# Sindbis Virus-Based Vectors for the Oncolytic Immunotherapy of Solid Tumors

**Innovative, efficacious, and safe treatment for ovarian and other types of cancers.**

### Technology

The Meruelo research group has developed a Sindbis virus (SV) vector platform for the treatment of advanced metastatic cancers. This platform leverages the tumor-biased laminin receptor-mediated entry of SV and the virus's ability to be systemically delivered to target tumors throughout the body. The innovators have assessed the incorporation of a wide selection of exogenous immunomodulatory cargo within the vector to provide efficient tumor clearance. The lead candidate vector expresses two immunomodulatory molecules, interleukin-12 (IL-12) and an agonistic OX40 antibody. IL-12 is a key cytokine that stimulates anti-tumor activity of Natural Killer cells, while OX40 is a secondary co-stimulatory immune checkpoint molecule that promotes Effector T Cell expansion and survival within the tumor microenvironment to help eradicate tumors. Extensive preclinical testing of the lead SV vector in a mouse model of high-grade serous ovarian carcinoma demonstrated optimal tumor tropism and induction of a potent anti-tumor immune response that provided long-term protection against tumor re-challenge even after 5 months. These vectors have been the basis of two completed NIH SBIR grants that provided $4.4 million in funding and pre-IND submission, and as such, have a detailed package of mechanistic, toxicology, biodistribution, pharmacokinetics, and manufacturing data. NYU is now seeking a partnership to lead the clinical development of this promising platform for the treatment of ovarian cancer and other solid tumors.

### Background

Ovarian cancer and other solid tumors such as prostate and lung cancers, remain difficult to treat and highly lethal due to properties of the tumor microenvironment that facilitate metastasis, impair immune surveillance, and mediate therapy resistance. Oncolytic virus therapeutics have emerged as a treatment for these cancers, and are currently in clinical stages of development. However, these oncolytic viruses often require invasive administration into the tumor site and have limited efficacy against metastatic disease. As a naturally blood-borne virus, SV and the associated vectors developed by the Meruelo group offer a novel treatment approach to these cancers, providing effective systemic delivery for targeting metastasis, while limiting entry and subsequent expression of immunomodulatory molecules to the tumor microenvironment.

### Development Stage

This innovation has been the subject of SBIR-funded pre-clinical development, including successful *in vivo* efficacy, toxicology, and GMP manufacturing. A pre-IND package of this innovation has been presented to the FDA and received written responses to guide subsequent IND submission.

**Technology ID**

MER02-24

**Category**

Life Sciences/Biologics
Life Sciences/Therapeutics/Oncology
Life Sciences/Platform Technology
Life Sciences/Drug Delivery Systems
Life Sciences/Genetic Engineering
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## Applications

- **Treatment of LAMR-expressing tumors:** Ovary, breast, stomach, melanocytes, lung, and uterus tumors all overexpress LAMR
- **Treatment of metastatic cancers**

## Advantages

- **Systemic delivery:** Sindbis viral vectors are suitable for targeting tumors throughout the body, unlike other agents that require direct tumor administration.
- **Broad applicability:** Sindbis viral vectors can be used for the treatment of various types of cancers due to widespread entry receptor expression on tumors.
- **Enhanced anti-tumor immune response:** The platform induces a potent anti-tumor immune response involving both CD8 and CD4 T cells.
- **Long-term protection:** The platform provides long-term protection against tumor re-challenge and possible patient relapse.
- **Transitory:** The vector is replication defective due to splitting of the genome and removal of the endogenous packaging signal.

## Intellectual Property

NYU holds a portfolio of issued and pending worldwide patent applications for the method of treating LAMR-expressing tumors with Sindbis virus vectors harboring combinations of immunomodulatory proteins, check-point inhibitors, or costimulatory antibodies.

**Issued patents:**

- US8114961B2
- US8093021B2
- US8282916B2
- AU2014318015B2
- CA2922835C
- CN105705163B
- EP3041500B1
- US10010628B2

## References

1. Opp, S.; Hurtado, A.; Pampeno, C.; Lin, Z.; Meruelo, D. , https://doi.org/10.3390/cells12010077