



Neuren (NEU) - ASX Announcement

28 May 2019

Chairman's Address at 2019 Annual Meeting of Shareholders

Before I begin, I am required to advise you that this Address contains some forward-looking statements that are subject to risks, which may cause the actual outcomes to differ from the outcomes anticipated in this Address.

Overview

As a small company, Neuren Pharmaceuticals is undertaking ground-breaking work developing novel drug therapies for a range of serious neurodevelopmental conditions. This work is both challenging and exciting, but most importantly we never lose sight of its real purpose, which is ultimately to make life better for the many patients and families who are impacted by these medical conditions. We are frequently reminded of the importance of our work and the need to make real progress towards an approved drug therapy as quickly as we possibly can. That said, we must at the same time continue to apply the highest level of diligence and care when executing on these development programs. Novel drug development is seldom a straightforward, quick or inexpensive undertaking. But regardless, whether it's for our patient families, for the company, or for you the shareholders, we all share the same ultimate goal.

Within this context, I am pleased to report that Neuren is in its strongest position yet. Our lead drug trofinetide is set to commence Phase 3 later this year, and this program is fully funded by our US partner ACADIA, which brings tremendous capabilities and commitment to the trofinetide programs. This commercial partnership has the potential to deliver revenue to Neuren of many hundreds of millions of dollars if the drug is successful in the US and equally importantly we have retained the rights to trofinetide outside North America, with full access to the clinical and regulatory data generated by ACADIA.

The ACADIA partnership has already provided to Neuren a very large step-up in terms of access to resources and capabilities across the clinical, regulatory and manufacturing functions which are essential for the preparation and execution of Phase 3. The two companies are working very effectively together across a wide range of activities. The final design of the trial, approved by the FDA, was informed by the results of Neuren's Phase 2 pediatric trial, which were published at the end of March in the highly regarded peer-reviewed medical journal *Neurology*[®]. The publication was also the basis for an editorial in the journal titled "Turning the tide on targeted treatments for neurodevelopmental disorders".

Another important benefit flowing from the ACADIA partnership is that it has allowed Neuren to allocate funding and resources to the development of our second drug compound NNZ-2591. This novel neurotrophic drug holds great promise and is fast becoming a very exciting and important part of our overall company strategy.



Rett Syndrome Program

I would like to provide more specific comments on the current status of the Rett syndrome program. In the last 12 months Neuren successfully completed the non-clinical toxicology studies required to support the longer duration of dosing in the Phase 3 trial, as well as ultimately supporting the New Drug Application filing with the FDA.

Manufacturing of trofinetide has been a key element of the preparation leading into the Phase 3 trial. A brief reminder that the Phase 3 trial itself has to be conducted using the commercial (“to-be-marketed”) product, which has required significant changes to the Phase 2 product supply arrangements and a large investment for manufacturing of both the drug substance as well as the finished drug product liquid formulation and packaging.

The scale-up activities, production scheduling and patient supply logistics are all progressing well and are now at an advanced stage. Some technical work relating to stability and quality testing remains ongoing, however I am pleased to report that we are on target to commence the Phase 3 trial in Q4 2019. It means that the timeline ACADIA published when the partnership was announced back in August – commencing the trial in H2 2019 and a New Drug Application in 2021 – has remained unchanged.

There are two parts to the Phase 3 program – treatment with trofinetide or placebo for 12 weeks to produce efficacy results, followed by treatment with trofinetide for 40 weeks to provide longer term safety data. The time taken to enrol approximately 180 patients will determine when the efficacy results are available, since the trial will end when the last patient enrolled completes her 12 weeks of treatment. We anticipate that patient enrolment will again benefit from strong support from the Rett community.

Regarding the Fragile X program, you may recall that the FDA Division of Psychiatry required further non-clinical safety data before we could proceed with clinical trials in pediatric patients, or with a treatment duration longer than 4 weeks. Further trials were also dependent upon obtaining drug supply from the scaled up supply chain. ACADIA and Neuren are now working to design the most efficient development plan for Fragile X.

NNZ-2591 neurodevelopmental disorders pipeline

Turning now to our second drug, NNZ-2591. This is a patented compound sourced from the original library of synthetic peptides developed by Professor Margaret Brimble and her medicinal chemistry team at Auckland University. It is a smaller molecule than trofinetide, being a cyclic dipeptide and it has demonstrated broad applicability across a number of neurodevelopmental conditions, all of which feature a degree of impairment in the functional connectivity between brain cells.

In February we announced positive results in an animal model of Phelan-McDermid syndrome and earlier this month we were excited to announce a further set of very clear and compelling results in separate animal models of Pitt Hopkins syndrome and Angelman syndrome. These genetic neurodevelopmental conditions display strong over-lap of signs and symptoms and they may also be co-



diagnosed with autism. We anticipate that all of these conditions meet the criteria for Orphan Drug designation and based on these recent animal results we are already working to submit the necessary Orphan Drug applications.

The Neuren team has accumulated a lot of experience from the trofinetide program and this is being readily applied to the benefit of the NNZ-2591 program. We are already well underway with a number of activities which includes the manufacturing of NNZ-2591 drug substance to be used in non-clinical safety studies. These data are required to support a submission for an Investigational New Drug application with the FDA and then to initiate human clinical trials. Neuren is planning a Phase 1 safety and PK study in Australia before commencing Phase 2 trials in patients in the second half of 2020.

Torreya process

In February, we appointed Torreya, a global investment bank specialising in life sciences, as Neuren's corporate advisor. Our objective is to evaluate all potential corporate transactions, be it for individual products, defined territories, or Neuren's entire business. A formal process commenced in April and we are well advanced in terms of engaging with third parties in the US, Europe and Japan. Our expectation at this stage is that the process will complete in Q3 2019.

Financial position

Neuren's cash reserves as at 30 April 2019 were approximately A\$20 million. We continue to maintain a very low overhead expenditure which gives us the capacity to invest in both the remaining phase 3 preparatory activities as well as the IND-enabling work for NNZ-2591 to which I have already referred.

Given that all payments from ACADIA are received in USD, the recent strength in the USD has a positive impact on the value of those payments for Neuren. It also provides a natural hedge for our NNZ-2591 development expenditure, most of which is in USD.

The Lanstead funding arrangement that was put in place in mid-2017 served the company very well for the first 12 months, providing the necessary funding for critical activities that were key in getting Neuren into its current strong position. Nevertheless, I must acknowledge that more recently the arrangement has been a source of contention and at times frustration with shareholders who have expressed concerns. I am able to confirm that the Lanstead funding arrangement will naturally conclude at the end of June and to the extent that it may have been an impediment to either the share price or our ability to attract new investors, then this should be removed.

Outlook and value

I commented in my letter to shareholders in the recently published annual report that notwithstanding our very much stronger position, we are reminded that being a small company on the ASX with relatively low liquidity and long development timelines, the price at which shares are traded may not always appropriately reflect the intrinsic risk-adjusted value of the underlying assets.



As shareholders ourselves and owning approximately 10% of Neuren, the board and management are extremely disappointed with the price the market has placed on Neuren since the deal with ACADIA in August 2018 was announced. Neuren owns valuable assets in both trofinetide and NNZ-2591 and this in large part is why the Board initiated the corporate process with Torrey.

We remain firmly of the view that the market is underestimating the value of ACADIA as a partner in North America and as such the likelihood of Phase 3 success, as well as ascribing little if any value to trofinetide in markets outside the US, or for that matter the potential value of NNZ-2591. We are fully committed to achieving the key development milestones for both trofinetide and NNZ-2591, while we actively engage with interested parties to evaluate the best mechanism through which we can achieve a better value recognition for our shareholders.

Concluding remarks

During the year we changed the composition of the Board quite significantly with the addition of three new directors. We now have a majority of independent non-executive directors together representing broad industry experience which is highly applicable to Neuren. It is a great pleasure working with my fellow Board members and I thank them for their constant guidance and encouragement.

Finally, my gratitude to the Neuren team. They are a small, highly capable and dedicated team that consistently delivers exceptional work.

Thank you.

Richard Treagus, Executive Chairman

About Neuren and NNZ-2591

Neuren Pharmaceuticals Limited (Neuren) is a biopharmaceutical company developing new therapies for neurodevelopmental disorders with high unmet need. Neuren completed Phase 2 development of its lead drug candidate trofinetide for Rett syndrome and has completed a Phase 2 clinical trial in Fragile X syndrome. The programs in Rett syndrome and Fragile X syndrome have each been granted Fast Track designation by the US Food and Drug Administration and Orphan Drug designation in both the United States and the European Union. Neuren has granted an exclusive license to ACADIA Pharmaceuticals Inc. for the development and commercialization of trofinetide in North America, whilst retaining all rights to trofinetide outside North America.

Neuren is advancing the development of its second drug candidate NNZ-2591, a synthetic analog of the neurotrophic peptide, cyclic glycine proline (cGP), which occurs naturally in the brain. NNZ-2591 has demonstrated efficacy in pre-clinical models of Phelan-McDermid syndrome, Angelman syndrome, Pitt Hopkins syndrome, Fragile X syndrome, memory impairment, Parkinson's disease, stroke, traumatic brain injury, peripheral neuropathy and multiple sclerosis.



Contact:

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

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.