**Supplemental Figure 1: TAM receptor and ligand expression in MDSCs were elevated in tumor bearing mice.**

**A.** Representative flow cytometry dot plots of splenic MDSCs. **B.** The percentage of M-MDSCs and PMN-MDSCs in the spleen of tumor-bearing WT, *Axl-/-*, *Mertk-/-* and *Tyro3-/-* mice quantified by flow cytometry. n=5 \*P<0.05 \*\*\*P<0.001. Significance calculated using the unpaired *t* test. All data are mean ± SEM. **C.** Representative flow cytometry dot plots of tumor MDSCs. **D.** MDSC gating strategy: Gated on lymphocytes, CD11b+ cells, then Ly6C+Ly6G- for M-MDSCs and Ly6intLy6G+ for PMN-MDSCs.

**Supplemental Figure 2: TYRO3, AXL and MERTK promoted MDSC immune suppressive function.**

**A.** UNC4241 (trans-4-((2-((4-fluorophenyl)amino)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-2-yl)pyrimidin-4-yl)amino)cyclohexan -1-ol) is a pan-TAM and Flt3 inhibitor (n = 6 for IC50s and n = 4 for Kis) (Zhang et al., 2013). It has a long half-life (8.17 h), moderate clearance (66.82 mL/min/kg), and large volume of distribution (36.12 L/kg) in an intravenous route and excellent oral bioavailability (90%) at 10 mg/kg dose in mice. **B.** trans-4-((5-bromo-2-((4-Fluorophenyl)amino)pyrimidin-4-yl)amino)cyclohexan-1-ol (2) To a suspension of 1 (30.6 g, 100 mmol) and 4-fluoroaniline (14.1 mL, 150 mmol) in MeCN (350 mL) was added a 4.0 M HCl solution in 1,4-dioxane (90 mL, 360 mmol). The resulting mixture was heated under reflux overnight. After cooled to room temperature, the suspension was filtered, and the precipitate was washed with CH2Cl2 (2X). The filtrate was concentrated to provide the HCl salt of the desired compound 2 as a pale white solid (42 g, 100%). MS (ESI) for [M+H]+ (C16H19BrFN4O+): calculated. m/z 381.06; found m/z 381.10. **C.** Survival of FACS sorted MDSCs cultured with 300nM UNC4241 were measured by MTS assay at 24, 48 and 72 hours. **D.** Flow analysis for macrophage and dendritic cell markers after MDSCs were cultured in 300nM UNC4241 for 72 hours. \*\* p<0.01, NS not significant **E.** Flow analysis for Ly6C and Ly6G markers of MDSCs cultured in 300nM UNC4241 for 72 hours.

**Supplemental Figure 3: Pan-TAM inhibitor UNC4241 inhibited MDSC capabilities and T cell suppression.**

**A.** IFN-γ ELISPOT analysis of WT, *Axl-/-*, *Mertk-/-* and *Tyro3-/-* MDSC’s suppression of OVA-stimulated T cell proliferation. Representative of 2 independent experiments. n=3/group \*\*P<0.01 \*\*\*P<0.001. Significance calculated using the unpaired *t* test. All data are mean ± SEM. Flow cytometry analysis of MDSCs incubated with GM-CSF for 3 days for markers of (**B.**) dendritic cells (CD11c+MHCII+) and (**C.**) macrophages (CD11b+F4/80+). Representative of 2 independent experiments. n=3/group \*P<0.05 \*\*\*P<0.001. Significance calculated using the unpaired *t* test. All data are mean ± SEM. eFluor 450 stained MDSCs implanted into mice with tumor cells were resected 3 days after implantation and eFluor 450+ cells were analyzed for markers of (**D.**) dendritic cells (CD11c+MHCII+) and (**E.**) macrophages (CD11b+F4/80+). Representative of 2 independent experiments. n=3 \*\*P<0.01 \*\*\*P<0.001. Significance calculated using the unpaired *t* test. All data are mean ± SEM. **F.** BRAFV600EPTEN-/- tumor cells and WT, *Axl-/-*, *Mertk-/-* or *Tyro3-/-* MDSCs were implanted at a 1:10 MDSC:tumor ratio. n=5 \*P<0.05 \*\*P<0.01. NS not significant. Significance calculated using the unpaired *t* test. All data are mean ± SEM.

**Supplemental Figure 4: UNC4241 delayed tumor growth, promoted T cell infiltration and augmented anti-PD-1 therapy.**

**A.** Analysis of *Axl*, *Mertk* and *Tyro3* RNA levels in BRAFV600EPTEN-/- cells compared to J774 cells by qRT-PCR (left) and protein levels by Western blot (right). **B.** Proliferation of BRAFV600EPTEN-/- cells treated with the indicated concentrations of UNC4241 for 24, 48 or 72 hours measured by MTS assay. **C.** Splenocytes were pre-treated with saline vehicle or UNC4241 then washed and analyzed for OVA-stimulated CD8 proliferation. n=3 **D.** Flow cytometry analysis of tumor infiltrating dendritic cells and macrophages. Representative images. n=9

**Supplemental Figure 5: TAMs facilitated MDSC action through Stat3 signaling.**

**A.** BM-MDSCs were serum starved for 2 hours, then pre-treated with 1μM p38 Inhibitor for 1 hour if applicable then treated with 200ng/ml GAS6 for 15 minutes at 37°C. MERTK was immunoprecipitated and samples were analyzed by Western blot using the indicated antibodies. Data are representative of 3 independent experiments. **B.** BM-MDSCs were serum starved for 2 hours, then pre-treated with 1μM pJNK Inhibitor for 1 hour if applicable then treated with 200ng/ml GAS6 for 15 minutes at 37°C. MERTK was immunoprecipitated and samples were analyzed by Western blot using the indicated antibodies. Data are representative of 3 independent experiments. **C.** BM-MDSCs were serum starved for 2 hours, then pre-treated with 1μM pERK Inhibitor for 1 hour if applicable then treated with 200ng/ml GAS6 for 15 minutes at 37°C. MERTK was immunoprecipitated and samples were analyzed by Western blot using the indicated antibodies. Data are representative of 3 independent experiments.

**Supplemental Figure 6: The frequency of TAM RTK+ MDSCs was increased in Metastatic Melanoma Patients.**

**A.** Gating strategy for human MDSCs. The number of AXL+, MERTK+ and TYRO3+ M-MDSCs (**B.**), PMN-MDSCs (**C.**) and e-MDSCs (**D.**) in the blood of healthy donors and metastatic melanoma patients were quantified by flow cytometry. n=25 healthy, n=15 melanoma ns=non-significant \*\*P<0.01 \*\*\*P<0.001 Mann-Whitney test. All data are mean ± SEM.