ModeX™ THERAPEUTICS
an OPKO Health Company

A phase 1/2a first-in-human clinical trial evaluating MDX2001, a multi-specific antibody in patients with advanced solid tumor malignancies (NCT06239194)

A. Minchom[1], K. Culm[2], L. Makris[2], M. Johnson[3], D. Sommerhalder[4], J. Henry[5], E. Garralda[6], J. Merchan[7], M. Yang[8], A.-L. Goenaga[9], D. Burzyn[2], Z.-Y. Yang[10], R. Wei[10], J. Mascola[11], G. Abbadessa[12], G. Nabel[13], E. Dumbrava[14]

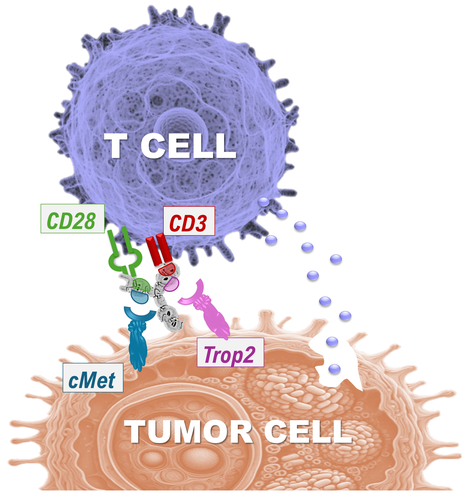
Institutions: [1]Drug Development Unit, ICR - Institute of Cancer Research, London, United Kingdom, [2]Clinical Development, ModeX Therapeutics, An OPKO Health Company, Weston, United States of America, [3]Lung Cancer Research, Sarah Cannon Research Institute-Cancer Centre, Nashville, TN, United States of America, [4]Department of Oncology, NEXT Oncology, San Antonio, United States of America, [5]Research, SCRI - Sarah Cannon Research Institute, Nashville, United States of America, [6]Early Drug Development Dept., Vall d'Hebron University Hospital, Barcelona, Spain, [7]Department of Medicine, Sylvester Comprehensive Cancer Center, Miami, United States of America, [8]Program Management, ModeX Therapeutics, An OPKO Health Company, Weston, United States of America, [9]Clinical Development, ModeX Therapeutics, An OPKO Health Company, Weston, MA, United States of America, [10]Research, ModeX Therapeutics, An OPKO Health Company, Weston, United States of America, [11]CSO, ModeX Therapeutics, An OPKO Health Company, Weston, United States of America, [12]CMO, ModeX Therapeutics, Inc. - An OPKO Health Company, Weston, United States of America, [13]CEO, ModeX Therapeutics, An OPKO Health Company, Weston, United States of America, [4]Investigational Cancer Therapeutics Department, The University of Texas MD Anderson Cancer Center - Main Building, Houston, United States of America. E-mail: kerry.culm@modextx.com

European Society for Medical Oncology Congress 2025 - 1584TiP

Background

MDX2001 is a tetraspecific antibody recognizing CD3 and CD28 on T cells, and c-MET and TROP2 on tumor cells. Anti-CD3 provides the primary signal for T cell activation; anti-CD28 delivers the secondary signal for enhanced T cell activation, survival, and proliferation.

Combinatorial targeting of c-MET and TROP2 by MDX2001, either on the same or different cancer cells, can **provide more effective engagement on tumor cells,** and may better address **tumor heterogenicity** and the development of retreatment **resistance** due to antigen downregulation. Preclinical studies with MDX2001 (Figures 1 and 2) demonstrate potent antitumor activity with no CD28-superagonist activity and minimal T cell activation in the absence of tumor cells [1].



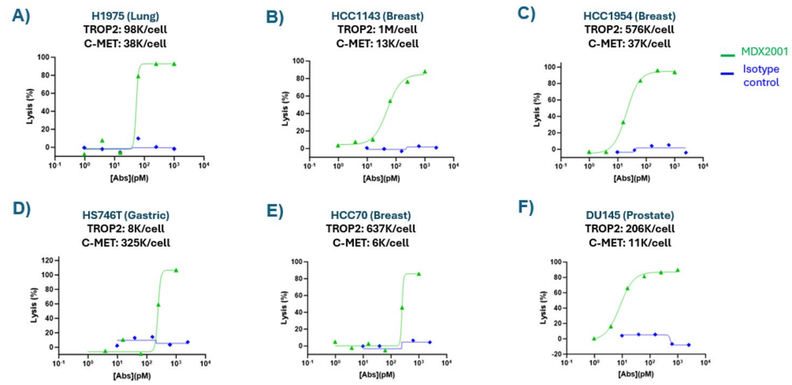


Figure 1. MDX2001 triggers robust *in vitro* tumor cytolytic activity when added to co-cultures of PBMCs and tumor cells.

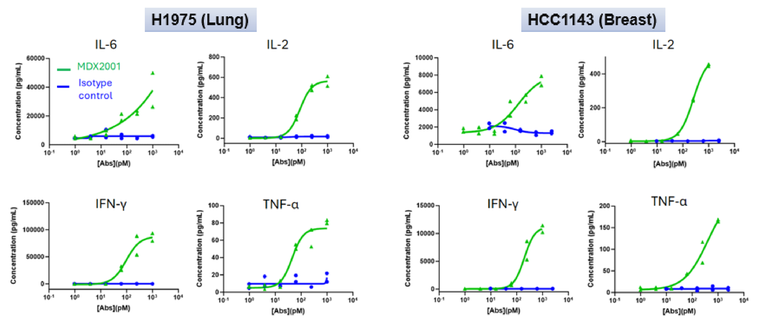
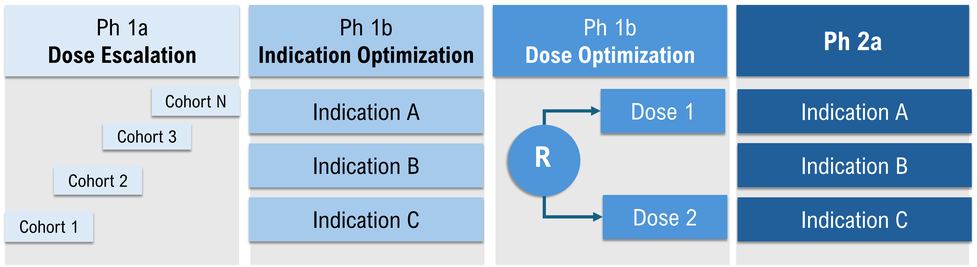


Figure 2. MDX2001 induces potent T cell activation in the presence of target tumor cells.

MDX-2001-101 Study Design



Key Inclusion Criteria

- Patients must be ≥ 18 years of age
- Histologically or cytologically confirmed diagnosis of metastatic solid tumors
- Eastern Cooperative Oncology Group (ECOG) performance status 0-1
- All patients should have at least 1 measurable disease per RECIST v1.1. An irradiated lesion can be considered measurable only if progression has been demonstrated on the irradiated lesion.
- Adequate hematologic, hepatic and renal function and appropriate contraceptive use for clinical trial participation.
- Capable of giving signed informed consent

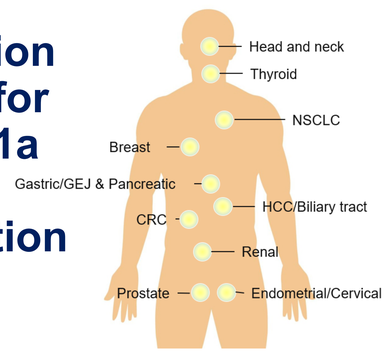
Key Exclusion Criteria

- Any clinically significant cardiac disease
- Unresolved toxicities from previous anticancer therapy
- Prior solid organ or hematologic transplant
- Known untreated, active, or uncontrolled brain metastases
- Known positivity with human immunodeficiency virus (HIV), known active hepatitis B or C, or uncontrolled chronic or ongoing infectious requiring intravenous treatment.
- Receipt of a live-virus vaccination within 28 days of planned treatment start
- Participation in a concurrent clinical study in the treatment period.
- Known hypersensitivity to MDX2001 or any of its ingredients

Study Objectives

Primary	○ Safety and tolerability in patients with advanced solid tumor malignancies ○ Identify a recommended Phase 2 dose ○ Assess the anti-tumor efficacy in patients with selected advanced solid tumor malignancies *(Phase 1b/2)*
Secondary	○ Further characterize anti-tumor efficacy and clinical benefit ○ Characterize pharmacokinetics and immunogenicity ○ Characterize relationship of baseline target protein expression in tumor tissue and clinical benefit
Exploratory	○ Evaluate potential biomarkers in tumor tissue and blood pre- and post-treatment that may predict or correlate with response to MDX2001

Tumor Indication Focus for Phase 1a Dose Escalation



1. Ling Xu et al. Beyond bispecifics: MDX2001, a novel tetraspecific antibody targeting T lymphocyte activation and survival enhancing receptors (LASER) directed to TROP2 and C-MET in solid tumor malignancies. Presented at SITC, November 2024, Abstract 1287.