INV043 DRAMATICALLY IMPROVED IMMUNE CHECKPOINT INHIBITOR EFFECTIVENESS WHEN USED IN COMBINATION, ACHIEVING ~80% TUMOUR CONTROL IN PRECLINICAL STUDIES

Highlights:

- **Topically applied INV043 in combination with an immune checkpoint inhibitor (ICI) resulted in ~80% of subjects being tumour-free. The study was conducted by Peter Mac using immune competent anal squamous cell carcinoma (ASCC) *in vivo* models**
- **ICIs, the standard of care for the treatment of several cancers, are a class of immunotherapy drug. Despite widespread clinical use as a monotherapy, ICI effectiveness is typically limited to a small proportion of patients**
- **Results support previous findings by Hudson Institute using intratumorally administered INV043 in combination with ICIs on another cancer type (triple negative breast cancer)**
- **Opens additional treatment options for upcoming clinical trial programs that span multiple cancers**
- **ASCC has potential to be designated as an orphan indication – leading to an expedited regulatory approval process**
- **The findings reinforce the potential for collaboration partnerships using combination therapies to extend the patent life of blockbuster ICIs**
- **Global ICI market forecast to grow at 16.8% CAGR to reach US$189 billion by 2032[1]**

MELBOURNE (AUSTRALIA) 04 March 2024: Invion Limited (ASX: IVX) ("**Invion**" or the "**Company**") is pleased to announce the findings from a study by the Peter MaCallum Cancer Centre (**Peter Mac**) on the effect of INV043, when used in combination with an immune checkpoint inhibitor (**ICI**) therapy. ICIs are a type of immunotherapy and is the standard of care for the treatment of several cancers. Despite widespread use of ICIs, the patient response rate can be as low as 12.5%[2].

The key findings from the *in vivo* study using immune competent mouse models with anal squamous cell carcinomas (**ASCC**) include:

- The combination therapy using INV043 with ICIs led to ~80% control of ASCC tumours at the study endpoint, compared with ICI therapy alone, which achieved ~12% control.
- The results were statistically significant (p=0.0037).
- The mice under combination treatment maintained a healthy weight while under treatment and no negative side effects from the combination therapy were noted.

"It's very exciting to see how well INV043 worked in combination with an anti-PD-1 therapy, where standalone ICI therapy typically has a very low response rate," said Professor Rob Ramsay, Senior Scientist at Peter Mac.

"These results demonstrated exceptional, consistent, and highly significant tumour control. And when considered with the prior Hudson findings, provide a strong indication that a high level of control may also be achieved in clinical trials across a number of cancers."

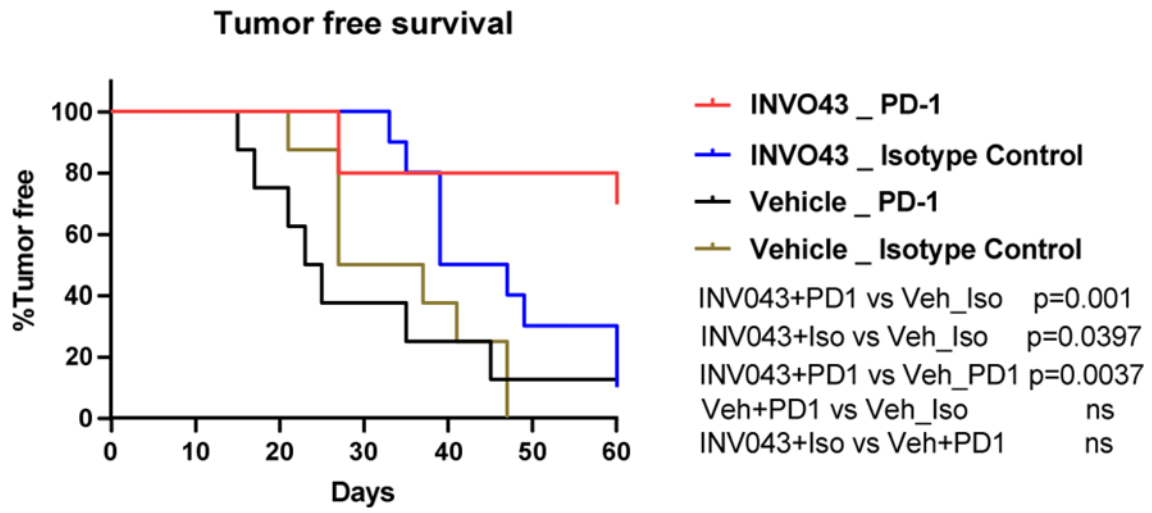
[1] https://www.alliedmarketresearch.com/immune-check-point-inhibitors-market

[2] https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2762389

Anal cancers require new options for treatment. The current management depends upon surgery plus chemotherapy and/or radiotherapy that has not substantially changed in decades. Anal cancers belong to a group of ano-genital tumours that are in genuine need of better treatment options.

Invion has received independent advice that anogenital cancer has the potential to be designated as an orphan indication, which leads to an expedited and lower cost path through the regulatory approval process.

The Peter Mac study independently validates Proof of Concept (**PoC**) research conducted at the Hudson Institute of Medical Research (**Hudson Institute**) where a reduction in tumour size of approximately 65% was achieved in mice implanted with triple negative breast cancer tumours and treated with INV043 intratumorally when compared to an ICI alone.



A log-rank (Mantel-Cox) test of the treatments is shown above with the parameters of one cycle of treatment followed by tumour monitored until the end points when the tumour size reaches 1500mm (indicated by 0% tumour-free on the y-axis) or 60 days, whichever occurs first.

Significance of the results

ICI therapies have limited effectiveness against several cancer types as a monotherapy despite its widespread clinical use[3]. Combining INV043 with ICI demonstrates enhanced clinical response in "cold" tumours (a tumour that is unlikely to trigger a strong immune response).

INV043 presents an attractive opportunity to pharmaceutical groups that own ICI drugs to develop new combination therapies to improve clinical outcomes, develop new intellectual property, and extend the patent life of their blockbuster ICI therapies[4]. The global ICI market was valued at US$40.1 billion in 2022, and is projected to reach $189.4 billion by 2032, growing at a CAGR of 16.8% from 2023 to 2032[1].

[3] Adel Naimi et al, (2022). Tumor immunotherapies by immune checkpoint inhibitors (ICIs); the pros and cons: Cell Communication and Signaling

[4] https://www.fiercepharma.com/special-report/top-15-blockbuster-patent-expirations-coming-decade

"These compelling findings demonstrate the potential of INV043 for use in combination with immune checkpoint inhibitors, to substantially improve patient outcomes", said Invion's Executive Chairman and Chief Executive Officer, Thian Chew.

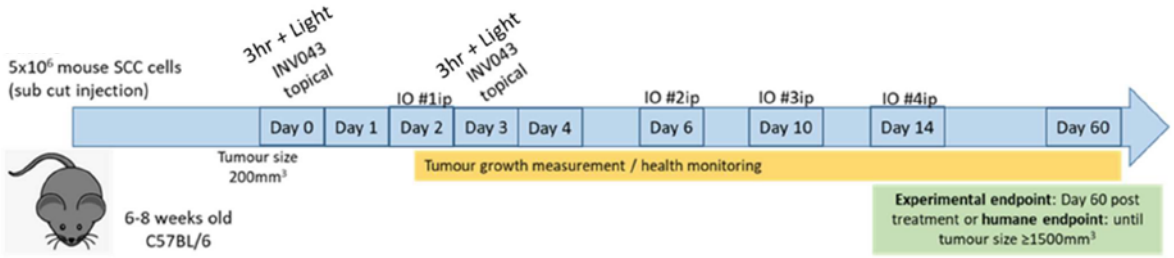
"The high impact opportunity to improve widely used ICI therapies, and ability to develop new combined IP with potential partners, provides us multiple pathways to commercialise Photosoft™ technology, which we look to further demonstrate in our clinical trials."

Michael Cho, founder of RMW Cho Group and originator of Photosoft, which INV043 is derived from, commented: "We are thrilled to see our joint efforts, in conjunction with Peter Mac, demonstrate an impressive level of control on ASCCs."

Details of the study

The study aimed to explore the role of the immune system in C57BL/6 recipient mice bearing anal squamous cell carcinoma (ASCC) lines injected subcutaneously when treated with INV043 with and without check point inhibition blockade.

A topical formulation of INV043 was used in this study – the same that Invion is using in its planned Phase I/II clinical trials for non-melanoma skin cancer.



Six- to eight-week-old C57BL/6 mice with a subcutaneous injection of ASCC lines were separated into four groups with eight to ten mice per group (n=8-10/group). Treatment groups included mice treated with single therapy anti-PD-1 alone, INV043 alone, the combination of both, and a control group.

Tumours were allowed to reach 200 mm^3 prior to application of INV043 in ointment (or vehicle control) for three hours then exposed to laser light. This was repeated 48 hours later. ICIs were injected every four days up to four rounds of treatment.

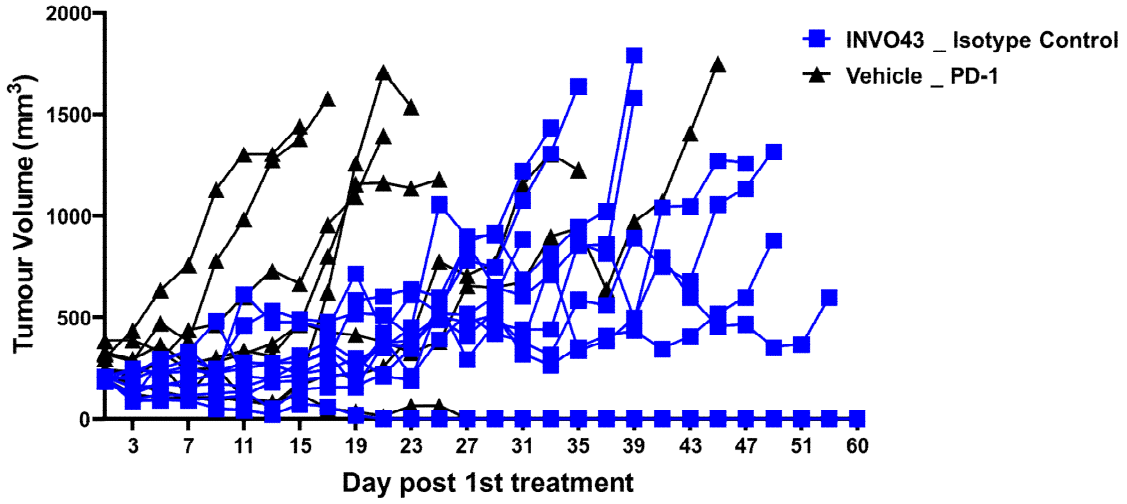
Statistical significance between groups was calculated using one-way ANOVA with Tukey's multiple comparisons test. A P-value of ≤ 0.05 was considered statistically significant (although it should be noted that with such a small sample size, the P-value should be considered representative only).

No effect on mouse wellbeing or weight gain over time was observed. As with other treatments with INV043, no visible scarring was observed in the mice where complete tumour control was achieved.

The following graphs below illustrate the level of control of each treatment.

INV043 Alone vs ICI Alone

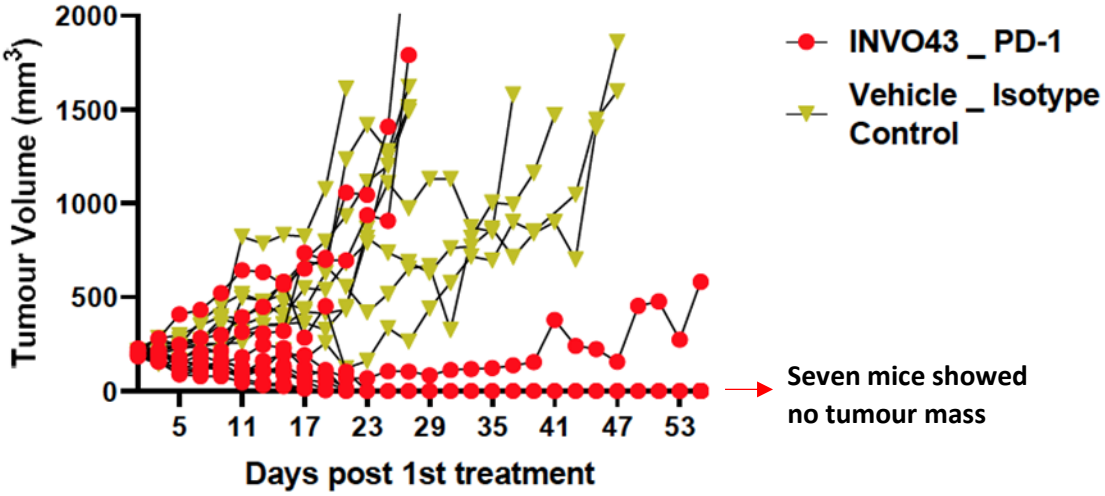
The application of INV043 alone achieved a significantly lower tumour volume than the INV043 group (as highlighted below).



Note: Each line denotes an individual animal. If the line does not reach 60 days, the animal reaches the ethical end point of a tumour >1,500mm³.

Combination INV043 and ICI vs Untreated Group

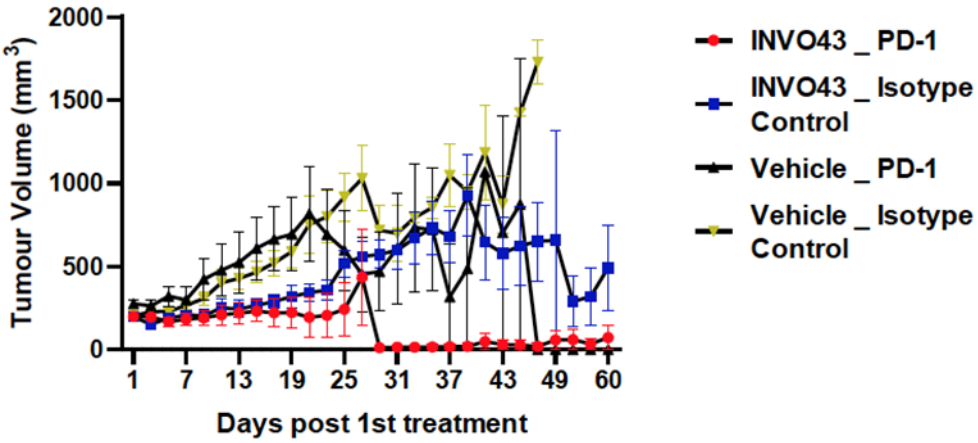
80% of the tumours treated with the combination of INV043 and ICIs showed tumour control. 70% showed no tumour volume at the end of the testing period of 60 days, and 10% had increased volume which was subsequently found from histology work to be pus contain no evidence of cancer.



Note: Each line denotes an individual animal. If the line does not reach 60 days, the animal reaches the ethical end point of a tumour >1 500mm³

Average Tumour Volumes in Different Groups

Average tumour volumes were substantially lower in combination treatment group. Standalone INV043 exhibited lower tumour volumes than standalone ICIs as all PD-1 treated mice reached an ethical endpoint of tumour size >1500mm^3.



This announcement was approved for release by Invion's Board of Directors.

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About Invion

Invion is a life-science company that is leading the global research and development of the Photosoft™ technology for the treatment of a range of cancers, atherosclerosis and infectious diseases. Invion holds the exclusive Australia and New Zealand license rights and exclusive distribution rights to Hong Kong and the rest of Asia Pacific, excluding China, Macau, Taiwan and Japan, to the Photosoft technology for all cancer indications. It also holds the exclusive rights to the technology in Asia and Oceania, excluding China, Hong Kong, Taiwan, Macau, the Middle East and Russia for atherosclerosis and infectious diseases, and subsequently acquired the rights to the United States, Canada and Hong Kong for infectious diseases. Research and clinical cancer trials are funded by the technology licensor, RMW Cho Group Limited. Invion is listed on the ASX (ASX: IVX).

About Photodynamic Therapy (PDT)

Invion is developing Photosoft™ technology as a novel next generation Photodynamic Therapy (PDT). PDT uses non-toxic photosensitisers and light to selectively kill cancer cells and promote an anti-cancer immune response. Less invasive than surgery and with minimal side

effects, PDT offers an alternative treatment option aimed at achieving complete tumour regression and long-lasting remission. PDT has also demonstrated broad-spectrum activity across multiple infectious diseases, including bacteria, fungi and viruses. Photosoft has the potential to address the global challenge of antibiotic-resistant "superbugs".