Sorafenib induces cathepsin B-mediated apoptosis of bladder cancer cells by regulating the Akt/PTEN pathway. The Akt inhibitor, perifosine, enhances the sorafenib-induced cytotoxicity against bladder cancer cells.

### Supplementary Figure 1: A,B) 5637 and T24 cells treated with sorafenib (10 μM panel A and 20 μM panel B) or with vehicle for 12, 24 h, were stained with Ann V-FITC and PI and...
analyzed by FACS. Data are expressed as percentage of positive cells ± SD of three separate experiments. **p<0.01 vs vehicle-treated cells; ##p<0.01 vs 12h of sorafenib treatment. No statistical significant difference was found between untreated and vehicle-treated cells or comparing different times of vehicle-treatment each other (data not shown).

Supplementary Figure 2: Pazopanib docked into the catalytic groove of CB.

A) Pazopanib/CB complex is showed indicating the active site (light pink of the protein surface) inside the catalytic groove.

B) Cys29 and the amino acids involved in the H-bond formation.
Supplementary Figure 3: Sorafenib does not modulate phosphorylation levels of SHP-1 in T24 BC cells. Lysates from T24 BC cells treated with sorafenib (20 µM) for 1, 3 or 6 h or with vehicle for 1 h were separated via 9% SDS-PAGE and probed using anti-phospho-SHP-1, anti-SHP-1 and anti-GAPDH Abs. One representative experiment out of three independent experiments is shown. No statistical significant difference was found between untreated and vehicle-treated cells or comparing different vehicles-treatment each other (data not shown). Data shown are relative to T24 cell line and are representative of BC lines analyzed.