

21 August 2026

Sydney, Australia

Xolatryp® Demonstrates Significant and Sustained Cardioprotection in Preclinical Doxorubicin Study

Highlights:

- Xolatryp® significantly protected cardiac function against progressive doxorubicin-induced cardiotoxicity in a preclinical study, with benefits across four key measures of heart performance.
- Magnitude of functional protection was comparable to dexrazoxane, the only approved cardioprotective agent, and was evident at Week 3 and sustained through Week 5, demonstrating a longitudinal treatment effect rather than an isolated terminal finding.
- Histopathology blinded analysis supported functional findings, with myocardial injury reduced from predominantly moderate focal injury with doxorubicin alone to predominantly mild focal injury with Xolatryp.
- Together with Nyrada's [previously reported tumour-model data showing anti-tumour activity with Xolatryp alone and additive activity with doxorubicin](#), the findings support Xolatryp's potential as a differentiated adjunct to anthracycline therapy – an area of significant unmet clinical need.

Nyrada Inc (ASX:NYR), a clinical stage biotechnology company focused on developing Transient Receptor Potential Canonical (TRPC) ion channel inhibitors to treat a range of medical conditions, is pleased to report the results of its cardiomyopathy study.

Background and Unmet Need

Anthracycline chemotherapy cardiotoxicity remains an important clinical limitation as cardiac injury is dose-dependent and cumulative. Doxorubicin is a potent anthracycline drug, widely used as a first-line treatment for both solid and metastatic tumours. It is often used in combination with other agents and forms part of the standard regimen for treating liver cancer, breast cancer, leukemias, lymphomas (Hodgkin and non-Hodgkin), sarcomas (bone and soft tissue), bladder, lung, and ovarian cancers, among others. In use since the 1970s, doxorubicin is considered a "backbone drug" in oncology.

The development of anthracycline-induced cardiac dysfunction can ultimately necessitate dose reduction, treatment interruption, or discontinuation of otherwise effective anticancer therapy. Dexrazoxane is an established cardioprotective agent, but its use is not routine across the broader population of patients receiving anthracyclines.

Historically, use of dexrazoxane in the clinic has been relatively restricted, reflecting limitations in approved indications, concerns regarding potential effects on anticancer efficacy and secondary malignancies, and additional haematological toxicity. [Current cardio-oncology guidelines](#) support consideration of dexrazoxane particularly in patients receiving high cumulative anthracycline doses or those at high or very-high cardiovascular risk.



There remains a significant unmet clinical need for cardioprotective therapies that can be deployed more broadly alongside anthracycline therapy to reduce cumulative cardiac injury while preserving the anticancer efficacy of treatment.

Study Results

Nyrada has completed a preclinical study evaluating Xolatryp in a model of doxorubicin-induced cardiotoxicity. Doxorubicin is one of the most widely used anthracycline drugs. In this study, Xolatryp was assessed against doxorubicin alone. Dexrazoxane was used as a positive control in the study.

Doxorubicin treatment weakened the heart's ability to pump and empty blood effectively. The heart squeezed less strongly, as shown by lower ejection fraction (EF) and fractional shortening (FS), and more blood remained in the heart after each beat, shown by increased end-systolic volume (ESV) and a larger heart chamber size during contraction (LVIDs). Overall, these changes indicate reduced heart pumping function.

Xolatryp significantly attenuated all four components of this phenotype. Protection was statistically significant across each parameter at Week 3 and was sustained through Week 5, by which point doxorubicin-induced dysfunction had progressed substantially. This longitudinal pattern is consistent with sustained cardioprotection rather than an effect confined to a single timepoint.

Functional cardioprotection with Xolatryp was comparable to that observed with dexrazoxane, with mean changes numerically favouring Xolatryp across all four systolic parameters.

Table 1. Mean percentage change from baseline in key echocardiographic parameters at Week 3 and Week 5

Parameter	Time	Doxorubicin	Xolatryp + Doxorubicin	Dexrazoxane + Doxorubicin	Xolatryp protection vs Doxorubicin	Xol vs Dox <i>p</i> -value*
EF ↑ better	W3	-35.9%	-21.2%	-28.0%	41% less decline	0.0014
	W5	-46.0%	-30.3%	-32.6%	34% less decline	<0.0001
FS ↑ better	W3	-45.3%	-28.6%	-38.1%	37% less decline	0.0024
	W5	-55.5%	-38.8%	-42.5%	30% less decline	0.0013
ESV ↓ better	W3	+196.5%	+123.6%	+164.7%	37% less increase	0.0022
	W5	+233.4%	+160.6%	+278.0%	31% less increase	0.0007
LVIDs ↓ better	W3	+48.5%	+33.8%	+42.1%	30% less increase	0.0248
	W5	+57.4%	+41.9%	+64.2%	27% less increase	0.0193

* Repeated-measures Two-way ANOVA with Holm-Sidak post hoc (n = 12 per group)

The study was not designed or powered to establish superiority over dexrazoxane, and no such conclusion should be drawn.

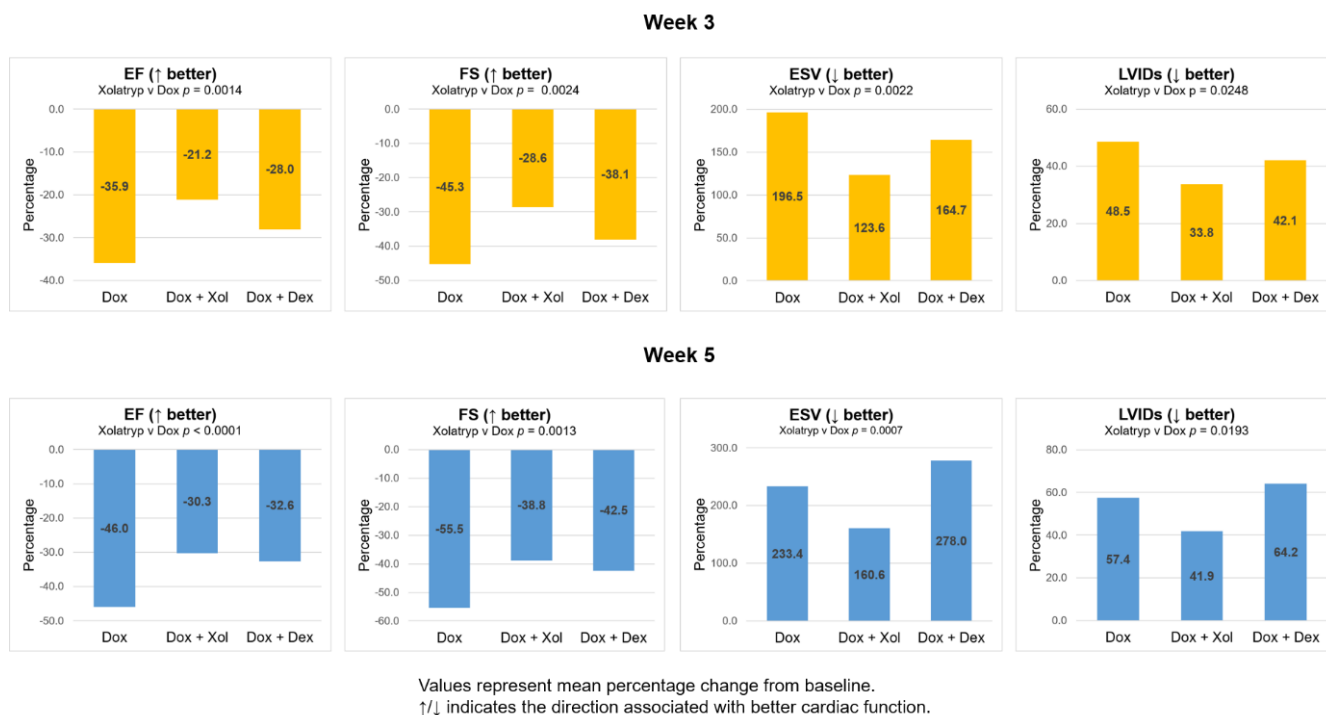


Figure 1. Xolatryp Protects Multiple Measures of Cardiac Systolic Function at Week 3 and Week 5

Xolatryp was associated with an approximately 19 per cent reduction in cardiac troponin I (cTnI) at Week 5 relative to doxorubicin alone, a difference that approached but did not reach statistical significance ($p = 0.0535$). Dexrazoxane produced a statistically significant reduction in cTnI. The comparatively modest effect on cTnI, despite significant preservation of cardiac function, may indicate a cardioprotective profile distinct from [dexrazoxane](#).

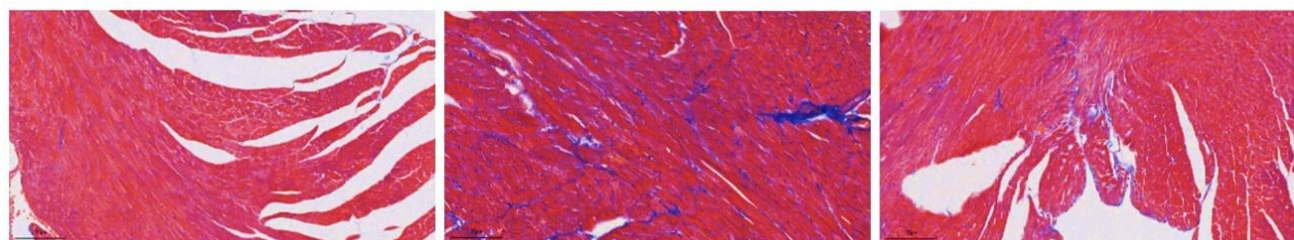
Additionally, heart rate remained comparable across treatment groups, indicating that the preservation of cardiac function with Xolatryp was not attributable to a compensatory increase in heart rate.

Structural and histopathological findings were also supportive of the functional results.

Histopathological examination, performed blinded, confirmed a clear doxorubicin-induced injury phenotype, comprising disordered myocardial fibres, focal myofiber rupture, widened intercellular spaces, interstitial oedema, and focal inflammatory-cell infiltration, with Masson's trichrome staining showing focal collagen proliferation and fibrotic lesions (Figure 2).

Mean myocardial collagen content was reduced from 17.4 per cent with doxorubicin alone to 13.2 per cent with Xolatryp, a numerical reduction of approximately 24 per cent that did not reach statistical significance and is therefore regarded as supportive rather than confirmatory.

Overall injury severity in Xolatryp-treated animals was reduced from predominantly moderate focal myocardial injury to predominantly mild focal injury, the same characterisation applied to the dexrazoxane positive-control group.



Vehicle: Normal tissue

- Predominantly red muscle fibres
- Minimal blue collagen

Doxorubicin

- Moderate tissue injury
- Increased blue collagen deposition

Doxorubicin + Xolatryp

- Mild tissue injury
- Reduced blue collagen compared to doxorubicin alone

Figure 2. Representative Masson's trichrome-stained sections of rodent heart at the end of the 5-week study. Collagen stains blue and myocardium (heart muscle tissue) stains red. Doxorubicin treatment resulted in increased collagen deposition and myocardial injury compared with vehicle (normal). Co-treatment with Xolatryp (32 mg/kg) reduced collagen deposition and improved myocardial architecture.

Anti-tumour Activity

[In Nyrada's earlier preclinical tumour model](#), Xolatryp showed anti-tumour activity as a single agent and combining it with doxorubicin improved anti-tumour activity over doxorubicin alone. Taken together, the separate cardiac and tumour studies support the potential for Xolatryp to protect cardiac function while preserving, and potentially enhancing, the anticancer activity of doxorubicin.

Nyrada CEO James Bonnar commented: "These results significantly strengthen the rationale for developing Xolatryp in the oncology setting. Xolatryp provided sustained protection against doxorubicin-induced cardiac dysfunction across multiple measures of heart function, with functional protection broadly comparable to dexrazoxane.

"Combined with our previous finding that Xolatryp has anti-tumour activity and enhances the response to doxorubicin in a tumour model, we believe Xolatryp has the potential to offer an important new approach to anthracycline therapy, protecting cardiac function while preserving, and potentially enhancing, the anti-cancer effect."

Study Design

The 5-week study used a rodent model of progressive doxorubicin-induced cardiomyopathy in which animals (n = 12 per group) received repeated weekly doxorubicin exposure. Xolatryp (32 mg/kg daily) was administered subcutaneously beginning 10 minutes after doxorubicin (5 mg/kg) and every 3 hours thereafter, for four doses per day over three days (8 mg/kg per dose). Dexrazoxane (50 mg/kg) was included as an established positive control given 30 minutes before doxorubicin.

Echocardiography was performed 46–48 hours after doxorubicin administration and before Xolatryp dosing on Day 3, a time point at which Xolatryp, from the preceding dose would be expected to have substantially cleared. cTnI was measured approximately 24 hours after doxorubicin.



At study completion, cardiac tissue underwent H&E (haematoxylin and eosin) and Masson's trichrome histopathology, including quantitative assessment of myocardial collagen. An independent contract research organisation (CRO) undertook blinded analysis of the heart sections.

Xolatryp Targets Both Sides of the Anthracycline Therapeutic index

This cardiac study and the previously reported tumour study address both sides of the anthracycline therapeutic-index equation: preservation of cardiac function during doxorubicin exposure and additive anti-tumour activity when Xolatryp is combined with doxorubicin.

Anti-Tumour Activity	Cardioprotection
Separate tumour model:	Week 5 EF change from baseline:
Xolatryp alone: -32% tumour volume	Doxorubicin: -46.0%
Doxorubicin alone: -41%	Doxorubicin + Xolatryp: -30.3%
Doxorubicin + Xolatryp: -57%	Doxorubicin + dexrazoxane: -32.6%
~39% improvement in anti-tumour activity vs Dox alone	Xolatryp vs Doxorubicin: $p < 0.0001$

Conclusion and Next Steps

This study demonstrated significant, sustained protection of cardiac systolic function with Xolatryp during repeated doxorubicin treatments. The effect was consistent across multiple independent echocardiographic measures and supported by histopathology, with the magnitude of functional cardioprotection broadly comparable to dexrazoxane.

Combined with separate preclinical evidence that Xolatryp has anti-tumour activity and can enhance the anti-tumour response to doxorubicin, these results support further development of Xolatryp as a differentiated adjunct to anthracycline therapy, with the potential to improve the therapeutic index of cancer treatment.

Nyrada will now assess the design and feasibility of a potential Phase Ib clinical trial of Xolatryp in the oncology setting.



Glossary of Key Terms

Anthracyclines	A widely used class of anti-cancer medicines that includes doxorubicin. Their use can be limited by cumulative damage to the heart.
Cardiotoxicity	Damage to the heart caused by a medicine or other treatment. Anthracycline cardiotoxicity can result in progressive impairment of heart function and, in severe cases, heart failure.
cTnI (cardiac troponin I)	A protein released into the blood following injury to heart muscle cells. Increased cTnI is commonly used as a biomarker of myocardial injury.
Dexrazoxane	An established cardioprotective medicine used in selected patients receiving anthracycline chemotherapy. It was included in the study as a positive-control benchmark for cardioprotection.
Dox / Doxorubicin	An anthracycline chemotherapy used to treat a broad range of cancers. Its cumulative use can cause dose-dependent cardiac injury.
EF (ejection fraction)	The percentage of blood in the left ventricle pumped out with each heartbeat. A decline in EF indicates impaired systolic heart function.
ESV (end-systolic volume)	The volume of blood remaining in the left ventricle after contraction. An increase in ESV can indicate impaired ventricular contraction and emptying.
FS (fractional shortening)	An echocardiographic measure of how much the left ventricle contracts during each heartbeat. A reduction in FS indicates impaired systolic function.
LVIDs (left ventricular internal diameter at end-systole)	The internal diameter of the left ventricle after contraction. An increase in LVIDs can indicate reduced contractile performance and ventricular dysfunction.
Masson's trichrome staining	A histological staining technique used to identify and quantify collagen and fibrosis in tissue.
Myocardium / myocardial	The muscular tissue of the heart responsible for contraction and pumping blood.
Phenotype	The set of observable traits or physical characteristics of a living thing.
Systolic function	The ability of the heart, particularly the left ventricle, to contract and pump blood effectively.
TRPC3/6/7	Members of the transient receptor potential canonical family of ion channels. Xolatryp is a selective inhibitor of TRPC3, TRPC6 and TRPC7.



About Xolatryp®

Xolatryp is a small-molecule inhibitor of TRPC3/6/7 channels designed to limit excessive Ca²⁺ entry related to multiple disease pathologies.

[A Phase I clinical trial to assess the safety, tolerability, and pharmacokinetics has been successfully completed](#) and a [Phase IIa clinical trial](#) has commenced to assess the safety and preliminary efficacy of Xolatryp in reducing cardiac reperfusion injury in patients with ST-Elevation Myocardial Infarction (STEMI) undergoing PCI.

Key Links:

Corporate Presentation - <https://bit.ly/4v0QgXE>

Foundation Studies

- GLP study results – <https://bit.ly/4d8VYkX>
- Phase I trial results – <https://bit.ly/3Nt0GzH>

Cardiac Studies

- Phase IIa PROTECT-MI website - <https://www.protect-mi.com>
- Phase IIa study fact sheet – <https://bit.ly/4bcDlKj>
- Preclinical cardioprotection study 1a - <https://bit.ly/4sigwMZ>
- Preclinical cardioprotection study 1b - <https://bit.ly/4rmOsXn>
- Preclinical cardioprotection study 2 - <https://bit.ly/40jHpUg>

Oncology Studies

- Preclinical anti-tumour study - <https://bit.ly/49rWOa0>
- Preclinical cardioprotection pilot study - <https://bit.ly/3QS1VKm>

Stroke Study

- Preclinical stroke study - <https://bit.ly/4sygHmH>

TBI Study

- Preclinical TBI study - <https://bit.ly/40fhrRT>

About Nyrada Inc.

Nyrada Inc. is a clinical-stage biotechnology company focused on the discovery and development of innovative small-molecule therapies, specifically targeting Transient Receptor Potential Canonical (TRPC) ion channels. The company's lead candidate, Xolatryp®, has shown efficacy in preclinical cardioprotection, neuroprotection, and oncology models and has completed a first-in-human Phase I clinical trial. A Phase IIa clinical trial has commenced to assess the safety and preliminary efficacy of Xolatryp in reducing cardiac reperfusion injury in patients with ST-Elevation Myocardial Infarction (STEMI) undergoing PCI. Nyrada Inc. (ARBN 625 401 818) is incorporated in Delaware, US, with limited liability for its stockholders.

www.nyrada.com

Authorised by John Moore, Non-Executive Chair, on behalf of the Board.

Investor & Media Enquiries:

Dimitri Burshtein

T: 0491 789 391

E: info@nyrada.com

Company Secretary:

David Franks

T: 02 8072 1400

E: David.Franks@automicgroup.com.au

Forward-Looking Statements

This announcement may contain forward-looking statements. You can identify these statements by the fact they use words such as "aim," "anticipate," "assume," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "predict," "project," "plan," "should," "target," "will" or "would" or the negative of such terms or other similar expressions. Preclinical results may not translate to humans. Forward-looking statements are based on estimates, projections, and assumptions made by Nyrada about circumstances and events that have not yet taken place. Although Nyrada believes the forward-looking statements to be reasonable, they are not certain. Forward-looking statements involve known and unknown risks, uncertainties and other factors that are in some cases beyond the Company's control that could cause the actual results, performance, or achievements to differ materially from those expressed or implied by the forward-looking statement.