

PH15

PH15 is in early stage development for the treatment of cognitive impairment

In vitro and in vivo pharmacological studies revealed that PH15 binds to GPC-peripheral receptors in the nasal passages in a dose dependent manner. In vitro and in vivo toxicology studies showed that PH15 is well tolerated in laboratory animals at concentrations 100-fold higher than the dose proposed to use in clinical studies. FMRI studies in human volunteers performed at the Institute of Neuroscience of Stanford University, California, revealed that intranasal administration of PH15 activates human brain areas related to the anterior gyrus cingulate (hippocampus, hypothalamus, limbic system, anterior thalamus, frontal and temporal cortex) in a dose dependent manner and this effect is significantly better than the effect of placebo-control.

Pherin Pharmaceuticals conducted a double blind, randomized, placebo-controlled pilot study in sleep deprived healthy volunteers (N=10) to compare the effects of its proprietary pherine PH15 nasal spray, placebo and orally administered caffeine, using quantitative computer simulation tests for assessment of cognitive performance and reaction time. The results show that intranasal administration of 1.6 microgram PH15 nasal spray improved cognition. This was revealed by a faster reaction time to identify synchronous and randomly presented visual stimuli in volunteers treated with PH15 nasal spray. This effect was statistically significantly better than the effect of placebo, and also than that of 400 milligram of caffeine administered orally.

Of particular interest is the significant effect produced by PH15 nasal spray during a cognitive challenge when the volunteers had to identify stimuli administered in random fashion, a situation that requires increased attention. The reaction time after intranasal administration of 1.6 mg PH15 was faster and statistically significantly more regular than the reaction time after administration of placebo or 400 mg oral caffeine. Due to the rapid onset of effect of PH15 nasal spray, the low dose needed to obtain significant improvement and the absence of side or adverse effects reported in the study, we expect that PH15 nasal spray will have considerable market potential for cognitive enhancement.

Indication : Cognitive Improvement - Cognitive deficits are characterized clinically by progressive loss of memory, cognition, reasoning, judgment and emotional stability that can gradually lead to profound mental deterioration. In an example of such disorders, Alzheimer's Disease (AD) is a common cause of progressive mental failure (dementia) in aged humans. Such disorders have been observed in varied races and ethnic groups worldwide and present a major current and future public health problem. These disorders are currently estimated to affect about two to three million individuals in the United States alone. A large number of healthy individuals (seniors, menopausal women, individuals suffering of general tiredness and stress) also complain annually of decreased performance or cognition. Several studies have shown that individuals complaining of insomnia due to several different causes score very low when challenged with cognitive performance situations. In the US.. alone, these conditions address a market estimated to be \$2 billion annually.

Current therapies to treat cognitive deficiency include estrogen, cholinergic agonists and OTC products. These therapies have well known side effects or have been proven to have similar efficacy to placebo.