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Sydney, Australia

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Noxopharm Limited

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Board of Directors Mr Peter Marks Chairman Non-Executive Director

Dr Graham Kelly Chief Executive Officer Managing Director

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- NYRADA INC OPENS CAPITAL RAISE: MEMORANDUM RELEASED
 - Noxopharm US subsidiary to raise AU\$6M
 - To fund R&D pipeline of 3 pre-clinical drug assets.

Sydney, 1 December 2017: Noxopharm is pleased to announce that its US subsidiary, Nyrada Inc ('Nyrada'), has released an Information Memorandum relating to the raising of AUD\$6M by placement of common stock to sophisticated non-US investors.

1,500,000 New Shares are being offered at a price of AU\$4.00 per share ('Offer'). Each 3 New Shares have 2 attached New Options with an expiry date of 30 November 2020 and an exercise price of AU\$6.00.

The funds being raised will be used to create a corporate infrastructure, including the appointment of a core scientific team, and to progress the development of the Company's 3 pre-clinical drugs assets – NYX-104, NYX-205 and NYX-330.

On 6 November 2017, Noxopharm shareholders approved the transfer of 2 nononcology assets (NYX-104 and NYX-205) to Nyrada, and the acquisition by Nyrada of a third drug asset (NYX-330) from a third party.

The Offer opens 1 December 2017 and closes on 15 December 2017.

A copy of the Memorandum can be obtained by contacting <u>prue.kelly@nyrada.com</u>.

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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 sensitise cancer cells to radiotherapy. NOX66 is the first pipeline product, with later generation drug candidates under development.

About Nyrada Inc.

Nyrada Inc is a Delaware-registered US biotechnology company, established as a subsidiary of Noxopharm to focus on non-oncology drug development. Nyrada has 3 drug assets: NYX-104 (excitotoxicity inhibitor), NYX-205 (anti-inflammatory) and NYX-330 (PCSK9 inhibitor).

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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.

NYRADA, Inc Information Memorandum

This is an Information Memorandum to raise A\$6,000,000 for NYRADA, Inc by issuing 1,500,000 shares of Common Stock at A\$4.00 per share



Important Notices

This Information Memorandum ('Memorandum') relates to the issue of common securities in Nyrada, Inc ('Nyrada' or the 'Company'), a corporation registered in the State of Delaware.

We are offering for sale shares of common stock of the Company and attaching options outside of the United States of America (USA) in an offshore transaction in accordance with regulations promulgated under the Securities Act of 1933, as amended (the 'Securities Act'), solely to non-U.S. persons who qualify as 'accredited investors', as that term is defined in Regulation D under the Securities Act.

These securities are subject to restrictions on transferability and resale in the USA or to U.S. persons (as defined in Regulation S) and may not be transferred or resold in the USA except or to U.S persons except as permitted under the Securities Act and the applicable state securities laws, pursuant to registration or exemption therefrom, and may not be sold or otherwise transferred except in accordance with the requirements and conditions described in this Memorandum.

Investors should be aware that they will be required to bear the financial risks of this investment for an indefinite period of time. Hedging transactions involving these securities may not be conducted unless in compliance with the Securities Act.

An investment in the Company involves a high degree of risk (see Sections 9 and 10). An investment in the Company is suitable only for sophisticated investors and requires the financial ability and willingness to accept the high risks inherent in an investment in the Company.

Prospective investors may wish to retain their own professional advisors to review and evaluate the economic, tax and other consequences of investing in the offering and should not construe the contents of this Memorandum, or any other information furnished by the company, as legal or tax advice.

This Memorandum has been prepared by the Company and no representation or warranty is made by any other person as to the accuracy or completeness of the information contained herein. The exhibits attached to this Memorandum constitute an integral part hereof.

The securities offered hereby have not been registered under the Securities Act. The offering contemplated by this Memorandum will be made in reliance upon an exemption from the registration requirements of the Securities Act for offers and sales of securities which do not involve any public offering. There will be no public market for the interests, and there is no obligation on the part of any person to register the interests under the Securities Act or any state securities laws.

This Memorandum shall not constitute an offer to sell or the solicitation of an offer to buy, nor shall there be any sale of interests in the Company, in any jurisdiction in which such offer,

solicitation or sale is not authorized or to any person to whom it is unlawful to make such offer, solicitation or sale. No person has been authorized to make any representations concerning the Company which are inconsistent with those contained in this Memorandum. Prospective investors should not rely on any information not contained in this Memorandum.

Forward-Looking Statements

This Memorandum contains forecasts and other forwardlooking statements concerning the Company. These statements are based on a number of assumptions, expectations and estimates developed by the Company that, while considered reasonable by the Company, are inherently subject to significant uncertainties and contingencies, many of which are beyond the Company's control or reflect future business decisions which are subject to change.

Recipients of this information are advised that the forecasts included in this Memorandum are forward-looking statements and therefore are inherently speculative. Due to the subjective judgments and inherent uncertainties of statements about future events, there can be no assurance that the Company's actual future results, or subsequent forecasts, will not vary significantly from the forecasts and other forward-looking statements set out in this Memorandum. The inclusion of the forward-looking statements set out in this Memorandum should not be regarded as a representation or warranty with respect to their accuracy or the accuracy of the underlying assumptions or that the Company will achieve or is likely to achieve any particular results.

No Guarantee of Listing or Other Liquidity Event

The Company intends to seek a listing on an appropriate securities exchange at a time considered appropriate by the Board and its advisors. However, there is no definite listing timetable and neither is there any certainty that the Company will be accepted for listing in any jurisdiction.

Nor can the Board provide any guarantee of trade sale, merger or takeover that would otherwise crystallise a liquidity event for shareholders. No application for quotation of the New Shares offered under this Memorandum on any securities exchange will be made in the interim.

Liquidity of the securities of the Company offered under this Memorandum for the period it remains unlisted, therefore cannot be guaranteed.

Director Consent

Each director has given and before issue of this Memorandum has not withdrawn his consent to be named as management of the Company.

Table of Contents

Im	Important Notices			
Tal	Table of Contents			
1.		Chief Executive's Letter		
2.				
	2.1	The Offer		
	2.2			
	2.3			
	2.4			
3.		Company Operations Overview		
5.	3.1	Vision		
	3.2			
	3.3	5		
	3.4			
	3.5			
	3.6			
4.		NYX-104: Inhibitor of Excitotoxicity	9	
	4.1	-		
	4.2			
	4.3	-		
	4.4			
	4.5			
5.		NYX-205: Anti-inflammatory drug		
5.	5.1	Inflammation Overview		
	5.2			
	5.3			
	5.4			
	5.5			
6.		NYX-330: Anti-LDL cholesterol drug		
	6.1	Hypercholesterolemia		
	6.2			
	6.3			
	6.4			
	6.5			
7.		Use of Funds	17	
8.		Share Capital		
	8.1			
	8.2	Share capital Stockholders' agreement		
-				
9.		Securities laws		
	9.1	US Securities laws		
	9.2			
10	•	General risks	20	
11		Specific risks and challenges	21	
12		Directory	22	
13		Glossary	23	
14				
	14.			
	14.			
	14.	3 Payment	24	
	14.	4 Minimum-maximum subscription	24	
	14.	5 Individual subscription	24	
	14.	6 Enquiries	24	
	14.	7 Allotment	24	

1. Chief Executive's Letter

Dear Investor

On behalf of the management of Nyrada, Inc ('Nyrada' or the 'Company'), it is my pleasure to present this opportunity to you.

The Issue of shares in Nyrada under this Information Memorandum provides investors with the opportunity to own shares in a new US-registered biotechnology company. The Company's strategy is to develop its starting drug assets over the next 12 months to a point that would support a listing on an appropriate exchange as soon as practicable.

The Company's core activity is drug development, focusing on small molecules with potential therapeutic benefit in areas of significant medical need.

The Company is commencing with three identified drug assets, each addressing major community diseases of significant unmet medical need.

NYX-104:

a drug that blocks a self-destructive process in the human nervous system known as excitotoxicity. To be administered following a stroke or traumatic head or spinal injury that Nyrada believes, for the first time, offering the ability to limit the extent of the primary damage, with the aim of reducing both rehabilitation times and the extent of permanent loss of function.

NYX-205:

- an anti-inflammatory drug intended to treat the painful condition of peripheral neuropathy, a common condition in diabetics and cancer patients undergoing chemotherapy.
- the same anti-inflammatory action the basis of a drug to treat the debilitating conditions of ulcerative colitis and sclerosing cholangitis, those conditions one of the major reasons for liver transplantation.

NYX-330:

 a drug intended to replace the out-of-patent statin drugs in the treatment of high blood cholesterol levels.

The Company believes that each drug asset has sufficient proof of principle for it to be confident that each asset is a potential first-in-class drug prospect with considerable therapeutic and commercial opportunity.

Investors need to understand that each asset is early-stage. We estimate between about 1 and 2 years before we anticipate them being considered as ready to enter human clinical study. That means we have a considerable way to go before we will see any commercial return on investment. And while any investment carries risk, drug development carries a particularly high level of risk associated with substantial hurdles to overcome in bringing a new drug to market. Despite that there is a high degree of confidence by management in the Company's future prospects, I strongly urge you to seek professional advice in evaluating that risk.

Should you decide to invest, then we look forward to welcoming you as a shareholder in Nyrada and in what we believe will be an exciting and rewarding journey.

Yours faithfully, Graham Kelly, PhD Chairman and CEO 23 November 2017

2. Summary of the Offer

2.1 The Offer

Nyrada is offering for subscription up to 1,500,000 common stock ('New Shares') and up to 1,000,000 options ('New Options') in the Company at an issue price of A\$4.00 per New Share to raise up to A\$6,000,000 ('Offer').

Each 3 New Shares have 2 attached New Options. The New Options have an expiry date of 30 November 2020 and an exercise price of A\$6.00.

Outline of the Offer		
Amount to be raised	New shares to be issued	Share price
A\$6,000,000	1,500,000	A\$4.00
Options under the offer	Expiry date	Exercise price
1,000,000	30 November 2020	A\$6.00

The Offer is not underwritten. The New Shares are common stock and are ranked pari passu with the Company's current issued shares.

2.2 Capital structure post-raise

Nyrada has valued each of its 3 drug assets equally at A\$10M, giving an overall pre-money valuation of A\$30M. A A\$6M investment represents a 16.7% stake in the Company immediately post-raise. If the New Options are exercised in full and subject to the Company not issuing any further equity prior to the exercise of the New Options, that stake becomes 25%, ranking with Noxopharm (50% of the equity) and Altnia (25% of the equity). Neither the Company nor Altnia are likely to participate in any future capital raisings, making it inevitable that those equity positions will be diluted. However, it is the aim of both companies to retain meaningful positions.

Proposed Capital Structure					
	Noxopharm	Altnia	New Shares	New Options	Total Issued Capital
Fully Diluted Capital Structure	5,000,000 (50%)	2,500,000 (25%)	1,500,000 (15%)	1,000,000 (10%)	10,000,000 (100%)

2.3 Use of proceeds

The Offer will raise A\$6,000,000 before expenses if all applications are accepted. The funds are intended to provide working capital for at least 15 months by permitting the Company to:

- Rent office facilities;
- Hire staff (key executives, scientists, support staff) aligned with its program of progressing small molecule drugs in non-oncology fields; and
- Continue with the development of its 3 drug assets (two assets in the neurodegenerative field, and one asset in the cardiovascular field) up to the stage of conducting IND-enabling studies.

2.4 Closing date for acceptance

The key dates for the Offer are as follows:

Summary of Important Dates	
Information Memorandum and application forms issued	30 November 2017
Intended closing date for lodgement of applications	15 December 2017
Intended date for issue of New Shares and New Options	6 January 2018

3. Company Operations Overview

3.1 Vision

Nyrada is a drug development company. It is commencing business with 3 drug assets each:

- wholly owned by the Company
- believed by the Company to be first-in-class
- stemming from technological developments believed by the Company to represent important breakthroughs in drug development and which are expected to provide the Company with a highly competitive advantage, and
- addressing an area of significant unmet clinical need.

Within the general category of the pharmaceutical industry, Nyrada sees itself as a biotechnology company, as opposed to a biopharmaceutical or pharmaceutical company. This means that it sees its purpose as early-stage drug development, with the eventual aim of taking each drug sufficiently far into the clinic in order to confirm its utility and to maximise its value, as the basis for seeking a licensing partnership.

While flexibility in aims and strategies need to be a fundamental tenet of the biotechnology business to take advantage of unexpected opportunity, Nyrada believes that its core strength lies in proprietary know-how in several key areas of innovative drug development technology, one of which is the ability to deliver a chemical class of drugs based on a diphenolic molecular structure across the blood-brain barrier. The Company proposes to build on that know-how to develop a growing portfolio of novel therapeutics in areas of major community need.

Two of the starting drug assets are in the field of neurobiology and the third in the cardiovascular field. To the extent that it is possible at this early stage to project a long-term drug development strategy, a growing focus on drugs to treat neurodegenerative diseases and conditions appears most likely, given the substantial unmet need in this field. The Company has an established working relationship with an eminent Australian neurosciences research group, and the aim is to make this the foundation of a growing alliance between Australian, European and US neuroscience and neuro-clinical research groups.

3.2 Objectives

	Madium term objectives (by and 2021)
The Company will concentrate over the next 2	Medium-term objectives (by end 2021)
years on developing its current pipeline assets: NYX-104, NYX-205, NYX-330. The Company has a minimum target by the end of 2019 of having IND applications submitted to the US FDA on all 3 drugs, and of having an IND granted on at least 1 of those assets.	Have all 3 drug assets in or through Phase 1 first-in-human clinical trials.
	Have initiated a broad-based neurosciences drug discovery alliance with US, Australian and European researchers.
	To have formed a business relationship with a major pharmaceutical or biotechnology company on at least 1 drug asset.

3.3 Operations

Nyrada is a US corporation registered in the State of Delaware. The Company proposes to conduct its business in the US, more particularly in the State of New York:

- reflecting the origins of its name ... [an acronym of New York R & D Alliances]
- to take advantage of significant funding and taxation incentives currently being offered by the State of New York to attract biotechnology businesses
- in expectation of anticipated alliances with the significant resource of universities, hospitals and research institutions in the New York - Connecticut – Boston biotechnology corridor.

The Company intends to be headquartered in White Plains, NY, with early-2019 the projected timetable for the establishment of headquarters there.

In the short-term (Nov 2017 – Dec 2018), the business will be housed in the Sydney offices of Australian biopharma company, Noxopharm Ltd ('Noxopharm'). This arrangement will serve three purposes in this formative stage of the Company's life:

to mitigate costs by sharing offices and support staff,

to provide ready access to Noxopharm scientific and management resources, and

to allow Group CEO, Graham Kelly, regular contact and supervision of the Company's R&D endeavours.

By end-2018, it is anticipated that Nyrada will be sufficiently staffed, resourced and independent in its business activities to begin the process of relocation to the US.

For the foreseeable future, the Company proposes to conduct its business on a virtual model, with scientific staff project managing R&D programs with research institutions globally on a contractual or collaborative basis. This model minimises overheads and maximises flexibility in being able to adjust and adapt to changing directions, an inevitable feature of drug development.

3.4 Staffing & Management

A 3-stage approach to staffing and management is to be adopted:



For the next 12 months, it is proposed that Nyrada will operate with approximately 6-7 full-time employees.

These will be a Chief Scientific Officer supported by 3-5 post-doctoral scientists (1-2 scientists per drug asset) and a US-based executive (Senior VP, US Operations).

For at least the first year of operations, it is proposed that Noxopharm Group CEO (Dr Graham Kelly) will act as CEO of the Company. In 2019, as the Company starts to build its portfolio of assets. A CEO and other required key executives will be recruited progressively.

For the first 12 months, Nyrada will be housed within the Noxopharm Sydney offices, providing access to the office management, manufacturing, chemistry and clinical affairs resources within Noxopharm on a contractual basis.

3.5 Board

For the Company's formative stage (2018), it is proposed to have a small Board of 3 directors comprising made up of Dr Graham Kelly, Mr Josiah Austin and a new non-executive director post-raise.

By 2019, the Board will expand to include at least 1, possibly 2, additional non-executive directors (US citizens).

3.6 Listing

The Company is being formed with the intention of eventually becoming a listed company. Clearly there can be no guarantees of that aim ever being fulfilled for a variety of reasons that include the Company failing to meet listing requirements or the Company's Board and shareholders deciding that it is in the Company's interest to remain unlisted. Neither is it possible to give anything more than an indicative timetable for such a process.

Nevertheless, it remains a starting intention to develop the Company's pipeline assets to the point of proof-ofconcept justifying IND-enabling studies, which represents a key inflection point in any drug development process, providing a basis for an objective market valuation. The aim is to seek a listing at that point in conjunction with a public offering.

The most likely market is the NASDAQ Global Market.

4. NYX-104: Inhibitor of Excitotoxicity

4.1 Excitotoxicity Overview

Excitotoxicity is a major degenerative condition of humans. It is responsible for a significant number of deaths and disabilities and extended rehabilitation times for a wide range of conditions affecting the brain, spinal cord and peripheral nerves. It remains almost completely untreated.

Excitotoxicity is a self-generating, secondary disease process that accompanies any situation causing injury or death of nerve cells (neurons):

- Physical injury (trauma, stroke, concussion),
- Degenerative processes (Alzheimer's, Parkinson's, Huntingdon's),
- Demyelinating diseases (motor neurone disease, multiple sclerosis),
- Infections, and
- Severe epilepsy.

Accelerated dementia in footballers and boxers, and hearing loss in soldiers and musicians...these are all the result of excitotoxicity.



Excitotoxicity is consequent to the primary injury...it is triggered by injured neurons, irrespective of what caused the original injury.

Excitotoxicity is as the name suggests - toxicity resulting from over-excitement of nerve cells.

The diagram below shows a normal **synapse**...the junction between two nerve cells (axons) across which an electrical signal needs to pass. Each brain cell can be connected with upwards of 1,000 other brain cells, producing, by some estimates, over 1,000 trillion synapses in the human brain.



When the electrical signal reaches the end of the first nerve cell, it triggers the release of a small number of chemicals known as neurotransmitters into the synaptic space. These include chemicals such as glutamate. The role of glutamate is to interact with glutamate-receptors on the receiving nerve cell. Activation of these receptors results in the flow of calcium (Ca++) ions into the nerve cell. This calcium then triggers a series of events that fires an electric signal in the receiving brain cell.

When a brain cell is injured, a natural response is to dump its stores of neurotransmitters, flooding each synapse with glutamate and resulting in a glutamate overload for the dozens or hundreds of healthy brain cell connected to that one injured brain cell. That glutamate overload then causes excessive stimulation of the glutamate receptors, which in turn let in far more calcium ions than normal, and over-stimulating the receiving nerve cell to the point where it dies itself.

That is excitotoxicity ... the process by which a single injured brain cell can cause the death of dozens or hundreds of healthy brain cells to which it is connected.

This cascade of death of brain cells radiates out from the original site of injury over days and weeks following the original injury. By the time it stops, the final area of damage can be up to 10-times that of the original injury.

Stroke or concussion might result in an area of brain dying that of itself might cause minimal and short-lived symptoms of paralysis. But the resulting area of excitotoxicity can be large enough to cause considerable paralysis requiring extensive rehabilitation, or leaving permanent disability, or even leading to death of the patient.

4.2 The Breakthrough

Despite considerable effort on the part of pharmaceutical companies, no drug has been developed that effectively inhibits excitotoxicity in the clinic. It remains an area of substantial unmet clinical need.

A recent breakthrough in the field was made by a team of neurobiologists led by Professor Gary Housley, Director of the Translational Neuroscience Facility, School of Medical Sciences, University of NSW, Sydney.

This team has identified a key series of steps in the glutamate overload-calcium ion channel basis of excitotoxicity. Within these steps, a particular protein known as transient receptor protein channel 3 (TrpC3), appears to be pivotal to the process, actively mobilising stores of calcium ions in the receiving brain cells that end up killing the cells.

The Company worked with the UNSW team to find a drug that would inhibit TrpC3, or more particularly, to find a drug that would inhibit the kinase responsible for phosphorylating (and thereby activating) TrpC3. And for such drug to be able to cross the blood-brain barrier.

4.3 Current Status of NYX-104

Proof-of-concept

- •First-in-class family of compounds identified able:
- •to inhibit drug target (glutamate-induced TrpC3 activity) in vitro
- •to cross blood-brain barrier (in rats)
- •to block excitotoxicity damage in an animal (mouse) model of cerebral stroke.

Lead optimisation

- •Two drug candidates currently identified. Lead optimisation to be determined on basis of mouse studies of pharmacokinetics and toxicity.
- •Development of intravenous dosage forms of both candidates currently being undertaken.

4.4 Key milestones for 2018

1. Confirm lead candidate compound

2. Identify PK profile and performed absorption, tissue distribution, metabolism and excretion studies (rats)

3. Determine MTD and 7-day acute toxicity studies in mice

4. Work-up large animal model of stroke

5. Optimise small-scale (100 gm) manufacturing process

6. Hold meeting with regulators (in an identified jurisdiction) to identify scope of pre-clinical studies

4.5 SWOT Analysis: NYX-104

Strengths

- Novel, first in class drug
- Targets novel protein that may be patented
- Using proprietary drug delivery technology to cross blood-brain barrier
- No toxicity anticpated
- No known competitors

Weaknesses

• Efficacy dependent on drug delivery

Opportunities

- · Large markets in stroke, TBI, concussion
- Unmet midical needs

Threats

None known

5. NYX-205: Anti-inflammatory drug

5.1 Inflammation Overview

Inflammation is a natural response by the body to tissue damage and infection. It is an essential step in repairing damage. The inflammatory process is a complex interplay of many moving parts, with that complexity tightly regulated by the body so that it responds, repairs and then retreats. Occasionally something intervenes to upset that tight control and the inflammatory process becomes dysfunctional, essentially turning into a disease process itself on top of the original insult. The development of anti-inflammatory drugs has been driven by the need to counteract abnormal over-expressions of inflammation.

The inflammatory cascade and its treatment can be summarised in the following diagram.



There are 3 main families of chemicals produced by the body that undertake the complex inflammation processes: leukotrienes, prostaglandins and thromboxane. Leukotrienes and prostaglandins are made mainly by white blood cells and immune cells; thromboxane is made mainly by blood-borne platelets.

The most commonly prescribed anti-inflammatory drugs are known as non-steroidal anti-inflammatory drugs (NSAIDs) that block the production of both prostaglandins and thromboxanes. They work by blocking enzymes known as cyclooxygenases (so-called COX inhibitors) that convert arachidonic acid to prostaglandins and thromboxane. Aspirin, indomethacin (Indocid), ibuprofen, paracetamol and diclofenac are commonly used COX inhibitors.

In knocking out both prostaglandins and thromboxane, COX inhibitors are seen as relatively blunt instruments. Prostaglandins and thromboxane have both independent functions as well as functions that balance each other...all part of the intricate interplay at work in inflammation. Targeting both, without allowing for the individual contributions of each to different types of inflammation, has long been recognised as a crude therapeutic approach to the treatment of inflammatory diseases across different tissue types where different types of underlying disease states are at play.

For example, thromboxane, rather than prostaglandins, are thought to play key roles abnormal inflammatory processes in the brain (Alzheimer's), liver (non-alcoholic steatohepatitis), large bowel (inflammatory bowel disease) and arteries (atherosclerosis).

This has led in recent years to the refinement step of developing drugs that block the production of thromboxane without affecting the production of leukotrienes and prostaglandins. One way of achieving this is to inhibit the enzyme downstream of the COX enzymes that is responsible for making thromboxane, the so-called thromboxane synthase enzyme.

5.2 Development of NYX-205

To date, only 1 selective thromboxane synthase has been developed, but remains registered only in Italy and untested in inflammatory conditions except peripheral arterial disease.

One other thromboxane synthase is known to have been discovered. The drug NV-52, was developed by Australian biotech company, Novogen Ltd, in the early-2000s as a thromboxane synthase inhibitor with inflammatory bowel disease (IBD) as its therapeutic target. In vitro, NV-52 reduced thromboxane B(2) levels by 40% and was effective in suppressing colonic inflammation in a rat model of IBD. NV-52 underwent a Phase 1a study in Australia in healthy volunteers in 2006, where it proved to be well tolerated.^{1,2}

NV-52 was part of a portfolio of drug assets sold by Novogen to US biotech company, MEI Pharma Inc, in 2010. The relevant has been allowed to lapse.

Nyrada is re-purposing this molecule because it believes that it represents a significant opportunity and is confident that it can bring additional proprietary IP that

- (a) will extend the use of the drug to indications beyond IBD, and
- (b) will provide a strong proprietary IP position.

The key to the additional enabling IP is the LIPROSE drug delivery technology which converts the original molecule into a modified pro-drug form, designed to provide significant additional drug-like features including

- protection from Phase 1 and 2 metabolisms
- extended half-life
- ability to cross the blood-brain and blood-nerve barriers.

The latter feature is a critical outcome in being able to consider using the drug to treat inflammatory conditions of the brain, spinal cord and peripheral nerves.

This modified form of the drug is known as NYX-205. A highly advantageous feature of NYX-205 is that the its core drug component has undergone human testing.

1. Howes LG et al. Nv-052: a novel thromboxane synthase inhibitor for the treatment of inflammatory bowel disease. Expert Opin Investigat Drugs 16, 1255 (2007).

2. Howes LG et al. Phase 1b single- and multiple-dose pharmacokinetic study of oral NV-52 in healthy volunteers. Drugs R D 9, 159 (2008).

5.3 Current Status of NYX-205

Nyrada proposes to bring NYX-205 into the clinic in the first instance in cancer patients to treat peripheral neuropathy associated with chemotherapy. This intractable and painful condition has no current therapies, and for patients with a limited lifespan, represents a major unmet need.

Nyrada believes that it will be possible to accelerate the entry of NYX-205 into the clinic to test its therapeutic benefit in this condition.

5.4 Key milestones for 2018

1. Complete small animal studies of carboplatin-induced peripheral neuropathy and demonstrated protective effect of NYX-205

2. Identify PK profile and performed absorption, tissue distribution, metabolism and excretion studies (rats)

- 3. Determine MTD and 28-day acute toxicity studies in mice
- 4. Optimisemid-scale (500 gm) manufacturing process
- 5. Hold meeting with regulators (in an identified jurisdiction) to identify scope of pre-clinical studies

5.5 SWOT Analysis: NYX-205

Strengths

- Novel, first in class drug
- No marketed thromboxane synthase inhibitor
- Using proprietary drug delivery technology to cross blood-brain and blood-nerve barriers
- No toxicity anticpated
- No known competitors

Weaknesses

- Efficacy dependent on crossing blood-brain and blood-nerve barriers
- Efficacy dependent on role of thromboxane in disease processes

Opportunities

- Large markets in peripheral neuropathy, neuroinflammation, ulcerative colitis, sclerosing cholangitis
- Considerable unmet medical needs in global markets

Threats

• Patent challenges

6. NYX-330: Anti-LDL cholesterol drug

6.1 Hypercholesterolemia

Cholesterol, an essential building block of cells, occurs in the body in 2 main forms: low-density lipoprotein (LDL) and high-density lipoprotein (HDL). Normal health, particularly blood vessel health, requires these 2 forms to be at a ratio no greater than 3.5 to 1. If the LDL:HDL ratio exceeds this level, LDL cholesterol starts depositing in the walls of arteries, eventually producing the disease known as atherosclerosis and increasing the individual's risk of heart disease and stroke. HDL levels are largely genetically determined and therefore relatively fixed. LDL levels, on the other hand, are affected by a wide range of variables including diet, stress, exercise levels, etc. Across many developed countries, LDL:HDL ratios are considered unhealthy in up to 10% of adults.

So-called statin drugs have been the standard approach for the past 20 years for lowering LDL levels. They do this by blocking the production of LDL cholesterol by the liver. In broad terms, statins only achieve desired LDL levels in about half of treated patients. Nevertheless, in 2012, statin drugs were the biggest-selling class of pharmaceutical in the world with sales of US\$40 billion, although that position has changed dramatically in recent years with statin patents now expiring.

6.2 PCSK9 Inhibitors

Just over 10 years ago, a new target was identified that was predicted to lead to a superior class of LDL-lowering drug over the statins, in addition to creating a new patented drug opportunity. That target is a plasma protein known as PCSK9.

LDL cholesterol particles are removed from blood by LDL receptors (LDLR) present on the surface of liver cells. The resulting LDL particle-LDLR complex is internalised by the liver cell where the cholesterol broken down, and the LDLR then recycled to the outside of the cell where it grabs another LDL particle. In this loop, there is no net loss of LDL receptors, with the whole process being critical to holding down LDL cholesterol levels in the blood.



The opportunity had been identified to develop a drug that blocked the ability of PCSK9 to bind to the LDL particle-LDLR complex once it formed. With that binding blocked, the LDLRs would avoid being degraded, and would be recycled to continue their role in removing LDL particles from blood. Ideally, that drug would be a small molecule drug, able to be taken orally, daily, and with a high degree of safety given that it would need to be taken on a long-term basis.

The binding site on the surface of the PCSK9 protein that attached to the LDLR protein was identified, leading to efforts to find a drug that attached to that binding site, providing a physical block that would prevent PCSK9 from binding to the LDLR protein. Those efforts proved unsuccessful, with the LDLR binding site on PCSK9 proving to be unsuitable for getting a small molecule drug to attach there.

The pharmaceutical industry consequently went down the road of seeking to cover much of the surface of PCSK9 with an antibody, effectively inhibiting its ability to bind to the LDLR. In 2015, the first monoclonal antibody product (evolocumab) entered the market to significant acclaim, achieving target LDL levels in 90% of individuals when used in conjunction with statins, and achieving a significant reduction in the risk of heart disease and stroke when used with statins compared to statins alone.

Despite its proven health benefits, evolocumab has a significant cost (\$14,000 p.a.), as well as needing to be injected fortnightly or monthly (for life). This serves to limit use of the drug to patients in whom statins alone are ineffective or too toxic.

NYX-330 is the result of Australian computational chemists identifying a previously unrecognised pocket on the surface of PCSK9, allowing a small molecule to be designed binds to the pocket and effectively blocks binding between PCSK9 and LDLR.

6.3 Current Status of NYX-330

To the best of the Company's knowledge:

- NYX-330 is the only small molecule inhibitor of PCSK9 under development
- The lead drug candidate has been identified
- It has been shown to have an acceptable PK profile in mice

Immediate tasks for NYX-330

- Compare LDL cholesterol-lowering in obese mouse model of NYX-330 vs Lipitor
- Develop oral formulation
- Determine off-target activity
- Conduct acute toxicity studies in rodents

6.4 Key milestones for 2018

1. Complete mouse proof-of-concept study comparing NYX-330 with Lipitor for lowering LDL cholesterol

2. Develop oral formulation with acceptable bio-availability

3. Determine extent of off-target kinase inhibitory activity

4. Conduct acute 7-day toxicity study in mice

6.5 SWOT Analysis: NYX-330

Strengths

- Novel, first in class drug
- Patentable, novel family of molecules
- No known competitors

Opportunities

- Patented replacement for statin drugs
- Alternative to monoclonal antibodies to PCSK9

Weaknesses

- Safety yet to be determined
- Requires development of oral dosage formulation

Threats

None Known

7. Use of Funds

A\$000s	2018	2019
R&D Costs		
NYX-104	820ª	1250 ^b
NYX-205	650ª	1350 ^b
NYX-330	520ª	1600 ^b
Salaries		
Scientists / support staff	1,040 ^c	2,000 ^d
Executive	500 ^e	1,250 ^f
Noxopharm	150 ^c	0
Board	0	400
Other		
Rent	60 ^h	120 ⁱ
Legals	300	350
Patents	50	100
Travel	200	350
Total	4,290	8,870
+20% contingency		
Total	5,510	10,664

a Primary (in vitro) and secondary (animal studies) proof-of-principle

b Completion of IND-enabling studies

c 6 scientists

d 10 scientists/project managers

e Part-time CEO; part-time US COO

f Full-time CEO, COO, CFO

g Contract use of Noxopharm support personnel

h Shared office space with Noxopharm

i US office space

Note. Use of funds and funding requirements assumes no external non-dilutive funding. The Company intends applying for funds from a variety of sources including the US Army Medical Research and Materiel Command where successful grants have the potential to cover much of the development costs of NYX-104 and NYX-205.

8. Share Capital

8.1 Share capital

As at the date of this Memorandum, the Company has 10,000 shares on issue owned as follows:

Current share capital structure	
6,670 Shares	Noxopharm Limited
3,330 Shares	Altnia Holdings Pty Limited ('Altnia')

To accommodate the proposed issue of New Shares and New Options, the Company will notify the U.S. Securities and Exchange Commission of the following 3 steps:

- 1. Expansion of the existing share capital from 10,000 to 7,500,000 so that the current ownership of the Company will change to:
 - a. 5,000,000 shares. Noxopharm Limited
 - b. 2,500,000 shares. Altnia Holdings Pty Limited.
- 2. Creation of 1,500,000 new shares ('New Shares').
- 3. Creation of 1,000,000 new options ('New Options').

The Company intends to introduce incentive share plans for key executives and employees in accordance with US market standards following completion of the Offer.

In the case of key executives, these will be shares linked to key performance milestones. The quantum of these shares has not been determined and will be the subject of negotiation between the Board and future key executives. Other employees will be issued stock under a standard Employee Share Scheme (ESS) on a salary-based pro rata basis. The issue of Performance Shares and ESS Shares is standard within the pharmaceutical industry and will be essential in attracting and holding key staff, as well as incentivising staff to the benefit of the Company.

8.2 Stockholders' agreement

Each investor to whom the Company issues New Shares and New Options will be required to accede to the Company's stockholders' agreement. The stockholders' agreement regulates the ownership, voting and transfer of shares of common stock, the governance of the Company and certain other matters relating to the Company.

The stockholders' agreement provides that, if the Company fails to achieve certain milestones or the Board determines that the Company will not undertake further financing for the development, research, use, licence or commercialization of NYX-330, Altnia may reacquire NYX-330 in return for the Company redeeming all of the outstanding shares of capital stock of the Company held by Altnia.

The stockholders' agreement also provides that, if the Company elects to sell, assign or transfer NYX-330 to a third party, Altnia has a right of first and last refusal in relation to the sale, assignment or transfer.

Otherwise, the stockholders' agreement contains terms and conditions customary for an agreement of its nature.

A copy of the Company's stockholders' agreement will be provided to prospective investors upon request.

9. Securities laws

9.1 US Securities laws

As a Delaware corporation, the Company is subject to the securities laws of the United States, including the registration requirements under the Securities Act of 1933, as amended (the "Securities Act"). The offering of Shares pursuant to this Memorandum is being made pursuant to exemptions from the registration requirements of the Securities Act provided by Regulation D and Regulation S, each promulgated under the Securities Act. Accordingly, the offering of New Shares is not being made to U.S. Person, as that term is defined in Regulation S, or to any persons in the United States, and is only being made to investors that are "accredited investors" as that term is defined in Regulation D. Each investor will certify in such investor's subscription agreement that such investor is not a U.S Person and is an accredited investor.

In addition, investors will be subject to certain transfer restrictions. During the one-year period following the closing of this offering, the New Shares and New Options being offered under this Memorandum may only be transferred in a transaction not subject to the registration requirements of the Securities Act by virtue of compliance with Rule 904 of Regulation S thereunder - namely,

- (i) the offer of the New Shares and New Options was not made to a person in the United States;
- (ii) (A) at the time the proposed transferee of the New Shares and/or New Options agreed to purchase the New Shares and New Options, the transferee was outside the United States or the investor and any person acting on the investor's behalf reasonably believed that the transferee was outside the United States or
- (B) and neither the investor nor any person acting on the investor's behalf knows (or at such time knew) that the transaction has been (or was) pre-arranged with a buyer in the United States;
- (iii) no directed selling efforts have been made in contravention of the requirements of Regulation S;
- (iv) the transaction is not part of a plan or scheme to evade the registration requirements of the Securities Act; and

(v) if the investor is (x) a dealer or a person receiving a selling concession, fee or other remuneration in connection with such transfer, or (y) an officer or director of the Company or a distributor who is an affiliate of the issuer or such distributor solely by virtue of holding such position, then the investor has complied with the additional conditions set forth in Rule 904(b) of Regulation S.

An investor wishing to transfer New Shares and/or New Options during such one-year period will also have to certify to the Company that the investor has complied with these transfer restrictions and will also have to present to the Company a certificate from the proposed transferee that the transferee is not a U.S. Person and is not acquiring the New Shares and/or New Options for the account or benefit of a U.S. Person.

These restrictions and procedures will be set forth in the form of subscription agreement. The New Shares and New Options will also be certificated, and each certificate will bear a legend that sets forth these transfer restrictions.

9.2 Australian Securities laws

For purposes of Australian securities law, the New Shares and New Options are not being offered with the purpose that they be sold or transferred or the subject of any grant, issue or transfer any interests in or options over them. Investors must agree that they are acquiring the New Shares and New Options for their own account and not with a view to the resale, distribution or other disposition thereof.

By accepting this offer of New Shares and New Options, an investor represents, warrants, undertakes and agrees for the benefit of the Company and its affiliates that, if the investor is in Australia, it is one of the following:

- a 'Sophisticated Investor' within the meaning of section 708(8) of the *Corporations Act 2001* (Cth) ('Corporations Act'); or
- a 'Professional Investor' within the meaning of section 708(11) of the Corporations Act; or
- (iii) an entity which is otherwise exempt from the requirement for the Company to give you a disclosure document (prospectus) under Chapter 6D of the Corporations Act;

and the Company may require the investor produce a certificate under section 708(8)(c) of the Corporations Act.

These restrictions and procedures will be set forth in the form of in each investor's subscription agreement.

10. General risks

R&D

There are multiple reasons why drug candidates fail to reach the regulatory review process. The 3 main reasons are failing to deliver a meaningful therapeutic benefit, having unacceptable toxicity, and having poor drug-like behaviour in areas such as bioavailability and pharmacokinetics. However, there are many other reasons too numerous to detail here. Also, failure often is not known until the drug candidate reaches a Phase 3 registration study, which can be very late in the drug development program, meaning that considerable moneys can be expended before failure is recognised. The 3 Nyrada drug assets are early-stage, which means that critical R&D issues such as efficacy and toxicity are yet to be tested in humans.

Regulatory approval

Even if the Company considers that it has developed any one of its 3 drug assets to a point of being ready for submission to any regulatory authority for marketing approval, there are numerous reasons why such approval might be denied or delayed. The Company will work closely with regulatory affairs advisors throughout the entire drug development process (embracing clinical trials, submission and approval phases) in order to identify the regulatory requirements and to maximise the likelihood of meeting those requirements, but success cannot be guaranteed for a variety of unforeseen reasons including by way of example, a change in the regulatory landscape in any one jurisdiction after completion of the clinical study

Manufacturing

Each of the Company's current drug assets involve a 2-step manufacturing process.

The first step with all 3 assets involves synthesis of the active molecule, known as the Active Pharmaceutical Ingredient (API). The 3 APIs currently are being manufactured by a contract manufacturer in India. While the process of drug synthesis uses commonly available raw materials and requires standard chemical synthetic processes, it will be necessary to scale-up the current micro-scale process, exposing the Company to potential delays due to problems associated with supply of raw materials and plant reliability. The Company proposes to mitigate this risk by using 2 contract manufacturers, one in India and the other in either the US or Switzerland. In each case, the contract manufacturer needs to hold the appropriate licences from both the FDA and the EMA.

The second step is the formulation of the final product involving the blending of the API with various excipients and production of the final dosage form. Again, this phase will be conducted by experienced contractors holding the appropriate licences.

This reliance on contractors exposes the Company to potential problems such as interruption of supply of raw

materials and maintenance issues with manufacturing plant. Again, these risks can be mitigated to some degree by the use of multiple suppliers and contractors.

Funding

Drug development is expensive, requiring funding for a period typically of 7 years. While the Company's explicit strategy is to licence each drug asset before reaching large Phase 3 clinical studies, the Company may have to be prepared to take each drug asset into a Phase 2 proof-of-concept clinical study. The Company intends to seek non-dilutive funding in the form of government and foundation grants as much as possible to offset R&D and clinical study costs, but notwithstanding that, the Company is going to need to raise additional funds in the absence of any revenue from licence fees and royalty streams. The Company will need to raise those funds from capital markets and thereby will be susceptible to the usual factors affecting market sentiment.

Key personnel

Successfully delivering on the Company's R&D and commercial strategies will require the ongoing involvement of certain key personnel such as Dr Graham Kelly. The Company will implement a succession-planning strategy as soon as practicable, but until that is in place, the Company would be at serious risk of disrupted leadership for an unidentified period of time if Dr Kelly was unavailable.

Intellectual property

Successful commercialisation of the Company's 3 drug assets will depend very considerably on achieving patent grant for each asset. The Company relies on the advice of patent attorneys on the novelty and inventiveness, and therefore likely patentability, of the intellectual property underpinning each of the Company's drug assets. While all reasonable care and effort is taken in the lodgement of any patent application to ascertain novelty and inventiveness, as well as the absence of infringement of others' patents, there can never be any certainty that patent offices in individual territories will grant a patent.

Competition

The Company is unaware of any drugs under development that would be regarded as directly competitive to the Company's current 3 drug assets, but there can be no certainty about that. Other companies with greater resources than Nyrada may develop similar drugs faster than Nyrada, or better-performing drugs.

Stock Markets

Investors need to consider risks common to small-cap biotechnology stock investments including share price volatility and inordinate sensitivity to news flow. While the Company remains unlisted, liquidity may remain restricted.

11. Specific risks and challenges

NYX-104

The main risk with this drug asset is that it will not cross the blood-brain barrier in humans.

NYX-104 has proven successful in blocking the extent of excitotoxicity over 5 days in mice with a cerebral infarct. The drug was administered as a suppository dosage formulation using the LIPROSE drug delivery technology, pointing to an ability to cross the blood-brain barrier in mice. Also, NYX-104 is an analog of the drug, idronoxil, which has been shown to cross the blood-brain barrier in rats when delivered rectally using the LIPROSE technology. On that basis there is no reason to believe that NYX-104 will be unable to cross the human bloodbrain barrier given the common behavioural characteristics of the mammalian blood-brain barrier, but this is yet to be tested in humans.

Mice treated daily for 5-days with NYX-104 showed no signs of acute toxicity or intolerances, pointing to a high therapeutic index for this drug. Humans also have shown a high tolerance to idronoxil, suggesting that NYX-104, an idronoxil analog, will be similarly well tolerated in humans, but this remains to be confirmed.

NYX-205

NYX-205 is a modified, pro-drug form of an older drug known as NV-52. NV-52 is a confirmed potent inhibitor of thromboxane synthase in vitro, and oral NV-52 has demonstrated efficacy in a mouse model of ulcerative colitis. Oral NV-52 also has been given to healthy volunteers in a Phase 1a pharmacokinetic and acute safety study. Nyrada has modified NV-52 with the LIPROSE technology to create an esterified pro-drug form known as NYX-205. The modification has two purposes: (a) to improve the drug's drug-like performance by extending its half-life in the body; and (b) to enable it to cross both the bloodbrain barrier and blood-nerve barrier.

The LIPROSE technology has proven successful in enabling drugs chemically related to NYX-205 to cross the blood-brain barrier, and therefore there is no reason to believe that this will not be the case also with NYX-205, but this is yet to be confirmed both in animals and humans.

NYX-330

The two key challenges with this drug asset are (a) the development of an oral dosage formulation, and (b) confirmation of a high therapeutic index (safety) given its long-term use.

NYX-330 shows good bio-availability and desirable metabolic and pharmacokinetic profiles when injected into animals, but poor oral bio-availability. The latter is a relatively common challenge in the pharmaceutical industry and there are a variety of means of addressing the problem. Nevertheless, there is no certainty that the problem can be solved, in which case alternative means of drug delivery will need to be found.

Dosing healthy individuals on a long-term basis demands a high level of safety. Preliminary standard screening assays show only minimal off-target activity, but this has yet to be looked at more extensively and to be tested by animal toxicology studies.

12. Directory

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13. Glossary

Blood-brain barrier:	A layer of endothelial cells and brain cells that controls the entry of chemicals into the brain. Permitted chemicals are actively transported into the brain.
Blood-nerve barrier:	A similar barrier to the blood-brain barrier that controls the entry of chemicals into peripheral nerves.
Ca++:	Calcium ions
CNS:	Central Nervous System (brain, spinal cord)
Excitotoxicity:	Death of neurons from being over-stimulated (over-excited). This occurs when neurons are injured by trauma or disease.
Glutamate:	The most common form of neurotransmitter in the brain.
Hypercholesterolaemia:	an excess of cholesterol in the bloodstream.
LDL cholesterol:	Low-density lipoprotein cholesterol, commonly referred to as 'bad' cholesterol. Elevated LDL levels are associated with an increased risk of heart disease.
LIPROSE:	Lipid Protective Shield (owned by Noxopharm)
NASH:	(Non-Alcoholic SteatoHepatitis) Fatty inflammation of the liver in people who do not abuse alcohol. It is typically a chronic condition that causes no symptoms or very mild symptoms but can sometimes cause progressive scarring and cirrhosis of the liver.
Neuron:	an electrically excitable brain cell that receives, processes, and transmits information through electrical and chemical signals.
Neurotransmitters:	Chemicals that enable electrical signals to be passed between neurons.
PCSK9:	The PCSK9 gene provides instructions for making a protein that helps regulate the amount of LDL cholesterol in the bloodstream.
Peripheral nerves:	Nerves that connect the central nervous system with the rest of the body.
Peripheral neuropathy:	An inflammatory condition affecting peripheral nerves charecterised by pain and loss of function.
Ulcerative Colitis (UC):	Severe form of inflammatory bowel disease (IBD). Causes swelling, ulcerations, and potential loss of function of the large intestine.

14. Application

14.1 How to apply for New Shares and New Options

Complete the application form in accordance with the instructions set out in the form. Completed application forms must be forwarded to reach the Company no later than 5:00pm Australian Eastern Standard Time on 15th December 2017. Except as required by US law, application forms may not be withdrawn by an applicant after delivery in accordance with this Memorandum.

By lodging an application form in respect of the offer contained in this Memorandum, each applicant declares and warrants to the Company that it is entitled to subscribe to this Offer under the laws governing their place of residence.

14.2 Special conditions

The Company has no special conditions or priority allocations.

14.3 Payment

The completed application form must be accompanied by evidence of payment in full at the rate of A\$4.00 per New Share for which you apply. No consideration is payable for the New Options, as each 3 New Shares have 2 attached New Options.

Funds are to be remitted electronically to the following trust account:

APP Securities Pty Limited Trust Account No2 BSB: 332-027 Account Number: 000 0553 894 884

All funds received by the Company under this Memorandum will be held in trust until close of the Offer and its issue of the New Shares.

14.4 Minimum-maximum subscription

The minimum subscription for the Offer is AUD\$4,000,000 being subscription moneies for 1,000,000 New Shares and 667,000 New Options. The maximum subscription is AUD\$6,000,000 for 1,500,000 New Shares and 1,000,000 New Options.

14.5 Individual subscription

The minimum subscription for investors is A\$40,000 being for 10,000 New Shares and 6,667 New Options.

14.6 Enquiries

If you have any questions in relation to this Memorandum, please contact

Dr Graham Kelly Tel: +61 429 854 390 Email: graham.kelly@nyrada.com

14.7 Allotment

The New Shares and New Options are expected to be allotted and certificates despatched by 6 January 2018.

The Company reserves the right to withdraw the issue at any time and refund acceptance moneys to applicants without interest. The Company may close this Offer early or extend the closing date for acceptances. In such case, the important dates listed above will be affected.

