**Title:** “Safety, tolerability and preliminary efficacy of AB-2004, a gut-restricted molecule targeting microbial metabolites, in an adolescent population with autism spectrum disorder (ASD)”

**Abstract:** Research has shown that the gut flora of autistic children is different compared with non-autistic children. In preclinical mouse models, Axial identified certain bacteria-derived metabolites (neuroactive microbial metabolites) that are produced in the gut and reach the brain resulting in altered neuronal network development and characteristics associated with autism. Axial is developing AB-2004, a novel gut-restricted therapeutic that removes these metabolites from the gastrointestinal (GI) tract, as a treatment of co-morbid challenges associated with ASD.

A study of AB-2004 was conducted as an open label, single cohort, 8-week multiple dose escalation study in 12 to 17 year old autistic males designed to establish safety, tolerability, and adherence to the three-times-per-day dosing regimen. Twenty-six subjects at three sites in Australia and New Zealand successfully completed the study. Safety was assessed by spontaneously reported adverse events as well as physical exams, blood samples, and urine samples. Exploratory endpoints included changes in key neuroactive microbial metabolites, changes in core and non-core autistic traits, and GI symptoms.

AB-2004 was found to be safe and well-tolerated with no drug-related adverse events. Significant reductions in plasma and urinary levels of several neuroactive microbial metabolites over the 8-week treatment were also observed, demonstrating target engagement of AB-2004 in the GI lumen. Additionally, irritability and anxiety assessment scores, as measured by the Aberrant Behavior Checklist-Irritability Subscale and Pediatric Anxiety Rating Scale, respectively, showed significant improvement over the 8-week treatment. Taken together, these data support that AB-2004 is safe and well-tolerated and justifies further evaluation as a treatment for autistic people.