PHARMACOTHERAPEUTICS OF INTRANASAL SCOPOLAMINE: FDA REGULATIONS AND PROCEDURES FOR CLINICAL APPLICATION

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Space Motion Sickness (SMS) is commonly experienced by astronauts and often requires treatment with medications during the early flight days of a space mission. Bioavailability of oral (PO) SMS medications is often low and highly variable; additionally, physiological changes in a microgravity environment exacerbate variability and decrease bioavailability. These factors prompted NASA to develop an intranasal dosage form of scopolamine (INSCOP) suitable for the treatment of SMS. However, to assure safety and efficacy of treatment in space, NASA physicians prescribe commercially available pharmaceutical products only. Development of a pharmaceutical preparation for clinical use must follow distinct clinical phases of testing, phase I through IV to be exact, before it can be approved by the FDA for approval for clinical use.

After a physician sponsored Investigative New Drug (IND) application was approved by the FDA, a phase I clinical trial of INSCOP formulation was completed in normal human subjects and results published. The current project includes three phase II clinical protocols for the assessment of pharmacokinetics and pharmacodynamics (PK/PD), efficacy, and safety of INSCOP. Three clinical protocols that were submitted to FDA to accomplish the project objectives: 1) 002 – A, a FDA Phase II dose ranging study with four dose levels between 0.1 and 0.4 mg in 12 subjects to assess PK/PD, 2) 002 – B, a phase II clinical efficacy study in eighteen healthy subjects to compare efficacy of 0.2 (low dose) and 0.4 mg (high dose) INSCOP for prophylactic treatment of motion-induces (off-axis vertical rotation) symptoms, and (3) 002 – C, a phase II clinical study with twelve subjects to determine bioavailability and pharmacodynamics of two doses (0.2 and 0.4 mg) of INSCOP in simulated microgravity, antiorthostatic bedrest.

All regulatory procedures were competed that include certification for Good laboratory Procedures by Theradex®, clinical documentation, personnel training, selection of clinical research operations contractor, data capturing and management, and annual reporting of results to FDA were successfully completed. Protocol 002 – A was completed and sample and data analysis is currently in progress. Protocol 002 – B is currently in progress at Dartmouth – Hitchcock Medical Center and Protocol 002 – C has been submitted to the FDA and will be implemented at the same contractor site as 002 - A. An annual report was filed as required by FDA on the results of Protocol 002 – A.

Once all the three Phase II protocols are completed, a New Drug Administration application will be filed with FDA for Phase III clinical assessment and approval for marketing of the formulation. A commercial vendor will be identified for this phase. This is critical for making this available for treatment of SMS in astronauts and military personnel on duty. Once approved by FDA, INSCOP can be also used by civilian population for motion sickness associated with recreational travel and other ailments that require treatment with anticholinergic drugs.