Paradigm's Two Arthritis Phase 2 Clinical Trials on Schedule

Highlights

- Paradigm's phase 2b, randomised double-blind placebo-controlled multicentre study to evaluate the effects of pentosan polysulfate sodium (PPS) on pain in participants with knee osteoarthritis and concurrent subchondral bone marrow lesions (n=100). Recruitment of nearly 25% complete and well ahead of schedule. Expected read-out Q4 CY2018.
- Phase 2a, randomised, double-blinded placebo-controlled clinical trial treating a total of 24 participants across four sites in Victoria and Queensland. Patients with Ross River virus (RRV) induced arthralgia (painful joints) are being evaluated for safety, tolerability and effects on disease symptoms of PPS subcutaneous injections. Recruitment of over 60% completed and also well ahead of schedule. Expected read-out Q2 CY2018.
- Paradigm previously announced the successful completion of its Phase 2a clinical trial in bone marrow lesions (BML) (bone bruising) as a result of an anterior cruciate ligament (ACL) injury. The primary endpoint of safety & tolerability was met along with the secondary endpoint of reduction of bone marrow lesion volume.
- This means in 2017, Paradigm successfully completed one phase 2 clinical trial along with the commencement of two additional phase 2 clinical trials in arthritis.

Melbourne 23 November 2017 Paradigm Biopharmaceuticals Ltd (ASX: PAR) today announced that its two arthritis phase 2 clinical trials are ahead of schedule meaning commercially valuable phase 2 randomised double-blind placebo-controlled data will be available in CY 2018.

Phase 2b - Osteoarthritis / Bone Marrow Lesions – Update

A phase 2b, randomised double-blind placebo-controlled multicentre study to evaluate the effects of pentosan polysulfate sodium (PPS) on pain in participants with knee osteoarthritis and concurrent subchondral bone marrow lesions (n=100).

Recruitment Status

- Trial is ahead of schedule, with 23 (23%) of participants recruited to date
- Recruitment of 23% from just two sites. All five sites will be operational from early January 2018.
- Recruitment will be paused over the next few weeks to ensure full functionality of the trial sites and participant adherence over the Christmas/New Year period

Paradigm is very pleased with the initiation of the trial and expects the strong momentum to continue. Injectable PPS has the potential to be a 'break-through' in the treatment of osteoarthritis (OA), where current therapies do not have adequate pain-relieving effects, provide no protection for the degenerating joint structures and are also associated with significant adverse side effects.

It is estimated that the size of the market is US$5 billion per annum[1] and this figure could potentially be multiples higher if new, effective, patented treatments such a PPS are commercialised.

OA also remains the most common form of joint disease globally. In the US alone, it affects more than 27 million adults,[2] while in Australia, arthritis affects around 3 million people. In both countries, the condition is a leading cause of pain and disability among the elderly and a cause of life-years lost due to disability.

The results from this phase 2b clinical trial are expected in Q4 CY2018.

Click here for Clinical Trial Details:
https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=373400&isReview=true

Phase 2a - Viral Arthritis – Ross River Virus - Update

Phase 2a, randomised, double-blinded placebo-controlled clinical trial treating a total of 24 participants across four trial sites in Victoria and Queensland. Patients with Ross River virus (RRV) induced arthralgia (painful joints) are being evaluated for safety, tolerability and effects on disease symptoms of PPS subcutaneous injections.

Recruitment Status

- Trial recruitment is strong with over 60% of participants recruited
- Influx of participants expected over the coming months as mosquito numbers rise
- Results read-out on track for mid 2018

Paradigm remains confident that the trial will recruit fully, and will complete on time and within budget. Results from the pilot study are expected to provide important safety data, and efficacy signals will be evaluated to design subsequent larger trials. Paradigm hopes that the phase 2a trial will demonstrate the potential of PPS as an effective treatment for patients with persistant symptoms following Ross River virus infection, where a treatment is desperately needed.

Click here for Clinical Trial Details:
https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=372925&isReview=true

Ross River on the rise in Australia

The incidence of Ross River virus in Victoria has spiked over 2017, with high amounts of rainfall and warm weather resulting in an unusually high number of infections. A total of 1,911 cases had been identified in the first 7 months of the year – an 86.2% increase on 2016's total.

---

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

[2] http://ard.bmj.com/content/annrheumdis/early/2017/07/12/annrheumdis-2017-211396.full.pdf

Potential for Ross River to be the next Zika virus

Interestingly, recent research has found that Ross River virus has the potential to become a global epidemic, similar to the recent global outbreak of Zika virus. It was previously thought that the mosquito-borne virus could only sustain itself among marsupials, which kept the disease endemic to Australia and Papua New Guinea. But research fellow at the University of Adelaide Professor Philip Weinstein said he and his partners at the Australian National University (ANU) found the disease silently planting roots in the South Pacific.

"It's really only in the last few years [it became apparent] when tourists returning to their home countries ... were diagnosed with Ross River virus after travelling in the Pacific," Professor Weinstein said.

Professor Weinstein said the new finding meant that even though there were no marsupials in the Pacific Islands, the virus was seemingly able to maintain itself there anyway. He warned that if the virus could sustain itself in areas where there were no marsupials, "then it could sustain itself anywhere in the world".

"That certainly means that it could be another global outbreak like Zika or Chikungunya a few years before that, another mosquito-borne virus that suddenly went global," he said.[3]

Phase 2a - ACL/BML – Result Overview

An open label clinical trial to investigate the safety, tolerability and efficacy of PPS in the treatment of participants with a ruptured Anterior Cruciate Ligament (ACL) injury and a Bone Marrow Lesion (BML)

Recruitment status

Phase 2a clinical trial has been closed out, and met its primary objective of safety and tolerability. Unexpectedly, results in the pilot trial show a statistically significant reduction in bone marrow lesion volume and effusion – synovitis volume compared with baseline.

Primary Endpoint

The company received the top line results following analysis of safety data on 11 participants in the open label trial to evaluate pentosan polysulfate (PPS) for the treatment of bone marrow lesions occurring after acute cruciate ligament (ACL) injuries.

PPS was administered as a course of 6 intramuscular injections, given over 3 weeks. All participants tolerated the injections and no serious adverse events were reported. There were no clinically significant changes in clinical laboratory parameters (haematology and biochemistry) or physical examination results over the treatment period or at 8 weeks follow-up.

The data confirms injectable PPS met the clinical trials primary endpoints of safety and tolerability.

Secondary Endpoint

Reduction in bone marrow lesion (BML) volume post administration of PPS. BML volume was assessed by an independent, blinded reviewer at Professor Flavia Cicuttini's Monash University research facility.

[3] https://www.adelaide.edu.au/news/news90662.html

9 of the 11 participants completed the course of treatment, while two participants withdrew for family and other reasons unrelated to PPS treatment.

Baseline MRIs

The changes in BML and effusion-synovitis from baseline to End of Study were examined in 9 patients:

- 6/9 (66.6%) patients showed reduction in BML
- 8/9 (88.8%) had reduction in effusion-synovitis
- a significant reduction in BML volume in lateral tibia [p=0.046]
- a marginally significant reduction for total tibia [p=0.06]
- a significant reduction in BML maximal area in lateral tibia [p=0.03] and total tibia [p=0.02]
- a significant reduction in effusion-synovitis volume in suprapatellar pouch [p=0.02] and total knee [p=0.01]
- a significant reduction in effusion-synovitis maximal area in suprapatellar pouch [p=0.03] and total knee [p=0.04].

These results indicate that PPS has potential to significantly improve recovery from acute ACL injury, with significant improvement in both bone marrow lesion volumes and effusion volumes, functional improvement and improved long term outcomes for patients. These data will be written up and submitted for peer-review publication.

Post the release of the Phase 2a ACL/BML results, Paradigm is receiving increased interest from athletes and sport physicians alike in the potential for PPS to be a treatment option for acute bone bruising injuries. This is in addition the very strong interest shown by retired sportsmen and women who are seeking treatments for joint related injuries and early onset OA.

Mr. Rennie, Paradigm's CEO said "Paradigm has a reputation of delivering on its milestones. The fact Paradigm has two phase 2 clinical trials running concurrently and both ahead of schedule is testament to the highly experienced, operational, clinical and regulatory staff at Paradigm and the commitment and dedication of the clinical trial sites across Australia. There is a very high level of interest in the Paradigm clinical trials, another important factor in the very rapid recruitment of clinical trial participants. The clinical trials are aimed at diseases for which there are very few safe and effective drugs meaning Paradigm is focusing on market sectors where there are high levels of unmet medical needs and high levels of commercial interest. Investors will also note that the completion of phase 2 clinical trials are major value inflection points. I am very pleased to report to the Paradigm shareholders that we are ahead of schedule with both our phase 2 clinical trials and more and regular updates will occur in 2018".

FOR FURTHER INFORMATION PLEASE CONTACT:

Paul Rennie
Director & CEO
Paradigm Biopharmaceuticals Ltd
Level 2, 517 Flinders Lane, Melb, VIC, 3000, AUSTRALIA
ABN: 94 169 346 963
Web: http://paradigmbiopharma.com/
Email: prennie@paradigmbiopharma.com