



Neuren (NEU) - ASX Announcement

28 April 2015

CHAIRMAN'S ADDRESS AT ANNUAL SHAREHOLDERS' MEETING

Good morning Ladies and Gentlemen. Welcome to our Annual Shareholders' Meeting in Melbourne. It is my pleasure to present Neuren's achievements for the financial year ended 31 December 2014 and to provide an update on the overall position of the company and progress of the trofinetide development program.

I am required to remind you that this report contains some forward-looking statements that are subject to risks, which may cause the outcomes to be different from our anticipated outcomes.

In my report to you this morning I wish to touch on three key areas. These are:

1. Neuren's strategy and progress
2. Update on the product development activities for trofinetide
3. Neuren's financial position

Neuren's Strategy and Progress

Neuren's strategy is to demonstrate the broad therapeutic applicability of our patented drug candidates in brain injury, neurodevelopmental and neurodegenerative disorders, and to progress selected applications towards commercialisation in large world markets.

We are fully committed to progressing the development of trofinetide as quickly as we can, while at all times maximising the commercial value to Neuren and our shareholders.

Our strategy is further defined by focusing the company's efforts on the following core elements:

Firstly, our ability to demonstrate human clinical benefit from treatment with trofinetide in selected patient groups for which there are few or no effective drug therapy options.

Secondly, our ability to access favourable regulatory pathways with the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

Thirdly, our ability to differentiate and protect the value of our intellectual property through patents as well as exclusivity periods associated with "Orphan Drug" designations and Paediatric Exclusivity programs in the major markets.

And finally, optimising the trofinetide manufacturing processes, the physical attributes and the unit costs of the drug substance for the commercial supply of drug product.



Against this background I am pleased to report that Neuren has made substantial and important progress over the last 12 months.

The World Health Organisation has proposed “trofinetide” as the International Non-proprietary Name for our lead molecule, which was previously designated by Neuren as NNZ-2566.

A pivotal development came in November 2014 when we announced the successful results of our first Phase 2 clinical trial of trofinetide in Rett syndrome. I will provide more detailed comments on this study, but in summary, the results exceeded our expectations and placed Neuren in a strong position to advance the development of trofinetide in this indication. Subsequent to these results we successfully obtained Orphan Drug designation for Rett syndrome from the FDA and earlier this month we completed our Orphan Drug submissions to the EMA for both the Fragile X syndrome and Rett syndrome indications. The Orphan Drug designations are extremely valuable commercially given the seven (US) and ten (EU) years of market exclusivity that they confer.

While the FDA did not grant our request for Breakthrough Therapy in March 2015, this did not alter our view of the clinical benefit observed or the significance of the study results, and we continue to work closely with the FDA under the Fast Track designation that has already been granted. We are at an advanced stage of preparation for a meeting with the FDA during which we will discuss the remaining regulatory requirements to obtain marketing authorisation for trofinetide in Rett syndrome.

Parallel to the work being undertaken on our clinical programs, we continue to allocate resources and make good progress in respect of the toxicology, chemistry, manufacturing and controls sections of the trofinetide development program. This recognises the importance of advancing all these elements in support of a pivotal development program and ultimately a successful New Drug Application. We are working closely with our advisors to ensure that we optimise the overall trofinetide data package, the commercial manufacturing process and the finished product attributes.

Update on Product Development Programs for trofinetide

I would like to provide some more detailed comments in relation to our four clinical programs.

Rett syndrome

The top-line results from our Phase 2 clinical trial in Rett syndrome, announced in November last year, demonstrated clinical benefit from treatment with trofinetide. The study also confirmed that the drug is well tolerated, with no safety concerns identified.

Having previously released the key findings of the study, I would like to provide further emphasis on a few important points.

Firstly, the study provided robust evidence of clinical improvement in 3 of the core efficacy outcome measures, with no clinically significant worsening in the remaining 3 core measures. Our pre-specified



criteria for success required improvement in 2 or more of the outcome measures. Of the successful outcome measures, two were clinician-assessed and one was caregiver-assessed. These measures were specifically designed to capture improvement of the core signs and symptoms of Rett syndrome.

Secondly, although there was some evidence of drug effect in the 35mg/kg low dose, this effect was more pronounced, and showed clear separation from placebo at the 70mg/kg higher dose level, which satisfied our pre-specified criteria.

Thirdly, notwithstanding that the study comprised only 28 days of treatment, we found that the magnitude of the treatment effect increased with time, i.e. across the duration of the study, and that the observed effects subsequently waned upon discontinuation of the study drug.

Finally, I would like to make some remarks in relation to the analysis of the study. A small, exploratory study such as this does not readily lend itself to conventional statistical methods more applicable to larger or pivotal trials. In recognising this fact, we chose to focus instead on quantifying a pattern of benefit across multiple outcome measures. The data were subjected to both group-level analysis and subject-level analysis, then “stressed” by utilising a permutation test method. This latter test is an accepted method for ascertaining the probability of observing the combined degree of clinical benefit in both the group level and the subject level analysis by chance alone, a phenomenon often referred to as a “false-positive” result. This probability was determined for our efficacy data set to be 2.3% ($p=0.023$).

Expert opinion on the analysis of the study and the results obtained has given us strong encouragement to explore the effect of trofinetide in a younger patient population and potentially to use a higher dose and longer duration of treatment.

We anticipate that in our upcoming meeting with the FDA we will have the opportunity to test our assumptions on study design, patient selection and dosing, as well as gain detailed input on the other remaining elements of the Rett syndrome development program.

Fragile X syndrome

Neuren’s phase 2 double-blind, placebo controlled clinical trial of trofinetide in Fragile X syndrome commenced in the US in January 2014. The trial is designed to assess the safety, tolerability and efficacy of trofinetide in approximately 60 male subjects with Fragile X syndrome.

In December we indicated that the initial enrolment rate into the study was slower than expected and that we would open additional trial sites in two stages, starting with 3 sites in January. The enrolment rate has already improved and we expect this to accelerate, with 5 further sites joining the study. Together with a broad awareness campaign in conjunction with the Fragile X Association of America (FRAXA) and the National Fragile X Foundation (NFXF), these remedial actions have kept us on track to complete subject enrolment and to present our analysis of the top line results in Q4 2015. Despite these



enrolment challenges, which reflect the very significant commitment required from participants and their families, we are in all other respects satisfied with the way in which the trial has been conducted.

I should remind you that the FDA has already granted Orphan Drug and Fast Track designation to trofinetide for the treatment of Fragile X syndrome.

INTREPID (Moderate to severe traumatic brain injury)

Neuren's ongoing Phase 2 trial using intravenous trofinetide in moderate to severe traumatic brain injury is designed to enrol 260 subjects, assessing safety, efficacy and brain injury biomarkers.

Following our action to increase the number of US trauma centres participating in the trial and the completion of two large competing trials, we have seen a steady increase in the subject recruitment rate and as such we expect the study to complete enrolment in coming months with top line results expected to be made available in Q4 2015.

Concussion (mild traumatic brain injury)

The phase 2 trial in mild traumatic brain injury, i.e. concussion, makes use of the oral dosage form of trofinetide and aims to enrol 132 subjects. The study has been designed to assess safety, efficacy and brain injury biomarkers.

The trial commenced in September 2014 at Fort Bragg, North Carolina with the US Army's 82nd Airborne Division. The logistics involved in the enrolment of service personnel at a military base have proven to be challenging and as we announced in December, Neuren is expanding the trial to include two civilian hospital sites in the US. These new sites are at an advanced stage of preparation and we will make a further assessment of the overall study timelines when we gain experience on the rate of enrolment at these hospitals.

Neuren's financial Position

In order to better reflect our business environment and financial risks, our reporting currency was changed from New Zealand dollars to Australian dollars effective 1 January 2014.

Neuren's consolidated loss after tax for the year ended 31 December 2014 was A\$8.3 million and our cash reserves at 31 March 2015 were A\$20.1 million.

There are presently 1.66 billion shares on issue and 95 million share options and equity performance rights remain outstanding, 83 million of which are held by Neuren's leadership team and Lang Walker interests.



Concluding remarks

In conclusion, we anticipate that the balance of 2015 will see further important milestones, notably our meeting with the FDA to discuss the remaining development requirements for Rett syndrome, decisions from the EMA on our Orphan Drug applications and the completion and top-line results of the Fragile X and INTREPID traumatic brain injury studies.

We continue to register a high level of interest in Neuren's drug development programs from a range of global and speciality pharmaceutical companies. This is naturally very encouraging and potentially provides Neuren with a range of strategic alternatives, which the Board will carefully consider at the appropriate time. In the meantime we will continue to build a strong level of agreement with the FDA on the balance of the Rett syndrome program, and work diligently on the completion of our three remaining phase 2 clinical trials.

I wish to thank the Neuren team for their concerted efforts, my fellow Board members for their support and guidance, the patients, parents and clinicians that make our clinical trials possible, and our shareholders for the support and faith that they have placed in Neuren.

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 pre-clinical 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.

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