Press release

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DEINOVE

DEINOVE is now ready to start Phase II clinical trial for its antibiotic compound DNV3837

- ***Having reached a sufficient number of clinical centers, Phase II clinical trial testing the antibiotic candidate DNV3837 in Clostridioides[1] (Clostridium) difficile infections will start this summer in the United States and Germany***
- ***This trial will be conducted as part of an active Investigational New Drug (IND) authorization and a recently updated version of the clinical protocol***
- ***The production of the first commercial batch of DNV3837 has been successfully initiated***

DEINOVE (Euronext Growth Paris: ALDEI), a French biotech company that uses a disruptive approach to develop innovative antibiotics and bio-based active ingredients for cosmetics and nutrition, **announced that all the conditions are in place for the upcoming start of the Phase II trial testing the antibiotic candidate DNV3837 for the treatment of *Clostridioides difficile* infections.**

DNV3837 is a *first-in-class* antibiotic candidate targeting the treatment of *Clostridioides difficile* infections (CDIs), a disease classified as a priority by the WHO and one of the global leading causes of healthcare-related infections[2]. DNV3837 has demonstrated a promising efficacy profile, and acceptable tolerance in Phase I trials. It has obtained a QIDP designation and a *Fast Track* status[3].

DNV3837 will now enter Phase II trial for the treatment of CDIs. The clinical protocol has recently been adjusted and allows the trial to be conducted under the IND initially granted for the compound.

This multicentric open-label trial will be conducted both in Germany and the United States. Under the updated protocol, the number of sites, necessary for the implementation of its Phase II, has been reached. The inclusion of the first patient is planned for mid-2019. Medpace (Nasdaq: MEDP) was chosen as the Clinical Research Organization to oversee the trial.

In parallel, DEINOVE has started the production of the first DNV3837 batch on a commercial scale, in accordance with good manufacturing practices. This batch will be used in order to prepare enough material for conducting Phase III trial. CMC (Chemistry, Manufacturing, and Controls) operations in the United States have been contracted to a recognized CMO and the

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[1] The Clinical & Laboratory Standards Institute (CLSI) recently changed *Clostridium difficile*'s name to *Clostridioides difficile*. The Centers for Disease Control and prevention (CDC) have since adopted this new classification.
[2] Source: CDC
[3] "*Fast Track*" status facilitates the development of the molecule through a faster and more flexible regulatory review of the application. This status is granted by the FDA to drugs under development that meet critical and unmet therapeutic needs.

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first production steps have been successfully completed in accordance with the agreed specifications.

Georges GAUDRIAULT, Scientific Director of DEINOVE, states: *" Clostridioides difficile infections represent a pathology associated with a strong medical need. There is no efficient and approved IV drug for the treatment of severe CDIs. This is the reason why the investigation centers selected for this trial are extremely committed and motivated by the start of this trial - they are well aware of the need at stake. In addition, with the start of the production of the first commercial batches, we are now ready for the next development stages. »*

ABOUT *CLOSTRIDIOIDES DIFFICILE* INFECTIONS

40% of patients suffering a *Clostridioides difficile* infection (CDI) have severe forms, with mortality rates as high as 50%. Over the past 20 years, ICDs have tended to increase significantly in incidence and severity, particularly due to the development of new hypervirulent strains and the high risk of recurrence. The US Center for Disease Control and Prevention recently identified CDIs as one of the leading causes of healthcare-associated infections before *Staphylococcus aureus* (MRSA[4]) infections. In 2011, about half a million Americans were infected and more than 29 000 patients died within 30 days of diagnosis[5]. This disease does not affect the United States only, recent studies[6] show that the incidence of this type of infection is vastly underestimated in other parts of the world such as Europe and Asia.

To date, there are no therapeutic solutions for patients with severe gastrointestinal infections. Since the oral route is compromised, the available treatments, which are mostly oral treatments, struggle to reach the intestine because of the patient's pathological condition (reduced gastrointestinal motility, intubation, intestinal perforation, etc.), and the few antibiotics that could be administered intravenously (IV), do not cross the gastrointestinal barrier and therefore do not reach the site of infection.

ABOUT THE DNV3837 ANTIBIOTIC CANDIDATE

DNV3837 – a prodrug of the DNV3681 molecule (also known as MCB3681) – is a narrow-spectrum, hybrid oxazolidinone-quinolone synthetic antibiotic targeting only Gram-positive bacteria. It is developed as a highly active 1st line treatment targeting *Clostridioides difficile*.

It has demonstrated significant efficacy and superiority to reference treatments (fidaxomicin in particular) against isolates of *C. diff.*, regardless of their virulence (including the hyper virulent strain NAP1).

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[4] MRSA : meticillin-resistant *Staphylococcus aureus*
[5] Burden of *Clostridioides difficile* Infection in the United States - Fernanda C. Lessa, The New England Journal of Medicine, 2015
[6] Balsells E, Shi T, Leese C, Lyell I, Burrows J, Wiuff C, Campbell H, Kyaw MH, and Nair H (2019) Global burden of *Clostridium difficile* infections: a systematic review and meta-analysis. J Glob Health 9:010407

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DNV3837 is an intravenous antibiotic that, when converted to its active form DNV3681, crosses the gastrointestinal barrier and accumulates in the intestinal lumen, allowing it to precisely target the infection site. Several Phase I trials (on approx. an hundred healthy volunteers) have shown a high concentration of the antibiotic in stools, a strong marker of its presence in the intestine. It has also demonstrated its ability to eliminate *C. diff.* bacteria without altering the gut microbiota in the long term. It has also shown an acceptable tolerance profile during Phase I trials.

FDA granted the DNV3837 program with *Qualified Infectious Disease Product* (QIDP) designation and *Fast Track* status.

ABOUT DEINOVE

DEINOVE is a French biotechnology company, a leader in disruptive innovation, which aims to help meet the challenges of antibiotic resistance and the transition to a sustainable production model for the cosmetics and nutrition industries.

DEINOVE has developed a unique and comprehensive expertise in the field of rare bacteria that it can decipher, culture, and optimize to disclose unsuspected possibilities and induce them to produce biobased molecules with activities of interest on an industrial scale. To do so, DEINOVE has been building and documenting since its creation an unparalleled biodiversity bank that it exploits thanks to a unique technological platform in Europe.

DEINOVE is organized around two areas of expertise:

- **ANTIBIOTICS, new-generation anti-infective agents**: DEINOVE is preparing to enter a first antibiotic candidate into Phase II. The Company is also pursuing the systematic exploration of biodiversity to supply its portfolio with new leads, drawing notably on partnerships with Naicons, bioMérieux, and Institut Pasteur (AGIR program supported by Bpifrance).
- **BIOACTIVES, Active ingredients of natural origin** with cosmetics as the first market and potential in nutrition and health: DEINOVE already markets a first innovative active ingredient, a second in partnership with Greentech, while two others are in development with Oléos (Hallstar Group). It also runs a program in animal nutrition with Avril Group. Several other partnerships are also being planned.

Within the Euromedecine science park located in Montpellier, DEINOVE employs 62 employees, mainly researchers, engineers, and technicians, and has filed more than 310 patent applications internationally. The Company has been listed on EURONEXT GROWTH® since April 2010.

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