

ASX Announcement

Imugene's B cell immunotherapy & oncolytic virotherapy platforms featured at ESMO Congress

Sydney, Australia, 24 October 2023: Imugene Limited (ASX: IMU), a clinical stage immuno-oncology company, is pleased to announce that its B cell immunotherapy HER-Vaxx and CF33 oncolytic virotherapy CHECKVacc featured this week at the ESMO Congress, currently being held in Madrid 20-24 October 2023.

The European Society for Medical Oncology (ESMO) Congress is the most influential oncology platform for clinicians, researchers, patient advocates, journalists, and healthcare industry representatives from all over the world.

The presentation titles featuring Imugene's HER-Vaxx and CHECKVacc are the following:

Poster 1536P: HERIZON: A Phase 2 study of HER-Vaxx (IMU-131), a HER2-targeting peptide vaccine plus standard of care chemotherapy in patients with HER2+ advanced stomach Cancer – dose-dependent anti-cancer antibodies correlating with improved clinical outcome. Presenter: Dr Joshua Tobias, Medical University of Vienna.

Highlights and conclusions

- As previously reported 27 June 2022 compared to chemotherapy alone, HER-Vaxx vaccination resulted in a statistically significant overall survival benefit.
- As previously reported at ESMO GI 30 June 2023 HER-Vaxx treatment produced statistically significant robust anti-HER2 antibody responses ($p < 0.0001$).
- In this new presentation HER-Vaxx-based vaccination of patients with HER2-overexpressing gastric cancer validates the mechanism of action by demonstrating; (1) induced anti-HER2 antibody responses ($p < 0.001$) with dose-dependent functionality in binding to human HER2-expressing gastric cancer cells, (2) intracellular phosphorylation inhibition of the HER2 receptor and (3) inhibiting the cancer signalling pathway kinases Akt and MAPK.
- The presented data further validate the proof of concept for the first-in-class B-cell immunotherapy HER-Vaxx.



Poster 472P: Prevention of metastasis formation by combination therapy targeting HER2 and PD-L1 in HER2-expressing tumors based on observed efficacious vaccination against HER2-positive tumors. Presenter: Dr Joshua Tobias, Medical University of Vienna.

Highlights and conclusions

- In the preclinical setting (in vivo mouse studies): Targeting HER-2/neu by HER-Vaxx vaccination was associated with concomitant PD-L1 upregulation and the HER2 receptor's downregulation of expression in the same tumors, resulting in a significantly higher ratio of PD-L1 to HER-2/neu positive metastases.
- In the clinical setting (Phase 1b HERIZON study): Targeting HER2 by HER-Vaxx vaccination was also associated with the upregulation of PD-L1 and downregulation of HER2 expression in the evaluated patient's primary tumor, conceivably influencing the final disease progression observed in the patient.

Tumoral upregulation of PD-L1 and downregulation of HER2 expression have both been linked to resistance and subsequent metastasis development following treatment with the standard of care monoclonal antibody trastuzumab.

These observations suggest that targeting HER2 induces upregulation of PD-L1 and a combination therapy targeting both HER2 and the PD1/PD-L1 axis with an immune checkpoint inhibitor may be used clinically and synergistically to treat metastatic HER2+ cancers with prevention of new metastasis development and immune evasion.

Poster Session

#4581: Induction of an Inflammatory Tumor Microenvironment with Oncolytic Virus CF33-hNIS-antiPD-L1 Intratumoral Injection in Patients with Metastatic Triple Negative Breast Cancer (mTNBC). Presenter: Dr Jamie Rand, City of Hope.

Highlights and conclusions

- Intratumoral (IT) treatment with CF33-hNIS-anti-PD-L1 is safe and well-tolerated at dose levels 1 through 3.



- CF33-hNIS-anti-PD-L1 IT injection induces tumor infiltration of CD4+ and CD8+ T-cells which are critical immune cells signalling localised immune activation connected to CF33-hNIS-anti-PD-L1 injection.
- Significant upregulation of PD-L1 within the tumor microenvironment (TME) further suggests immune activation by CF33-hNIS-anti-PD-L1, an important precursor for immune clearance of tumors.
- SPECT imaging after treatment with CF33-hNIS-anti-PD-L1 showed enhancement at injected lesions in 75% of patients, suggesting local viral replication and hNIS expression. This shows successful tracking of viral replication using non-invasive imaging studies.

This clinical trial is ongoing to further assess dose escalation, tumor response, and TME changes at later timepoints and higher dose levels.

The posters are available on Imugene's website, <https://www.imugene.com/conference-presentations>

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About Imugene (ASX:IMU)

Imugene is a clinical stage immuno-oncology company developing a range of new and novel immunotherapies that seek to activate the immune system of cancer patients to treat and eradicate tumours. Our unique platform technologies seek to harness the body's immune system against tumours, potentially achieving a similar or greater effect than synthetically manufactured monoclonal antibody and other immunotherapies. Our pipeline includes an off-the-shelf (allogeneic) cell therapy CAR T drug azer-cel (azercabtagene zapreleucel) which targets CD19 to treat blood cancers. Our pipeline also includes multiple immunotherapy B-cell vaccine candidates and an oncolytic virotherapy (CF33) aimed at treating a variety of cancers in combination with standard of care drugs and emerging immunotherapies such as CAR T's for solid tumours. We are supported by a leading team of international cancer experts with extensive experience in developing new cancer therapies with many approved for sale and marketing for global markets.

Our vision is to help transform and improve the treatment of cancer and the lives of the millions of patients who need effective treatments. This vision is backed by a growing body of clinical evidence and peer-reviewed research. Imugene is well funded and resourced, to deliver on its commercial and clinical milestones. Together with leading specialists and medical professionals, we believe Imugene's immuno-oncology therapies will become foundation treatments for cancer. Our goal is to ensure that Imugene and its shareholders are at the forefront of this rapidly growing global market.

Release authorised by the Managing Director and Chief Executive Officer Imugene Limited.