Autifony Therapeutics announces positive results from Phase I study of AUT00206, a first-in-class Kv3 modulator for treatment of schizophrenia

Demonstrated dose dependent changes in Mismatch Negativity latency in healthy volunteers;

Phase Ib Ketamine challenge study initiated in Manchester

London, UK - 10th January 2017 - Autifony Therapeutics Limited ("Autifony"), which is pioneering the development of novel pharmaceutical treatments for serious disorders of the central nervous system, today announced positive findings from a Phase Ia clinical trial of AUT00206, a first-in-class Kv3 modulator in development for the treatment of schizophrenia, as well as the start of the first of two Phase Ib studies with the molecule.

The results of the Phase 1a study provide encouraging confirmation of human target engagement, and support progression of AUT00206 in schizophrenia. In particular, these biomarker findings provide the first clinical evidence for the hypothesis that modulating Kv3 channels has the potential to treat schizophrenia.

The Phase Ia study in healthy volunteers assessed the effects of AUT00206 on Mismatch Negativity (MMN) latency, which is of considerable interest as a central pharmacodynamic biomarker of sensory processing deficits in schizophrenia. MMN latency increases have been associated with cognitive deficits in patients with schizophrenia and mild cognitive impairment[1,2].

AUT00206 was associated with a significant reduction in MMN latency eight hours after dosing on Day 1. There was also a correlation between individual C_{max} values (maximum concentration of AUT00206 in blood plasma) and MMN latency, which approached statistical significance.

Schizophrenia is a debilitating mental illness for which existing treatments often provide inadequate efficacy and troubling side effects. There have been few new successful treatment approaches in recent years, hence there is strong interest in new mechanisms that might deliver improvements, particularly in the treatment of cognitive and negative symptoms of the disorder. Preclinical data suggest that AUT00206 may indeed have such potential, which would represent a major breakthrough for patients.

The biomarker evaluation was part of a Phase I study designed to assess the safety, tolerability and pharmacokinetics of AUT00206 in relation to dose in over 60 healthy volunteers, as reported on 1 August 2016. Single and multiple ascending oral doses of AUT00206 were evaluated in a double blind, randomised, placebo controlled clinical trial in the UK. AUT00206 was shown to be safe and very well tolerated, with plasma pharmacokinetics confirming drug concentrations at levels required to generate a clinical effect, as predicted by preclinical models. MMN and other measures of brain activity were evaluated in a subset of 32 healthy volunteers. The MMN latency changes were seen at doses and plasma concentrations that were shown to be safe and well tolerated.

Autifony also announced today the initiation of a Phase Ib study to evaluate the effects of AUT00206 on Blood Oxygen Level Dependent (BOLD) signals during a ketamine challenge in healthy male subjects. The study, which is being carried out by Professor Bill Deakin at the University of Manchester, follows a

preclinical ketamine challenge study that demonstrated significant effect of AUT00206. The clinical study will recruit 16 healthy volunteers in a four-way crossover design.

A further Phase Ib study of AUT00206 in schizophrenia patients investigating clinical biomarkers of efficacy will soon be initiated, and conducted in collaboration with Dr Oliver Howes at the Institute of Psychiatry, Psychology and Neuroscience (IoPPN) Kings College London. The programme is supported by the Biomedical Catalyst, jointly funded by Innovate UK and the Medical Research Council, who also contributed important enabling funding towards the preclinical stages of the programme in collaboration with the Universities of Manchester and Newcastle.

Dr Charles Large, Chief Executive Officer of Autifony Therapeutics commented: "These positive findings on Mismatch Negativity latency with AUT00206 provide the first clinical evidence to support its potential for the treatment of patients with schizophrenia."

"Following the successful completion of this AUT00206 Phase Ia study, the Phase Ib ketamine challenge study, initiated by our collaborators in Manchester, will further investigate the effects of AUT00206 in the brain. We are keen to confirm our findings in patients with schizophrenia soon," he added.

References:

1. Toyomaki A, Kusumi I, Matsuyama T, Kako Y, Ito K, *et al.* (2008) Tone duration mismatch negativity deficits predict impairment of executive function in schizophrenia. Prog Neuro-Psychopharmacol Biol Psychiatry 32: 95–99
2. Ji L-L, Zhang Y-Y, Zhang L, He B and Lu GH. (2015). Mismatch negativity latency as a biomarker of amnestic mild cognitive impairment in Chinese rural elders. Frontiers in Aging Neuroscience. doi: 10.3389/fnagi.2015.00022

-ENDS-

About Autifony Therapeutics Ltd

Autifony Therapeutics is an independent UK based biotechnology company formed in 2011 as a spin-out from GSK, which retains equity in the company. The Company is focused on the development of high value, novel medicines to treat serious diseases of the central nervous system. It is funded by SV Life Sciences, Imperial Innovations plc, Pfizer Venture Investments, International Biotechnology Trust PLC, and UCL Business plc. www.autifony.com

About AUT00206

AUT00206 is a novel, orally active small molecule designed to selectively modulate Kv3 potassium channels.

Preclinical studies using models relevant to the pathophysiology of schizophrenia suggest that AUT00206 has the potential to treat cognitive and negative symptoms of schizophrenia, as well as positive symptoms with fewer side effects than current anti-psychotic drugs. Cognitive and negative symptoms are poorly treated by antipsychotic drugs and are associated with significant functional impairment and reduced quality of life for patients.

About Schizophrenia

Schizophrenia remains a major healthcare challenge throughout the world. Patients with the condition have a poor quality of life and prognosis. Antipsychotics are the main treatment but in up to a third of people with schizophrenia, the illness shows a poor response to these drugs. Particularly debilitating are cognitive symptoms of schizophrenia, such as poor decision making, attention and memory, and negative symptoms, such as social withdrawal and anhedonia, which make work and relationships difficult to sustain. Side effects of the currently approved antipsychotic drugs are also problematic, including weight gain, diabetes, heart disease, movement disorders and sexual dysfunction. There is a clear need for more effective drugs with fewer side effects.

See 'The Abandoned Illness', a report by the Schizophrenia Commission, November 2012.

About Innovate UK

Innovate UK is the new name for the Technology Strategy Board – the UK's innovation agency. Taking a new idea to market is a challenge. Innovate UK funds, supports and connects innovative businesses through a unique mix of people and programmes to accelerate sustainable economic growth. For further information visit www.gov.uk/innovateuk

About Biomedical Catalyst

Catalysts are run jointly by Innovate UK and the Research Councils. A Catalyst is a form of research and development funding which focuses on a specific priority area and aims to help take projects from research to as close to commercial viability as possible. The Catalyst model supports projects in priority areas where the UK research base has a leading position and where there is clear commercial potential. Current Catalysts include: Biomedical Catalyst, Agri-tech Catalyst and the Industrial Biotechnology Catalyst.

For more information, please contact:

Autifony Therapeutics Limited

Dr Charles Large, Chief Executive Officer

E: charles.large@autifony.com

Instinctif Partners

Sue Charles, Tim Watson, Alex Bannister

T: +44 (0) 20 7866 7860

E: Autifony@instinctif.com