Press Release

Montpellier
October 5, 2022
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DEINOVE to present data on DNV3837 at the ESCMID/ASM conference in Dublin

- New key preclinical results and a case study excerpted from our ongoing phase II clinical trial
- DNV3681 *in vitro* efficacy is superior to vancomycin and similar to the gold standard, fidaxomicin
- The prodrug DNV3837 is rapidly converted to DNV3681 *in vivo* and the active drug mostly concentrates in the GI tract
- The use of DNV3837 is a potential paradigm shift for CDI treatment

DEINOVE (Euronext Growth Paris: ALDEI), a French biotech company, pioneer in the exploration and exploitation of bacterial biodiversity to address the urgent, global challenge of antibiotic resistance, announces that a poster titled « *DNV3837, a parenteral GI tract-targeted treatment for* Clostridioides difficile *infection* » is to be presented at the ESCMID/ASM conference taking place in Dublin, from October 4 to 7.

The new preclinical data presented show that DNV3681 is highly efficient against 333 clinical isolates of *Clostridioides difficile*, and its efficacy is superior to vancomycin and similar to the gold standard, fidaxomicin.

Preclinical and clinical data show that the prodrug DNV3837 is rapidly converted to DNV3681 *in vivo* and that the active drug mostly concentrates in the GI tract. This unusual pharmacokinetic profile could be explained by a strong efflux of the active drug by the intestinal efflux pumps from the blood to the GI lumen.

The patient case presented suffers from a severe *Clostridioides difficile* infection. His White Blood Cells count, an inflammatory marker, rapidly dropped after inclusion, remained in the upper limit during 8 days and was normal at the end of the treatment. The diarrhea episodes improved after 6 days of treatment and came back to normal 10 days after treatment after a transient constipation period. DNV3681 concentrations in feces were several order of magnitude higher than DNV3681 MIC90[1].

Georges Gaudriault, Chief Scientific Officer of DEINOVE who attended the ESCMID/ASM conference in Dublin specifies: « *The use of DNV3837 is a potential paradigm shift. The intestine is a complex organ and CDI is not simply a topical disease*

[1] MIC : Minimale Inhibitory Concentration. MIC90 is the lowest concentration inhibiting, in 18 to 24 hours, the multiplication of 90 % of clinical isolates.

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of its epithelium. In order to treat efficiently the infection and avoid the persistence and/or recurrence of the infection, it is critical to treat this organ as a whole. DNV3837 is the first parenteral drug targeting the intestine and generating high exposure of DNV3681 in the intestinal tissue, as showcased today. »

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ABOUT *CLOSTRIDIOIDES DIFFICILE* INFECTIONS (CDI)

More than 40% of hospitalized patients with *Clostridioides difficile* infection (CDI) have been classified as severe disease associated with higher morbidity and mortality[2]. The Centers for Disease Control and Prevention (CDC) identifies CDI as one of the leading causes of hospital-acquired infections, ahead of even MRSA[3] infections. In the United States, it is estimated that CDI causes nearly half a million disease cases each year, and approximately 29,300 deaths[4]. This condition is not limited to the United States and recent studies[5] show that the incidence of this type of infection is greatly underestimated in other parts of the world, such as Europe and Asia.

To date, there is no proven therapeutic solution for CDI patients with severe vomiting, ileus and toxic megacolon. The oral route being compromised, the available treatments, which are mostly oral, have difficulty reaching 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 do not cross the gastrointestinal barrier and therefore do not reach the infection site.

ABOUT THE DNV3837 ANTIBIOTIC CANDIDATE

DNV3837 – a prodrug[6] 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 first-line treatment targeting *C. diff*. It has demonstrated significant activity and superiority to reference treatments against isolates of *C. diff.*, regardless of their virulence (including the hyper virulent BI/NAP1/027 strain).

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[2] Zar FA et al. Clin Infect Dis. 2007 Aug 01; 45(3):302-7.

[3] MRSA: methicillin-resistant *staphylococcus aureus*

[4] Guh AY, Mu Y, Winston LG et al. N Engl J Med 2020;382:1320–30

[5] 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

[6] Prodrug: substance whose transformation in the body results in an active product

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DEINOVE
INVESTING DARK BIODIVERSITY

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 approximately 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 demonstrated its ability to eliminate *Clostridioides* bacteria without affecting the gut microbiota.

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

For more information on the DNV3837 Phase II clinical trial in *Clostridioides difficile* infections, visit ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT03988855

ABOUT DEINOVE

DEINOVE is a French biotechnology company pioneering the exploration of a new domain of life, unexplored at 99.9%: the “microbial dark matter”. By revealing the metabolic potential of rare bacteria or still classified as uncultivable, it tackles a global health and economic challenge: antimicrobial resistance.

The new therapies discovered and developed by DEINOVE target superbugs (microbes that have become resistant to one or more antimicrobials) that cause life-threatening infections which are now spreading at high speed.

This breakthrough approach gave rise to one of the world’s first specialized microbiotechnology platforms and a unique collection of nearly 10,000 rare strains and thousands of bacterial extracts. Today, DEINOVE is conducting several development programs, of which its first antibiotic candidate is currently evaluated in a Phase II clinical trial in severe *Clostridioides difficile* infections, one of the world’s first emergencies. The Company has also developed new bacterial micro-factories that address the other issue in the race against antimicrobial resistance: the industrial production of these rare and low concentrated compounds with often too complex chemical structures to be generated by chemical synthesis.

Located at the heart of the Euromedecine park in Montpellier, DEINOVE has been listed on EURONEXT GROWTH® (ALDEI - code ISIN FR0010879056) since 2010. The Company has around 50 employees and relies on a network of world-class academic, technological, industrial and institutional partners.

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