INTRODUCTION

- Agonists of TLRs (7/8) are currently being evaluated in clinical trials to determine their anti-tumor effect.
- Efficacious plasma levels of TLR 7/8 agonists have resulted in Grade 3 or 4 adverse effects (fever and lymphopenia).

RESULTS

INTRODUCTION (CONTINUED)

- NKTR-262 is a small molecule agonist of TLR 7/8 designed to be retained in the tumor micro-environment.
- Upon intratumoral delivery, NKTR-262 provides sustained intratumoral engagement of the TLR 7/8 pathway to promote an immune stimulatory stimulus.

- The preclinical prodrug pharmacokinetics of NKTR-262 resulted in higher and longer plasma exposures compared to the unmodified agonist.

RESULTS

Higher intratumoral (T26) retention of NKTR-262 compared to the unmodified agonist

NKTR-262 exhibited lower systemic proinflammatory cytokine induction after intratumoral (T26) injection compared to the unmodified agonist, consistent with reduced drug peak concentration in plasma.

- NKTR-262 was incubated in plasma or buffer, and NKTR-262 active species concentrations were determined using a qualified LC-MS/MS method.

- Oxidative metabolism of the NKTR-262 active species was mostly CYP3A4-mediated.

CONCLUSIONS

- The produg concept of NKTR-262 was clearly demonstrated by the formation of NKTR-262 active species in NKTR-262 in plasma from all preclinical species and human in vivo.

REFERENCES