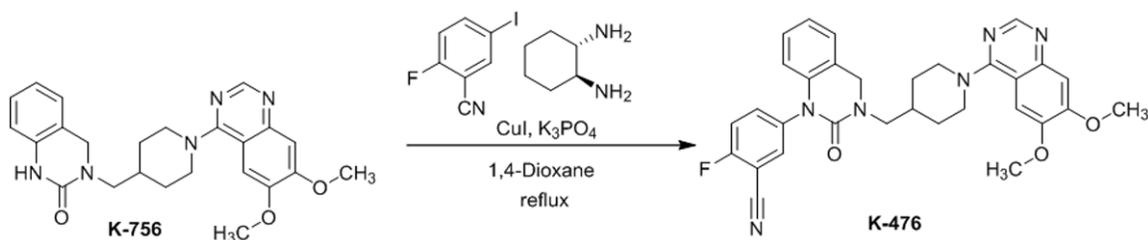


# TNKS inhibitor K-476 enhances antitumor activity of anti-PD-L1 antibody

## Supplementary Methods and Data

### Preparation of K-476



5-(3-[[1-(6,7-dimethoxyquinazolin-4-yl)piperidin-4-yl]methyl]-2-oxo-3,4-dihydroquinazolin-1(2H)-yl)-2-fluorobenzonitrile (K-476).

3-[[1-(6,7-dimethoxyquinazolin-4-yl)piperidin-4-yl]methyl]-3,4-dihydroquinazolin-2(1H)-one (K-756) was obtained by the previously reported method [1]. K-756 (50 mg, 0.12 mmol), copper(I) iodide (44 mg, 0.23 mmol), trans-1,2-cyclohexanediamine (26 mg, 0.23 mmol), 2-fluoro-5-iodobenzonitrile (114 mg, 0.46 mmol) and tripotassium phosphate (98 mg, 0.46 mmol) were stirred in 1,4-dioxane (1.0 mL) at 100°C for 5 hours. To the reaction mixture, a saturated aqueous sodium bicarbonate solution was added and the resulting mixture was extracted with ethyl acetate. The organic layer was treated with diatomaceous earth and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (a chloroform/methanol mixed solvent), whereby 5-(3-[[1-(6,7-dimethoxyquinazolin-4-yl)piperidin-4-yl]methyl]-2-oxo-3,4-dihydroquinazolin-1(2H)-yl)-2-fluorobenzonitrile (K-476) (40 mg, yield: 63%) was obtained.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 8.67 (s, 1H), 7.66-7.57 (m, 2H), 7.39-7.31 (m, 1H), 7.24 (s, 1H), 7.16-7.01 (m, 4H), 6.19 (d, *J* = 8.4 Hz, 1H), 4.61 (s, 2H), 4.21-4.17 (m, 2H), 4.02 (s, 3H), 3.98 (s, 3H), 3.46 (d, *J* = 7.0 Hz, 2H), 3.12-3.05 (m, 2H), 2.14-2.09 (m, 1H), 1.93-1.89 (m, 2H), 1.65-1.52 (m, 2H).

ESI-MS *m/z* calculated for C<sub>31</sub>H<sub>30</sub>FN<sub>6</sub>O<sub>3</sub>: 553 [M + H]<sup>+</sup> found 553.

### Reference

- [1] Nomoto Y, Obase H, Takai H, Hirata T, Tteruhashi M, Nakamura J and Kubo K. Studies on cardiotoxic agents. I. Synthesis of some quinazoline derivatives. *Chem Pharm Bull (Tokyo)* 1990; 38: 1591-1595.