REVEAL: A phase 1/2, open-label, multicenter, dose escalation and dose expansion study of NKTR-262 [TLR 7/8 agonist] plus NKTR-214 [CD122 bystander agonist] with or without nivolumab (nivo) in patients (pts) with locally advanced or metastatic solid tumor malignancies

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BACKGROUND

- Immune system activation with checkpoint inhibitors has proven to be an effective strategy for inhibiting tumor growth and prolonging survival. However, anti-PD-1 therapies, such as nivolumab, depend on pre-existing T-cell infiltration within the tumors for optimal efficacy.
- Toll-like-receptor (TLR) stimulation can induce differentiation of functional antigen presenting cells in the tumor environment and reduce immune suppression in tumors, facilitating T-cell priming.

OBJECTIVES

- Evaluation of the safety and tolerability, and define the maximum tolerated dose (MTD) or recommended phase 2 dose (RP2D) of NKTR-262 [TLR 7/8 agonist] plus NKTR-214 [CD122 bystander agonist] in combination with nivolumab (nivo).
- Evaluate the anti-tumor activity of the doublet and the triplet by assessing the objective response rate (ORR) per RECIST 1.1 Response Evaluation Criteria In Solid Tumors version 1.1.
- Evaluate the safety and tolerability, and define the maximum tolerated dose (MTD) or recommended phase 2 dose (RP2D) in patients with advanced or metastatic solid tumor malignancies.

REVEAL STUDY:

Sample Dose Escalation Scheme: Simultaneous 3+3 Design (Phase 1)

| Phase 1 Dose Escalation | Phase 2 Expansion | Phase 2 Triplet
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<tr>
<td>Cohort 1</td>
<td>Cohort 2</td>
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<td>Cohort 5</td>
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<td>Cohort 7</td>
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- Dose modifications of NKTR-262 (dose escalation or de-escalation) may be adjusted based on clinical observations as per the sample dose escalation scheme.

ELIGIBILITY

- Key Inclusion Criteria
  - Histologically confirmed diagnosis of a locally advanced (not amenable to curative therapy such as surgical resection) or metastatic cancer of the following histologies: melanoma, Merkel cell carcinoma, triple-negative breast cancer (TNBC), ovarian carcinoma, sarcoma, or carcinoma of unknown primary.
  - Eastern Cooperative Oncology Group (ECOG) performance status 0 to 1
  - Measurable disease per RECIST 1.1

- Key Exclusion Criteria
  - Pregnancy or lactation.
  - Known central nervous system (CNS) metastases.

- Status
  - Phase 1 dose escalation portion of REVEL is open and recruiting. REVEL Phase 2 is scheduled to open in the first half of 2019 (NCT03458364)