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Noxopharm Limited

ABN 50 608 966 123

Registered Office:
Suite 1 Level 6
50 Queen St
Melbourne VIC 3000
Australia

Operations Office:
Suite 3 Level 4
828 Pacific Highway
Gordon NSW 2072
Australia

IDRONOXIL DATA PROVIDES HOPE TO TREAT SECONDARY BRAIN CANCERS

- **Secondary brain cancer major cause of death in patients with breast cancer, lung cancer and melanoma**
- **Secondary brain cancer at least 3-times incidence of primary brain cancer**
- **Limited treatment options, poor survival prospects**
- **Idronoxil now shown to make brain cancer drug more effective by up to 1000-times.**

Sydney, 19 June 2017: Noxopharm announces that it has taken an important first step in its objective of using its front-line drug, NOX66, to treat secondary cancers of the brain, in what is considered by the Company to be a world-first opportunity.

Summary
Secondary cancer of the brain involves cancers that start outside of the brain (e.g. breast, lung, skin) and then spread to the brain, as distinct from the better known primary brain cancers that originate in and remain in the brain.

Secondary brain cancer is a prominent cause of death of cancer patients, with the incidence of secondary brain cancer estimated to be at least 3-times greater than that of primary brain cancer. This year in the US, 26,000 people are expected to be diagnosed with an aggressive primary brain cancer; the exact number of cases of secondary brain cancer is unknown, with US estimates ranging between 75,000 – 250,000. Any form of cancer can spread to the brain, with breast cancer, lung cancer and melanoma accounting for many cases; kidney cancer, colorectal cancer and leukaemias also can to spread to the brain.

Noxopharm currently is working with universities and research institutions in Australia and Hong Kong with the goal of bringing NOX66 into the clinic in

2018 to treat aggressive brain cancer. This objective is based on the confirmed ability of idronoxil to cross the mammalian blood-brain barrier when dosed as NOX66. Having the ability to achieve high levels of idronoxil within the brain presents the dual opportunity of converting current chemotherapy and radiotherapy practices into far more potent therapies.

The Company is engaged in pre-clinical studies to determine the optimal combination (chemotherapy or radiotherapy) for primary brain cancer in adults, primary brain cancer in children, and secondary brain cancer in adults.

The data reported here today relates specifically to the treatment of secondary brain cancer using chemotherapy.

The key development is the finding that the active component of NOX66, idronoxil, has been shown in the laboratory to enhance the cancer cell-killing effect of the chemotherapy drug, temozolomide (TMZ), against breast cancer and melanoma cells by up to 1000-times.

Potential Significance

The significance of this finding lies in the fact that TMZ is the best-known chemotherapy drug that can reach cancers within the brain by crossing the blood-brain barrier, a barrier that normally prevents drugs from accessing brain tissue. Most patients with secondary brain cancer have a poor prognosis because surgery and radiation are the only common options for treatment, with the position of the cancer often making them inaccessible to surgery.

Chemotherapy has shown to be relatively ineffective in secondary brain cancer, in large part because of the general high level of resistance of the cancers to TMZ. Consistent with that, in the study reported here, extraordinarily high levels of TMZ were required to kill the breast cancer and melanoma cells (IC_{50} > 1000 uM); these are levels that would be lethally toxic in the body. Idronoxil sensitised the cancer cells to TMZ to the extent that effective killing of the cancer cells was achieved at levels considered safe to use.

As a result, the Company believes that this finding provides an opportunity to convert a chemotherapy drug (TMZ) with little or no effect on secondary brain cancers, into a more potent drug capable of delivering a meaningful anti-cancer effect where no standard drug therapy currently exists.

Today's finding also offers the prospect of being able to use TMZ to treat secondary brain cancer at the same time as other more potent chemotherapy is being used to treat metastatic deposits of cancer located elsewhere in the body, with the prospect of NOX66 boosting the effectiveness of chemotherapy across the whole body.

Graham Kelly, Noxopharm CEO, said, "The blood-brain barrier is a key hurdle in delivering more effective treatments for patients with cancers involving the brain. We know that TMZ crosses that barrier, as does idronoxil, at least in animals when delivered in the form of NOX66. So here we have two drugs capable of reaching cancerous lesions within the brain and which we now know act in a highly synergistic way."

"I need to stress that this is in vitro data, so it needs to be seen in that context. But it is the critical first step that we needed to verify and for that reason should not be under-estimated. To the best of my knowledge, this is the first time that anyone has reported being able to turn the fairly modest anti-cancer action of TMZ, into a potent cancer-killing effect. If that effect can be reproduced in the clinic, even in part, it should translate into a meaningful boost to the drug's anti-cancer effect."

Kelly added, "I also want to stress that this outcome relates just to secondary brain cancer. While we would expect NOX66 to provide a similar boost to the effectiveness of TMZ in the treatment of primary brain cancers, the particularly aggressive nature of many primary brain cancers in adults and children means that we are focusing on the use of NOX66 to augment the effect of combined radiotherapy and chemotherapy in those situations."

About Secondary Brain Cancer

Any form of cancer is capable of spreading (metastasizing) to the brain, but the cancers most likely to spread there are lung, breast, colorectal, kidney and bladder cancer, melanoma, and leukaemia. The overall 5-year survival rate for patients with secondary brain cancer is 2.4%. The incidence of secondary brain cancer is unknown, but is variously estimated at between 3 and 10-times that of malignant primary brain cancers.

About Temozolomide (TMZ)

TMZ is a cytotoxic chemotherapy drug that works by alkylation of DNA. Other alkykating agents (eg. cisplatin, carboplatin, cyclophosphamide) are more potent anti-cancer agents and enjoy greater use than TMZ. The ability of TMZ to cross the blood-brain barrier (largely unique among chemotherapy drugs) means that its use is limited largely to the treatment of brain cancer; it is approved for the treatment of primary brain cancers - glioblastoma multiforme and astrocytoma. It is not approved for the treatment of secondary brain cancers, but nevertheless is sometimes used, but with limited effect. TMZ also is used in some cases for the treatment of some non-brain cancers.

About NOX66

NOX66 is an innovative dosage formulation of the experimental anti-cancer drug, idronoxil, developed specifically to preserve the anti-cancer activity of idronoxil in the body and to enhance its drug-like behaviour.

Idronoxil is a kinase inhibitor that works by inhibiting a range of enzymes including sphingosine kinase and PI3 kinase that regulate cell pro-survival mechanisms and which are over-expressed in cancer cells. Idronoxil also inhibits external NADH oxidase Type 2 (ENOX 2), an enzyme responsible for maintaining the transmembrane electron potential (TMEP) in the plasma membrane of cancer cells and whose expression is limited to cancer cells. Inhibition of these 3 key enzymes results in disruption of key downstream pro-survival mechanisms including resistance mechanisms, sensitizing the cancer cell to the cytotoxic effects of both chemotherapy drugs and radiotherapy.

About Noxopharm

Noxopharm is an Australian drug development company with offices in Sydney, Melbourne and Hong Kong. The Company has a primary focus on the development of drugs to address the problem of drug-resistance in cancer cells, the major hurdle facing improved survival prospects for cancer patients. NOX66 is the first pipeline product, with later generation drug candidates under development. The Company also has initiated a pipeline of non-oncology drugs.

INVESTOR AND MEDIA ENQUIRIES: Prue Kelly

E: info@noxopharm.com T: + 61 2 9144 2223

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