25 mL) was added triethylamine (2.50 mL, 17.9 mmol, 2.83 equiv.) and stirring continued for 30 min. The mixture was then cooled to 0 °C and benzoyl chloride (2.20 mL, 19.0 mmol, 1.19 equiv.) added dropwise over the course of 30 min and the mixture was left to stir for an additional 30 min at this temperature and at rt for a further 18 h. The reaction mixture was then concentrated *in vacuo* and the crude material redissolved in EtOAc (50 mL) and washed with 1M HCl, 1M NaOH and brine. Drying over anhydrous MgSO<sub>4</sub>, filtration and concentration *in vacuo* afforded a colourless solid that was recrystallised from boiling hexane-ethyl acetate to yield **32** (2.85 g, 80 %) as long colourless needles. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.69 (2H, d, *J* = 8 Hz), 7.48 (1H, dddd, *J* = 8, 6, 1 and 1 Hz), 7.40 (2H, t, *J* = 7 Hz), 7.33 (2H, t, *J* = 8 Hz), 7.27-7.22 (3H, m), 6.20 (1H, bs), 3.72 (2H, dt, *J* = 7, 6 Hz), 2.94 (2H, t, *J* = 7 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 167.6, 139.1, 134.8, 131.5, 129.0, 128.9, 128.7, 126.9, 126.7, 41.3, 35.8; HRMS: (ESI) *m/z* calcd for C<sub>15</sub>H<sub>15</sub>NNaO [M+Na]<sup>+</sup>: 248.1046, found: 248.1041; TLC: R<sub>f</sub> 0.31 (40% EtOAc/hexane). The experimental data was in good agreement with that previously reported (Gualtierotti, J.-B.; Schumacher, X.; Fontaine, P.; Masson, G.; Wang, Q.; Zhu. *J. Chem. Eur. J.* **2012**, *18*, 14812-14819).



**N-Phenylethylacetamide (33)**: According to the method used for **2** above, phenethylamine hydrochloride (1.11 g, 6.35 mmol) was reacted with acetyl chloride (650 μL, 9.14 mmol, 1.44 equiv.) to afford a colourless semi-solid that was purification by flash chromatography (EtOAc) to afford **2** (932 mg, 90%) as a colourless solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.31 (2H, tm, *J* = 7 Hz), 7.25-7.16 (3H, m), 5.56 (1H, bs), 3.51 (2H, dt, *J* = 7, 6 Hz), 2.81 (2H, t, *J* = 7 Hz), 1.93 (3H, s); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 170.2, 139.0, 128.9, 128.8, 126.6, 40.8, 35.8, 23.4; HRMS: (ESI) calcd for C<sub>10</sub>H<sub>13</sub>NNaO [M+Na]<sup>+</sup>: 186.0889, found: 186.0884; TLC: R<sub>f</sub> 0.21 (EtOAc). The experimental data was in good agreement with that previously reported (Pelagalli, R.; Feroci, M.; Chiarotto, I; Vecchio, S. *Green Chem.* **2012**, *14*, 2251-2255).



**3-Methyl-N-Phenylethylbutanamide (34):** Prepared according to the method used for **2** above, phenethylamine hydrochloride (1.07 g, 6.77 mmol) was reacted with isovaleryl chloride (1.10 mL, 9.02 mmol, 1.33 equiv.) to afford a colourless solid. Recrystallisation from refluxing hexane/ethyl acetate afforded **3** (1.07 g, 77%) as long colourless needles. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.31 (2H, tm, *J* = 7 Hz), 7.25-7.16 (3H, m), 5.43 (bs), 3.53 (2H, q, *J* = 7 Hz), 2.82 (2H, t, *J* = 7), 2.08 (1H, br d, *J* = 7 Hz)\*, 1.98 (2H, d, *J* = 7 Hz), 0.92 (6H, d, *J* = 6 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 172.6, 139.1, 128.9, 128.8, 126.6, 46.3, 40.6, 35.9, 26.2, 22.3; IR: cm<sup>-1</sup> HRMS: (ESI) *m/z* calcd for C<sub>13</sub>H<sub>19</sub>NNaO [M+Na]<sup>+</sup>: 228.1359, found: 228,1352; TLC: R<sub>f</sub> 0.21 (hexane/EtOAc, 1:1). The experimental data was in good agreement with that previously reported (Morkunas, B.; Galloway, W. R. J. D.; Wright, M.; Ibbeson, B. M.; Hodgkinson, J. T.; O'Connell, K. M. G.; Bartolucci, N.; Della Valle, M.; Welch, M.; Spring, D. R. *Org. Biomol. Chem.* **2012**, *10*, 8452-8464).



## Quantification of Autophagy Inhibitor Western Blots

The AlphaView SA (ProteinSimple) software was used to quantify the bands obtained by Western blotting. The total number of pixel grey levels were determined in the selected band area and then normalized to the GAPDH loading control. The results are shown in Fig. S6, S7 and S8.

$$\text{Signal} = (\text{Band} - \text{Background}) / (\text{GAPDH band} - \text{Background})$$

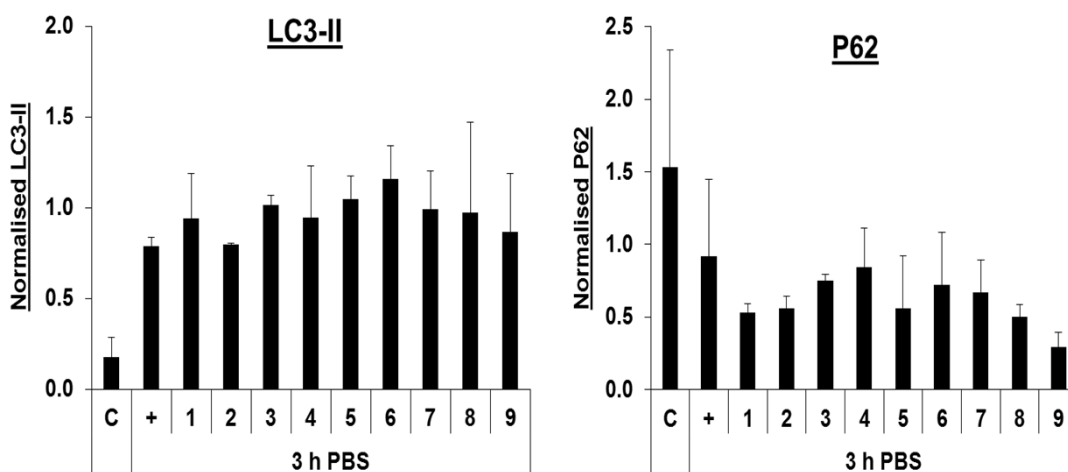


Figure S6. Compounds 1-9 from Fig. S1.

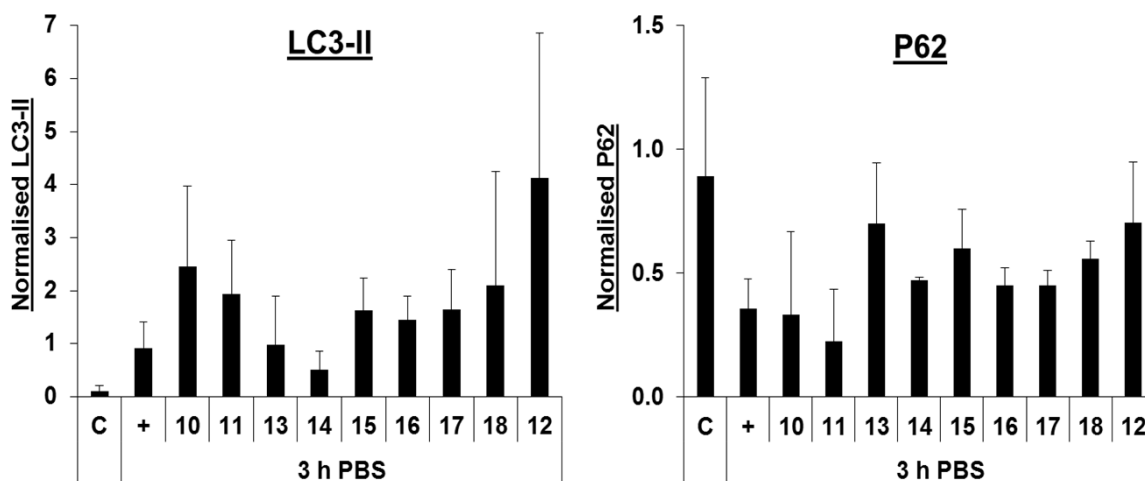
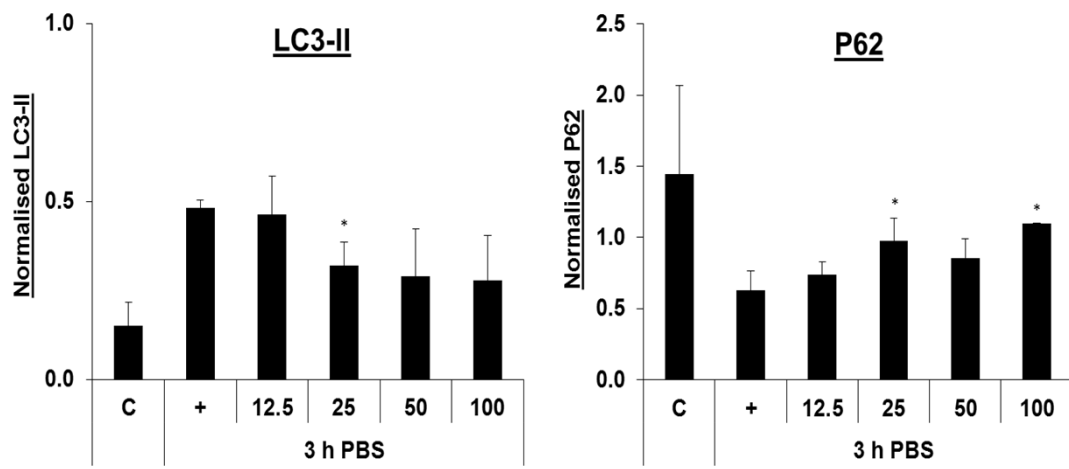


Figure S7. Compounds 10-18 from Fig. 2.



**Figure S8.** Autophagy inhibitor 14 ( $\mu\text{M}$ ) (Fig.3). \*, paired  $t$ -test,  $P < 0.05$  compared to “+”.