Here, we evaluated the immuno-oncologic impact and anti-tumor efficacy of immune responses, contributing to the evasion of cancer cells from immune surveillance.

**SUMMARY**

The TAM family of receptor tyrosine kinases (RTKs), including TYRO3, AXL, and MER, have been implicated in the pathogenesis and progression of many cancer types. In cancer cells, overexpression of TAM RTKs is associated with mechanisms of resistance and mesenchymal phenotypes. In immune cells, however, TAM RTKs play a key homostatic role as negative regulators of immune responses, contributing to the evasion of cancer cells from immune surveillance.

**RESULTS**

- RXDX-106 inhibited phosphorylation of TYRO3, AXL, and MER
- RXDX-106 completely inhibited tumor growth in NIH 3T3/TAM
- RXDX-106 inhibited ligand mediated AXL/MER activation on BMDM
- RXDX-106 inhibited phosphorylation of TYRO3, AXL, and MER
- RXDX-106 inhibited AXL- and MER-dependent phagocytosis

**CONCLUSIONS**

- RXDX-106 is a potent and selective TAM/c-MET inhibitor
- RXDX-106 is a highly potent, selective, and pseudo-irreversible inhibitor of TAM RTKs with durable target inhibition.
- RXDX-106 completely inhibited tumor growth as a single agent and in combination with anti-PD-1 antibody in the syngeneic CT26 model.
- RXDX-106 is a pseudo-irreversible biochemical profile (data not shown) drives greater cell-based potency and duration of target inhibition.

**ACKNOWLEDGEMENTS**

Working Model of RXDX-106 Mechanism of Action

**Figure 1.** Time course of the 4T1 breast cancer xenograft. Tumor volumes were measured at the indicated time points. *; p<0.05, **; p<0.01, ***; p<0.001

**Figure 2.** Axl and Mer Dependent Phagocytosis

**Figure 3.** Tumor Growth

**Figure 4.** Working Model of RXDX-106 Mechanism of Action

**Figure 5.** Effects of RXDX-106 on T cell response

**Figure 6.** Tumor volume and survival of 4T1 mouse breast carcinoma model

**Figure 7.** Anti-tumor and Pro-inflammatory Immune Response in syngeneic CT26 model

**Figure 8.** T-cell response

**Figure 9.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 10.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 11.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 12.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 13.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 14.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 15.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 16.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 17.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 18.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 19.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 20.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 21.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 22.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 23.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 24.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 25.** Macrophage NK cell Cancer cell DC T cell RXDX-106

**Figure 26.** Macrophage NK cell Cancer cell DC T cell RXDX-106