Intestinal barrier dysfunction is a key feature of active disease and predict relapse and serious complications. Engineered drugs approved in IBD have limited effects on endoscopic remission and improvement in mucosal healing, driving a critical need for therapies which lead directly to mucosal healing. We have identified a microbial protein, SG-2-0776, that directly improves barrier function and reduces fibrogenesis in vitro and in vivo with potential to become a drug of mucosal healing. SG-2-0776 was identified through a novel algorithm, multi-technology meta-analysis (MTMA), using murine biopsies from Ulcerative Colitis (UC) patient and control subjects. Two bacterial strains, Eubacterium eligens and Akkermansia muciniphila were significantly reduced in UC samples. Screening of proteins predicted to be secreted from these strains using in vitro transmembrane electrical resistance (TEER) and wound healing assays, identified SG-2-0776, a novel protein, which significantly improved epithelial barrier integrity and reduced fibrogenesis. Administration of recombinant SG-2-0776 protein showed improvement in intestinal barrier function, reduced inflammation and fibrosis in rodent models of colitis. Moreover, SG-2-0776 was expressed in and reduces fibrogenesis in UC samples. Screening of proteins predicted to be secreted from these strains using transmembrane electrical resistance (TEER) and wound healing assays, identified SG-2-0776, a novel protein, which significantly improved epithelial barrier integrity and reduced fibrogenesis. Administration of recombinant SG-2-0776 protein showed improvement in intestinal barrier function, reduced inflammation and fibrosis in rodent models of colitis. SG-2-0776 was expressed in Lactococcus lactis subsp. lactis and reduces fibrogenesis in vitro and in vivo.

**REFERENCES**


**SUMMARY**

- **Indication:** Inflammatory bowel diseases (IBD)
- **Administration:** Oral, via engineered delivery
- **Target:** Inflammatory bowel disease
- **Clinical scores**
  - **Day -7 to -2**
    - Clinical scores: PR
  - **Day 1 to 5**
    - Clinical scores: PR
  - **Day 6 to 10**
    - Clinical scores: PR admin
- **Readout**
  - **Day 1 to 5**
    - Tissue Collection: Euthanasia and Tissue Collection
  - **Day 6 to 10**
    - Protein: L. lactis

**CONCLUSION**

- SG-2-0776 is a novel protein that induces direct mucosal healing and has the potential to become a differentiated therapeutic agent in IBD to treat patients with ineffective responses to standard care.
- SG-5-00455 enables the gut targeted delivery of SG-2-0776.
- We expect to file IND in 2022 and begin clinical development in IBD in 2023.