ASX RELEASE 19 November 2026

# Independent Phase 3 analysis supports new ROW trial for iPPS

## Key Highlights

- **Independent analysis confirms the previously reported ROW findings:** TrialKey's exploratory analysis showed statistically significant results favoring iPPS for Weekly Average Daily Pain (wADP) at Day 112 (the primary endpoint), physical function and patients' overall improvement in the rest-of-world (ROW) cohort, findings are consistent with Paradigm's earlier internal analysis.
- **The findings provide a basis to assess a potential ROW trial:** The independent review strengthens the rationale for further investigation of iPPS. The proposed pathway would build on the ROW findings and overall PARA_OA_012 findings, with study design, execution and evidence requirements informed by the data and regulatory discussions.
- **US development remains a goal alongside the ROW pathway:** Paradigm plans to consult the US FDA on the PARA_OA_012 results and further consider pathway for development in US.
- **The Board's proposal remains to preserve the iPPS opportunity:** The proposal seeks a funded pathway forward combining clinical development, regulatory engagement, funding and restructuring. This proposal has not yet been presented to creditors for approval, and further development remains subject to funding, the administration process and applicable approvals.
- **The ROW findings support further investigation:** The interim futility outcome remains unchanged, with no clear treatment advantage overall or in the US, but clear signals in the exploratory analysis of the ROW cohort. The ROW analyses are exploratory and are not adjusted for multiple comparisons but were consistent concordant across missing data sensitivity analyses.

**Paradigm Biopharmaceuticals Limited** (Administrators Appointed) (ASX: PAR) (Paradigm or the Company) provides an update on TrialKey's independent analysis of its PARA_OA_012 Phase 3 knee osteoarthritis study and the proposed pathway for injectable pentosan polysulfate sodium (iPPS).

The independent review supports advancing iPPS into a new ROW trial as the near-term priority, with US development remaining part of Paradigm's longer-term clinical development plan. The analysis was conducted on the existing trial data.

## What the independent analysis found

The interim report, dated 16 November 2026, was prepared by TrialKey Pty Ltd, a wholly owned subsidiary of Pathkey.AI Limited (ASX: PKY), based on de-identified participant data provided by Paradigm

This exploratory post-hoc analysis compared Day 112 results in the US and ROW. In PARA_OA_012, ROW comprised Australia, Hong Kong and Moldova. It accounted for baseline pain, osteoarthritis severity, and other factors in the protocol prespecified analysis.

In ROW, iPPS showed statistically significant benefits over placebo for wADP, WOMAC function, and Patient Global Impression of Change (PGIC), which measures patients' perceived overall improvement. WOMAC pain also favored iPPS, but that result was not statistically significant.

These findings support the prior report of Paradigm's internal ROW analysis announced on 15 October 2026. The independent analysis examined several study populations and used different methods, so the results are not identical.

As reported in the Company's 15 October 2026 announcement, Paradigm's internal ROW analysis included observed Day 112 wADP assessments for 95 participants (45 receiving iPPS and 50 receiving placebo). That analysis reported an adjusted treatment difference of −1.105 points on the 0–10 pain scale in favour of iPPS (95% confidence interval −1.733 to −0.476; p=0.0007). In the same previously reported Company analysis, Day 112 results also favoured iPPS for WOMAC physical function (p=0.0026), WOMAC pain (p=0.0147) and patients' overall assessment of improvement (PGIC; p=0.0032).

## Understanding the US result

In the US, the iPPS and placebo groups showed similar responses. Placebo-group improvement was greater in the US than in ROW, but was not shown to be comparatively higher than with other external osteoarthritis study benchmarks reviewed by TrialKey.

The review identified a higher proportion of scheduled injections recorded as not given in the US, as well as gaps in pain records. Treatment delivery, data completeness and site performance therefore need further assessment. Expectations, natural changes in symptoms, prior pain treatment and differences in care or follow-up may also contribute to the observed treatment responses. None of these has been established as a specific cause of the US result.

## Important limits to the findings

The overall interim futility result is unchanged. In the exploratory ROW analysis, estimated treatment differences at Day 112 for pain, physical function and patient-reported overall improvement favoured iPPS and were statistically significant in the reported analyses.

TrialKey's report is interim. Its calculations need to be reconciled with the sponsor's official analysis. Missing data and analysis assumptions may affect interpretation. The findings support further investigation, not a conclusion that a future trial will succeed or that a regulatory pathway is confirmed.

TrialKey's analysis did not include an assessment of safety. The safety findings from the interim analysis, as reviewed by the independent Data Safety Monitoring Board (DSMB) and previously reported by the Company, were consistent with the safety profile observed in prior iPPS clinical studies.

## Assessing a potential ROW trial

TrialKey's report states: "There is a data-based reason to investigate another trial outside the USA."

The proposed focus is to assess a potential ROW trial that builds on the encouraging findings and addresses lessons from PARA_OA_012. Specific countries and sites would be assessed on their ability to recruit suitable participants, deliver treatment and collect reliable data.

As outlined in the earlier ROW results announcement, the Board's proposal aims to preserve iPPS and establish a funded path forward, combining clinical development, regulatory engagement, funding and restructuring options.

The proposed clinical development pathway would focus on a trial informed by the independent analysis and earlier clinical evidence. Regulatory discussions would guide the study design and evidence required, while the review of PARA_OA_012 would inform improvements to treatment delivery, site oversight and data collection. The scope and timing of the program would be determined alongside funding arrangements and the administration process.

## US development remains an option

The focus on a potential ROW trial does not rule out further US development. Before pursuing another US study, Paradigm plans to assess and resolve the operational issues identified in PARA_OA_012 and consult the US Food and Drug Administration (FDA) on the 012 results and requirements for any further study. These steps would inform whether and how a future US study could proceed.

Paradigm also plans engagement with other relevant regulators as the ROW option is assessed. No regulatory pathway or approval has been confirmed, and the design, countries, timing and funding of any future trial remain to be determined.

## Administration process

The Board's proposal to preserve the iPPS program has not been presented to or approved by creditors. It will be considered through the administration process alongside other options. There is no certainty that a proposal will be accepted, funding secured or further development commenced. Any proposed deed of company arrangement remains subject to the applicable creditor decision and other required approvals.

The Company will update the market when further material information becomes available.

-ENDS-

## Forward Looking Statements and Disclaimer

This announcement summarises TrialKey's independent interim analysis and distinguishes it from the Company's previously reported internal analysis. The Administrators have not independently verified the underlying data or analyses and make no representation as to their accuracy or completeness. The information is provided to keep the market informed.

Statements regarding a potential future study, regulatory engagement, funding, restructuring and continued development are forward-looking and subject to risks and uncertainties. Actual outcomes may differ materially. No assurance is given that any proposal will be approved, funding secured, trial commenced or regulatory approval obtained.

Authorisation for release by the Voluntary Administrators.

To learn more please visit: www.paradigmbiopharma.com

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Christopher Pattinson and Hayden White of FTI Consulting were appointed as joint and several voluntary administrators of Paradigm Biopharmaceuticals Limited (Administrators Appointed) ACN 169 346 963 on 29 September 2026.

# Appendix

## Previously reported ROW findings

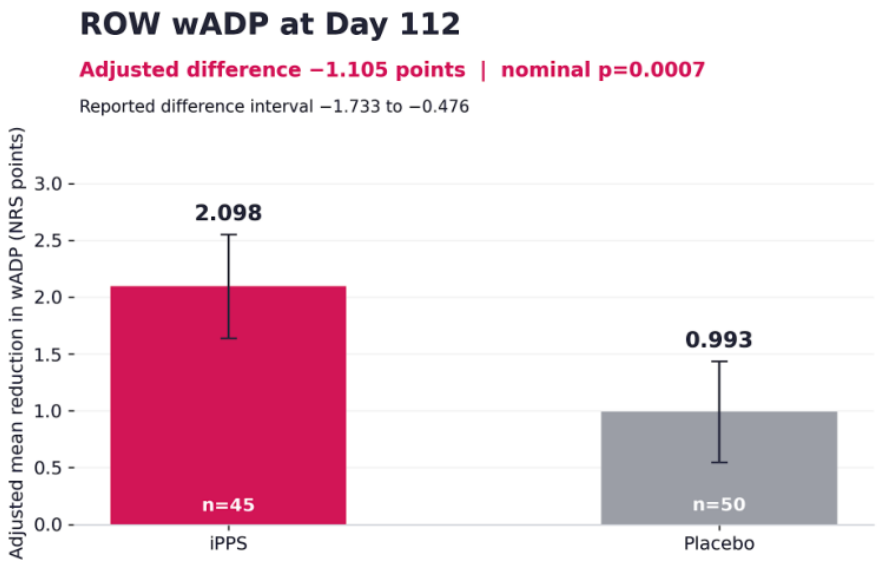



Figure 2. ROW Day 112 wADP: adjusted LS mean changes from baseline, shown as positive reductions. Supplied intervals; n assessed at visit.

Figure 2: At Day 112, the Company's observed-data analysis showed greater adjusted wADP improvement with iPPS than placebo. The bars show each group's improvement; the reported between-group difference was 1.105 points in favour of iPPS (nominal p=0.0007; 95 observed assessments).

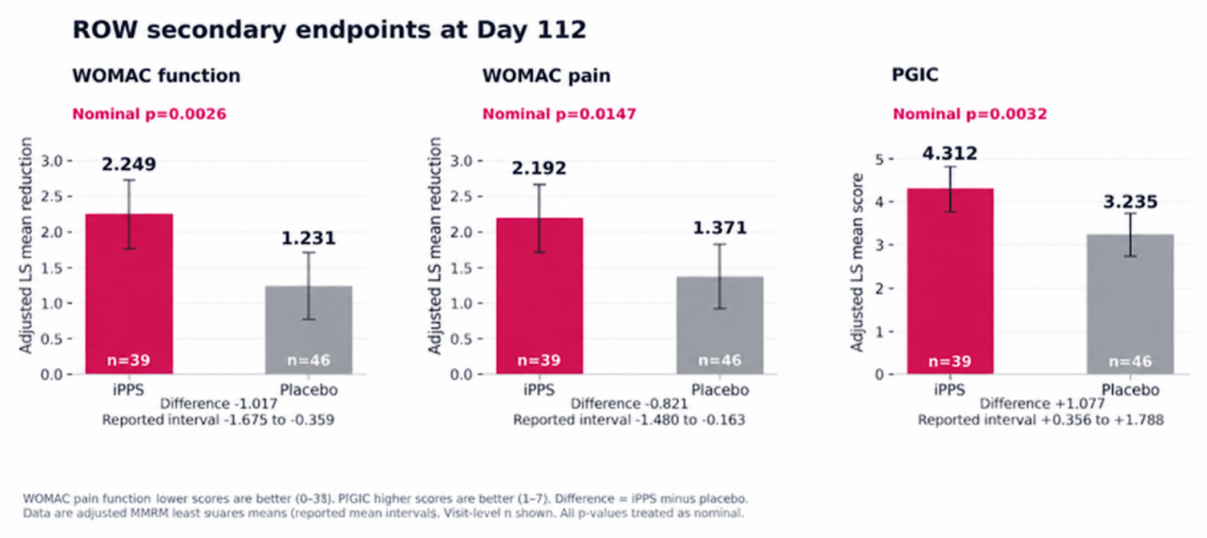



Figure 6. ROW Day 112. Pain/function: adjusted LS mean changes from baseline, shown as positive reductions. PGIC: adjusted LS mean score. Whiskers: supplied model mean intervals.

Figure 6: The Company's Day 112 analysis also reported differences favouring iPPS for WOMAC function, WOMAC pain and PGIC (nominal p=0.0026, 0.0147 and 0.0032 respectively; 39 iPPS and 46 placebo assessments). These outcomes involve overlapping participants, rather than separate confirmations of efficacy.

## Weekly average daily pain over time

Previously reported Company analysis | 15 October 2026

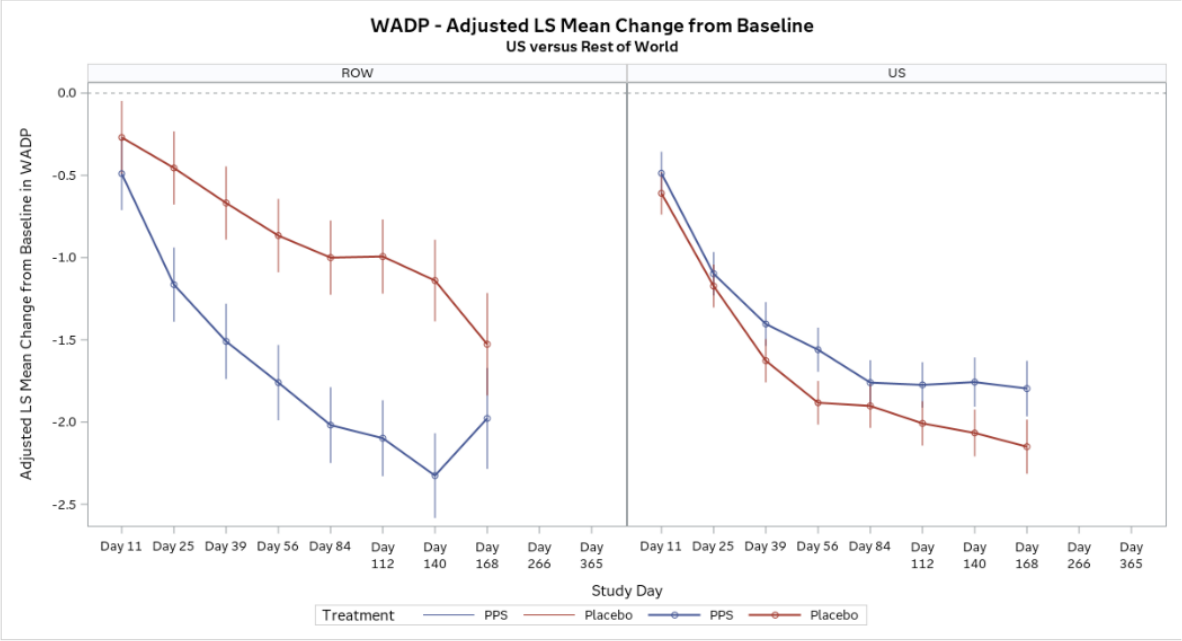



Figure 3. wADP adjusted LS mean change from baseline. Blue: iPPS; red: placebo. More negative values mean greater pain relief. ROW: left; US: right.

Figure 3 shows the Company's previously reported adjusted wADP changes over time. In ROW (left), iPPS showed greater numerical improvement than placebo, with separation narrowing at Day 168. The prior release reported only 25 observed Day 168 assessments versus 95 at Day 112 and a Day 168 treatment-difference confidence interval including zero; the later estimate is less precise.

## Physical function over time

Previously reported Company analysis | 15 October 2026

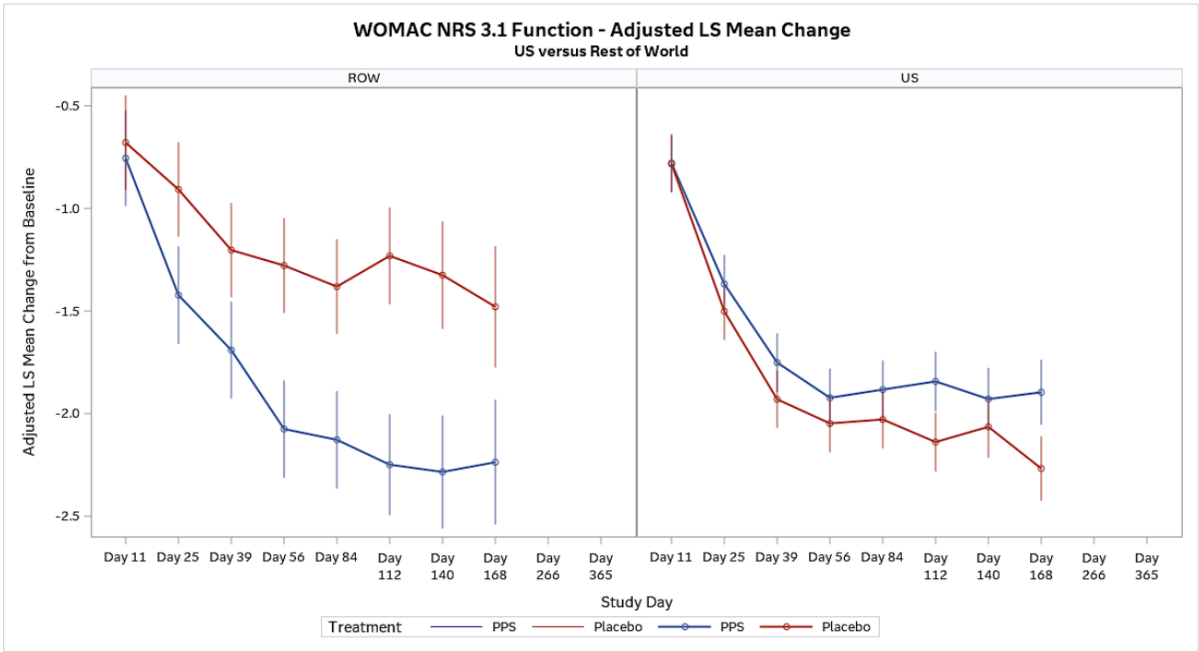



Figure 4. WOMAC function adjusted LS mean change from baseline. Blue: iPPS; red: placebo. More negative values mean greater improvement.

Figure 4 shows the Company's previously reported adjusted WOMAC function changes. In ROW (left), the iPPS curve indicates greater numerical improvement than placebo across the plotted follow-up assessments. At Day 112, the reported adjusted difference was 1.017 points in favour of iPPS (nominal p=0.0026). The curves alone do not establish statistical significance at every visit.

## WOMAC pain over time

Previously reported Company analysis | 15 October 2026

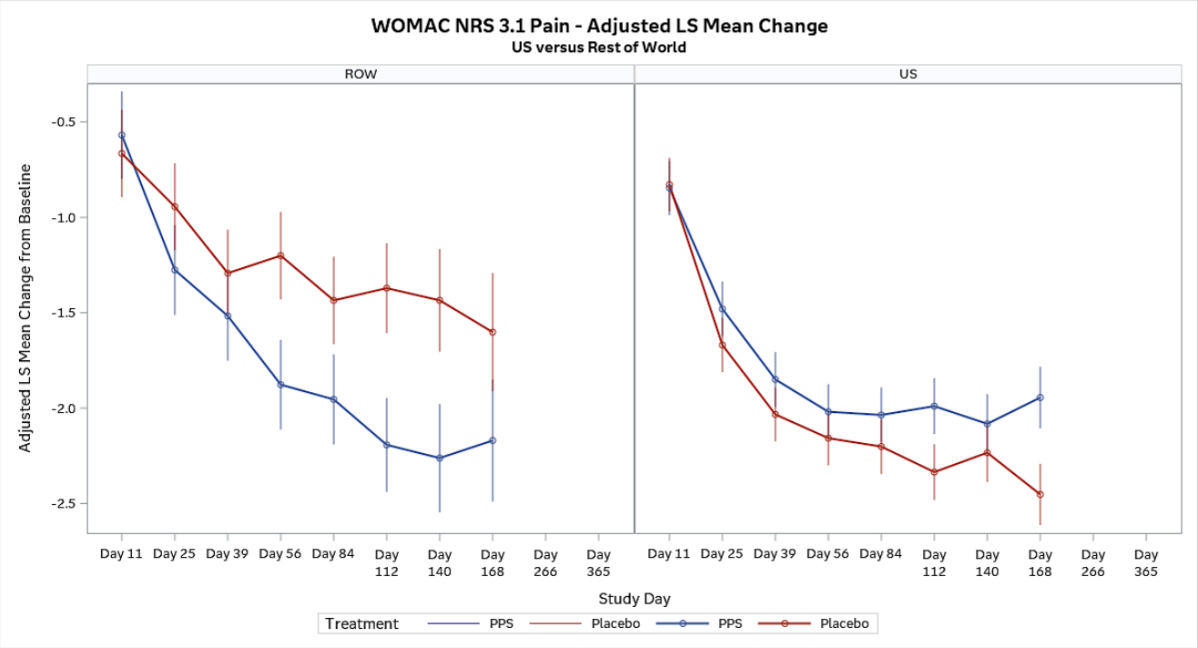



Figure 5. WOMAC pain: adjusted LS mean change from baseline. Blue: iPPS; red: placebo. More negative = more relief.

Figure 5 shows the Company's previously reported adjusted WOMAC pain changes. The ROW panel (left) shows greater numerical improvement with iPPS than placebo across the plotted follow-up assessments. The Company reported a Day 112 difference of 0.821 points in favour of iPPS (nominal p=0.0147). This is a separate pain measure from wADP, assessed in overlapping participants; the plotted separation does not establish significance at every visit.

Source: Paradigm's internal ROW analysis announced to the ASX on 15 October 2026.