InDex Pharmaceuticals publishes mechanism of action data for cobitolimod in scientific journal

February 25, 2020 – InDex Pharmaceuticals Holding AB (publ) today announced the publication of scientific data on the mechanism of action of cobitolimod, the company's lead drug candidate in development for the treatment of moderate to severe ulcerative colitis. The paper, published in the peer-reviewed *Journal of Crohns and Colitis (JCC)*, shows that the Toll-like receptor 9 (TLR9) agonist cobitolimod can modulate the immune system in ulcerative colitis by balancing the mucosal Th17/Treg cell response. The publication has also been highlighted in the journal podcast.

Cobitolimod recently met the primary endpoint in the phase IIb dose optimisation study CONDUCT as a novel therapy for moderate to severe ulcerative colitis with an outstanding combination of efficacy and safety. Ulcerative colitis is a debilitating chronic disease caused by inflammation of the large intestine. Accumulating evidence indicates that an imbalance between T helper 17 (Th17) and T regulatory (Treg) cells and their associated cytokines creates a pro-inflammatory state in ulcerative colitis. The scientific data now published in JCC demonstrate that cobitolimod mediates immunomodulatory effects both in an experimental colitis model as well as in blood and tissue samples of ulcerative colitis patients leading to a rebalanced Th17/Treg cell immune response.

"Cobitolimod is an innovative drug candidate with a unique mechanism of action for the treatment of ulcerative colitis. The highly interesting data presented in this paper clearly show that cobitolimod can induce immunomodulatory effects in the colonic mucosa leading to decreased inflammation in a murine model of colitis", said Professor Markus Neurath of the University of Erlangen-Nürnberg. "The fact that cobitolimod was able to balance the Th17/Treg cell response both in a mouse model, *in vitro* in cells from UC patients and in patients treated with cobitolimod in a clinical study demonstrates the robustness of the results. Cobitolimod represents a truly exciting first-in-class approach to targeted treatment of colonic inflammation."

Treatment with cobitolimod demonstrated therapeutic efficacy in the standard experimental model of colitis. At the same time, Th17 cells and pro-inflammatory IL17 and IL6 cytokines were significantly decreased, and Treg cells and IL10 positive immune cells were significantly increased after cobitolimod treatment. In line with these data, cobitolimod significantly decreased IL17 and significantly increased the expression of the anti-inflammatory cytokine IL10 in immune cells from ulcerative colitis patients *in vitro*. Furthermore, analysis of colon biopsies of ulcerative colitis patients taken before and four weeks after administration of cobitolimod showed a significant induction of IL10 positive and a pronounced reduction of IL17 positive immune cells after cobitolimod treatment in patients responding to cobitolimod, which was not observed in placebo treated patients. In addition, Treg cells were significantly increased in the colon upon treatment with cobitolimod. Besides IL10 producing Treg cells, cobitolimod could also induce anti-inflammatory IL10 producing wound healing macrophages *in vitro* in cells from UC patients.

These data were obtained in collaboration with the University of Erlangen-Nürnberg in Germany, and has previously been presented at the congress of the European Crohn's and Colitis Organisation.

"We are very pleased with the publication of these results, which provide a deeper understanding of how cobitolimod mediates its anti-inflammatory effects. That JCC also chooses to highlight the data in their podcast, shows that there is a great interest from the scientific community," said Peter Zerhouni, CEO of InDex Pharmaceuticals. "This supporting mechanistic data fits very nicely with the successful clinical results obtained with cobitolimod in our phase IIb study CONDUCT."

The publication has the title "The TLR9 agonist cobitolimod induces IL10 producing wound healing macrophages and regulatory T cells in ulcerative colitis" and is available at http://ecco-jcc.oxfordjournals.org, Schmitt H et al. J Crohns Colitis, Manuscript Doi: 10.1093/ecco-jcc/jjz170.

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Cobitolimod in brief
Cobitolimod is a Toll-like receptor 9 (TLR9) agonist, that can provide an anti-inflammatory effect locally in the large intestine, which may induce mucosal healing and relief of the clinical symptoms in ulcerative colitis. Cobitolimod is a first-in-class compound under development for moderate to severe ulcerative colitis and recently met the primary endpoint in the phase IIb study CONDUCT with an outstanding combination of efficacy and safety. Data from four previous completed placebo-controlled clinical trials support the efficacy and safety demonstrated in the CONDUCT study. Cobitolimod is also known as Kappaproct® and DIMS0150.

InDex Pharmaceuticals in brief
InDex is a pharmaceutical development company focusing on immunological diseases where there is a high unmet medical need for new treatment options. The company's lead asset is the drug candidate cobitolimod, which is in late stage clinical development for the treatment of moderate to severe ulcerative colitis - a debilitating, chronic inflammation of the large intestine. InDex has also developed a platform of patent protected discovery stage substances, so called DNA based ImmunoModulatory Sequences (DIMS), with the potential to be used in treatment of various immunological diseases.

InDex is based in Stockholm, Sweden. The company's shares (ticker INDEX) are traded on Nasdaq First North Growth Market Stockholm. Redeye AB with e-mail certifiedadviser@redeye.se and phone number +46 8 121 576 90 is the company's Certified Adviser. For more information, please visit www.indexpharma.com

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