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PARA_OA_002 Phase 3 Clinical Trial Update

KEY HIGHLIGHTS

- Stage 1 (dose selection) of the PARA_OA_002 phase 3 clinical trial completes recruitment. The final stage 1 participants are currently completing the protocol-mandated screening and randomization which is expected to be complete early in Q3 CY2023.
- Paradigm is on track to conclude dose selection once all stage 1 participants reach 84 days post initial treatment. Post dose selection, newly recruited participants will proceed to stage 2 of PARA_OA_002 with the most effective dose. Additionally, PARA_OA_003 the confirmatory study will proceed with the selected dose.
- Paradigm has achieved its target by (i) activating 120 clinical trial sites across 7 countries and (ii) initiating a number of innovative recruitment initatives.
- The timeline for Paradigm's New Drug Application (**NDA**) with the US FDA remains on track.
- The independent Data Monitoring Committee recommends, based on two formal safety reviews, to proceed, with the pivotal Phase 3 clinical trial, without modification. The most recent DMC review occurred on June 20, 2023.

Paradigm Biopharmaceuticals Ltd (ASX:PAR) ("Paradigm" or "the Company"), a late-stage drug development company focused on delivering new therapies to address unmet medical needs, is pleased to provide an update on the recruitment progress for the PARA_OA_002 phase 3 clinical trial evaluating the change from baseline in pain and joint function following injectable pentosan polysulfate sodium (**iPPS**) compared to placebo in participants with knee osteoarthritis (**OA**).

Paradigm can confirm that participants have been identified for completion of stage 1 of the PARA_OA_002 clinical trial. Paradigm expects the final participants in screening to be randomised during Q3 this calendar year. Once all participants in stage 1 are randomised and reach the pre-specified timepoint, the data monitoring committee (**DMC**) will select the optimal dose for proceeding to stage 2. Following dose selection, the PARA_OA_003 confirmatory trial can commence.

The DMC has to date conducted two formal safety reviews of the PARA_OA_002 clinical trial. The DMC is responsible for assessing safety and efficacy during the conduct of Paradigm's PARA_OA_002 study, as well as ensuring the validity and scientific merit of the trial. The recommendation from the reviews by the DMC were that the clinical trial proceed without modification.

The completion of stage 1 and dose selection remains within previously reported timelines, with dose selection and stage 2 activities of the PARA_OA_002 clinical trial to occur in 2H CY2023. The timeline for Paradigm's NDA with the US FDA remains on track.

Paradigm has been able to progress its recruitment with the assistance of several recruitment initiatives. The PARA_OA_002 clinical trial has activated 120 sites across 7 countries comprising Australia, the US and Canada in North America, the UK, Belgium, Poland and Czechia in the EU. As Paradigm has reached its target for site activation and these clinical trial sites have become familiar with the study design, Paradigm has been able to increase the number of participants directed to these sites through the utilisation of the recruitment initiatives. The implemented initiatives include the introduction of 1nHealth, SubjectWell, and Paradigm's partnership with NFL Alumni Health, which together have driven potential participants to study sites for screening and randomisation. Paradigm has recently launched a dedicated clinical trial website www.Hope4OA.com, an ethics-approved easy-to-use public-facing website for providing trial information and access to an eligibility questionnaire for Paradigm's OA clinical trials.

Paradigm's Managing Director, Mr Paul Rennie commented: "Our progress has been achieved by a team of dedicated professionals, which is very encouraging, since it augurs well for our upcoming clinical milestones. Over the last 6 months, we have achieved a rapid increase in pre-screening and patient enrolment numbers. Due to the multiple effective recruitment initiatives, we expect this recruitment rate to be maintained throughout stage 2 as well as the confirmatory PARA_OA_003 study."

The PARA_OA_002 trial

The purpose of PARA_OA_002, a two-stage, adaptive, randomised, double-blind, placebo-controlled, multicentre phase 3 clinical trial, is to measure the change from baseline in WOMAC pain and function with subcutaneous injections of iPPS compared with subcutaneous injections of placebo in participants with knee OA pain.

Stage 1 comprises approximately 468 participants randomised to receive one of three iPPS dose regimens or placebo for 6 weeks. The primary objective of stage 1 is to identify the optimal dose for stage 2 and for Paradigm's confirmatory trial. Selection of the selected dose is based on considerations of optimal efficacy and optimal safety.

Participants in stage 1 are randomly allocated to receive one of the following:

- 1.5 mg/kg calculated for ideal body weight (**IBW**) iPPS twice weekly,
- 2 mg/kg IBW iPPS once weekly + placebo once weekly,
- Fixed doses
    - 100 mg iPPS for ≤65 kg IBW once weekly + placebo once weekly, or
    - 150 mg iPPS for >65 to ≤90 kg IBW once weekly + placebo once weekly, or
    - 180 mg iPPS for >90 kg IBW once weekly + placebo once weekly
- Placebo twice weekly

In stage 2, approximately 470 participants will be randomised 1:1 to receive the selected iPPS dose regimen or placebo for 6 weeks.

Participants in stage 2 will be randomly allocated to receive:

- iPPS dose regimen selected by the DMC, or
- Placebo twice weekly.

The primary endpoint in the PARA_OA_002 study will be change from baseline at day 56 in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain. Secondary outcomes include change from baseline at multiple timepoints out to day 168 in WOMAC pain and function, Patient Global Impression of Change (PGIC), and Quality of Life (QoL).

Phase 3 Clinical Program Recruitment Initiatives

Hope4OA

To facilitate current and potential trial participants, Paradigm launched a new clinical trials website called Hope4OA.com. The website is designed for ease of use where potential participants can discover trial details and find answers to commonly asked questions. If interested, they are invited to complete an online questionnaire to determine their eligibility as a potential trial participant. The website hosts helpful explanations and instructional videos about clinical trials in general, as well as providing links to patient support and further information.

1nHealth

1nHealth is a global patient recruitment company that has established a strong reputation in the supporting full enrolment for pharma sponsors across a wide range of therapeutic areas. 1nHealth excels in engaging and enrolling participants through its patient-centric content and technology-enabled approach, making the process seamless for patients and for the study's research sites alike. Through the partnership with Paradigm, 1nHealth employs a thorough pre-screening process to ensure participants are more likely to meet eligibility criteria for the PARA_OA_002 clinical trial, enabling a more seamless enrolment process.

SubjectWell

SubjectWell is a leading recruitment platform that excels in connecting sponsors and researchers with eligible trial participants. Leveraging advanced technology and a vast network of potential participants SubjectWell streamlines the recruitment process making it faster and more efficient. Through their user-friendly interface, they match individuals to relevant clinical trials based on specific criteria, medical history demographics, and location. SubjectWell's capabilities extend beyond traditional recruitment methods, as they employ digital marketing strategies, social media outreach, and targeted advertising to reach a diverse pool of potential participants. Their data driven approach ensures high quality referrals optimising the enrolment process and enhancing the speed of trial completion.

NFL Alumni Health Research Partnership

Following the successful Expanded Access Program (EAP) where 10 ex-NFL players were treated with iPPS, Paradigm entered a research partnership with NFL Alumni Health (see ASX announcement 13 July 2022). NFL Alumni Health is a wholly owned subsidiary of NFL Alumni, offering informational resources, programs, services, and other benefits to both NFL Alumni members (former NFL players, coaches, executives, spouses, cheerleaders, and associate members). Since the formation of this partnership, Paradigm has conducted several presentations to NFL Alumni Chapter Presidents to provide information about osteoarthritis disease onset and progression, current treatment options, and clinical trials throughout the US. Through this partnership, Paradigm has seen strong interest from NFL Alumni members in accessing further information on the PARA_OA_002 clinical trial which has boosted enrolment numbers. This partnership with NFL Alumni Health is expected to continue throughout the phase 3 clinical program.

About Paradigm Biopharmaceuticals

Paradigm Biopharmaceuticals Ltd. (ASX:PAR) is a late-stage drug development company driven by a purpose to improve patients' health and quality of life by discovering, developing, and delivering pharmaceutical therapies. Paradigm's current focus is developing injectable (subcutaneous) pentosan polysulfate sodium (**iPPS**) for the treatment of diseases where inflammation plays a major pathogenic role, indicating a need for the anti-inflammatory and tissue regenerative properties of iPPS, such as in osteoarthritis (phase 3) and mucopolysaccharidosis (phase 2).

Forward Looking Statements

This Company announcement contains forward-looking statements, including statements regarding anticipated commencement dates or completions dates of preclinical or clinical trials, regulatory developments and regulatory approval. These forward-looking statements are not guarantees or predictions of future performance, and involve known and unknown risks, uncertainties and other factors, many of which are beyond our control, and which may cause actual results to differ materially from those expressed in the statements contained in this presentation. Readers are cautioned not to put undue reliance on forward-looking statements.

To learn more please visit: www.paradigmbiopharma.com

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