Date: 20 November 2017 **Sydney, Australia**

ASX: NOX

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PROMISING INTERIM CLINICAL DATA FOR NOX66

- **Patients with metastatic, late-stage cancers**
- **10 of 11 patients showing no disease progression following 3-months treatment with NOX66 in combination with low-dose carboplatin**
- **Well-tolerated drug combination.**

20 November 2017, Sydney: Noxopharm is pleased to release interim data from its first-in-human study of NOX66 being conducted in Georgia. The data was presented to the European Society of Medical Oncology Asia conference in Singapore on 18 November 2017.

The data shows promising outcomes both in terms of safety and disease control in patients receiving NOX66 in combination with a low dose of carboplatin. The Company notes that this is interim data, with the majority of patients yet to reach the end of the study, and in particular yet to include additional data from the higher dose of NOX66 considered by the Company to be the final clinical dose.

The headline data read-out is:

- 19 patients have been enrolled with late-stage (Stage 4) metastatic solid cancers (breast, ovarian, lung, prostate, head & neck)
- patients must have failed to respond to standard treatment options and be eligible for experimental drug therapy
- 11 of the 19 patients have been treated for 3 months with a combination of NOX66 and low-dose carboplatin
- only 1 of the 11 patients showed disease progression over this time; of the remaining 10 patients, 9 showed stable disease and 1 showed a partial response
- NOX66 alone and in combination with low-dose carboplatin was well tolerated and with no reported adverse events.

Study rationale
The majority of patients with metastatic disease involving solid cancers eventually run out of treatment options and experience unchecked

disease progression.

The hypothesis behind the current study is that a combination of NOX66 and carboplatin will block disease progression and provide a meaningful survival benefit in patients whose cancers have stopped responding to standard treatment options, including carboplatin.

Importantly, the Company is looking to see if this anti-cancer effect with NOX66 can be achieved in combination with a dose of carboplatin low enough to be well tolerated.

Carboplatin is one of the most commonly used chemotherapy drugs in the treatment of solid cancers. Its major adverse side-effect is suppression of bone marrow function, leading to low levels of white blood cells and greater susceptibility to infections. Avoiding this side-effect, which is common to many chemotherapies apart from carboplatin, has been identified as a major need in cancer care, particularly with the growing emergence of antibiotic-resistant superbugs.

Combination therapy
The study is testing NOX66 in combination with 2 dosages of carboplatin. Carboplatin typically is used within a dosage range designated AUC4 (lower end) and AUC6 (higher end). Dosages of AUC5 and AUC6 are more usual when carboplatin is used on its own. A dosage of AUC4, while generally well tolerated in terms of bone marrow function, typically is only marginally effective in most patients when used on its own, usually being reserved for when the drug is used in combination with other chemotherapy drugs.

The combination therapy typically is administered over 6 months in monthly cycles. Each cycle comprises a single intravenous injection of carboplatin each month; NOX66 is administered daily for 14 consecutive days, starting 1 day before each monthly carboplatin injection.

Study design summary
Patients must have late-stage, metastatic solid cancers of the following types: breast, ovarian, lung, prostate, head & neck. Patients must have progressed on standard treatments and have a minimum life-expectancy of 3 months.

Each patient undergoes 3 separate sequential treatment steps:

- Step 1 is a 3-week Run-In arm of NOX66 alone;
- Step 2 is NOX66 in combination with low-dose carboplatin for 3 months;
- Step 3 is NOX66 in combination with high-dose carboplatin for 3 months.

Nineteen patients have been divided into 2 cohorts depending on NOX66 dosage:
Cohort 1 (8 patients); receiving 400 mg NOX66 daily throughout the 3 steps.
Cohort 2 (11 patients); receiving 800 mg NOX66 daily throughout the 3 steps.

Tumour response is being assessed by radiological measurement (RECIST) at the conclusion of Steps 2 and 3 and compared to CT scans done immediately pre-Study.

Study status
The study is fully recruited (19 patients). Two patients dropped out voluntarily during Step 1; one patient was withdrawn due to disease progression after Step 2; one patient was withdrawn due to a severe adverse event in Step 3; one patient has completed all 3 steps and is off-study. All remaining 14 patients continue on-study, with the last patient due to have the 6-month scan in April 2018.

Results: *Safety data*
No adverse events were observed in Step 1 (NOX66 alone) at either dosage.
No adverse events have been observed in 13 patients who have completed Step 2 (NOX66 + low-dose carboplatin).
A serious adverse event (infusion reaction) occurred in one patient following the first intravenous injection of high-dose carboplatin in Step 3, leading to withdrawal of that patient from the study.

Results: Tumour response data
Of 11 patients with measurable disease (able to be measured by scans) who have been treated with NOX66 and low-dose carboplatin, only 1 of the 11 patients showed disease progressed after 3 months. The results are:

- 9 patients = stable disease (no disease progression)
- 1 patient = partial response
- 1 patient = progressive disease.

Of these 11 patients, 5 received 400 mg NOX66 daily (Cohort 1) and 6 received 800 mg NOX66 daily (Cohort 2). The one case of progressive disease (lung cancer) was in the 400 mg dose cohort, and the one case of partial response (prostate cancer) was in the 800 mg dose cohort. Five Cohort 2 patients are yet to complete Step 2.

Only 1 patient to date has completed Step 3 and continues to show stable disease.

Comment
Noxopharm CEO, Dr Graham Kelly, said, "The clinical team is highly encouraged by this data. NOX66 has proven to be well tolerated both on its own and in combination with low-dose carboplatin. Being able to deliver a meaningful clinical benefit to patients with late-stage cancer in a way that doesn't add to their burden by exposing them to debilitating or life-threatening side-effects, is a major aim of this Company."

"But it is the disease status of the patients that is worth noting. The patients coming into this study are all late-stage cancer patients with metastatic disease and with no remaining standard treatment options. So, to see only 1 of 11 patients show disease progression after 3 months of treatment on combined NOX66 and low-dose carboplatin is something that we regard as highly encouraging. We obviously cannot categorically rule out this effect being due to carboplatin alone, but that seems highly unlikely given both the treatment history of these patients and the considerable clinical experience of monthly carboplatin (AUC4) on its own delivering very marginal clinical benefit across most forms of cancer."

"It also is noteworthy that this effect has been achieved across a range of common cancers. And having achieved this without any serious toxicity essentially means that

we appear to be on our way of achieving one of two key aims that this study set out to achieve." Kelly added.

There are another 5 patients (Cohort 2) yet to complete their 3-months of low-dose carboplatin treatment, and all but 1 patient to complete their 3-months of treatment with high-dose carboplatin early next year.

Kelly added, "The anti-cancer drug scene in recent years has been dominated by the arrival of drugs that target the immune system and which have come to market to considerable acclaim. What is less well understood is that their benefits generally are limited to specific tumour types, with generally relatively modest response rates, and where the response where it does occur generally is of limited duration. All of this with side-effects that can be serious."

"If the interim outcome we are seeing in this study is confirmed once all data is in, and then confirmed in a larger, controlled study, then we are confident that NOX66 has the potential to become an important new anti-cancer drug in combination with carboplatin, offering hope for patients where little currently exists."

About the study
Study NOX66-001 is an open-label Phase 1a/Phase 1b study being conducted in Georgia in four FDA-audited clinical sites.

Assessment of tumour response
Tumour response is being assessed by standard RECIST parameters involving CT scans. RECIST (Response Evaluation Criteria in Solid Tumors) identifies up to 5 lesions in total whose longest diameter can be measured. These are termed *target* lesions; all other lesions are counted but not measured (*non-target lesions*).

- *Complete Response*: Disappearance of all target and non-target lesions.
- *Partial Response:* At least a 30% decrease in the sum of the longest diameters of target lesions; no new lesions.
- *Progressive Disease*: At least a 20% increase in the sum of the longest diameters of target lesions; or the appearance of 1 or more new lesions.
- *Stable Disease*: Neither sufficient shrinkage to quality for partial response, nor sufficient increase to qualify for progressive disease.

About carboplatin
Carboplatin is a cytotoxic chemotherapy approved for the treatment of breast, ovarian, lung, head & neck, and brain cancer, and neuroblastoma. The dosage normally is expressed as Area Under the Curve (AUC). Side-effects are common, with bone marrow suppression the major one, and nausea, peripheral neuropathy and allergic reactions generally less common.

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 radiotherapy.

About Noxopharm
Noxopharm is an Australian drug development company with offices in Sydney 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 that are held by subsidiary company, Nyrada, Inc.

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Forward Looking Statements
This announcement may contain forward-looking statements. You can identify these statements by the fact they use words such as “aim”, “anticipate”, “assume”, “believe”, “continue”, “could”, “estimate”, “expect”, “intend”, “may”, “plan”, “predict”, “project”, “plan”, “should”, “target”, “will” or “would” or the negative of such terms or other similar expressions. Forward-looking statements are based on estimates, projections and assumptions made by Noxopharm about circumstances and events that have not yet taken place. Although Noxopharm believes the forward-looking statements to be reasonable, they are not certain. Forward-looking statements involve known and unknown risks, uncertainties and other factors that are in some cases beyond the Company’s control that could cause the actual results, performance or achievements to differ materially from those expressed or implied by the forward-looking statement. No representation, warranty or assurance (express or implied) is given or made by Noxopharm that the forward-looking statements contained in this announcement are accurate and undue reliance should not be placed upon such statements.

SINGAPORE 2017 ESMO ASIA

NOXOPHARM

NOX66 PLUS CARBOPLATIN

- Phase 1 Signalling Study

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Abstract Number LBA2

DISCLOSURE SLIDE

The Authors are employees of the Sponsor Company, Noxopharm Limited

ABOUT NOX66

First-in-class inhibitor of tumour cell sphingosine kinase

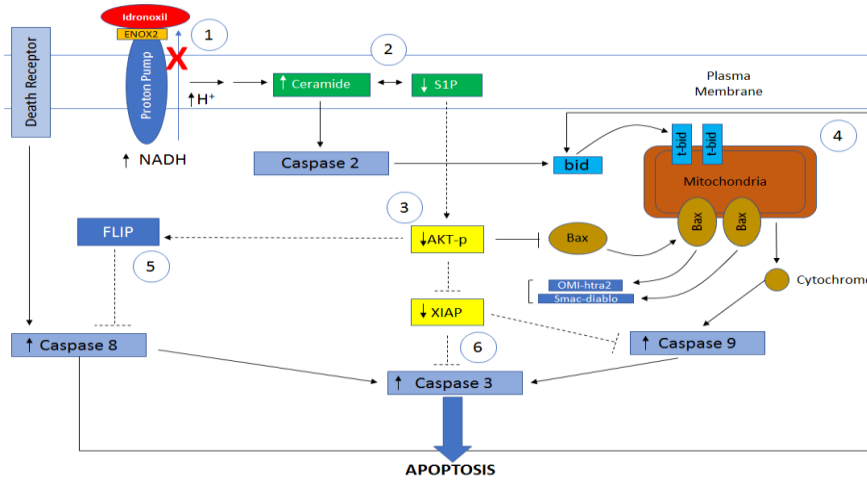
Idronoxil – inhibitor of external NADH oxidase–type 2 (ENOX2). *Oncogene*

- Inhibits sphingosine kinase
- Inhibits pro-survival signalling (S-1-P, Akt, PI3K)
- Inhibits DNA repair (PARP-1, topoisomerases 1 and 2)

Oral/IV dosage forms of idronoxil ineffective due to Phase 2 metabolism

NOX66 formulated as idronoxil in a hydrogenated fatty acid

- Blocks Phase 2 metabolism
- Creates 'pro-drug' form
- Improved drug-like features



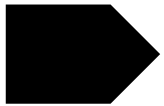
SINGAPORE 2017 ESMO ASIA

ABOUT NOX66

First-in-class inhibitor of tumour cell sphingosine kinase

Primary development as radio-sensitiser

- **External beam radiotherapy**
- **Brachytherapy (LuPSMA)**



- ❑ Increased response in irradiated lesions
- ❑ Abscopal response in non-irradiated lesions

Supplementary development as chemo-sensitiser

- ❑ Adjunct Rx with radiotherapy

RATIONALE

Idronoxil inhibits DNA repair following exposure to alkylating agents *(tumor cells only)*

Potent (10^3-10^4 x) sensitiser of carboplatin *in vitro*

? Increase response to carboplatin

? Allow carboplatin dose to be reduced

STUDY DESIGN

Phase: Phase 1, open label study

Patients: End-stage disease , metastatic solid tumours, no remaining standard treatments options

No. patients: 17 patients, 2 cohorts (400 mg and 800 mg NOX66).

1^0 objectives: Safety. PK.

2^0 objectives: Efficacy (RECIST) 3 and 6 months; ECOG Score; Biomarkers

Cohort 1: NOX66 400mg (Patients 1-8)	**RUN-IN** NOX66 MONOTHERAPY days 1-14	**+ CARBOPLATIN AUC=4** 3 x 28 Day cycles NOX66 days 1-7 Carboplatin Day 2	**+ CARBOPLATIN AUC=6** 3 x 28 Day cycles NOX66 days 1-7 Carboplatin Day 2
Cohort 2: NOX66 800mg (Patients 9-16)			
Replacement: NOX66 800mg (Patients 17-19)			

KEY INCLUSION / EXCLUSION CRITERIA

Tumour types = Breast, Lung, Head & Neck, Prostate, Ovarian

KEY Inclusion criteria	KEY Exclusion criteria
Histologically confirmed locally or metastatic advanced solid tumours	Tumour involvement Central Nervous System
At least 1 measurable lesion on CT or MRI scan	Patients who are breastfeeding or pregnant
ECOG performance scale of 0-1	Clinically significant uncontrolled cardiac disease or myocardial infarction within last 12 months; QTc of >470 msec on screening ECG
Adequate heamatologic, hepatic and renal function	Uncontrolled infection or systemic disease
Minimum life expectancy of 12 weeks	Any major surgery, radiotherapy, immunotherapy within the last 21 days (palliative radiation > 2 weeks permitted
Fertile patients agree to use of effective contraception during study and 90 days after last dose of NOX66	No concurrent chemotherapy or biologic therapy; chemotherapy with delayed toxicity within last 4 weeks
	History solid organ transplant
	Known unsuitability for treatment with carboplatin or suppository use

INTERIM RESULTS

Data available at 16th November 2017

Fully enrolled:

16 patients recruited originally:

- Cohort 1 – 8 patients NOX66 400 mg
- Cohort 2 – 8 patients NOX66 800 mg

- 2 voluntary withdrawals (1 each Cohort); 1 SAE withdrawal
- 3 replacement patients enrolled and added to Cohort 2
  - *Final* Cohort 1 – 7 patients
  - *Final* Cohort 2 – 10 patients

INTERIM RESULTS

Data available at 16th November 2017

RUN-IN (Phase 1a) Arm. NOX66 monotherapy. 14 consecutive days.

Cohort 1. 8/8 completed

Cohort 2. 7/8 completed. *1 patient voluntary withdrawal*

No AEs reported

INTERIM RESULTS

Data available at 16th November 2017

PHASE 1b. NOX66 + LOW-DOSE (AUC4) CARBOPLATIN

Cohort 1. All 7/8 completed (*1 voluntary withdrawal*); 2 non-evaluable disease

Cohort 2. 5/10 completed. (5 yet to complete)

Safety: No SAEs reported

RECIST:

Cohort 1. 4/5 stable disease; 1/5 PD; (+ *2 non-evaluable*)

Cohort 2. 4/5 stable disease; 1/5 partial response

INTERIM RESULTS

Data available at 16th November 2017

PHASE 1b. NOX66 + HIGH-DOSE (AUC6) CARBOPLATIN

Cohort 1. 1 completed

Cohort 2. 0 completed.

Safety: 1 SAE reported (infusion reaction)

RECIST:

Cohort 1. 1/1 stable disease after 6 months. *6 current*

Cohort 2. *4 current*

PRELIMINARY CONCLUSIONS

- NOX66 well tolerated
  - No Adverse Events considered related to NOX66 use
  - No SAEs with NOX66 + carboplatin (AUC=4) after 3 cycles

- After 3-months with NOX66 + carboplatin (AUC4):
  - 9/11 patients with SD
  - 1/11 patients with PR
  - 1/11 Patients with PD
- Preliminary data suggest NOX66 in combination with low-dose carboplatin may benefit patients who are resistant to or unable to tolerate standard dose carboplatin.