



Optionality Builds: Oncology Readout Supports Platform Story

Nyrada Inc.

Nyrada's 20 May preclinical oncology study readout adds a third therapeutic area to Xolatryp's platform. The study included a model of Huh7 hepatocellular carcinoma (a type of liver cancer), testing xolatryp as a monotherapy and in combination with doxorubicin. Two findings matter: Xolatryp showed direct anti-tumour activity as a monotherapy (32% tumour volume reduction vs vehicle) and an additive effect in combination with doxorubicin (57% reduction vs 41% for doxorubicin alone); and animals dosed with Xolatryp showed a favourable cardiac troponin I trend versus doxorubicin alone, the first in-vivo (meaning within a living thing) evidence that Xolatryp's cardioprotective mechanism extends to anthracycline-induced cardiotoxicity.

We do not re-rate the platform on this data just yet. The model has well-known limitations – immunocompromised mice, intratumoral dosing, n=6 dropping to n=4 in the combination arm at Day 14. But what the readout does is materially strengthen the anthracycline cardiotoxicity sub-thesis flagged in our initiation. A drug that protects the heart and enhances tumour kill is differentiated against dexrazoxane on the precise dimension where dexrazoxane has historically been constrained.

Our valuation framework remains anchored on the lead myocardial ischaemia-reperfusion injury (MIRI) indication. PT and recommendation unchanged. The PROTECT-MI Phase IIa, with first patient dosed in April 2026, remains the dominant near-term value driver.

Catalysts

The oncology readout creates several preclinical catalysts that did not exist at the time of our initiation. None are individually transformational, but cumulatively they progress the platform story:

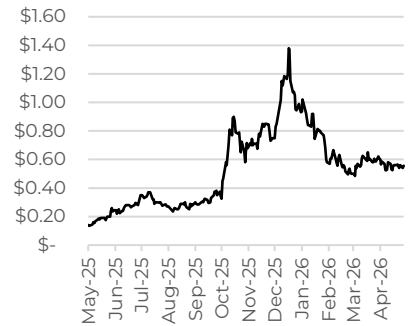
- **Preclinical cardiomyopathy study** – explicitly flagged in the 20 May announcement, designed to assess Xolatryp's ability to mitigate doxorubicin-associated cardiac injury in a dedicated model. This is the readout that would convert the troponin trend into a more substantive AICT case. Timing not guided.
- **Systemic dosing oncology studies** – the company has flagged this as future work. Intratumoral dosing is not clinically translatable; an IV or oral dosing study with comparable anti-tumour activity would be required before any oncology IND could be contemplated.
- **Additional tumour types** – Nyrada has flagged evaluation across other anthracycline-treated tumours (breast, lymphoma, sarcoma, leukaemia). Even one supportive readout in a more commercially relevant indication than HCC would strengthen the case.
- **PROTECT-MI PK/safety review on first 8 patients** – expected H1 2026, this remains the more important near-term de-risking event. A clean readout confirms target exposure and tolerability in the STEMI population.

Recommendation	SPEC BUY
Price Target	Unchanged \$1.04
Share Price	\$0.555
TSR	+87%

Company Profile

Market Cap	\$135.9M
Enterprise Value	\$129.2M
SOI (diluted)	297.6M
Free Float	54.6%
ADV (3-month)	\$196.3k
52-Week Range	\$0.095-1.435

Price Performance



%	1M	3M	12M
Absolute	-5.9%	-30.6%	311%
ASX/S&P200	-3.9%	-4.9%	2.6%

Company Overview

Nyrada Inc (ASX: NYR) is a clinical-stage biotechnology company developing Xolatryp, a first-in-class small-molecule TRPC ion channel inhibitor with dual applications in neuroprotection and cardioprotection. The company's lead programme targets myocardial ischaemia-reperfusion injury (MIRI) in STEMI patients, with a Phase IIa clinical trial commencing in Q1 2026 following a successful Phase Ia safety study. Xolatryp's mechanism also has demonstrated preclinical efficacy in stroke and traumatic brain injury, providing platform optionality across multiple high-unmet-need indications.

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Coverage:

[Initiation](#) 26 March 2026
[Update](#) 15 April 2026



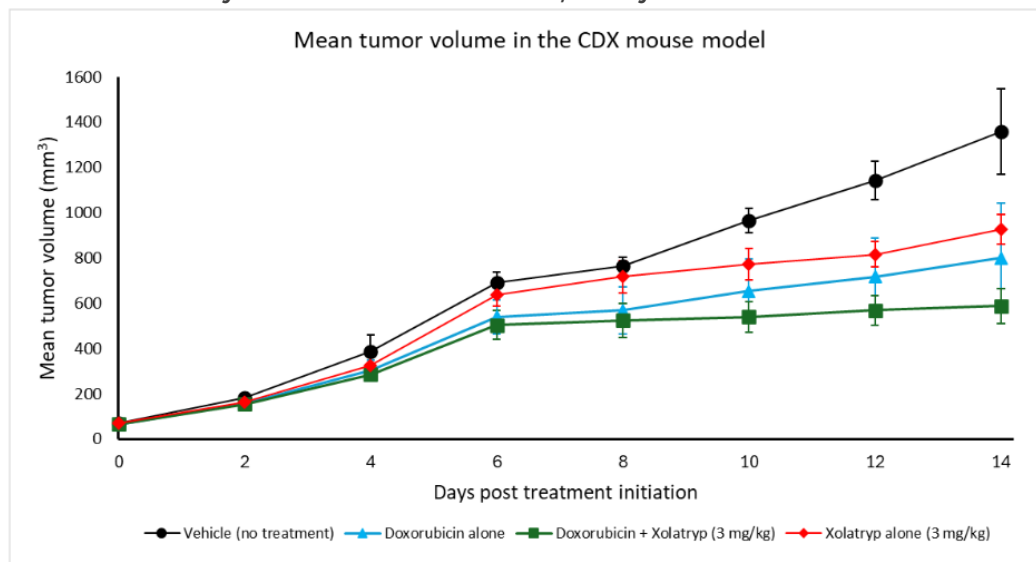
What Was Announced

In a Huh7 cell-line derived rodent xenograft model of liver cancer, Xolatryp was evaluated as a monotherapy (3 mg/kg intratumoral, daily) and in combination with doxorubicin (twice weekly), against doxorubicin monotherapy and vehicle control. Tumour volumes were measured over 14 days. The combination arm produced the greatest effect:

Figure 1: Tumour volume reduction vs vehicle control at Day 14 in the Huh7 CDX mouse model. Source: Nyrada Inc. ASX announcement, 20 May 2026.

Arm	Tumour volume reduction vs vehicle (Day 14)	Statistical significance
Doxorubicin + Xolatryp	57%	Significant from Day 4 (p=0.015)
Doxorubicin monotherapy	41%	Significant from Day 6 (p=0.0006)
Xolatryp monotherapy (3 mg/kg, intratumoral)	32%	Significant from Day 10 (p=0.003)

Figure 2: Mean tumour volume in the Huh7 CDX mouse model over 14 days post-treatment initiation. Source: Nyrada Inc. ASX announcement, 20 May 2026.



Two further findings warrant attention. First, animals in the Xolatryp arms (both monotherapy and combination) showed a favourable trend in plasma cardiac troponin I relative to doxorubicin alone – an in-vivo cardioprotective signal in the anthracycline setting. Second, Nyrada has lodged a provisional patent application for Xolatryp as an anti-cancer agent, complementary to the composition-of-matter patent published in March 2026.

What the Data Does (and Does Not) Show

The TRPC6/HCC mechanistic foundation is reasonably well-established.

Multiple groups have demonstrated TRPC6 overexpression in HCC tissue and its role in calcium-driven proliferation and chemotherapy resistance. The most directly comparable recent paper is Ji et al. (*European Journal of Pharmacology*, March 2026), which showed that BI-749327 – Boehringer Ingelheim's selective TRPC6 inhibitor – binds TRPC6 directly at the VSLD domain, suppresses TRPC6-mediated calcium influx and downstream PI3K/AKT/mTOR signalling, and inhibits HCC proliferation, migration, and EMT while promoting apoptosis. The Ji study, however, is primarily in vitro. Nyrada's data is one of the first in-vivo demonstrations of TRPC channel inhibition reducing HCC tumour volume in a xenograft model, which adds genuine value to the published literature.

One mechanistic distinction worth noting: BI-749327 is a *selective* TRPC6 inhibitor with 85-fold selectivity over TRPC3 and 42-fold over TRPC7. Xolatryp is a pan-TRPC3/6/7 inhibitor. TRPC3 and TRPC7 are also implicated in tumour calcium signalling, so pan-blockade could be beneficial, but selectivity is generally a clinical advantage where it can be achieved.

The Huh7 xenograft model has well-known limitations.

Immunocompromised mice cannot recapitulate the tumour-immune interactions that dominate modern HCC therapy. Intratumoral dosing – Nyrada used intratumoral administration in this study – is not clinically translatable; future studies will need to assess systemic dosing. The combination arm dropped to n=4 by Day 14 due to two premature deaths attributed to tumour lysis syndrome, which is a recognised complication of highly active anti-cancer therapy and manageable clinically, but does mean the Day 14 combination result rests on a small sample.

Where the Data Does Shift the Thesis

An interesting finding in this readout is the favourable cardiac troponin I trend in Xolatryp-treated animals receiving doxorubicin. This is the first in-vivo evidence that Xolatryp's cardioprotective mechanism extends from ischaemia-reperfusion injury to anthracycline-induced cardiotoxicity (AICT), and it sits on top of a meaningful body of literature linking TRPC6 specifically to doxorubicin-induced cardiac damage.

The biological rationale is well-supported. Norton et al. (*Frontiers in Cardiovascular Medicine*, 2022) showed that TRPC6 knockout mice are protected from doxorubicin-induced cardiomyopathy. Wu et al. (*Circulation: Genomic and Precision Medicine*, February 2026) identified a TRPC6 gain-of-function variant (A404V, 12% minor allele frequency in the general population) associated with doxorubicin-related cardiomyopathy in human patients: direct human genetic evidence that TRPC6 mediates AICT.

The commercial significance of an AICT cardioprotectant rests on what the existing standard of care does poorly. Dexrazoxane is the only FDA-approved agent for anthracycline-induced cardiotoxicity, with a global market estimated at US\$300–500m (market sizing estimates vary widely, with one report suggesting up to US\$1.4bn including all anthracycline-treated populations). Its uptake has been constrained for three reasons that have persisted for decades:

- Label restriction to cumulative doxorubicin doses ≥ 300 mg/m², meaning it is positioned reactively after substantial cumulative exposure rather than prophylactically from dose 1.
- Historical and disputed concerns that dexrazoxane reduces anti-tumour response rates, which slowed adoption even after regulatory authorities concluded the concern lacked consistency.
- Secondary haematologic malignancy concerns, particularly in paediatric use.

Xolatryp's data is positioned against precisely these constraints. The combination data showed enhanced anti-tumour activity (57% combination vs 41% doxorubicin alone) rather than interference – the inverse of dexrazoxane's principal historical liability. The troponin trend was observed alongside this enhanced anti-tumour effect, suggesting cardioprotection and chemotherapy potentiation are not in tension. A separate preclinical cardiomyopathy study is now underway to assess this hypothesis directly, and a positive readout would meaningfully strengthen the case for Xolatryp as a differentiated anthracycline adjunct.



Outlook

The lead indication remains MIRI. Xolatryp's clinical asset is in PROTECT-MI, a randomised, double-blind, placebo-controlled Phase IIa in approximately 100 STEMI patients undergoing primary PCI. First patient dosing was achieved in April 2026, with the first site activated on 22 April. The PK/safety review on the first 8 dosed patients is expected in H1 2026, with top-line data anticipated between Q4 2026 and H2 2027.

The oncology readout is platform optionality, not clinical de-risking of the lead programme. Anthracycline cardiotoxicity work is at preclinical stage; the dosing in this study was intratumoral and not clinically translatable; and any oncology or AICT clinical programme would require systemic dosing studies, formal IND-enabling work, and a separate clinical development pathway.

Our valuation framework remains: US\$500m global peak sales in MIRI, 10–15% cumulative probability of success, 3.0x risk-adjusted peak sales multiple, implying A\$0.87–A\$1.30 per share at the base case. Stroke and TBI remain unvalued. We add the AICT indication to that list of unvalued optionality. The argument for not valuing these indications has not changed: they remain preclinical, lack systemic dosing data, and any of them could in principle contribute materially to the eventual partnering or acquisition outcome. They sit in the optionality bucket, not the base case.



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