Neuren (NEU) – ASX Announcement **7 October 2024**

Neuren continues PMS Phase 3 preparations following positive FDA meeting

Highlights:

- **Constructive End of Phase 2 meeting with FDA, discussing proposals for the first ever pivotal clinical trial program for Phelan-McDermid syndrome**
- **Alignment reached on key aspects of NNZ-2591 Phase 3 trial program:**
    - **Single randomised, double-blind, placebo-controlled trial of treatment for 13 weeks in children aged 3 to 12 years with Phelan-McDermid syndrome**
    - **Participants may continue into an open-label extension study continuing treatment until commercial launch**
    - **One active treatment group versus placebo, with target dose equivalent to dose tested in Phase 2 trial**
    - **Less burdensome safety monitoring plan than Phase 2, subject to FDA review of the final protocol**
- **Neuren to submit further information to FDA to confirm endpoints for the primary efficacy assessment**
- **Preparations for Phase 3 advancing, including selection of service providers, identification of potential trial sites and manufacturing of NNZ-2591 supplies**

Investor Webinar 11am AEDT | Monday, 7 October 2024

You are invited to register using this link:

https://us06web.zoom.us/webinar/register/WN_Z5H9bF5DTbSs_f2IiUVaCw

Participants may submit questions at registration or during the session

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today announced positive outcomes from an End of Phase 2 Meeting with the US Food and Drug Administration (FDA) to discuss proposals for the first ever pivotal clinical trial program in Phelan-McDermid syndrome (PMS). There are no medications approved for PMS, which has severe quality of life impacts on those living with it, as well as on parents and siblings. At the FDA meeting alignment was reached on key aspects of the NNZ-2591 Phase 3 program, with Neuren to submit further information to confirm endpoints for the primary efficacy assessment.

Neuren CEO Jon Pilcher commented: "We are pleased with the outcomes of a very collaborative meeting with the FDA and are eager to move forward in our mission to develop NNZ-2591 as a first approved treatment for Phelan-McDermid syndrome, which has an overwhelming unmet need."

The single pivotal Phase 3 trial will be a randomised, double-blind, placebo-controlled trial of treatment for 13 weeks in children aged 3 to 12 years with PMS. Participants may continue into an open-label extension study continuing treatment until commercial launch. There will be one active treatment group versus placebo, with a target dose equivalent to the dose tested in the Phase 2 trial. Based on the safety data from the Phase 2 clinical trial, Neuren proposed a less burdensome safety monitoring plan for the Phase 3 and open label extension trials, which was considered reasonable by the FDA, subject to review of the final protocol.

This study is the first ever pivotal clinical trial in PMS, which means there is no precedent for efficacy assessment. Primary efficacy endpoints for the Phase 3 trial were considered in depth at the meeting, with a range of potential options discussed. The FDA has requested that Neuren submit further existing information before agreeing the final selection of the endpoints.

Next steps

Neuren is currently compiling the further information on efficacy endpoints and updating the Phase 3 trial protocol. Each of these will be submitted to the FDA for review. In the meantime, Neuren is well advanced in the selection of service providers for the Phase 3 program and has commenced identification of potential trial sites. The campaign to manufacture the required supplies of NNZ-2591 is continuing on schedule. Further information on estimated timelines and costs will be provided after the efficacy endpoints are confirmed.

About Phelan-McDermid syndrome

Phelan-McDermid syndrome is caused by a deletion or other change in the 22q13 region of chromosome 22, which includes the *SHANK3* gene, or a mutation of the gene. PMS is also known as 22q13 deletion syndrome. The *SHANK3* gene codes for the shank3 protein, which supports the structure of synapses between nerve cells in the brain. It is estimated that between 1 in 8,000 and 1 in 15,000 people have PMS. There are no medications, drugs, or therapies specifically for PMS, which has an overwhelming unmet medical need. PMS has severe quality of life impacts on those living with it, as well as on parents and siblings. The most common characteristics are moderate to severe developmental and intellectual impairment and developmental delay, delayed or absent speech, symptoms of autism, low muscle tone, motor delays, mild to severe epilepsy, behavioural problems and difficulties with socialization, activities of daily living and self-care.

Further information about PMS is available at: www.pmsf.org and www.cureshank.org

About Neuren

Neuren is developing new drug therapies to treat multiple serious neurological disorders that emerge in early childhood and have no or limited approved treatment options. Recognising the urgent unmet need, all programs have been granted "orphan drug" designation in the United States. Orphan drug designation provides incentives to encourage development of therapies for rare and serious diseases.

DAYBUE™ (trofinetide) is approved by the US Food and Drug Administration (FDA) for the treatment of Rett syndrome in adult and pediatric patients two years of age and older. Neuren has granted an exclusive worldwide licence to Acadia Pharmaceuticals Inc. for the development and commercialisation of trofinetide.

Neuren's second drug candidate, NNZ-2591, is in Phase 2 development for multiple neurodevelopmental disorders, with positive results achieved in Phase 2 clinical trials in Phelan-McDermid syndrome, Pitt Hopkins syndrome and Angelman syndrome.

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ASX Listing Rules information

This announcement was authorized to be given to the ASX by the board of directors of Neuren Pharmaceuticals Limited, Suite 201, 697 Burke Road, Camberwell, VIC 3124

Forward-looking Statements

This announcement contains forward-looking statements that are subject to risks and uncertainties. Such statements involve known and unknown risks and important factors that may cause the actual results, performance or achievements of Neuren to be materially different from the statements in this announcement.