



Chronos Therapeutics Announces Positive Pre-Clinical Proof of Concept Studies for its Orexin-1 Antagonist Project Initially Targeting Binge Eating Disorder

Oxford, UK 2 May 2018: Chronos Therapeutics Ltd (Chronos) the private biotech company focused on ageing diseases, brain and nervous system disorders, announced today that the lead compound in its addiction programme, CT-010018 an orexin-1 antagonist, demonstrated positive pre-clinical proof of concept (POC) results in an *in vivo* model of binge eating disorder (BED). BED is a psychiatric condition, is classified in the American Psychiatric Association handbook, DSM-5 and is more common than anorexia and bulimia combined. Vyvanse (lisdexamfetamine dimesylate) is currently the only medication approved to treat moderate to severe binge eating disorder in adults.

Orexin-1 antagonism is viewed as one of the most attractive targets in BED. Targeting this brain system has the promise to provide effective treatment of BED with no abuse liability, anhedonia, anorexia or somnolence.

Dr Fraser Murray, CSO said: *“We are encouraged by these results demonstrating the efficacy of CT-010018 in a pre-clinical model of BED, an area where a large unmet medical need remains. This result provides a solid foundation from which to advance CT-010018 towards clinical development.”*

Dr Huw Jones, CEO commented: *“These positive pre-clinical results demonstrate our ability to deliver potentially market-leading profiles with speed and capital efficiency. We have three programmes targeting BED, MS Fatigue and the fatal motor neurone disease ALS. Each programme is delivering exciting data as we progress towards the clinic.”*

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Notes to Editors

About Chronos Therapeutics

Chronos Therapeutics Ltd is a privately held Oxford, UK-based biotechnology company focused on diseases of ageing, brain and nervous system disorders. Chronos has a dedicated laboratory in Oxford which screens for activity of drugs in brain disease through its proprietary platform, Chronoscreen™.

The company has an extensive library of re-purposed molecules showing promise for brain and neurological diseases. The lead compound, RDC5, is being developed for the fatal neurodegenerative disease, Amyotrophic Lateral Sclerosis (ALS). A phase 1 study is complete for RDC5 and the company anticipates completing Investigational New Drug (IND) activities in 2019 in anticipation of starting a Phase 2a clinical study in ALS patients.

Chronos recently acquired three new chemical entity (NCE) development programmes for CNS diseases. The most advanced programme is initially targeting fatigue associated with multiple sclerosis. The company's orexin-1 antagonist programme is following closely behind and expected to enter the clinic at a similar time. Other, earlier programmes address serious behavioural and neurodegenerative conditions.

Chronos' major shareholders include Vulpes Life Sciences, Odey Asset Management, the University of Oxford, an affiliate of Shire PLC, the Board and Management. For additional information, please visit: www.chronostherapeutics.com

About Addictive Behaviours

There are a number of addictive behaviours that represent significant unmet medical needs and require novel treatments. Chronos is targeting binge eating, alcohol and nicotine addictions.

Binge eating is an eating disorder where a person feels compelled to overeat on a regular basis through regular "binges" or consumption of very large quantities of food over a very short period of time, even when they are not hungry. The condition tends to first develop in young adults, although many people do not seek help until they are in their 30s or 40s. There is a 1 in 30 to 1 in 50 chance of a person developing binge eating disorder at some point during their life and it can lead to a variety of health problems that can, in extreme circumstances, be life-threatening. Whilst more women suffer from the condition than men, binge eating is not particularly uncommon in men with the prevalence ratio of approximately 1.5 women for every man with the disorder.

Nicotine and alcohol addiction: Addiction involves repeated use of a psychoactive substance (such as nicotine or alcohol) causing a user to be intoxicated with a compulsion to take the preferred substance and often a determination to obtain the substance by almost any means. Addicts also have difficulty in modifying or stopping substance use. They build up tolerance to the addictive substance, sometimes requiring more and more for the same effect and develop



withdrawal syndromes when use is interrupted.

Addiction to nicotine via tobacco kills one person prematurely every six seconds and 50% of long term smokers according to World Health Organisation (WHO) reports, with tobacco attributed deaths predicted to rise to 8 million globally a year by 2030. The US Centers for Disease Control and Prevention (CDC) also notes that about 480,000 Americans die every year from smoking-related causes involving cancers (chiefly lung cancer), stroke, heart disease and chronic obstructive pulmonary disease (COPD).

Excessive alcohol use (as caused by addiction or binging) has caused 10% of deaths among working-age adults aged 20-64 years in the USA with economic costs in 2010 in the USA alone of \$249 billion. The WHO also estimates that harmful alcohol use causes 3.3 million deaths a year, globally. Short-term health risks, most often the result of binge-drinking, include accidents, injuries, alcohol poisoning and risky sexual behaviours. Over a longer time excessive alcohol use can lead to chronic diseases including high blood pressure, cancers, mental health and social problems.

About Multiple Sclerosis and Fatigue

An estimated 2.3 million people globally have multiple sclerosis (MS) according to the Multiple Sclerosis International Federation. Fatigue is the most common symptom of the disease. It occurs in 75% to 95% of patients with MS and as many as 40% of patients have described it as the single most disabling symptom of the disease.

There are two major types of fatigue in MS. These two types of fatigue are probably separate problems related to the MS. The first type is a general feeling of tiredness. It may feel as if one has not slept the night before. This feeling may be worse in the afternoons or after activity. People may feel that they are unable to do as many tasks without getting tired as they did before. A second type of fatigue is muscular. In this type, there is increased weakness after repeated activity. Often, this occurs with walking. People may find that they are dragging one leg or are more unsteady.

About Amyotrophic Lateral Sclerosis (ALS)

The motor neurone disease Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig's Disease) is a fatal neurodegenerative disease characterised by progressive death of the primary motor neurones in the central nervous system. Symptoms include muscle weakness and muscle wasting, difficulty in swallowing and undertaking everyday tasks. As the disease progresses, the muscles responsible for breathing can fail, gradually causing dyspnoea or difficulty in breathing.

ALS has an average prevalence of 2 per 100,000. Prevalence is higher in the UK and USA than in many other countries, up to 5 per 100,000. There are estimated to be over 50,000 patients in the USA and 5,000 patients in the UK with the condition. Mortality rates for ALS



sufferers are high with 10-year survival after diagnosis below 10% and average survival of 39 months from diagnosis. There is only one drug currently approved for treatment in the EU and as of 2017, two drugs approved for the condition in the USA.