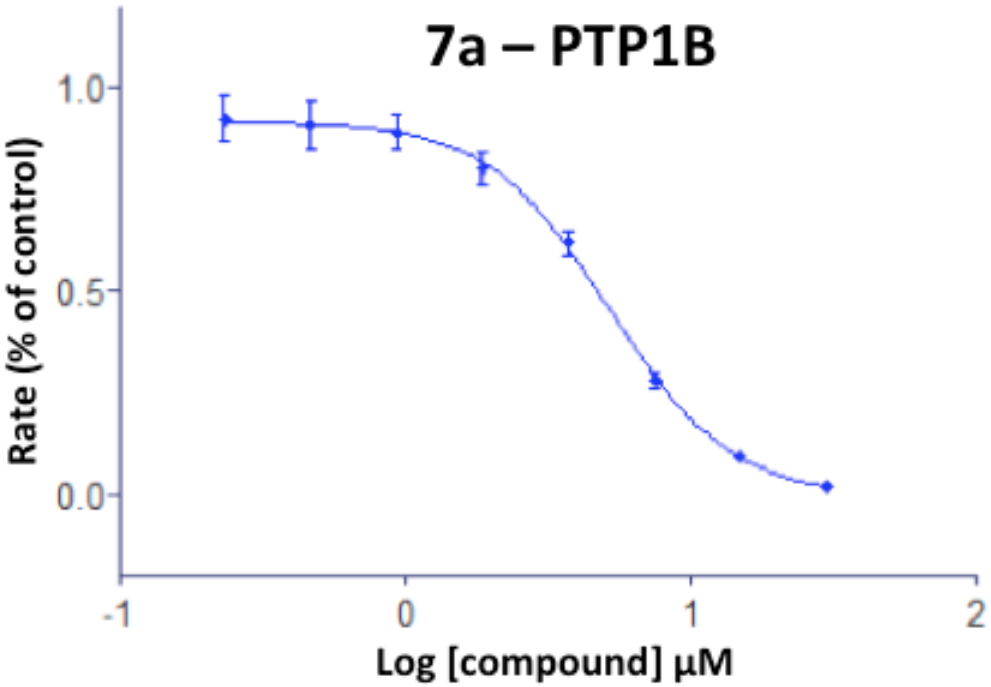

Fig. S1A. Graphs used for IC_{50} value determinations of **7a** against PTP1B. Dose-response data points represent the mean value of 3 trials

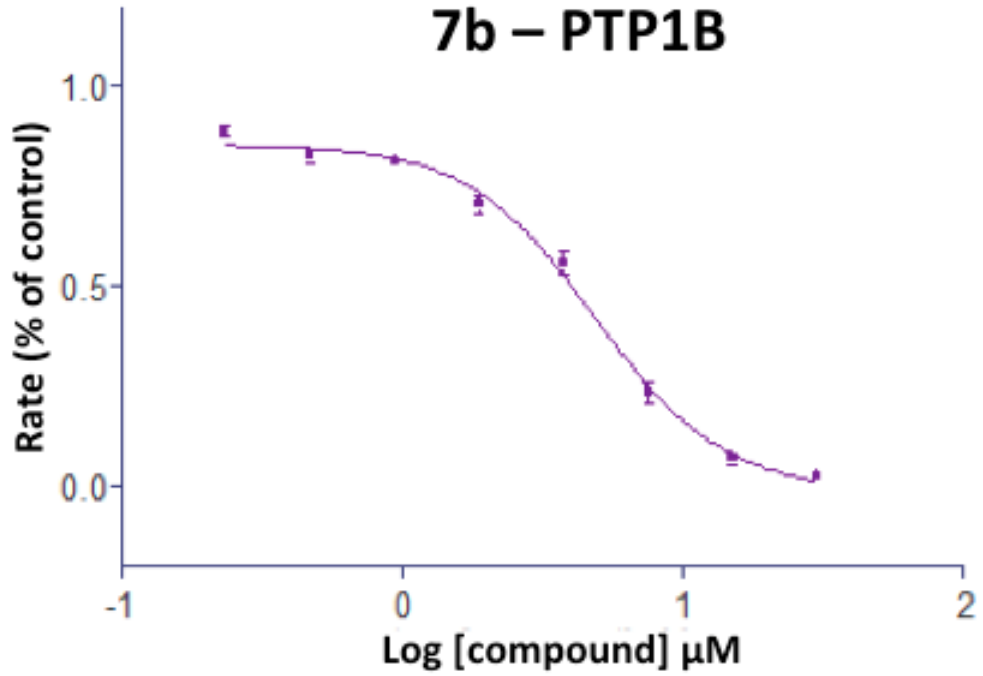

Fig. S1B. Graphs used for IC_{50} value determinations of **7b** against PTP1B. Dose-response data points represent the mean value of 3 trials

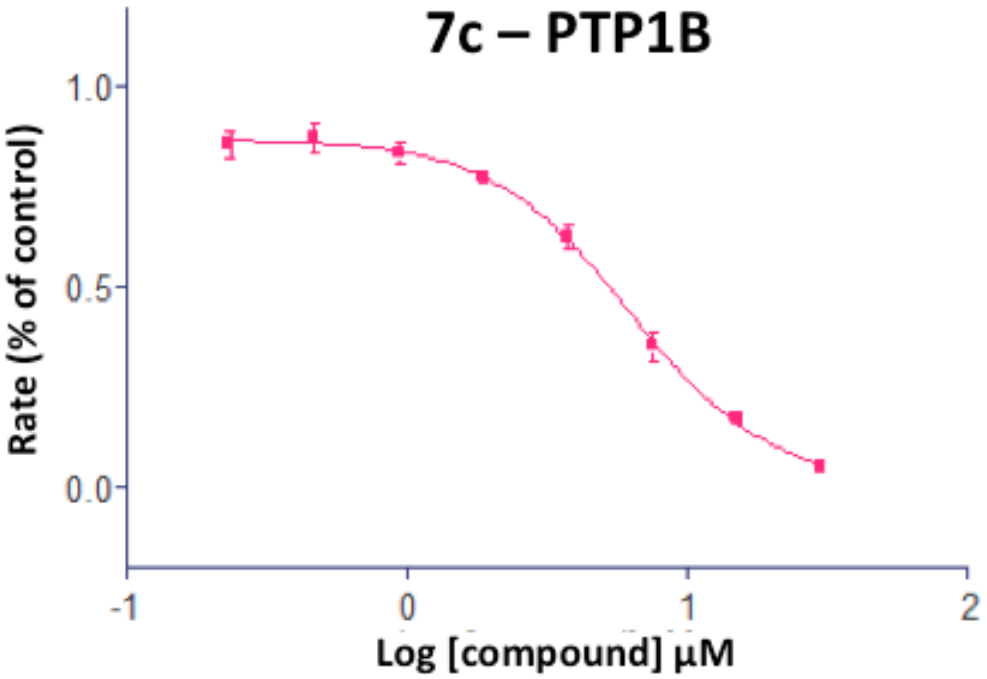

Fig. S1C. Graphs used for IC_{50} value determinations of **7c** against PTP1B. Dose-response data points represent the mean value of 3 trials

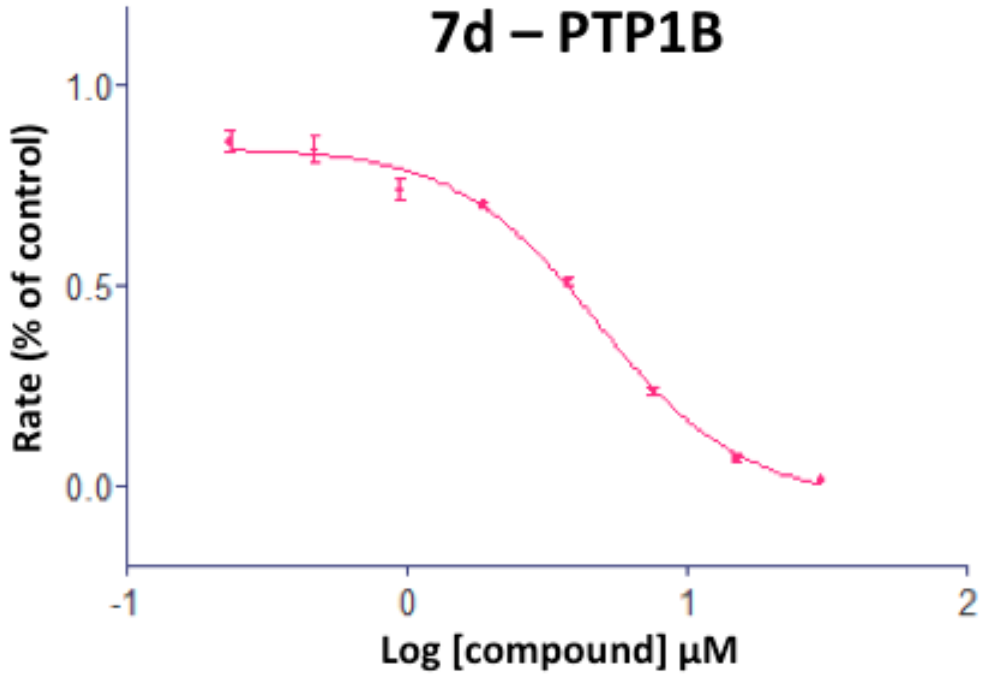

Fig. S1D. Graphs used for IC_{50} value determinations of **7d** against PTP1B. Dose-response data points represent the mean value of 3 trials

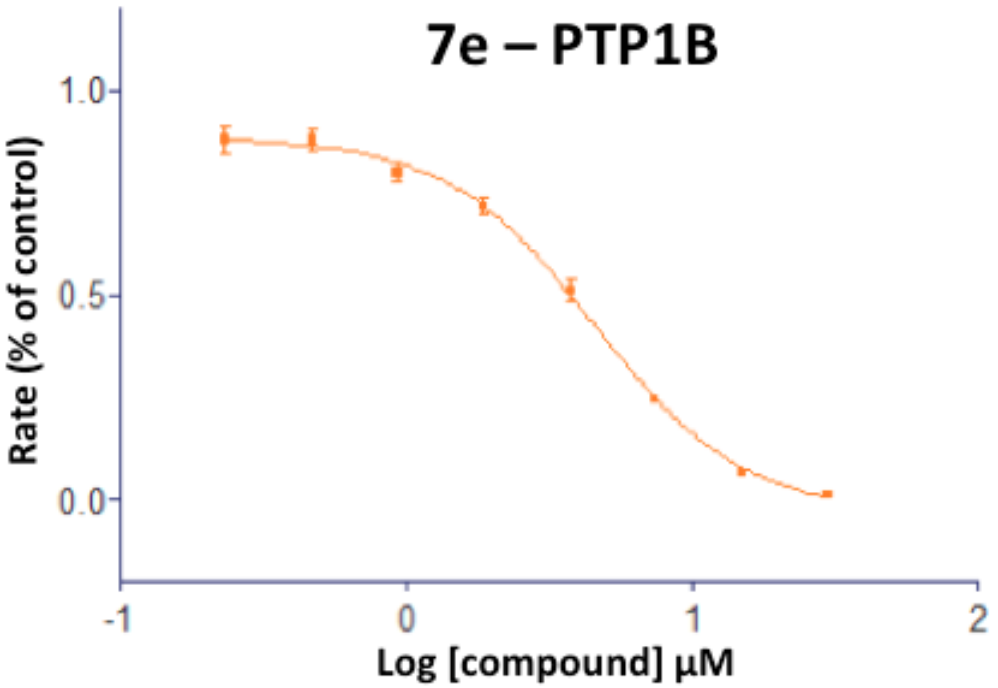

Fig. S1E. Graphs used for IC_{50} value determinations of **7e** against PTP1B. Dose-response data points represent the mean value of 3 trials

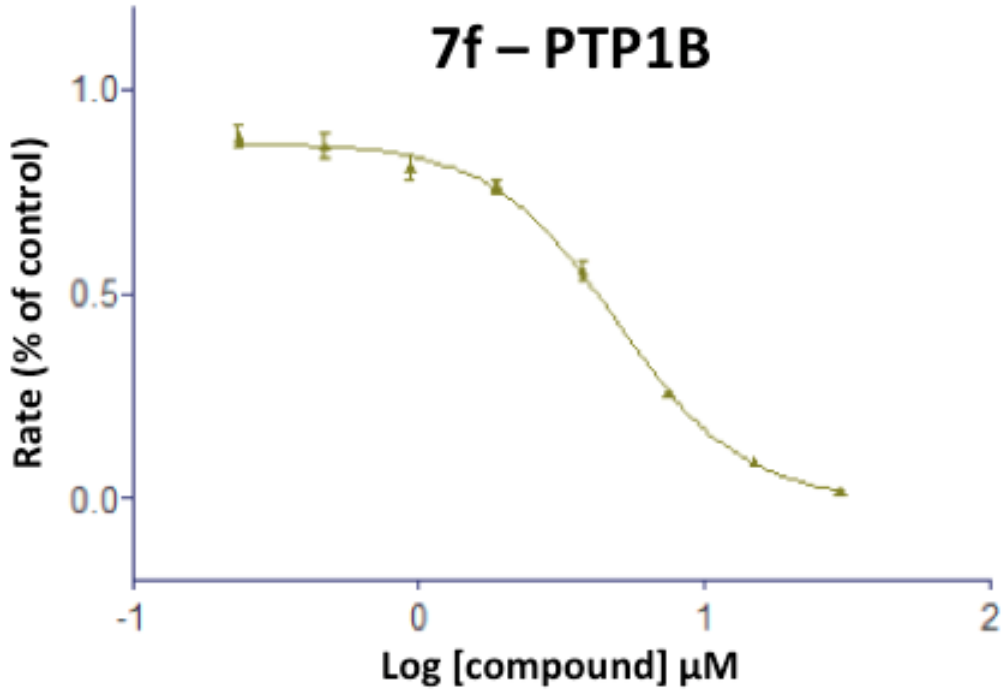

Fig. S1F. Graphs used for IC_{50} value determinations of **7f** against PTP1B. Dose-response data points represent the mean value of 3 trials

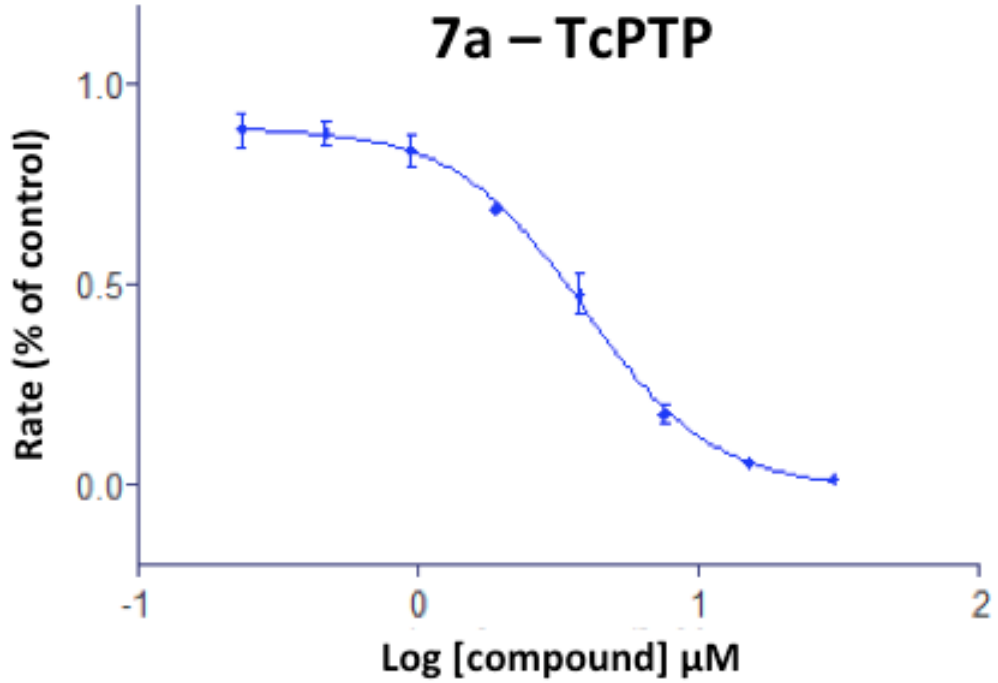

Fig. S1G. Graphs used for IC_{50} value determinations of **7a** against Tc-PTP. Dose-response data points represent the mean value of 3 trials

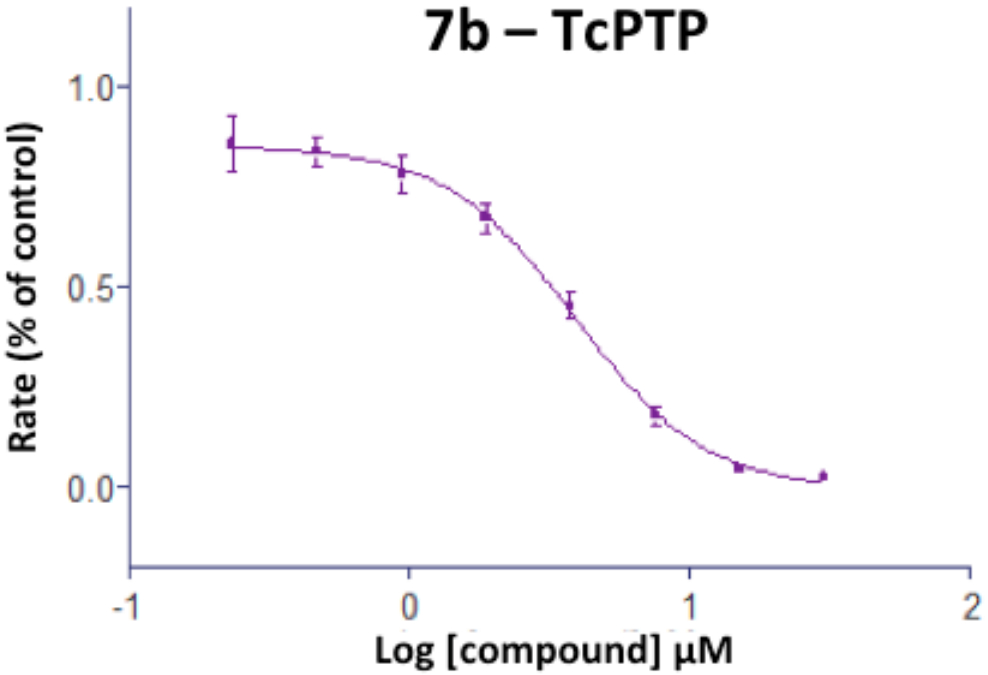

Fig. S1H. Graphs used for IC_{50} value determinations of **7b** against Tc-PTP. Dose-response data points represent the mean value of 3 trials

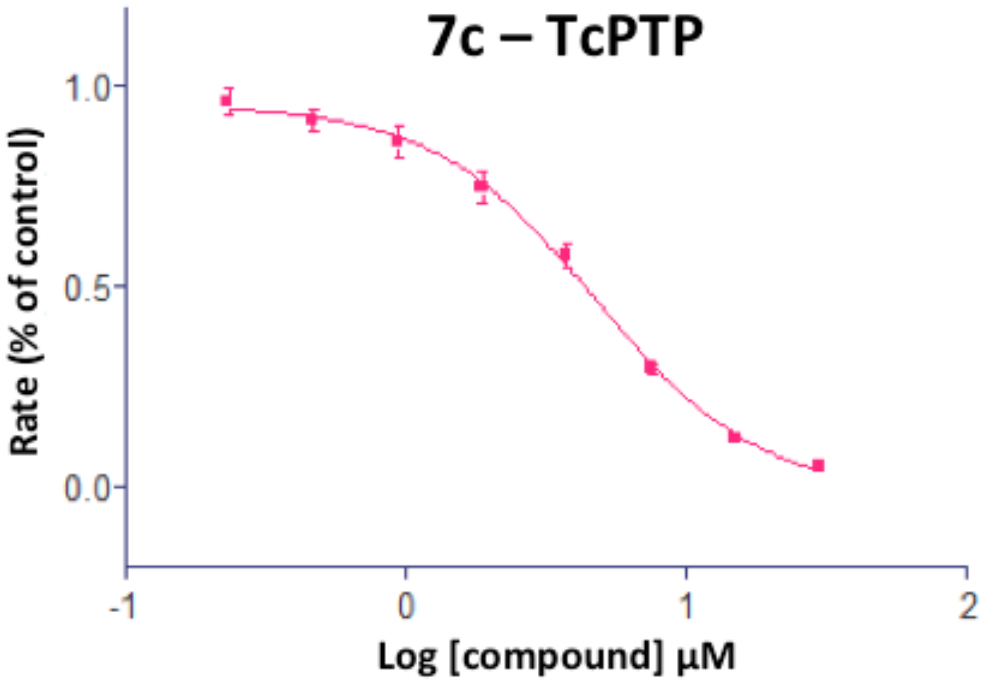

Fig. S1I. Graphs used for IC_{50} value determinations of **7c** against Tc-PTP. Dose-response data points represent the mean value of 3 trials

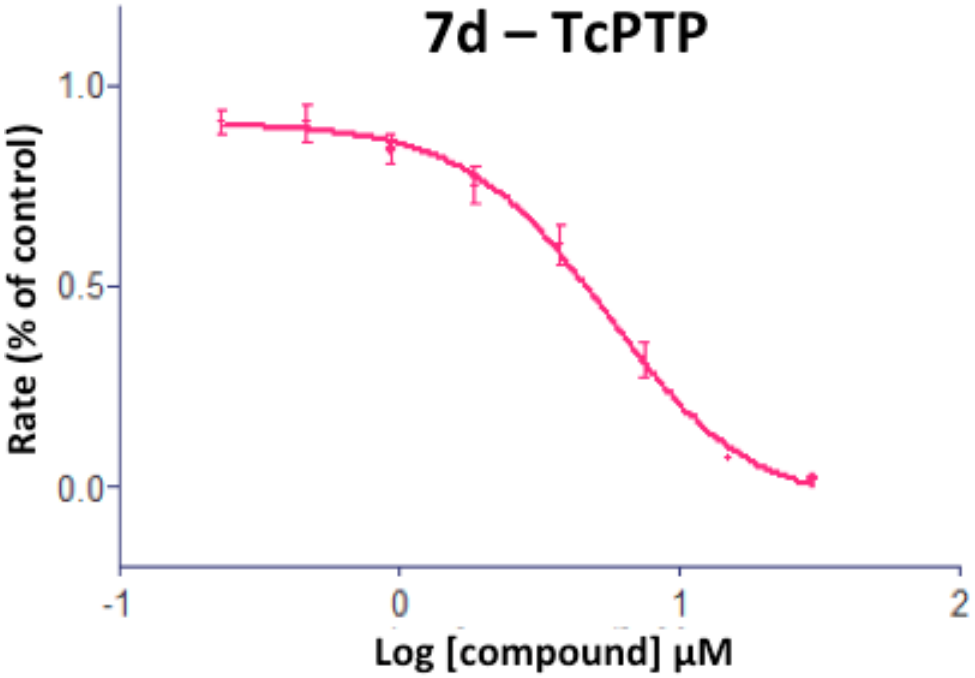

Fig. S1J. Graphs used for IC_{50} value determinations of **7d** against Tc-PTP. Dose-response data points represent the mean value of 3 trials

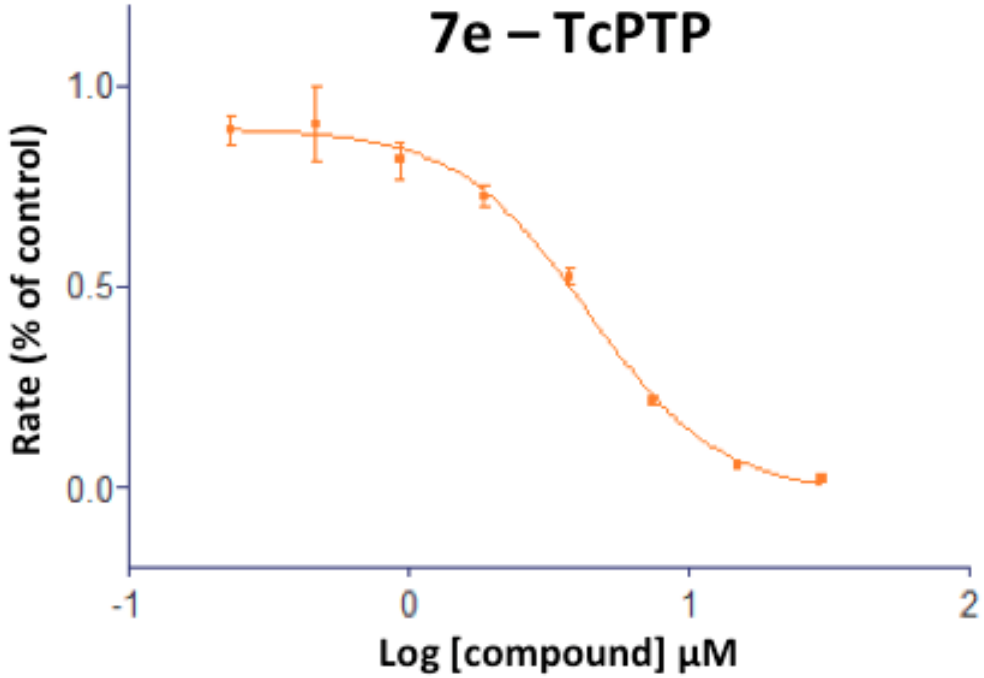

Fig. S1K. Graphs used for IC_{50} value determinations of **7e** against Tc-PTP. Dose-response data points represent the mean value of 3 trials

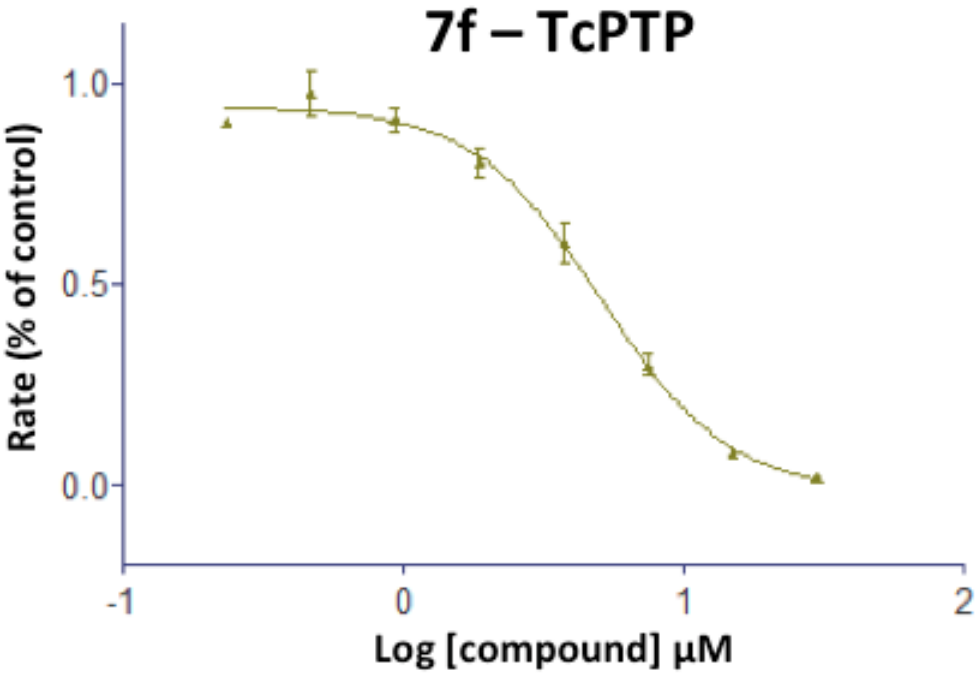

Fig. S1L. Graphs used for IC_{50} value determinations of **7f** against Tc-PTP. Dose-response data points represent the mean value of 3 trials

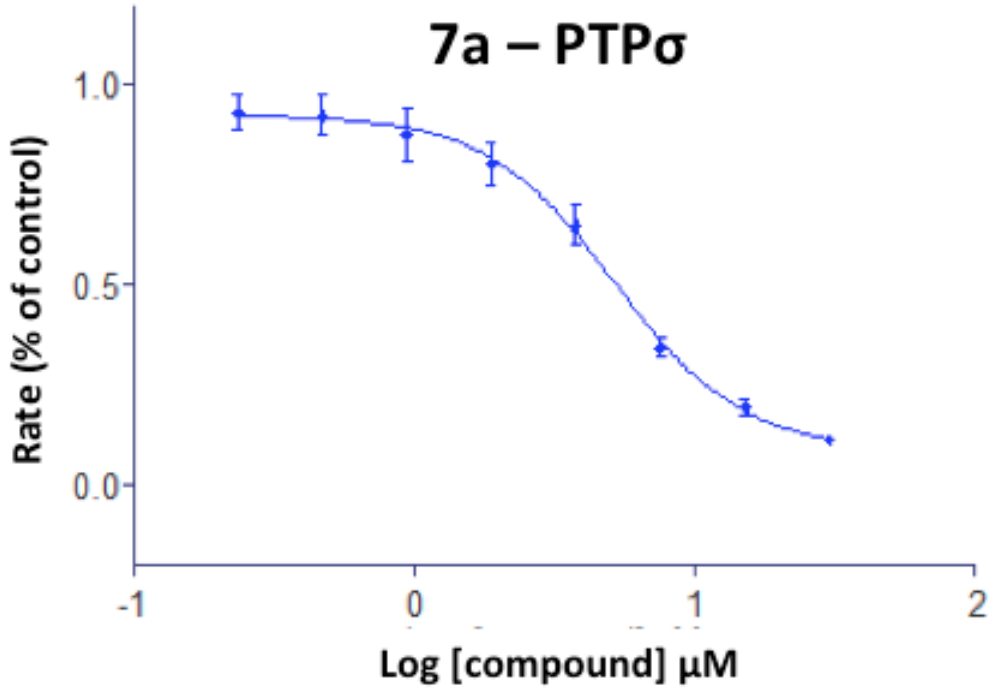

Fig. S1M. Graphs used for IC_{50} value determinations of **7a** against PTPσ. Dose-response data points represent the mean value of 3 trials

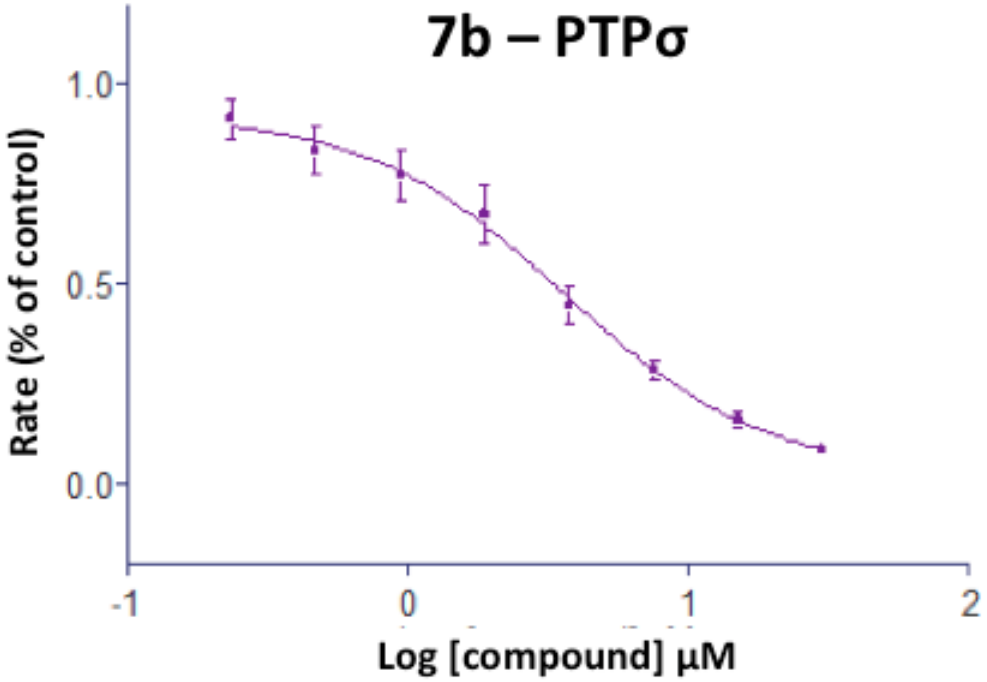

Fig. S1N. Graphs used for IC_{50} value determinations of **7b** against PTPσ. Dose-response data points represent the mean value of 3 trials

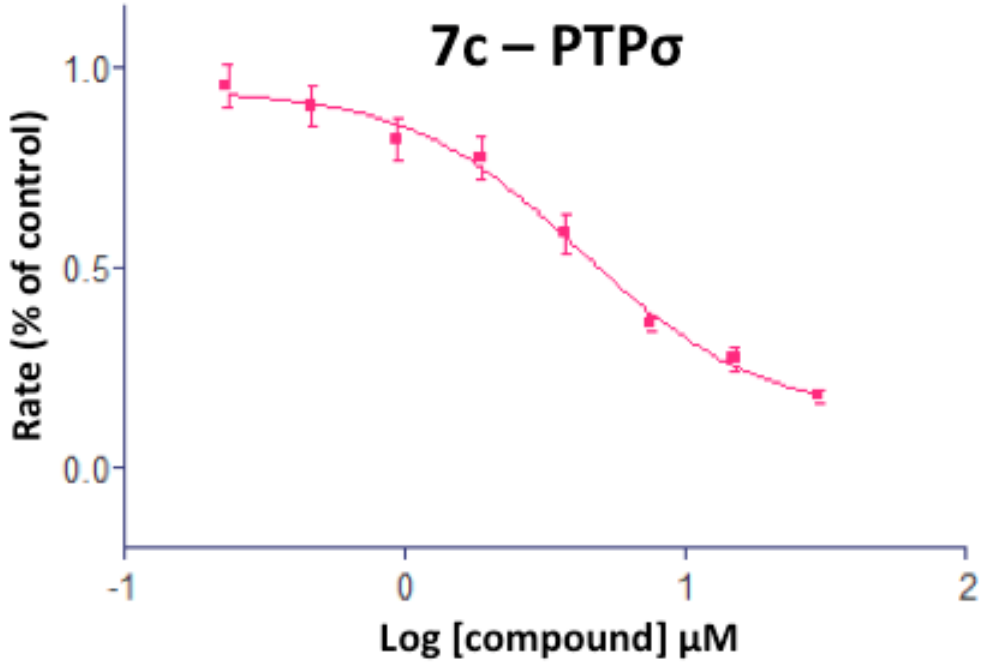

Fig. S1O. Graphs used for IC_{50} value determinations of **7c** against PTPσ. Dose-response data points represent the mean value of 3 trials

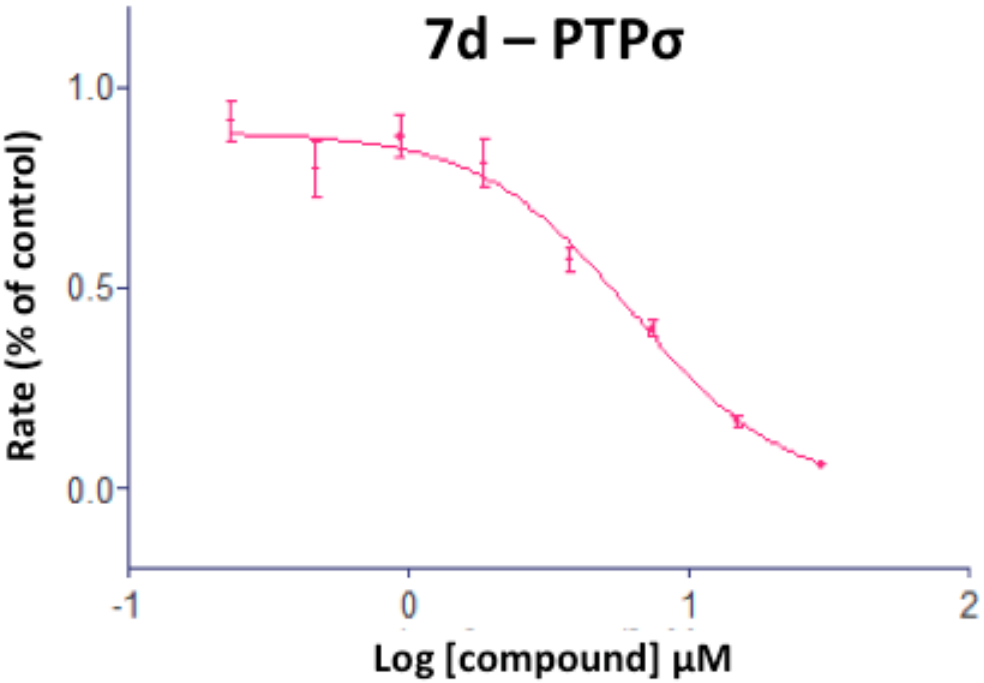

Fig. S1P. Graphs used for IC_{50} value determinations of **7d** against PTPσ. Dose-response data points represent the mean value of 3 trials

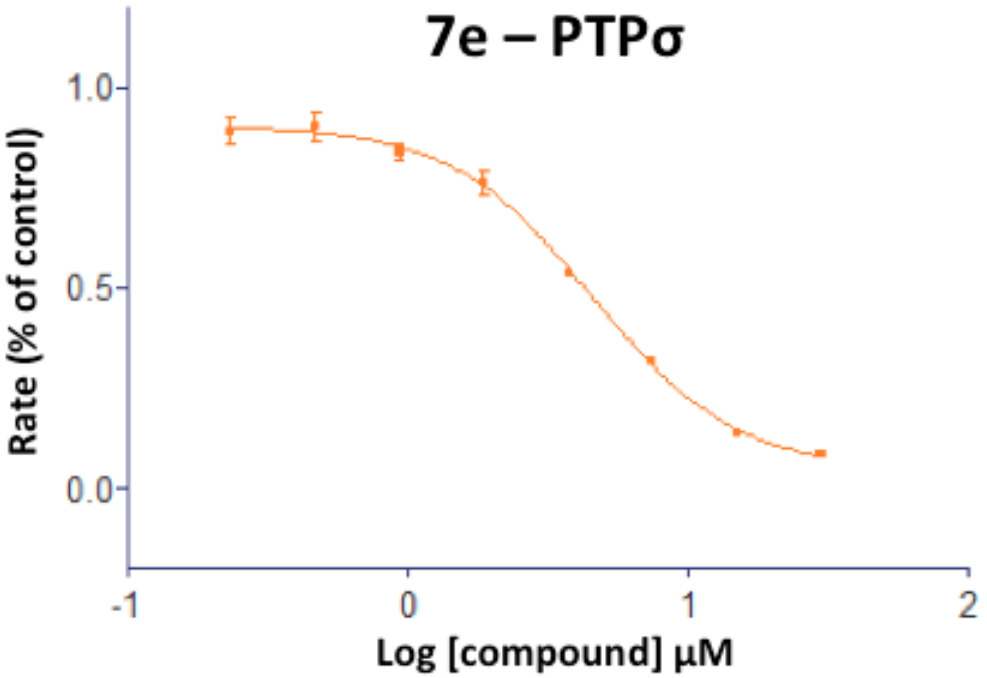

Fig. S1Q. Graphs used for IC_{50} value determinations of **7e** against PTPσ. Dose-response data points represent the mean value of 3 trials

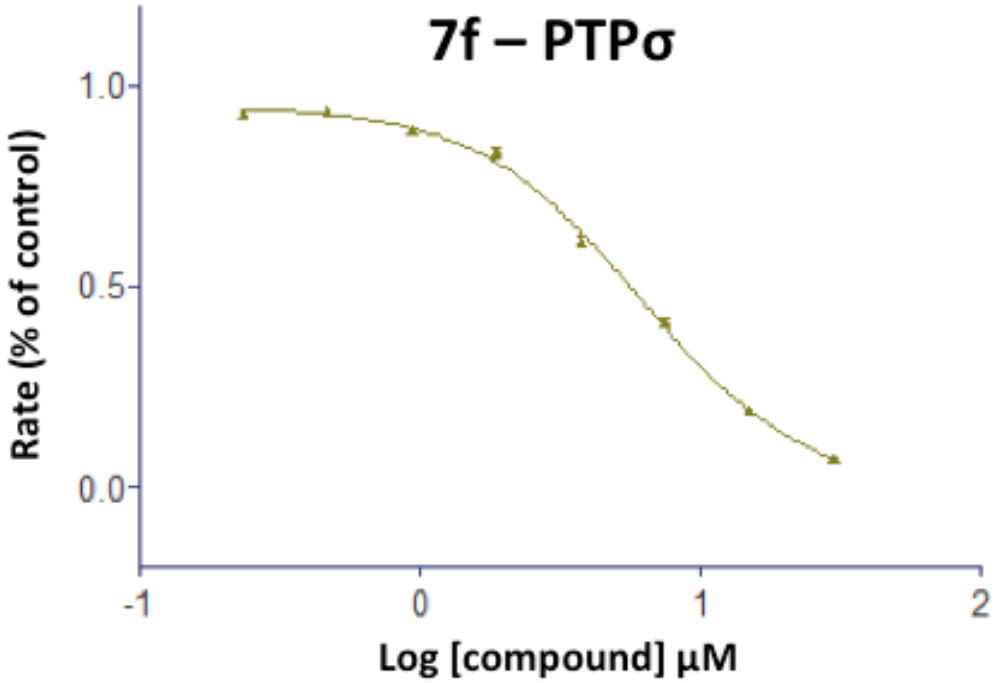

Fig. S1R. Graphs used for IC_{50} value determinations of **7a** against PTPσ. Dose-response data points represent the mean value of 3 trials

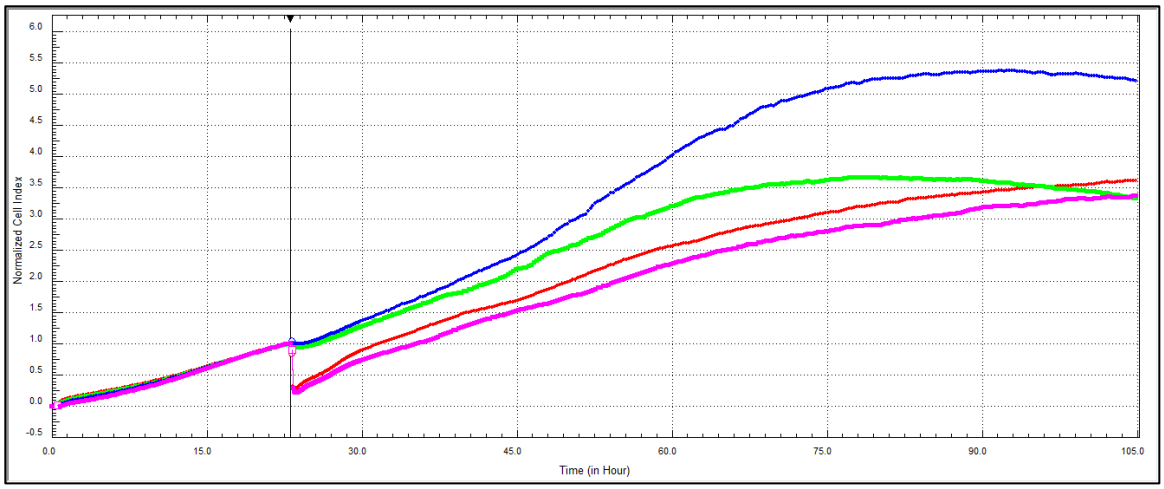

Fig. S2A. xCELLigence cytotoxicity control data. Measurements taken over 105 hrs for CHO-IR cells in DMSO (purple line) and 0.4, 10 and 50 μM salicylic acid (blue, green and red lines respectively). Administration of additive demarcated by vertical line on graph.

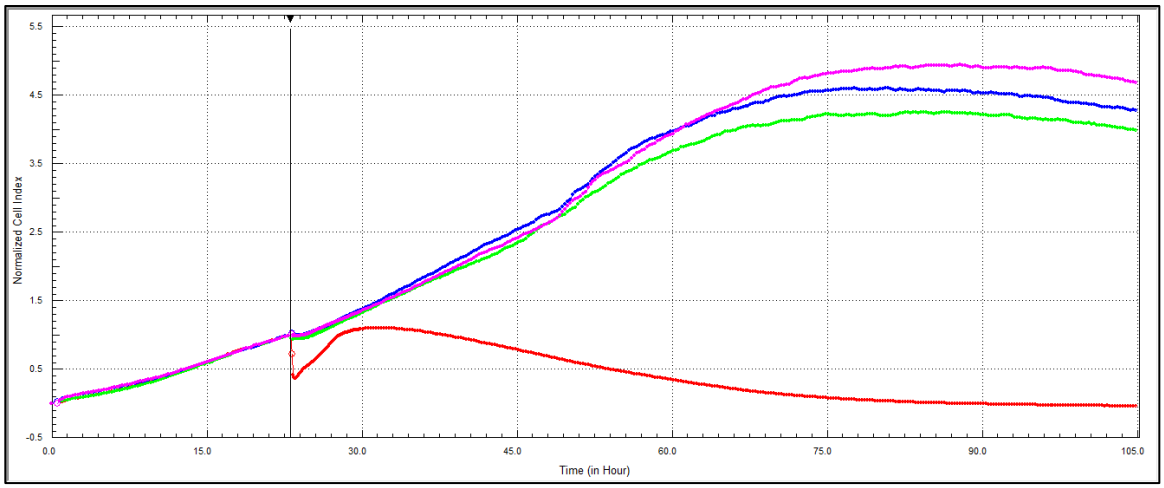

Fig. S2B. xCELLigence cytotoxicity data for **7a**. Measurements taken over 105 hrs in CHO-IR cells incubated with 0.4, 2, 10 and 50 μM concentrations of **7a** (purple, blue, green and red lines respectively). Administration of additive demarcated by vertical line on graph.

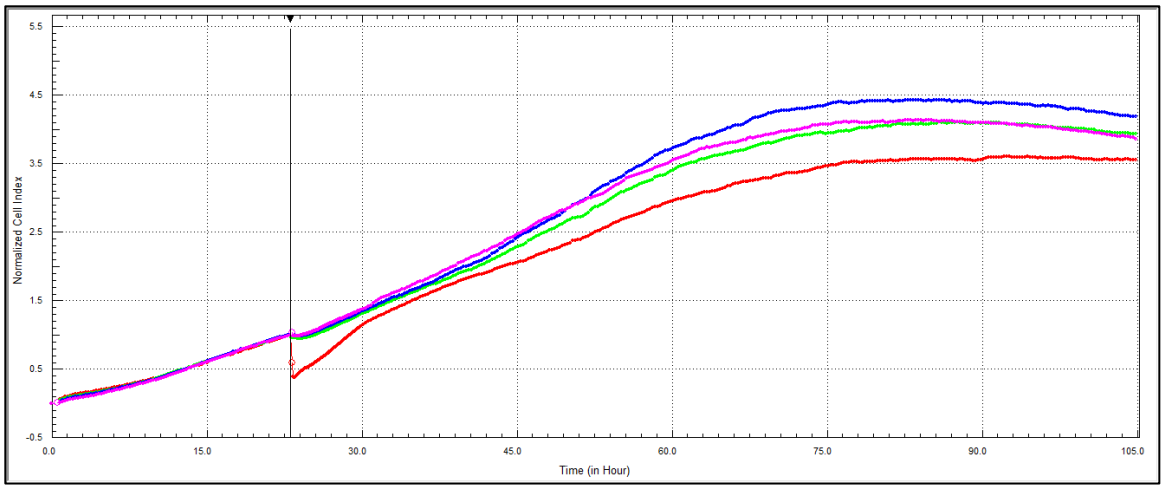

Fig. S2C. xCELLigence cytotoxicity data for **7b**. Measurements taken over 105 hrs in CHO-IR cells incubated with 0.4, 2, 10 and 50 μM concentrations of **7b** (purple, blue, green and red lines respectively). Administration of additive demarcated by vertical line on graph.

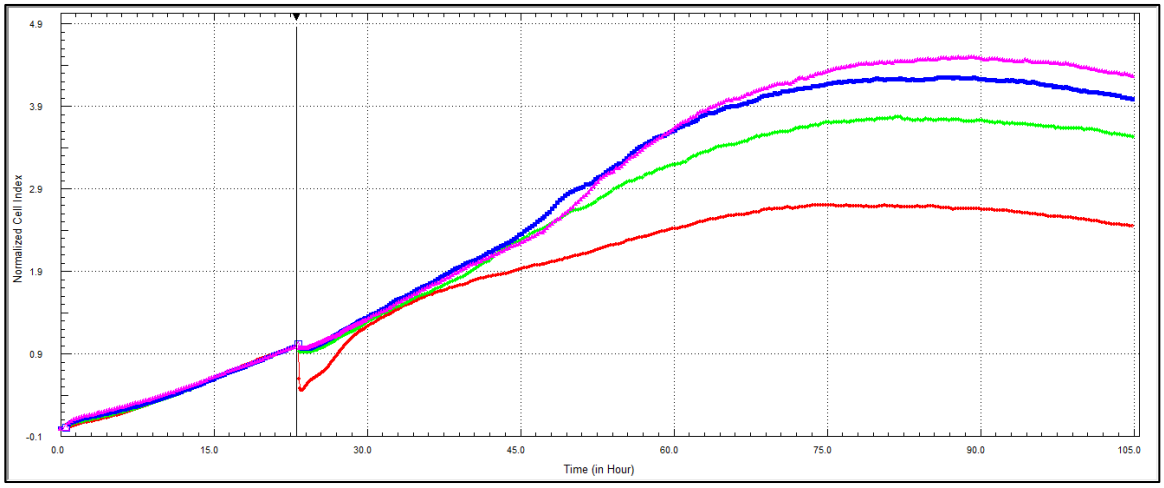

Fig. S2D. xCELLigence cytotoxicity data for **7c**. Measurements taken over 105 hrs in CHO-IR cells incubated with 0.4, 2, 10 and 50 μM concentrations of **7c** (purple, blue, green and red lines respectively). Administration of additive demarcated by vertical line on graph.

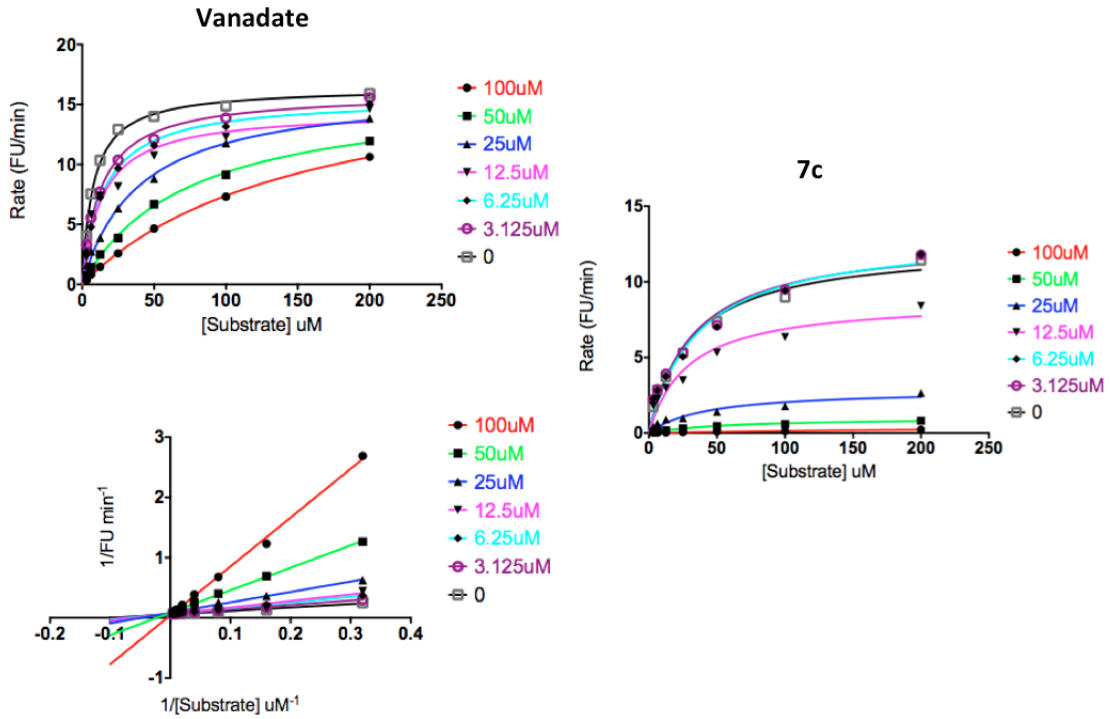

Fig. S3: Michaelis-Menten control data for Vanadate and experimental **7c** data. Curves represent the hydrolysis of DiFMUP and subsequent fluorescent detection at 450 nm (excitation of 358 nm). Below curves is shown Lineweaver-Burke transforms . V_{max} decreases and K_m increases for **7c** as a function of substrate concentration, indicative of mixed inhibition.

Materials and Methods

Reagents., Papain and BSA were purchased from Sigma. HEPES was purchased from Fisher. DiFMUP was purchased from Invitrogen and Z-Phe-Arg-pNA from Cederlane. Compound 1 was described in (Stuible et al. ChemBioChem 2007).

Preparation of GST-fusion proteins. GST-PTP were prepared as in (Stuible et al. ChemBioChem 2007). Purified GST-PTPs used are catalytic domain of PTP1B and TC-PTP, Full length MKPX and PRL2A/S (active mutant) and D1D2 of LAR and Sigma. All PTP were the human form.

Buffers : Enzyme reactions were performed in 50mM HEPES pH7.0 in which 3mM DTT and 0.1mg/mL BSA were added fresh. DiFMUP was used as substrate for all assays with GST-PTP. For Papain assay the substrate Z-Phe-Arg-pNA was used.

Kinetic measurments using DiFMUP as substrate: The hydrolysis of DiFMUP was conducted in black 96-well plates (Corning) in a final volume of 100µL at 25°C. The reaction was monitored by measuring excitation/emission 358/450 (for DiFMUP) or abosrbance 405nM (for Z-Phe-ARG-pNA) using Varioskan plate reader (Thermo electron). Kinetic measurements were monitored over 10 minutes in 30 seconds intervals

and rates were calculated using the slope (relative unit/min). Enzyme dilution was determined by choosing a reaction rate comprise in a Fluorometric range of 5-15 Fluorescence units/min (DiFMUP) or 0.3 OD_{405nm} units (Z-Phe-ARG-pNA).

Compound Screening: Inhibitors were diluted in DMSO and kinetic reactions were performed in 1% DMSO final. 10uM compound were used for initial screen with DiFMUP as substrate. Compound inhibiting any of the PTP were selected for a Papain screen to rule out oxidative molecules. A substrate concentration equivalent to the Km value for each enzyme was used.

IC50 assay: For IC50 a serial dilution starting at 30uM was made in assay buffer. IC50 reactions were performed in less than 2% DMSO final. IC_{50} values were derived by a sigmoidal dose-response(variable slope) curve using GraphPad Prism software. A substrate concentration equivalent to the Km value for each enzyme was used for IC_{50} determinations. The reported data are average of at least three independent experiments.

Cell culture, inhibitor treatment and lysate preparation. Cell lines were maintained in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% fetal bovine serum (FBS) and 1x gentamicin (Wisent). For FLT3-ITD/PTP1B expression, 293T cells were plated at $1x10^6$ cells/well in 6-well plates 20 h prior to transfection. Cells were transfected with 0.5 □g hFLT3-ITD-HA DNA, 0.25 □g PTP1B DNA, and 1.5 □l Lipofectamine 2000 (Invitrogen) for 6 h according to the manufacturer's directions. Following transfection, cells were serum-starved in 0.1% FBS DMEM overnight. For inhibitor treatment, media was then replaced with 0.1% FBS DMEM containing 1% DMSO and 10uM of compounds 7a, 7b and 7c, and cells were incubated a further 6 h. Cells were lysed in mRIPA with complete protease inhibitors(Roche) Vanadate and Sodium fluoride and analyzed by Western Blot.

For insulin time-course assays, CHO-IR cells were used. Prior to treatment, cells were serum-starved for 2 h in plain DMEM, then media was replaced with DMEM containing 1% DMSO and 1, 5 or 10 □M of inhibitors. After an extra 3 h incubation, human insulin (Humulin R, Eli Lilly), diluted in starvation media, was added at 10 nM for 15minutes. Cell lysates were prepared and analyzed as described above. Quantification of band intensity was performed by densitometry using ImageJ software (NIH).