

# A Phase 1b/2, open-label, multicenter, dose-escalation and dose-expansion study of NKTR-255 plus cetuximab as a salvage regimen in patients with solid tumors

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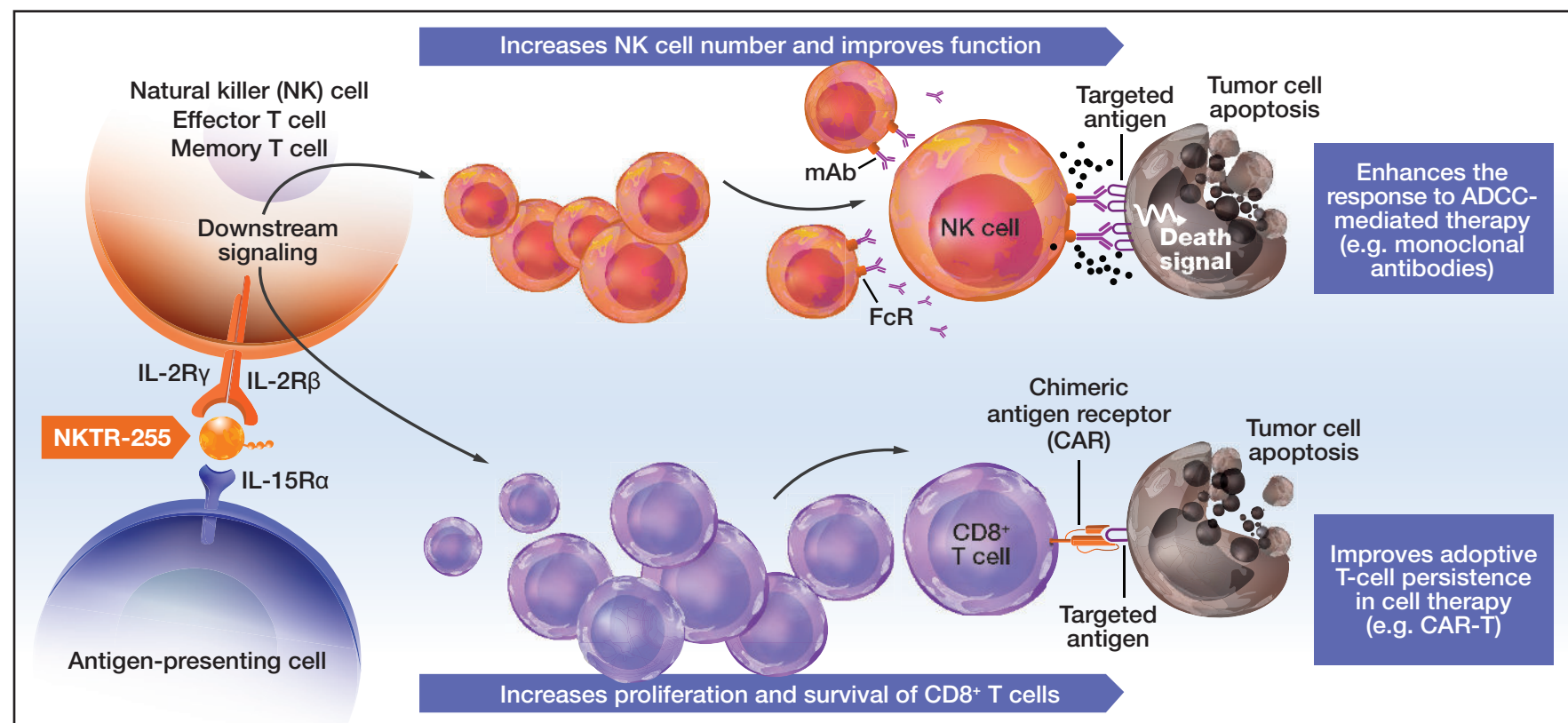
M. Altan<sup>1</sup>, A. Patnaik<sup>2</sup>, M. Barve<sup>3</sup>, L. Dunn<sup>4</sup>, P. Cobb<sup>5</sup>, A. Rosenberg<sup>6</sup>, S. Sharma<sup>7</sup>, A. Sukari<sup>8</sup>, Z. Lee<sup>9</sup>, M. Marcondes<sup>9</sup>, J. Zalevsky<sup>10</sup>, M. Tagliaferri<sup>9</sup>, A. Sacco<sup>11</sup>

<sup>1</sup>Department of Thoracic-Head & Neck Medical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; <sup>2</sup>Clinical Research, South Texas Accelerated Research Therapeutics (START), San Antonio, TX, USA; <sup>3</sup>Mary Crowley Cancer Research Center, Texas Oncology, Dallas, TX, USA; <sup>4</sup>Head and Neck Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; <sup>5</sup>St. Vincent Frontier Cancer Center, St. Vincent Healthcare, Billings, MT, USA; <sup>6</sup>Hematology/Oncology Department, University of Chicago, Chicago, IL, USA; <sup>7</sup>Hematology and Medical Oncology, Honor Health Research Institute, Scottsdale, AZ, USA; <sup>8</sup>Head and Neck Medical Oncology, Karmanos Cancer Center, Detroit, MI, USA; <sup>9</sup>Clinical Development, Nektar Therapeutics, San Francisco, CA, USA; <sup>10</sup>Research and Development, Nektar Therapeutics, San Francisco, CA, USA; <sup>11</sup>Moore's Cancer Center, University of California San Diego, La Jolla, CA, USA

## BACKGROUND

- There is an unmet need for new therapies that can boost NK cell number and function, with the purpose of aiding current approved therapies for HNSCC and CRC<sup>1</sup>
- NKTR-255 is a polymer-conjugated rhIL-15 agonist, which provides sustained PD responses without the need for daily dosing (**Figure 1**)<sup>2</sup>
- In preclinical models, NKTR-255:
  - Induced proliferation and activation of NK cells<sup>2</sup>
  - Promoted survival and expansion of CD8<sup>+</sup> T cells<sup>2</sup>
  - Induced NK cells with the potential for greater antitumor activity compared with IL-15 superagonists<sup>3</sup>
  - Enhanced antitumor activity of tumor-targeted antibodies with an ADCC mechanism<sup>2</sup>

**Figure 1. NKTR-255 engages with the IL-15R $\alpha$ /IL-2R $\beta$  receptor complex to boost NK cell number and CD8<sup>+</sup> T-cell expansion, proliferation, activation, function, and survival<sup>2</sup>**



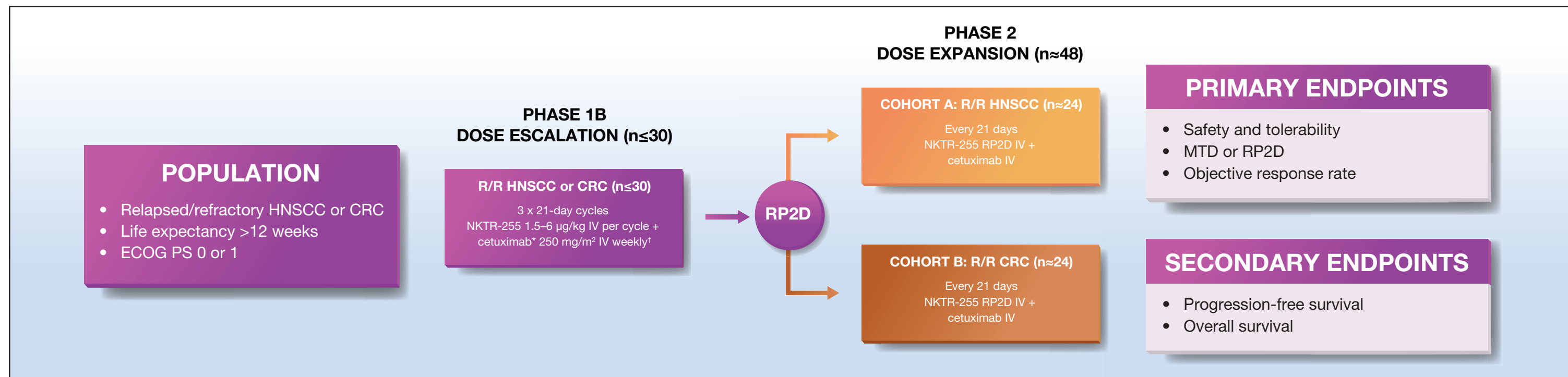
ADCC, antibody-dependent cellular cytotoxicity; CAR, chimeric antigen receptor; CAR-T, CAR T-cell therapy; CD, cluster of differentiation; FcR, Fc receptor; IL-2R, interleukin-2 receptor; IL-15R, interleukin-15 receptor; mAb, monoclonal antibody; NK cell, natural killer cell.

## STUDY

### Design

- A phase 1b/2 (NCT04616196) multicenter, open-label, dose-escalation, and dose-expansion study to evaluate the safety and antitumor activity of NKTR-255 plus cetuximab in patients with metastatic R/R HNSCC or CRC (**Figure 2**)
- In the dose-escalation phase,  $\leq 30$  patients will receive NKTR-255 every 21 days plus cetuximab weekly
  - Until the MTD and/or RP2D is determined, successive cohorts of 2–4 patients will receive ascending doses of NKTR-255
  - Patients who achieve optimal (partial or complete) response will be given the choice to continue NKTR-255 as maintenance therapy every 28 days
- In the dose-expansion phase,  $\approx 48$  patients from the R/R HNSCC and CRC cohorts will receive the RP2D of NKTR-255 plus cetuximab every 21 days
  - Patients will be treated until disease progression or unacceptable toxicity

**Figure 2. Phase 1b/2 dose-escalation and dose-expansion study design of NKTR-255 plus cetuximab in patients with R/R HNSCC and CRC**



\*On day -7, cetuximab 400 mg/m<sup>2</sup> IV will be given as a loading dose.

\*Patients who achieve optimal (partial or complete) response, will be given the option to continue NKTR-255 (every 28 days) as maintenance therapy.

CRC, colorectal cancer; IV, intravenous; MTD, maximum tolerated dose; RP2D, recommended phase 2 dose; R/R HNSCC, relapsed/refractory head and neck squamous cell carcinoma.

### Eligibility criteria

#### Key inclusion criteria

- ✓  $\geq 18$  years of age
- ✓ Locally advanced or metastatic HNSCC or CRC, not amenable to curative therapy, with measurable disease per RECIST v1.1
- ✓ Life expectancy  $>12$  weeks as determined by the Investigator
- ✓ ECOG PS 0 or 1
- ✓ No prior cetuximab or other EGFR-targeted therapy (phase 2 only)\*

#### HNSCC

- ✓ Disease progression on 1L/2L platinum-based chemotherapy or anti-PD-(L)1 checkpoint inhibitor
- ✓ Prior treatment with checkpoint inhibitor occurred  $\geq 4$  weeks before enrollment
- ✓ Ineligible for platinum-based chemotherapy or chemoradiation due to decline in renal function and/or intolerance

#### CRC

- ✓ Confirmed *KRAS* wild-type EGFR<sup>+</sup> tumor for phase 2 enrollment
- ✓ Received or intolerant to  $\geq 2$  prior cancer treatments in the metastatic setting
- ✓ Patients with microsatellite instability-high or deficient mismatch repair tumors must have received checkpoint inhibitors

\*Unless cetuximab was given as part of a primary treatment approach, with no progressive disease for at least 4 months following the end of prior cetuximab treatment.

#### Key exclusion criteria

- ✗ Prior treatment with an investigational agent/device or anti-cancer treatment  $\leq 28$  days before study treatment
- ✗ Active, known, or suspected autoimmune disease that requires systemic treatment  $\leq 3$  months from enrolment or requires systemic corticosteroids or immunosuppressants\*
- ✗ Surgery/radiotherapy or approved tyrosine kinase inhibitors  $\leq 14$  days before study treatment†
- ✗ Prior treatment with IL-2 or IL-15 at anytime, or systemic interferon alpha  $\leq 6$  months before enrollment
- ✗ Contraindication to, or unable to receive cetuximab, including those with prior Grade 4 infusion-related reactions
- ✗ HNSCC patients requiring anticoagulation therapy
- ✗ Prior treatment with warfarin for CRC patients  $\leq 14$  days before study treatment

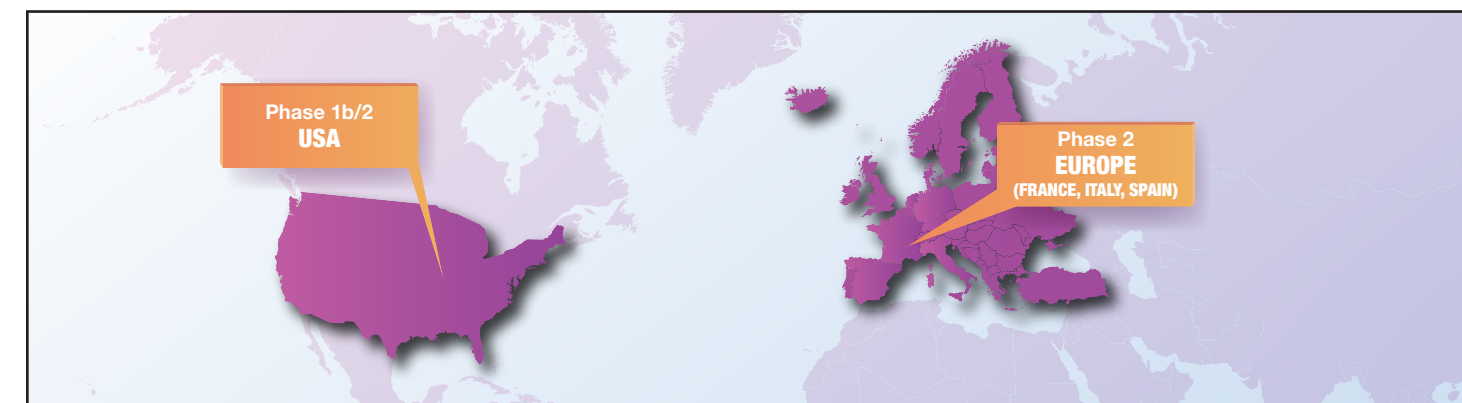
\*Exceptions include any patient on  $\leq 10$  mg prednisone or equivalent, patients with vitiligo, hypothyroidism stable on hormone replacement, Type 1 diabetes, Graves' disease, Hashimoto's disease, alopecia areata, eczema, psoriasis, or with Medical Monitor approval.

†Patients receiving sunitinib, sorafenib, vemurafenib, dabrafenib, or cobimetinib  $\leq 14$  days before administration of the first dose of study drug(s) will be excluded.

### Status

- This study is currently enrolling in the USA and plans to open in Europe for phase 2 (**Figure 3**)
- Enrollment is complete for the NKTR-255 1.5 and 3.0  $\mu\text{g/kg}$  dose levels
- Please visit ClinicalTrials.gov and search for NCT04616196 to find out the latest information on this study

**Figure 3. Locations of active or planned clinical trial sites**



## ABBREVIATIONS

1L, first-line therapy; 2L, second-line therapy; ADCC, antibody-dependent cellular cytotoxicity; CAR-T, chimeric antigen receptor T-cell therapy; CD, cluster of differentiation; CRC, colorectal cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HNSCC, head and neck squamous cell carcinoma; IL, interleukin; IV, intravenous; MTD, maximum tolerated dose; NK, natural killer; PD, pharmacodynamic; RECIST, Response Evaluation Criteria in Solid Tumors; rh, recombinant human; RP2D, recommended phase 2 dose; R/R, relapsed/refractory.

## ACKNOWLEDGMENTS

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The study was approved by the institutional review board of each participating site and informed consent is obtained from all patients.

## DISCLOSURES

M. Altan has served as an advisor to GlaxoSmithKline and Shattuck Labs, and has received institutional funding for research from Adaptimmune Therapeutics, Bristol Myers Squibb, Genentech, GlaxoSmithKline, Jounce Therapeutics, Lilly, Merck, Nektar Therapeutics, Novartis, and Shattuck Labs.

## REFERENCES

- Kivimäe S, et al. *J Immunother Cancer* 2019;7(Suppl. 1):P619.
- Shah N, et al. *Future Oncol* 2021;doi: 10.2217/fo-2021-0576. Online ahead of print.
- Miyazaki T, et al. *J Immunother Cancer* 2021;9:e002024.

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