



Neuren (NEU) - ASX Announcement

29 June 2017

2017 Annual Shareholders' Meeting Chairman's Address

This morning we have announced an important financing that provides Neuren with the funding to approach both our anticipated meeting with the FDA Division of Neurology and partnering discussions in a strong position, whilst at the same time being able to commit to continuing the key activities on the critical path for commencing a Phase 3 trial.

Despite the Rett syndrome Phase 2 trial results in March 2017 exceeding expectations, Neuren's share price has subsequently been under pressure. This is likely for two reasons - firstly some uncertainty around our funding position and secondly the need for feedback from the FDA with respect to our forward-looking plans. We have now removed the funding uncertainty and we expect to receive that feedback from the FDA within the next 3 months.

The structure and timing of the financing is particularly suited to the current needs and future prospects of the Company. We are not activating the previously approved facility to issue shares to Walker Corporation, which we put in place as a contingency until 30 June 2017. This means that the shareholdings of Lang Walker interests will remain below 20%.

Following the announcement of the Rett syndrome study results in March, Neuren has continued to receive a wide level of interest in the trofinetide programs from pharmaceutical companies around the world. We have nevertheless formed a view that partnering options are better considered once Neuren has met with the FDA. As always, the Board is guided by two important principles, these being, speed to market for the families affected by these conditions and maximising the commercial value to Neuren and our many shareholders who ultimately make this important work possible.

I will now provide a brief update on the business status and outlook, beginning with the Rett syndrome program.

Rett syndrome program

In March of this year we announced the results from the Phase 2 clinical study in girls aged 5 to 15 with Rett syndrome, in which the highest dose of trofinetide (200mg/kg twice daily) demonstrated statistically significant and clinically meaningful improvements across three syndrome-specific efficacy measures. As I stated in our Annual Report, the results were deeply encouraging and greatly increased the confidence of Neuren and the leading Rett syndrome clinical experts with whom we are working to develop this therapy. This data, along with that generated from our first Rett syndrome study, provided a strong basis to move forward with the remaining steps of development.



We have requested a meeting with the FDA Division of Neurology and we anticipate the meeting will be conducted in Q3 2017. We will present our plans for the remaining development towards a New Drug Application and will seek agreement from the FDA regarding the design of a single Phase 3 study, including the dosing regimen and endpoint selection. We are fortunate to have the input of key clinical, regulatory and statistical experts going into our planning. We expect that the outcome of the FDA meeting will allow us to confirm the costs and timelines of the program and in turn, this will inform our approach to partnering and funding alternatives in Q4 2017.

In advance of the FDA meeting, there are key manufacturing and non-clinical activities that are on the critical path in order to commence a Phase 3 trial. In the absence of the funding announced this morning, we would not be able to commit to initiating these activities, which would lead directly to a delay for the Phase 3 trial. The cash flow associated with these key activities will occur across H2 2017 and H1 2018, but in many cases the work cannot start without committing to the full financial impact. The key activities that we can now commit to initiating are:

- Conclude the optimization of the drug substance manufacturing process for commercial supply
- Conclude the stability testing and analytical validation of the new to-be-marketed liquid drug formulation
- Conduct a 6 months' dosing toxicity study in rodents, which is required for a Phase 3 trial and subsequently to support a New Drug Application to the FDA

Other development programs

Fragile X - Neuren previously conducted a Phase 2 clinical trial in 70 males aged 12 to 45 years with confirmed Fragile X syndrome. After a relatively short treatment period of 28 days, improvements were seen across core symptoms of Fragile X syndrome including higher sensory tolerance, reduced anxiety, better self-regulation and more social engagement.

We are currently designing the next clinical trial, which will likely enrol younger children and examine higher doses with longer treatment duration. The study will also seek to refine the outcome measures that may be used in a Phase 3 trial. Completion of the 6 months' dosing toxicity study in rodents for the Rett syndrome program should mean that the treatment duration options for the next Fragile X trial are not limited to 6 weeks as was the case for the Rett syndrome pediatric trial.

Traumatic Brain Injury - Neuren and the US Army are discussing the feasibility of a second trial in either severe, or moderate to severe TBI, using RBANS as a primary efficacy measure, a more tightly defined patient population, combined with substantially higher doses and a longer duration of treatment. At the present time, the commencement of such a study remains subject to US Army funding.



FXTAS - In the Annual Report, we described a new indication for trofinetide, being Fragile X-associated Tremor Ataxia syndrome (FXTAS). There is currently no approved drug therapy for this neurodegenerative disorder, which typically affects males over 50 years of age. We believe that a drug development program for FXTAS is likely to meet the criteria for orphan drug designation. The first stage of the development program is to generate efficacy data in animal models of the disease, which can potentially be used to support applications to the FDA and the European Medicines Agency for orphan drug designation. We will provide more details of our plans during H2 2017.

Commercial exclusivity

In May 2017, we announced the approved grant of two new patents in the United States and Europe. The new patent in the US covers the use of trofinetide in Fragile X syndrome and the new patent in Europe covers the use of trofinetide in autism spectrum disorders, including both Rett syndrome and Fragile X syndrome. When issued, each new patent will expire in 2032.

Neuren already owns issued patents in the US concerning the use of trofinetide to treat Rett syndrome and in Australia for the use of trofinetide to treat autism spectrum disorders. Each of these patents expires in 2032.

Supplementing the issued composition of matter patents and the orphan drug designations already granted in both the US and Europe, these new patents provide lengthy and valuable commercial protections.

Financial position and capital structure

Neuren's cash reserves at 31 March 2017 were A\$1.6 million. In our quarterly cash flow report for March 2017, we estimated cash of A\$1.0 million at 30 June 2017 and indicated that expenditure had reduced significantly following the completion of the Rett syndrome clinical trial. The funding announced today from Lanstead Capital, Rettsyndrome.org and Neuren's directors and management will provide additional cash of A\$3 million in July 2017 and a further A\$8.5 million in 18 monthly instalments, subject to the value sharing agreement with Lanstead.

After issue of all the placement shares, there will be approximately 2 billion ordinary shares on issue. We intend to consolidate the shares into a smaller number in order to remove an impediment to investment for some US institutions. We will provide details and a timetable for the consolidation in due course. Under New Zealand law, shareholder approval is not required.

Concluding remarks

In conclusion, I am pleased to report that Neuren is now in a well-funded position, with an even stronger suite of patents, two orphan drug indications and class-leading phase 2 clinical data in Rett syndrome.



We are looking forward to meeting with the FDA in the next quarter and having the opportunity to discuss and agree the remainder of the Rett syndrome development program.

Finally, I wish to thank the Neuren team for their ongoing commitment and enthusiasm at all times, as well as my fellow Board members and our clinical experts who are always available and willing to assist no matter what. A special mention to the team at Rettsyndrome.org (RSO), who provide tremendous support and more specifically have seen fit to invest in the future of trofinetide as part of this latest funding.

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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