Press release

MONTPELLIER
JULY 15, 2020
6:30PM CEST

DEINOVE

DNV3837 antibiotic candidate: the Phase II trial continues in the United States, despite a disrupted context due to the COVID-19 outbreak

DEINOVE (Euronext Growth Paris: ALDEI), a French biotech company that uses its lead generation platform to develop innovative anti-infective drugs, **is pursuing the Phase II clinical trial of its antibiotic candidate DNV3837, in a context where U.S. hospitals are still fighting the COVID-19 pandemic. The Company thanks the clinicians for their commitment to this trial, as they face an unprecedented health crisis.**

DNV3837 targets the treatment of *Clostridioides difficile* gastrointestinal infections (CDI), a pathogen classified as urgent threat by the U.S. Centers for Disease Control and Prevention (CDC). A Phase II clinical trial, launched in early 2020 in the United States, is evaluating the efficacy of DNV3837 in patients, following promising Phase I data. To date, DEINOVE is the only French biotech with a small molecule in clinical development, fully owned by the company, in the field of antibiotics.

This trial continues in the United States despite the COVID-19 outbreak. Several of the investigation centers have maintained their clinical research activities and continue to screen and include patients. DEINOVE scientific team and the CRO Medpace are closely monitoring the situation.

« We are grateful to the clinicians for doing their utmost to ensure that the clinical trial runs smoothly. We are surrounded by a team that is aware of the therapeutic stakes and the potential of our solution in development, and we thank them for this. In the current health conditions in the United States, where hospitals are overcrowded, we could have feared a suspension of the trial, » **says Dr. Yannick Plétan, Acting Chief Medical Officer responsible for the clinical trial.** *« Conversely, the COVID-19 outbreak - which mainly affects the elderly - and the heavy antibiotic treatments administered to combat possible bacterial co-infections, are factors conducive to the development of severe* Clostridioides difficile *infections targeted by DNV3837. We are concerned, however, about the irrational use of antibiotics, which would have long-term public health consequences. »*

On June 1st of this year, the WHO warned of the increasing rates of antimicrobial resistance, boosted by the current health crisis. *" The COVID19 pandemic has led to an increased use of antibiotics, which ultimately will lead to higher bacterial resistance rates that will impact the burden of disease and deaths during the pandemic and beyond,"*, **worried Dr Tedros Adhanom**

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Ghebreyesus, WHO Director-General[1]. According to him, the threat of antimicrobial resistance is *"one of the most urgent challenges of our time* ". He also recalled that only small proportion of COVID-19 patients need antibiotics to treat subsequent bacterial infections.

ABOUT *CLOSTRIDIOIDES DIFFICILE* INFECTIONS (CDI)

40% of patients suffering a *Clostridioides difficile* infection (CDI) have severe forms, with mortality rates as high as 50%. Over the past 20 years, CDIs 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 (CDC) recently identified CDIs as one of the leading causes of healthcare-associated infections before *Staphylococcus aureus* (MRSA[2]) infections. In 2017, in the United States, there were an estimated 223,900 cases in hospitalized patients and 12,800 deaths[3]. This disease does not affect the United States only, recent studies[4] 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[5] 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. difficile*, regardless of their virulence (including the hyper virulent BI/NAP1/027 strain).

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. a 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

[1] https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---01-june-2020
[2] MRSA: meticillin-resistant *Staphylococcus aureus*
[3] https://www.cdc.gov/drugresistance/biggest-threats.html#cdiff
[4] 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
[5] Prodrug: substance whose transformation in the body results in an active product

demonstrated its ability to eliminate *Clostridioides* bacteria without affecting the gut microbiota. It has also shown an acceptable tolerance profile.

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

ABOUT THE PHASE II CLINICAL TRIAL TESTING DNV3837 IN CDI

The antibiotic candidate DNV3837 has been in a Phase II trial since the end of January 2020. The purpose of this trial is to evaluate its efficacy in CDI (through monitoring of symptoms, stool analysis, etc.), as well as to consolidate the safety and pharmacokinetic data.

This trial is taking place in the United States in two stages:

- In the first phase, a cohort of 10 patients with moderate to severe CDI is treated with DNV3837. At the end of this phase, the DSMB[6] has scheduled to review the interim results.
- The second phase involves 30 patients with severe CDI. This is an open-label randomized trial testing DNV3837 (in 2/3 of patients) against an approved standard of care[7] (1/3 of patients) for comparison purposes.

[6] DSMB - *Data Safety Monitoring Board:* a group of independent experts tasked to review the data generated during the trial and make recommendations on patient safety as well as trial relevance and validity.

[7] Standard treatments approved in the United States for the treatment of CDIs include vancomycin, fidaxomicin and metronidazole (all three antibiotics). The choice will be at the discretion of the clinicians.

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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 drugs**: A first antibiotic candidate is now in Phase II. The Company is also pursuing the systematic exploration of biodiversity to supply its portfolio with new leads, drawing notably on partnerships with bioMérieux and Naicons (AGIR program supported by Bpifrance).
- **BIOACTIVES, Active ingredients of natural origin** with cosmetics as the first market. DEINOVE already markets four cosmetic active ingredients, proprietary or developed in partnership with Greentech and Hallstar France, and has a number of products in development.

Within the Euromedecine science park located in Montpellier, DEINOVE employs 60 employees, mainly researchers, engineers, and technicians, and has filed more than 300 patent applications internationally. The Company has been listed on EURONEXT GROWTH® since April 2010.

CONTACTS

Investors
Coralie Martin
Communication, Marketing and Investor Relations
Ph.: +33 (0)6 46 62 47 50
coralie.martin@deinove.com

Media
ALIZE RP
Caroline Carmagnol
Ph.: +33 (0)6 64 18 99 59
deinove@alizerp.com

Visit www.deinove.com

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