MedinCell demonstrates *in vivo* the efficacy of the first injectable combining surgical anesthesia and 3 days opioid free postoperative pain management

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In vivo studies have demonstrated that mdc-CMV offers surgical anesthesia and a minimum of 3 days of analgesia after a single preoperative injection.

The MedinCell team has selected the _lead formulation_ of the product and is launching its regulatory preclinical development.

Based on ropivacaine, mdc-CMV is the only known product able to achieve these two therapeutic objectives. Ropivacaine is a local anesthetic already widely used with a favorable risk/benefit profile.

mdc-CMV aims to:

- ✓ **improve and simplify postoperative pain management,**
- ✓ **reduce the risk of developing chronic pain after an inadequate management of postoperative pain,**
- ✓ **avoid the use of opioids.**

mdc-CMV targets a substantial number of surgical procedures: in the United States alone, 30 million operations performed under anesthesia require postoperative pain management every year.

mdc-CMV is the fourth MedinCell product entering regulatory development (the most advanced is currently in clinical phase 3 in the US). It is also the first fully-owned program of the company to reach this stage.

Human clinical trials should start in the first half of 2020.

The strengths of the project: a single injection combining anesthesia and non-opioid analgesia

mdc-CMV combines the BEPO® technology of MedinCell with a pharmaceutical ingredient already widely used: ropivacaine. *In vivo* studies demonstrate, on mini pigs, that a perineural injection of the product could allow local surgical anesthesia, followed by at least three days of analgesic effect. In vivo studies also showed the apparent safety profile of the product.

Anesthesia / Analgesia combination after a single injection could make mdc-CMV a unique product on the market. Main anticipated benefits to **improve postoperative pain management** are:

- ✓ **A significant reduction in the risk of chronic pain appearing** following a surgical procedure.
- ✓ **An alternative to the opioids currently extensively used for the treatment of postoperative pain.** Opioids cause numerous side effects in patients. Their use for pain management can also lead to abuse and addiction. It is currently a major public health issue, particularly in the United States where opioids are responsible for 130 deaths a day according to CDC, the US federal public health agency.
- ✓ **A reduction in hospital stays, their associated costs and nosocomial infection risks.** Outpatient treatment could be facilitated.

mdc-CMV could be used for a large range of surgical procedures, notably in orthopedic field. **The opioid-free postoperative pain management market is growing** with players such as Pacira (Exparel®) or Heron Therapeutics (HTX-011, currently awaiting market authorization). These products use bupivacaine, which is more toxic at cardiac and neurological levels than ropivacaine.

MedinCell develops a **multimodal approach to opioid-free pain management** with, in addition to the mdc-CMV program:

- mdc-CWM, for the treatment of postoperative pain and inflammation in orthopedic surgery currently in phase 2 clinical trials in the United States,
- mdv-NVA, for the treatment of chronic post traumatic peripheral neuropathic pain over 4 weeks currently in the lead formulation selection phase.

Next steps for the product portfolio

The launch of regulatory preclinical studies with mdc-CMV is part of the ongoing momentum to expand the portfolio of MedinCell, which includes both in-house products and products developed within the framework of partnerships. mdc-CMV is the fourth product of MedinCell currently in development, thus joining the three most-advanced programs of the Company for which major milestones are expected in the upcoming months:

- Currently in a Phase 3 clinical study in the United States, the efficacy results of the mdc-IRM program for the maintenance treatment of schizophrenia should be available by the end of the year.
- The results of the Phase 2 clinical trial currently ongoing in the United States with the mdc-CWM product for the treatment of postoperative inflammation and pain in orthopedic surgery are also expected this year.
- In the CNS field, the mdc-TJK program could enter clinical development by the end of the summer.

The portfolio of MedinCell also includes six other products in various therapeutic areas that are currently in the lead formulation selection phase, developed in-house or with the support of partners. Some of them could also enter regulatory preclinical development in the coming months.

Addressing a number of different therapeutic areas and indications, **all the products in the portfolio of MedinCell are based on active pharmaceutical ingredients already widely used with demonstrated efficacy and safety.** These programs have a particularly attractive risk/benefit profile and can be entitled to accelerated development processes.

Public data concerning the in vivo studies are available in the Corporate Presentation of MedinCell, which can be downloaded from the website invest.medincell.com.

About MedinCell

MedinCell is a pharmaceutical company that develops a portfolio of long-acting injectable products in various therapeutic areas by combining its proprietary BEPO® technology with active ingredients already known and marketed. Through the controlled and extended release of the active pharmaceutical ingredient, MedinCell makes medical treatments more efficient, particularly thanks to improved compliance, i.e. compliance with medical prescriptions, and to a significant reduction in the quantity of medication required as part of a one-off or chronic treatment. The BEPO® technology makes it possible to control and guarantee the regular delivery of a drug at the optimal therapeutic dose for several days, weeks or months starting from the subcutaneous or local injection of a

simple deposit of a few millimeters, fully bioresorbable. Based in Montpellier, MedinCell currently employs more than 130 people representing over 25 different nationalities.

Glossary

Lead formulation selection

The lead formulation selection is the first stage for all programs. It enables a prototype of the product to be obtained that complies with the targeted specifications, notably the duration of action and the dose of active ingredient to be regularly released. For each product, a new combination of polymers is created, thus making each formulation unique and exclusive.

Preclinical regulatory development

Launched after the development of the prototype, non-clinical development includes a series of studies and operations aimed at confirming the product's viability, testing its safety and establishing the scientific bases and regulatory strategy necessary for all applications for clinical trial approval.

Clinical development

Clinical development includes three major trial phases undertaken on human cohorts:

- Phase 1 includes healthy volunteers to assess their tolerance to the treatment.
- Phase 2 is carried with a limited group of sick patients to assess the treatment's efficacy, the drug's optimal dose and any side effects.
- Phase 3 is undertaken with a large number of sick patients to compare the treatment's efficacy to that of a placebo or standard of care. If successful, this is the final step before the marketing of the product.

NB: as the products developed by MedinCell use active ingredients that are already widely known and marketed, they can be exempt from certain clinical studies.

In Vivo Studies

Tests conducted in non-human living systems to study the activity of a drug candidate.

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