



Neuren (NEU) - ASX Announcement

31 May 2016

2016 Annual Shareholders' Meeting Chairman's Address

Good morning Ladies and Gentlemen. It is my pleasure to present Neuren's achievements for the year ended 31 December 2015, and to provide an update on the overall position of the company and our progress with the trofinetide development programs.

I am required to remind you that today's address contains some forward-looking statements that are subject to risks, which may cause the actual results to differ from our anticipated outcomes.

Update on product development programs for trofinetide

Neuren has continued to make important progress with the development of trofinetide over the last 12 months and I would like to provide some more detailed comments in relation to our key clinical programs.

Rett syndrome

Firstly, I will update you on our Rett syndrome program, which is the most advanced of the indications that we are targeting with trofinetide. The top-line results from our Phase 2 clinical trial in adults and adolescents with Rett syndrome, which were announced in November 2014, provided evidence of clinical benefit following treatment with trofinetide, and confirmed that the drug was well tolerated, with no safety concerns identified.

Subsequently, in 2015 we were granted orphan drug designation for Rett syndrome in both the US and Europe, and in November we were issued a new US patent for the treatment of Rett syndrome. Both of these provide significant and valuable commercial protections for trofinetide in this treatment indication.

Over the last 12 months we have continued to seek guidance from our clinical experts as well as the FDA – Division of Neurology Products. Given the preliminary evidence of efficacy and the strong safety and tolerability profile of trofinetide, we received encouragement to move quickly into testing trofinetide in a younger patient group, using higher doses and treating for longer.

In January 2016 we commenced the Rett syndrome paediatric trial in the US. This is a double-blind, placebo-controlled study design using a maximum dose of up to 200mg/kg twice daily, enrolling girls aged 5-15 years and a longer treatment period. We now have 8 sites activated in the US and we expect a total of 12 clinical sites ultimately to participate.



With 14 subjects already enrolled and a further 14 scheduled for their first visit, the clinical sites have made a good start and we are anticipating completion of the trial in the fourth quarter of 2016, with top-line results becoming available in the first quarter of 2017.

In relation to progress on the key regulatory matters, we have had a series of interactions with the FDA and I am pleased to report that we have now reached agreement on the construct of the primary outcome measure considered acceptable for use in a pivotal registration study. The measure, which is derived from the Motor Behavior Assessment used by clinicians in the Rett syndrome natural history study, has been carefully designed to capture potential improvement in the core signs and symptoms of Rett syndrome.

Subject to the results from our paediatric trial, we are planning to commence a single pivotal phase 3 study in Rett syndrome during 2017.

Fragile X syndrome

In December 2015, we announced top line results from our Phase 2 trial in adults and adolescents with Fragile X syndrome. These results established proof of concept, with the preliminary evidence of efficacy and good safety profile providing a rationale to move forward with developing trofinetide for Fragile X syndrome.

We and our clinical experts have now met with the FDA - Division of Psychiatric Products in order to discuss our proposed plans for the development of trofinetide in Fragile X. This is the first time that Neuren has interacted with this Division and therefore it was an important opportunity to advance our thinking in relation to patient selection, dose levels and the type of clinical outcome measures that may be appropriate for use in future registration trials.

We are encouraged by our discussions with the FDA, during which it was recognised that the broad mechanisms of action of trofinetide make it appropriate to use a novel approach to the assessment of Fragile X patients. We will now work with the FDA to refine and validate some of the behavioural measures that form part of our Fragile X Syndrome Rating Scale. The Division also requested that we provide data from the non-clinical toxicity studies that we are conducting before commencing clinical trials in paediatric patients. Some of the studies are already underway, and all will be completed in 2017. We will also be able to provide the Division with safety and tolerability data from our paediatric trial in Rett syndrome. Once the Division is satisfied that we have provided sufficient information, we expect to be in a position to commence a paediatric study in Fragile X.

Traumatic Brain Injury

Top-line results from our Phase 2 clinical trial of trofinetide in moderate to severe traumatic brain injury (the "INTREPID" trial) were announced last month. The results once again confirmed the good safety profile of trofinetide, although results from the pre-specified core efficacy measures led us to conclude that higher doses, along with a more tightly defined patient selection, will be required in order to



demonstrate efficacy in those measures if further studies are to be conducted. The RBANS score, which was included as an exploratory efficacy measure that assesses cognitive function, did provide us with evidence of a drug effect and we are conducting a deeper analysis of the data to fully understand the implications of this. RBANS is a battery of objective cognitive tests completed by the patient, which is commonly used to assess dementia, as well as being validated for use in TBI.

The US Army has requested that Neuren proposes the optimum design of a possible follow on clinical study. Funding for such a study will be subject to further discussions with the Army.

Our concussion trial presently being conducted with the US Army at Fort Bragg will form part of the overall TBI review, which we expect to be completed in the third quarter of 2016. In the meantime, all expenditure related to the concussion program has been placed on hold.

In parallel with our clinical studies, we continue to make good progress with the toxicology, chemistry, manufacturing and controls sections of the trofinetide development program. This work is necessary to ensure that all key elements in support of a pivotal trial and ultimately a successful New Drug Application remain on track.

Neuren's financial position

Neuren's consolidated loss after tax for the year ended 31 December 2015 was A\$13.4 million and our cash reserves at 31 March 2016 were A\$11.0 million.

There are presently 1.8 billion shares on issue and 76 million share options and equity performance rights remain outstanding, 64 million of which are held by Lang Walker interests and Neuren's leadership team.

While the current funding, including further contributions from rettsyndrome.org, R&D tax rebates and the exercise of share options, is sufficient to complete our Rett syndrome paediatric trial in 2016, additional funding will be required for trials planned for 2017 onwards.

Our primary objective remains to progress the development of trofinetide as quickly as we can, while at the same time seeking to maximise the commercial value to Neuren and our shareholders.

Guided by these objectives the Neuren Board is closely evaluating a range of potential sources of funding, including partnering arrangements and strategic investments from third parties. There is of course a need to balance the near-term funding requirements of the business with the longer-term potential value of trofinetide. And to this very point, the Board is carefully considering the risks and benefits associated with the timing of securing additional funding relative to the Rett syndrome paediatric study completion. We will keep shareholders fully updated as appropriate.



Concluding remarks

In concluding this update, I wish to thank the Neuren team for their commitment and dedication to these very important programs, my fellow Board members for their constant availability and involvement; and as always, our gratitude to the patients, parents and clinicians that make our clinical trials possible, as well as to you our shareholders for your ongoing support.

Thank you.

Richard Treagus, Executive Chairman

About Neuren

Neuren Pharmaceuticals Limited (Neuren) is a biopharmaceutical company developing new therapies for brain injury, neurodevelopmental and neurodegenerative disorders. The novel drugs target chronic conditions as well as acute neurological injuries. Neuren presently has a clinical stage molecule, trofinetide in Phase 2 clinical trials as well as NNZ-2591 in preclinical development.

Forward-looking Statements

This ASX-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.

For more information, please contact:

Dr Richard Treagus, Executive Chairman: rtreagus@neurenpharma.com ; +61 417 520 509