COSMA Clinical Study Protocol

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CLINICAL STUDY PROTOCOL

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AN OPEN LABEL, PROSPECTIVE, RANDOMISED, COMPARATIVE, TWO ARM CLINICAL STUDY TO EVALUATE THE EFFECTIVENESS OF GAMING PLATFORM - COSMA SOFTWARE FROM CEREBRUM MATTER LTD IN SUBJECTS WITH MILD DEMENTIA ASSOCIATED WITH MILD NEUROCOGNITIVE DISORDER AND ALZHEIMER'S DISEASE WITH EARLY ONSET.

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1. PROTOCOL SYNOPSIS

COSMA SOFTWARE ON EARLY ONSET DEMENTIA	
PROJECT NUMBER	AHC/195/RDD/CR/EE/19
PROTOCOL NUMBER	AHC/PSY/051/19
THERAPEUTIC AREA	Psychiatry
SPONSOR	Cerebrum Matter Limited, UK
CRO	Aurous HealthCare R & D India Pvt. Ltd., India.
SCIENTIFIC TITLE	An Open Label, Prospective, Randomised, Comparative, Two Arm Clinical Study to Evaluate the Effectiveness of Gaming Platform - COSMA Software from Cerebrum Matter Ltd in Subjects with Mild Dementia associated with Mild Neurocognitive Disorder and Alzheimer's Disease with Early Onset.
PUBLIC TITLE	Clinical Study to Test Effectiveness of Gaming Software (COSMA) in Patients with Mild Dementia
INDICATION	Mild Dementia associated with Mild Neurocognitive Disorder (MND) and Alzheimer's Disease (AD) with Early Onset.
CLINICAL PHASE	N/Ap. Proof of Concept
TYPE OF STUDY	Non-Interventional, Device Based Study.
INVESTIGATORS	Neuro-Psychologists, Psychiatrist and/or Neurologists
CDSCO APPROVAL	Not Required.
TREATMENT DURATION	28 days for each enrolled subject.
STUDY POPULATION	Adult subjects between 40 and 65 years (both ages and sexes inclusive) with Mild Dementia associated with Mild Neurocognitive Disorder and Alzheimer's Disease with Early Onset.
STUDY DESIGN	An Open Label, Prospective, Randomised, Comparative, Two Arm Clinical Study

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STUDY AIMS	1. To evaluate whether a software based Gamified Platform can support cognitive and mood improvement in clinically demented patients; MND and early AD. 2. To investigate whether brainwaves (measured via EEG) while using the sponsor's software COSMA, would impact executive functions and motor responses in MND and early AD. 3. To improve the behavioral and psychosocial well-being in MND and early AD patients via our software (COSMA), using a scientific pathway (brainwave patterns) and understand the impact of the designed software that has on individuals with dementia.
STUDY OBJECTIVES	1. To assess and quantify changes in mood (psychological effect), executive functions (cognitive effect), behaviour and well-being in MND and early AD (to evaluate the differences in the above between pre and post-testing). 2. To assess increase in alpha waves and parietal & frontal lobe activation in EEG.
INCLUSION CRITERIA	1. Adult subjects between 40 and 65 years (both ages and sexes inclusive) with Mild Dementia associated with Mild Neurocognitive Disorder and Alzheimer's Disease with Early Onset. 2. Subjects with Clinical Dementia Rating (CDR) of ≤1.0 at the time of enrollment. 3. Subjects with Mini-Mental State Exam Score between 18 -23 at the time of enrollment. 4. Subjects who are educated, able to read and write English fluently 5. Subjects who can a computer/similar electronic device with minimal supervision. 6. Subjects who have a computer and an active high speed internet connection at home. 7. Subjects with a dedicated LAR or caretaker to address any study objectives in lieu of the subject. 8. Subject/LAR who is willing to give informed consent for participation, able to comprehend and understand the responsibilities during treatment period and follow up period.
EXCLUSION	1. Subjects with mental illness and/or neuropsychiatric disorders.

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CRITERIA	2. Subjects who are on anti-depressants, anti-psychotics and/or medication that may cause worsening in cognitive functions. 3. Subjects with significant primary visual impairments. 4. Any significant medical condition (e.g., significant psychiatric or neurological disorders, active alcohol/drug abuse, etc.), any medical condition that is unstable/poorly controlled or other factor (e.g., planned relocation) that the Investigator felt would interfere with study evaluations and study participation. 5. Subjects who have participated in any clinical study within 3 months from the date of enrolment. 6. Females who are pregnant or lactating or planning to become pregnant during the study period. 7. Subjects who mentally unable to comprehend the responsibilities and adhere to the stipulations of the protocol. 8. Subjects, who in the opinion of the Investigator/CRMC are not eligible for enrolment in the study.
STUDY OUTCOME MEASURES	1. **Apathy Evaluation Scale:** Improvement from baseline 2. **Trail Marking Test A :** Improvement from baseline 3. **Trail Marking Test B :** Improvement from baseline 4. **Dementia Severity Rating Scale:** Improvement from baseline 5. **Abbreviated Mental Test Score:** Improvement from baseline 6. **Clock Drawing Test :** Improvement from baseline 7. **Lawson-Brady : Instrumental Activities of Daily Living (IADL) Scale :** Improvement from baseline 8. **The Clinical Global Impressions Scale:** Improvement from baseline 9. **EEG :** Improvement from baseline
STUDY END POINTS	1. **Apathy Evaluation Scale:** Reduction of ≥10 scores from baseline. 2. **Trail Marking Test A:** Improvement of ≥5 seconds from baseline. 3. **Trail Marking Test B :** Improvement ≥ 10 seconds from baseline 4. **Dementia Severity Rating Scale:** Reduction of ≥5 scores from

	baseline. 5. **Abbreviated Mental Test Score:** Improvement of ≥3 scores from baseline. 6. **Clock Drawing Test:** Improvement of ≥3 scores from baseline. 7. **Lawson-Brady: Instrumental Activities of Daily Living (IADL) Scale :** Improvement of ≥2 scores from baseline. 8. **The Clinical Global Impressions Scale:** Score of ≤3 by end of study 9. **EEG:** Increase in alpha waves, parietal & frontal lobe activation.
NUMBER OF SUBJECTS	60 Subjects
TREATMENT ARMS	**Two Arm Study 2:2:1:1 Ratio** **TREATMENT ARM I : Mild Neurocognitive Disorder** ▪ **Cohort IA :** MND : 20 Subjects : COSMA Players ▪ **Cohort IB :** MND : 10 Subjects : Control Players **TREATMENT ARM II : Alzheimer's Disease with Early Onset** ▪ **Cohort IIA :** EAD : 20 Subjects : COSMA Players ▪ **Cohort IIB :** EAD : 10 Subjects : Control Players
INVESTIGATIONAL DEVICE	Gaming Platform - COSMA Software from Cerebrum Matter Ltd
CLASSIFICATION	Non-Invasive, Non-Interventional Device
DATA CAPTURING	COSMA Software, EEG Report, Questionnaires & Assessment WorkSheets; Case Report Form.
DATA SETS FOR STATISTICAL ANALYSIS	**EFFICACY ANALYSIS SET:** ▪ *Treatment Arm I vs Treatment Arm II* ▪ *Cohort IA vs Cohort IB* ▪ *Cohort IIA vs Cohort IIB* ▪ ***Per Protocol Set (PP Analysis Set):*** *60 Subjects (expected)* ▪ ***Intent to Treat (ITT Analysis Set) :*** *60 Subjects (subjects with minimum of paired data post baseline)* **SAFETY ANALYSIS SET:** ▪ *All subjects enrolled into the study*