



**Date: 4 October 2017**

**Sydney, Australia**

**ASX: NOX**

**Noxopharm Limited**

ABN 50 608 966 123

**Registered Office:**

Suite 1 Level 6  
50 Queen St  
Melbourne VIC 3000  
Australia

**Operational Office:**

Suite 3, Level 4  
828 Pacific Highway  
Gordon NSW 2072  
Australia

**Board of Directors**

**Mr Peter Marks**

Chairman  
Non-Executive  
Director

**Dr Graham Kelly**

Chief Executive Officer  
Managing Director

**Dr Ian Dixon**

Non-Executive  
Director

ASX Limited  
20 Bridge Street  
SYDNEY NSW 2000

**ESTABLISHMENT OF NYRADA INC. – EXTRAORDINARY  
GENERAL MEETING**

**Sydney, 4 October 2017:** As announced on 25 September 2017, Noxopharm Limited (ASX:NOX) has formed a subsidiary company in the US, Nyrada Inc. (**Nyrada**), for the purpose of developing non-oncology drug intellectual property (IP).

As previously announced, Noxopharm has agreed to transfer the total issued share capital of its two wholly-owned subsidiaries, Norbio No. 1 Pty Ltd ACN 619 956 722 and Norbio No. 2 Pty Ltd ACN 619 956 973, to Nyrada in consideration for 6,669 shares in Nyrada (**NorBio Agreement**).

Altnia Holdings Pty Ltd ACN 133 349 238 as trustee for the I. Dixon Family Trust, has agreed to transfer the total issued share capital of Cardio Therapeutics Pty Ltd ACN 167 825 201 to Nyrada in consideration for 3,329 shares in Nyrada (**Cardio Agreement**).

The NorBio Agreement and the Cardio Agreement together are the “**Proposed Transactions**”.

Noxopharm is calling an extraordinary general meeting (**EGM**) for the purpose of shareholders considering and, if thought fit, approving the Proposed Transactions.

The EGM is scheduled for Monday, 6 November from 10:00am Sydney time at the Company’s offices at Suite 3, Level 4, 828 Pacific Highway, Gordon NSW 2072.

Accordingly, we attach following documents:

- Notice of Meeting;
- Explanatory Statement;
- sample proxy form;
- Independent Expert Report; and
- Independent Valuation,

(together, the **EGM Notice of Meeting**).

Mailing of the EGM Notice of Meeting commenced today.

## Indicative timetable for implementing the Proposed Transactions

The indicative timetable for the Proposed Transactions has moved forward slightly to that announced on 25 September 2017. The new indicative timetable is set out below:

Event	Date
Announce the Proposed Transactions	25 September 2017
Call the extraordinary general meeting	4 October 2017
Hold the general meeting	6 November 2017
Complete the NorBio Agreement and the Cardio Agreement	10 November 2017

Note: this is subject to change.

For further information, please contact:

Karen Thompson

Tel: (02) 9144 2223

[info@noxopharm.com](mailto:info@noxopharm.com)

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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 address the problem of drug-resistance in cancer cells, the major hurdle facing improved survival prospects for cancer patients. NOX66 is the first pipeline product, with later generation drug candidates under development. The Company also has initiated a pipeline of non-oncology drugs.

### Investor & Corporate Enquiries:

Prue Kelly

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E: [info@noxopharm.com](mailto:info@noxopharm.com)

### Company Secretary:

David Franks

T: +61 2 9299 9690

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[www.noxopharm.com](http://www.noxopharm.com)



# Noxopharm Limited

ACN: 608 966 123

## Notice of Extraordinary General Meeting and Explanatory Statement

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Date of Meeting:	Monday, 6 November 2017
Time of Meeting:	10:00am AEDT Registration from 9:45am AEDT
Place of Meeting:	Suite 3, Level 4, 828 Pacific Highway, Gordon NSW 2072

This is an important document. It should be read in its entirety.

If you are in doubt as to the course you should follow, consult your financial or other professional adviser.

All Shareholders should refer to the Independent Expert Report enclosed with this Notice of Extraordinary General Meeting.

The Independent Expert, Moore Stephens (Vic) Pty Ltd, has concluded that the Norbio Acquisition, the Cardio Acquisition and the Transaction are **fair and reasonable** to non-associated Shareholders.



4 October 2017

Dear Shareholder

I invite you to read and consider the information contained in this Notice of Meeting, which relates to the proposed establishment of a company called Nyrada Inc., which will be engaged in drug development in various non-oncology fields.

You are being asked to consider and then vote on 2 Resolutions.

If both Resolutions are approved, the end result will be the creation of a new drug development business in which Noxopharm will hold 66.7% of the total issued share capital and, by virtue of which, you will have an indirect shareholding. Nyrada will be a US company, based in the State of New York, and which your Board believes has the potential to become a significant drug development company with a global presence.

Noxopharm began as a dedicated oncology company, and everything that has happened since we were admitted to ASX in 2016 has served only to confirm that strategy. The emerging potential of NOX66, plus the ongoing development of the Company's second- and third-generation anti-cancer products, means the Company has a full book of work for the foreseeable future. Your Board believes that NOX66 has very significant commercial potential, and realising that potential means staying focused in terms of attention and capital resources.

Nevertheless, the Company now finds itself in the position of owning intellectual property with potential applications outside of the oncology field and which, in the Board's view, has potentially significant commercial value. Nyrada stems from the Board's intention to realise that value.

Creating our lead product, NOX66, meant developing a means of making its active component, idronoxil, behave in a considerably better drug-like manner than had been the case previously. This included preserving the activity of the drug in the body, keeping it in this active state in the body for considerably longer, and giving it the ability to cross the blood-brain barrier to treat brain cancer. And with that discovery came the realisation that we had developed a proprietary drug delivery platform that potentially was applicable to other drug candidates with a similar chemistry to idronoxil that could be used to treat conditions other than cancer.

A number of these 'other drug candidates' already had been shown by others to have promise in the treatment of various degenerative conditions of the brain, but that promise failed to translate into the clinic, in large part because of the impenetrability of the blood-brain barrier to this class of drug. Noxopharm believed that its proprietary drug delivery platform potentially held the ability finally to make that translation possible. That belief was put to the test by a team of eminent Australian neuroscientists who, working with an animal model of neurodegenerative disease, were able to confirm the success of one of the Company's non-oncology drugs in the treatment of this disease.

That success then raised the prospect of being able to deliver drugs, not just across the blood-brain barrier, but also across the blood-nerve barrier (a similar barrier to the blood-brain barrier affecting peripheral nerves). The blood-nerve barrier has proved a block to effective treatment of various diseases involving peripheral nerves.

The Company then identified 2 drug candidates:

- NYX-104 (an inhibitor of excitotoxicity) intended to minimise the loss of brain function associated with head and spinal trauma and stroke; and
- NYX-105 (an anti-inflammatory compound) intended to treat loss of peripheral nerve function (peripheral neuropathy) associated with diabetes and chemotherapy, and to treat ulcerative colitis and inflammatory bowel disease.

Both drugs then were transferred to 2 wholly-owned subsidiaries of Noxopharm, known as Norbio No. 1 Pty Ltd and Norbio No. 2 Pty Ltd respectively.

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Each of these indications are significant community concerns of substantial unmet medical need, which led the Board to believe that it had a responsibility to put that intellectual property to work for Shareholders. But it also believed that by keeping it within Noxopharm, this new opportunity would struggle to gain the attention and resources it deserves in the face of the Company's primary goal of bringing NOX66 through to market.

Having considered various options, the Board came to the view that a separate company, with its own management, staffing and capital resources, represented the best value proposition for Shareholders by virtue of maximising ownership of the intellectual property. The rationale for establishing this new entity in the US was a belief that the intellectual property potentially would be valued higher in that territory.

The Company then became aware of a 3<sup>rd</sup> drug candidate owned by Cardio Therapeutics Pty Ltd, a company controlled by Dr. Ian Dixon, a non-executive Director of the Company. That drug candidate belongs to a class of drugs currently the subject of considerable pharmaceutical industry attention known as PCSK9 inhibitors, intended to treat patients with high blood cholesterol levels. With the so-called *statin* drugs now coming to the end of their patent lives, PCSK9 inhibitors have emerged as the next generation cholesterol-lowering drugs. The Company reviewed the drug candidate owned by Cardio and came to the view that it was a first-in-class candidate of considerable scientific novelty and of potential significant commercial value.

The Board believes that the 3 drug candidates represent a unified story of 3 small molecule, non-oncology drugs, each pertinent to areas of significant topical interest and commercial potential.

The plan you are being asked to consider involves a Transaction in 2 steps, each requiring Shareholder approval, with each step being the subject of a separate resolution.

**Resolution 1** relates to the transfer of Norbio No. 1 and Norbio No. 2 to Nyrada (**Norbio Acquisition**).

**Resolution 2** relates to the acquisition by Nyrada of Cardio (**Cardio Acquisition**).

If approved by Shareholders, Nyrada will be a semi-independent company with its own management, staff and a separate Board of Directors, the majority of whom will be US citizens, with myself as Executive Chairman.

Nyrada is intended to be self-sufficient in terms of funding, with that company seeking a capital-raising following the Transaction receiving Shareholder approval.

This Notice of Meeting and the attached Explanatory Statement contains the details of the Transaction and I encourage you to read it and the enclosed Independent Expert Report and then to vote in support the Resolutions.

If you have any further questions about the Transaction, please do not hesitate to contact me.

Yours sincerely

A handwritten signature in black ink, appearing to read "Graham Kelly", written over a light blue horizontal line.

Graham Kelly  
CEO & Managing Director

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## NOXOPHARM LIMITED

ACN: 608 966 123

### NOTICE OF EXTRAORDINARY GENERAL MEETING

Notice is hereby given that the Extraordinary General Meeting of Noxopharm Limited ACN 608 966 123 will be held at the Company's offices at Suite 3, Level 4, 828 Pacific Highway, Gordon NSW 2072 on Monday, 6 November 2017 at 10:00am AEST.

The attached Explanatory Statement is provided to supply Shareholders with information to enable Shareholders to make an informed decision regarding the Resolutions set out in this Notice. The Explanatory Statement is to be read in conjunction with this Notice.

This Notice should be read in its entirety. If Shareholders are in doubt as to how they should vote, they should seek advice from their accountant, solicitor or other professional adviser prior to voting.

All Shareholders should refer to the Independent Expert Report enclosed with this Notice.

#### 1. Agenda - Ordinary Business

##### Resolution 1 Approval of Norbio Acquisition

To consider and if thought fit, to pass the following resolution as an ordinary resolution:

*"That, for the purposes of Chapter 2E of the Corporations Act, ASX Listing Rule 10.1 and for all other purposes, the acquisition by Nyrada of the entire issued share capital of Norbio No. 1 and Norbio No. 2 from the Company on the terms and conditions set out in the Explanatory Statement is approved."*

##### Resolution 2 Approval of Cardio Acquisition

To consider and if thought fit, to pass the following resolution as an ordinary resolution:

*"That, subject to Resolution 1 being passed, for the purposes of Chapter 2E of the Corporations Act, ASX Listing Rule 10.1 and for all other purposes, the acquisition by Nyrada of the entire issued share capital of Cardio from Altnia and the issue of 3,329 Nyrada Shares to Altnia on the terms and conditions set out in the Explanatory Statement are approved."*

#### Voting Exclusions

In accordance with ASX Listing Rule 14.11 and (where relevant) the Corporations Act, in relation to:

- (a) **Resolution 1:** The Company will disregard votes cast on Resolution 1 by Nyrada, Altnia Holdings Pty Ltd as trustee for the I. Dixon Family Trust, or any of their associates, including Dr. Ian Dixon. However, the Company need not disregard a vote on Resolution 1 if it is cast by a person as a proxy for a person who is entitled to vote in accordance with the directions of the Proxy Form or it is cast by a person who is entitled to vote, in accordance with a direction on the Proxy Form to vote as the proxy decides.
- (b) **Resolution 2:** The Company will disregard votes cast on Resolution 2 by Nyrada, Altnia Holdings Pty Ltd as trustee for the I. Dixon Family Trust, or any of their associates, including Dr. Ian Dixon. However, the Company need not disregard a vote on Resolution 2 if it is cast by a person as a proxy for a person who is entitled to vote in accordance with the directions of the Proxy Form or it is cast by a person who is entitled to vote, in accordance with a direction on the Proxy Form to vote as the proxy decides.

## 2. Determination of voting entitlement

For the purpose of determining a person's entitlement to vote at the Meeting, a person will be recognised as a shareholder and the holder of Shares if that person is registered as a holder of those Shares at 7:00pm AEST on Wednesday, 1 November 2017.

## 3. Votes

Unless a poll is demanded in advance of voting on a resolution, voting on each resolution will initially be by way of a show of hands. On a show of hands, each member present in person or by proxy or, in the case of a body corporate, by a representative, shall have one vote.

On a poll, every member present in person or by attorney or by proxy or, in the case of a body corporate, by a representative, shall have one vote for each share held by him, her or it.

## 4. Proxies

A Shareholder entitled to attend and vote is entitled to appoint a proxy to attend and vote instead of the Shareholder. Where the Shareholder is entitled to cast two or more votes, the Shareholder may appoint two proxies and may specify the proportion or number of votes each proxy is appointed to exercise.

If the Shareholder appoints two proxies and the appointment does not specify the proportion or number of the Shareholder's votes each proxy may exercise, each proxy may exercise half of the votes. A proxy need not be a Shareholder.

To be effective, the instrument of appointment of a proxy (and power of attorney or other authority, if any, under which it is signed or a certified copy of that power or authority) must be received by the Company by 10:00am AEST on Saturday, 4 November 2017:

- by mail to the Company at PO Box 2226, Strawberry Hills NSW 2012;
- personally to the Company at Suite 310, Level 3, 50 Holt Street, Surry Hills NSW 2010; or
- by facsimile to +61 (0)2 8583 3040.

If you choose to appoint a proxy, you are encouraged to direct your proxy how to vote on by marking either "For", "Against" or "Abstain" on the form of proxy for that item of business.

Subject to the voting restrictions set out in the Voting Exclusion Statement, the Chairperson will vote undirected proxies on, and in favour of all Resolutions.

A form of proxy accompanies this Notice.

## 5. Questions and Comments by Shareholders at the Meeting

A reasonable opportunity will be given to Shareholders to ask questions and/or make comments on the management of the Company at the Meeting.

## 6. Corporate Representatives

Any corporation which is a member of the Company may authorise (by certificate under common seal or other form of execution authorised by the laws of that corporation's place of incorporation, or in any other manner satisfactory to the chairperson of the Meeting) a natural person to act as its representative at any Extraordinary General Meeting.

For and on behalf of the Board of Directors:



**David Franks**  
Company Secretary  
Noxopharm Limited  
Dated: 4 October 2017



## EXPLANATORY STATEMENT

This Explanatory Statement is intended to provide Shareholders with sufficient information to assess the merits of the Resolutions contained in this Notice.

The Directors recommend that Shareholders read this Explanatory Statement and the Independent Expert Report in full before making any decision in relation to the Resolutions.

**Resolution 2 is conditional upon Resolution 1 being approved. If Resolution 1 is not passed, then both Resolutions will be taken to have been rejected by Shareholders and the Transaction will not proceed. If Resolution 1 is passed and Resolution 2 is not passed, the Norbio Acquisition will proceed but the Cardio Acquisition will not proceed.**

### The Transaction

#### 1. Background

Nyrada Inc. (**Nyrada**) is a company incorporated in the USA. The Company and Altnia Holdings Pty Ltd ACN 133 349 238 as trustee for the I. Dixon Family Trust (**Altnia**) own the shares in Nyrada equally.

Nyrada is controlled by the Company within the meaning of section 50AA of the Corporations Act. Accordingly, Nyrada is a child entity of the Company for the purposes of ASX Listing Rules and is an entity controlled by the Company for the purposes of Chapter 2E of the Corporations Act.

Resolution 1 relates to the acquisition of the total issued share capital of Norbio No. 1 Pty Ltd ACN 619 956 722 (**Norbio No. 1**) and Norbio No. 2 ACN 619 956 973 (**Norbio No. 2**) by Nyrada from the Company (**Norbio Acquisition**). Collectively Norbio No. 1 and Norbio No. 2 are the “**Norbio Original Subsidiaries**”.

Resolution 2 relates to the acquisition of the total issued share capital of Cardio Therapeutics Pty Ltd ACN 167 825 201 (**Cardio**) by Nyrada from Altnia (**Cardio Acquisition**).

Together, the Norbio Acquisition and the Cardio Acquisition comprise the “**Transaction**”.

#### 2. The Transaction

##### ***Rationale behind Nyrada***

It is the view of the Board that the Transaction, which results in the establishment of a non-oncology drug development business to be conducted by Nyrada, represents the best way to grow shareholder value for intellectual property that is not in line with the current oncology focus of the Company but which, in the opinion of the Board, holds significant commercial potential.

On 23 November 2016, the Company announced that its NOX66 delivery technology had resulted in its active component, idronoxil, crossing the blood-brain barrier in rats. NOX66 involves a proprietary drug delivery system known as LIPROSE (lipid protective shield), which is designed to ensure that idronoxil retains its anti-cancer potency once it reaches the bloodstream of cancer patients. The ability of LIPROSE to go one step further and deliver idronoxil into the brain was an unexpected, but significant, discovery.

The blood-brain barrier is a robust barrier that serves to exclude foreign chemicals from accessing brain tissue. While serving a vital protective function to protect the brain from potentially harmful compounds, it also inadvertently prevents many drugs from accessing the brain that are intended to deliver therapeutic benefit.

The blood-brain barrier represents an effective barrier to medicine’s ability to treat conditions of the brain and spinal cord. The ability of NOX66 to cross the blood-brain barrier led the Company to form the view that LIPROSE might address this problem by delivering into the brain compounds with a similar chemistry to idronoxil (but with different targets to cancer).

A similar barrier exists with peripheral nerves, serving to restrict the entry of drugs into peripheral nerves. In developing a drug delivery platform that enables drugs to cross the blood-brain barrier, the Company is confident that the same platform will enable drugs to cross into peripheral nerves, potentially enabling such drugs to treat various forms of peripheral neuropathy.

Accordingly, the Company undertook two pre-clinical studies intended to identify compounds chemically related to idronoxil that potentially could treat two key brain and peripheral nerve pathologies associated with many neurological conditions – excitotoxicity and neuro-inflammation. Those studies identified two drug candidates (**Non-Oncology Drug Assets**), which, in the view of the Board, represent first-in-class drug opportunities.

The Company then became aware of a third drug asset (**PCSK9 Program**) owned by a company controlled by Dr. Ian Dixon, a Director of the Company. Please see page 7 of this Explanatory Statement for further information in relation to the PCSK9 Program. Once the Board (other than Dr. Ian Dixon) reviewed the PCSK9 Program, the Board (other than Dr. Ian Dixon) came to the view that the PCSK9 Program was a significant opportunity that would complement the Non-Oncology Drug Assets. This was for three reasons. First, the PCSK9 Program provided an element of de-risking by extending the reach of Nyrada into a completely different family of molecules with a completely different drug action. Second, PCSK9 inhibitors have the opportunity to replace the so-called *statin drugs* which have been the mainstay of treatment of high blood cholesterol levels for 25 years but which are approaching the end of their patent life. Third, the Non-Oncology Drug Assets and the PCSK9 Program have the commonality of all being small molecules for non-oncology indications.

***Why the opportunity is not being retained directly by the Company***

It is the view of the Board that the Company has a major commercial opportunity with its front-line drug, NOX66. Ongoing research and development is looking to build on that opportunity with 2<sup>nd</sup> and 3<sup>rd</sup> generation products. Bringing through to market a drug that the Board believes has the potential to become a standard of care in oncology, in addition to other generation drugs, demands a clear focus by management of the Company and a clear quarantining of resources.

The Company was admitted to ASX as an oncology company and the Board believes that it is in the best interests of the Company to remain focused on this area of significant need. Further, the market profile of, and investors in, oncology research and non-oncology research are different and operate on different timeframes, urgency, funding and market perception.

It is proposed that the development of the non-oncology capability in Nyrada should not impact the assets and progress of the Company. The Directors have considered the Company's position and believes that it is in the best interests of the Company to preserve its limited resources and for the Company to maintain its focus on oncology. However, the Directors also consider that ignoring the opportunities of the Non-Oncology Drug Assets is not a viable option. The potential opportunity to develop two first-in-class drugs in areas of significant unmet clinical need in the community is considered by the Board to be too great to ignore. Further, given the early stage of development of the Non-Oncology Drug Assets, licensing the Non-Oncology Drug Assets to a third party is unlikely. Accordingly, the Directors have considered the Company's options to realise the potential of the Non-Oncology Drug Assets and the most appropriate way is to place them into a separate company that will be able to seek its own funding.

The Transaction gives the Company an opportunity to maintain an interest in Nyrada without adversely affecting the Company or its progress. The Directors believe that the combination of the Norbio Original Subsidiaries and Cardio will be attractive to investors and, if the trials are successful, the Company's interest in Nyrada could be a valuable asset of the Company.

The Company has, in conjunction with Altnia, incorporated Nyrada in the US because they believe that the market for potential investors for the Non-Oncology Drug Assets and the PCSK9 Program in the US is much larger and will provide more opportunity to Nyrada to fund the research and development of the Non-Oncology Drug Assets and the PCSK9 Program. Further, being based in the US will provide Nyrada with easier access to

significant grant funding opportunities, collaboration with US research institutions, and analysts with expertise in specific areas of disease.

***Consequences if a Resolution does not pass***

If Resolution 1 passes but Resolution 2 does not pass, Nyrada and the Company will proceed with the Norbio Acquisition.

If Resolution 1 does not pass (which, as Resolution 2 is conditional upon Resolution 1, means that Resolution 2 also does not pass), the Non-Oncology Drug Assets will likely undergo limited further development.

***Nyrada – Shareholdings***

Nyrada currently is owned jointly by the Company and Altnia. Upon completion of the Transaction, the Company will own 66.7% of the total issued share capital of Nyrada and Altnia will own 33.3% of the total issued share capital of Nyrada.

The Company has obtained Independent Valuation of the intellectual property rights held by Norbio No. 1, Norbio No. 2 and Cardio. The Independent Valuation is set out in Annexure B. The independent valuer determined that each Non-Oncology Drug Asset and the PCSK9 Program are roughly of equivalent value.

Accordingly, each of the Company's and Altnia's shareholding in Nyrada upon completion of the Transaction represents the value of the intellectual property that the relevant entity is, subject to Shareholder approval, providing to Nyrada.

If Resolution 2 is not approved by Shareholders and completion of the Cardio Transaction does not occur, Altnia is required to transfer its shares in Nyrada to the Company. If this occurs, Nyrada will be a wholly-owned subsidiary of the Company.

**Norbio No. 1 Intellectual Property – *Inhibitor of excitotoxicity***

Norbio No. 1 owns all intellectual property rights associated with a drug that seeks to reduce the impact of trauma and stroke on brain function.

Any event that causes acute damage to the brain (stroke, physical trauma, repeated concussion, severe epilepsy) has two consequences. The first is the immediate death of those brain cells (neurons) directly involved in the trauma. The second consequence is delayed, occurring over the following week, and involves the death of an even greater number of neurons. This secondary event, known as ***excitotoxicity***, typically results in up to 10 times more brain cells dying than were immediately injured by the trauma.

In excitotoxicity, brain cells are dying as a result of being over-stimulated. It is not a disease in itself, but a second-stage disease process where healthy, undamaged brain cells die as a result of being exposed to excessive levels of chemicals released from the brain cells damaged by the original trauma.

Damaged neurons respond by dumping their stores of chemicals responsible for stimulating nerve impulses. These chemicals are known as neurotransmitters and include chemicals such as glutamic acid. This sudden spike in brain levels of glutamic acid results in the surrounding healthy neurons being over-stimulated, which in turn results in those brain cells' death. These healthy, undamaged neurons, now dying, then dump their neurotransmitters causing their neighbouring healthy neurons to die, and so on. This cascade of brain cell death progressively expands the region of death of brain cells out from the original injury up to 10 times that of the original injury.

This expanded area of brain cell death is believed to account for the protracted rehabilitation times, poor recovery rates, and even death following traumatic head and spinal damage and stroke. The long-term harmful effects of repeated concussion in certain sports (for example, football and boxing) are the result of

excitotoxicity. For example, hearing loss associated with prolonged exposure to loud noise (e.g. military personnel) is the result of excitotoxicity.

An eminent team of neurophysiologists at the University of New South Wales recently identified a key mechanism responsible for excitotoxicity. It involves a protein known as *short transient receptor potential channel 3 (TrpC3)*, which responds to glutamic acid overload by allowing healthy nerve cells to be excessively stimulated to the point of death.

The Company originally identified a compound, NYX-104, with the capacity *in vitro* to block the ability of TrpC3 to respond to an overload of glutamic acid. NYX-104 belongs to the same chemical family (benzopyran) as idronoxil, the active component in NOX66. In light of the fact that the LIPROSE drug delivery technology enabled the passage of idronoxil across the blood-brain barrier, the same delivery platform was applied to NYX-104. The Company subsequently successfully obtained proof-of-concept that NYX-104 can inhibit the extent of excitotoxicity in a model of human stroke in a mouse. Delivered daily for 5 days after the model of human stroke, NYX-104 reduced the cascade of death of brain cells extending out from the original trauma to a significant degree.

Based on this key pre-clinical proof-of-concept evidence, the Company believes that NYX-104 may be a first-in-class drug with significant commercial potential.

The ability to deliver a drug that can limit the degree of brain cell death shortly after stroke or traumatic injury to the brain or spinal cord holds significant promise of shorter rehabilitation times and fewer long-term disabilities for sufferers of acute brain damage.

The Company has assigned all intellectual property rights associated with NYX-104 to Norbio No. 1. A provisional patent application in respect of NYX-104 was lodged in the United States on 15 September 2017.

At this point in time, the clinical indications most likely to be pursued first by Norbio No. 1 are stroke and traumatic brain injury.

If Resolution 1 is passed by Shareholders, the scope of work for the development of NYX-104 over the next 12 months includes:

- development of different dosage forms of NYX-104;
- tissue distribution and brain PK studies; and
- pre-IND animal toxicology studies.

The 12-month budget for the development of NYX-104 is US\$1.8 million. It is intended that this will be funded by the raising of capital by Nyrada and not from the Company's funds.

## **Norbio No. 2 Intellectual Property – *Inhibitor of neuro-inflammation***

Norbio No. 2 owns all intellectual property rights associated with a drug that seeks to block inflammation both within the brain and in peripheral nerves.

Inflammation is a partner pathology process with excitotoxicity in any disease or event that damages neurons, both within the central nervous system (brain, spinal cord) and in peripheral nerves (for example, in limbs). In the brain, inflammation contributes to the disease process following trauma, stroke, or neurodegenerative diseases (for example, Alzheimer's, Parkinson's, amyotrophic lateral sclerosis, multiple sclerosis); in peripheral nerves, it contributes to peripheral neuropathies including diabetic neuropathy and toxicity from chemotherapy.

The compound, NYX-105, has been identified by Noxopharm as having the desired anti-inflammatory properties considered pertinent to neuro-inflammatory processes in the brain, spinal cord and peripheral nerves. Similar to NYX-104, NYX-105 belongs to the same chemical family as idronoxil, meaning that the

LIPROSE drug delivery technology should be able to facilitate its delivery across the blood-brain barrier and blood-nerve barrier.

At this point in time, the initial (human) clinical indication to be targeted by Norbio No. 2 is peripheral nerve damage associated with chemotherapy.

The Company has assigned all intellectual property rights associated with NYX-105 to Norbio No. 2. A provisional patent application in respect of NYX-105 was lodged in the United States on 15 September 2017.

If Resolution 1 is passed by Shareholders, the scope of work for the development of NYX-105 over the next 12 months includes:

- formulation of an intravenous dosage form;
- proof-of-concept in animal model of carboplatin-induced neuropathy;
- tissue distribution and PK studies; and
- pre-IND animal toxicology studies.

The 12-month budget for the development of NYX-105 is US\$1.9 million. It is intended that this will be funded by the raising of capital by Nyrada and not from the Company's funds.

### **Cardio Intellectual Property – Inhibitor of PCSK9**

Cardio owns the intellectual property rights in a drug development program known as the 'PCSK9' Program. The objective of the PCSK9 Program is the development of a drug that seeks to lower LDL cholesterol levels in patients with hypercholesterolaemia and which offers significant clinical advantage over current drug therapies.

The target of the drug is *proprotein convertase subtilisin/kexin type 9 (PCSK9)*, and the role of the drug is to block the ability of the PCSK9 protein to bind to the low-density lipoprotein (LDL)-receptor complex. In so doing, more LDL is removed from the blood.

PCSK9 is now identified as a preferred drug target in the treatment of elevated levels of LDL cholesterol, with anti-PCSK9 therapy based on monoclonal antibodies providing better response rates and superior cardiovascular health benefits than the drugs known as 'statin drugs' which have dominated this field for the past 25 years.

Early attempts by pharmaceutical companies to develop a 'statin-like' drug (that is, an oral small molecule drug) targeting the PCSK9-LDLR interaction failed, leading to the alternative approach of monoclonal antibodies, of which two have been marketed since 2015. Both monoclonal drugs have to be administered by injection on a fortnightly or monthly basis, come at significant cost, and their use is limited to patients where other therapies have failed or are not well tolerated.

A team of Australian chemists has managed to design a small molecule that effectively blocks PCSK9's ability to bind to the LDL-receptor complex. A provisional patent application in respect of the PCSK9 Program was lodged in Australia on 17 March 2017.

If Resolution 2 is passed by Shareholders, the scope of work over the next 12 months for the development of the PCSK9 Program includes:

- confirmation of Alt-30 as the lead drug candidate;
- proof-of-concept study in a transgenic mouse model;
- formulation of an oral dosage form;
- tissue distribution and PK studies; and
- pre-IND animal toxicology studies.

The 12-month budget for the development of the PCSK9 Program is US\$2.5 million. It is intended that this will be funded by the raising of capital by Nyrada and not from the Company's funds.

## Resolution 1 Approval of Norbio Acquisition

### 3. Background

Resolution 1 relates to the Norbio Acquisition, being the acquisition of the total issued share capital of Norbio No. 1 and Norbio No. 2 by Nyrada from the Company.

#### *Summary of Norbio Acquisition*

As announced on 25 September 2017, the Company has entered into a share sale and subscription agreement with Nyrada in relation to the Norbio Acquisition (**Norbio Agreement**).

The material terms of the Norbio Agreement are as follows:

- **Consideration:** in consideration for the total issued share capital of Norbio No. 1 and Norbio No. 2, the Company will receive fully paid ordinary shares in Nyrada so that, after completion of the Norbio Agreement and the Cardio Agreement, its shareholding in Nyrada is equal to 66.7% of the total issued capital of Nyrada (**Nox Consideration Shares**); and
- **Conditions Precedent:** completion under the Norbio Agreement is conditional upon:
  - the Company obtaining any approvals for the transactions contemplated by the Norbio Agreement which are required under the Corporations Act or the ASX Listing Rules, including any approvals which are required under Chapter 2E of the Corporations Act and ASX Listing Rule 10.1; and
  - the Company obtaining any necessary approvals to the transactions contemplated by Norbio Agreement from ASIC or ASX.

The Norbio Agreement otherwise contains terms and conditions considered customary for an agreement of its nature.

If completion does not occur under the Cardio Agreement, Nyrada will become a wholly-owned subsidiary of the Company.

#### *Summary of Norbio No. 1's and Norbio No. 2's Assets*

Norbio No. 1 owns the intellectual property rights in a drug known as NYX-104. Norbio No. 2 owns the intellectual property rights in a drug known as NYX-105. For more information in relation to the intellectual property rights held by Norbio No. 1 and Norbio No. 2, see section 2 of this Explanatory Statement.

### 4. ASX Listing Rule 10.1

ASX Listing Rule 10.1 provides that an entity must ensure that neither it, nor any of its child entities, disposes a substantial asset to, amongst other persons, a related party or a child entity of the entity without the approval of the holders of the entity's ordinary securities.

Nyrada is both a related party and a child entity of the Company for the purposes of ASX Listing Rule 10.1.

#### *Substantial asset*

For the purposes of ASX Listing Rule 10.1, an asset is substantial if its value, or the value of the consideration for it is, or in ASX's opinion is, 5% or more of the equity interests of the entity as set out in the latest accounts given to ASX under the ASX Listing Rules.

The equity interests of the Company as defined by the ASX Listing Rules and as set out in the latest accounts given to ASX under the ASX Listing Rules (being for the twelve months ending 30 June 2017) were \$2,467,514. 5% of this amount is \$123,375.

As the value of the total issued share capital of Norbio No. 1 and Norbio No. 2 is more than 5% of the equity interests of the Company as set out in the latest accounts given to ASX under the ASX Listing Rules, the completion of the Norbio Agreement will result in the disposal of a substantial asset.

### ***Related party***

For the purposes of ASX Listing Rule 10.1, a related party of a public company includes an entity that acts in concert with a related party of the public company on the understanding that the related party will receive a financial benefit if the public company gives the entity a financial benefit. Altnia is controlled by Dr. Ian Dixon and, therefore, is a related party of Noxopharm. As completion of the Cardio Acquisition is conditional upon completion of the Norbio Acquisition, Altnia will only receive a financial benefit, being shares in Nyrada, if the Company gives a financial benefit to Nyrada, being the share capital of Norbio No. 1 and Norbio No. 2.

Therefore, Nyrada is, in addition to being a child entity of the Company, a related party of the Company for the purposes of ASX Listing Rule 10.1.

### ***Requirement for shareholder approval***

As a result of the above conclusions, the completion of the Norbio Acquisition will result in the disposal of a substantial asset to a child entity and a related party and the Company is therefore required to seek Shareholder approval under ASX Listing Rule 10.1.

## **5. Independent Expert Report**

ASX Listing Rule 10.10.2 requires a notice of meeting containing a resolution under ASX Listing Rule 10.1 to include a report on the transaction from an independent expert.

The Independent Expert Report set out in Annexure A sets out a detailed independent examination of the Norbio Acquisition, the Cardio Acquisition and the Transaction to enable Shareholders to assess the merits of the Norbio Acquisition, the Cardio Acquisition, and the Transaction and decide whether to approve Resolution 1 and Resolution 2. The Independent Expert has concluded that the Norbio Acquisition, the Cardio Acquisition and the Transaction are **fair and reasonable** to Shareholders whose votes are not to be disregarded on Resolution 1 and Resolution 2.

Shareholders are urged to carefully read the Independent Expert Report to understand its scope, methodology of the valuation and the sources of information and assumptions made.

The Independent Expert Report is also available on the Company's website at [www.noxopharm.com](http://www.noxopharm.com). If requested by a Shareholder, the Company will send to the Shareholder a hard copy of the Independent Expert Report at no cost.

## **6. Chapter 2E of the Corporations Act**

For a public company, or an entity that the public company controls, to give a financial benefit to a related party of the public company, the public company or entity must:

- obtain the approval of the public company's members in the manner set out in sections 217 to 227 of the Corporations Act; and
- give the benefit within 15 months following such approval,

unless the giving of the financial benefit falls within an exception set out in sections 210 to 216 of the Corporations Act.

The transfer of the total issued share capital of Norbio No. 1 and Norbio No. 2 by the Company to Nyrada in accordance with the terms of the Norbio Agreement constitutes a financial benefit and Nyrada is a related party of the Company for the purposes of the Transaction by virtue of section 228(7) of the Corporations Act. For an explanation as to how section 228(7) of the Corporation Act applies, see section 4 of this Explanatory Statement.

None of the exceptions set out in sections 210 to 216 of the Corporations Act apply to the transfer of the total issued share capital of Norbio No. 1 and Norbio No. 2 to Nyrada. As a result, the Company seeks Shareholder approval for the transfer of the total issued share capital of Norbio No. 1 and Norbio No. 2 by the Company to Nyrada under Chapter 2E of the Corporations Act.

The following information is provided in accordance with section 219 of the Corporations Act.

***The related parties to whom Resolution 1 would permit the financial benefit be given***

Nyrada Inc, and if Resolution 2 is passed, Altnia Holdings Pty Ltd ACN 133 349 238 as trustee for the I. Dixon Family Trust (controlled by Dr. Ian Dixon, a Director of the Company)

***The nature of the financial benefit***

The financial benefit to Nyrada is the total issued share capital of Norbio. No 1 and Norbio No. 2, which are currently wholly-owned subsidiaries of the Company.

The financial benefit to Altnia is the issue of the Altnia Consideration Shares by Nyrada to Altnia. Upon completion of the Cardio Agreement and the Norbio Agreement, the capital structure of Norbio will be as follows:

<b>Shareholder</b>	<b>Number of Nyrada Shares</b>	<b>% or Nyrada Shares on issue</b>
Altnia Holdings Pty Ltd ACN 133 349 238 as trustee for the I. Dixon Family Trust	3,330	33.3%
Noxopharm Limited ACN 608 966 123	6,670	66.7%

***Other information that is reasonably required by members to make a decision and that is known to the Company or any of the Directors***

There is no other information known to the Company or any of the Directors, except that the Company has obtained taxation advice that it should be eligible for scrip-for-scrip rollover relief for any capital gains tax payable on the disposal the total issued share capital of Norbio No. 1 and Norbio No. 2 to Nyrada.

***Directors' recommendation***

Each of the Directors of the Company (Dr. Ian Dixon abstaining) recommends that you vote in favour of Resolution 1.

The reasons for this recommendation are that the Directors (other than Dr. Ian Dixon) believe that the establishment of a non-oncology research business to be conducted by Nyrada (which is implemented by the Norbio Acquisition):

- maximises the development opportunities for the Non-Oncology Drug Assets;
- maximises the Company's development opportunities for oncology drugs by removing a potentially dilutive and distractive asset;
- potentially maximises the market valuation of the Non-Oncology Drug Assets; and



- provides an opportunity for assets held by subsidiaries of the Company that currently have minimal market value to be realised, with the possibility that such realisation will increase the value of the Company's assets and consequently its share price.

## Resolution 2 Approval of Cardio Acquisition

### 7. Background

Resolution 2 relates to the Cardio Acquisition, being the acquisition of the total issued share capital of Cardio by Nyrada from Altnia.

Altnia is controlled by Dr. Ian Dixon, a Director.

#### *Summary of Cardio Acquisition*

As announced on 25 September 2017, Nyrada has entered into a share sale and subscription agreement with Altnia and Dr. Ian Dixon in relation to the Cardio Acquisition (**Cardio Agreement**).

The material terms of the Cardio Agreement are as follows:

- **Consideration:** in consideration for the total issued share capital of Cardio, Altnia will receive fully paid ordinary shares in Nyrada so that, after completion of the Norbio Agreement and the Cardio Agreement, its shareholding is equal to 33.3% of the total issued capital of Nyrada after completion of the Norbio Acquisition (**Altnia Consideration Shares**). The Altnia Consideration Shares will be subject to a restriction agreement, the details of which are provided below;
- **Conditions Precedent:** completion under the Cardio Agreement is conditional upon:
  - the Company obtaining any approvals for the transactions contemplated by the Norbio Agreement which are required under the Corporations Act or the ASX Listing Rules, including any approvals which are required under Chapter 2E of the Corporations Act and ASX Listing Rule 10.1; and
  - the Company obtaining any necessary approvals to the transactions contemplated by Norbio Agreement from ASIC or ASX;
- **Inter-conditionality:** completion of the Cardio Agreement is conditional upon completion of the Norbio Agreement;
- **Termination:** if the Cardio Agreement is terminated for any reason prior to completion, Altnia must transfer the one share that it holds in Nyrada to Nyrada (as a share buy-back) or as directed by Nyrada for \$1 within 10 Business Days of the date of termination of the Cardio Agreement; and
- **Guarantee:** Dr. Ian Dixon guarantees Altnia's due and punctual performance of its liabilities under the Cardio Agreement and, as a separate and additional liability, indemnifies Nyrada against any loss or liability which Nyrada suffers, incurs or is liable for at any time, arising from any default or delay in the due and punctual performance of Altnia's obligations under the Cardio Agreement.

The Cardio Agreement otherwise contains terms and conditions considered customary for an agreement of its nature.

#### *Restriction agreement*

ASX requires that the Altnia Consideration Shares are subject to a restriction agreement. This restriction agreement will also cover any other shares that Altnia holds in Nyrada. The restriction agreement will be in a form substantially similar to Appendix 9A of the ASX Listing Rules. The term of the restriction agreement will be 12 months, commencing on the later of the date on which the restriction agreement is executed and the date of issue of the Altnia Consideration Shares. At completion under the Cardio Agreement, Altnia must provide to Nyrada a counterpart of the restriction agreement duly executed by Altnia.

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### ***Summary of Cardio's Assets***

Cardio owns the intellectual property rights in a drug development program known as the 'PCSK9' Program. For more information in relation to the 'PCSK9' Program, see section 2 of this Explanatory Statement.

## **8. ASX Listing Rule 10.1**

ASX Listing Rule 10.1 provides that an entity must ensure that neither it, nor any of its child entities, acquires a substantial asset from, amongst other persons, a related party of the entity without the approval of the holders of the entity's ordinary securities.

The Company and Altnia own the shares in Nyrada equally. Nyrada is a child entity of the Company for the purposes of ASX Listing Rule 10.1, as Nyrada is controlled by the Company within the meaning of section 50AA of the Corporations Act.

### ***Substantial asset***

For the purposes of ASX Listing Rule 10.1, an asset is substantial if its value, or the value of the consideration for it is, or in ASX's opinion is, 5% or more of the equity interests of the entity as set out in the latest accounts given to ASX under the ASX Listing Rules.

The equity interests of the Company as defined by the ASX Listing Rules and as set out in the latest accounts given to ASX under the ASX Listing Rules (being for the twelve months ending 30 June 2016) were \$2,467,514. 5% of this amount is \$123,375.

As the value of the total issued share capital of Cardio is valued at more than 5% of the equity interests of the Company as set out in the latest accounts given to ASX under the ASX Listing Rules, the completion of the Cardio Acquisition will result in the acquisition of a substantial asset by a child entity of the Company.

### ***Related party***

For the purposes of ASX Listing Rule 10.1, a related party of a public company includes an entity controlled by a director of the public company.

Dr. Ian Dixon, a Director, is the sole director of Altnia. Further, Dr. Ian Dixon and his wife own all of the shares in Altnia and are the appointors of the I. Dixon Family Trust. As a result, he controls Altnia. Therefore, for the purposes of ASX Listing Rule 10.1, Altnia is a related party of the Company.

### ***Requirement for shareholder approval***

As a result of the above conclusions, the completion of the Cardio Agreement will result in the acquisition of a substantial asset by a child entity of the Company from a related party of the Company and the Company is therefore required to seek Shareholder approval under ASX Listing Rule 10.1.

## **9. Independent Expert Report**

ASX Listing Rule 10.10.2 requires a notice of meeting containing a resolution under ASX Listing Rule 10.1 to include a report on the transaction from an independent expert.

The Independent Expert Report set out in Annexure A sets out a detailed independent examination of the Cardio Acquisition, the Norbio Acquisition and the Transaction to enable Shareholders to assess the merits of the Cardio Acquisition, the Norbio Acquisition and the Transaction and decide whether to Resolution 1 and Resolution 2. The Independent Expert has concluded that the Cardio Acquisition, the Norbio Acquisition and the Transaction are **fair and reasonable** to Shareholders whose votes are not to be disregarded on Resolution 1 and Resolution 2.

Shareholders are urged to carefully read the Independent Expert Report to understand its scope, methodology of the valuation and the sources of information and assumptions made.

The Independent Expert Report is also available on the Company’s website at [www.noxopharm.com.au](http://www.noxopharm.com.au). If requested by a Shareholder, the Company will send to the Shareholder a hard copy of the Independent Expert Report at no cost.

**10. Chapter 2E of the Corporations Act**

For a public company, or an entity that the public company controls, to give a financial benefit to a related party of the public company, the public company or entity must:

- obtain the approval of the public company’s members in the manner set out in sections 217 to 227 of the Corporations Act; and
- give the benefit within 15 months following such approval,

unless the giving of the financial benefit falls within an exception set out in sections 210 to 216 of the Corporations Act.

The Company controls Nyrada. The issue of the Altnia Consideration Shares by Nyrada to Altnia in accordance with the terms of the Cardio Agreement constitutes the giving of a financial benefit by Nyrada to Altnia, which is a related party of the Company by virtue of it being controlled by Dr. Ian Dixon, a Director.

None of the exceptions set out in sections 210 to 216 of the Corporations Act apply to the issue of the Altnia Consideration Shares to Altnia. As a result, the Company seeks Shareholder approval for the issue of Altnia Consideration Shares to Altnia under Chapter 2E of the Corporations Act.

The following information is provided in accordance with section 219 of the Corporations Act.

***The related parties to whom Resolution 2 would permit the financial benefit be given***

Altnia Holdings Pty Ltd ACN 133 349 238 as trustee for the I. Dixon Family Trust (controlled by Dr. Ian Dixon, a Director)

***The nature of the financial benefit***

The financial benefit is the issue of the Altnia Consideration Shares by Nyrada to Altnia. Upon completion of the Cardio Agreement and the Norbio Agreement, the capital structure of Nyrada will be as follows:

<b>Shareholder</b>	<b>Number of Nyrada Shares</b>	<b>% or Nyrada Shares on issue</b>
Altnia Holdings Pty Ltd ACN 133 349 238 as trustee for the I. Dixon Family Trust	3,330	33.3%
Noxopharm Limited ACN 608 966 123	6,670	66.7%

***Other information that is reasonably required by members to make a decision and that is known to the Company or any of the Directors***

There is no other information known to the Company or any of the Directors.

***Directors’ recommendation***

Each of the Directors of the Company (Dr. Ian Dixon abstaining) recommends that you vote in favour of Resolution 2.

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The reasons for this recommendation are as follows:

- a small molecule drug that inhibits PCSK9 represents a potential significant commercial opportunity; and
- the current status of the development of the PCSK9 Program is sufficiently advanced to have lowered the risk of failure of the PCSK9 Program to a reasonable degree.

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### GLOSSARY

In the Notice of Meeting and Explanatory Statement the following terms have the following meanings:

**AEST** means Australian Eastern Standard Time.

**Altnia** means Altnia Holdings Pty Ltd ACN 133 349 238 as trustee for the I. Dixon Family Trust.

**Altnia Consideration Shares** has the meaning given to that term in section 7 of the Explanatory Statement.

**ASIC** means the Australian Securities and Investments Commission.

**ASX** means ASX Limited.

**ASX Listing Rules** or **Listing Rules** means the listing rules of ASX.

**Board** means the board of directors of the Company.

**Cardio** means Cardio Therapeutics Pty Ltd ACN 167 825 201.

**Cardio Acquisition** has the meaning given to that term in section 1 of the Explanatory Statement.

**Cardio Agreement** has the meaning given to that term in section 7 of the Explanatory Statement.

**Company** or **Noxopharm** means Noxopharm Limited ACN 608 966 123.

**Constitution** means the Company's constitution.

**Corporations Act** means *Corporations Act 2001* (Cth).

**Director** means a current director of the Company.

**Explanatory Statement** means the explanatory statement to this Notice of Meeting.

**Independent Expert Report** means the independent expert report in relation to the Norbio Acquisition, the Cardio Acquisition and the Transaction, which is set out in Annexure A.

**Independent Valuation** means the independent valuation of the intellectual property rights held by Norbio No. 1, Norbio No. 2 and Cardio, which is set out in Annexure B.

**Meeting** means the Extraordinary General Meeting of the Shareholders of the Company to be held at 10:00am on Monday, 6 November 2017, to which the Notice of Meeting and Explanatory Statement relate.

**Non-Oncology Drug Assets** has the meaning given to that term in section 2 of the Explanatory Statement.

**Norbio Acquisition** has the meaning given to that term in section 1 of the Explanatory Statement.

**Norbio Agreement** has the meaning given to that term in section 3 of the Explanatory Statement.

**Norbio No. 1** means Norbio No. 1 Pty Ltd ACN 619 956 722.

**Norbio No. 2** means Norbio No. 2 Pty Ltd ACN 619 956 973.

**Norbio Original Subsidiaries** means Norbio No. 1 and Norbio No. 2.

**Nox Consideration Shares** has the meaning given to that term in section 3 of the Explanatory Statement.

**Notice** or **Notice of Meeting** means this notice of meeting.

## NOTICE OF EXTRAORDINARY GENERAL MEETING

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**Nyrada** means Nyrada Inc.

**Nyrada Shares** means fully paid ordinary shares in Nyrada.

**PCSK9** has the meaning given to that term in section 2 of the Explanatory Statement.

**PCSK9 Program** has the meaning given to that term in section 2 of the Explanatory Statement.

**Resolution** means a resolution referred to in the Notice.

**Share** means a fully paid ordinary share in the capital of the Company.

**Shareholder** means a holder of Shares.

**Transaction** means the Cardio Acquisition and the Norbio Acquisition.

Words importing the singular include the plural and vice versa.

All references to currency are in Australian dollars.

**NOXOPHARM LTD**

ACN 608 966 123

Registered Office: Suite 1, Level 6, 50 Queen Street, Melbourne VIC 3000

**CERTIFICATE OF APPOINTMENT OF CORPORATE REPRESENTATIVE**

---

*(Name of the body corporate making the appointment, in block letters)*

**hereby certifies that it has appointed**

---

*(Name of the appointee or if the appointment is to be by reference to a position held, the position held in the body corporate making the appointment, in block letters)*

**to act as its representative at the Extraordinary General Meeting of shareholders Noxopharm Ltd to be held on Monday, 6 November 2017 and at any meeting held subsequent and pursuant to an adjournment of that meeting.**

Dated this \_\_\_\_\_ day of \_\_\_\_\_

Executed for and on behalf of: ) (\* Affix common seal  
 ) here if required

---

in accordance with its constitution by: )  
 )

---

Director /  
Sole Director and Sole Company Secretary  
*(please delete one)*

---

Director/Company Secretary  
*(please delete one)*

**This form of appointment may be sent to the Company (or its share registry) in advance of the meeting or submitted at the time of registration before or during the meeting.**

(\*) The common seal of the body corporate making the appointment must be affixed if required by its constitution.

**NOXOPHARM LIMITED**  
**ACN 608 966 123**

Registered Office: Suite 1, Level 6, 50 Queen Street, Melbourne VIC 3000

If you propose to attend and vote at this Extraordinary General Meeting, please bring this form with you. This will assist in registering your attendance

[EntityRegistrationDetailsLine1Envelope]  
[EntityRegistrationDetailsLine2Envelope]  
[EntityRegistrationDetailsLine3Envelope]  
[EntityRegistrationDetailsLine4Envelope]  
[EntityRegistrationDetailsLine5Envelope]  
[EntityRegistrationDetailsLine6Envelope]

[BARCODE]

**Holder Number:**  
[HolderNumber]

**APPOINTMENT OF PROXY**

I/We being a member/s of **NOXOPHARM LIMITED ACN 608 966 123 (Company)** and entitled to attend and vote hereby appoint.

<b>A</b>	the Chair of the Meeting (mark box)	<input type="checkbox"/>	OR if you are NOT appointing the Chair of the Meeting as your proxy, please write the name of the person or body corporate (excluding the registered security holder you are appointing as your proxy)	<input style="width: 90%;" type="text"/>
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Or failing the person/body corporate named, or if no person/body corporate is named, the Chair of the Meeting, as my/our proxy to act generally at the meeting on my/our behalf and to vote in accordance with the following instructions (or if no directions have been given, as the proxy sees fit) at the Extraordinary General Meeting of the Company to be held at Suite 3, Level 4, 828 Pacific Highway, Gordon NSW 2072 at 10:00am on Monday, 6 November 2017 and at any adjournment of that meeting. Where more than one proxy is to be appointed or where voting intentions cannot be adequately expressed using this form an additional form of proxy is available on request from the share registry. Proxies will only be value and accepted by the Company if they are signed and received at the Company's registered office no later than 48 hours before the meeting.

The Chair intends to vote undirected proxies IN FAVOUR of resolutions.

Should you desire to direct your proxy how to vote on any resolution please insert  in the appropriate box below.

Resolutions		For	Against	Abstain*
Resolution 1	That, for the purposes of Chapter 2E of the Corporations Act, ASX Listing Rule 10.1 and for all other purposes, the acquisition by Nyrada of the entire issued share capital of Norbio No. 1 and Norbio No. 2 from the Company on the terms and conditions set out in the Explanatory Statement is approved.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 2	That, subject to Resolution 1 being passed, for the purposes of Chapter 2E of the Corporations Act, ASX Listing Rule 10.1 and for all other purposes, the acquisition by Nyrada of the entire issued share capital of Cardio from Altnia and the issue of 3,329 Nyrada Shares to Altnia on the terms and conditions set out in the Explanatory Statement are approved.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

\*If you mark the Abstain box for a particular Resolution, you are directing your proxy not to vote on your behalf on a show of hands or on poll and your votes will not be counted in computing the required majority on a poll.

**B** PLEASE SIGN HERE This section *must* be signed in accordance with the instructions overleaf to enable your directions to be implemented

<b>Securityholder 1</b>	<b>Securityholder 2</b>	<b>Securityholder 3</b>
<input style="width: 90%; height: 20px;" type="text"/>	<input style="width: 90%; height: 20px;" type="text"/>	<input style="width: 90%; height: 20px;" type="text"/>
Director / Sole Director and Company Secretary / Individual	Director/Company Secretary / Individual	Director / Individual

<hr/> Contact Name	<hr/> Contact Daytime Telephone or Email	<hr/> Date
--------------------	--	------------



## PROXY INSTRUCTIONS:

### Generally

A shareholder entitled to attend and vote at the Court ordered meeting convened by the Notice is entitled to appoint not more than 2 proxies to vote on the shareholder's behalf. A proxy need not be a shareholder. The proxy appointed may be a standing appointment for all general meetings until it is revoked. Additional proxy forms are available from the Company.

If a representative of a shareholder or proxy is to attend the meeting the appropriate "Certificate of Appointment of Corporate Representative" must be produced prior to admissions. A form of the certificate appears on page 21.

### Appointing Two Proxies

A shareholder entitled to cast 2 or more votes may appoint 2 proxies. Where 2 proxies are appointed, if the appointments do not specify the percentage or number of votes that each proxy may exercise, each proxy may exercise one half of your votes. Fractions of votes will be disregarded.

### Signing Instructions

Individuals:	The shareholder must sign personally.
Joint Holdings:	If the holding is in more than 1 name, all of the shareholders must sign.
Company:	Where the company has a sole director who is also the sole company secretary, this form must be signed by that person. If the company (pursuant to section 204A of the Corporations Act) does not have a company secretary, a sole director can also sign alone. Otherwise this form must be signed by a director jointly with either another director or a company secretary. Please sign in the appropriate place to indicate the office held.
Power of Attorney:	The attorney must sign and the power of attorney must be deposited at the Company's registered office for inspection and return, when the proxy is lodged.

### Lodgement of a Proxy

Proxy forms (and the power of attorney, if any, under which the proxy form is signed) must be lodged at, or send by facsimile transmission to, the offices of the Company so that it is received no later than 10:00am on Saturday, 4 November 2017.

### Documents may be lodged:

IN PERSON	Noxopharm Ltd, Suite 310, Level 3, 50 Holt St, Surry Hills NSW 2010
BY MAIL	Noxopharm Ltd, P.O. Box 2226, Strawberry Hills NSW 2012
BY FAX	Noxopharm Ltd, (02) 9199 9600.

### Your Address

This is your address as it appears on the Company's share register. If this information is incorrect, please make the correction on the form and sign it. Security holders sponsored by a broker (in which case your reference number overleaf will commence with an "X") should advise your broker of any changes. You cannot change ownership of your share using this form

**Annexure A – Independent Expert Report**

The Independent Expert, Moore Stephens (Vic) Pty Ltd, has concluded that the Norbio Acquisition, the Cardio Acquisition and the Transaction are **fair and reasonable** to non-associated Shareholders.



MOORE STEPHENS

[www.moorestephens.com.au](http://www.moorestephens.com.au)

Serious about Success®

**NOXOPHARM LIMITED**  
**RELATED PARTY TRANSACTION REQUIRING SHAREHOLDER APPROVAL UNDER**  
**CHAPTER 2E OF THE CORPORATIONS ACT AND ASX LISTING RULE 10.1**

**Independent Expert's Report**

**8 SEPTEMBER 2017**

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8 September 2017

The Directors  
Noxopharm Limited  
Suite 1  
Level 6, 50 Queen Street  
MELBOURNE VIC 3000

Dear Sirs,

## INDEPENDENT EXPERT'S REPORT

### RELATED PARTY TRANSACTION REQUIRING SHAREHOLDER APPROVAL UNDER CHAPTER 2E OF THE CORPORATIONS ACT AND ASX LISTING RULE 10.1

As Directors of Noxopharm Limited (**Noxopharm**, or **Company**) you have requested Moore Stephens (Vic) Pty Ltd (**Moore Stephens**) to prepare an Independent Expert's Report (Report) in relation to a proposed transfer of assets to a USA incorporated subsidiary (**NYRADA**) and to issue shares in NYRADA to the Company and a related party in exchange for the rights to a prospective non-cancer therapeutic drug compounds.

The Proposal (as described in Section 1.1 below) will be presented to Noxopharm Shareholders for approval at an Extraordinary General Meeting to be held on or about 9 November 2017 (**EGM**).

You have requested Moore Stephens to provide an opinion on whether the Cardio Acquisition and the Transfer, the subject of Resolutions 1 and 2 in the Notice of Meeting (**NOM**), is fair and reasonable to the non-associated shareholders of the Company (**Noxopharm Shareholders**).

Unless otherwise specified, all dollar amounts in the Report are in Australian Dollars (AUD) and all terms have the same meaning as in the NOM.

## 1. INTRODUCTION

### 1.1 Background

1. Noxopharm (ASX: **NOX**) is an Australian publically listed company engaged in the development of compounds to address the problem of drug and radio-resistance in cancer cells, the major hurdle facing improved survival prospects for cancer patients. The first pipeline product is NOX66, with later generation drug candidates under development in an R&D program. The Company's Initial Public Offering of its shares on the Australian Securities Exchange raised \$6 million in August 2016.
2. The Company also has a number of prospective compounds targeting non-cancer therapeutic drugs. The Company intends to transfer (**Transfer**)<sup>1</sup> two compounds, NYX-104 and NYX-105 (**NOX Assets**) to the NYRADA subsidiary for an approximately 2/3rd equity interest in NYRADA. The remaining approximately 1/3rd equity interest of NYRADA will be issued to Dr. Ian Dixon (or his associate) to acquire another prospective non-cancer therapeutic compound known as PCSK9, (**Dixon Asset**) (**Cardio Acquisition**). The Company has filed provisional patents for the NOX Assets.

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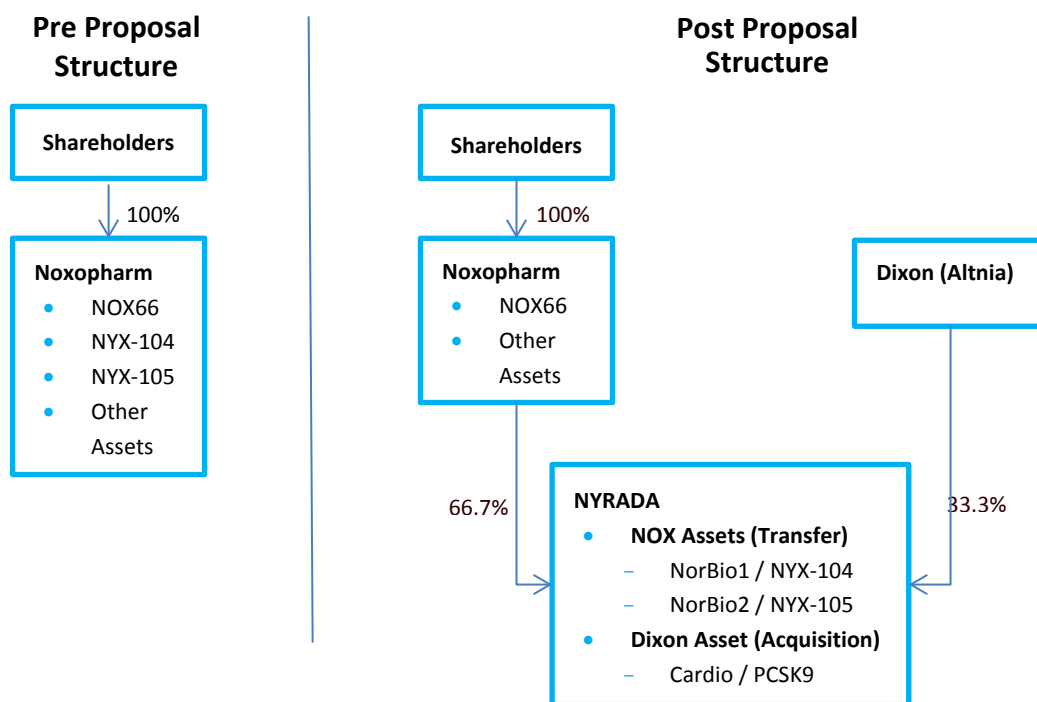
<sup>1</sup> The Transfer will include a series of steps and interposed entities being **NorBio 1** and **NorBio 2** (who will hold NYX-104 and NYX-105).

3. The Company's intention is then to raise funding for NYRADA to undertake further development of the three drug assets. The details, pricing and strategy of any fund raising is not finalised and the prospect of a fundraising is not a pre-condition of the Transfer and Cardio Acquisition.
4. The Transfer of assets to NYRADA is considered by the Directors as a disposal of substantial assets to a related party as set out in the NOM. The issue of NYRADA shares to Dr Ian Dixon (or his associate) is considered a related party transaction as he is also a Director of Noxopharm.
5. Details of the Proposal will be communicated to the Company's Shareholders by way of the NOM and accompanying Explanatory Memorandum.
6. Elements of the transaction are interdependent such that the Transfer and the Cardio Acquisition are therefore for the purposes of our Independent Expert Report referred to as the **Proposal**.

## 1.2 Cardio Acquisition

7. On 24 August 2017, Noxopharm announced a successful capital raising placement of 16.67 million shares at 33 cents per share raising \$5.5 million. This will result in the total of number of shares on issue of 101.84 million. The new capital is intended to accelerate clinical development of Noxopharm's core NOX66 drug development platform and does not relate to the Proposal. As such the capital raising does not form part of our analysis of the Proposal. No changes or dilution to the number of Noxopharm shares on issue are contemplated as part of the Proposal. The non-associated Noxopharm shareholders hold circa 100 million shares or 98.3% of the total shares on issue.
8. In addition to the above shareholding there are 22.6 million options outstanding with an exercise price of 30 cents expiring 28 February 2021.
9. We have disregarded the impact of Pre Proposal options in our fairness assessment as their potential dilutive impact (if any) is present regardless of whether existing shareholders approve the transaction or not.
10. The Transfer is the subject of Resolution 1 and the Cardio Acquisition is the subject of Resolution 2 in the NOM. An overview of each of the resolutions for which shareholder approval is sought is set out below:
  - *Resolution 1: Approval of NorBio 1 and 2 Acquisition.* This resolution is to approve the Transfer of the NOX Assets to NYRADA.
  - *Resolution 2: Approval of the Cardio Acquisition.* This resolution is to approve the acquisition by NYRADA of the Dixon Asset and the issue of shares in NYRADA to Dr. Ian Dixon's associate.

Full details in respect of each Resolution are set out in the Notice of Meeting and Explanatory Memorandum. A diagram of the Pre and Post Proposal structure is as follows:



- We highlight from the above diagram that Noxopharm Shareholders interest in the core oncology development program, NOX66 and other assets of Noxopharm, is unchanged Pre and Post Proposal<sup>3</sup>.
- The Cardio Acquisition and the Transfer (**Resolutions 1 and 2**) are the subject of our opinion and are, for the purposes of this Report, referred to collectively as **the Proposal**.

**2. PURPOSE AND SCOPE OF THIS REPORT**

- Noxopharm is a publically listed company incorporated in Australia and accordingly is subject to the regulations of the *Corporations Act 2011 (the Act)*, as well as ASX Listing Rules.
- Chapter 2E of the **Act** requires a public company to obtain shareholder approval when the company provides a financial benefit to a related party. However, under the Act shareholder approval is not required when the terms of the transaction are “no worse than on an arm’s length basis”.
- ASX Listing Rule 10.1 requires where there is an acquisition or disposal of a substantial asset from/to a related party or child entity, such transaction must be approved by shareholders. ASX Listing Rule 10.1 makes no exemption for benefits provided on “arm’s length terms”. The Directors are of the view that the Transfer of assets to NorBio 1 and 2 is the transfer of a substantial asset, as set out in the NOM. As described above, the Cardio Acquisition is an acquisition of an asset from a related party.

<sup>3</sup> Not shown in the above diagram is Noxopharm’s Pre Proposal interest in NYRADA which has been incorporated on an equal joint venture basis with Dixon / Altnia as set out in Section 1 of the Explanatory Memorandum. This is not shown as Pre Proposal NYRADA has no assets.

16. Notwithstanding the Directors' view that the Transfer and the Cardio Acquisition terms are "arms length", the Directors have determined that good governance is for the Cardio Acquisition and the Transfer to be approved by shareholders before proceeding to completion.
17. In accordance with the requirements of the Act, ASX Listing Rules and ASIC Regulatory Guides, the Directors of Noxopharm have engaged Moore Stephens to prepare an Independent Expert's Report for Noxopharm Shareholders to comment on the fairness and reasonableness of the Transfer and the Cardio Acquisition under the Proposal, to be included in the Explanatory Memorandum to be issued to Noxopharm shareholders.

### 3. EXECUTIVE SUMMARY OPINION

#### 3.1 General

18. Our report has been prepared having regard to ASIC Regulatory Guide 76 "Related Party transactions" (RG 76), Regulatory Guide 111 "Content of Expert's Reports" (RG 111), and Regulatory Guide 112 "Independence of Experts" (RG 112).
19. In forming our view of the Proposal we have had regard to the current value of Noxopharm Shares, and the financial impact (i.e. "Fairness" / quantitative assessment) and other qualitative aspects (i.e. "Reasonableness") of the Proposal for Noxopharm Shareholders.
20. In respect of our "Fairness" assessment, this assignment is also a Valuation Engagement as defined by Accounting Professional & Ethical Standards Board professional standard APES 225 'Valuation Services' (APES 225).
21. We have considered the terms of the Proposal in its entirety as outlined in the NOM and in this Report and as a result of our review and considering all the factors we are of the opinion that the Proposal is **fair and reasonable** to Noxopharm Shareholders.

#### 3.2 Fairness (quantitative assessment)

22. RG 111.57 states that a proposed related party transaction is 'fair' if the value of the financial benefit to be provided by the entity to the related party is equal to or less than the value of the consideration being provided to the entity. This comparison should be made:
  - a) assuming a knowledgeable and willing, but not anxious, buyer and a knowledgeable and willing, but not anxious, seller acting at arm's length; and
  - b) for control transactions, on the basis referred to in RG111.11.
23. The below table summarises the value of the NOX Assets and NYRADA equity interest therein provided compared to the value of the Dixon Asset acquired.



Table 2: Summary of value provided compared to asset acquired

\$ million	Low	Medium	High
Value of NOX Assets pre Proposal	Nil	4.65	8.94
Equity interest in NOX Assets provided	33.3%	33.3%	33.3%
<b>A) Value of NOX Asset provided as consideration</b>	<b>Nil</b>	<b>1.53</b>	<b>2.95</b>
Value of DIXON Assets acquired	Nil	2.60	5.25
Noxopharm's equity interest in the Dixon Assets	66.7%	66.7%	66.7%
<b>B) Noxopharm's equity interest in the Dixon Assets</b>	<b>Nil</b>	<b>1.72</b>	<b>3.47</b>
<b>Value difference (B-A, rounded)</b>	<b>Nil</b>	<b>0.19</b>	<b>0.52</b>

24. The above values at the Medium and High range are drawn from the independent technical specialist (**Acuity**) report commissioned by Noxopharm which accompanies the NOM. The Low range estimate of nil value is drawn from our own assessment which has been formed with the assistance of a technical specialist (**MSV Technical Specialist**) engaged directly by us.
25. Given that the Acuity report was commissioned by Noxopharm for the purposes of establishing the exchange value of assets under the Proposal, Moore Stephens commissioned the MSV Technical Specialist to opine on Acuity's report. The MSV Technical Specialist did not undertake a separate valuation and his work was solely based upon a review of the Acuity report. The MSV Technical Specialist concluded that the approach taken by Acuity in its valuation is reasonable. However it is the MSV Technical Specialist's practice to value pre-clinical assets or drugs with patents at the provisional stage at nil value.
26. Whilst we are satisfied with Acuity's report for our assessment purposes and we concur with the MSV Technical Specialist that due to the high degree of uncertainty in the assumptions underpinning Acuity's valuation, it is prudent to show a nil value at the Low range in Table 2. Not shown in Table 2 is Acuity's low range estimate of value of circa \$0.6 million for each of the (two) NOX Assets and (one) Dixon Asset.
27. Table 2 shows that the value difference between the value consideration paid and the asset value received is either nil to positive \$0.19-0.52 million. On this basis, the Proposal is likely to be fair to Noxopharm Shareholders and no financial benefit is given to Dixon in the Cardio Acquisition or Nyrada in the Transfer.
28. RG 111.53 also states that the Expert should consider the overall effect of the related party transaction. We consider the overall effect by comparing the Pre and Post proposal value of Noxopharm shares for the non-associated Noxopharm Shareholders.
29. The financial impact of the Proposal to Noxopharm Shareholders, based on the assessed value of Noxopharm shares held by them using the adopted valuation methodologies and basis, is summarised in the Table 3 below.

Table 3: Summary of Proposal on Noxopharm Shareholders per share value

Cents per share (rounded)	Low	Medium	High
Value of Noxopharm shares Pre Proposal	32.9	32.9	32.9
Value of Noxopharm shares Post Proposal	32.9	33.1	33.4
<b>Value accretion / (dilution)</b>	<b>Nil</b>	<b>0.2</b>	<b>0.5</b>

30. We have assessed the Pre Proposal value of Noxopharm to Noxopharm Shareholders to be 32.9 cents based upon the current implied liquid minority market value. Our adjustments to market value were to deduct unavoidable transaction costs of the Proposal.
31. In assessing the value of Noxopharm shares post Proposal we have also adopted an adjusted market value methodology. Our adjustments to market value were to add the net value difference between the NOX assets and the Dixon Assets drawn from Table 2.
32. Based on Table 3 above, we determine that the value of Noxopharm Shares post Proposal is nominally greater than the value of Noxopharm Shares pre Proposal under both the Medium and High values. At the Low value (i.e. Nil) the Proposal is neither value accretive or dilutive.
33. Based upon the foregoing assessment in accordance with ASIC guidelines, we are of the opinion that overall the Proposal is likely to be **fair** to Noxopharm Shareholders.

### 3.3 Control premium

34. RG 111.11 suggests that when assessing the value of a company's shares for the purposes of approval under Item 7 of s611 (i.e. a share issue akin to a takeover offer) the expert should consider a premium for control. An acquirer could be expected to pay a premium for control due to the advantages they will receive should they obtain 100% control of another company.
35. Whilst the concept of control in RG 111.11 is incorporated by reference in RG 111.57 in respect of related party transactions, in our view the substance of the Proposal is not a control transaction and the consideration of control premiums (or lack thereof) is unwarranted.
36. This is because under the Proposal, Noxopharm shareholdings are unchanged pre and post Proposal. In addition whilst Noxopharm's equity interest in the NOX Assets is diluted from 100% in exchange for acquiring the Dixon Assets, at the conclusion of the Proposal Noxopharm will still hold a 66.7% controlling interest in NYRADA which will hold the NOX Assets.

### 3.4 Other qualitative factors of the proposal

37. In assessing if the advantages of the Proposal outweigh the disadvantages we have had regard to the following:

#### Advantages of the Proposal

- The Proposal is fair.
- The Proposal is non-cash and does not impact Noxopharm's solvency.
- Noxopharm Shareholders will gain an interest in a complimentary IP asset that may be able to better realise the value of existing NOX Assets.
- Transaction costs may be partly recovered from NYRADA, (subject to a future capital raising).
- Transfer of the non-oncology IP assets to NYRADA may assist Noxopharm to focus on its core oncology asset NOX66.
- There is no selective treatment of any Noxopharm Shareholder.
- There is unlikely to be any change in the liquidity of Noxopharm's securities as a result of the Proposal.

Disadvantages of the Proposal
If the Proposal is NOT approved

- Other than gaining an interest in the NOX Assets at fair value, there is no other special value given to Dixon.
- The valuation of the NOX Assets and the Dixon Assets is subject to a high degree of uncertainty.
- It is likely that NYRADA will require further funds to develop its products post Proposal and such funds may be dilutive to Noxopharm Shareholders. The Company's plans for a fund raising are as yet unformed.
- A possible transfer of NOX Assets directly to the NYRADA (USA) may crystallise a tax liability.
- The NOX Assets are unlikely to be developed further by Noxopharm for the foreseeable future and as a result there is limited potential to realise any value.
- The Board advises that there are no other offers capable of acceptance in respect of the NOX Assets.

38. In our opinion the position of Noxopharm Shareholders is more advantageous post Proposal than pre Proposal and therefore the Proposal is **reasonable** to Noxopharm Shareholders.

### 3.5 Summary of opinion

39. On balance of all the matters considered we are of the view that the Proposal is **fair and reasonable** to Noxopharm Shareholders.

## 4. GENERAL DISCLOSURES AND LIMITATIONS

### Changes in market conditions

40. Our analysis and conclusions are based on market conditions existing at the date of this Report. A limitation of our conclusion is that market conditions may change between the date of this Report and when the various aspects of the transaction are concluded.

### Individual shareholder circumstances

41. Acceptance or rejection of the Proposal is a matter for individual shareholders based upon their own views of value, risk, and portfolio strategy. Noxopharm Shareholders who are in doubt as to the action that they should take in relation to the Proposal should consult their professional advisor.

### Entirety of Report

42. This summary opinion should be read in conjunction with and not independent of the remainder of this Report.

43. The Report should also be read in conjunction with the Notice of Meeting to which this Report is attached. Terms in this Report are, unless otherwise noted, consistent with terms and description referred in the Notice of Meeting.

*Noxopharm Limited  
Independent Expert's Report – 8 September 2017  
Related party transaction requiring shareholder approval*

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Yours faithfully

**Moore Stephens (Vic) Pty Ltd**

Holder of Australian Financial Services License No.247362

A handwritten signature in black ink, appearing to read "G. Graco". The signature is fluid and cursive, with a large initial "G" and a trailing flourish.

**GARY GRACO**  
**Director & Authorised Representative**

## 5. DISCLOSURES AND LIMITATIONS

44. This Report has been prepared at the request of the Directors of Noxopharm for the purposes of assisting Shareholders in their evaluation of the Proposal.
45. The Report is not intended to serve any other purpose and should not be relied upon by any other person for any other purpose. In preparing this Report, Moore Stephens has relied upon financial and other information provided by Noxopharm. Furthermore, we have relied upon the representations and opinions of the management of Noxopharm and Dixon.
46. We believe that (unless stated otherwise) the information provided was reliable, complete and not misleading and there is no reason to believe that any material facts have been withheld. However, we have not conducted any separate due diligence or audit investigations to assess the correctness or completeness of this information. Information, judgements and representations have been evaluated through analysis, enquiry and review to the extent practicable. However, it must be appreciated that such information is not always capable of external verification or validation.
47. Acceptance or rejection of the Proposal is a matter for individual shareholders based upon their own views of value, risk, and liquidity preference and portfolio strategy. Noxopharm Shareholders who are in doubt as to the action that they should take in relation to the Proposal should consult their professional advisor.
48. The opinion of Moore Stephens is based on economic market and other conditions prevailing on the date of this Report. Such conditions can change significantly over a relatively short period of time.

## 6. REGULATORY FRAMEWORK

### 6.1 Corporations Act & ASX Listing Rules

49. Chapter 2E of the **Act** requires a public company to obtain shareholder approval when the company provides a financial benefit to a related party. However, under the Act shareholder approval is not required when the terms of the transaction are “no worse than on an arm’s length basis”.
50. ASX Listing Rule 10.1 requires where there is an acquisition or disposal of a substantial asset from/to a related party or child entity, such transaction must be approved by shareholders. ASX Listing Rule 10.1 makes no exemption for benefits provided on “arm’s length terms”. The Directors are of the view that the Transfer of assets to NorBio 1 and 2 is a substantial asset, as set out in the NOM. As described above, the Cardio Acquisition is an acquisition of an asset from a related party.
51. Notwithstanding the Directors’ view that the Transfer and the Cardio Acquisition terms are “arms length”, the Directors have determined that good governance is for the Cardio Acquisition and the Transfer be approved by shareholders before proceeding to completion.
52. In accordance with the requirements of the Act, ASX Listing Rules and the ASIC Regulatory Guides, the Directors of Noxopharm have engaged Moore Stephens to prepare an Independent Expert’s Report for Noxopharm Shareholders to comment on the fairness and reasonableness of the Transfer and the Cardio Acquisition under the Proposal, to be included in the Explanatory Memorandum to be issued to Noxopharm shareholders.

### 6.2 Guidelines issued by ASIC on acquisitions agreed to by shareholders

53. ASIC has issued ASIC Regulatory Guide 76 “*Related Party transactions*” (**RG 76**) Regulatory Guides 111 – *Content of Experts Reports* (**RG111**) and Regulatory Guide 112 – *Independence of Experts* (**RG112**). We highlight the following from RG111 that are pertinent to this Report.

- RG111.55 *Generally, ASIC expects an expert who is asked to analyse a related party transaction to express an opinion on whether the transaction is 'fair and reasonable' from the perspective of non-associated members. This analysis is specifically required where the report is also intended to accompany meeting materials for member approval of an asset acquisition or disposal under ASX Listing Rule 10.1*
54. RG111.53 states that whether a related party transaction is fair and reasonable should not be applied as a composite test, but that there should be a separate assessment of whether the transaction is "fair" and "reasonable". These concepts are explained further:
- RG 111.57 A proposed related party transaction is 'fair' if the value of the financial benefit to be provided by the entity to the related party is equal to or less than the value of the consideration being provided to the entity. This comparison should be made:*
- a. assuming a knowledgeable and willing, but not anxious, buyer and a knowledgeable and willing, but not anxious, seller acting at arm's length; and*
  - b. for control transactions, on the basis referred to in RG 111.11.*
- RG 111.58 Where the proposed transaction consists of an asset acquisition by the entity, it is 'fair' if the value of the financial benefit being offered by the entity to the related party is equal to or less than the value of the assets being acquired.*
55. RG 111.53 also states that where a related party transaction is made up of a number of separate components, the expert should consider the overall effect of the related party transaction.
56. We have necessarily considered the ASIC guidance in our analysis. The methodology that we have used to form an opinion as to whether the Proposal is fair and reasonable, is summarised as:
- **Fairness** – This assessment of the value difference between the value provided and the value received; as well as the overall impact on Noxopharm Shareholders by comparing the pre and post Proposal share values.
  - **Reasonableness** – we have analysed other significant factors, which shareholders should consider prior to accepting or rejecting the Proposal, including the advantages and disadvantages of the Proposal and the alternatives available if the Proposal is not approved.

### 6.3 Guidelines issued by ASIC on technical expertise

57. In preparing our Report we have also considered ASIC guidelines on expertise:
58. RG 111.119 For technical matters beyond the expert's expertise, an expert should retain a specialist to advise them (e.g. a geologist to provide an opinion on recoverable ore the subject of mining tenements, or a traffic forecast report in relation to a toll road): see RG 112.67–RG 112.69
- RG 112.67 It is the expert's responsibility to:*
- (a) determine that a specialist's assistance is required on a matter that must be determined for the purposes of the report;*
  - (b) select the specialist and ensure that the specialist is competent in the field;*
  - (c) negotiate the scope and purpose of the specialist's work and ensure that this is clearly documented in an agreement (though the agreement may be with the commissioning party or the expert); and*
  - (d) be satisfied that the specialist is independent of, and is perceived to be independent of, the commissioning party and any other interested party.*

RG 112.68 We consider best practice would be for the expert to pay the specialist its fees and recover those fees from the commissioning party.

59. Moore Stephens do not have expertise in assessing highly technical drug compounds or their prospects of commercialisation or valuation. The Acuity report was commissioned by the Company and not by Moore Stephens. Therefore consistent with RG 112.67-68 above we commissioned the MSV Technical Specialist to provide guidance to us on its suitability for our assessment.

#### 6.4 Guidelines on valuation engagements

60. This report has also been undertaken in accordance with the requirements set out in Accounting Professional and Ethical Standards Board professional standard 225 "Valuation Services" (APES 225).
61. A valuation engagement is defined by APES 225 as "Engagement or Assignment to perform a Valuation and provide a Valuation Report where the Member is free to employ the Valuation Approaches, Valuation Methods, and Valuation Procedures that a reasonable and informed third party would perform taking into consideration all the specific facts and circumstances of the Engagement or Assignment available to the Member at that time".

## 7. PROFILE OF NOXOPHARM

### 7.1 Company overview

62. Noxopharm is a publically listed company engaged in the development of compounds to address the problem of drug and radio-resistance in cancer cells, the major hurdle facing improved survival prospects for cancer patients. The first pipeline product is idronoxil NOX66, with later generation drug candidates under development in an R&D program. The Company's Initial Public Offering of its shares on the Australian Securities Exchange raised \$6 million in August 2016 at 20 cents per share.
63. The Company's Initial Public Offering of its shares on the Australian Securities Exchange raised \$6 million in August 2016. Since then there have been a number developments with the Company's formulation of idronoxil as NOX66 for the treatment of late-stage cancer. The major developments are detailed below.
- The Company commenced the clinical trial program during the 1Q'CY17, being the first of an expected seven clinical trials in the program.
  - The Company has moved into new premises as a result of its expanded infrastructure needs. The Company has also employed additional personnel to ensure there is sufficient personnel to complete the clinical trial program. This resulted in an increase in administrative and corporate costs.
  - The Company has taken steps to scale up production of NOX66 to meet its growing clinical trial needs as well as an anticipated potential provision for future programs. This has involved investing in its own interim small-scale manufacturing plant with a capacity of >100,000 doses per day.
  - 4.2m shares were released from escrow in April 2017, taking the free-float shares on issue to 38.3m. There remains 46.9m shares on escrow (55% of shares on issue) until 9 August 2018.
  - The Company embarked on a further capital raising of \$5.5 million at 33 cents per share on 24 August 2017, (Aug-17 Raising).

### 7.2 Share capital

64. Noxopharm has as of 8 September 2017, 101,838,096 fully paid ordinary shares on issue held by a total of 1,067 shareholders. Table 3 below sets out the top shareholders:

Table 4: Top shareholders

Rank	Name	Shares (000's)	%
1	MILLIGENE PTY LTD*	31,028	30.5%
2	DRH SUPERANNUATION PTY LTD*	6,871	6.7%
3	ANGLO MENDA PTY LTD*	6,171	6.1%
4	RGT CAPITAL FUND NO 5 (NOXO) PTY LTD	3,939	3.9%
5	GOODRIDGE NOMINEES PTY LTD	3,034	3.0%
6	RHLC PTY LTD	2,500	2.5%
7	SUBURBAN HOLDINGS PTY LIMITED	1,982	1.9%
8	UURO PTY LTD	1,800	1.8%
9	HELIUM MANAGEMENT PTY LTD*	1,766	1.7%
10	JOHN W KING NOMINEES PTY LTD	1,036	1.0%
	<b>Total Top 10 holders of Ordinary fully paid shares</b>	<b>60,127</b>	<b>59.0%</b>
	<b>Other Shareholders</b>	<b>41,711</b>	<b>41.0%</b>
	<b>Total</b>	<b>101,838</b>	<b>100.0%</b>

Source: Noxopharm management, Computershare

65. Table 4 shows the top 10 shareholders of Noxopharm accounting for 59.0% of total issued capital. The shareholders in Table 4 marked with an "\*" account for 45.8 million of the total of 46.9 million shares subject to escrow until 9 August 2018. The largest shareholding relates to Mr Graham Kelly, a Director of Noxopharm. In total current directors of Noxopharm hold a relevant interest in approximately 33% of total issued capital.
66. In addition to the above shareholding there are 22.6 million options outstanding with an exercise price of 30 cents expiring 28 February 2021. All options released from escrow on 9 August 2017.

### 7.3 Financial performance

67. A summary of Noxopharm's consolidated statement of comprehensive income for the period 27 October 2015 to 30 June 2016 (audited)<sup>4</sup> and for the financial year ended 30 June 2017<sup>2</sup> (audited), are shown in Table 4 below.

Table 5: Noxopharm Statements of Comprehensive Income

\$'000s	30-Jun-16 (audited)	30-Jun-17 (audited)
Other income	-	194
<b>Total revenue</b>	-	<b>194</b>
Corporate Administration expenses	(211)	(1,126)

<sup>4</sup> An audit report with an unmodified opinion was issued by William Buck Chartered Accountants dated 30 September 2016 for the 30 June 16 year and 31 August 2017 for the 30 June 2017 year. .



\$'000s	30-Jun-16 (audited)	30-Jun-17 (audited)
Research and Development expenses	(143)	(816)
Depreciation	(3)	(30)
Finance Fee expenses	(2)	(11)
Consulting, Employee & Director expenses	(345)	1,256
<b>Loss before income tax</b>	<b>(705)</b>	<b>(3,046)</b>
Income tax benefit	-	-
<b>Total comprehensive loss for the period</b>	<b>(705)</b>	<b>(3,046)</b>

Source: Noxopharm Financial Reports

68. Table 5 above shows that the Company is engaged in research and development and administration thereof and has not yet commercialised its development assets. Other income is primarily R&D tax incentives and interest.

#### 7.4 Financial position

69. A summary of Noxopharm's consolidated Statement of Financial Position as at 30 June 2016 (audited), and 30 June 2017 (audited) are summarised in Table 6 below.

Table 6: Noxopharm Statements of Financial Position

\$'000s	30-Jun-16 (audited)	30-Jun-17 (audited)
Cash and cash equivalents	161	2,459
Trade and other receivables	39	63
Other	106	47
<b>Total current assets</b>	<b>306</b>	<b>2,567</b>
Property, plant and equipment	17	64
Other	-	197
<b>Total non-current assets</b>	<b>17</b>	<b>261</b>
<b>TOTAL ASSETS</b>	<b>323</b>	<b>2,829</b>
Trade and other payables	(283)	(291)
Employee entitlements	(14)	(70)
<b>Total current liabilities</b>	<b>(297)</b>	<b>(361)</b>
<b>TOTAL LIABILITIES</b>	<b>(297)</b>	<b>(361)</b>
<b>NET ASSETS</b>	<b>26</b>	<b>2,468</b>
Contributed equity	731	6,218
Accumulated losses	(705)	(3,751)
<b>TOTAL EQUITY</b>	<b>26</b>	<b>2,468</b>

Source: Noxopharm Financial Reports

70. Table 6 above shows:

- Cash on balance sheet is from the August 2016 IPO, less operating costs incurred to date;
- No value of the R&D assets under development has been recognised. Other non-current assets mainly reflects rental deposits and bank guarantees;
- Capital reflects the initial seed funding and \$6 million raised at the August 2016 IPO, less fund raising costs.

#### 7.5 NOX Assets

71. In addition to its main R&D program, NOX66, Noxopharm has also developed non-oncology compounds which are to be transferred as part of the Proposal. The status of these are (source: Acuity report and Directors):

- TRPC3 Inhibitor – lead candidate (NYX-104) has been validated in vitro as an inhibitor of TRPC3-mediated glutamate-induced calcium overload and validated in an animal model of stroke as an inhibitor of excitotoxicity. Excitotoxicity is the progressive death of brain cells resulting from the dumping of neurotransmitters (glutamate) from injured brain cells. It follows acute brain injury such as stroke, head trauma/concussion and severe epileptic seizure;
- Thromboxane Synthase Inhibitor – a compound previously evaluated in humans has been modified (NYX-105) by Noxopharm with its LIPROSE technology platform to improve its drug-like qualities, including the ability to cross the blood brain barrier. NYX-105 is directed at inhibiting inflammatory processes within the brain in various neurodegenerative diseases (Alzheimer's, Parkinson's, Huntington's, motor neuron disease, multiple sclerosis) and in peripheral nerves (peripheral neuropathy: chemotherapy toxicity, diabetes).

72. Acuity states that it is unlikely that any of these projects is sufficiently advanced to attract licensing opportunities in the immediate term. Noxopharm confirms that it has no intention of seeking a partnership until after first-in-human studies at the earliest. Further details of these compounds are set out in the Acuity report and the NOM.

## 8. PROFILE OF THE DIXON ASSET<sup>5</sup>

73. The Dixon asset is held by a company called Cardio Therapeutics Pty Ltd (**Cardio**). Dixon has represented to Noxopharm that Cardio holds no assets or liabilities other than the Dixon Asset (PCSK9 compound/program) and that it has never traded on a commercial basis, has lodged no tax returns and has no bank account or employees.

74. Cardio is engaged in a drug discovery and development program around small molecule inhibitors of the PCSK9-LDLreceptor interaction to treat a variety of conditions including hypercholesterolemia. A provisional patent was lodged in March 2017. A number of compounds have been identified as inhibiting binding between PCSK9 and the LDL-receptor. Current studies aim to confirm proof-of-concept in an animal model. Acuity states it is unlikely that this project is sufficiently advanced to attract licensing opportunities in the immediate term. Noxopharm has confirmed that it has no intention of seeking a partnership until after first-in-human studies at the earliest, and most likely after Phase 2.

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<sup>5</sup> Source: Noxopharm management, Dixon and the Acuity report

9. FURTHER BACKGROUND TO THE PROPOSAL

9.1 ACUITY REPORT

75. Our assessment is based on the opinion of Acuity for the valuation of the NOX Assets and the Dixon Asset. The Acuity report is included in the NOM. In summary the Acuity range of values are:

Table 7: Summary of Acuity values

\$ million	Low	Preferred	High
NOX asset NYX-104	0.58	2.36	4.74
NOX Asset NYX-105	0.67	2.29	4.20
<b>Total NOX Assets</b>	<b>1.25</b>	<b>4.65</b>	<b>8.94</b>
Dixon Asset PCSK9	0.63	2.60	5.25
<b>Total NYRADA Assets</b>	<b>1.88</b>	<b>7.25</b>	<b>14.19</b>
<i>Dixon Asset % of total</i>	<i>33.5%</i>	<i>35.8%</i>	<i>37.0%</i>

Source: Acuity report

76. Table 7 shows that the Acuity report shows a wide range of values for the assets from \$1.9 million to \$14.2 million with a preferred value of \$7.3 million.

77. Acuity adopted a probabilistic adjusted discounted cash flows methodology resulting from continued development and possible IP licensing of the assets. Probability estimates of successful development and commercialisation of each asset was drawn from studies of comparable drug development success rates. Acuity considered but dismissed alternate cost based or market based valuation methods on the basis of lack of reliable data.

78. Acuity also assumes ongoing funds (which is not presently available, but assumed to be sourced by NYRADA fund raising) to develop the assets. The report states that “Noxopharm only proposes to fund the business of Nyrada until the end of 2017 when Nyrada is expected to have independent capital resources”.

79. As Acuity was engaged by the Company and not by Moore Stephens, consistent with ASIC guidelines on expertise, we engaged the MSV Technical Specialist to review the Acuity Report.

80. The MSV Technical Specialist concluded that the approach taken by Acuity in its valuation is reasonable. However it is the MSV Technical Specialist’s practice to value pre-clinical assets or drugs with patents at the provisional stage at nil value.

81. Whilst based on the review of the methodology undertaken by the MSV Technical Specialist we are satisfied with Acuity’s report for our assessment purposes, we concur with the MSV Technical Specialist that due to the high degree of uncertainty in the assumptions underpinning Acuity’s valuation it is prudent to show a nil value at the Low range.

9.2 Step plan for implementation of the Proposal

82. Noxopharm has provided us with details of a step plan on how the Proposal is expected to unfold. We are instructed that this step plan has been formulated in conjunction with the Company’s tax advisers. This is summarised as:

- **STEP 1&2:** Noxopharm establishes wholly owned Australian subsidiaries (**NOX Subsidiaries**) and transfers the NOX Assets to these subsidiaries. As these will be part of Noxopharm’s tax consolidated group, no tax implications arise on the transfer.

- **STEP 3:** Noxopharm and Altnia Holdings (an associate of Dixon) establish NYRADA Inc. (USA) as an equal joint venture for a nominal capital contribution, (this step has already occurred). As NYRADA has no assets, no tax consequences arise on its formation. NYRADA is not part of Noxopharm's tax consolidated group.
  - **STEP 4:** Noxopharm transfers the shares in the NOX Subsidiaries holding the NOX Assets to NYRADA in exchange for NYRADA Shares. Noxopharm considers that whilst the transfer of the NOX Subsidiaries shares is a Capital Gains Tax (**CGT**) event, roll-over relief should be available to defer CGT on a scrip for scrip basis. We note that there are a number of legislative requirements for the scrip for scrip roll-over provisions to apply and the ability to apply the roll-over is dependent on those requirements being satisfied. We have not factored any taxes risk into our fairness assessment as the primary advice from Noxopharm's tax advisors is that roll over relief will be available and the likelihood of tax losses being available to Noxopharm to offset any gain on the deconsolidation (CGT event) of the NOX subsidiaries.
    - Altnia also transfers its shares in Cardio Tx to NYRADA in exchange for NYRADA shares.
    - At the conclusion of Step 4, Noxopharm will hold 66.7% of the shares in NYRADA and Altnia (Dixon) will hold 33.3%.
83. Following implementation of the Proposal, Noxopharm intends to seek further funding for NYRADA. These plans are not yet formulated and are not part of the Proposal, however we note that such fund raising is likely to dilute both Noxopharm's and Altnia's interests in NYRADA.
84. It is also possible that a US investor may require the transfer of NYRADA's Australian assets direct to the US entity via an in specie liquidator's distribution. This would represent a disposal of the assets by the Australian entities with the CGT or capital allowances provisions applying to determine the taxable gain or loss. The Australian tax legislation contains specific provisions regarding liquidators distributions which would need to be applied at that time. These provisions may result in a deemed dividend applying to NYRADA in respect of the distribution of assets received. As the deemed dividend would be a dividend paid to a non-resident, cash leakage on account of dividend withholding tax would be highly probable in such a transaction, which would be dilutive to all NYRADA shareholders. As this outcome will depend upon the decisions of as yet unknown US investor(s) we consider this eventuality too remote for our fairness assessment of the Proposal.

## 10. BASIS OF ASSESSMENT OF THE PROPOSAL

85. In assessing whether the Proposal is fair and reasonable from the perspective of Noxopharm Shareholders, we have had regard to the criteria set out in RG111, RG170 and APES 225.
86. The following factors have been considered in our evaluation of the advantages and disadvantages to Noxopharm Shareholders:
- The value difference between the value provided and the value received;
  - The fair value of Noxopharm Shares Pre Proposal and the fair value of Noxopharm Share Post Proposal;
  - The alternatives available to Noxopharm if the Proposal does not proceed;
  - Other qualitative advantages and disadvantages of the Proposal to Noxopharm; and
  - Any other factors which may have a material impact.
87. The following sections set out details of our assessment of fairness (Section 11), whether a control premium is received (Section 12) and other qualitative aspects of the Proposal (Section 13).

**11. ASSESSMENT OF FAIRNESS (QUANTITATIVE ASSESSMENT)**

**11.1 Overview**

88. Section roadmap:

- Section 11.2 compares the value of the interest in the NOX Assets transferred with the interest in the Dixon Asset acquired.
- Section 11.3 determines the value of Noxopharm Shares Pre Proposal.
- Section 11.4 determines the value of Noxopharm Shares Post Proposal.
- Section 11.5 summarises overall the financial impact of the Proposal.

89. ASIC Regulatory Guide 111 outlines the appropriate methodologies a valuation expert should consider when valuing assets or securities. The use of different methodologies is however, dependent upon individual circumstances, the nature of the company and availability of information.

90. The following summarises the various methodologies we have considered:

<b>Market Based</b>	Business or equity is determined by reference to comparable market buy/sell transactions or quoted market prices ( <b>QMP</b> ) if the company is listed on an exchange.
<b>Income Based</b>	Value is determined by reference to capitalised future maintainable earnings ( <b>CME</b> ) or discounted cash flows ( <b>DCF</b> ) derived by the business
<b>Asset Based</b>	Value is determined by reference to the sale or realisable proceed of individual assets or groups of assets in an entity

We provide more details of the available valuation methodologies in **Appendix B** of this Report.

**11.2 Comparative value of NOX Assets to Dixon Asset**

91. In assessing the value of NOX Assets compared to the Dixon Asset, we have used the values determined by Acuity as reviewed by the MSV Technical Specialist. The Acuity report considered all of the methodologies outlined in Section 11.1 as noted in Paragraph 78.

92. The below table summarises the value of the NOX Assets and NYRADA equity interest therein provided as consideration, compared to the value of the Dixon Asset Acquired.

Table 8: Summary of value provided compared to asset acquired

\$ million	Low	Medium	High
Value of NOX Assets pre Proposal	Nil	4.65	8.94
Equity interest in NOX Assets provided	33.3%	33.3%	33.3%
<b>A) Value of NOX Asset provided as consideration</b>	<b>Nil</b>	<b>1.53</b>	<b>2.95</b>
Value of DIXON Assets acquired	Nil	2.60	5.25
Noxopharm's equity interest in the Dixon Assets	66.7%	66.7%	66.7%
<b>B) Noxopharm's equity interest in the Dixon Assets</b>	<b>Nil</b>	<b>1.72</b>	<b>3.47</b>
<b>Value difference (B-A, rounded)</b>	<b>Nil</b>	<b>0.19</b>	<b>0.52</b>

93. The above values at the Medium and High range are drawn from the independent technical specialist (**Acuity**) report commissioned by Noxopharm which accompanies the NOM and set out in Table 7 (Paragraph 76). The Low range estimate of nil value is drawn from our own assessment which has been informed by the MSV Technical Specialist engaged directly by us for the reasons set out in Section 9.1 above.
94. Table 8 shows that the value difference between the value of the consideration provided and the asset value received is either nil to positive \$0.19-0.52 million. On this basis, the Proposal is likely to be fair to Noxopharm Shareholders as no financial benefit is given to Dixon or NYRADA in the Transfer and Cardio Acquisition.

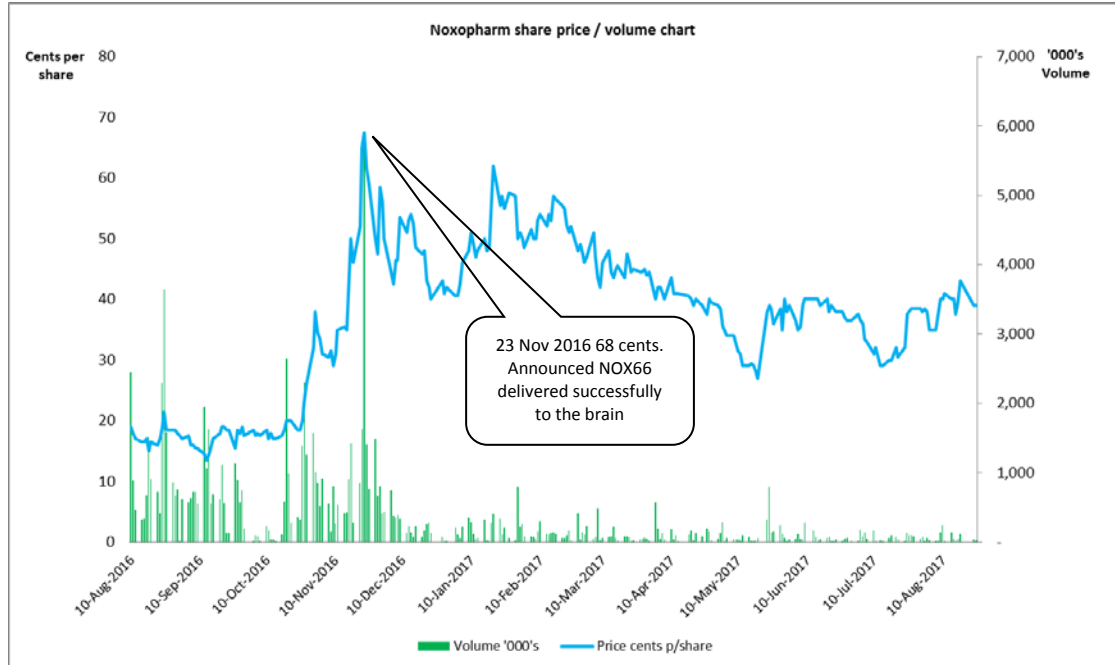
**11.3 Value of Noxopharm shares Pre Proposal**

95. RG 111.53 also highlights that the Expert should consider the overall effect of the related party transaction. We consider the overall effect by comparing the Pre and Post proposal value of Noxopharm shares for the non-associated Noxopharm shareholders. In assessing the value of Noxopharm, we considered all of the methodologies outlined in Section 11.1.

*Market based value – Quoted Market Price*

96. Given that Noxopharm is a listed company on the ASX, we have considered the quoted market price of Noxopharm shares as a method for determining the value of Noxopharm shares, noting however that the quoted market value is reflective of a minority interest in the Company. We have analysed the Noxopharm share price for the last 12 months, (noting a trading halt on 23 August 2017).
97. The following chart shows recent trading in Noxopharm's shares to 23 August 2017 when the Aug-17 capital raising was announced. Since the capital raising, the trading has settled within the 33 cents per share range:

Chart 3 – Noxopharm share price and trade history



Source: Eikon Thomson Reuters and MSV analysis

Table 9: Noxopharm volume trading

Period	Last 3 mths	Last 6 mths	Last 12 mths
Total shares traded #'000's	4,180	11,143	75,370
As % of total issued capital	4.91%	13.08%	88.49%
Price (cents)			
High	43	51	68
Low	27	27	14
Total value of trades (\$AUD, 000's)	1,562	4,423	27,775
VWAP (cents)	37	40	37

Source: Eikon Thomson Reuters and MSV analysis

98. The chart and table above shows the price of Noxopharm Shares has traded on average around 37-40 cents in the last 12 months. There has been significant trading volumes over the last 12 months representing 89% of the total shares on issue. Most of the trading occurred in the period between the August 2016 IPO (at 20 cents per share) and 23 November 2016 when it was announced that their core drug platform NOX66 was successfully delivered to the brain. Trading since that date has been more subdued, (5% and 13% in the last 3 to 6 months respectively), however on 24 August

2017 it was announced that \$5.5 million had successfully been raised at 33 cents per share. As of 4 September 2017, the share price was 33 cents per share, or an implied market capitalisation of \$33.6 million.

99. RG 111.69 states that an expert should consider “*the quoted price for listed securities, where there is a liquid and active market*”.
100. In our view liquidity is represented (amongst other factors) by 25-50% of the total number of shares being traded over the course of a year, or about 0.5%-1.0% per week. The trading activity in the last 6 months exhibits characteristics of a traded stock at the low end of these amounts, however the Aug-17 capital raising represents 19% of the capital on issue prior to the raising. We therefore consider that the market price likely provides a meaningful and liquid value of Noxopharm as a whole. Therefore we have utilised the implied market capitalisation of \$33.6 million (as at 4 September 2017) in our analysis.
101. Given that no announcement concerning the Transfer of the NOX Assets (or the Cardio Acquisition of the Dixon Asset) has been made it is uncertain from our analysis whether these assets are valued by the market or not. We observe that Company announcements and investor presentations throughout CY2017 and the 24 August 2017 capital raise have all referred to prospects and plans for NOX66 and no reference has been made to the NOX Assets that are the subject of the Proposal.
102. As previously highlighted, the Noxopharm Shareholders interests in NOX66 are unchanged as a result of the Proposal.

#### *Income based value*

103. We have not undertaken a whole of Company valuation based on either the CME or DCF methodology, given the Company has not prepared any reasonable<sup>6</sup> budgets or forecasts given the primary assets are still in development stage and as yet there are no commercial business operations. Acuity was not commissioned to value the NOX66 asset.
104. We also considered adopting a revenue multiple based approach which can be an appropriate form of CME valuation for loss making entities – but similarly have been unable to do this without any reasonable forecasts provided by management.

#### *Asset based value*

105. We considered the net asset value (**NAV**) methodology on a going concern basis. However we do not consider this an appropriate methodology to assess Noxopharm shares. Under the going concern basis<sup>7</sup>, an asset based valuation will estimate the value of net assets at its fair market value and will not account for realisation costs. This method involves making any necessary adjustments required to reflect the fair market value of the net assets of the business.
106. Given that the net assets and liabilities of Noxopharm based on the audited balance sheet as at 30 June 2017 (refer Table 6) do not record the value of development assets, (either at cost or fair market value) we do not consider this method appropriate compared to the market based value method.
107. We have made notional adjustments to the Noxopharm market based value to bring the net value difference of the NOX Assets and Dixon Assets to account, (refer Table 8) and to account for

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<sup>6</sup> i.e. consistent with ASIC guidelines as described in Section 6.3.

<sup>7</sup> We are cognisant that the assumption of going concern is only valid due to the ability of Noxopharm to continue to raise funds for ongoing drug development, as recently demonstrated by the 24 August 2017 capital raising.



transaction costs that will, or are likely to occur, up until the expected date of completion which will have an impact on the share value of Noxopharm.

108. The following table may illustrate the adjusted market value of Noxopharm and other pro-forma adjustments to include costs and transactions up until the Proposal date:

Table 10: Adjusted Pre-Proposal market value

Pre Proposal value	Ref	Low	Medium	High
<b>\$'000's</b>				
Market value 4 Sept. 2017 (101.8m@33cps)	Table 6	33,607	33,607	33,607
Unavoidable transaction costs		(113)	(113)	(113)
<b>Adjusted Pre Proposal market value \$AUD</b>		<b>33,494</b>	<b>33,494</b>	<b>33,494</b>
No. of shares ('000's)		101,838	101,838	101,838
Pre-proposal value cents per share		32.9	32.9	32.9

109. Table 10 above shows the adjusted market value of Noxopharm Pre Proposal to be estimated as \$33.5 million or 32.9 cents per share comprised of:

- The implied market value of Noxopharm based upon current trading at 33 cents per share.
- Managements estimate of unbooked unavoidable transaction costs relating to the Proposal. These are largely comprised advisor fees and the costs of establishing NYRADA. Management state that this cost will be recovered from NYRADA when it completes its capital raising. In the absence of further details on NYRADA's capital raising we have included the cost within the analysis of the Proposal.

110. We therefore consider for the purposes of our assessment the adjusted market value of Noxopharm shares Pre Proposal to be **32.9 cents per share**.

#### 11.4 Value of Noxopharm shares Post-Proposal

111. We summarise the valuation of Noxopharm Shares post-Proposal in Table 11 below:

Table 11: Summary of Noxopharm Post-Proposal value

Post Proposal value	Ref	Low	Medium	High
<b>\$'000's</b>				
Adjusted Pre Proposal market value \$AUD	Table 6	33,494	33,494	33,494
Add value difference of Proposal	Table 8	nil	190	520
<b>Adjusted Pre Proposal market value \$AUD</b>		<b>33,494</b>	<b>33,684</b>	<b>34,014</b>
No. of shares ('000's)		101,838	101,838	101,838
Pre-proposal value cents per share		32.9	33.1	33.4

112. Table 11 above shows the adjusted market value of Noxopharm Post Proposal to be estimated as \$33.5 million to \$34.0 million comprised of:

- The adjusted Pre Proposal market value taken from Table 10.

- The net value difference between the value of the NOX Assets consideration paid and the Dixon Asset received, taken from Table 8.

113. We therefore consider for the purposes of our assessment the adjusted market value of Noxopharm shares Post Proposal to be in the range of **32.9 to 33.4 cents per share**.

**11.5 Summary of financial impact of the proposal on Noxopharm shareholders**

114. The following Table summarises the financial impact of the Proposal on Noxopharm Shareholders:

*Table 12: Summary of Proposal on Noxopharm Shareholders*

Cents per share (rounded)	Ref	Low	Medium	High
Value of Noxopharm shares Pre Proposal	Table 10	32.9	32.9	32.9
Value of Noxopharm shares Post Proposal	Table 11	32.9	33.1	33.4
<b>Value accretion / (dilution)</b>		<b>Nil</b>	<b>0.2</b>	<b>0.5</b>

115. Based upon our forgoing analysis, under both the Medium and High scenarios the Proposal may be nominally accretive in the value of Noxopharm Shareholders interests in the Company. At the Low value the Proposal is neither value accretive or dilutive.

116. Based upon the foregoing assessment in accordance with ASIC guidelines, we are of the opinion that overall the Proposal is likely to be **fair** to Noxopharm Shareholders.

**12. ASSESSMENT OF CONTROL PREMIUM**

117. RG 111.11 suggests that when assessing the value of a company's shares for the purposes of approval under Item 7 of s611 (i.e. a share issue akin to a takeover offer) the expert should consider a premium for control. An acquirer could be expected to pay a premium for control due to the advantages they will receive should they obtain 100% control of another company.

118. Whilst the concept of control in RG 111.11 is incorporated by reference in RG 111.57 in respect of related party transactions, in our view the substance of the Proposal is not a control transaction and the consideration of control premiums (or lack thereof) is unwarranted.

119. This is because under the Proposal, Noxopharm shareholdings are unchanged pre and post Proposal. In addition whilst Noxopharm's 100% equity interest in the NOX Assets is diluted in exchange for acquiring the Dixon Asset, at the conclusion of the Proposal Noxopharm will still hold a 66.7% controlling interest in NYRADA which holds the NOX Assets.

13. ASSESSMENT OF REASONABLENESS (QUALITATIVE ASSESSMENT)

120. In assessing if the Proposal is reasonable of Noxopharm Shareholders, we have had regard to the following:

Advantages of the Proposal	<ul style="list-style-type: none"> <li>• The Proposal is fair.</li> <li>• The Proposal is non-cash and does not impact Noxopharm's solvency.</li> <li>• Noxopharm Shareholders will gain an interest in a complimentary IP asset that may be able to better realise the value of the existing NOX Assets.</li> <li>• Transaction costs may be partly recovered from NYRADA, (subject to a future capital raising).</li> <li>• Transfer of the non-oncology IP assets to NYRADA may assist Noxopharm to focus on its core oncology asset NOX66.</li> <li>• There is no selective treatment of any Noxopharm Shareholder.</li> <li>• There is unlikely to be any change in the liquidity of Noxopharm's securities as a result of the Proposal.</li> <li>• Other than gaining an interest in the NOX Assets, for which fair value is received, there is no other special value given to Dixon.</li> </ul>
Disadvantages of the Proposal	<ul style="list-style-type: none"> <li>• The valuation of the NOX Assets and the Dixon Assets is subject to a high degree of uncertainty.</li> <li>• It is likely that NYRADA will require further funds to develop its' products post Proposal and such funds may be dilutive to Noxopharm Shareholders. The Company's plans for a fund raising are as yet unformed.</li> <li>• A possible transfer of NOX Assets directly to the NYRADA (USA) may crystallise a tax liability.</li> </ul>
If the Proposal is NOT approved	<ul style="list-style-type: none"> <li>• The NOX Assets are unlikely to be developed further by Noxopharm for the foreseeable future and as a result there is limited potential to realise any value.</li> <li>• The Board advises that there are no other offers capable of acceptance in respect of the NOX Assets.</li> </ul>

121. In our opinion the position of Noxopharm Shareholders is more advantageous post-Proposal than pre Proposal, and therefore the Proposal is **reasonable** to Noxopharm Shareholders.

14. OPINION ON THE PROPOSAL

122. On the basis of our analysis, and for the reasons outlined in the preceding sections, we consider that the Proposal is **fair and reasonable** to Noxopharm Shareholders.

## **APPENDIX A - Qualifications, Independence, Declarations and Consents**

### **Statement of Qualifications, Independence, Declarations and Consents**

#### **Qualifications**

Moore Stephens is a leading global accounting and consulting group, with a network of 276 independent firms and 626 offices across 108 countries. Founded in London in 1907, our success stems from our niche industry focus, enabling us to provide an innovative and personal service to our clients. Our policy is to be regarded by clients as the first port of call for all their business and personal finance decisions.

The Moore Stephens philosophy is to cater for our clients' needs wherever required, but not to grow for the sake of size alone. As a result, our client-orientated culture has developed over a number of years, which ensures that we are able to provide a highly personalised service.

The AFSL licence (No 247262) allows Moore Stephens to act for clients only in the capacity of providing reports in relation to certain corporate transactions or to provide general financial product advice on certain classes of financial products. Senior directors at Moore Stephens specialise in such advice and regularly perform corporate and asset valuations and advice on company restructures, acquisitions and proposals. Moore Stephens, acting through different directors also performs audits on the accounts of Australian companies.

The primary person responsible for preparing this Report on behalf of Moore Stephens is Gary Graco (Dip. Bus Studies – Accounting, ACA) with the assistance of staff, who has a significant number of years of experience in relevant corporate matters including valuations, independent expert reports and investigating accountant engagements.

#### **Independence**

Moore Stephens considers itself to be independent in terms of Regulatory Guide 112 issued by ASIC relating to independence of experts and has developed and issued an opinion and report on an unbiased basis.

Moore Stephens and its related entities or any of its Directors or Partners have not had within the previous two years, any shareholding in the Company or Dixon. During the 2 years period to this report Moore Stephens and its related entities have not provided any professional services to the Company.

None of Moore Stephens, Gary Graco, nor any other member, director, partner or employee of any of Moore Stephens has any interest in the opinion reached by Moore Stephens except that we are entitled to receive professional fees for the completion of this Report based on time incurred at normal professional rates. With the exception of these fees no parties will receive any other benefits, whether directly or indirectly, for or in connection with issuing this Report.

#### **Disclaimers**

This Report has been prepared at the request of the Directors of the Company and was not prepared for any other purpose than stated in this Report in Section 2. This Report has been prepared for the sole benefit of the Directors and the Non-associated Shareholders of the Company. This Report should not be used or relied upon for any purpose other than as set out in Section 2. Accordingly, Moore Stephens expressly disclaims any liability to any person (other than the Directors or Non-associated Shareholders of the Company) who relies on our Report, or to any person at all who seeks to rely on the Report for any other purpose not set out in Section 2.

**Appendix C** identifies the sources of information upon which this Report has been based. To the extent we have used historical information we are entitled to rely upon the information. Any forecast information which has been referred to in this Report has been prepared by the relevant entity and is generally based upon best estimate assumptions about events and management actions that may or may not occur.

Accordingly Moore Stephens cannot provide any assurance that any forecast is representative of results or outcomes that will actually be achieved.

The opinions given by Moore Stephens in this Report are given in good faith, based upon our consideration and assessment of information provided to us by the Directors and executives of the parties to the Proposal; and in the belief on reasonable grounds that such statements and opinions are correct and not misleading, (unless otherwise stated in the Report). This Report has been prepared with care and diligence.

Advanced drafts of this Report were provided to the Directors of the Company. Minor changes for factual content were made to this Report. There was no alteration to the methodology or conclusions reached as a result of discussions related to drafts of the Report.

Moore Stephens' opinion is based on prevailing conditions at the date of this Report including market, economic and other relevant circumstances. These can change over relatively short time period and any subsequent changes in these conditions in the value either positively or negatively.

#### **Indemnity**

The Company has agreed that it will indemnify Moore Stephens and its employees and officers in respect to any or all losses, claims, damages and liabilities arising as a result of or in connection with the preparation of this Report, except where the claim has arisen as a result of wilful misconduct or negligence by Moore Stephens.

#### **Consent**

This Report has been prepared at the request of the Company and may accompany the Notice of Meeting to be given to shareholders.

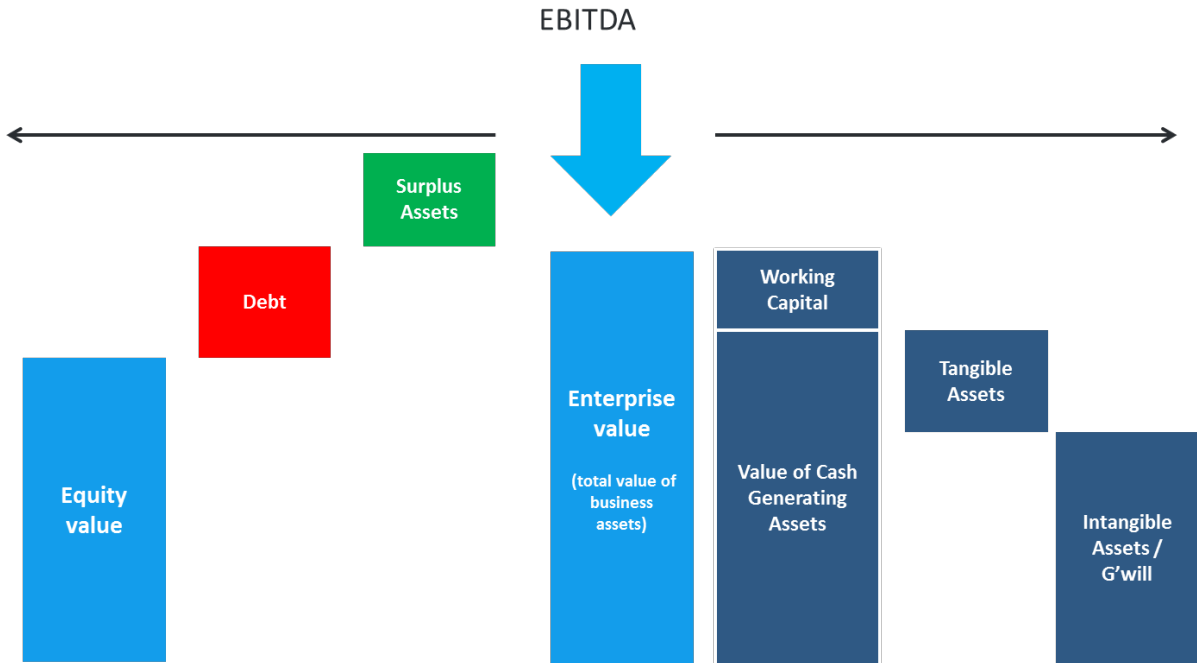
Moore Stephens consents to the issuing of this Report and the form and context to which it is to be included with the Notice of Meeting. Other than the Report, Moore Stephens has not been involved in the preparation of the documents or other aspects of the Proposal or the Notice of Meeting to which this Report may be attached. Accordingly, we take no responsibility for the content of the Notice of Meeting or the Proposal as a whole. Neither the whole nor any part of this Report nor any reference thereto may be included in any other document without prior written consent of Moore Stephens as to the form and context to which it appears.

APPENDIX B - Overview of Valuation Methodologies and principles

Type	Method	Description	When method used
Income Approaches	<b>Discounted Cash Flow</b>	<p>The Discounted Cash Flow (DCF) method derives the value of a business on a controlling basis based on the future cash flows of the business discounted back to a present value at an appropriate discount rate (cost of capital). The discount rate used will reflect the time value of money and the risks associated with the cash flows.</p> <p>The DCF Method requires:</p> <ul style="list-style-type: none"> <li>Forecasting cash flows over a sufficient long period (at least 5 years and usually 10 years)</li> <li>Assessing an appropriate discount rate (typically derived using judgment and aids such as the Capital Asset Pricing Model (CAPM)). The cost of equity (Ke) can be built up from first principles or benchmarked against comparable companies ("Co-Co") or transactions ("Co-Tran"), and</li> <li>Estimation of the terminal value (value of the business into perpetuity) at the end of the period (typically derived using the capitalisation of earnings method).</li> </ul>	<ul style="list-style-type: none"> <li>Reasonably accurate forecast cash flows (minimum 5 years).</li> <li>Earnings or cash flows expected to fluctuate from year to year.</li> <li>Business is in start-up or turn around phase.</li> <li>Specific projects that have a finite or infinite life, for example, mining projects.</li> </ul>
	<b>Capitalisation of Maintainable Earnings</b>	<p>The Capitalisation of Maintainable Earnings (CME) method is the most commonly used valuation method. It involves the application of a capitalisation multiple to an estimate of the Future Maintainable Earnings (FME) of the business. The FME must be maintainable by the business and must not include one-off gains or losses. The capitalisation multiple will reflect the risk, time value of money and future growth prospects of the business.</p> <p>The appropriate capitalisation multiple is determined with reference to the observed multiples of entities whose businesses are comparable ("Co-Co") to that of the business being considered and/or comparable transactions, ("Co-Tran").</p>	<ul style="list-style-type: none"> <li>The business has a history of profits with a reasonably consistent trend and that trend is expected to continue.</li> <li>The business has an indefinite life.</li> <li>Cash flow forecasts are not available.</li> </ul>
	<b>Capitalisation of Dividends</b>	<p>This method involves the capitalisation of forecast future maintainable dividends. The maintainable level of dividends is estimated by assessing the expected level of future maintainable earnings and</p>	<ul style="list-style-type: none"> <li>Valuation is for a minority interest.</li> <li>Stable business.</li> <li>High payout ratios.</li> </ul>

Type	Method	Description	When method used
		the dividend policy of the entity. The appropriate capitalisation rate reflects the investor's required rate of return.	
	<b>Yield Based</b>	This method is primarily used for property assets and involves capitalising forecast distributions by an estimated future maintainable yield. The yield or rate is determined based on analysis of comparable entities.	<ul style="list-style-type: none"> <li>Commercial or investment properties including retail, industrial and commercial.</li> </ul>
<b>Market Approach</b>	<b>Market</b>	<p>This method values a company based on the traded prices of its equity on a public market/exchange. The approach can adopt the prevailing spot rate of the company's securities at valuation date or the Volume Weighted Average Price (VWAP over a set trading period i.e. the preceding 30, 60 or 90 trading days to the valuation date).</p> <p>In the absence of market data specific to the company, the market approach can also be used by examining market values for comparable companies ("Co-Co") or comparable transactions ("Co-trans"). Comparable transactions may be observed as being based upon a widely used industry practice such as a multiple of revenue instead of earnings.</p>	<ul style="list-style-type: none"> <li>Company's equity is listed on public market/exchange i.e. ASX.</li> <li>Securities in the company are actively traded on the market/exchange.</li> <li>As above for comparable companies or transactions</li> </ul>
	<b>Asset Approach</b>	<b>Asset Based</b>	<p>Asset based valuation involve separating the business into components that can be readily sold, such as individual business units or items of plant and equipment, and ascribing a value of each component based on the amount that could be obtained if sold.</p> <p>The asset value can be determined on the basis of:</p> <ul style="list-style-type: none"> <li>Orderly realisation</li> <li>Liquidation</li> <li>Going concern</li> </ul>
<b>Cost approach</b>		<p>The value of an asset determined by:</p> <ul style="list-style-type: none"> <li>replacement cost (in basic terms, the cost of replicating functionality).</li> <li>reproduction cost (in basic terms, the cost of recreating the asset).</li> </ul>	The cost-based approach can be used to derive market value where market or income factors are difficult to obtain or estimate with reliability (for example, for some intangible assets).

Valuation principles



In adopting an income approach, a multiple of EBITDA or a DCF of cash flows is typically used to determine Total Enterprise Value (TEV), which represents the total value of the business assets. Any excess over tangible and identified intangible assets (moving right in the diagram above) represents goodwill.

Moving left in the diagram above, adjustments are made to TEV to add surplus assets and deduct debt so as to determine equity value. Surplus assets are any assets that are not required to generate the business's earnings or cash flows.

Further discounts may be applied to equity to determine a minority or illiquid value.



## APPENDIX C - Documents and Information Relied Upon

1. Draft Notice of Meeting and Explanatory Memorandum received 5 September 2017.
2. Noxopharm 30 June 2016 and 30 June 2017 audited accounts
3. Acuity's Report(s), draft dated 1 August 2017, final 10 September 2017
4. Noxopharm's Step Plan and associated tax advice issued by Addison's Lawyers
5. Discussions and correspondences with Noxopharm management and advisors.
6. MSV Technical Specialists opinion on the Acuity Report, dated 4 September 2017.
7. [www.asx.com.au](http://www.asx.com.au); Thomson Reuters Eikon; and various other websites and public domain information services.

## Moore Stephens (Vic) Pty Ltd Financial Services Guide

**This Financial Services Guide is dated 8 September 2017  
and forms part of the Independent Limited Assurance Report.**

Moore Stephens (Vic) Pty Ltd (ACN 052 362 348) (**Moore Stephens**) holds Australian Financial Services Licence no 247262 authorising it to provide general financial product advice in relation to various financial products such as securities, interests in managed investment schemes, and superannuation to wholesale and retail clients. Moore Stephens has been engaged by Noxopharm Limited (**Noxopharm** or **the Company**) to provide an Independent Experts Report (**the Report**) for inclusion with the Notice of Meeting of Shareholders to be held on or about 9 November 2017 to consider resolutions associated with related party transactions.

The *Corporations Act, 2001* requires Moore Stephens to provide this Financial Services Guide (**FSG**) in connection with its provision of this Report. Moore Stephens does not accept instructions from retail clients. Moore Stephens provides no financial services directly to retail clients and receives no remuneration from retail clients for financial services. Moore Stephens does not provide any personal retail financial product advice to retail investors nor does it provide market-related advice to retail investors.

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This Report contains only general financial product advice. It was prepared without taking into account your personal objectives, financial situation or needs. You should consider your own objectives, financial situation and needs when assessing the suitability of this Report to your situation. You may wish to obtain personal financial product advice from the holder of an Australian Financial Services Licence to assist you in this assessment.

When providing reports in the form of this Report, Moore Stephens's client is the Company to which it provides the report. Moore Stephens receives its remuneration from the Company. In respect of this Report and other services, Moore Stephens will receive a fee based upon normal professional rates plus reimbursement of out-of-pocket expenses from the Company. Directors or employees of Moore Stephens or other associated entities may receive partnership distributions, salary or wages from Moore Stephens. Moore Stephens and its authorised representatives, employees and associates may from time to time have relationships with the issuers of financial products.

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Moore Stephens has internal complaints-handling mechanisms. If you have concerns regarding this Report, please contact us in writing to Mr Kevin Mullen, Moore Stephens (Vic) Pty Ltd, Level 18, 530 Collins Street, Melbourne, Vic, 3000. We will endeavour to satisfactorily resolve your complaint in a timely manner. In addition, a copy of our internal complaints handling procedure is available upon request.

## Glossary

Abbreviated Term	Definition
Act	The <i>Corporations Act 2001</i>
Acuity report	Valuation report by Acuity commissioned by the Company valuing the NOX Assets and the Dixon Asset dated 10 September 2017
AFSL	Australian Financial Services Licence
Altnia	An associate of Dixon which owns the interest in Cardio and the Dixon Asset Pre Proposal
ASIC	Australian Securities and Investment Commission
ASX	Australian Securities Exchange
Cardio	Cardio Tx – owns the Dixon Asset
Cardio Acquisition	The acquisition of an interest in the Dixon Asset
Company	Noxopharm Limited, (ASX:NOX).
Directors	Directors of the Company
Dixon	Dr Ian Dixon, a Director of the Company and the related party the subject of the Cardio Acquisition and Altnia, the vendor of Cardio
Dixon Asset	A prospective non-cancer therapeutic compound known as PCSK9 to be acquired from Dr Ian Dixon (or his associate).
EM	Explanatory Memorandum
Moore Stephens	Moore Stephens (Vic) Pty Ltd - AFSL Holder 247362
MSV Technical Specialist	Technical specialist commissioned by Moore Stephens to review the Acuity Report
NAV	Net Asset Value
NorBio 1 and 2	Interposed entities that will own the NOX Assets as part of the Proposal
NOM	Notice of meeting
NOX Assets	Two prospective non-cancer therapeutic compound known as NYX-104 AND NYX-105
Noxopharm Shareholders	Noxopharm shareholders not associated with the Proposal

---

Abbreviated Term	Definition
NYRADA	NYRADA Inc., a company incorporated in the USA for the purposes of acquiring interests in the NOX Assets and Dixon Asset.
Proposal	The Transfer and Cardio Acquisition
Report	This Independent Expert Report prepared by Moore Stephens in relation to the Proposal
RG 111	ASIC Regulatory Guide 111 - Content of Experts Reports
RG 112	ASIC Regulatory Guide 112 - Independence of Experts
Shares	Fully paid ordinary shares in the Company
Transfer	The transfer of the NOX Assets to NYRADA (or entities interposed between Noxopharm and Nyrada)

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10 September 2017

The Directors  
Noxopharm Limited  
PO Box 824  
Turrumurra  
NSW 2074

Dear Sirs

### *Review of Programs and Valuation of Nyrada, Inc.*

This report has been prepared at the request of the Board of Noxopharm Ltd (Noxopharm). Noxopharm is a drug development company that listed on the Australian Securities Exchange (ASX) in August 2016 focussed on the development of the experimental anti-cancer drug, NOX66. This report concerns the valuation of a new subsidiary company of Noxopharm known as Nyrada, Inc (Nyrada).

## **1. Executive Summary**

### **1.1 Company Rationale**

It is our understanding that a key factor in the development of NOX66 has been the creation of a proprietary drug delivery technology platform designed to prevent degradation of the product's active drug, idronoxil, in the body. We further understand that this technology platform involves the interaction of idronoxil with a lipid that serves to create a drug-lipid construct considerably improving the drug-like qualities of the idronoxil. The drug-lipid construct had an unexpected consequence in that it readily delivered idronoxil across the normally largely impenetrable blood-brain barrier (BBB) and that NOX66 delivered relatively large amounts of idronoxil with a relatively long half-life in the brain.

While this discovery creates obvious opportunities for the use of NOX66 in the treatment of brain cancer, it is a discovery that Noxopharm believes presents significant opportunities in the treatment of a range of diseases of the central nervous system (CNS) beyond cancer.

Idronoxil, is a drug based on a diphenolic chemical scaffold. The significance of this lies in the considerable body of research showing that diphenolic compounds have therapeutic potential in a wide range of neurological diseases, but which has not translated into marketed products, in large part because of the impenetrability of the BBB.

That led Noxopharm to the realisation that its ability to deliver idronoxil to the brain presented an opportunity to realise the therapeutic potential of these and related compounds more generally in the treatment of a range of neurodegenerative diseases and disorders.

Noxopharm then conducted a limited research program based on the opportunity to treat the conditions known as *excitotoxicity* and *neuroinflammation*, two prime components of the pathogenesis of many CNS degenerative conditions. Over the past 12 months the Company has progressed both of these opportunities to the point of identifying lead candidate compounds with confirmed on-target activity in both cases. The two lead compounds are identified as NYX-104 and NYX-105 respectively.

Noxopharm believes that the identification of these two compounds is a significant commercial opportunity, addressing diseases of significant community cost and with high unmet need. While significant progress has been achieved to date with minimal expenditure, further progress will require considerable funding.

The Noxopharm Board has considered its position and believes that it is in the best interests of shareholders that the listed entity preserves its resources and maintains its focus on oncology, and that the most appropriate way to realise the potential of these two non-oncology drug assets is to place them into a separate company that will be able to seek its own funding.

Having taken that decision, the opportunity then presented to acquire a third drug development asset, itself a small molecule non-oncology therapeutic known as a PCSK9 inhibitor and owned by Cardio Therapeutics Pty Ltd (Cardio), a company independent of Noxopharm and owned by Dr Ian Dixon, a Non-Executive Director of Noxopharm.

## 1.2 Nyrada Pipeline

The three drug development programs that will be advanced by Nyrada are:

### 1. **NYX-104** - *An inhibitor of TrpC3.*

Short transient receptor potential channel 3 (TrpC3) has recently been identified by a research team at the University of New South Wales (UNSW) as a key regulator of excitotoxicity, a pathological condition of the brain associated with stroke, concussion and many neurodegenerative diseases.

A collaboration between Noxopharm and the UNSW has identified NYX-104 as an effective inhibitor of TrpC3, potentially protecting healthy neurons against damage.

Nyrada intends to develop NYX-104 as a treatment to minimise damage following CNS trauma (stroke, repeat concussion, severe epileptic seizure, spinal damage).

### 2. **NYX-105** - *Thromboxane synthase inhibitor.*

Thromboxane is one of the key components of inflammation. Inhibiting the activity of thromboxane synthase, blocks the formation of thromboxane by platelets, without affecting other components of the inflammatory cascade. Thromboxane has been implicated in the pathogenesis of a number of inflammatory diseases including inflammatory bowel disease (IBD), which includes ulcerative colitis (UC) and Crohn's Disease; non-alcoholic steatohepatitis (NASH) and neurodegenerative diseases such as Alzheimer's Disease.

Nyrada will focus on using the Noxopharm proprietary drug delivery mechanism in two ways:

- (i) to provide NYX-105 with enhanced drug-like activities in the treatment of IBD and NASH; and
- (ii) to deliver NYX-105 across the BBB to treat neuro-inflammatory processes.

3. **ALT-30 - A PCSK9 inhibitor.**

The project to be acquired from Cardio is a drug to inhibit the activity of proprotein convertase subtilisin/kexin type 9 (PCSK9). PCSK9 is a validated drug target for the treatment of elevated cholesterol, with two monoclonal antibody products currently enjoying market success in the treatment of familial hypercholesterolaemia.

ALT-30 is the lead candidate compound with confirmed ability to inhibit binding between PCSK9 and the low density lipoprotein (LDL) cholesterol receptor.

Nyrada proposes to develop ALT-30 as an oral, small molecule inhibitor of PCSK9 function for the general treatment of hypercholesterolaemia.

### 1.3 This Report

The Board of Noxopharm requested Acuity Technology Management Pty Ltd (Acuity) to prepare valuations of the three drug programs. In the first instance, the valuations will be used by the Noxopharm Board to determine the amount of equity to be granted to Dr Ian Dixon in return for the acquisition by Nyrada of Cardio. In addition, Dr Dixon's position as a member of the Noxopharm Board makes this a related party transaction that will require shareholder approval. Hence a second purpose of the project valuations is to support an Independent Expert Report to shareholders, to be prepared by a third party, aiming to validate that the transaction is fair and reasonable.

Acuity specialises in the appraisal and valuation of IP and knowledge-based intangible assets, including in-process R&D (IPR&D). Acuity has experience in valuing medical devices, diagnostic systems, pharmaceuticals, genetic and recombinant DNA technologies, stem cell therapies and complementary & alternative medicines. Details of our qualifications and experience are summarised in an Attachment to this valuation opinion. Further details can be found at [www.acuitytechnology.com](http://www.acuitytechnology.com).

The cash flow models used in the following valuations make an assumption that the further development and commercialisation of programs is not limited by funding. A lack of sufficient capital could undermine the valuation.



## 1.4 Summary of Valuation

Our analysis of the IP and the markets for the proposed products of the research programs suggests an after-tax valuation for Nyrada as at 1 July 2017 of approximately **\$7.25 million**. The assessment assumes that human applications are licensed out following Phase 2 studies by Nyrada with the licensee assuming ongoing development costs while Nyrada receives royalties on the sale of products.

Component after-tax valuations are:

TRPC3 inhibitor,	\$2.36 million in the range \$0.58 to \$4.74 million,
Thromboxane synthase inhibitor,	\$2.29 million in the range \$0.67 to \$4.20 million, and
PCSK9 inhibitor,	\$2.60 million in the range \$0.63 to \$5.25 million.

The range is consistent with the market capitalisations of early stage or pre-clinical Australian biotech companies.

It is our opinion that all three projects, being discovery or pre-clinical, considering the ranges of valuations and taking into account the errors associated with input assumptions, are of roughly equivalent value.

All programs are valued on their potential to be used in a single medical condition. The thromboxane inhibitor product, in particular, and the TRPC3 inhibitor have the potential to be of clinical utility in many other indications and consequently may have greater valuations than presented in this analysis. The PCSK9 product is a “first-in-class” development and, although the potential market is extremely high, its current valuation is constrained by the need for demonstrable clinical safety of the proposed molecule.

At valuation date, the status of development may be summarized as discovery and pre-clinical:

- TRPC3 Inhibitor – lead candidate (NYX-104) identified and currently undergoing validation in an animal model of stroke. It is a variant on a compound already confirmed by Noxopharm as crossing the BBB of rats and as safe for human administration;
- Thromboxane Synthase Inhibitor – a compound previously evaluated in humans has been modified (NYX-105) by Noxopharm to improve its drug-like qualities, including the ability to cross the BBB. This new construct requires proof-of-concept *in vivo*; and
- PCSK9 Inhibitor – ALT-30 is confirmed as binding to and inhibiting PCSK9. Current studies aim to confirm proof-of-concept in an animal model.

It is unlikely that any of these three projects are sufficiently advanced to attract licensing opportunities in the immediate term. Nyrada has indicated no intention of seeking a partnership until after first-in-human studies at the earliest, and after Phase 2 preferably.

Although a number of techniques suitable for valuing intangible assets were considered, the principle method used is based on a probability adjusted discounted cash flow (DCF) using revenue forecasts and expenses developed by Acuity and drawing on budgets and other financial information provided by Nyrada along with an analysis of pharmaceutical company metrics. The method is considered the most suitable for IPR&D in the pharmaceuticals field. The financial models are based on cash flow projections that may be achieved following further research and commercialisation of the IP with probability and discount rate adjustments based on an examination of risks to the successful completion and exploitation of the IP.

The development of each product involves risks commonly encountered in drug development and published statistics provide a reasonable basis for estimating the likelihood of success in reaching market and generating revenues from sales, or licence fees and royalties. Our valuation methodology considers these risks through the application of probabilities of success in obtaining marketing approvals in the proposed indications. It also utilises insights into the technical likelihood of discover and pre-clinical success, areas where there is scant statistical information. The overall probability of successful transition to market approval used in our modelling for valuation purposes is in the range 4.3% to 5.6%. There are many other areas for potential error in predicting cash flows relating to the size of the treatable populations, selling price, estimates of strength and quality of competition, clinical development costs and development times. These all impact on the valuation and are difficult to estimate with accuracy at this stage.

Although drug development follows a well-trodden pathway and the risks and likelihoods of success are well understood, it is difficult to predict the potential for early stage, discovery programs to create a novel and effective molecule that will enter human trials and to understand the precise niche that any product, once launched, will fulfill. A valuation based on future earnings is likely to be imprecise, hence a broad range, while a valuation based on comparables analysis is unreliable due to the limited number of licensing transactions occurring while still in a research phase and the paucity of publicly traded entities. In our opinion, historical expenditures are a poor indicator of value.

This report presents valuations from two perspectives:

- That of Nyrada, as originator, which will out-license the IP prior to entry into late stage clinical trials to avoid costs and mitigate risks; and
- That of a licensee, or licensees, which will need to realize a return on the investment in the product licences and the further development of products.

The major focus is for a valuation based on the IP's potential for license to a major pharmaceutical or biotechnology company and represents the value that Nyrada may realise through such a transaction. In a licensing arrangement, the net gain from commercializing the IP is generally split between licensee and licensor, often in a ratio of three to one, the "25% rule", and possibly up to 50:50 for a fully developed and approved product. In this case, we have apportioned 75% to the licensee and 25% to the licensor for all three programs on the basis that the Company is likely to complete Phase 2 studies before licensing. The royalty rate is adjusted to achieve these splits.

Full-development and exploitation by Nyrada, if it were to occur, has the advantage that there will be no sharing of net benefits with another party and a valuation based on such an approach may result in a higher figure than achieved through licensing. However, such a commercialization strategy does entail greater risks and costs relative to those faced by big pharma and, as a consequence, a lower probability of success will translate to a valuation lower than might otherwise be expected.

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## 2. Background

### 2.1 The TrpC3 Inhibitor – NYX-104

Any damage to neurons (the primary cells in the brain and spinal cord) causes them to dump their chemical neurotransmitters resulting in surrounding healthy neurons being subject to over-stimulation by an excess of neurotransmitters. That damage can be in the form of trauma (concussion, spinal trauma), impaired blood supply (stroke) or neurodegenerative disease (Alzheimer's disease, etc).

One of the key actions of neurotransmitters is to increase calcium influx into neurons, leading to an electrical impulse in the receiving nerve cell. Neurotransmitter overload, however, risks causing excessive calcium influx into the cell, resulting in the cell becoming over-excited and then dying, a process termed *excitotoxicity*.

Excitotoxicity is a progressive pathological event, causing a cascade of brain cell death. Following stroke, excitotoxicity is estimated to cause six to ten times more death of brain cells over the ensuing week than caused by the original injury. It is generally accepted that excitotoxicity accounts for the bulk of neuronal damage in many CNS diseases.

For that reason, excitotoxicity has been identified as a key target for drug development to assist in blocking the cascade of death of brain cells following acute brain injury or chronic brain diseases. To date, no drug has successfully been tested in the clinic.

A critical step in this objective has now been taken by the UNSW, with a research group in the Faculty of Medicine identifying a key protein. TrpC3 has been shown to play a gate-keeper role in the excitotoxicity process. In response to a barrage of glutamate (the main neurotransmitter), TrpC3 responds by opening up calcium channels and allowing toxic levels of calcium to enter the neuron, eventually killing the cell.

The UNSW research team has identified a particular isoform of TrpC3 (alternative spliced protein) as being responsible for a higher rate of calcium ion ( $\text{Ca}^{++}$ ) influx than previously thought. Using an *in situ* model involving measuring glutamate-induced  $\text{Ca}^{++}$  influx into isolated human neuronal cells, the team has shown definitively that inhibition of this form of TrpC3 blocks  $\text{Ca}^{++}$  influx and preserves the integrity of the cell.

Using that same *in situ* screen, NYX-104 has been identified as a potent inhibitor of the relevant TrpC3 isoform. The inhibitory mechanism of action has yet to be identified but is assumed to be due to inhibition of phosphorylation of TrpC3 stemming from a direct inhibitory effect of NX-104 on the protein's activating tyrosine kinase.

NYX-104 currently is undergoing testing in a mouse stroke model for its ability to block the extent of death of brain cells associated with excitotoxicity

## 2.2 Thromboxane Synthase Inhibitor – NYX-105

Inflammatory processes are recognised as a key component of the pathology associated with a wide range of traumatic CNS conditions and neurodegenerative diseases: Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, motor neuron disease (MND) and multiple sclerosis.<sup>1</sup>

Neuro-inflammation and excitotoxicity are the two prime components of CNS diseases and the Noxopharm strategy is to seek to achieve important uniqueness in addressing both pathologies.

The rationale in using a thromboxane synthase inhibitor in the treatment of neuro-inflammation is recent data pointing to a key role of platelets and thromboxanes in this form of inflammation.<sup>2</sup> No selective thromboxane synthase inhibitor has previously been looked at in the treatment of neuro-inflammation.

Thromboxane synthase is responsible for production of key inflammatory eicosanoids, Thromboxane A<sub>2</sub> and Thromboxane B<sub>2</sub>, TxA<sub>2</sub> and TxB<sub>2</sub> respectively, which play key roles in neuro-inflammatory pathology associated with cerebral ischaemic damage and neurodegenerative diseases.

Known inhibitors of thromboxane synthase: ifetroban for example - a thromboxane receptor antagonists; and dual action, picotamide which inhibits thromboxane synthase as well blocking the thromboxane receptor; do not cross the BBB and are of little benefit in treating neurological disorders. The clinical relevance of using such inhibitors remains untested.

A series of novel synthetic isoflavone analogues was developed in the early-2000s by Novogen Ltd as selective inhibitors of thromboxane synthase, with NV-52 subsequently identified as the lead compound and taken into a Phase 1 clinical study.<sup>3</sup> NV-52 was developed specifically to inhibit the production of thromboxane without inhibition of cyclooxygenase (COX) 1 and 2, the latter generated upstream of thromboxane formation in the arachidonic acid pathway.

Novogen's interest in NV-52 was in treating IBD and ulcerative colitis (UC) specifically. There is an increased production of specific prostaglandins which are thought to be protective to gastrointestinal mucosa. NV-52 demonstrated a high degree of protection from disease in the standard mouse model of human IBD, the dextran-induced colitis which produces a pathology mimicking human IBD.

NV-52, in common with all diphenolics, is subject to extensive Phase 2 metabolism in the human body which Noxopharm believes would potentially significantly compromise its therapeutic effect in IBD, as well as blocking its ability to cross the BBB.

NYX-105 is a chemically modified form of NV-52 designed to augment its therapeutic potential in the case of IBD and to cross the BBB in the case of neurodegenerative diseases.

---

<sup>1</sup> Chen W-W, *et al.* Role of Neuroinflammation in Neurodegenerative Disease (Review). Mol Med Reports 13:3391, 2016

<sup>2</sup> Horstman LL, *et al.* Role of Platelets in Neuroinflammation: A Wide Angle Perspective. J Neuroinflammation 7:10, 2010.

<sup>3</sup> Howes LG, *et al.* NV-52: A Novel Thromboxane Synthase Inhibitor for the Treatment of Inflammatory Bowel Disease. Expert Opin Investig Drugs 16(8):1255, 2007.

The targeted conditions for NYX-105 are neuro-inflammation and IBD. The current valuation is premised on demonstration of efficacy in UC. The Company intends to pursue this clinical indication with what it believes will have a greater chance of success compared to the original NV-52 program.

IBD comprises two different syndromes: UC and Crohn's disease. UC is characterised by inflammation that is limited to the mucosa and submucosa of the colon (principally the rectum and distal colon) and consists of a continuous area of inflammation. The incidence of UC in the population varies between 3 and 15 per 100,000.

Thromboxanes are produced in excess not only in inflamed gut mucosa, but also by isolated intestinal and peripheral blood mononuclear cells and in the uninflamed bowel in Crohn's disease. Their cellular source is likely to include platelets, neutrophils, and endothelial and epithelial cells as well as mononuclear cells.

IBD is well known to be associated with dysregulation of detoxifying activity in affected mucosal cells. While levels of UDP-glucuronosyl transferase/sulfatase activity have not been measured, levels of many other detoxification enzymes (glutathione transferase, acetylation enzymes, methyltransferases) are known to be increased. If, as Noxopharm suspects, UDP-glucuronosyl transferase/sulfatase activities are also increased, then the original unprotected molecule (NV-52) would be at increased risk of Phase 2 metabolism and therefore have greatly diminished bio-activity. NYX-105 is designed to protect the molecule from Phase 2 metabolism, thereby preserving the drug's activity.

While NV-52 was protective in the mouse dextran sulphate model of IBD, the considerable difference known to exist in Phase 2 metabolism between rodents and humans leads Noxopharm to believe that there is a real prospect that NV-52 would not have been effective in humans.

NYX-105 is a pro-drug that offers the prospect of ensuring that the anti-inflammatory effect of the compound is retained.

### **2.3 PCSK9 Inhibition – ALT-30**

When the levels of cholesterol in the blood are too high (6.5 mmol/l or higher), the condition is called hypercholesterolemia or dyslipidemia. It is generally thought that lowering cholesterol back to within the normal range prevents plaque formation in the blood vessels and reduces the likelihood of cardiovascular incidents such as heart attack and stroke. Cholesterol (like all other lipids) is insoluble in water, and is carried in the blood bound to a protein structure, forming molecules called lipoproteins. The two types of lipoprotein that are particularly important in atherosclerosis and heart disease are LDL and high density lipoproteins (HDL). LDL transports cholesterol from the liver (where cholesterol is synthesized) to peripheral tissues of the body, whereas HDL removes excess cholesterol from peripheral tissues, taking it back to the liver to be broken down. Epidemiological studies have associated higher levels of LDL-cholesterol and lower levels of HDL-cholesterol in the blood with increased risk of coronary heart disease.

The current preferred modality for reducing plaques and cardiovascular risk is through restricting cholesterol synthesis. Statins are a class of small molecule compounds that inhibit HMG-CoA reductase, a rate-limiting enzyme in cholesterol biosynthesis, thereby reducing LDL-cholesterol in humans. Statins effectively reduce cholesterol levels 20% to 50% and the associated cardiovascular disease risk by about 30%, but residual risks for developing cardiovascular disease remain.

Statins have been amongst the highest revenue generating drugs for several decades and, although the prescribing levels continue to increase, revenues are declining as branded drugs come off patent and generic statins enter the market.

A second approach to constrain cholesterol levels is to limit cholesterol intake from the diet. Ezetimibe inhibits an intestinal epithelial membrane protein, Niemann-Pick C1-Like 1 (NPC1L1), to reduce cholesterol absorption and accordingly lowers LDL-cholesterol by about 20%. The cardiovascular risk reduction from ezetimibe, however, is yet to be proven in clinical studies.

In recent years, PCSK9 has emerged as a target of significant interest as an alternative to statins and new source of revenues for drug companies. Cholesterol carried in LDL particles is readily taken up by its cognitive plasma membrane receptor, LDL-R, on liver and other tissue. Cholesterol is delivered eventually to the lysosomal compartment, and receptors either recycle back to plasma membrane or are degraded in lysosomes. PCSK9 plays a major role in regulating hepatic LDL-R protein levels and thus circulating LDL-cholesterol in humans by binding to the extracellular portion of LDL-R with the PCSK9/LDL-R complex moving into the cell where it is degraded such that there is no LDL-R recycling back to the plasma membrane. The net effect is reduced removal of LDL-cholesterol from the circulation. The inhibition of PCSK9 has been shown to effectively reduce circulating LDL-cholesterol by conserving LDL-R.

The cell surface LDL-R interaction has been proven to be an unsuitable site for small molecule targeting. The PCSK9 binding site on LDL-R has been identified and is known to be well conserved across species which means that cross-species testing of an LDL-R-binding drug is feasible.

The Cardio program started with computational modelling of constitutively preserved PCSK/LDL-R binding site. The company subsequently identified a groove adjacent to the attachment site on LDL-R and has shown this to be suitable for binding small molecules. Filling this groove has now been confirmed as blocking PCSK9/LDL-R binding.

## **2.4 Intellectual Property**

### **2.4.1 Patents Covering Noxopharm IP**

We understand that the patent situation is a work in progress with Noxopharm's attorneys, Freehills, actively reviewing existing patent applications and preparing new ones.

The current situation is that Noxopharm filed a patent in April of this year that covered the NOX66 delivery method for its modified idronoxil, referred to as idronoxil-C. The active compound appeared in the blood stream where it displayed a considerably better pharmacokinetic (PK) profile compared to idronoxil given intravenously (IV) or orally; plus an ability to cross the BBB. The nature of idronoxil-C is now known to be a pro-drug form that endows the compound with these more desirable drug-like properties.

Separate patents are currently being written for these pro-drug forms of both NYX-104 and NYX-105, along with claims covering their different clinical applications. The NYX-104 patent is in the name of NorBio No. 1 Pty Ltd and NYX-105 in the name of NorBio No. 2 B Pty Ltd. It is intended that these two wholly-owned subsidiary companies of Noxopharm will roll over into Nyrada.



The Company intends to have both patents filed by the time the Acuity document goes public and, once completed, enable verification that separate patents having been filed with the US Patent Office under the PCT system for both NYX-104 and NYX-105. We understand that these patents will cover composition of matter for the pro-drug structures, along with usage claims across a wide range of clinical applications.

Nyrada will not be in breach of any patent concerning NV-52. Patent application, WO2006/108212, filed by Novogen and subsequently allowed to lapse, claims isoflavanoids (including NV-52) specifically for the treatment of inflammatory diseases, including IBD (not neuro-inflammation). The compound is therefore unpatentable *per se* due to this prior disclosure, and protection for NYX-105 will derive from the novel pro-drug structure and new claimed uses.

#### 2.4.2 Patent Covering Cardio IP

Cardio is the owner of an Australian Provisional Patent filed on 17 March 2017. The provisional is titled: *Heterocyclic inhibitors of PCSK9*, and claims a class of small molecules that binds extracellular PCSK9 thereby preventing its interaction with the LDL receptor.

This is a composition of matter patent and provides the highest level of protection for a pharmaceutical.

Patents for all three drug assets are provisional, benefiting from the priority date of the filings, and full PCT specifications must be lodged within 12 months of the provisionals. Once a PCT is filed it will undergo examination by the national patenting authorities and, if granted, benefit from a 20 year from filing date monopoly on the invention.

### 3. Research Findings

#### 3.1 Noxopharm Research

##### 3.1.1 TRPC3 Inhibitor

The initial studies conducted by UNSW used the naturally-occurring plant isoflavonoid, genistein. The basis being that one of genistein's many biological properties is an ability to block calcium channel activity in cells. After identifying TrcP3 as a key drug target in excitotoxicity, the UNSW research team confirmed in their *in situ* model that genistein moderately blocked glutamate-activated TrcP3 activity. However, genistein was not considered a suitable drug candidate in humans because of its high rate of metabolism and inability to cross the BBB.

Noxopharm then supplied UNSW with a number of compounds related to genistein, but in contrast to genistein, able to be protected from metabolism and able to cross the BBB. NYX-104 proved to be highly effective at blocking TrpC3 activity *in vitro*.

NYX-104 is currently undergoing a proof-of-concept study in a mouse model of stroke (laser-induced ischaemic lesions of the cerebrum and cerebellum) in collaboration with the UNSW. It is proposed that on receipt of that proof-of-concept data, that NYX-104 then will undergo routine pre-clinical studies in the lead up to a first-in-human study.

### 3.1.2 Thromboxan Synthase Inhibitor

NV-52 is supported by solid evidence of proof-of-principle in an animal model. In published studies conducted by Novogen, the compound demonstrated a high degree of protection from disease in the standard mouse model of human IBD (dextran-induced colitis), which produces a pathology mimicking the human condition.

A Phase 1 study of intravenous NV-52 in healthy volunteers then showed it to be well tolerated and with a PK profile considered at the time to be therapeutically relevant.<sup>4</sup> There is no evidence of any further development of the compound after that time, with this period coinciding with the sale of Novogen assets to MEI Pharma, Inc in about 2010.

Noxopharm has converted NV-52 into a pro-drug form along the lines of idronoxil-C, which displays the following key advantages:

- Protection from Phase 2 drug metabolism;
- Increased half-life from 45 minutes to approximately nine hours; and
- Ready passage across the BBB.

Under Nyrada, the project will pursue two main development streams:

- Neuro-inflammation (particularly peripheral neuropathy associated with chemotherapy and diabetes); and
- IBD, specifically UC.

The latter forms the basis of the current valuation as NV-52 is known to be effective in rodent models and a sound hypothesis exists for a modified formulation likely to be effective in humans.

## 3.2 Cardio Research

Cardio's investigations identified a groove adjacent to the attachment site on LDL-R and has shown this to be suitable for binding small molecules. Filling this groove has now been confirmed as blocking PCSK9/LDL-R binding.

A small molecule library was subsequently screened for binding to this site, leading to a standard medicinal chemistry structure-activity relationship (SAR) analogue development program. ALT-30 has been identified as the lead candidate with a 70 nM inhibitory activity, lack of significant off-target activity, and an appropriate PK profile in mice.

The current research program is evaluating ALT-30 in a transgenic hypercholesterolaemic mouse model followed by the development of an oral dosage form.

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<sup>4</sup> Howes LG, et al. Phase 1b Single- and Multiple-Dose Pharmacokinetic Study of Oral NV-25 in Healthy Volunteers. *Drugs R D* 9(3):159, 2008.

### 3.3 Terms of IP Acquisition

NorBio No. 1 Pty Ltd and NorBio No. 2 Pty Ltd are to be rolled over by Noxopharm Ltd into Nyrada, with Noxopharm receiving 100% shares in the latter entity. Nyrada then will own fully all IP relating to NYX-104 and NYX-105.

The purchase of Cardio Therapeutics Pty Ltd by Nyrada will be the subject of shareholder approval at a General Shareholder Meeting given that the involvement of Dr Dixon in this transaction makes it a related party transaction. A report in accordance with Australian Securities and Investment Corporation (ASIC) Regulatory Guideline RG 111, *Content of Experts reports* and RG 112, *Independence of Experts*, will be presented to shareholders prior to voting.

We understand that Moore Stephens Lawyers will be appointed to prepare the Independent Expert Report and will rely on Acuity's report in providing an opinion as to whether the proposed transaction is fair and reasonable to Noxopharm shareholders.

### 3.4 Development and Commercialization Plans

Development and commercialization strategies for all three drug assets (should Noxopharm shareholders grant the necessary approvals) will rest in the hands of the Nyrada Board. However, we understand that Noxopharm with its majority shareholding in Nyrada will control the Nyrada Board through nominee directors. On that basis, Acuity has taken note of the stated intentions of the Noxopharm Board in respect of the short-term objectives it believes will be set for Nyrada.

Nyrada will concentrate over the next six months on two key objectives: (a) establishing proof-of-concept in animal models; and (b) optimising dosage delivery formulations. From there, standard pre-clinical studies will be undertaken across all programs. Those studies will need to focus on all required pre-Investigational New Drug studies in the lead up to first-in human clinical studies. Those pre-clinical programs are anticipated to take 18-24 months.

The Noxopharm Board has indicated its intention to take at least two, if not all three, programs through to the conclusion of Phase 2 clinical studies at which time the strategy will be to seek a marketing partner to take the drugs through the Phase 3 and registration process.

Longer-term, the strategy for Nyrada is:

- To remain a developer of small molecule drugs;
- To be active across a variety of therapeutic fields (other than oncology); and
- To in-license drug opportunities rather than to develop in-house drug discovery resources.

## 4. Markets and Competition

### 4.1 Stroke

A stroke is the result of disruption of blood to the brain and hence nutrients and oxygen to brain cells or neurons. Blood may be interrupted or stop moving through an artery because the artery is blocked, known as an ischaemic stroke, or ruptures, haemorrhagic stroke. The area of brain damage is called a cerebral infarct.

Neurons die rapidly following the infarct due to oxygen and glucose deprivation. Excitotoxicity is a primary mechanism of neuronal injury to nearby cells and intervening in this process may prevent extensive functional damage.

The brain is particularly prone to ischaemic damage. Unlike the immediate ischaemic damage that is observed in other tissues, a transient period of cerebral ischemia (approximately 10 minutes) can produce profound neuronal damage that only becomes evident three days after the event and continues progressively for months. The delayed and progressive nature of neuronal damage following cerebral ischemia points to a wide time window for therapeutic intervention and emphasizes the importance of understanding the nature of ischaemic neuronal death.

According to the World Health Organisation (WHO), 15 million people suffer stroke worldwide each year. Of these, five million die and a similar number are permanently disabled.<sup>5</sup> The WHO places the global incidence of stroke at around 200 cases per 100,000 inhabitants, although data vary among countries. Stroke incidence ranges from 240 per 100,000 in Dijon, France (standardized to the European population aged 45–84 years), to about 600 per 100,000 in Novosibirsk, Russia.<sup>6</sup>

Stroke is Australia's second single greatest killer after coronary heart disease and a leading cause of disability. In 2012, Australians suffered around 50,000 new and recurrent strokes. Every year, more than 795,000 people in the US have a stroke. About 610,000 of these are first or new attacks.

Most strokes (87%) are ischaemic (caused by thrombosis or embolisms) and the rest (13%) are haemorrhagic (caused mainly by rupture of blood vessel or aneurysm).

Data from the US Agency for Healthcare Research and Quality's HCUPnet<sup>7</sup> database reports emergency department data for *Cerebral artery occlusion, unspecified with cerebral infarction* (diagnosis code 434.91), as 397,994 visits in 2014 with 318,714 admissions (the remainder discharged). Data from hospital admissions has 355,345 admissions for 4.5 days hospitalisation and mean cost of US\$43,089 and national bill of US\$15.341 billion.

The number of stroke events in Europe is projected to rise from 1.1 million in 2000 to 1.5 million per year by 2025, largely due to the ageing population.<sup>8</sup> In the EU27 countries, the annual economic cost of stroke is an estimated €27 billion: €18.5 billion (68.5%) for direct costs and €8.5 billion (31.5%) for indirect costs. An additional €1.1 billion is calculated for the value of informal care.<sup>9</sup>

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<sup>5</sup> World Health Organisation. Global Burden of Stroke ([http://www.who.int/cardiovascular\\_diseases/en/cvd\\_atlas\\_15\\_burden\\_stroke.pdf](http://www.who.int/cardiovascular_diseases/en/cvd_atlas_15_burden_stroke.pdf)).

<sup>6</sup> Grysiewicz RA, *et al.* Epidemiology of Ischaemic and Hemorrhagic Stroke: Incidence, Prevalence, Mortality and Risk Factors. *Neurol Clinics* 26(4):871, 2008.

<sup>7</sup> <https://www.ahrq.gov>.

<sup>8</sup> Truelsen T, *et al.* Stroke Incidence and Prevalence in Europe: A Review of Available Data. *Eur J Neurol* 13:581, 2006.

<sup>9</sup> British Geriatrics Society. Human and Economic Burden of Stroke. *Age Ageing* 38:4, 2009.

Stroke is the most prevalent cardiovascular disease and the most prevalent neurological disease in Asia. Many countries in East and Southeast Asia have higher mortality rates from stroke than from ischaemic heart disease, the opposite of Western countries. In Japan, stroke rates have declined in recent decades but recent studies suggest the age-adjusted incidence of total stroke for men being approximately 500 per 100,000 person-years and 380 per 100,000 for women with 75.4% ischaemic.<sup>10</sup>

The critical role of calcium influx mediated by the N-methyl-D-aspartate receptor (NMDA-R) in stroke pathogenesis suggests that NMDA-R antagonists and post-synaptic calcium channel blockers may be effective against stroke. A recent review of drug development and studies has been presented by Lai, *et al.*<sup>11</sup> The drug MK-801 is a potent and selective uncompetitive NMDA-R antagonist that readily crosses the BBB, allowing systemic administration. Notably, MK801 is one of the most widely studied NMDA-R antagonists in neurodegeneration research, and has been widely demonstrated to be effective in *in vitro* and *in vivo* models of ischaemic/anoxic neuronal death.

None of the drugs designed to target the NMDA-R directly have been approved for clinical use in stroke treatment, and several of these compounds have failed clinical studies in unexpected ways. The reason for this lack of clinical success is likely multi-factorial. Two possible explanations are that (i) NMDA-R blockers produce many side effects due to the prevalence of neurological functions requiring these receptors, and (ii) NMDA-R blockers have a short therapeutic window for drug administration, as they are effective only when administered before or immediately following stroke. A major drawback of NMDA-R antagonists is their side effects, including the dysfunction of neurological processes that require the NMDA-R and the reversible induction of pathology related to neuronal morphology. A number of NMDA-R antagonists that were under development have been discontinued from further human clinical studies, partially due to concerns about pathomorphological changes that were observed in neurons from animals treated with the earlier experimental compounds like MK-801 and phencyclidine.

Two notable compounds are the NMDA-R glycine-binding site antagonists, gavestinel (GV150526) and licostinel (ACEA1021), which were developed with the intention of reducing the side effects that are observed with conventional NMDA-R antagonists that target the glutamate-binding site or the NMDAR channel pore. Gavestinel and licostinel are strongly protective against ischaemic neuronal damage *in vivo*.

The role of TrpC3 channels in excitotoxicity and the potential to block these has been reviewed by Hartmann, *et al.*<sup>12</sup> Development of an effective blocker of TrpC3 channels will reduce mortality and morbidity from ischaemic brain injury, along with progressive expansion of brain injury from trauma, and glutamate excitotoxicity from epilepsy.

Perth-based Metavone Ltd issued a prospectus in 2016 stating that it was developing oral isoflavone drugs primarily for treatment of cancer and neurodegenerative diseases. That company reports that several of their compounds have the ability to cross the BBB which for clarification was based on computer predictions rather than on confirmed animal studies, with those computer predictions most likely not taking into account the high rate of Phase 2 metabolism of isoflavones in humans.

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<sup>10</sup> Toyoda K. Epidemiology and Registry Studies of Stroke in Japan. *J Stroke* 15(1):21, 2013.

<sup>11</sup> Lai TW, *et al.* Excitotoxicity and stroke: Identifying Novel Targets for Neuroprotection. *Prog Neurobiol* 115:157, 2014.

<sup>12</sup> Hartmann J, *et al.* TRPC3 Channels are Required for Synaptic Transmission and Motor Coordination. *Neuron* 59:392, 2008.

## 4.2 Ulcerative Colitis

In the US, it is currently estimated that about 1.0 to 1.3 million people suffer from IBD with 238 cases per 100,000 adults.

Many agents are available for the treatment of both forms of IBD and the selection of the most ideal therapeutic regimen depends on several factors including disease severity, response to previous treatment, and co-morbidities. Though various treatment algorithms exist in the literature, clinical treatment for both forms of IBD remains highly personalized to each individual. Since there is no cure for either form of the disease, the goal of treatment is to induce and maintain remission of symptoms.

Aminosalicylic acids (5-ASAs) are recommended for both types of IBD. Conventional corticosteroids do not require direct contact with the inflamed tissue but rather work to decrease inflammation throughout the body. For inducing remission in mild to moderate UC, this drug class is perceived to be the most effective and is administered to patients who are inadequate responders to 5-ASAs and/or antibiotics. Corticosteroids are also known to cause serious side effects. Also useful are anti-tumour necrosis factor (TNF) antibodies which attach to and block a protein produced by immune cells called TNF. They are generally used later in the IBD treatment algorithm in patients who respond inadequately to corticosteroids. Such treatment on a chronic basis can be highly expensive.

## 4.3 Hypercholesterolaemia

The current armory of cholesterol-lowering drugs includes statins, absorption inhibitors, nicotinic acid (niacin) derivatives, bile acid sequestrants (resins) and fibrates. Statins, HMG-CoA reductase inhibitors, have been the mainstay of the industry since the late 1980s.

The market for cholesterol drugs used to fight dyslipidaemia is expected to remain amongst leading drug sales and to grow to US \$31 billion by 2022, according to a Health Exchange report.<sup>13</sup>

By 2011, global sales of statins and other lipid-regulating drugs had reached a dramatic high of US\$39.1 billion. At that time, Pfizer's Lipitor® was the world's leading drug with annual sales of US\$12.5 billion. During the years that followed, things quickly began to change. Global sales of statins and other lipid regulators fell more than 32% between 2011 and 2017. Transparency Market Research reported the market for dyslipidemia drugs as US\$17.9 billion in 2014 but expected a decline 10.3% compound annual growth rate (CAGR) between 2015 to 2023.<sup>14</sup>

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<sup>13</sup> Britt R. Cholesterol Drugs will Continue to be Market Leader for a Decade; Report. Health Exchange 20 Aug 2013 (<http://blogs.marketwatch.com/health-exchange/2013/08/20/cholesterol-drugs-will-continue-to-be-market-leader-for-a-decade-report>).

<sup>14</sup> Transparency Market Research. Dyslipidemia Drugs Market – Global Industry Analysis, Size, Share, Growth, Trends and Forecast 2015-2023.

According to market analysts, Visiongain, the statin Crestor® (rosuvastatin, AstraZeneca), was the global leader in 2014 with sales of US\$5,911 billion holding 32.2% market share in a market worth \$18,346 billion.<sup>15</sup> The analysts estimated that revenues of cholesterol lowering drugs would reach \$24.6 billion in 2019. Crestor sales in 2015 were US\$5.427 billion down 8.2%.

Crestor, however, like other statins before it, is losing value as patents expire and lower cost generics gain market entry although research firm, Decisions Resources, believes that generic growth is not enough to offset new drivers of market growth. Newer cholesterol-fighting medications known as PCSK9 and CETP inhibitors will drive new market sales and that is expected to counterbalance the loss in sales from the rise in generic medications.

According to Medscape, Crestor® sales were \$6.090 billion in the US to June 2015 followed by absorption inhibitor, Zetia® (ezetimibe, Merck and Co, known as Ezetrol® in other markets) at \$2.159 billion and, Lipitor® \$252 million.<sup>16</sup> Lipitor® (atorvastatin, Pfizer) was an early casualty of generic competition, having been leader and declining from US\$5.157 billion in 2012 in the US and \$2.061 billion in 2014. Between April 2014 to March 2015 prescriptions of Crestor were 21,478,776 in the US, the second most prescribed drug while sales value was fifth.<sup>17</sup>

While generally effective at lowering cholesterol levels, many patients experienced adverse, often serious, side effects, while some patients were not reaching cholesterol lowering treatment goals with statins alone. Lawsuits were filed against Pfizer after it was found that Lipitor may increase the risk of developing diabetes, severe muscle pain, and other serious health problems. AstraZeneca, the manufacturers of Crestor also had lawsuits filed against it by patients who had suffered side effects. From the global highpoint in 2011, sales of statins and other lipid-regulators subsequently fell every single year. By 2015 they had plummeted to US\$26.5 billion, a fall of over 32%.

Forbes magazine reported total cholesterol lowering prescriptions to be 214 million in 2012. Of these, 50,000 prescriptions were non-statins.<sup>18</sup> Of the non-statins in 2012, fibrates led with 23,000 prescriptions and fenofibrates, such as Tricor® (fenofibrate, AbbVie) and generic versions, 17,000.

Drug companies seeking to fill a failing market for proprietary statins have taken to the development of PCSK9 inhibitors. These have been shown to further decrease LDL-cholesterol by 50–70% when administered as monotherapy or in combination therapy with statins.<sup>19</sup> Current inhibitors are monoclonal antibodies directly binding the PCSK9 protein. Antibodies, as proteins, require I/V administration to avoid breakdown in the gut and they can be expensive.

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<sup>15</sup> Cholesterol-Lowering Drugs Market Forecast 2015-2025: Opportunities in PCSK9 Inhibitors, CETP Inhibitors, MTTP Inhibitors, ApoB Inhibitors and PPAR Agonists. Product code: PHA0076. Visiongain (<https://www.visiongain.com/Report/1527/Cholesterol-Lowering-Drugs-Market-Forecast-2015-2025>).

<sup>16</sup> Brooks M. 100 Best-selling, Most Prescribed Branded Drugs Through March. Medscape News & Perspective Aug 13, 2015.

<sup>17</sup> Brown T. 100 Best-selling, Most Prescribed Branded Drugs Through March. Medscape News & Perspective May 6, 2015.

<sup>18</sup> Herper M. As Statins Soar, use of other Cholesterol Medicines Declines. Forbes 29 May 2013 (<https://www.forbes.com/sites/matthewherper/2013/05/29/as-statins-soar-use-of-other-cholesterol-medicines-declines/#17fd12741f6b>).

<sup>19</sup> Value of Cholesterol Lowering Medications. Pfizer ([http://www.pfizer.com/files/health/VOM\\_Statins\\_DEC\\_2016.pdf](http://www.pfizer.com/files/health/VOM_Statins_DEC_2016.pdf)).

In 2015, the US Food and Drug Administration (FDA) approved two different PCSK9 medications for use in patients with heterozygous familial hypercholesterolemia and for patients with cardiovascular disease that require additional lowering of LDL-cholesterol. The first of these injectable drugs, produced by Sanofi and Regeneron, is Praluent® (alirocumab) while the second, developed by Amgen, Repatha® (evolocumab), also has approval in Europe.<sup>20</sup> Following patent litigation by Amgen, the sale of Praluent® was banned in 2016.<sup>21</sup> Pfizer also has a PCSK9 inhibitor under development.

Experts initially estimated that the new medications would cost US\$7,000 to \$12,000 a year, far more expensive than many existing statin drugs. Repatha® (evolocumab) has a current list price of £170 per dose in the UK, taken fortnightly via a pre-filled pen injection. Over the course of a year this is more than £4,400 per patient.<sup>22</sup> Statins are incredibly cheap in comparison, costing the UK National Health Service (NHS) about £200 a year per patient. The Daily Mail reports that around 45% of patients at high risk for cardiovascular disease cannot adequately lower their cholesterol levels with statins. However, others point out that Repatha® comes with its own side effects, including the common cold in 5% of patients and throat infections in 3%.

Praluent® was launched in the US with a US\$40-a-day price, \$14,600 annually.<sup>23</sup> In defending the price, Sanofi noted that estimated costs for a patient who has suffered a heart attack or similar cardiovascular problem range from \$50,000 to \$119,000 over one year. Repatha® in Australia costs \$42.63, or \$24,492 a year.

More than 73 million US adults, or nearly one-third, have high LDL-cholesterol, according to the Centers for Disease Control and Prevention and are candidates for Praluent®. An estimated 6.3 million patients cannot control their LDL levels with statins alone. And another 3.3 million are thought to be unable to tolerate statins due to side effects, but there are no formal criteria to identify these patients.

Sales of both Praluent® and Repatha® have been minimal to date, US\$75 million and \$83 million through the first nine months of 2016, respectively because insurance companies have largely refused to provide reimbursement. The research firm GlobalData forecast that the entire class of PCSK9 drugs could generate sales of US\$17.8 billion by 2023 while Credit Suisse estimates sales for the entire class - including drugs from Amgen and Pfizer - will reach US\$10 billion by 2019. One estimate suggests that, while Praluent® is not marketed, the long-term peak sales for Repatha® could reach US\$3 to 4 billion.

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<sup>20</sup> Dennis B. New Cholesterol-lowering Medications Likely to Trigger Fight over Prices. The Washington Post 21 July 2015.

<sup>21</sup> Heurstein A. After Stunning Loss to Amgen in Patent Case, Regeneron Plans to Join Sanofi in Appeal. The Street 6 Jan 2017 (<https://www.thestreet.com/story/13944621/1/regeneron-cholesterol-lowering-drug-banned-from-u-s-market-in-stunning-loss-to-amgen-in-patent-case.html>).

<sup>22</sup> Spencer B. An Alternative to Statins? New Drug which 'Halves Cholesterol' with Fewer Side Effects goes on Sale in the UK Tomorrow. Daily Mail Australia 7 January 2016 (<http://www.dailymail.co.uk/health/article-3216517/An-alternative-statins-New-drug-halves-cholesterol-fewer-effects-goes-sale-UK-tomorrow.html#ixzz4lRQW5Hrd>).

<sup>23</sup> CBS/AP 27 July 27, 2015 (New cholesterol lowering drug Praluent far more expensive than statins (<http://www.cbsnews.com/news/praluent-cholesterol-lowering-drug-high-cost-statin-alternative>)).



PCSK9 drugs in development include:

- Drugs binding PCSK9
  - Pfizer, bococizumab in Phase 3,
  - Novartis AG, LTG209, in Phase 2,
  - Roche, RG7652 in Phase 2,
  - Alder Biopharmaceuticals, ALD306, preclinical;
- Drugs targeting RNA
  - Alnylan Pharmaceuticals, Idera Pharmaceuticals and Santaris Pharma A/S, all preclinical;
- Small molecules that block PCSK9 secretion from cells
  - In preclinical with Shifa Biomedical;
- Small molecules inhibitors
  - In preclinical with Serometrix and Shifa Biomedical.

Cholesterol drugs remain the second-largest number of dispensed prescriptions in the US according to IMS Health's 2015 National Prescription Audit, which counted 258 million total prescriptions. It is not possible to predict the sales volume nor the impact that PCSK9 inhibitors will have on the market share of statins in the future. It is possible that the potential for generic versions of top-selling medications will make prescribers more likely to take a more cost-effective route, rather than recommend the highly expensive injectable drugs.

At least one study has suggested the current, monoclonal-based PCSK9 inhibitors are not cost effective.<sup>24</sup>

#### 4.4 Advantages & Risks of the Nyrada Programs

Our valuation methodology employs a risk adjusted net present value ("rNPV") approach which requires estimates of the likelihoods of the therapy development program's transitioning through the well-defined stages of evaluation. Over the past two decades there have been several publications presenting suitable data, most of which are derived from US and European clinical trial activity, from which we are able to extract indication-specific information.

Table 1 lists probabilities for drugs across all indications, both new chemicals (referred to as New Molecular Entities or NMEs) and biologicals, once they enter the clinical stages of development. The probabilities are the likelihoods that a drug will successfully complete a particular stage of investigation and move to the next stage. The cumulative probability is the likelihood that it will complete all stages.

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<sup>24</sup> Kazi DS, et al. Cost-effectiveness of PCSK9 Inhibitor Therapy in Patients with Heterozygous Familial Hypercholesterolemia or Atherosclerotic Cardiovascular Disease. JAMA 316(7):743, 2016.

**Table 1: Published Success Rates for Drug Development Programs**

Successful completion of:	Transitional Probability <sup>25</sup>			
	Abrantes-Metz <i>et al</i> <sup>26</sup>	Kola & Landis <sup>27</sup>	Kaitlin <sup>28</sup> & DiMasi, <i>et al</i> <sup>29</sup>	Hay, <i>et al.</i> <sup>30</sup>
Phase 2	80.7%	68%	71%	64.5%
Phase 2	57.7%	38%	45%	32.4%
Phase 3 studies	56.7%	55%	64%	60.1%
Registration	N/A	77%	93%	83.2%
<b>Cumulative probabilities</b>	<b>26.4%</b>	<b>11%</b>	<b>19%</b>	<b>10.4%</b>

Overall, there is about a 10% to 20% chance that a new drug entering clinical trials for the first time will achieve approval and it is recognised that the likelihoods have declined over time.

Kola and Landis break out Neurology as 75% Phase 1, 33% Phase 2, 71% Phase 3 and 86% registration. Overall, the likelihood of approval (LOA) from entering the clinic to approval is 15.1%.

Hay, *et al.* provide the most recent data and present it in a manner suitable for isolating LOAs for different disease classifications. They report neurology as having an average LOA from initiation of trials to approval of just 9.74%. Cardiovascular fairs worse at 7.1%.

Clearly, data for discovery and preclinical stages of development are less easily come by because these research programs are not registered with a regulatory body and many are often killed-off by the researchers with no public notification. In addition, one would expect a high level of variability as such work depends on the basis of discovery, ie. directed at an established target or new target, a screening program, a serendipitous discovery, or other; the type of molecule - NME, biological, natural, etc; and on the skills and resources of the investigators. It is our usual approach to base preclinical estimates on an objective experience-based risk analysis. However, one published report provides some examples<sup>31</sup>:

<sup>25</sup> Transitional probability is the likelihood of a drug successfully completing the particular stage of testing, i.e. moving from one clinical trial phase to the next.

<sup>26</sup> Abrantes-Metz, R, *et al.* Pharmaceutical Development Phases: A Duration Analysis. Working Paper No. 274. US Federal Trade Commission: Bureau of Economics, 2004.

<sup>27</sup> Kola I & Landis J. Can the Pharmaceutical Industry Reduce Attrition Rates. *Nature Reviews Drug Discovery* 3:711, 2004.

<sup>28</sup> Kaitlin K. Deconstructing the Drug Development Process: The New Face of Pharmaceutical R&D. Presented at Bernstein Research Conference June 15, 2011.

<sup>29</sup> DiMasi JA, *et al.* Trends in Risks Associated With New Drug Development: Success Rates for Investigational Drugs. *Clin Pharmacol Ther* 87(3):272, 2010.

<sup>30</sup> Hay M, *et al.* Clinical Development Success rates for Investigational Drugs. *Nature Biotech* 32(1):40, 2014.

<sup>31</sup> Early Stage Valuation. Avance ([http://www.avance.ch/downloads/avance\\_early\\_stage\\_valuation.pdf](http://www.avance.ch/downloads/avance_early_stage_valuation.pdf)).

**Table 2: Likelihoods of Success in Pre-clinical Development of Drugs**

Phase	Time	Cost	Success rate
<b>Preclinical</b>			
In vitro	1 year	\$1 mil	67%
In vivo	1-2 years	\$1-2 mil	75%
Toxicology	1-2 years	\$1-2 mil	80%
<b>Total</b>	<b>3-5 years</b>	<b>\$3-5 mil</b>	<b>40.2%</b>
<b>CMC<sup>32</sup> Preclinical</b>		\$1-2 mil	
<b>IND</b>	3-6 mos	\$0.5-1 mil	67%

All three Nyrada programs are at a pre-clinical stage of development with the definitive lead compound reasonably elucidated.

The average pre-tax cost involved in developing a new prescription pharmaceutical has most recently been estimated at US\$2.5 billion.<sup>33</sup> The analysis includes accounting for additional drug candidates required to ensure that achieving one is successful. In other words, for one product approved, a company must fund, on average, 10 compounds entering a Phase 2 study (and all these costs are taken into account). Increases in the cash outlays to conduct clinical trials and higher drug failure rates have contributed to dramatic increases in R&D costs over the last two decades.

The key attributes of the Nyrada research programs are:

- TrpC3 Inhibitor – a number of molecules have been identified with confirmed ability to inhibit the TrpC3 target and to block glutamate-activated calcium influx into human neuronal cells and a lead candidate has been identified; the lead candidate is a closely related analogue of idronoxil-C which has been confirmed in rat studies to cross the BBB and which is without safety concerns in humans; the lead candidate is readily synthesized and the pro-drug form is novel and therefore patentable.
- Thromboxane Synthase Inhibitor – the core compound (NV-52) has confirmed efficacy in a rodent model of IBD. It has been confirmed as safe in animal toxicology studies; has been tested in two Phase 1 human clinical studies; is readily synthesized; and is able to be modified to a pro-drug form.
- PCSK9 Inhibitor – ALT-30 is confirmed able to bind to PCSK9 and block attachment to the LDL receptor. It is a small molecule offering significant advantages over anti-PCSK9 monoclonal antibodies in the method by which it can be delivered, orally vs. I/V, and cost of manufacture.
- Patent applications have been (or will shortly be) filed for all three programs. Although no patents have been granted, and there is a risk that they may not grant, each program should benefit from a long patent life – in excess of 20 years;

<sup>32</sup> Chemistry Manufacturing and Controls.

<sup>33</sup> DiMasi JA. Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs. Co-authors Grabowski HG & Hansen RW. Briefing. Cost of Developing a New Drug. Tufts Centre for the Study of Drug Development. 18 November 2014.

- All are small molecules and, we are advised, easy to synthesize.

Excluding general company and funding risks inherent with early-stage biotechnology companies, the risks to technical and commercial success include:

- Noxopharm only proposes to fund the business of Nyrada until the end of 2017 when Nyrada is expected to have independent capital resources. To that extent, Nyrada will be reliant on the support of the capital markets to provide both initial and ongoing funding. The high cost of drug development makes the Company's ability to continue to raise funds a critical risk factor in its success;
- Nyrada will be reliant on others to manufacture drugs in compliance with regulatory guidelines. They will be reliant on the ability of those contractors to continue to meet exacting regulatory standards;
- Even if Nyrada or its licensees receive regulatory approval to market product candidates, the market may not be receptive to their commercial introduction. Acceptability depends on both the patient acknowledging the products' benefits and relative superiority, as well as the prescribing physician's endorsement;
- The success of Nyrada will be dependent on key employees and consultants, as the Company grows it is going to have to recruit new, skilled personnel;
- The proposed products compete to varying degrees with numerous other drug and biotechnology companies including many in dyslipidaemia and IBS treatments. Many have substantially greater financial and other resources and are able to expend more funds and effort than Nyrada on R&D and promotion. Although a larger company with greater resources will not necessarily have a higher likelihood of receiving regulatory approval for a particular product or technology, the company with a larger R&D expenditure will be in a position to support more development projects simultaneously and bring its products to market more rapidly. Competitors may develop more effective, more affordable or more convenient products. These competing products may render Nyrada's product candidate obsolete. These companies also compete in recruiting qualified scientific and management personnel;
- Time to market is critical with any new technology, particularly in the medical area where patent life is compromised by protracted clinical trials and regulatory approvals. Adequate capital and competent skills are essential to expediting development and commercialization;
- Delays in the roll-out of the product, due to factors such as patient recruitment and slow regulatory approvals can adversely affect the valuation.

We have considered these risks in preparing our valuation – see also the Sensitivity analysis (Section 6.2.5).

## **5. Intangible Assets Valuation Methodologies**

The valuation of Nyrada resides largely with its IP which includes patent applications (and proposed applications) and experimental data.

The valuation of a mature company tends to follow a methodology that draws heavily on its historical income, either by performing a net present value of expected future earnings, the confidence in which derives from past activity, or capitalisation of maintainable earnings. Another technique considers the orderly realisation of assets. In the case of Nyrada, the sole assets are IPR&D, generally regarded as an intangible asset (IA). There are no historical cash flows available for extrapolation and no current product sales, and there is uncertainty that product development will be completed successfully.

Techniques used for valuing IA, including IPR&D, generally fall into three main categories<sup>34</sup>:

1. Cost Based;
2. Market Based; and
3. Revenue Based.

### 5.1 Cost Based Methods

There are several cost approach valuation methods, the most common being the reproduction cost method and the replacement cost method. Regardless of the type of cost being estimated (eg. reproduction, replacement or other) five components of cost are generally included in the analysis being: Materials; Labour; Overhead; Developer's Profit; and Entrepreneurial Incentive. The last factor is often difficult to estimate.

In considering historical costs as a basis for replacement or reproduction it must be assumed that all expenditure on a product's development, has been targeted and cost effective (not always valid assumptions in R&D), and that another party wishing to recreate the IP does not have the benefit of the current owner's acquired knowledge nor is he precluded by patents in exploiting his "reproduction". These constraints often negate the use of historical costs. Others argue strongly that historical expenditures are irrelevant for IP simply because the value to an acquirer cannot be correlated with the developer's costs.<sup>35</sup> For example, how do you compare a program that has had \$3 million spent on it, but has yet to identify a lead candidate and therefore has no bioavailability or pharmacokinetic data, and has no *in vivo* proof-of-concept with a program that has spent significantly less but has identified a lead compound, has confirmed its bioavailability and acceptable PK, and has been shown to work in a mouse model? Surely, the size of the potential market is also relevant – a company could spend a vast sum on developing a drug that has an incidence of 1 in 100,000 while another spends less to access an illness affecting a considerable fraction of the population.

Although drug development is extremely costly, future benefits are considered to be worthy of the investment and deals to acquire promising, IPR&D programs are often an order of magnitude higher than the past expenditure. Patents provide a market monopoly for the inventions and it would be very difficult for a third party to replicate the technology with equivalent specificity and activity without infringing the patents.

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<sup>34</sup> Reilly RF & Schweihl RP. Valuing Intangible Assets, McGraw Hill (NY) 1998.

<sup>35</sup> Razgaitis R. Early-Stage Technologies. Valuation & Pricing. Wiley (NY) 1999.

Historical costs, in the case of Nyrada involve UNSW expenditure (which may include lead investigator's time, grant funds, unrecorded student involvement and access to other resources) plus an inestimable overhead for the University as well as patent costs (irrespective of whether they provide adequate protection for the discoveries), all previous expenditure by Noxopharm on NOX66 with an apportionment to the NYX-104 project and an apportionment of all work on the delivery system and its patent; Novogen's expenditure on NV-52 with an extraction of what is relevant to NYX-105, and allowance for unpaid involvement by Drs Kelly and Dixon, and others involved with PCSK9, plus Cardio's equipment and facility allocation. We doubt whether these expenses can be reasonably assessed.

The Cost Based method was therefore not employed.

## 5.2 Market Based Methods

Techniques based on analysis of transactions between companies, equity valuations or capitalisations of comparable companies have considerable merit in the biotechnology sector. There are thousands of transactions taking place in the industry every year where one company licenses IP from another or enters into a collaborative venture. There are also many fund raisings, both private placements and IPOs, which may be used as analogies.

Comparison is possible only where a transaction relates to an identifiable unit of IP or platform technology that is reasonably analogous or, in the case of the value placed on a company, where that company is virtually single purpose and technically equivalent to the subject company or IP. Such criteria are often difficult to meet and comparable analyses are usually used only to support the values derived with other methodologies or to provide a "ball park" estimate.

A market analysis should realistically be undertaken by comparing companies or transactions of products at similar stages of development, ie. discovery/candidate selection. In Australia, where early stage listing is rare but not uncommon there are few companies in the fields targeted by Nyrada, while pre-clinical listing in the US and Europe is even less likely and licensing deals unusual.

Nonetheless, an analysis of some relevant companies is presented in Section 6.1 of this report.

## 5.3 Discounted Cash Flow Method

The technique most commonly employed is based on a DCF analysis. To assume any level of credibility, the DCF must be based on sound cash flow predictions, with justifiable assumptions regarding sales estimates, expenses and revenue timings. These are then net present valued using a discount rate, often following probability adjustment, that recognises the time value of money and risks involved in achieving the forecast cash flows.

The "Beta Factor" of a particular investment is a reflection of its risk expressed as a fraction of the volatility to that of a market portfolio, ie. a portfolio of stocks sufficiently diversified so as to reflect average market movements. The rate of return on the market portfolio will, by definition, fluctuate identically with the market and therefore its Beta Factor is one. Investments with Beta Factors lower than unity are less volatile than the market and thus would be expected to have a risk premium lower than the overall market premium.

The “Risk Premium” represents the premium over the Risk Free Rate that an investor requires to invest in the market portfolio. Typically, the risk premium associated with the equity market, as determined by the Centre for Research in Finance at the Australian Graduate School of Management, over the longer term is around 6-7%.

Using the 30-year US bond yield of 4.6%, and applying a Beta range of 1.2 to 1.5 as determined by Loh and Brooks<sup>36</sup> for DNA and biochemistry companies a discount rate of approximately 13% to 15% nominal is derived.

Discount rate adjustments have been used in the past to account for risk associated with realising projected cash flows. For example, a high risk project may be discounted at 45% which could be three or four times the weighted average cost of capital for the venture. Such practices seldom apply to the valuation of IP and IPR&D as they fail to recognise the fact that once the research has been completed the risk has been resolved. However, where there may be compounding risk such as an anticipated increase in competition or a changing economic environment, modest discount rate premiums may have relevance.

Our preferred methodology for IPR&D is generally not to apply discount rate premiums over and above the CAPM but to use a risk analysis and probability adjust cash flows.<sup>37, 38</sup> The procedure explicitly recognises the time profile of the risk by probability adjusting the cash flow using literature- or experience-based probabilities and applying these at the time points at which the risk is apparent.

The American Institute of Certified Public Accountants (AICPA) has issued a Practice Aid stipulating the approach to be adopted when valuing IPR&D in pharmaceutical and other high technology sectors.<sup>39</sup> The Practice Aid states that, whilst valuations of in-process R&D may still be carried out using traditional discounted cash flow techniques; the preferred approach is to use expected cash flows arrived at using decision analysis techniques and probability analysis. The resulting cash flows may then be discounted at a rate close to the cost of capital as the risks are deemed to have been dealt with in the probability analysis. In the AICPA’s opinion, the explicit assessment of the probabilities associated with the possible cash flow outcomes provides computational transparency compared with selecting a discount rate purportedly commensurate with the risks.

## 6. Valuation Opinion

### 6.1 Comparables Analysis

There are, not surprisingly, very few listed biotechnology companies with their most advanced drug candidate having not completed pre-clinical assessment and sometime from initiation of human studies. A few recent examples in Australia are:

- In 2016, Metavone Limited issued a prospectus to list on the ASX. The company is in pre-clinical development of isoflavone compounds for the treatment of cancer and neurological

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<sup>36</sup> Loh J & Brooks P. Valuing Biotechnology Companies: Does Classification by Technology Type Help? *J Comm Biotechnology* 14(2):118, 2008.

<sup>37</sup> Boer FP. *The Valuation of Technology: Business & Financial Issues in R&D*. Wiley (New York), 1999.

<sup>38</sup> Bogdan B & Villager R. *Valuation in Life Sciences: A Practical Guide*. Springer Verlag (Berlin), 2007.

<sup>39</sup> Aaron AV, Bitton VR (co-chairs), *et al*. *Assets Acquired in a Business Combination to be used in Research and Development Activities*. AICPA, New York. 2013.

disorders. It has identified and filed patents on a large number of novel compounds which it claimed on the basis of computer predictability to be able to cross the BBB; they also claimed them to be effective against cancer cells grown in *in vitro* culture. The company valued its IP at \$4.33 million. The capital raise, seeking \$5.0 million, was terminated – blamed on “poor market conditions”.

- AdAlta Limited, in 2016 raised capital to take its lead candidate into Phase 1 trials at a directors’ valuation of \$15 million prior to the issuance of new shares. The first application of its platform technology, in development for over a decade, is for the treatment of idiopathic pulmonary fibrosis, a rare, chronic and ultimately fatal disease. The company’s current capitalisation is \$25.3 million while holding \$7.5 million in cash at 31 March 2017.
- Recce Limited issued a prospectus in 2015 raising \$2.5 million at a pre-investment valuation of \$8.19 million. The company aimed to commence safety and toxicology on synthetic polymer antibiotics and had granted patents. The company now has a market capitalisation of \$14.8 million.
- Noxopharm, with one product in Phase 1 trial and several in pre-clinical development, has a current market capitalisation of \$28.1 million (undiluted). Although the market may not be fully appraised of the potential of its non-cancer assets the valuation includes the two programs to be transferred to Nyrada.

The above analysis indicates that a reasonable valuation of Nyrada’s preclinical assets is in the range \$4.0 million to \$15 million.

## 6.2 Revenue Based Analysis

Individual financial models have been prepared for Nyrada for the following indications:

- TrpC3 inhibitor in stroke;
- Thromboxane synthase inhibitor in UC; and
- PCSK9 inhibitor for dyslipidemia.

We have concentrated largely on the markets in the developed world due to the dominance of these markets and the fact that novel and potentially expensive treatments in these indications are likely to have delayed acceptance into developed regions.

In the cases of stroke and UC the lack of effective treatments or cures and adequate data suggest market development base on incidence or prevalence data for these indications. Information on the numbers of individuals with elevated cholesterol and at risk of cardiovascular disease is less reliable. Cholesterol lowering drugs are prescribed to large numbers of patients with usage growing. We have, therefore, modelled PCSK9 by comparison with the statins market.



We have developed financial projections based on the available information for the term of the anticipated patent expiry date for each product. Thus, for example, the valuation term for PCSK9 is 21 years from filing of the provisional on the assumption that a full PCT application is lodged on the anniversary, to March 2038. We have ignored the potential for sales beyond that term, even though there may be available an additional five or more years resulting from patent extensions in the major pharmaceutical markets (including USA). The assumption is, however, that the sub-licence will be granted only to assured expiry of the patent. Furthermore, there is the potential for all products to be extended into indications other than those modelled, especially the two neurological programs. These other uses have not been considered at this stage.

Included in the analysis is a valuation of Nyrada based on the three programs and current tangible assets. A valuation of the Company may make the assumption of life to perpetuity, achievable through greater R&D investment and the development of additional products, and include residual values in the models. We have not considered life beyond the patents' expiry of the three programs.

Time frames for finalisation of lead development, clinical trials, approvals and market launch are based on realistic schedules as outlined in the following sections.

The models for the products assume selling of product by a licensee or licensees following completion of Phase 2 with initial testing in patients providing both safety and efficacy evidence. Subsequently, the drugs will be developed, by the licensees.

Revenues are based on estimates of market size deriving from published incidence and prevalence data, a treatment cost as may be anticipated from trends for NMEs and estimated market shares or, for PCSK9, the likelihood of receiving revenues of a defined level based on current drug sales.

Phase 1 development expenses for twenty patients under a Clinical Trials Notification (CTN) in Australia is estimated to be approximately US\$0.5 million. Phase 2 costs involve the submission of an Investigational New Drug (IND) Application with the USA FDA (or equivalent body) will be international multicentre and be outsourced to a Contract Research Organisation (CRO).

Phase 3 clinical trial costs, borne by the licensee, are based on estimates of numbers of patients required in the various trial phases as extracted from clinical trials information for neurology/dyslipidemia drugs,<sup>40</sup> multiplied by a per patient evaluation cost as available from published literature. It is assumed that these estimates include the manufacturing of trial drugs and licensee company overheads. Additional expenses are included for preparation and submission of regulatory dossiers and post market surveillance. The COGS and corporate overheads are based on an examination of annual reports for major pharmaceutical companies.

The financial models prepared by Acuity present two cash flows – one for the licensor, Nyrada, and one for the drug's licensee or licensees. The licensee is responsible for late stage clinical trials, regulatory costs and other commercialisation expenses and it can be expected to pay to Nyrada milestone fees and royalties.

Nyrada meets the cost of preclinical development, and Phase 1 and 2 developments. Nyrada's revenues are the result of payments from the licensee. Nyrada satisfies its obligations to Noxopharm and Cardio through issuance of equity with no royalties payable.

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<sup>40</sup> <http://www.ClinicalTrials.gov>

It is assumed that capital assets are not acquired and held by Nyrada.

The cash flows are probability adjusted using published data on drug development success rates (see Section 4.4) with probabilities applied at the time point where development hurdles are passed. Probabilities are cumulative.

The objective of modelling the licensee's cash flow as well as the licensor's is to apportion the net benefit of the technology's commercialisation between the two parties as a basis for determining royalty rates and milestone payments.

It should be appreciated that the sum of the licensee and licensor valuations provides an overall project valuation as may be the case in the hands of a party fully capable of exploiting the technology and with the cost structures of a major pharmaceutical company (in other words royalties and cash payments are cash neutral in the two party models). The valuation based on a licensor's projected returns is what may be expected from a fair and reasonable licensing deal. The economies of scale and advanced infrastructure are not available to the start-up, and the risk profile is significantly greater such that the worth is less for the licensor.

In determining the licensor's valuation of the IP in its current form we deduct tax at an international rate of 35% and tax losses are carried forward to profitability.

Cash flows are discounted at an appropriate discount rate that reflects industry risks but with no additional premiums.

The valuation date is 1 January 2017. The cash flow models are in US currency as it is expected that international pricing will be based on USD.

The following sections summarises assumptions for the individual clinical applications.

### **6.2.1 TRPC3 for Stroke**

The following assumptions apply to the modelling of TRPC3 inhibitor for Stroke as initial indication:

- With reference to published incidence data, we have estimated that there are approximately 795,000 new occurrences of stroke in the US each year of which 87% are ischaemic. In Europe, there are 1,350,000 strokes with 87% ischaemic and in Japan, 440/100,000 with 75% ischaemic.
- The growth in incidence is 1% per annum.
- The market penetration by Nyrada is 15%, there being no adequate neuroprotective drugs and knowledge that only five or six prescription drugs are generally approved for any indication.

- The cost for a course of treatment is estimated at US\$4,500 and US\$3,000 in the other regions. The cost of a standard 100 mg vial of tissue plasminogen activator (TPA, Activase®, Genentech), a clot dissolving drug used following stroke, was US\$6,400 in 2014 in the US.<sup>41</sup> At the same time, Medicare reimbursement to hospitals for TPA-treated patients increased by just 8%, from US\$11,173 in 2006 to \$12,064 in 2013. More than half (53%) of the total reimbursement amount goes to pay for the drug.
- Preclinical development, including manufacturing development, will require a further two years and cost US\$2,000,000. Further animal studies are estimated at US\$250,000.
- We have conservatively estimated that the Company is unlikely to initiate human studies within 24 month. We have assumed that a first-in-human study will be a Phase 1 safety and PK study in six patients post-stroke. The cost of such a trial, including cost of drug, patient costs and data management is estimated at US\$600,000.
- A Phase 1b dose-escalating safety followed by Phase 2 intent-to-treat clinical trials to be undertaken by Nyrada following submission of an IND Application in the USA, will require 18-24 months. The overall cost of a Phase 1b/Phase 2a study program is US\$14.0 million.
- A Phase 3 study, to be conducted by a licensee, could be expected to take three years to conduct and to require approximately 1,000 patients, followed by 12 months for approval in the USA and Europe. The Japanese market will lag by 12 months. A four times multiple has been assumed compared to a Phase 1b/2a program.
- On approval, sales grow to reach peak after 3 years and remain at peak for 5 years. Sales (volume and/or price) to the incident group decline at 5% per annum due to the entry of competition.
- Revenues continue to the date of expiry of the US provisional patent filed on 6 April 2017.
- The Cost of Goods Sold (COGS) is 29.1% of selling price based on an analysis of industry averages for pharmaceutical companies.
- Selling, General and Administrative (SG&A) expense to the licensee is 28.2% of selling price.
- Although a company's R&D expenditure as may be presented in annual reports is not relevant to already marketed drugs, DiMasi, *et al.*<sup>42</sup> found from a survey of ten multinational pharmaceutical companies that approximately 15% of overall R&D expenditures are related to improvements to drugs that have been approved. Hence, we have added a further 2.5% (15% of the 17.0% of turnover spent on R&D as per annual reports) to overheads.

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<sup>41</sup> Brooks M. Cost of Thrombolysis Outpaces Reimbursement in Stroke. Medscape 23 Feb 2016 (<http://www.medscape.com/viewarticle/859245>).

<sup>42</sup> DiMasi JA, Hansen RW & Grabowski HG. The Price of Innovation: New Estimates of Drug Development Costs. J Health Econ 22:151, 2003.

- Regulatory dossier preparation and submission has been assumed to be US\$2.5 million for the USA. Two million dollars has been allowed for post-market surveillance.
- We have included on the licensor side administrative cost subsequent to out-licensing of 0.5% of revenues to cover accounting and audit charges, and general office expenses as related to this product solely.
- Royalties are receivable from the licensee with the amount adjusted, in the absence of milestone payments, to achieve an approximately 25% split in earnings before interest and tax (EBIT). (License fees and milestones payments can be expected and the models allow for their inclusion, however, the overall valuation is unaffected whether there are payments and a royalty or merely a higher royalty.) The analysis computes royalties of 10.2% of sales revenue to derive the split. Based on a Licensing Executives Society (LES) analysis, the royalty is reasonable for a Phase 2 product after allowance for the fact that the LES analysis included milestone payments.<sup>43</sup>
- The cash flows have been risk adjusted with cumulative probabilities applied at the time points where stages are completed using data from Hay, *et al.* for neurological drugs – being the most recent published analysis. The preclinical estimates of 60% is a judgement by Acuity that there remains a risk arising from the fact that the idronoxil-isomer still needs to undergo rigorous safety testing (not viewed as a high risk). Hay, *et al.*'s estimated Phase 1 likelihood 62.4% has been retained although NOX-66 has been evaluated in human trials previously.

The analysis is in constant 2017 dollars and no consideration has been allowed for inflation. The discount rate of 15% is therefore real.

The modelling shows product sales commencing in 2026 and a potential peak of around US\$1.5 billion annually (non-probability adjusted). The overall LOA is 5.6%. They projections show expected revenues will approach US\$78 million per annum once peak penetration has been achieved.

Discounting the probability adjusted pre-tax cash flows for the licensee yields a valuation of approximately US\$14.9 million and for Nyrada, US\$5.0 million. The Nyrada amount is what the Company can expect to achieve as the result of out-licensing the IP following a Phase 2 study.

As royalties and milestones payments paid between the parties are “cash neutral” in the overall collaboration, the sum of the licensee and licensor valuations is the overall project valuation. The pre-tax figure is US\$19.8 million and Nyrada’s cut, 25% of this.

An after-tax, probability adjusted valuation as a stand-alone project<sup>44</sup> is around US\$2.2 million and, at an exchange rate of 0.76 USD:AUD, \$2.8 million. An “effective” discount rate, the rate that would achieve the same valuation in the absence of probability adjustment, is 36.6%.

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<sup>43</sup> Global BioPharmaceutical Royalty Rates & Deal Terms Survey. LES USA/Canada. Licensing Executives Society International (LESI). December 2012.

<sup>44</sup> As “stand alone” tax losses are carried forward to profitability for this particular project as if it were the only project being conducted by the Company. In presenting a Company valuation the combined profitability is considered in determining when tax is payable.

## 6.2.2 Thromboxane Synthase Inhibitor in Ulcerative Colitis

The modelling is analogous to stroke with a number changes in inputs.

In determining relevant treatable population, we used data from DataMonitor Healthcare for prevalence of UC and diagnosed population in the major markets.

Market penetration assumes 12% of prevalent diagnosed patients as there are options, albeit largely ineffective, but no consistently effective drug. The selling price is assumed \$4,000 per annum for chronic treatment in the US and \$3,000 in other regions.

We have reduced the development time by 12 months due to the favourable experience of NV-52.

The likelihoods of success are again based on neurology drugs with an 60% pre-clinical probability this being a pro-drug form of the Novogen drug in a condition where efficacy was not seen in human UC trials. Although NV-52 has been safely administered to humans in properly managed clinical trials we have held with the Phase 1 likelihood as determined by Hay, *et al.* of 62.4%. The overall LOA for this product is 5.6%.

Again, the analysis uses a 25% split of net benefit to Nyrada.

The analysis determines a before tax risk adjusted valuation of US\$14.4 million for the licensee and in Nyrada's hands as a licensor of \$4.8 million. The stand-alone after tax valuation is US\$2.2 million, A\$2.8 million.

The estimated effective discount rate is 40.9%.

It should be appreciated that the projected Nyrada primary application of the thromboxane synthase technology is neuro-inflammation and UC is an early and obvious target. Diseases such as MND, which will rely on *in vivo* human demonstration that the pro-drug crosses the BBB and is efficacious, may constitute bigger markets, at least from a pricing perspective, and can be expected to double or better the valuation presented here.

## 6.2.3 PCSK9 Inhibitor in Hypercholesterolemia

The revenue forecast for the PCSK9 project is based on the inhibitor achieving a sales level as the average peak for the nine approved statin dyslipidemia drugs. The drugs include Lipitor's 2006 peak sales of US\$12.886 billion. The product is now off patent and several generic atorvastatin products have diminished sales. Crestor (rosuvastatin) at US\$7.0 billion at peak is the current market leader but is also subject to generic challenge. The average of peak sales of the nine branded statins is US\$3.65 billion, including failed Baycol.

The model proposes that the Nyrada product will achieve 50% of this level of sales on the premise that statins, as a class, will remain firmly entrenched as a reliable treatment (statins themselves did not face viable competition from cholesterol lowering drugs with alternative modes of action) and be available at a lower consumer price than when they dominated the market. Hence, with annual prescription growth of 2%, sales of the PCSK9 inhibitor exceed US\$2.0 billion after 2029 – a modest prediction relative to the spectacular performance of statins.

Time frames for finalisation of clinical trials, approvals and market launch are similar to those expected for the TrpC3 program with two years before entering human trials. As the definitive candidate molecule has reasonably been determined, but oral bioavailability and *in vivo* safety have yet to be demonstrated, we have applied a pre-clinical probability of 60% and Phase 1 probability of 60.6%, as per Hay, *et al.* for cardiovascular drugs for an overall LOA of 4.3%.

COGS and SG&A, as for the other two products, are based on pharmaceutical company metrics.

Considering the impact of the loss of exclusivity of statins to drug company revenues and the fact that current biologic PCSK9 inhibitors have been approved for selective marketing, albeit cumbersome to administer and costly, we view a positive outcome as a highly attractive licensing proposition. We have applied a split of benefits of 25%.

The model computes a royalty of 14.8% payable by the licensee to Nyrada if licensed following a Phase 2 proof-of-concept.

The analysis suggests a valuation of US\$5.5 million pre-tax for Nyrada for a combined IP valuation of US\$21.9 million. The stand-alone, after tax valuation is US\$1.5 million, A\$1.9 million.

The effective discount rate is 40.4%.

#### 6.2.4 Company Valuation

Treating Nyrada as a single corporate entity with three projects in development and adjusting for tax on a consolidated basis results in an overall after tax valuation of US\$7.2 million with an approximate equal breakdown of project valuations. Working capital of 5% of revenues has been included – which assumes Nyrada is effectively a virtual company. The pharmaceutical industry working capital as a fraction of revenue is 24% but all of these firms are conducting their own manufacturing, warehousing, distribution and marketing.

The company tax rate has been assumed to be 35% with consolidated program losses carried forward to profitability in 2028. Probability adjusted royalty revenues exceed of \$27 million in 2030.

The assessment assumes that Nyrada has no utilizable current tax losses and no financial or physical assets.

The apportionment of the valuation across the three projects is determined from the individual projects' pre-tax valuations.

The following after tax valuations at 1 July 2017 have been determined:

**Table 3: Component and Consolidated After Tax Valuations for Nyrada**

Program	Valuation (A\$'mil)	Fraction of Overall Value
TRPC3 Inhibitor	2.36	32.6%
Thromb Syn Inhibitor	2.29	31.5%
PCSK9 Inhibitor	2.60	35.9%
Nyrada	7.24	

### 6.2.5 Sensitivity Analysis

As many input parameters to the models are, at best, estimates and may change with time and as development advances, we subjected these to a perturbation analysis. Various inputs were adjusted across ranges considered realistic or time frames extended or brought forward by 12 months while retaining the value apportionment (except where this itself was the variable). The fixed apportionment was achieved by adjusting the royalty rates. The impact of increasing or decreasing the split was also examined. The findings are presented in Table 4.

In the following table, variations were applied to the programs individually (other than the discount rate and tax rate which are uniformly applied across all programs) and the valuation reported as a component of the overall Company valuation. The variances to the base parameters reflect the ranges of the inputs that may realistically be expected.

**Table 4: Sensitivity Analysis on the Individual Programs**

Variable, Expected Range	TRPC3		ThrombSyn		PCSK9	
	Valuation \$'000	Variance %	Valuation \$'000	Variance %	Valuation \$'000	Variance %
Base After Tax Valuation	2,362		2,286		2,600	
Discount Rate:						
12.5%	5,228	+121	4,905	+115	6,447	+148
17.5%	338	-86	343	-85	287	-89
LOA:						
+10%	2,675	+13	2,573	+13	2,925	+13
-10%	2,086	-12	2,026	-12	2,307	-12
Sales Revenue:						
+30%	4,743	+100	4,198	83	5,252	+102
-30%	579	-76	665	-71	630	-76
Pre-licence Expenses:						
+50%	822	-65	798	-65	807	-69
-50%	4,370	+85	4,197	+84	5,740	+121
Licensee Devt, COGS and SG&A:						
+10%	448	-81	376	-84	302	-88
-10%	3,828	26	3,825	21	4,790	32
Tax Rate:						
+15%	1,768	-25	1,711	-25	1,946	-25
-15%	2,878	+62	2,785	+67	3,169	+84
Split of Benefits:						
+20%	3,204	+36	3,101	+36	3,528	+36
-20%	1,519	-36	1,470	-36	1,673	-36
Development Time						
Delay 12 months	1,378	-42	1,409	-38	1,566	-40
Advance 12 months	3,407	+44	3,096	+35	3,668	-41

The discount rate is a major factor in determining the valuation of the programs and the Company and the analysis exemplifies the inordinate impact that premiums to the discount rate can have on long-term R&D projects. At current and expected future interest rates, affecting the cost of capital, it is reasonable to expect that a rate lower than 15% will prevail well into the future. By comparison large pharma weighted average cost of capital (“WACC”) averages 7.4% with a range of 3.1% to 11%. An upper range discount rate of 17.5% as used in this analysis applies too high a premium. Risk have been largely accounted for in the probability adjustments while the discount rate premium is intended to reflect the unknown future economic factors.



Estimation of revenues, from our experience, is always the factor most subject to error as it incorporates estimates of population likely to be subject to disease, the subset which will be of relevance, selling price of the treatment and market penetration/competition. All are subject to error and combined this may well exceed 30% of forecasts. Such a variance, plus or minus 30%, imparts a range of valuations between minus 70% and plus 100%. In our opinion, this adequately presents an acceptable range for each of the programs' valuations.

Other factors of significance are:

- LOA, there is reason to suspect that the Noxopharm developments have a higher than average likelihood of success since NYX-105 is based on a drug that has been evaluated in humans previously, ensuring a high chance of safety;
- Nyrada expenditure on development prior to licensing is a significant factor although we have possibly overestimated development and trial costs to ensure a conservative valuation;
- Partners' development and operating expenses, factors outside Nyrada's control, which influence the Company's share of net benefits from commercialised products;
- Tax rate, and we have allowed for a range between 30% and 40% - in comparison with drug companies' effective rates these are high;
- Split of benefits, the result of the ability of Nyrada to negotiate an appropriate deal. The PCSK9 project has the potential to negotiate a greater split; and
- Delay or expedition of program development times. Experience would suggest that delays are more likely.

In our opinion, the range of revenues from -70% to +100% encompasses all potential variations to input parameters.

## 7. Discussion & Conclusions

Our rNPV analysis suggests, not unreasonably, that all three programs have similar worth at around \$2.3 to \$2.6 million each. These are early stage programs with considerable work to be undertaken before the candidate molecules or definitive formulations are validated, and chemical synthesis finalized. Patents have yet to be granted covering the relevant discoveries.

**Table 5: Summary of valuations and Ranges**

Program	After-tax Valuation (\$'000)	Low (\$'000)	High (\$'000)
TRPC3 Inhibitor	2.36	0.60	4.74
Thromb. Synth. Inhibitor	2.29	0.67	4.20
PCSK9 Inhibitor	2.60	0.63	5.25

Based on the foregoing analysis we offer the opinion that all three projects have similar valuations and the overall Company after-tax valuation is around \$7.25 million

As there is further discovery work to be followed by formal clinical trials overall time frames are approximate. Revenues are at least a decade away and there is room for considerable competition to emerge and for markets to change. A comparables analysis provides little guidance while suggesting that the current appraisal is “in the ball park”. The valuation ranges, by definition, are broad.

The strength of having three programs is that risks are spread and the chance of one highly successful product is significant. The models do not allow for the benefit of synergy.

We have utilised a licensing model based on the advice of Noxopharm that it believes that Nyrada will seek to out-license following a proof-of-concept Phase 2 study and knowledge that this is the most probable route for a biotech company.

There are generally two broad-brush approaches to the preparation of a DCF for a start-up company or technology developer. The first is to assume that the company/researcher undertakes all development and exploitation itself, in which case modelling includes production, marketing and administrative costs as well as full development expenses; while the second approach is a licensing model in which income derives from milestone payments and royalties and there are no significant expenses once the IP has been licensed out.

In a licensing arrangement, the royalty rate is negotiated such that the buyer realises a level of return which ensures he can operate profitably even under the most adverse of circumstances and compensates for the risks he has taken in commercialising the IP. Commonly, as a rule-of-thumb, a step-up factor of approximately four is required to make the investment attractive - often referred to as the 25% rule.<sup>45, 46</sup> The splits analysis is done on the basis of before tax cash flows as the putative licensee's tax affairs are seldom known. As a technology gets closer to market it is likely that the licensor can demand a higher fraction and after a successful proof-of-efficacy in humans this is likely to be the case. However, we have conservatively held with 25% in our modelling. There is reason to believe that these projects will be highly attractive to big pharma and a higher split could be anticipated.

A full development model should include in the analysis capital expenditure for a production facility, or an additional margin on COGS where contract manufacturing is anticipated, and greater working capital requirements. In addition, a small company will not have the economies of scale in production, marketing and administrative overheads available to an established pharmaceutical giant. The likelihood of successfully taking development through clinical trials and regulatory approvals is potentially lower for a small company relative to big pharma. For this reason, a valuation based on full exploitation using typical big pharma costs and probabilities is not realistic for a start-up operation or the technology inventor. Such a valuation is not appropriate for negotiating a licence because both parties, licensor and licensee, need to realise a return.

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<sup>45</sup> FP Boer (Reference 37), page 255.

<sup>46</sup> R Razgaitis. Valuation and Pricing of Technology-based Intellectual Property. Wiley (NY), 2003, page 204.

A venture capitalist, for the sake of discussion, may apply a 45% to 55% discount rate to the cash flow forecasts (with no probability adjustments) when presented by a start-up compared to a figure of 7% to 10% when the same cash flows are proffered by a pharmaceutical giant. (Our models suggest discount rates of 35% to 40% will produce equivalent valuations in the absence of probability factors.)

Although due diligence was applied to estimation of revenues there is an inherent inability to prognosticate on potential sales of any new and unproven product. In valuing this IP, there is no past business activity by which to gauge the potential for future success. The discount rate attempts to compensate for the lack of objectivity surrounding the modelling.

## 8. Sources of Information

We have prepared our valuation using publicly accessible information and other documents provided by Noxopharm. Most of the assumptions on the timings and costs for the development of the proposed products are our own although we did discuss these with the Company, and the market shares, COGS and other expenses were also developed by Acuity.

In preparing our assessment, we held discussions with:

- **Dr Graham Kelly**, Managing Director of Noxopharm; and
- **Dr Ian Dixon**, Managing Director of Cardio.

In addition, we were provided with the following non-public documents:

- **Information Memorandum. NorBio Pharm Ltd** (IM. Short. 2April.docx) supplied to Acuity in an email from G Kelly on 2 April 2017.
- **NorBio Pharm. A New Public US Biotechnology Company** (*NORBIO PHARM Slide Deck.pptx*) supplied to Acuity in an email from G Kelly on 5 May 2017.
- **NorBio Pharm Pty Ltd, An Overview of NX-104 (Project Diltnia)** (*David overview NX-104.docx*) supplied to Acuity in an email from G Kelly on 15 June 2017.
- **NorBio Development Plans** (*Acuity Development Plans.docx*) supplied to Acuity in an email from G Kelly on 18 June 2017.
- **Housley G. A New Vision for the Treatment of Brain Injury from Glutamate Excitotoxicity – Stroke, Epilepsy, Trauma.** University of New South Wales. 18 February 2016.
- **US Provisional Patent, Isoflavonoid composition with improved pharmacokinetics**, filed by Noxopharm on 6 April 2017.
- **Altnia<sup>47</sup> PCSK9 Technical Summary** (*Altnia\_PCSK920170117\_non\_confidential VII.pptx*).

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<sup>47</sup> Altnia Pty Ltd is a company owned by Dr I Dixon as is Cardio Therapeutics Pty Ltd. We understand that the relevant IP will transferred to Cardio.

- **Provisional Patent, *Heterocyclic inhibitors of PCSK9***, filed by Altnia Operations Pty Ltd on 17 March 2017.

Numerous graphs and charts were provided summarizing experimental data.

We conducted independent research of the scientific and medical literature, and patent databases through the World Intellectual Property Organization<sup>48</sup>, The European Patent Office<sup>49</sup> and the US Patent and Trademark Office<sup>50</sup>.

## 9. Disclaimer

The valuations make certain assumptions in relation to the revenue prospects. The projections used in the valuation derive from information which we have obtained from Noxopharm and Cardio, and publicly available sources.

In preparing this report we have relied on information provided by Noxopharm and Cardio, complemented by our own experience in drug development and independent searches of the literature. We can provide no assurance that material provided by the Company was complete and accurate although we have no reason to suspect that this was not the case. We have exercised all due care in verifying the information provided and found no reason to doubt the reliability of the information. We also relied on published and Company-confidential scientific reports as the main sources of past research and were not able to review raw data, methods of analysis therein or confirm that these reports contained all relevant findings.

A draft of this report was supplied to Noxopharm to confirm factual accuracy and some changes were made to reflect their comments.

Acuity does not guarantee that the outcomes described in this report will actually occur because of possible changes in the markets and the Company's own actions, which are beyond our ability to forecast. This report is provided for information only and is not a recommendation to purchase shares in Noxopharm or Nyrada.

Acuity has acted independently in preparing this report and neither its Director nor staff have any pecuniary or other interest in Noxopharm, its related entities or associates that could reasonably be regarded as affecting its ability to give an unbiased opinion. Acuity will receive normal professional fees for the preparation of this report and, with the exception of these fees, will not receive any other direct or indirect benefits.

We understand that this report may be relied upon by Moore Stephens in its preparation of an Independent Expert Report to shareholders concerning the proposed IP transfer. Other than for that purpose, neither Acuity nor any employee of Acuity undertakes responsibility in any way whatsoever to any person or organisation (other than Noxopharm) in respect of information set out in this report, including any errors or omissions here-in, arising through negligence or otherwise, however caused.

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<sup>48</sup> <https://patentscope.wipo.int>.

<sup>49</sup> <https://worldwide.espacenet.com>.

<sup>50</sup> <https://www.uspto.gov>.

It is our usual practice to prepare valuation reports having regard to the Policy Statements and Practice Notes issued by the ASIC in relation to Valuations, Expert Reports and Independence of Experts.

In the current circumstance where Noxopharm and Cardio actively are developing their respective platform compounds, while generating no income, the valuation draws primarily on the future potential of the Nyrada IP. As such, it is based on prospective financial information and excluded from use in public disclosure statements by ASIC. Acuity is not a holder of an Australian Financial Services Licence and this report is not a recommendation to invest in Noxopharm or Nyrada or any of the other entities mentioned in this report.

The cash flow model used in the valuation makes the assumption that Noxopharm (in the short-term) and Nyrada (in the longer-term) will, or will have, sufficient funds to support further development and maintenance of the IP, and to meet other obligations under the licensing agreements. We have not analysed the Noxopharm accounts in detail and cannot confirm that adequate funding and resources are available. Without adequate funds, the value of the IP may not be realised. Additionally, delays in research and/or in securing collaborations could impact severely on the valuation.

## 10. Experience and Qualifications

Acuity provides management consulting to technology based companies. The company is skilled in the development of business plans and the technical, commercial and financial analyses of engineering and science based projects. An area of special interest is the provision of advice to investors and financial institutions on the funding of high technology R&D and the exploitation of outcomes.

The current valuation was undertaken by Acuity's Managing Director, David Randerson. Dr Randerson specializes in the valuation of intangible assets, and business entities whose main assets are intangibles, with particular expertise in IP. Valuations have been performed for purposes of licensing, capital raising and investment, sale, depreciation and amortization, impairment, purchase price allocation, consolidation, mergers, acquisitions, stock options and goodwill.

Dr Randerson has experience with valuing pharmaceuticals, stem cells, medical devices, diagnostics, agriculture, biochemical and cell culture technologies and environmental products. In the fields of physical and applied sciences, he has valued software, internet, electronics, telecommunications, mining and petrochemical projects, process engineering, production engineering and automotive technologies. Research-in-process is of particular interest to Dr Randerson.

Dr Randerson has a Bachelor of Chemical Engineering (Monash University), Master of Science in Applied Science (UNSW) and a Doctorate of Philosophy in Biomedical Engineering (UNSW). He is a fellow of the Australian Institute of Company Directors and a member of the Institution of Chemical Engineers. An understanding of physical and life sciences, research and development, project management, probability and statistics, discounted cash flow methodologies, real options analysis, life cycle forecasting, engineering depreciation and functional obsolescence analysis, are amongst the important tools in which Dr Randerson has competence.

As principal of Acuity for 27 years, Dr Randerson has undertaken in excess of 280 valuations in biomedical sciences and 120 in applied sciences.

Yours sincerely

A handwritten signature in blue ink, appearing to read "D. Randerson", with a long horizontal line extending to the right.

David H Randerson, BE, PhD, FAICD  
Managing Director