**Brilacidin for Inflammatory Bowel Disease: A Novel, Non-Corticosteroid, Non-Biologic Drug Candidate in Clinical Development**

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### Introduction/Background

Brilacidin is being developed as a novel, non-corticosteroid, non-biologic treatment for Inflammatory Bowel Disease (IBD), with formulation development plans including oral tablets for the treatment of Ulcerative Colitis and Crohn’s Disease, and foam or gel for the treatment of mild-to-moderate Ulcerative Proctitis/Proctosigmoiditis (UP/UPS), two types of IBD. Brilacidin is a fully synthetic, non-peptidic, Host Defense Protein (HDP) marine with a molecular weight (free base) of 3,685 g/mol.

HDPs, also referred to as defensins, isolated from organisms across the phylogenetic spectrum form part of an innate immune system and serve as the first line of defense against microbial and/or viral infections. Apart from the ability of HDNs to kill bacteria by direct action (by both membrane and non-membrane destruction), they have a potential role in modulation of multiple cellular immune and inflammatory responses.

Brilacidin appears to be a non-antibiotic based largely on its inhibition of phosphodiesterases (PDE4 and PDE5) and its down regulation of pro-inflammatory cytokines. The drug candidate, which has been evaluated in clinical trials in three indications (serious skin infections, oral mucositis, IBD), also has a wide variety of pathogenic organisms. Apart from the ability of Brilacidin to kill bacteria by direct action (by both membrane and non-membrane destruction), they have a potential role in modulation of multiple cellular immune and inflammatory responses.

Brilacidin is being developed as a novel, non-corticosteroid, non-biologic treatment for mild-to-moderate Ulcerative Proctitis/Proctosigmoiditis (UP/UPS), two types of IBD. Brilacidin is a fully synthetic, non-peptidic, Host Defense Protein (HDP) marine with a molecular weight (free base) of 3,685 g/mol.

### Study Design

- **Study Schematic**
- **Clinical Remission in > 50% subjects (Day 42)**
- **Safety**
- **Conclusions**

### Clinical Remission in > 50% subjects (Day 42)

- **Primary Efficacy Endpoint:**
  - **Clinical Remission at Day 42/Week 6** (reported by Modified Mayo scoring)
  - **Clinical Remission:**
    - At Day 42
    - More than 60% subjects in each cohort achieved ≥1-point or more improvement
  - **Quality-of-Life (QoL) Instrument**
    - Short Inflammatory Bowel Disease Questionnaire (SIBDQ)
    - Improvement in Quality-of-life (QoL) (reported by H/T subjects after 6 week treatment)
    - At least half of subjects in cohorts B and C also showed ≥20-point or more improvement
  - **Safety**
    - No rectal bleeding (RB=0) at Day 42
    - 75% Cohort C (3 of 4)
    - 5 of 6 subjects Cohort B
    - 1 subject in Cohort C declined (3 of 4)

### Conclusions

- **Brilacidin exhibited favorable efficacy in UF/UPS (BD) across 3 dose-evaluation cohorts (40 mg, 100 mg, 200 mg as retention enema)**
  - **Phase 2, Open Label, Dose-Escalation Trial (3 dose levels/cohort)**
  - **Active Mild-to-Moderate Ulcerative Proctitis (UP)(Active Proctitis/Proctosigmoiditis (UPP)) (Treated 17 subjects)**
  - **No Blood seen Normal Normal or inactive disease**
  - **Improvement in Quality-of-life (QoL) (reported by H/T subjects after 6 week treatment)**
    - **Gastrointestinal (GI) symptoms**
      - **Short Inflammatory Bowel Disease Questionnaire (SIBDQ)**
        - Improvement in Quality-of-life (QoL) (reported by H/T subjects after 6 week treatment)
    - **At least half of subjects in cohorts B and C also showed ≥20-point or more improvement**
    - **Safety**
      - **No rectal bleeding (RB=0) at Day 42**
      - 75% Cohort C (3 of 4)
      - 5 of 6 subjects Cohort B
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### Further Information

- **Beverly, MA 01915**
- **Further Information**
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