

SCIENTIFIC ABSTRACT

Background

BHT-3021 is an antigen-specific immunotherapy agent in development as a treatment for treatment of Type 1 Diabetes (T1D). Treatment with BHT-3021 is expected to stop autoimmune destruction of the pancreas thereby preserving pancreatic β cell function.

BHT-3021 is a plasmid expression vector encoding full-length human proinsulin protein under the control of the cytomegalovirus immediate-early promoter/enhancer. Preclinical studies conducted at Bayhill using the murine homolog of BHT-3021 demonstrate efficacy in preventing development of diabetes in the Non-obese Diabetic (NOD) mouse model. This effect appears to be long-lasting as hyperglycemic NOD mice treated for 8 weeks did not develop diabetes during an additional 16 weeks of follow-up. Moreover for many hyperglycemic NOD mice, treatment with mouse homolog of BHT-3021 reversed hyperglycemia and restored normal blood glucose levels. This observation suggests that pancreatic damage can be reversed in patients if the autoimmune process can be stopped prior to complete destruction of residual beta-cell function. Mechanism of actions studies showed that the murine homolog of BHT-3021 decreased the immune response to autoantigens, particularly the response to insulin.

Study Design

This is a multi-center, randomized, double-blind placebo-controlled phase 1 trial in patients with type 1 diabetes. Subjects with T1D will be screened for eligibility. Key eligibility criteria are T1D diagnosed within 3 years of randomization, residual pancreatic β -cell function measured by stimulated C peptide level and a positive test for anti-insulin antibodies.

Two dose levels of BHT-3021 will be tested: 1.0 mg and 3.0 mg. A cohort of twelve Subjects will be treated at each dose level for a total of twenty-four subjects. Subjects will be randomized to BHT-3021 or placebo in a 3:1 ratio. BHT-3021 or BHT-placebo are administered intramuscularly weekly for 12 weeks (Weeks 0 to 11). Four weeks after the last dose of study drug (Week 15) each Subject undergoes a complete evaluation for safety, pancreatic function and anti-insulin immune after which the Subject's treatment assignment is unblinded. Subjects who received BHT-3021 enter Long Term Follow-up Period during which they are monitored for delayed adverse events, pancreatic function and anti-insulin immune responses. Subjects who received BHT-placebo subsequently receive 12 doses of open label BHT-3021 at their cohort's dose level. These cross-over Subjects are fully evaluated four weeks after the last dose of study drug after which they enter the Long Term Follow-up Period.

An independent Data Safety Monitoring Board (DSMB) will monitor patient safety and provide advice on trial operations.