

A Phase 1b, multi-center, single blinded, placebo-controlled, sequential dose-escalation study to assess the safety of topically applied AG013 in subjects receiving induction chemotherapy for the treatment of cancers of the head and neck

Principal investigator: Dr. B. Murphy, Vanderbilt-Ingram Cancer Center, Nashville, Tennessee

The purpose of this study is to investigate the safety, possible harms and side effects, of AG013 in subjects who are at risk for oral mucositis (OM) and to look for clinical indication of AG013 in the reduction of signs and symptoms of OM in patients receiving induction chemotherapy for the treatment of their head and neck cancer.

AG013 is made up of genetically modified (GM) bacteria called *Lactococcus lactis* (*L. lactis*). *L. lactis* that is not modified is commonly used to produce dairy products including yogurt, cheeses and milk. To make AG013, the DNA of *L. lactis* has been changed in the laboratory to secrete (release) a protein called human Trefoil Factor 1 (hTFF1). hTFF1 is normally secreted in saliva and intestines. Trefoil factor has been shown to be important in protecting and healing mucosal tissues, such as the tissue in the mouth, when these tissues are damaged by cancer therapies such as chemotherapy and radiation therapy.

In addition, ActoGeniX research has shown that local application of GM *L. lactis* strains, engineered to secrete hTFF1, to the oral cavity, reduce the severity and duration of radiation-induced OM in an animal model.

The proposed Phase 1b clinical trial will enroll subjects with head and neck cancer who develop OM during their first cycle of treatment with chemotherapy. OM is a painful, common toxicity of many forms of drug and radiation therapy used for the treatment of cancer. Subjects with OM get soreness, irritation, and ulcers in the mouth and may have a hard time eating, drinking or swallowing as a result of their cancer treatment.

During the second cycle of chemotherapy, eligible subjects will receive AG013 or placebo for 14 days at a frequency of one rinse, three rinses or six rinses per day.

Throughout the study, safety will be assessed by collecting and recording Adverse Events, laboratory assessments and the presence of the bacteria in blood. Vital signs, including temperature, systolic and diastolic blood pressures, heart rate and respiration rate, will be measured and recorded at the visit before treatment and once weekly during the treatment period.

A visual assessment of OM lesions using the WHO scoring system will occur each day during treatment. These daily assessments will be used to evaluate the effectiveness of AG013.

Information obtained from this research study may improve OM care. The final goal of the complete development program of AG013 is to reduce all the signs and symptoms of OM.