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Medincell and AIC Unveil New Positive Phase 3 Results for mdc-CWM: Major Subgroup Analysis Shows Reduced Pain and Opioid Use, and Accelerated Rehabilitation following Total Knee Replacement

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Analysis of a major subgroup of patients undergoing a first Total Knee Replacement (TKR), representing over 70% of the trial population (108 out of 151), revealed the following benefits when comparing patients treated with F14/mdc-CWM (n=51) to those in the control group (n=57)[1]:

- **70% reduction in the number of opioid users at 3 months post-surgery,**
- **28% reduction in the total quantity of opioids consumed during the first 3 months post-surgery,**
- **Lower daily knee pain over the endpoints of 3 and 7 days, 2 and 6 weeks, and 3 months post-surgery,**
- **Range of motion (ROM) milestone (100 degrees) achieved significantly faster,**
- **Significant improvements across multiple, independent assessments of pain, inflammation and function.**

The analysis of this large subgroup of patients undergoing their first TKR revealed a consistently greater treatment effect compared to the overall study population which also included patients receiving a second TKR.[2]

This subgroup of patients will be the primary focus of future clinical development, planned for 2025, provided FDA agreement.

F14/mdc-CWM is an innovative sustained-release, non-steroidal anti-inflammatory drug (NSAID) designed for targeted intra-articular delivery. Medincell's partner, Arthritis Innovation Corporation (AIC), conducted a phase 3 trial to evaluate F14's efficacy and safety in managing pain and inflammation following total knee replacement (TKR). The study compared outcomes between patients receiving multimodal analgesia (MMA) alone and those treated with MMA alongside a single intra-articular dose of F14 administered during surgery. The MMA regimen, defined by the study protocol and similar to current standard of care, included periarticular infiltration with bupivacaine, oral acetaminophen, and opioid pain medication.

Most notable outcomes were observed in a subgroup of patients representing over 70% of the trial population (108/151) who had not previously undergone TKR in their contralateral (non-study) knee. Within the subgroup, patients treated with MMA and F14 (n=51) compared to patients treated only with MMA (n=57):

- Took 28% fewer opioids in the 3 months following TKR with a difference in daily need for analgesia for the F14 group vs. control group that becomes evident from 2 weeks after surgery. The same analysis from 2 weeks to 3 months showed a 40% difference in opioid consumption, which could substantially impact opioid addiction following TKR surgery.
- Discontinued opioid use earlier, with only 4% of patients treated with F14 still taking opioids at 3 months compared to 14% of patients in the control group.
- Showed better knee Range of Motion at 2, 6 and 12 weeks, 3 and 12 months. Significantly more F14 patients achieved the flexion milestone of 100 degrees required for advancing rehabilitation and resuming activities of daily living by 6 weeks than controls.

Dr. Richard Malamut, Chief Medical Officer at Medincell, states:

"The analysis of this subgroup's results by AIC provides compelling evidence to support future regulatory development. It demonstrates that our product could be a valuable adjunct to the current standard-of-care multimodal analgesia for patients undergoing total knee replacement, potentially accelerating rehabilitation.

Importantly, it has the potential to significantly reduce opioid consumption - a critical finding as the United States continues to prioritize the fight against opioid overuse. This urgency is further emphasized by the forthcoming implementation of the NOPAIN Act, which aims to promote the use of non-opioid pain management solutions."

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[1] Source: F14 Clinical Phase 3 Study (100-CIP02; 2022-2024); Data on file. Arthritis Innovation Corporation - Toronto, Canada; ClinicalTrials.govID NCT05603832

[2] Results presented in May 2024; www.medincell.com/wp-content/uploads/2024/05/PR_Medincell_CWM_14052024_EN.pdf

Patients of the subgroup treated with F14 also reported substantial improvement over controls for:

- AUC NRS pain score[3] at each study endpoint, including 3 and 7 days, 2 and 6 weeks, and 3 months post-surgery (notably, these improvements were found whether or not statistical, after adjustments)
- Knee effusion (swelling) at 2 weeks, 6 weeks, and 3 and 12 months
- Timed Up and Go test[4] at 2 weeks, 6 weeks and 3 months
- Knee Society Score[5]: all domains and especially "Functional Activities", at 2 weeks, 6 weeks and 3 months
- SF-12 Health survey[6]: all domains and especially "Physical functioning" at 2 weeks, 6 weeks and 3 months

The subset analysis was pre-specified in the protocol as a sensitivity analysis[7], but not alpha-controlled for formal statistical testing[8].

Medincell's partner, AIC, is scheduled to meet with the U.S. FDA in Q1 2025 to establish the approval pathway for F14/mdc-CWM.

As a reminder, Medincell will hold a videoconference on Tuesday December 10th, 2024, to present the half-year financial results (April 2024-September 2024)

- **Meeting in French, 6:00 pm (CET): https://www.medincell.com/fr/live-fr/**
- **Meeting in English, 7:00 pm (CET): https://www.medincell.com/live-en/**

About Medincell

Medincell is a clinical- and commercial-stage biopharmaceutical licensing company developing long-acting injectable drugs in many therapeutic areas. Our innovative treatments aim to guarantee compliance with medical prescriptions, to improve the effectiveness and accessibility of medicines, and to reduce their environmental footprint. They combine active pharmaceutical ingredients with our proprietary BEPO® technology which controls the delivery of a drug at a therapeutic level for several days, weeks or months from the subcutaneous or local injection of a simple deposit of a few millimeters, entirely bioresorbable. The first treatment based on BEPO® technology, intended for the treatment of schizophrenia, was approved by the FDA in April 2023, and is now distributed in the United States by Teva under the name UZEDY® (BEPO® technology is licensed to Teva under the name SteadyTeq™). We collaborate with leading pharmaceutical companies and foundations to improve global health through new treatment options. Based in Montpellier, Medincell currently employs more than 140 people representing more than 25 different nationalities.

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[3] AUC by NRS refers to the "Area Under the Curve" (AUC) calculated using the Numerical Rating Scale (NRS) for pain assessment. NRS is a common way to measure pain, where patients rate their pain on a scale from 0 (no pain) to 10 (worst pain imaginable). AUC is a statistical method that measures the cumulative amount of pain experienced over a specific time period. It considers the changes in pain levels over time rather than looking at just one point. AUC by NRS summarizes the patient's overall pain experience over time based on their ratings on the NRS. It's often used in pain studies to compare the effectiveness of treatments. Lower AUC values mean less overall pain experienced during the studied period.

[4] The Timed Up and Go (TUG) test measures mobility, balance, and fall risk. It involves timing how long a person takes to stand from a chair, walk a short distance, turn, return, and sit. It's commonly used in clinical settings to assess functional mobility and monitor rehabilitation progress.

[5] The Knee Society Score (KSS 2011) is a comprehensive tool for assessing knee function and patient satisfaction after knee replacement. It evaluates pain, mobility, stability, and functional activities, including walking and stair climbing, along with patient-reported outcomes. It's widely used to track recovery and guide treatment decisions.

[6] The SF-12 Health Survey is a brief questionnaire that measures overall health and quality of life. It assesses physical and mental health through 12 questions, providing a summary of functional well-being and the impact of health conditions on daily life.

[7] A sensitivity analysis is a method used to determine how the results of a study, model, or analysis are affected by changes in its input variables or assumptions. It assesses the robustness of conclusions by identifying which variables have the most influence on the outcomes. In clinical trials, sensitivity analyses are often performed to ensure the findings are consistent across different scenarios, subpopulations, or statistical methods.

[8] Alpha-controlled for formal statistical testing means applying a pre-defined significance level (usually 0.05) to limit the risk of false-positive results in hypothesis testing.

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