INV043 SHOWN TO COMPLETELY REGRESS TNBC TUMOURS AND TRIGGER PROTECTIVE IMMUNITY

Highlights:

- Latest PoC pilot studies show complete regression of triple negative breast cancer (TNBC) *in vivo* following INV043 treatment
- TNBC is a hard-to-treat cancer that is resistant to most chemotherapies. It represents one of many cancer types where a strong clinical need exists for alternatives to current standard of care
- Tumour mass was undetectable two weeks after initial treatment and no scarring was evident
- There was no recurrence of disease and re-challenge with TNBC implant could not re-establish new tumours, suggesting the development of protective immunity
- Additional PoC tests being carried out by Hudson Institute

MELBOURNE (AUSTRALIA) 28 October 2021: Invion Limited (ASX: IVX) ("Invion" or the "Company") is pleased to announce the results from the latest Proof-of-Concept (PoC) studies undertaken by its research partner, Hudson Institute of Medical Research.

This pilot study used INV043 to treat immunocompetent mice that had been implanted with triple negative breast cancer (TNBC).

TNBC is an aggressive and metastatic tumour type that is innately resistant to most chemotherapies. These tumours are difficult to treat and have high mortality rates.

Results showed a complete regression in the tumour and appeared to have triggered an immune response that subsequently prevented the recurrence of TNBC.

The latest studies follow on from the initial successful PoC tests announced on 25 May 2021 which used immune-deficient mice.

Testing Approach

TNBC cells were implanted, establishing solid tumours in the mammary fat pad that rapidly metastasised.

The treatment group (n=3) with established tumours had INV043 injected intratumorally, and subsequently were illuminated with red light. No anaesthesia was required and no adverse effects were observed. Treatment was repeated nine days later.

There were three control groups. One was made up of untreated mice, while the remaining two groups consisted of mice that were either administered with light or with INV043 alone.

Details of Results

PDT treatment using INV043 resulted in complete tumour regression with no recurrence of disease. Moreover, there was no apparent scarring or other indication of prior tumour presence, and no evidence of either primary tumour or metastatic spread at autopsy.

As a preliminary probe of immune-mediated effects, mice that achieved remission were re-challenged by a second implantation of TNBCs at a new site. No new tumours could be established, suggesting the successful development of protective immunity following INV043 treatment, a key requirement to maintain long-term remission.

In the control groups, tumours enlarged rapidly and had reached endpoint (tumour size >100mm^2) by day 19 with autopsies showing the cancer had spread to the lungs and the abdominal fat pad. Control animals that received only INV043 or light treatment showed similar progression.

"INV043 has performed exceptionally well and is showing good promise as a potential treatment for TNBC as well as a range of other hard to treat cancers" said Dr Andrew Stephens, the Research Group Head, Ovarian Cancer Biomarkers, at Hudson Institute.

"Not only did INV043 completely regress the primary tumour, but it also appears to have prevented the cancer from returning or spreading to other parts of the body. This sets it apart from other cancer treatments."

Further PoC studies by Hudson Institute are ongoing, including a larger TNBC study (primary tumour model), as well as secondary study investigating the potential of INV043 to treat metastatic disease. Each study will include arms exploring potential synergies with other cancer therapies.

The Chairman and Chief Executive Officer of Invion, Thian Chew, commented:

"These results demonstrate the potential of Photosoft™ technology and its clinical relevance. Hudson Institute will continue to undertake further PoC studies using our novel treatment. The early success we have achieved sets the foundation for Invion to progress INV043 towards clinical trials.

"We are pursuing multiple pathways to develop the technology to treat a range of cancers and other insidious diseases, and I look forward to updating shareholders of these efforts as they advance."

Further details on the PoC pilot study can be found in the attached presentation at the end of this announcement.

This announcement has been approved by the Board of Directors.

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About Invion

Invion is a life-science company that is undertaking the global research and development of Photosoft™ technology for the treatment of a range of cancers, atherosclerosis and infectious diseases. Invion holds the exclusive Australia and New Zealand license rights to the Photosoft™ technology for all cancer indications and Asia Pacific (excluding Greater China) for atherosclerosis and infectious diseases. Research and clinical cancer trials are funded by the technology licensor, RMW Cho Group Limited, via an R&D services agreement with the Company. Invion is listed on the ASX (ASX: IVX). This announcement was approved for release by Thian Chew, Chairman of the Board.

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.

FINDINGS:
PROOF OF CONCEPT II

October 2021

INVION

PROOF OF CONCEPT II: PRIMARY TUMOUR PILOT RESULTS
REGRESSION OF TUMOUR, PROTECTIVE IMMUNITY, CLINICAL POTENTIAL

BACKGROUND

- Previously announced Initial Proof of Concept testing, performed on immune-deficient *in vivo* models, demonstrated effectiveness of INV043 in regressing multiple tumour types.
- Our next Proof of Concept testing, in collaboration with Invion's research partner, the Hudson Institute of Medical Research, comprised a Pilot Study using INV043 to treat triple negative breast cancer ("TNBC") as an *in vivo* primary tumour model, where immune systems were intact.
- TNBC is an aggressive and metastatic tumour type that is innately resistant to most chemotherapy. These tumours are difficult to treat and have high mortality rates.

FINDINGS

Pilot Study demonstrated that photodynamic therapy ("PDT") using INV043:

- Completely regressed established TNBC tumours in mice with no recurrence of disease.
- Left no apparent scarring or other indication of prior tumour presence.
- Mice that achieved remission were re-challenged by secondary implantation of TNBCs at a new site. No new tumours could be established in these animals, suggesting the successful development of protective immunity.

Additionally, INV043 was:

- Non-toxic up to 100x the therapeutic dose.
- Formulated for oral, injectable and topical delivery with tumour localisation via these routes successfully demonstrated.

CONCLUSION AND NEXT STEPS

These data suggest that INV043 provides strong anti-cancer activity and can induce an anti-tumour immune response, providing protective immunity required for long-term remission.

Further Proof of Concept work will look at extended primary and metastatic disease models, as well as explore potential synergies with other therapies.

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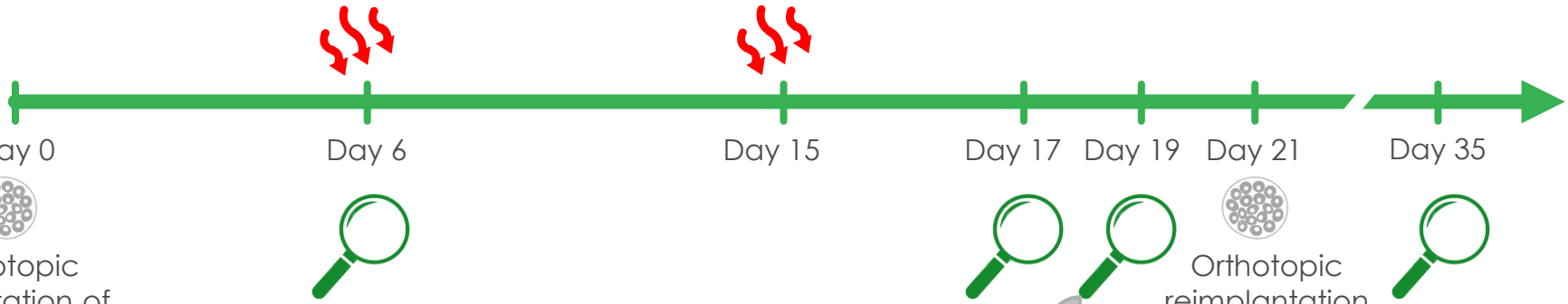
PROOF OF CONCEPT II: PRIMARY TUMOUR PILOT STUDY
FINDINGS: REGRESSION AND PROTECTION (I)

Treatment with established tumours (INV043 with light)

- INV043 was injected intratumorally (0.1mg/kg)
- 16 hours later, illuminated with red light
- No anaesthesia required, no adverse effects observed

Immune competent mice with TNBC (n=3/group)



TREATMENT GROUP	No adverse effects observed	Tumour regression observed	Tumour mass undetectable	No tumour detectable

CONTROL GROUPS:	(1) No treatment (2) INV043 alone (no light) (3) Light alone (no INV043)	• Enlarged rapidly and reached endpoint (tumour size >100mm^2) • Obvious metastatic involvement of lungs and abdominal fat pad at autopsy

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The research activities involving the use of animals were carried out in accordance with relevant guidelines and regulations as well as with appropriate Animal Ethics Committee approval.

PROOF OF CONCEPT II: PRIMARY TUMOUR PILOT STUDY
FINDINGS: REGRESSION AND PROTECTION (II)

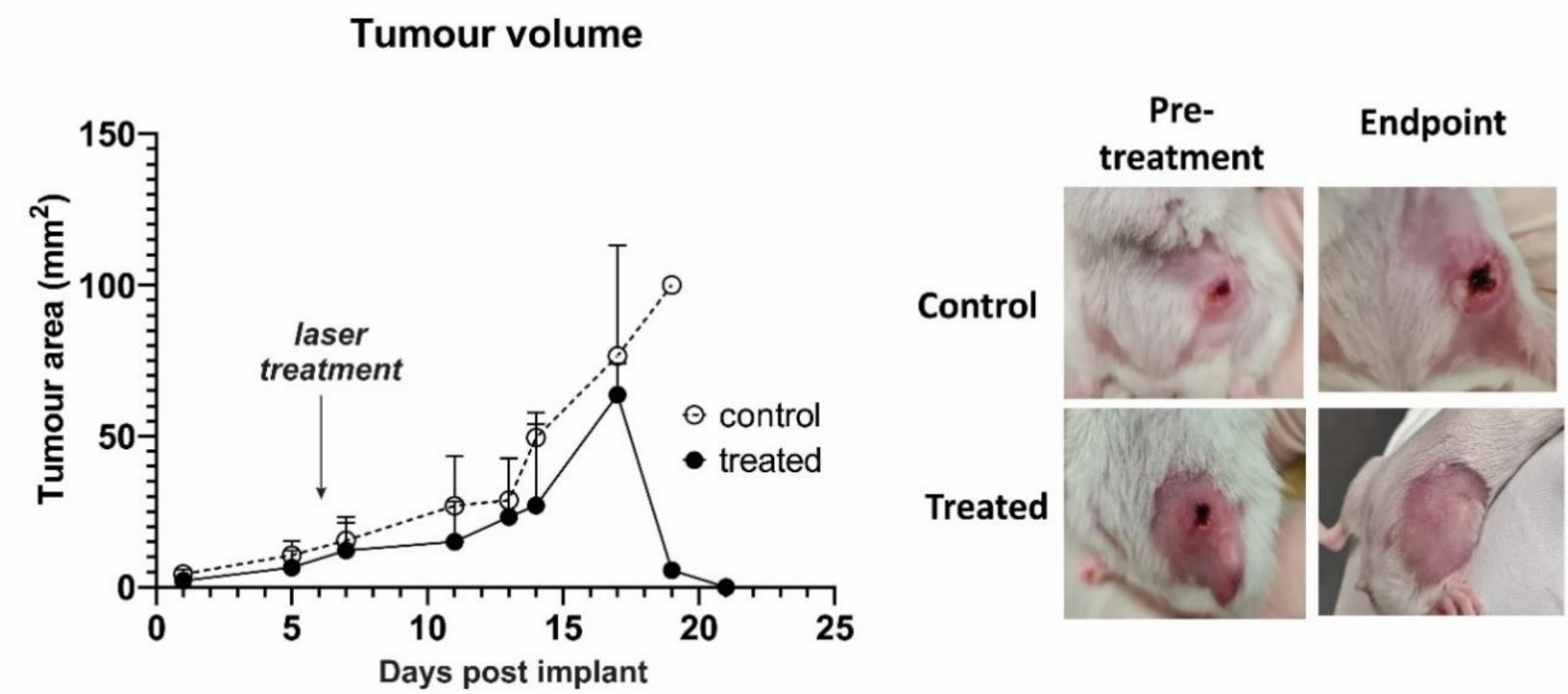

Figure 1. PDT using INV043 results in complete regression of established tumours. Mice with established 4T1 breast tumours were treated with INV043 PDT at days 6 and 13 post-implant. Tumour size was monitored until endpoint (tumour size $\geq$100mm^2). Treatment regressed established tumours to an undetectable level within 14 days of treatment (right). Moreover, no tumour regrowth was observed. *n=3/group; mean +/- SD*

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PROOF OF CONCEPT II: PRIMARY TUMOUR PILOT STUDY
FINDINGS: REGRESSION AND PROTECTION (III)

- **Complete regression of established tumours**
  - PDT treatment using INV043 treatment of triple negative breast cancers (TNBC) in immune-competent mice resulted in complete tumour regression with no recurrence of disease.
  - No apparent scarring or other indication of prior tumour presence; and no evidence of either primary tumour or metastatic spread at autopsy.
- **Favourable cosmetic outcome**
  - A common outcome of surgical interventions is scarring caused by removal of large areas of tissue. Whilst an undesirable side effect of surgery, it is largely unavoidable.
  - Following PDT with INV043 complete wound healing was achieved. No evidence of scarring following tumour resolution, no palpable mass and no visible evidence of tumours remaining at the treatment site (Figure 1, lower right).
  - PDT using INV043 eliminated cancerous cells and promoted complete wound healing, suggesting a desirable alternative to standard surgical interventions.
- **Protective immunity against cancer recurrence**
  - When previously treated mice were rechallenged with secondary tumour implant, no tumours could be grown. Indicates protective immunity against cancer recurrence, a key requirement to maintain long-term remission.
  - 4T1 TNBC metastasise rapidly in mice, generally involving the fat pad, lungs and bone. Mimics progression of human breast cancers, where removal of the primary cancer often not curative; and with TNBC, few therapeutic options available to resolve secondary tumours associated with metastatic disease.
  - Following resolution of tumours, mice were monitored. No tumour regrowth at primary implant site evident two weeks after tumour clearance. Also, no evidence found of metastatic disease at autopsy following treatment – suggesting induction of a systemic immune response with resulting clearance or prevention of metastasis.
  - Remaining mice received a second orthotopic implantation of 4T1 TNBC cells in the contralateral mammary fat pad. After 2 weeks, no tumour formation could be detected.

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PROOF OF CONCEPT II: PRIMARY TUMOUR PILOT STUDY

MULTIPLE ADMIN ROUTES, STRONG LOCALISATION, NON-TOXIC (I)

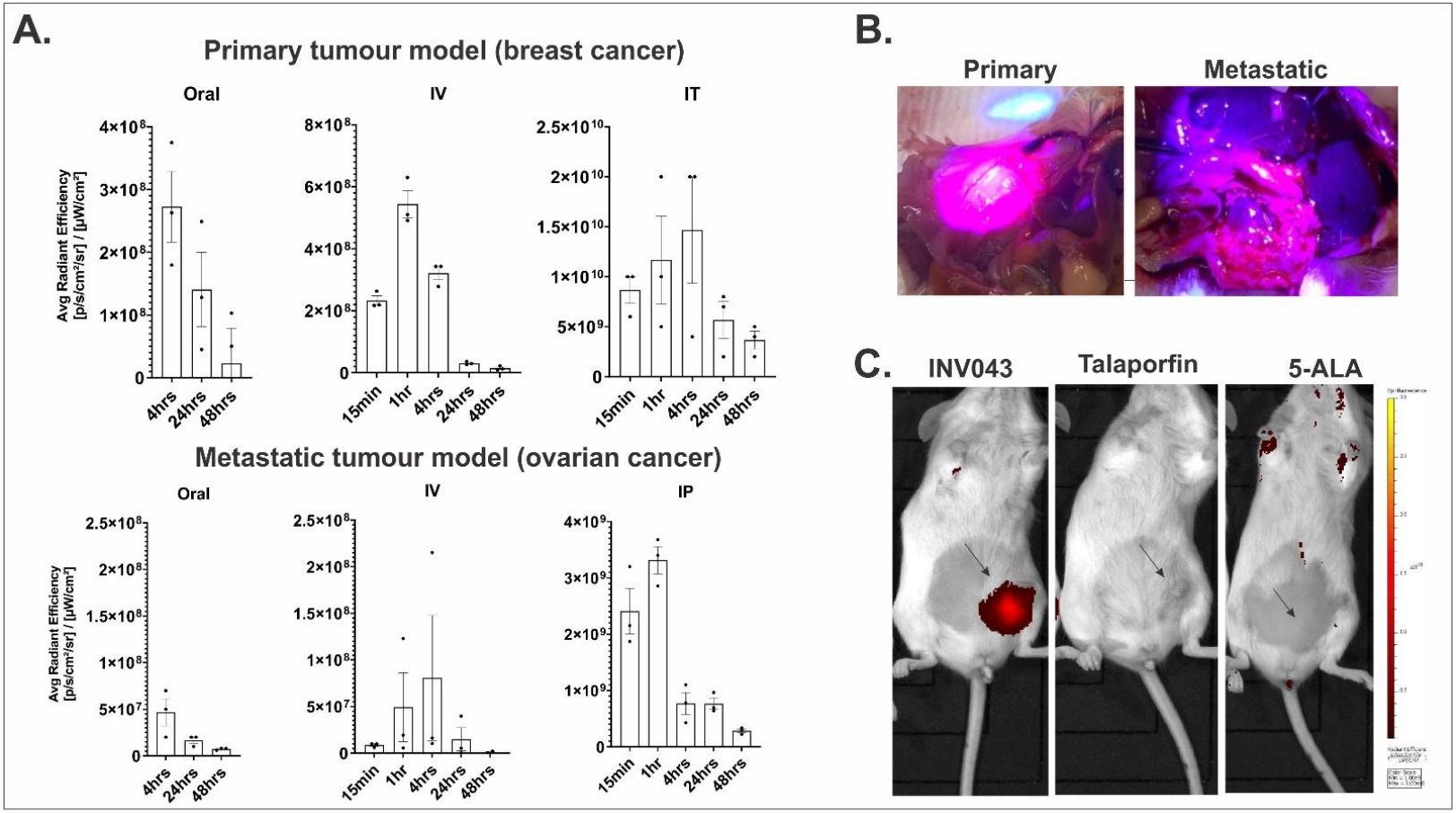

Figure 2. Localisation and retention of INV043 in tumours. (A). Quantitative analysis of tumour-associated INV043 fluorescence following administration by IV, ORAL and IT or IP as indicated. Tumours were either primary breast (upper panel) or disseminated peritoneal metastases (lower panel). n=3/group; mean +/- SD. (B). Visualization of INV043 fluorescence at autopsy. INV043 appears bright pink where localised in tissue; illumination is under blue light. In primary tumour (TNBC) INV043 was visualised as an intense red fluorescence. In metastatic disease (ovarian) INV043 was localised to individual metastatic nodules on multiple peritoneal surfaces, and in continuous omental mass.

(C) Localisation and retention of INV043 in primary breast tumours. Talaporfin Sodium and 5-ALA were imaged as comparators. Tumour site is indicated by arrow.

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PROOF OF CONCEPT II: PRIMARY TUMOUR PILOT STUDY
MULTIPLE ADMIN ROUTES, STRONG LOCALISATION, NON-TOXIC (II)

- **INV043 localises to tumour tissue via multiple administration routes**
  - INV043 formulated for oral, injectable and topical delivery. Tumour localisation via all of these routes successfully demonstrated *in vivo*.
  - Localisation of INV043 to tumour tissues assessed using intrinsic fluorescence of INV043 when stimulated under blue light. Mice injected at dose of 1mg/kg, and fluorescence in tumour tissue assessed 24 hours later. For comparison, two clinically used photosensitisers - Talaporfin sodium (the active ingredient of Laserphyrin™) and Aminolevulinic acid (5-ALA) – were similarly administered at the same dose, and their localisation assessed.
  - In all cases, INV043 localised strongly to tumour tissues with different kinetics dependent on the administration route (Figure 2A). Fluorescence easily visible to the naked eye, and localised preferentially to tumour tissue with rapid clearance from non-tumour areas (Figure 2B). Neither Talaporfin nor 5-ALA was accurately detected at the tumour site, suggesting either their fluorescence yield was not sufficient for imaging or their localisation was not comparable to INV043.
  - Thus, INV043 provided superior localisation and retention at the tumour site (Figure 2C), suggesting it is likely to have superior efficacy for cancer treatment.
- **Strong therapeutic profile: INV043 is non-toxic up to x100 therapeutic dose**
  - A maximum effective therapeutic dose of 0.1mg/kg had been determined, which is 100 times lower than the highest dose tested, demonstrating a strong therapeutic safety profile for clinical use.
  - Potential toxicity evaluated using escalating dose experiments in multiple mouse species (Balb/C, C57BL/6 and Swiss mice). Administration routes including intravenous (IV), intraperitoneal (IP), intratumoral (IT), subcutaneous (SC) and oral were evaluated, encompassing models of either solid or metastatic disease.
  - No adverse events recorded when INV043 administered at up to 10mg/kg IV or IP; or at up to 30mg/kg SC or orally. Of note, the determined therapeutic dose for INV043 was 0.1mg/kg IV; 100-fold lower than the maximum dose administered. A dose level demonstrating toxicity was not reached in these studies.
  - Thus, INV043 demonstrated an attractive safety profile for clinical use.

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