



DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government Owned Invention Available for License: Monoclonal Antibody (RO4) that Reacts with the Juxta-membrane Region of Mesothelin

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The National Cancer Institute (NCI) seeks research co-development partners and/or licensees for a novel monoclonal antibody (mAb), RO4, that can be used to treat mesothelin (MSLN) expressing cancers.

FOR FURTHER INFORMATION CONTACT: Inquiries related to this license opportunity should be directed to: Laurie Whitney, Ph.D., Unit Supervisor, NCI, Technology Transfer Center, Email: WhitneyL@mail.nih.gov or Phone: 240-276-5505.

SUPPLEMENTARY INFORMATION: Mesothelin (MSLN) is a surface antigen highly expressed in many solid tumors, such as mesothelioma, ovarian, and pancreatic cancers. MSLN is present at relatively low levels in mesothelial cells of healthy individuals, making it an ideal candidate for targeted therapeutics. However, the efficacy of MSLN-targeted agents is often reduced as a portion of the protein is shed from the cell surface and binds to available anti-MSLN antibodies. This reduces therapeutic engagement at the cell surface as shed MSLN acts as a decoy within tumor microenvironments, limiting antibodies from reaching and destroying tumor cells.

Researchers at the NCI developed a novel mAb, RO4, which specifically binds to the juxta-membrane region of MSLN to block shedding. RO4 binds to the same region of MSLN as a previously developed mAb, 15B6 (NCI Ref. #E-106-2017), but in a different conformation. This allows for increased binding affinity and specificity. CAR-T cells made with humanized RO4 demonstrated higher cytotoxicity both *in vitro* and *in vivo* compared to h15B6 CAR-Ts. Additionally, hRO4 exhibited broader binding across MSLN-positive cell types compared to h15B6, suggesting wider utility in patient populations.

Researchers at the NCI seek licensing and/or co-development research collaborations for further development of RO4 that can be used to treat MSLN-positive cancers.

“This Notice is in accordance with 37 C.F.R. § 404.4 Authority to grant licenses.”

NIH Reference Number: E-051-2024.

Related Technologies: E-106-2017 and E-033-2022.

Product Type: Therapeutic.

Therapeutic Area(s): Oncology | Immunology.

Development Stage: Pre-clinical (*in vivo* validation).

Publications:

- Onda M, et al. RO4, a high-affinity humanized antibody against the juxtamembrane region of mesothelin for targeted cancer therapy. (PMID41550974).
- Liu X, et al. Highly active CAR T cells that bind to a juxtamembrane region of mesothelin and are not blocked by shed mesothelin. (PMID35512094).

Patents: National Stage Applications.

Potential Commercial Applications:

- Treatment of various MSLN-positive cancers – including mesothelioma, ovarian and pancreatic cancer.
- Development of CAR T cells and bispecific antibodies to target MSLN and CD3.
- Development of Antibody-Drug Conjugates (ADCs) and Antibody-nanoparticle conjugates to deliver cytotoxic payloads to MSLN-positive tumors.

Competitive Advantages:

- Increased therapeutic effectiveness via avoiding shed decoy interference.
- Enhanced binding affinity and selectivity compared to earlier antibodies.
- Improved cytotoxicity across various MSLN-positive tumors.
- Versatility in use of CAR T cells and bispecific antibodies targeting MSLN and CD3.

Collaboration Opportunity: Researchers at the NCI seek licensing and/or co-development research collaborations for a novel monoclonal antibody (mAb), RO4, that can be used to treat MSLN expressing cancers.

Dated: August 7, 2026.

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Associate Director,

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National Cancer Institute.

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