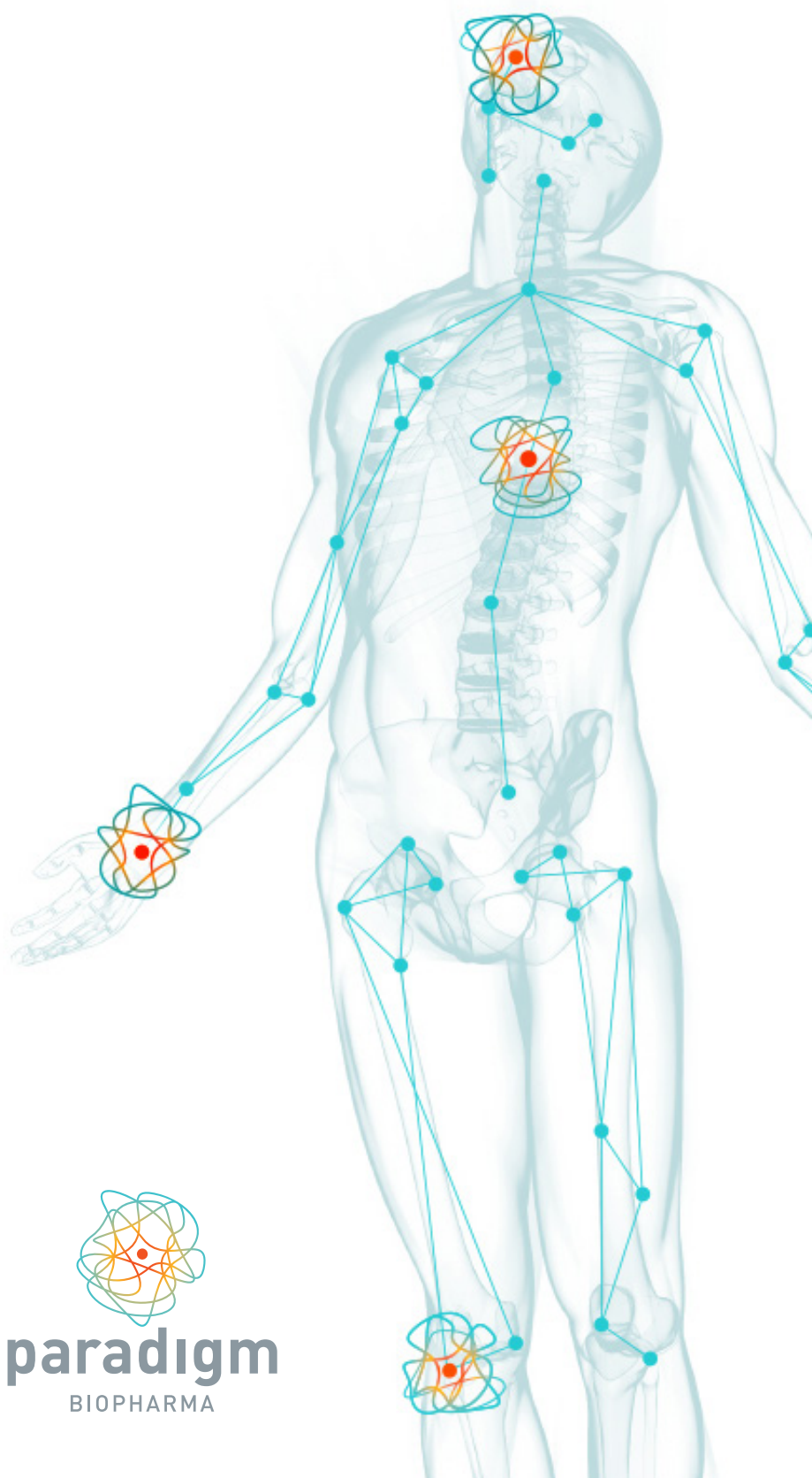


2017

SHAREHOLDER NEWSLETTER



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01 - CEO LETTER

RELEASE OF COMMERCIALY VALUABLE PHASE 2 TRIAL RESULTS IN CY2018

**DEAR
SHAREHOLDERS,
I WOULD LIKE
TO TAKE THIS
OPPORTUNITY TO
WISH YOU AND
YOUR FAMILY A
MERRY CHRISTMAS
AND HAPPY NEW
YEAR FOR 2018.**

The past 12 months have been an exciting period for Paradigm. We have achieved a number of key milestones that have set us up for a solid year in 2018.

Next year is expected to be a pivotal one for Paradigm with the release of results across a number of arthritis programs, namely:

- > Phase 2a trial for Ross River virus - final results expected June 2018,
- > Phase 2b trial for Osteoarthritis (OA) with concurrent Bone Marrow Lesions (BMLs) – final results expected Q4CY2018, and
- > OA with concurrent BML Real World Evidence (RWE) case studies.

Currently a number of orthopaedic surgeons and high-profile sports physicians are treating their patients, under the Therapeutic Goods Administration Special Access Scheme, with injectable PPS where current therapies have failed. Together, the orthopaedic surgeons and sports physicians are likely to report on between 75 to 100 cases in CY2018. As Paradigm receives reports from doctors it will report the findings to the market in cohorts of about 25 cases at a time. Results from the next cohort of 25 cases is expected in February 2018.

The release of these data will be a major value inflection point for our Company with the results being of significant interest to the Company's potential commercial partners. Please see the separate story in this newsletter for further details on these trials.

Those additional 75 case studies under the TGA's SAS Program will provide more valuable Real World Evidence data for our regulatory

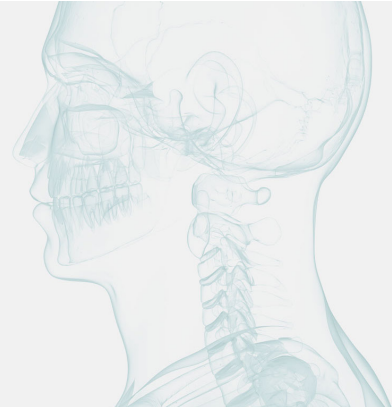
submissions. Please see the separate story in the newsletter which explains why this Real World Evidence data is so important for Paradigm.

Our alphavirus clinical trial programme is also expected to expand, with preparations for a Phase 2 clinical trial for Chikungunya (South America) continuing to progress well and on schedule. We anticipate strong interest from the US Department of Defense (DoD) in this program and will update the market accordingly.

I would like to take this opportunity to thank you for your support over the year and look forward to updating you in the New Year on our progress with these significant milestones. Once again, I wish you and your family all the very best for the holiday season.

PAUL RENNIE

**DIRECTOR & CHIEF EXECUTIVE
OFFICER**



02 - ANDREW WALKER

FORMER AFL STAR SUCCESSFULLY TREATED WITH PPS FOR OSTEOARTHRITIS

**FORMER AFL
PLAYER ANDREW
WALKER WAS
SUCCESSFULLY
TREATED WITH
PARADIGM'S
PENTOSAN
POLYSULFATE
SODIUM (PPS)
FOR OA UNDER
THE TGA SAS.**

Walker, who played for Carlton, had struggled throughout his AFL playing days with OA, which impacted not only playing career but also his everyday life.

Before treatment with PPS, Walker had five different surgeries on his knee, with 150ml of fluid causing the pain drained from his knee three times a week.

Following treatment with PPS, Walker's pain level reduced from 10 out of 10

to 2 out of 10. A 10-millimeter bone marrow edema had also shrunk to just 1-millimeter and Walker never had his knee drained after the PPS treatment.

The following link has Andrew (from the 14 min mark) talking about his condition and life pre and post treatment with PPS:

<https://www.youtube.com/watch?v=Zr5lZqDuPv0&feature=youtu.be>



THE IMPORTANCE OF REAL WORLD EVIDENCE DATA



IN OCTOBER, PARADIGM ANNOUNCED THE RESULTS FROM DOCTORS WHO TREATED A TOTAL OF 24 PATIENTS WITH OA AND BMLS THAT WERE TREATED WITH PPS UNDER THE TGA SAS.

In the 24 patients with a median age of 57.5 years (range 31 to 84 years), joint pain was reduced in 83% and knee function was improved in 80% of all cases treated.

These results followed the release of the peer-reviewed published case study of PPS in an additional patient with OA and BMLs in September.

These case studies are important to Paradigm as they provide Real World Evidence (RWE) data – i.e. the data from sources other than traditional clinical trials.

The United States Food and Drug Administration (US FDA) allows RWE data to be used in combination with Randomised Controlled Clinical Trials (RCCT) to support product registration for repurposed drugs such as PPS under the FDA 505(b)(2) regulatory pathway.

This follows the signing of the 21st Century Cures Act in December 2016, by which the US Congress tasked the FDA with developing a framework to evaluate how the use of data from sources other than traditional clinical trials could be used to support drug approvals.

This brings a further advantage to sponsors utilising the 505(b)(2) pathway, in addition to the already recognised benefit of streamlined development programs.

The act amended the US Federal Food, Drug, and Cosmetic Act by inserting, among other things, a provision to assess the potential for use of RWE in drug approval programs.

PARADIGM'S RWE CASES

People with OA and concurrent BML often present to their doctor with symptoms of painful joints (at rest, at night or with activity such as when walking up or down stairs) and decreased range of motion in the affected joint(s). When other pharmaceutical therapies have failed, injectable PPS has been used with success to reduce pain and improve joint function. Injectable PPS has also been used by doctors on elite athletes for acute and chronic sporting injuries. Again, where the current standard of care, corticosteroids, have failed to treat these sporting injuries, injectable PPS has been used with success. Currently, doctors from four AFL clubs are using PPS on sporting injuries that have failed standard of care (ie corticosteroids). At this time, Paradigm is not marketing the injectable PPS product for sale and injectable PPS can only be sourced by doctors for their patients under the TGA Special Access Scheme.

**BREAKOUT:
OSTEOARTHRITIS
IS THE MOST
COMMON FORM
OF JOINT DISEASE
WORLDWIDE**



US

27 million

OA affects more than 27 million adults¹

20% 

By 2030, approximately 20 percent of Americans (about 70 million people) will have passed their 65th birthday and will be at increased risk for the disease²

US\$81 billion

The financial burden has been estimated to be US\$81 billion in medical costs and US\$128 billion in total costs³

AUS



3 million 

Arthritis affects around 3 million people

19,000

19,000 hip replacements and 25,000 knee replacements are performed for OA patients each year⁴

AU\$475 million

Hip and knee replacements represent a direct healthcare cost in excess of \$475 and \$500 million respectively⁵

US\$5 billion

Size of the market is US\$5 billion per annum⁶

Paradigm's injectable PPS has the potential to be a breakthrough treatment for OA – a condition with a significant unmet medical need. Most current treatments prescribed for the condition do not have adequate pain-relieving effects, provide no protection for the degenerating joint structures and are also associated with significant adverse side effects.

<http://ard.bmj.com/content/annrheumdis/early/2017/07/12/annrheumdis-2017-211396.full.pdf>

<http://most.ucsf.edu/studyoverview.asp>

National Institute of Health; Emerging drugs for osteoarthritis; Hunter DJ and Matthews G 16(3): 479–491; 2011 September.

<https://www.mja.com.au/journal/2004/180/5/epidemiology-osteoarthritis-australia>

<http://www.hica.com.au/health-insurance-news/the-growing-cost-of-hip-and-knee-replacements>

National Institute of Health; Emerging drugs for osteoarthritis; Hunter DJ and Matthews G 16(3): 479–491; 2011 September.

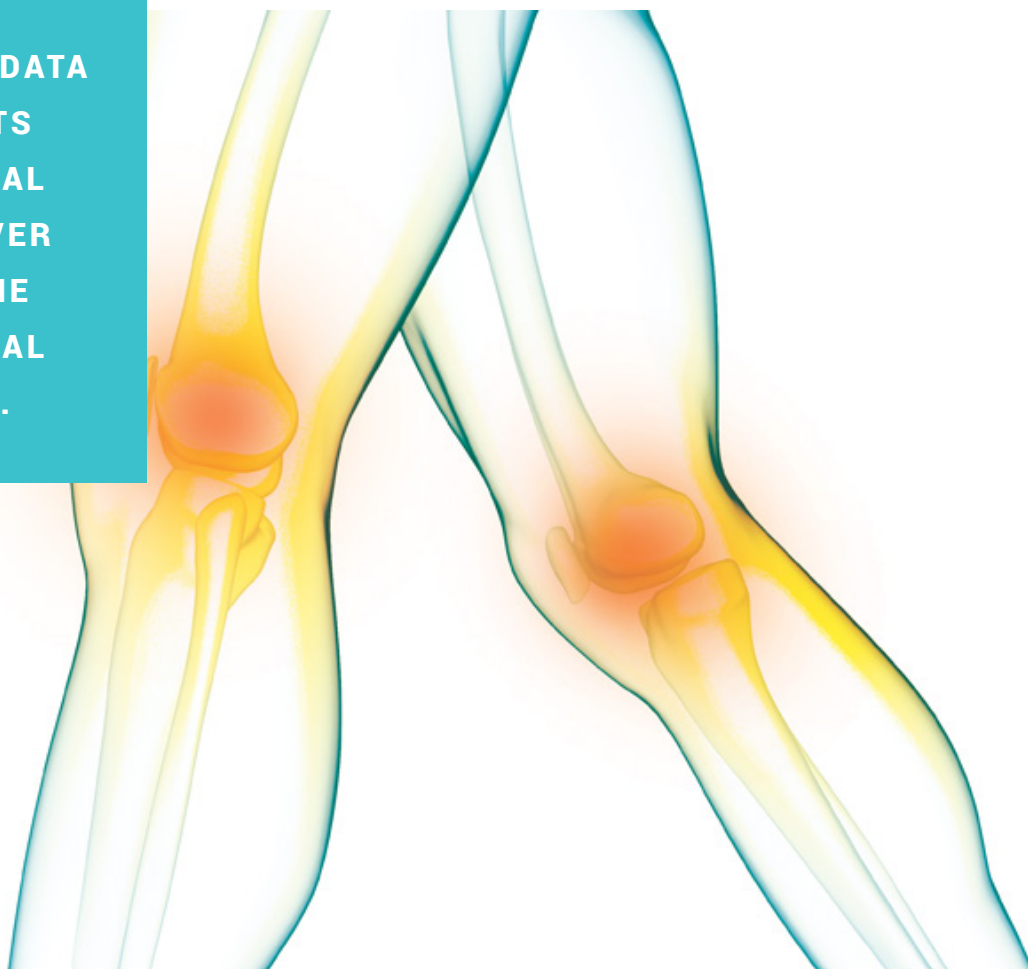
04

PIVOTAL PHASE 2 TRIAL RESULTS DUE IN 2018

IN 2018, PARADIGM WILL RELEASE COMMERCIALY VALUABLE PHASE 2 RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED DATA FROM BOTH ITS PHASE 2A TRIAL FOR ROSS RIVER VIRUS AND THE PHASE 2B TRIAL FOR OA/BMLS.

Importantly, as per the ASX Announcement on November 23, both trials are running concurrently and both are already ahead of schedule. The link to that announcement is here: <http://www.asx.com.au/asxpdf/20171123/pdf/43phcjkh2r8nyx.pdf>

For the Phase 2b trial for OA with BML, 23 out of 100 participants (23%) have been recruited to date from just two sites. All five sites for the trial will be operational from early January 2018 and Paradigm expects this strong momentum to continue.



The trial is a Phase 2b, randomised double-blind placebo-controlled multicentre study to evaluate the effects of PPS on pain in participants with knee OA and concurrent subchondral BMLs and results are expected in Q4 CY2018.

Paradigm's Phase 2a trial for Ross River virus (RRV) is also progressing strongly with more than 60% of participants recruited and an influx of participants expected over the coming months as mosquito numbers rise over the summer.

The trial is a randomised, double-blinded placebo-controlled clinical trial treating a total of 24 participants across four trial sites in Victoria and Queensland. Patients with RRV-induced arthralgia (painful joints) are being evaluated for safety, tolerability and effects on disease symptoms of PPS subcutaneous injections. Results are expected in Q2CY2018.

05

SUCCESS IN PHASE 2 ACL TRIAL

IN NOVEMBER, PARADIGM ANNOUNCED THAT ITS PHASE 2A CLINICAL TRIAL IN BMLS (BONE BRUISING) MET ITS PRIMARY ENDPOINT OF SAFETY AND TOLERABILITY.

Additionally, the secondary endpoint was met and showed a statistically significant reduction in BML volume.

These results indicate that PPS has potential to significantly improve recovery from acute anterior cruciate ligament (ACL) injury, with significant improvement in both bone marrow lesion volumes and effusion volumes, function improvement and improved long term outcomes for patients.

The Company received the top-line results following analysis of safety data on 11 people who participated in the phase 2a open label trial to evaluate PPS for the treatment of bone marrow lesions associated with acute ACL injuries.

06

CEO PAUL RENNIE INTERVIEW WITH ALAN KOHLER

IN NOVEMBER, PARADIGM'S CEO, PAUL RENNIE WAS INTERVIEWED BY SEASONED FINANCIAL JOURNALIST AND COMMENTATOR, ALAN KOHLER, FOR HIS "CEO OF THE DAY" SECTION OF THE CONSTANT INVESTOR NEWSLETTER.



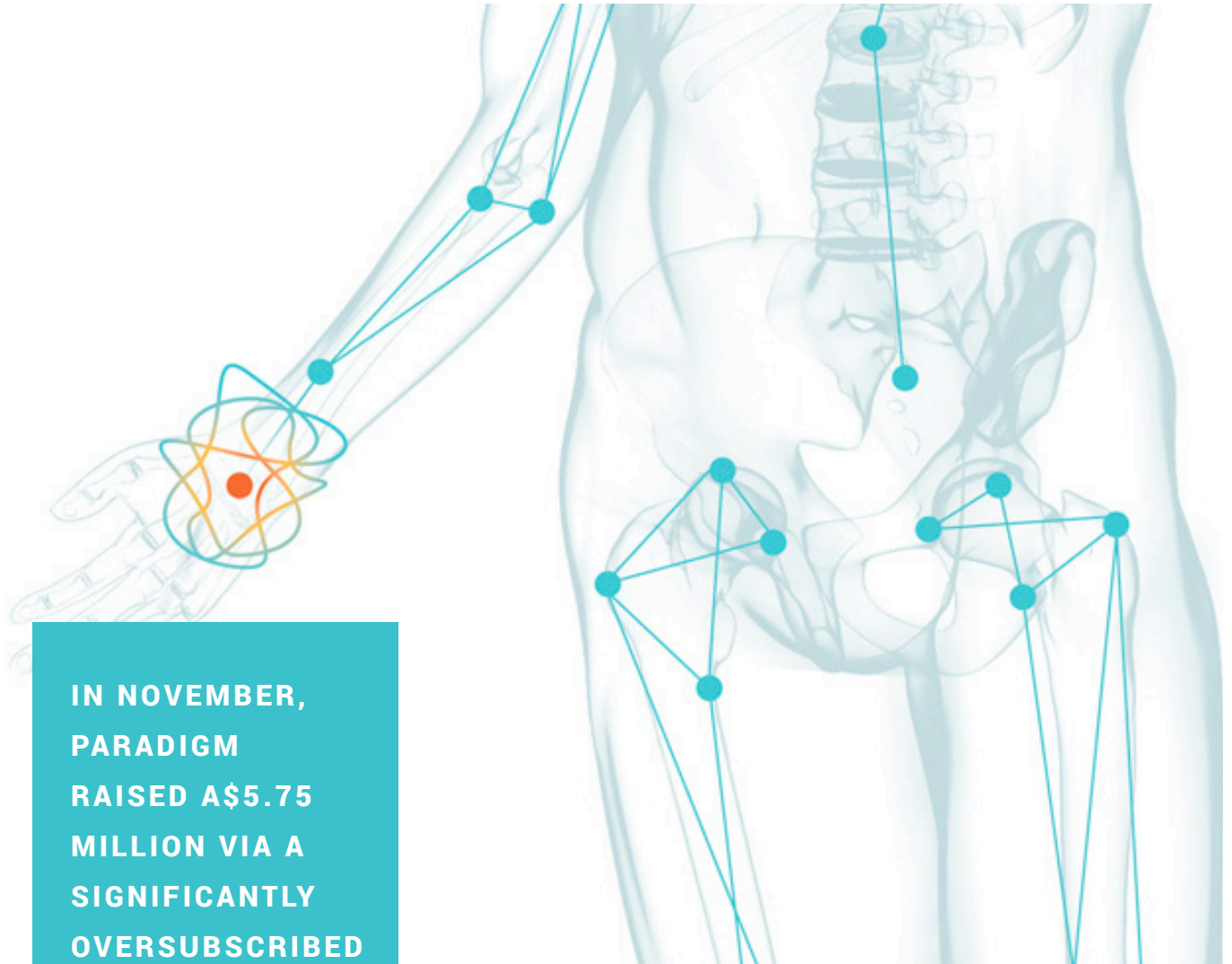
In the interview, Paul speaks about the advantages of working with a repurposed drug in PPS, the applications for the drug and the Company's upcoming pivotal Phase 2 trial results in 2018.

To read the transcript or listen to the audio interview, click here:

<https://theconstantinvestor.com/the-arthritic-paradigm/?free-pass> (may require subscription)

07

SIGNIFICANTLY OVERSUBSCRIBED PLACEMENT RAISES A\$5.75MN



IN NOVEMBER, PARADIGM RAISED A\$5.75 MILLION VIA A SIGNIFICANTLY OVERSUBSCRIBED PLACEMENT, PLACING THE COMPANY IN A STRONG POSITION TO ACCELERATE ITS PHASE 2 TRIALS FOR ROSS RIVER VIRUS AND OA.

The Placement was expanded due to very strong demand from existing and new institutional, sophisticated and professional investors.

The capital raising means the Company is well funded into CY2019 and importantly, post the completion of both the Phase 2 Ross River virus and 100 participant Phase 2b OA trials which are due to be completed at the end of CY2018.

The proceeds from the Placement will primarily be used to fund the Phase 2 OA trial as well as the ongoing generation of RWE data in subjects with OA and concurrent BMLs.