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PRE-CLINICAL DATA CONFIRMS RADIO-ENHANCING POTENTIAL OF NOX66 FOR PAEDIATRIC BRAIN CANCER

- **Diffuse Intrinsic Pontine Glioma (DIPG); highly aggressive and poorly responsive brain cancer of children**
- **Idronoxil (NOX66) significantly enhances ability of radiotherapy to kill DIPG cells.**

Sydney, 5 July 2018: Noxopharm (ASX: NOX) today releases pre-clinical data providing important proof-of-concept of the ability of idronoxil (the active drug in NOX66) to increase the killing effect of radiation on brain cancer cells.

The data has been generated via a collaboration with the Children's Cancer Institute (CCI) and is part of a broader program being conducted by Noxopharm into the use of idronoxil (as NOX66) as a radio-enhancer in the treatment of both primary and secondary brain cancers in adults and children. This particular collaboration with the CCI is looking at using NOX66 to enhance the ability of radiotherapy to treat diffuse intrinsic pontine glioma (DIPG), a highly aggressive and poorly responsive primary brain cancer of children.

Laboratory studies were conducted using primary cell cultures established by CCI from DIPG tumours. Idronoxil was able to kill these cancer cells on its own, but more importantly, sensitised the cells to radiation, leading to a significantly higher level of death of cancer cells using a constant dosage of radiation.

NOX66 brain cancer program
NOX is pursuing a broad program looking at the potential to use NOX66 to treat brain cancers in adults and children based on the following:

- The ability of idronoxil to readily cross the blood-brain barrier in animals
- The ability of idronoxil to kill highly chemotherapy-resistant glioblastoma multiforme (GBM) cancer cells
- The ability of idronoxil to kill GBM cells regardless of their MGMT gene expression
- The ability of idronoxil to sensitise cancer cells to radiation.

DIPG
DIPG is the most aggressive of all childhood cancers and is the leading cause of brain tumour-related death in children. There is no effective treatment for DIPG and all patients eventually die from this

disease. Radiotherapy is the only form of treatment currently that offers any transient benefit in DIPG. Approximately 90% of cases of DIPG respond to radiotherapy, but the responses generally are short-lived, lasting on average 6-9 months. DIPG arises in an area of the brain known as the pons, a part of the brainstem which controls many of the body's vital functions such as breathing and heart rate. The critical nature of these functions serves to limit the amount of radiation that can be applied. Following completion of radiotherapy, almost all DIPG cases recur locally within 12 months.

NOX and DIPG

Finding a way to render the DIPG cells more sensitise to radiation, without rendering the surrounding healthy brain tissue more radio-sensitive as well, has been identified as an urgent need. Noxopharm believes that NOX66 holds the potential to meet that need, and today's data goes towards supporting that belief. The pre-clinical program now enters the animal phase where DIPG tumours will be grown in the brains of mice (orthotopic xenografted tumours) and treated with a combination of NOX66 and radiotherapy. Success in that animal model opens the way for a clinical study in children.

Comment

Dr John Wilkinson, Noxopharm Chief Scientific Officer, said," Today's data fits in with other data showing idronoxil increasing the killing effect of radiation on lung and prostate cancer cells by 2- or 3-fold. The radio-enhancing effect of idronoxil therefore is looking to be independent of cancer type. On that score, it is worth noting that DIPG arises in the brain's glioma cells, or cells that provide the support structure of the brain. And these are the same cells involved in glioblastoma multiforme (GBM), the most common form of aggressive brain cancer in adults."

"That feeds into our broader objective of using NOX66 to sensitise primary brain cancer such as GBM in adults, as well as secondary brain cancers, in a way that allows the radiotherapy to be more effective, but without jeopardising the safety of healthy brain tissue."

"Treatment of children with DIPG currently relies mainly on radiotherapy, but the location of DIPG in the vitally important brainstem means that the amount of radiation that can be delivered needs to be limited and that accounts for the poor survival outcome with this cancer. Our aim with NOX66 is to provide a means of achieving greater killing of DIPG cells, equivalent to giving a higher dosage of radiotherapy but without inducing any more harm on healthy brain tissue. And obviously we hope to see that translate into longer survival," Wilkinson added.

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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, as well as inhibiting external NADH oxidase Type 2 (ENOX 2) which is 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 enzymes results in disruption of key downstream pro-survival mechanisms including resistance mechanisms, sensitizing the cancer cell to the cytotoxic effects of chemotherapy drugs and radiotherapies. Idronoxil also increases the activity of human NK cells.

About DIPG

DIPG accounts for 10% of all childhood brain tumours. Approximately 300 children are diagnosed with DIPG in the US each year. DIPG occurs in boys and girls equally, usually between the ages of 5 and 9, and does not generally occur in adults.

About Noxopharm

Noxopharm is a clinical-stage Australian drug development company with offices in Sydney and Hong Kong. The Company has a primary focus on the development of drugs to sensitise cancer cells to radiotherapy and chemotherapy.

About Children's Cancer Institute

Originally founded by two fathers of children with cancer in 1976, Children's Cancer Institute is the only independent medical research institute in Australia wholly dedicated to research into the causes, prevention and cure of childhood cancer. Forty years on, our vision remains unchanged – to save the lives of all children

with cancer and to eliminate their suffering. The Institute has grown to now employ more than 220 researchers, operational staff and students, and has established a national and international reputation for scientific excellence.

The CCI focus is on translational research, and has an integrated team of laboratory researchers and clinician scientists who work together in partnership to discover new treatments which can be progressed from the lab bench to the beds of children on wards in our hospitals as quickly as possible. These new treatments are specifically targeting childhood cancers, so safer and more effective drugs and drug combinations can be developed that will minimise side-effects and ultimately give children with cancer the best chance of a cure with the highest possible quality of life.

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