| Compound  | MIC<sub>50</sub> (µM) | MBC<sub>90</sub> (µM) | CC<sub>50</sub>_BHK21 (µM) | CC<sub>50</sub>_HepG2 (µM) | CC<sub>50</sub>_C6 glioma (µM) |
|-----------|------------------------|-----------------------|-----------------------------|-----------------------------|-----------------------------|
| 5         | 0.65±0.11              | 2.5-5                 | >50                         | >50                         | >50                         |
| 6         | 0.63±0.24              | 2.5-5                 | 13.75±0.87                  | 19.3±8.0                    | 8.10±1.55                   |
| 7         | 0.11±0.04              | 1.25-2.5              | 3.75±0.35                   | 4.50±0.28                   | >12.5                       |
| 8         | 9.67±1.45              | n.d.                  | >50                         | >50                         | >50                         |
| 9         | >20                    | n.d.                  | n.d.                        | n.d.                        | n.d.                        |

**Supplementary table S1. Initial structure-activity relationship of PI compounds.** The inhibitory activity (MIC<sub>50</sub>) was determined against *M. tuberculosis* H37Rv. The cidal activity (MBC<sub>90</sub>) and cytotoxicity (CC<sub>50</sub>) were determined after 5 days of exposure to a single dose of compound. Assays were carried out at least two times. MIC<sub>50</sub>: Minimum Inhibitory Concentration 50%; MBC<sub>90</sub>: Minimum Bactericidal Concentration 90%, CC<sub>50</sub>: Cyototoxic concentration 50%. n.d.: not determined.
### M. tuberculosis strain

| Glycerol: | AH9584 MIC (µM) | BE11677 MIC (µM) | E8133 MIC (µM) | W4 MIC (µM) |
|-----------|-----------------|------------------|----------------|-------------|
| +         | 0.43            | 1.09             | 0.67           | 0.07        |
| -         | > 20            | > 20             | > 20           | > 20        |
| Compound 1| 0.44            | 1.21             | 0.63           | 0.06        |
| -         | > 20            | > 20             | > 20           | > 20        |
| Compound 2| 0.005           | 0.022            | 0.016          | < 0.005     |
| -         | 0.008           | 0.022            | 0.016          | 0.016       |
| Rifampicin| 0.19            | 0.20             | 0.08           | < 0.005     |
| -         | 0.19            | 0.23             | 0.08           | 0.14        |

**Supplementary table S2. Activity of the PI compounds against four recent clinical isolates.**

The MIC$_{50}$ of compound 1 and 2 was tested in the presence (+) or absence (-) of glycerol. Rifampicin and isoniazid were used as reference compounds. The assay was repeated two times independently.