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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Paradigm Biopharmaceuticals

By TIM BOREHAM

ASX code: PAR

Share price: 35 cents

Shares on issue: 428,519,176

Market cap: $150.0 million

Executive chair: Paul Rennie

Board: Mr Rennie, Amos Meltzer, Matthew Fry (Dr Donna Skerrett stepped down in November last year to focus on her chief medical officer role).

Financials (year to June 30, 2025): revenue nil, loss of $18.8 million (previous deficit $59.4 million), cash $16.8 million (down 6%)

September quarter 2025: customer receipts $33,000, cash burn $6.51 million, cash of $19.8 million

Identifiable major holders: Paul Rennie and related entities 4.9%.

Who said free to air TV was in its death throes?

When the Seven news network ran a piece about Paradigm's knee osteoarthritis (OA) drug candidate a few months ago, the company received around 700 emails from sufferers keen to participate in the company's current phase III trial.

Perhaps that reflects the ageing OA-prone demographic of TV news viewers, while younger consumers rely on the internet thingie to be informed (or misinformed).

“There’s a huge amount of interest,” says Paradigm’s investor relations chief director Simon White. “Finding people is never the issue. It’s just about having the sites up and going to drive the volume through.”

After myriad delays, Paradigm finally is well underway with the keenly anticipated study. The trial tests the efficacy of the company’s Zilosul, pentosan polysulphate sodium (PPS), for mild to severe knee osteoarthritis.

The company hopes to have recruited half of the 466 targeted patients by the end of 2025, “or early next year at worst”.

Pitched at US Food and Drug Administration approval, the trial is being carried out at 15 local sites and 50 US ones, with a potential Hong Kong site as well.

“We are building momentum across both clinical and corporate fronts as we continue to advance our mission to change the treatment landscape for osteoarthritis,” says Paradigm CEO Paul Rennie.

What’s the fuss about?

PPS is an anti-inflammatory, heparin-like compound made from beechwood hemicellulose. In the past, the drug has been used to treat a bladder condition and deep-vein thrombosis.

PPS has been used on dogs and horses, without any safety concerns.

Currently, osteoarthritis commonly is treated with non-steroidal anti-inflammatory drugs or opioid-based painkillers, which are either ineffectual or undesirable.

Paradigm has an exclusive 25-year exclusive supply deal with the only approved PPS maker, Germany’s Bene Pharmachem.

Under the Bene Pharmachem compact, Paradigm has dibs on all patented human applications. These include respiratory distress syndrome, heart failure and rheumatoid arthritis.

Paradigm was founded by Paul Rennie and Graeme Kaufman and listed on the ASX on August 18, 2015, having raised $8 million at 35 cents apiece.

Mr Rennie was Mesoblast’s head of product development. Mr Kaufman was CSL’s chief financial officer through the plasma behemoth’s privatization and was Mesoblast’s vice president.

In November 2021, Mr Rennie ceded his chief executive role and continued as chair. But in November 2022 he returned to the CEO role.

The story to date

The company says osteoarthritis affects around 530 million people globally, 32 million in the US. Knee osteoarthritis accounts for 365 million of the worldwide tally.

Paradigm has been encouraged by ‘real world’ evidence from about 700 patients who have undergone the treatment, mainly under the local special access scheme (SAS).

These takers include numerous former AFL footballers, including Simon White who donned his boots for Carlton.

The oldest SAS patient is in his 80s.

One early patient was dosed in 2016 and still receives ‘top up’ treatment when required.

The company also treated 10 retired US National Football League players, under an expanded access scheme.

But ‘real world’ evidence is not enough, no matter how compelling.

In 2018, the FDA knocked back the company’s approval application and demanded a phase III trial.

Where’s the clinical evidence?

Paradigm’s clinical evidence so far consists of three-phase II trials – Para-OA-005, Para-OA-008 and Para-OA-002.

Para 005 achieved a primary endpoint of reduction in pain and improved function among its 121 subjects.

With 61 patients, Para 008 measured the change in the synovial fluid biomarkers associated with pain, inflammation and osteo-arthritis disease, relative to placebo. In October 2023 Paradigm reported “clinically meaningful outcomes” at 365 days compared to placebo.

These included significant pain reduction and functional improvements and durable improvements in stiffness, as measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire.

The company also reported reduced use of pain medication, with the placebo group resorting to paracetamol (or such) five times more than the treated group.

The 600-patient Para-OA-002 trial confirmed the minimum effective dose for the phase III study.

Getting to the pointy end

The current phase III trial is known as Para-OA-012.

Trial recruitment aside, the market's focus is on an interim analysis, covering the first 50 percent of patients at day 112.

In last week's September quarterly report, the company said strong screening performance meant the number of sites potentially could be reduced.

The interim readout is on track for a readout in mid-2026.

The Australian sites account for 30 percent of patients, while Florida sites are also "over-represented", given the state's senior demographic of sun-seeking, Trump voting retirees.

Paradigm's recruitment has been helped by protocol changes, in terms of reduced stringency monitoring based on safety data.

Mr White adds the local Therapeutic Goods Administration has perused the company's trial protocol, while the company might undertake a confirmatory trial in Europe.

Either FDA or European marketing approval likely would lead to Hong Kong assent – and an entrée to the Chinese market.

Restorative benefits?

While the trial is all about pain mitigation, the company is buoyed by previous trial data that suggests the drug actually may improve overall joint health.

In October 2023, Paradigm released data from magnetic resonance imaging (MRI) scans of 15 patients, suggesting Zilosul results in 'functional' improvement to the joints.

This outcome was well beyond the previous known effects of relieving pain and improving function. The key findings were that cartilage reduction had not just been halted but the volume of connective tissue had increased, with bone lesion damage reducing.

"We showed increased cartilage thickness and reduced inflammation and bone marrow lesions," Mr White says.

He notes a "durable effect" out to 12 months after six weeks' treatment, with reduced rescue medication relative to placebo.

"To deliver those results, you would think there was something happening with the underlying health of the joints."

Trial participants are undergoing MRIs to assess cartilage thickness and X-rays to measure joint space.

Oral delivery?

In late June, Paradigm said it would acquire an early-stage oral candidate for minor to mild osteoarthritis.

This is by way of purchasing the private Proteobioactives Pty Ltd, for up to $16.5 million.

Paradigm will test PPS with Proteobioactive's COX-2 inhibitor, called Coxib.

The idea is to improve drug 'bioavailability' - a shortcoming of many oral drugs.

The deal gives Paradigm exclusive global rights to develop and commercialize the PPS-Coxib combo (known as Pentacoxib) for mild knee osteoarthritis and the veterinary market (dogs and horses).

Proof of concept data shows meaningful pain reduction in patients with hand and knee osteoarthritis.

Pentacoxib is a potential alternative to existing non-steroidal anti-inflammatory drugs which don't improve joint structures.

"We are looking to do some formulation work," Mr White says. "Initially, we would target it at the vet market and then progress into human studies."

Proteobioactives was founded by Prof Peter Ghosh, who pioneered PPS research.

The deal involves an upfront $500,000 in cash and a $1 million milestone payment on completion of a phase II trial.

Paradigm pays a further $5 million on "successful completion" of a phase III trial.

A further $5 million is paid on FDA approval and a further $5 million is due on the sale of an FDA registered product.

About one-third of knee osteoarthritis sufferers have mild pain; moderate to severe pain accounts for the rest.

Finances and performance

In the year to June 2025 Paradigm reported a net loss of $18.8 million, an improvement on the previous $59.4 million deficit.

R&D expenditure declined to $17.7 million from the previous $50.6 million.

Cash declined 5.6 percent to $16.8 million.

Last week, the company reported a September quarter cash burn of $6.5 million and cash of $19.68 million.

In December last year, the company raised $16 million in a placement, at 40 cents apiece.

In February this year, the company issued free loyalty options, on a one-for-four basis. These listed instruments are exercisable by February 11, 2026 at 65 cents. If all of them were to be exercised the company would raise $63 million.

While the current share price is well shy of the strike price, management expects many holders will exercise their options, because of one-for-two ‘piggyback’ options. These are exercisable at $1 within two years.

In early July, Paradigm announced a $US27 million ($A41 million) convertible note with Obsidian Global Partners.

The company has drawn down the first $US7 million, with the remainder at the company’s discretion (in drawdowns of $5 million) over two years.

“We can use it, but we don’t have to,” Mr White says.

Over the last year Paradigm shares have ranged between 16 cents (late October last year) and 63 cents (early February this year).

The shares peaked at $4.17 in January 2020.

Eyeing the competitive landscape

Paradigm reckons that when it comes to other non-opioid knee OA pain treatments, the coast is clear.

Korea’s Kolon Tissue Gene has a potential therapy based on stem cell genetic modification. The program is in phase III, having been subject to an earlier FDA ‘clinical hold’.

Kolon has a market capitalization of around $650 million on the Korean exchange, while Paradigm is worth around $180 million.

Pending FDA approval, the Israel-based, Nasdaq listed Enlivex Therapeutics plans to advance its lead cell therapy asset, Allocetra, to phase IIb stage.

Enlivex’s mechanism of action involves reprograming “macrophages into their homeostatic state”.

A phase I/IIa study failed to have a statistically significant impact on the study’s entire patient population.

But three biweekly doses of the drug helped knee pain, function and stiffness in a primary osteoarthritis population.

Dr Boreham's diagnosis:

Mr White describes Paradigm as "a simple story" - and indeed it is.

The outcome is binary: phase III success opens the company to a massive, underserved market.

Hitting the secondary endpoints of actual knee repair would be a spectacular game changer.

Trial failure isn't worth contemplating.

"By granting fast-track designation, the FDA agreed there's a huge unmet need," Mr White says.

"Now it is about execution and staying on time".

Broker Bell Potter has no doubt about the significance of the trial.

"The search for a safe, well tolerated and effective non-opioid pain relief for osteoarthritis represents one of the Holy Grails for modern medicine, along with a cure for cancer and a treatment for dementia."

Meanwhile, Mr White was treated with Zilosul in 2019 and 2022 and reckons it's time for a top-up.

While he doesn't play footy anymore, Mr White still leads an active life.

"No-one that's been in severe pain want to go back to where they were."

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. His Holy Grail is finding his car keys.