**PIVOT-02 STUDY**

**BACKGROUND**

- Immune system activation with checkpoint inhibitors has proven to be an effective strategy for inhibiting tumor growth and prolonging survival.1
- Anti-PD-1 therapies, such as nivolumab, depend on pre-existing T-cell infiltration within the tumors for optimal efficacy.4
- Abundance and functional quality of tumor-infiltrating lymphocytes are positively linked with tumor response and improved survival with checkpoint inhibitors.1,4

**NKTR-214 MONOTHERAPY STUDY**

- A phase 1, multicenter, open-label, dose-escalation study (EXCEL) was conducted to assess the safety, preliminary efficacy, pharmacokinetics, and pharmacodynamics of NKTR-214 in 21 patients with locally advanced or metastatic solid tumors.2
- Outpatient regimen with convenient 15-minute IV dosing regimen every 2 or 3 weeks.
- NKTR-214 has a favorable safety and tolerability profile.2
- No evidence of immune-mediated AEs or organ-related inflammation (e.g., colitis, pneumonitis, dermatitis, hepatitis, enterocolitis).

**Design**

- Phase 1: dose-escalation phase in 24 patients with locally advanced or metastatic solid tumors.
- Phase 2: dose-expansion phase in 22 patients with metastatic melanoma.

**Eligibility for Dose Expansion Cohorts**

- All patients will be monitored for treatment response as well as for any side effects.
- Demonstrated adequate organ function within 14 days of treatment initiation.
- Known BRAF status for patients with melanoma.
- History of organ transplant that requires systemic immunosuppression.
- History of autoimmune disease that requires systemic immunosuppression.
- Evidence of clinically significant interstitial lung disease or autoimmune inflammatory diseases.
- Prior surgery or radiotherapy within 14 days of therapy.

**All patients will receive NKTR-214 plus nivolumab in combination with anti-PD1, a trial combining NKTR-214 plus nivolumab (PIVOT-02) was initiated.**

**Figure 1. NKTR-214 Mechanism of Action**

- Histologically confirmed diagnosis of a locally advanced or metastatic melanoma, NSCLC, or triple negative breast cancer.
- Known BRAF status for patients with melanoma.
- Immunologic (PD-1/L1) checkpoint inhibitors must have demonstrated disease progression during or following treatment with prior checkpoint therapy.
- Eastern Cooperative Oncology Group (ECOG) performance status 0-1.
- Measurable disease per RECIST 1.1.
- Demonstrated adequate organ function within 14 days of treatment initiation.
- Oxygen saturation ≥ 92% on room air.
- History of organ transplant that requires systemic immunosuppression.
- History of autoimmune disease that requires systemic immunosuppression.
- Evidence of clinically significant interstitial lung disease or autoimmune inflammatory diseases.
- Prior surgery or radiotherapy within 14 days of therapy.

**Figure 2. Sustained Exposure and Robust PD Changes After a Single Dose of NKTR-214**

- Transient increase in active cytokine species, reaching Cmax 1-2 days after single dose of NKTR-214 (C0 to C1D0) and was rapidly reversible with IV fluids.

**Figure 3. NKTR-214 Promotes T Cell Proliferation and Selectively Increases CD8+ T Cells in Tumor**

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