Date: 30 October 2019 **Sydney, Australia**

ASX Limited
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October Newsletter Released

- DARRT-1 Study data continues to indicate strong anti-cancer effect in late-stage prostate cancer
- Drug pipeline explained: glutamate-inhibition and cancer stem cells

Sydney, 30 October 2019: Noxopharm (ASX: NOX) releases its October Newsletter.

The leading article comments on the interim data from the DARRT-1 clinical study showing that a combination of Veyonda® and low-dose radiotherapy is stopping the growth of late-stage prostate cancer and providing durable pain relief in a high proportion of men.

The Newsletter also explains the Company's efforts in building a drug pipeline, including providing further details on the recently announced brain cancer treatment drug program and previously unannounced cancer stem cell drug program.

About Noxopharm
Noxopharm is a clinical-stage Australian drug development company with offices in Sydney and New York. The Company has a primary focus on the development of Veyonda® and is the major shareholder in Nyrada Inc, a spin-off company developing a pipeline of non-oncology drugs.

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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.

NOXOPHARM

FOCUS

THE NOXOPHARM NEWSLETTER

In this edition

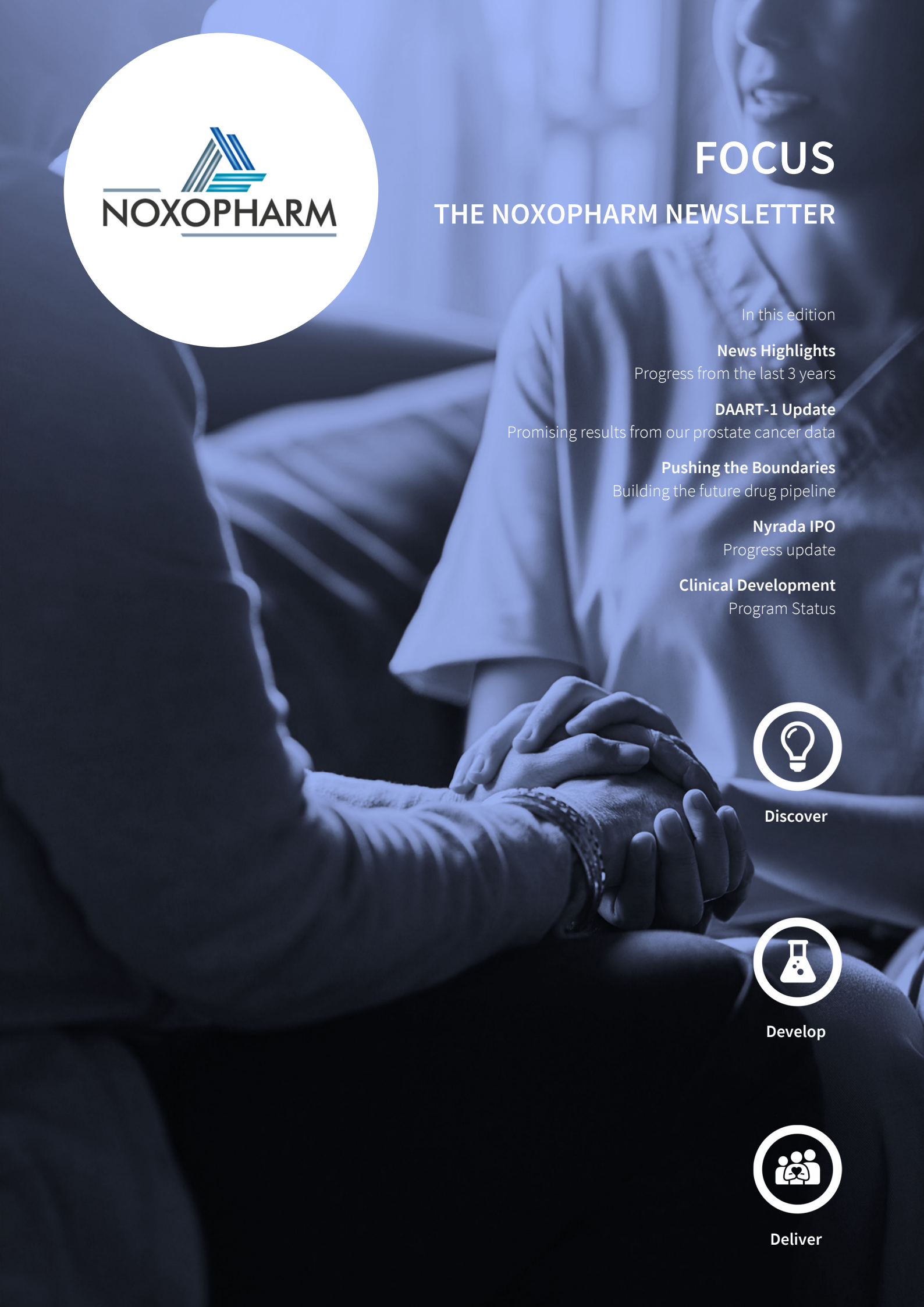
News Highlights
Progress from the last 3 years

DAART-1 Update
Promising results from our prostate cancer data

Pushing the Boundaries
Building the future drug pipeline

Nyrada IPO
Progress update

Clinical Development
Program Status



Discover

Develop

Deliver

News Highlights

PROGRESS

With the 3 year anniversary of the ASX listing, Noxopharm is primed for entry into the US market. In this short time, Noxopharm has made great strides in the following key areas:

Built robust collaborations - internationally and locally

Steadily increasing our footprint in the U.S. medical market through **conference presentations** and actively engaging with U.S.-based clinicians for study development, and in the investment sector through **investor roadshows**

Commenced engagement with the FDA by preparing an Investigational New Drug (IND) to enable us to conduct clinical studies in the U.S. clinical environment

Lodged 6 patent families around Veyonda®, the first of which has entered the national examination phase in 80 countries.

Designed a **robust Clinical Development Plan** based on encouraging preliminary results from our early trials that we believe will support the future of Veyonda® as a novel treatment in prostate cancer

Secured funding in excess of $A30M through successful capital raisings and positive grant outcomes

COLLABORATION

Collaboration is paramount to our success:

Advisory Boards: We have established a robust collaboration with world renowned experts in prostate cancer from both Australia and U.S. This provides both expert guidance on the clinical development of Veyonda® and the opportunity to further build on these key relationships along the way.

LuPIN program: Collaboration is evident in our ongoing relationship with St Vincent's Hospital in Sydney - with the principal investigator Associate Professor Louise Emmett – a key opinion leader in this field of theranostics. This investigator-led trial explores combining Veyonda® with ^{177}lutetium-PSMA-617 as a prostate cancer targeted therapy.

Universities: Pre-clinical collaborations with experts in state-of-the-art facilities are integral to our Drug Development Plan. We have partnered with University of NSW, Monash University, La Trobe University, Olivia Newton-John Cancer Research Institute, The Hudson Institute of Medical Research, the University of Hong Kong and the Chinese University of Hong Kong.

Final DARRT-1 data on its way

Just to refresh everyone's memory, DARRT is a combination of low-dose radiotherapy and Veyonda® intended to reset the body's immune system to attack and eliminate cancer cells, effectively immunising the body against cancer cells. We believe that the DARRT treatment protocol has the potential to become standard of care for many forms of late-stage prostate cancer. **DARRT-1 is testing this theory in prostate cancer.**

All men in the DARRT-1 study will have completed their 6-month follow-up in a matter of weeks (early-November). Following a review of their scans by a panel of independent radiation oncologists, we anticipate releasing the headline data in late-November 2019. That marks the end of the primary part of the study, although we will continue to follow the patients for 24-months to gather overall survival data. The full dataset then needs to undergo full validation and statistical review (a process typically taking 2-3 months), meaning that a final report on the primary data will be released early next year.

The story so far. The DARRT-1 study is in two parts:

- Part 1 is a dose-escalation arm (400/800/1200 mg Veyonda®) involving 14 men;
- Part 2 is a dose-expansion arm, using the highest (1200 mg) dose of Veyonda® in 11 men.

The men's clinical condition is reviewed at 3-months and 6-months. Of the 25 men initially enrolled, 22 were able to be evaluated by measures of PSA levels, pain scores and RECIST criteria. We are only reporting here on those 22 patients where their cancer was assessable by all 3 measures.

We have previously reported the 3-month and 6-month data for Part 1, and the 3-month data for Part 2. The coming final November data is the 6-month data for Part 2.

The following table combines all 22 patients regardless of Veyonda® dosage.

Figure: DARRT-1 Reported Patient Data Overview

	400, 800 and 1200 mg	
	3 months	6 months
No. of patients	22	11*
PSA Response	7 (32%)	2 (18%)
Pain Response	12 (55%)	6 (55%)
(mean pain response)	*(78%)*	*(73%)*
RECIST no. of patients	22	10
Stable disease	13 (60%)	7 (70%)
Partial response	3 (14%)	1 (10%)
Progressive disease	2 (9%)	2 (20%)

**Data for remaining 11 patients in Part 2 to be released late-Nov 2019*

Some explanations about these numbers.

1. The first point is the advanced nature of the disease in these men. The average starting PSA level across all 22 men was 623 ng/mL (range up to 5514; normal range varies depending on age but is usually regareded as 0-4 ng/ml). All men entered the study having progressed following all standard therapies.
2. A 'PSA Response' means that the PSA level has fallen by at least 50% compared to the start. This is regarded by doctors as a surrogate marker of a meaningful anti-cancer response. A number of men experienced PSA falls of less than 50%, but still showed a clinical response.
3. A 'Pain Response' means that pain levels have decreased by at least 30% compared to the start. In those men where there was a drop in pain levels, the fall was significant (78% and 73% at 3- and 6-months respectively). Pain relief is an important outcome in late-stage prostate cancer where secondary tumours tend to be in the skeleton, where their presence is liable to cause significant pain.
4. RECIST means radiographic assessment of disease status. RECIST measures the dimensions of tumours as well as counting tumours and categorises cases as Progressive Disease (PD), Stable Disease (SD), Partial Response (PR) or Complete Response (CR). SD means a change in the sum of all measured tumours of between +20% and -30% and no new tumours. PR means a change in the sum of all measured tumours of between -31% and -99% and no new tumours. This takes into account irradiated and non-irradiated tumours.

SOME OBSERVATIONS ABOUT THIS DATA

Across all 3 dosage groups, almost 3 out of 4 (73%) men showed stable disease or better at 3-months, and this was maintained at 6-months. Significant pain response was achieved in 55% of cases at 3-months and maintained at 6-months.

The Company sees this as a remarkable outcome given the advanced nature of these mens' disease status and the lack of any alternative treatment offering any meaningful way of halting the progression of the disease.

The simple outcome of halting disease progression (stable disease) for 6 months represents a potentially major achievement in this form of late-stage cancer characterised by extensive secondary disease in the skeleton, typically fairly rapid cancer growth, and considerable pain. The study formally finished at 6-months, with the effect of treatment on their long-term survival to be determined over 24-months.

These outcomes are exciting as they clearly are better than the experience of low-dose radiotherapy alone and go a long way to supporting the Company's belief that Veyonda® and the DARRT treatment can become a standard of care for late-stage prostate cancer.

It also is worth emphasising that these outcomes have been obtained without any notable side-effects beyond several cases of Grade 1 (lowest measurable level) dry mouth, oral mucositis, stomatitis and fatigue believed associated with the radiotherapy /Veyonda® combination.

DARRT-2

Given the encouraging data emerging from DARRT-1, planning is already underway under the watchful eye of our CMO, Dr Gisela Mautner, for what we hope will be the final step in our plans to bring the DARRT treatment to market.

We are looking to use a study design procedure known as 'adaptive design' that incorporates Phases 2 and 3 into the one study and greatly expedites the development process. Our ability to pursue this path is based on two key factors:

(i) the well-tolerated nature of DARRT, and

(ii) the apparent meaningful anti-cancer benefit being achieved.

DARRT-2 will be a multi-national study across Australasia, North America, UK and Europe.

A wide range of input has yet to come from our medical advisory boards, our contracted research organisation, our investigators, and, of course, the regulators. We believe the final treatment protocol will involve a single course (5 days) of radiotherapy and repeat courses (10 days) of Veyonda®. We hope to be recruiting patients this time in 2020.

We will be using the same form of radiotherapy in DARRT-2 that we used in DARRT-1 – external beam radiotherapy (EBRT). An alternative way of delivering radiotherapy to tumours is a more sophisticated (3-D computerised) way known as stereotactic body radiotherapy (SBRT) that delivers radiation in a more focused way and spares surrounding healthy tissue. It is quite possible that SBRT would be a better form of radiotherapy for DARRT. However, we are continuing with EBRT because currently it is far more widely available and considerably cheaper than SBRT. Whether we could achieve higher response rates with SBRT vs EBRT is something for the future. For the moment, our objective is to bring Veyonda® and the DARRT treatment regimen to market, and if the current outcomes we are seeing in DARRT-1 are repeated in DARRT-2, then we believe we will achieve our objective.

Our January Newsletter will contain more details about the planning processes now under discussion.

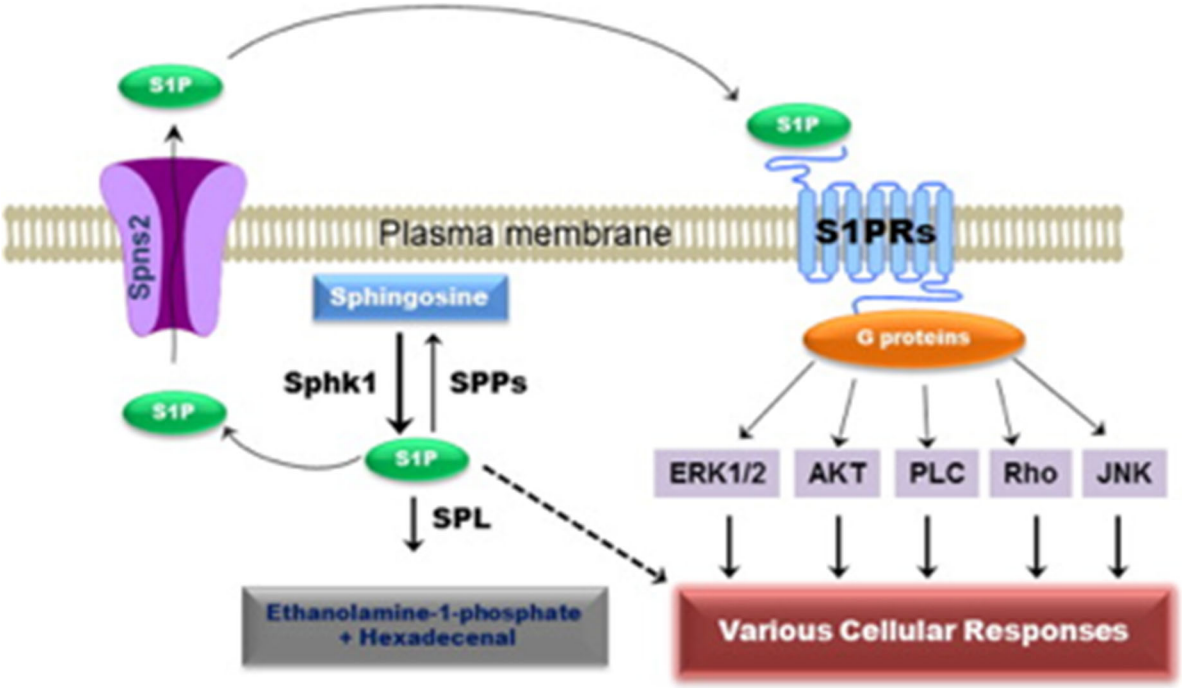
The key to the success of the DARRT treatment is a combination of two actions:

1. First, by exposing a small number (1 or 2) of individual tumours to low-dose radiation. Low-dose is critical because we only want to damage the tumour, not try and wipe everything out. Wiping 'everything out' means also getting rid of good cells such as those responsible for inflammation and immune responses, which are cells we want to preserve. The key to DARRT is setting up an inflammatory response that serves as a trigger to an immune response;
2. Second, irradiating the tumour in the presence of Veyonda® is meant to boost that modest, local immune response and turn it into a much stronger response, serving as a form of vaccination that we hope will extend body-wide. Transforming a local immune response into a strong, all-of-body immune response is known as an *abscopal response*.

HOW VEYONDA® WORKS

Veyonda® works by shutting down a signalling process in the cancer cell known as sphingosine-1-phosphate (S-1-P). S-1-P is an important regulator in all cells with multiple pro-survival roles, one of which is to make sure that any inflammatory-immune response to injury in any tissue doesn't get out of hand and turn into chronic inflammation such as autoimmune disease. Many cancers exploit this normal immune-dampening system by making very high levels of S-1-P, effectively blocking the ability of the body to mount inflammatory and immune responses to fight the cancer. By removing this block, Veyonda® is helping to restore the body's inherent ability to fight the tumour.

Figure: Schematic of the sphingosine-1-phosphate (S-1-P) pathway

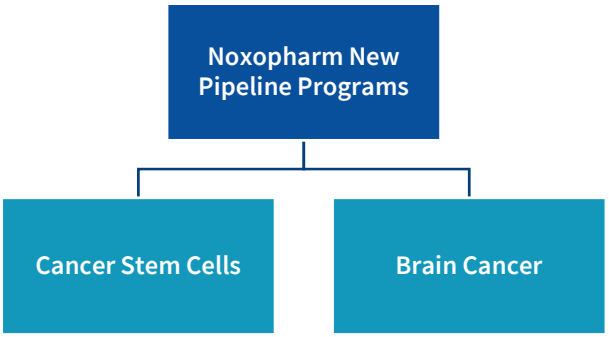


Pushing the Boundaries

As commercially valuable as we see Veyonda® based on its sales in due course, and as hopeful we might be of Veyonda® becoming a major new anti-cancer drug, and as much as we need to preserve the Company's resources to see this happen, the Company nevertheless needs to look to a future beyond Veyonda®.

If Noxopharm is to be more than one drug and more than a purpose-built buy-out play, then it needs a pipeline. And not just any pipeline, but one that continues the Veyonda® tradition of transformative medicines intended to disrupt common therapeutic practice. Noxopharm aims to be around for a while yet, with a vision of becoming a major drug discovery and drug development company noted for breaking-down frontiers. Not to the extent of distracting us from the main game, but quietly and steadily.

We have two such pipeline programs underway:



We hope to bring you more details of progress in both programs over coming months, but following is a glimpse of the frontiers that NOX is reaching out to.

NEW PIPELINE PROGRAMS

CANCER STEM CELLS

Veyonda® isn't going to work in every patient. That would be unrealistic. Where it doesn't always produce a favourable outcome, we believe the problem more than likely lies with a sub-population of cancer cells known as cancer stem cells. These are the Rambos of the cancer world – the toughest of the tough. Cancer stem cells are more resistant to chemotherapy and radiotherapy, plus can hide from immune cells while all other cancer cells around them are being killed by immune cells.

Cancer stem cells have the ability to change and adapt to anything that we can throw at them at the moment, mutating to fight another day. And the tumours they end up producing are clones of their toughness, which is why a patient's cancer gets increasingly less responsive to therapy with increasing lines of therapy.

Each line of therapy used selects out a small sub-population of resistant cells that then become the dominant population.

To maximise the benefit of Veyonda®, in the event of a non-response or a partial response to Veyonda®, we envisage being able to give the patient a drug that is able to kill or even slow down these recalcitrant cancer stem cells before they have a chance to multiply.

We have identified a family of molecules capable of doing this and have initiated a research program with the aim of bringing a candidate compound into the clinic in early-2021.

BRAIN CANCER

The main form of brain cancer in adults is glioblastoma multiforme (GBM) and it remains a major therapeutic challenge. Despite a lot of research, standard therapy remains surgical resection, followed by radiotherapy and the drug, temozolomide.

Immuno-oncology drugs have shown little benefit in GBM, with most research focusing on new chemotherapy drugs or re-purposing older chemotherapy drugs. The newer drugs have been designed to inhibit cell proteins such as P53, PI3K, Akt, MAPK or STAT3, which because these targets are non-selective, means that such drugs are viewed at best as offering temporary slowing of the cancer.

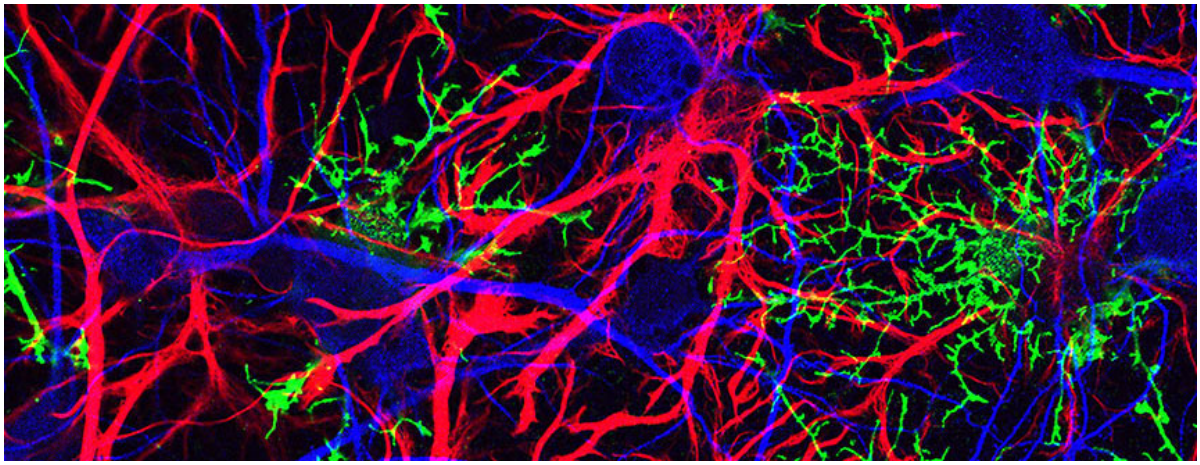
A new hope has emerged recently in this battle. It comes from the discovery that GBM tumours are similar to hormone-sensitive cancers such as breast cancer and prostate cancer. In the same way that the female sex hormone, estrogen, drives the growth of breast cancer cells, and the male sex hormone, testosterone, drives the growth of prostate cancer cells, so a chemical known as glutamate is driving the growth of GBM cells.

Glutamate is one of the most common chemicals in the brain. It is the main neurotransmitter responsible for how the brain's neurons communicate with each other.

The brain is made up of two main forms of cells – neurons and glial cells, with glial cells being more numerous. The old view was that neurons conducted the electrical impulses and was where all learning and memory resided, with the glial cells playing a more passive role, essentially providing a supporting structure. We now know that glial cells are a lot more active than that, and that brain function in all its glory is the result of a close working relation between neurons and glial cells.

In the following picture from a rat brain, the neurons are blue and the glial cells red (astrocytes) and green (oligodendrocytes).

Figure: The complex cellular architecture of the brain showing the neurons, glial cells, astrocytes and oligodendrocytes



Reprinted from Science News

Neurons communicate with other neurons through neurotransmitters such as glutamate. In a healthy brain, neurons also communicate with glial cells through glutamate. We now know that this line of communication between neurons and glial cells continues once glial cells become cancerous, with neurons sending them electrical signals resulting in the release of glutamate, with that glutamate acting as a driver of the growth of GBM. Glutamate has emerged as key to the growth of GBM[1].

But this problem extends one step further, in that the glutamate being received by the tumour leaks out into the surrounding healthy brain tissue, inducing a problem known as excitotoxicity that is responsible for seizures and death of healthy brain tissue, seriously exacerbating the cancer symptoms for the patient[2].

Unsurprisingly, blocking the action of glutamate is now seen as a potential whole new and productive approach to the treatment of GBM, not just slowing tumour growth, but potentially reducing the loss of brain function associated with GBM.

But there lies the challenge, how to block glutamate function in cancer without shutting down all brain function.

Noxopharm believes it may have the answer. It stems from the work Noxopharm initially did back in 2016 with a team of neuroscientists at UNSW. That collaboration led to the discovery of a compound (NYX-104) intended to be used in patients suffering a stroke or traumatic brain injury. It works by blocking the toxic effects of injured and dying neurons dumping their stores of glutamate. Importantly, NYX-104 was able to do this in an animal model of stroke in a highly selective way within the area of brain damage, without having any obvious inhibitory effect on the functions of the rest of the brain. That discovery led Noxopharm to form Nyrada Inc.

Noxopharm now intends to bring that expertise to the task of designing a glutamate-inhibitor that it hopes will improve the outcome for patients with GBM.

Sources
1. *Venkataramani V et al (2019) Nature 573, 532-538.*
2. *Ye ZC, Sontheimer H. (1999) Cancer Res 59, 4383-4391.*

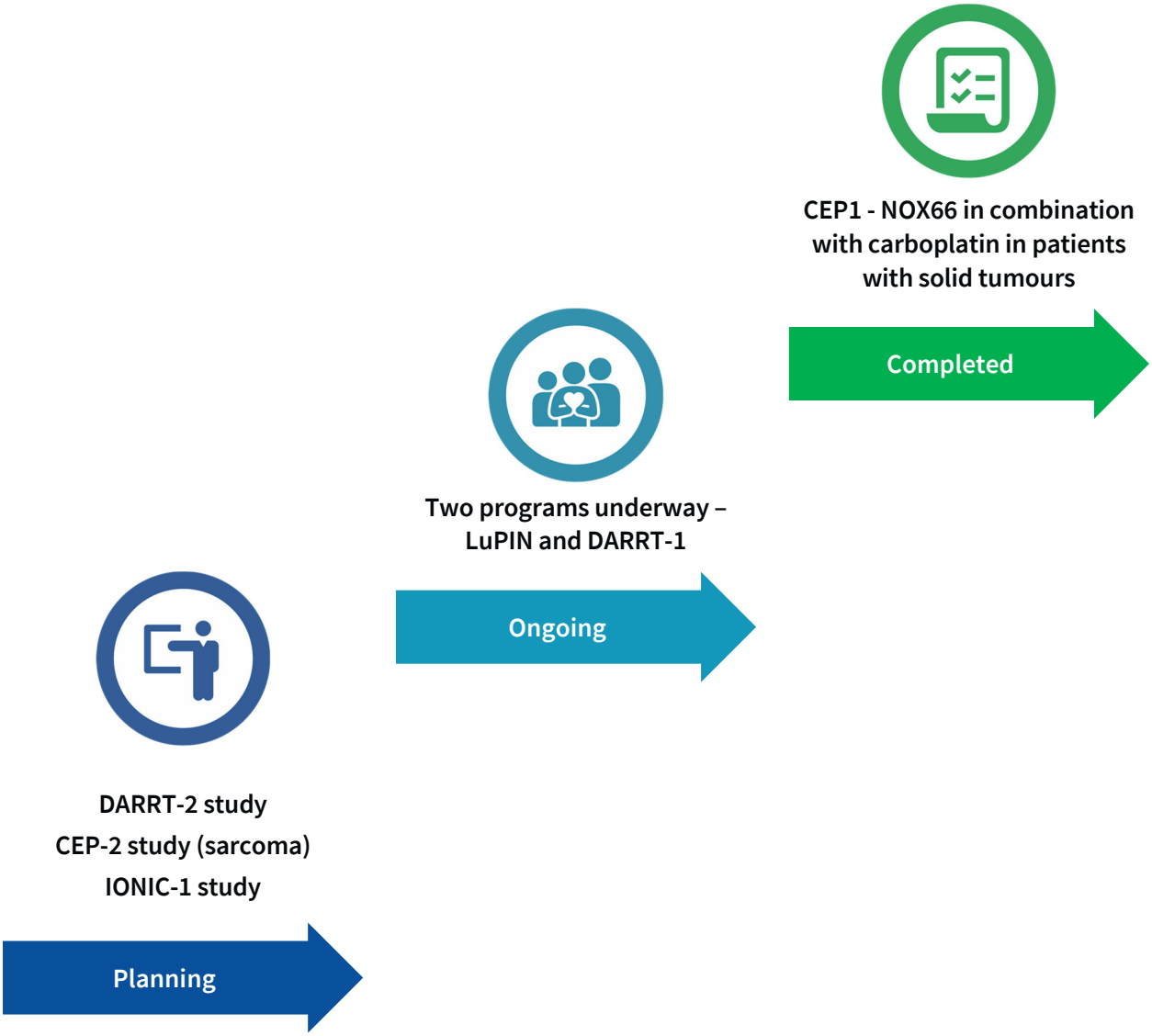
Nyrada Update

Nyrada Inc (Nyrada), the Company's partially owned subsidiary focusing on non-oncology drugs, grew out of a collaboration with Professor Gary Housley's team at UNSW Sydney and their work looking for a way to help patients suffering brain damage from a stroke or head trauma such as serious concussion. From those humble beginnings, Nyrada has secured three main drug development assets which show good promise to progress to clinical-stage testing in well-defined areas of unmet market need.

As announced on 15th August 2019, Nyrada engaged Alto Capital as Lead Manager and corporate advisor as it is investigating an Initial Public Offering on the ASX. Alto Capital (AFSL: 279099) specialises in raising capital for companies via Initial Public Offerings, Rights Issues, and Placements. The Company will update shareholders on any further progress as and when available.

Clinical Development Program

Making progress through strategic execution of the clinical development plan:



We will have more information to share with you on our website that we will add to as we progress. Please visit the website to find more about our story, our science, and our plans for the future.

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