DRUG DEVELOPMENT TOOL
LETTER OF SUPPORT
DDT-BMQ-000156

September 13, 2024

Nordic Bioscience A/S
Attention: Daniel Guldager Kring Rasmussen
Herlev Hovedgade 205-207
DK-2730 Herlev
Denmark

Dear Dr. Rasmussen:

The FDA is issuing this Letter of Support to encourage the further study of the biomarker CPa9-HNE, which quantifies a calprotectin S100a9 fragment generated from proteolytic cleavage of calprotectin by human neutrophil elastase. CPa9-HNE is a proposed biomarker measured in the serum and plasma of patients with inflammatory bowel disease (IBD), and it is intended to quantify activated neutrophils to provide a non-invasive, objective measure of endoscopic disease activity.[1] The most common indication for drugs being evaluated in IBD clinical trials is the treatment of patients with moderately to severely active ulcerative colitis or Crohn's disease, and endoscopic disease activity is an important component of clinical trial entry criteria. A blood-based biomarker such as CPa9-HNE, if successful, may enrich the trial population by identifying patients more likely to have moderately or severely active endoscopic disease. Furthermore, CPa9-HNE may reduce the number of unnecessary endoscopies by identifying patients whose disease activity does not meet the criteria for enrollment.

FDA supports your plan to study CPa9-HNE as an enrichment biomarker in IBD clinical trials and encourages you to seek qualification by submitting a letter of intent (LOI). To date, published and unpublished information show that the CPa9-HNE biomarker quantifies neutrophil activity and potentially neutrophil extracellular trap (NET) formation, which has been associated with inflammatory disease activity. Activated neutrophils are important in IBD as the neutrophil count in the lamina propria and epithelium is part of the histological assessment of inflammation in IBD patients[2]. If CPa9-HNE is formally proposed as a biomarker for qualification, analytical validation of the assay measuring CPa9-HNE, and validation of potential algorithms containing CPa9-HNE, should be performed as well as studies to support the clinical validation of CPa9-HNE as an enrichment tool.

[1] Mortensen, J. H. et al. A Specific Calprotectin Neo-epitope [CPa9-HNE] in Serum from Inflammatory Bowel Disease Patients Is Associated with Neutrophil Activity and Endoscopic Severity. J. Crohn's Colitis 1–14 (2022).
[2] Vespa, E. et al. Histological Scores in Patients with Inflammatory Bowel Diseases: The State of the Art. J. Clin. Med. 11, (2022).

FDA encourages data sharing and integrating data across trials to facilitate the development of promising drug development tools like CPa9-HNE. Any groups (academia, industry, government) that would like to join in this effort or have information or data that may be useful can contact Daniel Guldager Kring Rasmussen (dgr@nordicbio.com), Joachim Høg Mortensen (jhm@nordicbio.com), or view Nordic Bioscience's webpage (www.nordicbioscience.com).

Sincerely,

Jeffrey Siegel, M.D.
Director, Office of Drug Evaluation Science
Office of New Drugs
Center for Drug Evaluation and Research

Jessica J. Lee, M.D.
Director, Division of Gastroenterology
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

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Jeffrey Siegel

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Jessica Lee

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