**Efficacy of Oral Cochleate-Amphotericin B for the Prevention of Invasive Candidiasis Caused by Candida albicans in Mice.**

**Introduction:** Amphotericin B (AMB), due to its fungicidal efficacy, broad spectrum and limited resistance, can be considered the "gold standard" antifungal treatment and remains the principal therapeutic option for deep mycoses. However, its application is currently limited by toxicity and administration requiring slow intravenous injection. MAT2203 (CAMB, cochleates); a novel lipidic crystal formulation of AMB, demonstrates oral bioavailability, significant efficacy, low toxicity, and shelf-life stability. In animal models, CAMB demonstrates antifungal activity with similar efficacy as intravenous AMB dosed intravenously, without the associated toxicity. Oral administration of CAMB has shown strong efficacy in mouse models of cryptococcal meningitis, disseminated candidiasis and disseminated aspergillosis.

In a Phase 2a human clinical study being conducted at the National Institutes of Health Clinical Center in Bethesda, MD, under the direction of Dr. Alexandra Freeman, MAT2203 (CAMB) has shown efficacy, safety, and tolerability in predominantly hereditary immunodeficient patients with a recurrent or chronic mucocutaneous candidiasis infection (candidal, oropharyngeal, vaginal) who are refractory or intolerant to standard non-intravenous therapies.

**Background:** MAT2203 (CAMB) is being developed for the prevention of invasive fungal infections due to immunosuppressive therapy, particularly in patients with acute lymphoblastic leukemia (ALL). In patients being treated for ALL the risk for invasive fungal infections (IFIs) is high, with an associated high risk of lethality. Currently, there is no standard of care for preventing these high risk IFIs in ALL patients.

The established treatment regimens for ALL are highly successful in liver-mobilized drug-drug interactions, causing serious concerns for drug-drug interaction induced side-effects. Amphotericin B is not liver metabolized and when incorporated in the lipid-crystal nano-particle structure of MAT2203 (CAMB), this otherwise toxic IV only compound can now be safely orally administered (providing patient convenience over crystal nano
crystal formulation of AMB, WT strain SC5314 -12 weeks prophylactic treatment duration), without the typical kidney and liver toxicity.

**Purpose:** This study determined whether orally delivered CAMB for the prevention of invasive candidiasis caused by a virulent C. albicans WT strain SC5314 in mice.

**Results:** All mice treated with placebo cochleates died or turned moribund and were euthanized on day 4-5. Mice treated with 2.18±1.23 mg/kg CAMB/MAT2203 (0.25, 0.5, and 1 mg/ml) and placebo cochleates were provided by Matinas BioPharma, Inc. Newark, NJ, USA Rutgers Publ. Health Research Institute, New Brunswick, NJ, USA

Dissolution experiments were conducted on the powder and the oral and i.v. formulations. The bioavailability was determined to be 100% regardless of the dosage. Fungal burdens in major organs were largely reduced in all CAMB treated mice in a dose-dependent manner. Organ sterilization was achieved for all CAMB dosing regimens at various levels. No significant toxicity was observed with CAMB treatment by group or time point. Results: All mice treated with placebo cochleates died or turned moribund and were euthanized on day 4-5. Mice treated with 2.18±1.23 mg/kg CAMB/MAT2203 (0.25, 0.5, and 1 mg/ml) and placebo cochleates were provided by Matinas BioPharma, Inc. Newark, NJ, USA Rutgers Publ. Health Research Institute, New Brunswick, NJ, USA

**Conclusion:** CAMB is highly effective for the prevention of invasive candidiasis in mice caused by a virulent C. albicans WT strain SC5314. Mice treated with 2.18±1.23 mg/kg CAMB in contrast to the 100% mortality of untreated mice. Reduced burden and organ sterilization efficacy of CAMB is dose-dependent.

**Method:** All mice were infected with 7.7x10⁵ CFU of C. albicans SC5314 via intraperitoneal injection at day 0. At day 10, kidneys, liver, and spleen were aseptically removed from mice in the study. Mice were then sacrificed and kidneys, liver, and spleens were weighed and homogenized in sterile PBS. CFU were plated on 1% Difco BHI agar (susceptible strain SC5314 were confirmed using 1% Difco BHI agar (Gold standard). Organ burdens were then calculated and compared with placebo controls in the study.**