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**Towards a new therapeutic approach for Crohn's Disease:
Phase I/II results demonstrate the potential for the TNF-Kinoid
in this inflammatory bowel disease.**

Neovacs presents the results of the TNF-K-001 clinical study at the European Crohn's and Colitis Organisation (ECCO) Congress which clearly demonstrate the significant promise in terms of both safety and clinical activity of the TNF-Kinoid in Crohn's Disease.

- Crohn's Disease is a chronic inflammatory disorder that can affect any segment of the digestive tract. ⁽¹⁾ It is most frequently diagnosed between the ages of 20 and 30, and it has a prevalence in France of approximately one person per thousand of population. Its incidence is estimated at **5 patients per 100,000 population** per year. ⁽¹⁾
- Given its high incidence in young adults, the chronic and evolving natural course of the disease, the significant associated morbidity, and its impact on patient quality of life, Crohn's represents a **serious public health problem**. ⁽²⁾
- **Today, there is no cure for Crohn's Disease.** The objectives of today's therapies are sustained control of disease activity and providing patients with a satisfactory quality of life.
- Immunomodulators, and especially **TNF inhibitors**, which were a major advance in the fundamental treatment approach to severe disease manifestations, **have clear limitations** : Multiple studies have shown that, in long-term use, at least 20% of patients do not respond to TNF inhibitors⁽³⁾ and, after only one year of use, only one patient in two is still a responder. ^(4, 5, 6)
- **Given the limitations of current treatment options, Crohn's Disease remains an area of significant unmet medical need, and consequently many patients today do not have access to satisfactory therapy.**

Considering the major patient need for alternative therapies for this disease, Neovacs, a biotechnology company, has focused on developing a new approach based on a novel concept: active immunization to cytokine targets. Based on this platform, the TNF-Kinoid is in Phase II clinical development and is ultimately intended to treat patients suffering from moderate to severe Crohn's Disease who have failed treatment with a TNF-inhibiting monoclonal antibody.

The final results of the Phase I/II study show the excellent safety profile of the TNF-Kinoid

The study was conducted in 21 patients with moderate to severe Crohn's Disease (CDAI: 220-400). The study was an open-label, dose-escalation design, run at multiple clinical centers. The principal objectives were to evaluate the safety of the TNF-Kinoid and its ability to induce an immune response to TNF. Data was also collected allowing the calculation of each patient's Crohn's Disease Activity Index (CDAI), a composite score of disease attributes used to track disease severity.

Three different dose levels were administered on Days 0, 7 and 28: 60 µg (n=3), 180 µg (n=9) or 360 µg (n=9). Four patients received a maintenance dose at 6 months.

After at least five months of follow-up, no severe adverse event related to the TNF-Kinoid has been reported, nor has any unusual infection been observed. All patients completed the study according to the protocol.

Clear induction of an immune response to TNF

17 of the 21 patients treated showed the production of antibodies directed to TNF. Of the 21 subjects, only one of the three that received the lowest dose (60 µg) responded. At the higher doses, 180 and 360 µg, 89% of patients produced antibodies to TNF.

These results led to the conclusion that the 60 µg dose should not be included for evaluation in the Phase II program.

One patient in two in clinical remission one month after dosing

At week 8, one month after the administration of the last dose of the Kinoid, 70% of patients in the study showed a clinical response, defined as a decline in CDAI of 70 points or more, and half were in clinical remission (a CDAI score of 150 or less). These results were sustained until at least week 20, four months after the last dose, with 72% of patients showing a response and 44% in remission. Clinical remission is recognized as the most important measure against which to evaluate new therapies for Crohn's.

The presence of antibody at Week 8 is associated with remission at week 12

Patients with antibody to TNF at week 8 (14 out of the 21 in the study) had a more than 50% chance of being in clinical remission at Week 12. By contrast, patients without antibody at week 8 (7 out of 21) had a low probability (14%) of being in clinical remission at Week 12.

"These results are very encouraging." commented Guy-Charles Fanneau De La Horie, Neovacs' CEO *"They tend to suggest that the presence at Week 8 of antibodies induced by active immunization with the Kinoid are predictive of a good clinical response, exemplified by a high probability of achieving clinical remission at week 12, 2 months after the last dose. These data therefore speak to a potential clinical benefit that is both potent and durable."*

A reduction in intestinal inflammation and evidence of mucosal healing

During the study, the evolution of calprotectin in the stools was also followed in ten patients. Calprotectin is a marker for intestinal inflammation. The results showed a normal calprotectin level in 7 of the ten patients at week 12, a sharp decline over baseline in most cases, indicative of a substantial reduction in inflammation of the intestinal mucosa.

Further, colonoscopies undertaken in 9 patients showed mucosal healing in 6 of them.

In conclusion, noted Guy-Charles Fanneau De La Horie, *"Taken together, these results lead one to think that antibodies generated by immunization with the TNF-Kinoid have strong clinical activity"*

He added that *"This is the first time results like this have been seen using an active immunization approach to Crohn's with TNF as the target. The Phase II study we recently began is designed to provide statistically significant confirmation of these first clinical results from the TNF-K-001 trial."*

About Neovacs

Neovacs is a biotechnology company focused on an active immunotherapy technology platform (Kinoids™) with applications in autoimmune diseases and other chronic conditions. Neovacs' current portfolio consists of 3 drug candidates: TNF-Kinoid, IFNα-Kinoid and VEGF-Kinoid. The company's lead immunotherapy program (TNF-Kinoid) targets TNF-mediated chronic inflammatory diseases. For TNF-Kinoid, a Phase I/II clinical trial in Crohn's Disease has been completed and Phase II trials in rheumatoid arthritis (RA) and Crohn's Disease (CD) are ongoing. The clinical study in RA is also the focus of collaboration with the French diagnostics company BMD, with the goal of developing theranostic tools for personalized care in RA. Patient recruitment is complete in a Phase I/II trial of Neovacs' second product candidate (IFNα -Kinoid, an immunotherapy targeting interferon alpha) in the treatment of lupus. Neovacs' R&D has generated a broad patent estate.

For more information, visit the Neovacs website at www.neovacs.com

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