Press release

MONTPELLIER, FRANCE
JANUARY 27, 2020
7:30 AM CET

DEINOVE

Enrolment of first patient in Phase II trial testing DNV3837 in *Clostridioides difficile* infections

- **The Phase II clinical trial aims to evaluate the efficacy, safety and pharmacokinetics of DNV3837 in patients with *Clostridioides difficile* gastrointestinal infection (CDI).**
- **The trial will be conducted mainly in 15 centers in the United States, in two successive stages:**
  - **a cohort of 10 patients with moderate to severe CDI treated with DNV3837,**
  - **a randomized cohort study testing DNV3837 against standard of care in 30 patients with severe CDI.**
- **The final results of this trial are expected by the end of 2020.**
- **DEINOVE is the only French player to conduct a clinical trial with an antibiotic.**
- **On 17 January, the WHO warned about the extreme lack of new antibiotics and the threat posed by the antibiotic resistance.**

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, **announced the inclusion of the first patient in the Phase II trial testing DNV3837.**

DNV3837 targets the treatment of *Clostridioides difficile* infections (CDI), a disease classified as a priority by the WHO and one of the global leading causes of healthcare-related infections[1].

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. DNV3837 has demonstrated a promising efficacy profile and acceptable tolerance in Phase I trials (on healthy volunteers). It has also demonstrated its ability to eliminate *Clostridioides* bacteria without affecting the gut microbiota. It has been granted *Fast Track* status and QIDP designation[2].

[1] Source: CDC (US Centers for Disease Control and Prevention)
[2] '*Fast Track*' status facilitates the development of the molecule through a faster and more flexible regulatory review of the application. The QIDP designation gives the drug exclusive access to the market for an additional five-year period. These designations are granted by the FDA to drugs under development that meet critical and unmet therapeutic needs.

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The Phase II trial aims to evaluate the efficacy of DNV3837 in pathological conditions (through monitoring of symptoms, stool analysis, etc.), as well as to consolidate the safety and pharmacokinetic data of the antibiotic candidate.

This trial is concentrated in the United States. It will take place in two stages:

- In the first phase, involving 5 centers, a cohort of 10 patients with moderate to severe CDI will be treated with DNV3837. At the end of this phase, the DSMB[3] will review the interim results.
- The second phase will involve 30 patients with severe CDI and will be carried out in 15 investigation centers. This will be an open-label randomized trial testing DNV3837 (in 2/3 of patients) against an approved standard of care[4] (1/3 of patients) for comparison purposes.

The results of this clinical trial should be available by the end of 2020.

"The start of this Phase II clinical trial is a significant step forward for DEINOVE and a great hope for patients. We are very proud to provide a potential solution to this unmet medical need and, to this end, work with the best American specialists in this area. The investigation centers are very committed to conducting this trial which, in the event of positive results, will be an important milestone towards the registration of DNV3837," **said Dr Georges Gaudriault, Scientific Director of DEINOVE.**

This announcement echoes warnings issued by the WHO about the lack of antibiotics renewal. Dr Tedros Adhanom Ghebreyesus, Director-General of WHO, declared last January 17 « *Never has the threat of antimicrobial resistance been more immediate and the need for solutions more urgent* ».
https://www.who.int/news-room/detail/17-01-2020-lack-of-new-antibiotics-threatens-global-efforts-to-contain-drug-resistant-infections

[3] 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.
[4] 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 *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, 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[5]) infections. In 2017, in the United States, there were an estimated 223,900 cases in hospitalized patients and 12,800 deaths[6]. This disease does not affect the United States only, recent studies[7] 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[8] 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 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.

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[5] MRSA : meticillin-resistant *Staphylococcus aureus*
[6] https://www.cdc.gov/drugresistance/biggest-threats.html#cdiff 7
[7] 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
[8] Prodrug: substance whose transformation in the body results in an active product

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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 and potential in nutrition and health: DEINOVE is already marketing a first cosmetic active ingredient, a second in partnership with Greentech and plans to launch new assets in 2020. Several other cosmetic actives are in development, including with Oléos (Hallstar Group) and Dow. It also runs a program in animal nutrition with Groupe Avril.

Within the Euromedecine science park located in Montpellier, DEINOVE employs 60 employees, mainly researchers, engineers, and technicians, and has filed more than 350 patent applications internationally. The Company has been listed on EURONEXT GROWTH® since April 2010.

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