The PART THE CLOUD CHALLENGE to RESCUE (REverse, reStore, Cease and UndErstand) Brain Cell Degeneration in Alzheimer’s disease

Program Goal: The PART THE CLOUD CHALLENGE to RESCUE (REverse, reStore, Cease and UndErstand) Brain Cell Degeneration in Alzheimer’s disease will accelerate therapeutics and discovery of innovative compounds to be used in early clinical trials.

Background: Two hallmark pathologies in Alzheimer’s disease are the presence of amyloid beta (A-beta) fibrillar plaques and tau neurofibrillary tangles. Brain atrophy caused at least in part by neuronal loss is a prominent pathological feature of Alzheimer’s disease as well. Precise mechanisms of neuronal cell death remain uncertain, but multiple lines of evidence suggest that both A-beta and tau accumulation trigger a complex cascade of events that result in neuronal demise. Notably by the time an individual is overtly symptomatic with AD or even MCI a great deal of neuronal damage has occurred, and there is widespread amyloid and tau pathology. Thus, in symptomatic phase of dementia there is a pressing need to identify therapeutic strategies capable of preventing additional neuronal damage, reversing pre-existing damage or some combination of the two. Further there is growing evidence that dysfunction and even death of other types of brain cells may contribute to pathology, thus, there may be opportunities to target the health of astrocytes, oligodendrocytes and even microglia in order to halt and/or reverse the brain cell degeneration seen in Alzheimer’s disease.

Given that it may not be sufficient to target A-beta or tau in symptomatic disease, the Alzheimer’s Association believes that we must also develop potential therapeutics addressing neuronal fitness and regeneration. Further, given the uncertainty regarding precise mechanisms of neurodegeneration, the PTC Challenge to RESCUE Brain Cell Degeneration in Alzheimer’s will not only advance potential therapeutics, but will accelerate our understanding of processes involved in neurodegeneration. Identifying therapies that target brain cell health may have the potential to impact multiple aging-related diseases that impact the brain.
Program Description: The PTC Challenge to RESCUE Brain Cell Degeneration in Alzheimer’s will promote human studies to advance innovative ideas for early phase human trials (Phase 1 or Phase 2a proof of concept) that addresses therapies to target neuron cell health in Alzheimer’s disease – this could include, but is not limited to, therapies to address synaptic dysfunction, neurogenesis and neuronal protection. Up to six (6) projects will be awarded with $1 million to launch and carry forward the Phase 1 study in Alzheimer’s disease and the experimental approach that shows the most promise after 2 years (24 months) will be considered for a $4 million prize to continue the clinical path of development for the proposed therapeutic target. The Challenge aims to accelerate our knowledge of neuronal brain health and rapidly advance therapeutics in the clinical setting.

Applications for the PTC Challenge program will be accepted that include lead candidate therapeutic agents targeting neuronal growth factors, cell survival and cell cycle pathways, anti-apoptotic or anti-cell death mechanisms and related mechanisms. These targets should be at a stage that require early stage phase 1 testing prior to Proof of Concept (POC) Phase 2 or 3 efficacy studies, or with lead therapeutic agents that have already established human safety data and require a small-scale pilot Proof of Mechanism (POM) phase 2 study in preparation for larger-scale POC trials. Awards should be able to demonstrate significant advancement of the compound within two years (24 months) of the award. Funding will support Phase 1 or early Phase 2 studies (Phase 2a, including proof of concept, proof of mechanism) of new or repurposed drugs in normal individuals or individuals with preclinical or symptomatic Alzheimer’s disease (i.e. early human studies to set the stage for efficacy studies), including single and multiple dose studies to establish safety, brain penetration and/or target engagement and POM in preparation for larger proof of concept trials. Any proposal must have a clear relevance to Alzheimer’s disease and be translational in nature. While preliminary preclinical animal studies can be a component of the larger proposal and as a part of the study design, proposals must include human clinical trials for eligibility. Proposals should include a plan for how participants are being selected, for instance confirming that there are already Alzheimer’s disease related changes or neuronal or other cell death pathology in the individual; this can include fluid, imaging or other biological measures. All proposals should clearly and explicitly outline the type of study, the rationale for the study, the participant selection process, the methods for study, and outcomes. This can include use of appropriate biomarker measures (fluid, imaging or other) to identify participants and/or to confirm target engagement throughout the study as well, as applicable.

The PTC Challenge will fund best in class projects that effectively demonstrate that their proposal will translate into human trials of an experimental drug or drugs targeting neuronal health, with the future promise of improving cognition/function in individuals with neurodegenerative diseases.
Selection of Finalists: Up to six (6) projects will be selected as a finalist for this program. These projects will receive up to $1,000,000 (total) over 2 years to support their proposed study. Funding must span over two years with maximum per year of $700,000. Projects will be evaluated throughout the 2 years and at the conclusion for satisfactory progress and overall success toward achieving the milestones. After the initial 2 year period, if applicable, one of the projects with the most viable translation to advanced human trials will receive an additional award of up to $4,000,000 to advance the project forward.

Projects will be evaluated with special attention to clinical translational details for moving through the development pipeline, as well as their innovation and out of the box thinking to address these challenging questions.