RESULTS FROM RMWC FUNDED PHASE II PROSTATE CANCER TRIAL USING INV043 – STRONG SAFETY PROFILE AND 40% POSITIVE RESPONSE RATE

Highlights:

- **RMW Cho Group Limited (RMWC) has provided Invion a report authored by Scendea detailing a recently completed investigator-led Phase II prostate cancer trial using the photosensitiser INV043**
- **The trial results showed that INV043 administered sublingually (under the tongue) has a solid safety profile and demonstrated promising efficacy signals three months post treatment:**
  - **A regime of 6 cycles of INV043 treatments was very well tolerated by patients**
  - **No serious adverse events were experienced and all side effects reported were mild**
  - **40% of patients showed a positive response as measured by the RECIST 1.1 standard (10% had complete response)**
  - **44% of patients had negative PSMA-PET results 3 months post treatment**
- **The positive safety and efficacy signals for INV043 opens the potential for treatment of prostate cancer without the serious side effects associated with conventional treatments**
- **The safety data from the trial indicates potential for INV043 to be administered systemically in future clinical trials including via sublingual and IV routes**
- **The global prostate cancer market is expected to grow to ~US$27.5 billion by 2032 (8.7% CAGR from 2023 to 2032)[4]**
- **INV043 is the same active pharmaceutical ingredient that Invion is using in its Ph I/II skin cancer trial (topical formulation)**

MELBOURNE (AUSTRALIA) 18 September 2024: Invion Limited (ASX: IVX) ("**Invion**" or the "**Company**") wishes to announce that RMW Cho Group Limited (**RMWC**), the licensor of the Photosoft™ technology, has successfully completed a Phase II prostate cancer trial[1] (ACTRN12621000633886) using a sublingual (under the tongue) formulation of INV043, the same active pharmaceutical ingredient (API) in the topical formulation that Invion is using for its Phase I/II non-melanoma skin cancer trial.

RMWC provided Invion with a clinical study summary report collated by Scendea Limited (**Scendea**) using information received and relied upon from RMWC based on the results of the investigator-led and open label trial that was fully funded by RMWC. Scendea is a leading pharmaceutical development and regulatory consulting group.

The Phase II prostate cancer trial used six treatment cycles of INV043 as a monotherapy. It was found to be safe and well tolerated by patients with no serious adverse events experienced and all side effects reported were mild.

In terms of efficacy signals, 40% of patients showed a positive response to the treatment with 10% demonstrating complete regression as measured by the Response Evaluation Criteria in

[1] The existence of this trial was disclosed in multiple Invion presentations released to the ASX from 2021 (https://announcements.asx.com.au/asxpdf/20211109/pdf/452rfs8zcjklyd.pdf)

Solid Tumours (**RECIST**) 1.1 framework – a standard way to measure the response of a tumour to treatment.

Further, 44% of patients had negative Prostate Specific Membrane Antigen – Positron Emission Tomography (**PSMA-PET**) results three months post treatment (all patients were positive before the treatment).

The report concluded that "the favourable safety profile and the preliminary efficacy results are promising and warrant further investigation of INV043". Further details of the study are included in the sections below.

In contrast, radiotherapy, chemotherapy and surgery (which are currently mainstream treatment options) carry risks of significant side effects, such as urinary incontinence, bowel dysfunction, erectile dysfunction and /or infertility[2]. Due to these risks, the standard of care is to monitor the cancer until it progresses to a point where the benefits of these treatments outweigh the risks.

However, this approach may cause anxiety among patients who will have to live with the cancer without knowing if it will one day become more severe or even life-threatening.

Commenting on the results, Invion's Executive Chair and Chief Executive Officer (CEO) Thian Chew said:

> *"It's very exciting to see these results for our lead cancer candidate, INV043. The results showed that INV043 can be safely administered and activated with light to treat prostate cancer. It also highlighted its potential to be safely administered systemically to patients, including via sublingual and even IV routes.*
>
> *"Together with the positive efficacy signals from this trial, this points to the prospect of INV043 to become an effective treatment for prostate cancer without the devastating side effects that can be associated with conventional treatments."*

Prostate cancer is the second most common cancer in men[3]. The global prostate cancer market is expected to grow to around US$27.5 billion by 2032, representing a compound annual growth rate (CAGR) of 8.7% over the forecast period from 2023 to 2032[4].

Invion's patented lead Photosensitiser, INV043, was developed to preferentially target and accumulate in tumour cells, and not healthy cells. The trial design focused on the safety and efficacy of sublingually administrated INV043 as a monotherapy and the use of a laser probe to apply red light to the prostate/prostatic fossa using transurethral and/or transrectal intraluminal techniques.

On the back of these results, Invion is exploring opportunities to progress this program into a larger trial that may explore avenues to further improve response rates including combination therapies with immunotherapies, such as immune checkpoint inhibitors (**ICIs**). *In vivo* studies undertaken separately by the Peter MaCallum Cancer Centre and Hudson Institute of Medical Research found INV043 to dramatically improve the effectiveness of ICIs on various cancers[5].

[2] https://www.pcf.org/about-prostate-cancer/prostate-cancer-side-effects/
[3] https://www.wcrf.org/cancer-trends/prostate-cancer-statistics/
[4] https://www.precedenceresearch.com/prostate-cancer-market
[5] https://announcements.asx.com.au/asxpdf/20240304/pdf/0614byrl2c4ww0.pdf and https://announcements.asx.com.au/asxpdf/20220530/pdf/459ffkjbvdpjrg.pdf

Background to Study

A total of 75 patients were originally planned for the trial, but only 41 male patients with prostate cancer were enrolled because the trial was terminated early due to challenges related to disruptions from the COVID-19 pandemic. Of those, 31 were treated with photodynamic therapy (**PDT**): three (3) patients from Group A (biopsy proven primary prostate cancer) and 28 from Group B (primary prostate cancer diagnosed by PSMA-PET or MRI).

The first 25 patients (first cohort) were enrolled in the study during the COVID-19 pandemic lock downs in Melbourne, Australia. Ten dropped out of the study prior to treatment due largely to geographical or compliance reasons. For the remaining 15, collection of data and compliance with protocol specified assessments were challenging and inconsistent during this period. Therefore, a decision was made to focus on widely used endpoints for assessment of efficacy and safety only.

There were 16 patients aged between 50-80 years who were treated after the COVID-19 pandemic (second cohort). They were selected for analysis because they had complete and evaluable data. As the dose in the first cohort did not show any significant adverse events, the dose was doubled to 0.9ml for the second cohort of patients.

Clinical Trial Design

The clinical trial participants underwent a total of six (6) cycles of PDT treatments over a nine (9) week period, administered in rounds of two (2) cycles on sequential days with a 4-week interval before the subsequent rounds. Each PDT cycle consisted of two steps:

- Step 1: Sublingual administration of photosensitiser INV043.
- Step 2: Approximately 15-20 hours after dosing, 25 min of 660 nm laser light was administered.

The study's primary endpoint objective was to assess PDT treatment effectiveness using Response Evaluation Criteria in Solid Tumours (RECIST 1.1). Secondary endpoint objectives aimed to assess PDT safety and tolerability as well as further assess PDT effectiveness using standard outcome measures.

Based on the original trial protocol, it was planned that statistical analyses were performed using SPSS (PASW version 26). Statistical significance was set at $p<0.05$. Continuous variables were to be analysed between groups by Student t-test and analysis of covariance (ANCOVA), and categorical variables were to be analysed by Chi-square test.

However, due to the challenges created by the pandemic and the small number of evaluable patients, no formal statistical analysis was performed.

Safety Data on INV043

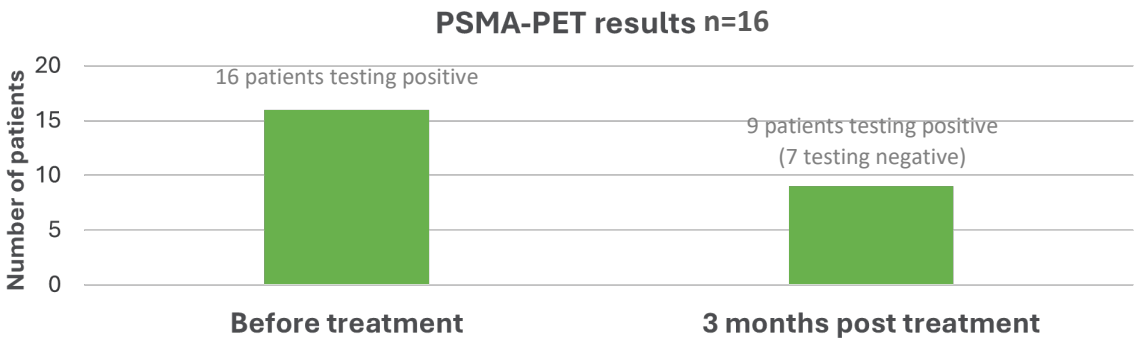
INV043 appeared to be safe and well-tolerated when administrated sublingually to patients over the six cycles of PDT treatments.

There were no serious adverse events (SAEs), life-threatening treatment emergent adverse events (TEAEs), or TEAEs leading to death reported in the study. All adverse events reported were mild and included fever, fatigue, headache and soreness.

There were also no clinically significant changes in vital signs, ECGs, or clinical laboratory parameters reported.

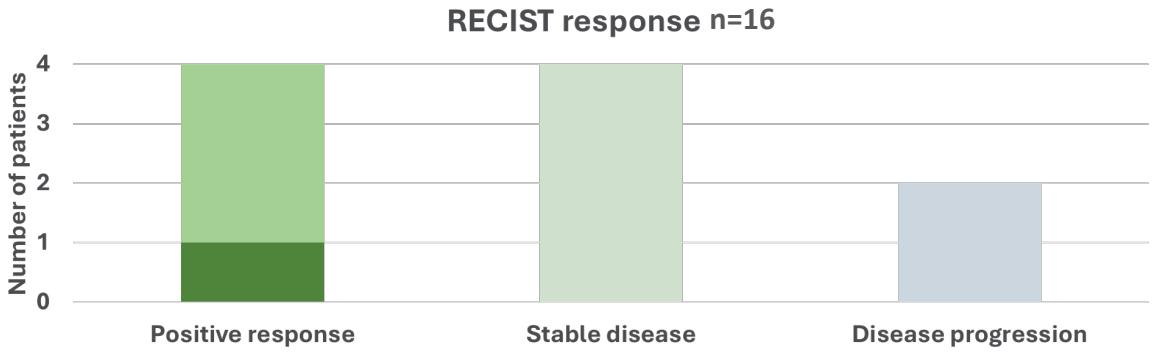
Efficacy Data: PSMA-PET

All patients in the second cohort were positive for prostate cancer prior to starting the treatment regime when scanned using a PSMA-PET scan, which is used to detect prostate cancer throughout the body. Three months post treatment, 44% (7 out of 16) showed a negative result in a follow-up PSMA-PET scan.



Efficacy Data: RECIST

Where possible, MRI scans were performed pre- and post-treatment to measure the size of lesions in the prostate. Out of the 16 evaluable patients in the second cohort, two (2) patients had undergone prostatectomy prior to the treatment and four (4) patients did not have MRI scans for various reasons (such as the presence of implants) and were excluded from the RECIST 1.1 analysis.



Of the remaining 10 evaluable patients, 40% showed a positive response and the breakdown of the results are:

- One (1) patient showed complete regression (no detectable lesion).
- Three (3) patients showed partial regression (>30% reduction in lesion size).
- Four (4) patients showed stable disease.
- Two (2) patients showed disease progression (>30% increase in lesion size).

The Phase II prostate cancer trial was funded by RMWC and sponsored by the National Institute of Integrative Medicine, Victoria.

This announcement was approved for release by the 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".