AVX-470 is an oral, enteric-coated, bovine-derived, polyvalent antibody designed to target TNF in the gastrointestinal (GI) tract without significant systemic exposure. AVX-470 was evaluated in a double-blind, placebo-controlled, first-in-human trial undertaken to explore the pharmacodynamics (bio-markers, clinical, endoscopic, histologic) and pharmacokinetics (tissue, stool, systemic bioavailability) of AVX-470. Immunogenicity & safety of 4 weeks of AVX-470 administration in patients with active ulcerative colitis (UC).

**Background & Aim**

AVX-470 was a well-tolerated drug with no drug-related SAEs, opportunistic infections or allergic reactions.

**Methods**

- 36 patients with active UC
- 13 centers in US, Canada, Belgium, and Hungary
- 4 weeks treatment, 3 ascending-dose cohorts 0.2 g/d, 0.4 g/d, and 0.8 g/d in divided doses
- Patients with high body mass index (BMI) were pre-screened to avoid dose escalation to AVX-470 3.5 g/day
- Colonscopic remission at Baseline and Week 4 — biopsy from cecal base, transverse, descending, sigmoid colon

**Demographics**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>43.6</td>
</tr>
<tr>
<td>BMI (mean)</td>
<td>27.2</td>
</tr>
<tr>
<td>Disease duration (mean)</td>
<td>9.62</td>
</tr>
<tr>
<td>Sex (%) Male:Female</td>
<td>61.1:38.9</td>
</tr>
<tr>
<td>Hispanic (%)</td>
<td>72.2</td>
</tr>
<tr>
<td>African-American (%)</td>
<td>1.1</td>
</tr>
<tr>
<td>White (%)</td>
<td>26.7</td>
</tr>
<tr>
<td>Other (%)</td>
<td>1.1</td>
</tr>
</tbody>
</table>

**Results**

AVX-470 reduces TNF in Colon: Direct Effect on Therapeutic Target

**Pharmacokinetics**

- **Stool**
- **Tissue**
- **Serum**

**Changes in Serum CRP Levels Across Treatment Arms & Duration**

- 3.5 g/day vs placebo — two-sided, two-sample paired t-tests
- Week 4 vs baseline CRP: paired analysis

**Clinical & Endoscopic Remission**

- **Remission**
- **Clinical Improvement**
- **Endoscopic Remission**

**Conclusions**

- AVX-470 was well-tolerated with no drug-related SAEs, opportunistic infections or allergic reactions.
- AVX-470 was stable in passage through the GI tract and was not associated with significant systemic exposures. No immunogenicity was observed.
- Bovine Ig was shown to penetrate the colonic mucosa, even in areas of normal endoscopic activity. However, prior dietary exposures interfered with detection of changes in tissue levels.
- Efficacy trends were observed across multiple parameters (clinical, endoscopic, biomarker) of disease activity, most favoring the 3.5 g/day dose group.

**Acknowledgements**

The authors would like to acknowledge Daniel E. Tracey, Brenda Lemos, Emma Erlich, Dave Keanes & Rutvi Patel (current and former employees of Avaxia Biologics) for their contributions to the biomarker analysis.

**Contact**

M. Scott Harris, M.D., Chief Medical Officer Avaxia Biologics Inc.
128 Spring St, Lexington, MA, USA
email: sharris@avaxiabiologics.com