PRESS RELEASE

TauRx Announces Results from Phase 3 Alzheimer's Disease Study, LUCIDITY, Assuring Path for Regulatory Submissions

- For people with early Alzheimer's (MCI), HMTM treatment resulted in sustained improvement in cognition over pre-treatment baseline, and normalisation of brain atrophy to a rate similar to healthy individuals
- For people with mild to moderate Alzheimer's, HMTM stabilised cognition and function and reduced rate of brain atrophy compared to historical matched individuals with AD
- HMTM is an oral drug with a strong safety profile, having no risk of amyloid related imaging abnormalities
- TauRx will present the Phase 3 findings at the Clinical Trials in Alzheimer's Disease (CTAD) conference on Wednesday, 30th November 2022, in San Francisco

Aberdeen, UK and Singapore, October 6, 2022

TauRx Pharmaceuticals Ltd is a global leader in tau-based research in Alzheimer's disease (AD). Pathological aggregation of Tau correlates with clinical disease severity and brain atrophy. It is a hallmark of the disease now generally recognised as an important potential target for treating AD.

Hydromethylthionine mesylate (HMTM) is a potent inhibitor of Tau aggregation pathology which is taken orally. The Phase 3 LUCIDITY study compared HMTM 16 mg/day with methylthioninium chloride (MTC) given at a dose of 4 mg twice weekly, the minimum required to prevent bias arising from potential urinary discolouration. The study was conducted in 598 patients with AD severity ranging from Mild Cognitive Impairment (MCI) through to the moderate stage of disease.

TauRx has now completed the first 12-month double-blind phase of the trial. The second 12-month open label period is ongoing, during which all participants receive HMTM 16 mg/day. All participants were required to have a positive amyloid-PET scan and not to be taking standard symptomatic treatments for AD.

Of those receiving MTC 4 mg twice weekly, the majority were unexpectedly found to have blood levels of active drug above the threshold needed to produce a clinical effect. In the absence of a true placebo, the trial as designed could not determine outcomes on primary clinical endpoints relative to a therapeutically inactive placebo as prespecified. In light of the evidence now available, TauRx does not believe that a valid blinded placebo-controlled trial of HMTM with clinical endpoints is technically feasible. TauRx has therefore analysed the data in terms of the relationship between blood concentration of drug and treatment effect, change from pre-treatment baseline, and comparisons against historical controls available from closely matched data from the Alzheimer's Neuroimaging Initiative (ADNI).

The overall baseline MMSE score was 21 for the study population spanning MCI through to moderate disease. There was minimal decline over the first 12 months in participants receiving the 16 mg/day dose on both coprimary cognitive and functional endpoints (1.3 ADAS-cog$_{11}$ units and -1.0

ADCS-ADL_{23} units). The expected decline over 12 months in an untreated population would be approximately 5 units on both scales.

In the 105 participants with MCI (baseline MMSE score 23) receiving the 16 mg/day dose, there was statistically significant cognitive improvement of 2 units over the pre-treatment baseline at 6 months (p=0.0002), 12 months (p=0.0391) and 18 months (p=0.0473) on the ADAS-cog_{13} scale. The mean change on the instrumental activities of daily living subscale of ADCS-ADL also remained above the pre-treatment baseline at 6, 12 and 18 months.

In the 147 participants with mild to moderate AD (baseline MMSE 20) receiving 16 mg/day, there was a 2.5 unit cognitive decline in the first 9 months and no further decline over the following 9 months. The functional decline on the ADCS-ADL scale was -2 units at 12 months and -3 units at 18 months representing a reduction in decline of about 75% relative to a published meta-analysis of publicly available placebo decline data from historical trials in mild to moderate AD.

Statistically significant reductions in disease progression as measured by change in cognitive function (p=0.0008) and brain atrophy (p<0.0001) were confirmed by comparisons of participants receiving the 16 mg/day dose against ADNI subjects who were closest to the study population by age and clinical severity. The differences remained statistically significant in both MCI and AD subgroups. As expected, LUCIDITY trial participants with MCI entered the study with more brain atrophy than ADNI healthy aging subjects and consistent with ADNI MCI subjects. Those treated with HMTM 16 mg/day had a rate of progression of brain atrophy that was significantly less than in ADNI MCI subjects (p<0.0001) and comparable to that seen in ADNI healthy aging subjects.

Recent trials that have tested treatments targeting amyloid have been conducted in comparable or milder populations than the MCI group in the LUCIDITY trial. When HMTM is compared to publicly available placebo decline data from these studies as a benchmark, the treatment effects on cognitive and functional decline are about three-fold larger over 18 months. The benefit seen with HMTM is clinically meaningful for people with Alzheimer's.

The safety profile seen in LUCIDITY remains strong and consistent with earlier published HMTM trial data. There were no treatment-related serious adverse events or evidence of amyloid related imaging abnormalities (ARIA).

On the outcome of the current data analysis, Professor Claude Wischik, Executive Chairman and co-founder of TauRx, explains, "This is the first time any treatment has produced evidence of sustained improvement over the individual's own pre-treatment baseline lasting 18 months at an early clinically detectable stage of AD, and stabilization of disease progression at more severe stages. The results in AD confirm published findings from two earlier HMTM Phase 3 trials. The availability of an accessible oral treatment which does not require expensive monitoring over routine clinical care opens up an opportunity to intervene before the onset of the cognitive and functional decline that lead to loss of independence.

"Tau pathology of the disease is now recognized as an important target for treatment, and it is encouraging that cognitive improvement is seen at such an early stage of the disease with a drug targeting Tau. The field has focused mainly on amyloid as a target for early intervention. Our data are consistent with the evidence that Tau pathology begins at least 20 years before clinical symptoms appear and is a viable first-line target for treatment."

To assist with next stages, TauRx has appointed strategic regulatory advisors in the UK, US and Canada, alongside naming Dr Richard Stefanacci, an established global key opinion leader in Alzheimer's, as Chief Medical Officer. Dr Stefanacci is a US-based Internist and fellowship trained Geriatrician who is an active physician caring for people with Alzheimer's daily.

Dr Stefanacci commented: "These data support our ability to pursue regulatory submissions. We look forward to making a significant difference addressing this global unmet need with a medication that is affordable, easy to administer, and safe. I'm very pleased to be joining the team and supporting the work we're undertaking to achieve our mission of bringing treatments to people affected by neurodegenerative diseases caused through protein aggregation – Alzheimer's is just the beginning."

On the appointment of Dr Stefanacci, Professor Claude Wischik said, "This is an exciting time for TauRx, and we are very pleased to welcome Dr Stefanacci as our Chief Medical Officer. His joining the dedicated team at TauRx is testament to our science and prospects for the future success of the company in helping to transform the lives of people with Alzheimer's and other neurodegenerative conditions, as well as the caregivers supporting them."

ENDS

ABOUT LUCIDITY
LUCIDITY is the only late-stage clinical trial specifically targeting the tau pathology of Alzheimer's. Aggregation of abnormal tau protein is one of the hallmark pathologies.

Additional data analysis is ongoing in relation to the 1-year open label phase of the trial, secondary endpoints including MRI volumetric brain scans, and exploratory endpoints. A summary of the LUCIDITY study protocol has recently been published in The Journal of Prevention of Alzheimer's Disease http://dx.doi.org/10.14283/jpad.2022.63).

https://www.luciditytrial.com

ABOUT TAURx PHARMACEUTICALS LTD
The TauRx group of companies was established in 2002 in Singapore, continuing a partnership with the University of Aberdeen, with primary research facilities and operation based in Aberdeen, UK. The company has dedicated the past two decades to developing treatments and diagnostics for Alzheimer's and other neurodegenerative diseases due to protein aggregation pathology.

Alzheimer's dementia is a leading cause of death throughout the world and one of the most important public health issues to be addressed globally. TauRx will contribute to addressing this unmet need with data from LUCIDITY and pursuit of Medicines and Healthcare products Regulatory Agency (MHRA) approval through the Innovative Licensing and Access Pathway (ILAP), having been granted an Innovation Passport, the first stage of the process, in May this year.

TauRx plans to submit HMTM for regulatory approval in the US and Canada in 2023, with other territories to follow, in line with its overall plans to commercialise HMTM and pursue clinical trials in other related neurodegenerative diseases.

https://www.taurx.com

TAU PATHOLOGY IN ALZHEIMER'S

Through dedicated research programs, it is understood that certain age-related factors lead to misfolding and aggregation of tau proteins, and the subsequent formation of tau tangles in Alzheimer's. These tangles disrupt and damage neuronal function, a process that begins many years before symptoms of dementia are seen. Tau pathology has been proven to correlate with the clinical decline (loss of memory and ability to care for oneself) commonly seen in people with Alzheimer's, establishing it as an important target for treatment. HMTM is a tau aggregation inhibitor, which effectively crosses the blood brain barrier to target the source of this damaging process.

Media Contacts **Leona Minellas, Communication Director** Aspect: The Strategic Communication Experts Leona.minellas@aspectreputation.com +44 (0) 7311 823947	**https://news.cision.com/taurx**