Background of the Disease:
INAD is an ultra-rare inherited neurological disorder. It begins within the first few years of life, and leads to a progressive impairment of movement, cognition, and vision. Its prevalence is extremely rare (<1,000,000), and it is inherited in an autosomal recessive pattern. Disease onset may start at 6 months of age with slowing of motor and cognitive development and regression of previously acquired skills. It is accompanied by rousing eye movements, strabismus and nystagmus. Hypotonia is initially accompanied by preserved / brisk reflexes and is more obvious in the lower than the upper extremities. Death usually occurs between the ages of 5 to 10 years, often from loss of bulbar function leading to aspiration pneumonia.

The genetic basis of INAD are mutations in the PLA2G6 gene (chromosome 22q12-q13) which encodes an 85 kDa group IV calcium independent phospholipase A2, (iPLA2). The enzyme is responsible for the selective hydrolysis of the sn-2 ester bond of glycerophospholipids to release free polyunsaturated fatty acids (PUFAs). This is a critical housekeeping function in all cells membranes but in particular those exposed to high oxidative stress such as mitochondrial membranes in high energy tissues.

Abstract:
The patient, a ~2.5-year-old female, had developed normally until about 15 months of age, and received a confirmed genetic diagnosis of PLA2G6-deficient INAD at around 28 months. At the initial visit, she presented with a loss of many developmental milestones. Her exam demonstrated difficulty with maintaining gaze with nystagmus and strabismus, no verbal output, hypotonia, and minimal motor activity. She also had poor bulbar function (dysphonia and required syringe feeding of liquids). At the trial start, she began dosing of 1.8 g, BID of RT001 1 g.

Results:
Starting within a month of dosing and continuing until the current one year anniversary of dosing, the patient has improved. Table 1 shows a detailed list of development milestones lost by the subject prior to drug treatment, and the observations of the treating physicians vs. the baseline assessment at the start of trial. These results were recorded in videotaped exams at baseline, 1 month, 3, 6, 9, and 12 months. Since stabilization of progression of lost development milestones is a major advance in therapy for INAD, we believe that these clear reversals justify additional trials of the stabilized PUFAs, RT001, in patients with classical INAD.

Conclusions
A severely affected child with semi-vegetative state and severely compromised vital functions at baseline has shown slow, progressive and sustained improvement over one year of treatment with RT001. Prominent improvements have been in bulbar and oculogyratory functions with mild improvements in temporo-frontal and human interactions. Despite improvements, she remains severely disabled, requiring constant supervision and attention despite treatment.