Care4Rare Year 2 (April 2014- March 2015)

Report for Fondation de l'Ataxie Charlevoix-Saguenay

Care4Rare is pleased to share our progress over the second year of this four year project, which is detailed in the enclosed report.

One of our Care4Rare activities is to identify therapeutic leads for rare diseases and ARSACS is included as one of the disorders studied in this pipeline. In the first year, we utilized bioinformatics approaches and an FDA drug screen using human fibroblasts (skin derived cell line), to identify compounds that may increase the expression of the *SACS* mRNA. Extensive follow-up studies excluded any of these potential "hits" as having an effect and so we are continuing to pursue therapeutic leads for ARSACS through additional avenues of investigation:

- An FDA screen using neuronal cells for diseases, such as ARSACS, that impact the central and peripheral nervous systems. Several drugs (including a shelved phase II Pfizer drug) have resulted in a potential increase in *SACS* expression in neuronal cells and these leads are being further investigated.

- Development of a screen to look at correcting the abnormal appearance of the mitochondria in fibroblasts derived from patients with ARSACS. In this so-called "cell phenotyping" approach, we will determine if modulation of cellular processes (via a 3,000 drug library from Pfizer) may correct the abnormal appearance of these cells. This may provide insight into which cellular pathways to investigate further to identify therapeutic targets.

We look forward to continued success and thank you for your support.

Sincerely,

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