2018 Year-end Business Update

Year-end review

We are pleased to report that at the end of 2018, Neuren stands in an immeasurably stronger position than some 14 months ago prior to our End of Phase 2 Meeting with the US Food and Drug Administration (FDA). Over this same period, Neuren has made meaningful progress towards the goal of ultimately making trofinetide available to patients around the world. The fact that our current market valuation does not properly reflect the intrinsic value of trofinetide is a source of disappointment, however as we continue to communicate the strength and value of the ACADIA partnership, advance our rest of world plans and accelerate the development of our second patented drug compound NNZ-2591, we expect that the market will better understand Neuren’s strong fundamentals and future prospects.

During the last 14 months Neuren has:

- Reached agreement with the FDA (Division of Neurology), endorsing our Phase 3 plan for Rett syndrome;
- Licensed trofinetide in North America to ACADIA Pharmaceuticals, a highly capable, committed and well-funded partner. ACADIA is providing substantial funding and execution capabilities for Phase 3 and commercialisation that were otherwise not available to Neuren;
- Retained strong participation in the future commercial value of trofinetide in North America through double digit percentage royalties plus milestone payments of up to US$455 million under the ACADIA agreement;
- Retained 100% of the rights to trofinetide outside North America, and ensured free and full access to utilise the US regulatory package for registration in other territories; and
- Received non-dilutive funding that enables us to advance the development of Neuren’s highly promising drug candidate NNZ-2591.

Since the ACADIA agreement was executed in August 2018, the strength of ACADIA as a partner has become even more apparent. In September, the FDA issued a clear statement reaffirming the positive benefit-risk profile of ACADIA’S product NUPLAZID®, which removed any level of prevailing uncertainty. In October ACADIA announced positive results from a Phase 2 trial of Pimavanserin for adjunctive treatment in patients with major depressive disorder, demonstrating quite clearly ACADIA’s capabilities in neurology drug development. And finally, in November ACADIA raised new capital of approximately US$316 million, which provides certainty around funding capabilities as trofinetide moves towards commencement of Phase 3.

The Neuren and ACADIA teams are working collaboratively on all the preparations for the Rett syndrome Phase 3 trial, which include manufacturing the drug supplies, finalising the trial protocols,
preparing clinical sites and completing standard non-clinical studies. All of these activities remain on track for commencement of the trial in the second half of 2019.

As we previously announced, until 31 January 2019 we are in a period of exclusive negotiations with ACADIA regarding the rights to develop and commercialize trofinetide in territories outside North America. ACADIA received this right of first negotiation under the terms of the agreement for North America.

Neuren will end the year with a very strong funding position. Our current cash reserves are approximately A$22 million and the pause of monthly settlements from Lanstead Capital for 120 days has concluded, with the next settlement due in December and 6 further settlements due in the first half of 2019.

Since announcing the ACADIA partnership we have taken the opportunity to raise Neuren’s profile, including meeting with US analysts and fund managers, commissioning analyst coverage and obtaining Australian media coverage. In 2019 we intend to build on this further, as we continue to communicate the very strong position that Neuren is now in and highlight the value opportunity for investors both in Australia and overseas.

**Advancing NNZ-2591**

An important consideration as part of the partnering discussions was for Neuren to retain the rights to our patented drug compound NNZ-2591. Following the ACADIA deal for trofinetide, Neuren now has the funding as well as the organizational resources to advance the development of this second novel compound. NNZ-2591 will therefore be a prominent focus for our company as we head into 2019.

We plan to develop NNZ-2591 as a therapy for neurodevelopmental disorders, including autism spectrum disorders, for which we have lengthy patent coverage and/or which may qualify for Orphan Drug designation. We will provide more information on the target indications in the near future.

We have established that NNZ-2591 has very high oral bioavailability and the pre-clinical work conducted to date has confirmed that this compound has broad activity within the central nervous system. We also believe that the manufacturing process for NNZ-2591 potentially may hold significant technical and commercial advantages.

Before we can file an Investigational New Drug application (IND) with the FDA and commence clinical trials, we are required to complete the standard characterisation and nonclinical safety studies. We intend to generate safety data to support clinical dosing for 12 weeks and clinical trials in children, which may remove the need to conduct short duration clinical studies in adults first, as was the case with trofinetide.
Analysts and valuations

On 5 December 2018 Pitt Street Research published a detailed initiation of coverage report on Neuren, including a valuation. We commissioned this research given that Neuren was lacking formal analyst coverage and that research from sell-side analysts is hard to come by when the company has no plans to raise capital.

Neuren is now covered by two analysts – Bell Potter and Pitt Street Research. In both cases, they value Neuren by risk adjusting estimated future cash flows (i.e. adjusting for a probability that the cash flows will occur) and then discounting those risk adjusted cash flows for the time value of money at the assumed cost of capital. The Pitt Street Research base case valuation of A$4.28 per share is significantly higher than the Bell Potter valuation of A$2.28 per share in the last report that was published in August 2018 after the ACADIA deal, mainly due to three factors:

- Bell Potter included nil value for trofinetide outside North America, whereas Pitt Street Research in its base case included A$53 million.
- Bell Potter included nil value for Neuren’s share in the sales proceeds of a potential Pediatric Rare Disease Priority Review Voucher, whereas Pitt Street Research in its base case included A$19 million.
- Bell Potter maintained the probability of achieving a marketing authorisation for Rett syndrome in the US at 40%, whereas Pitt Street Research assigned a probability of 71%.

The following table provides a comparison of key elements of the two valuations:

<table>
<thead>
<tr>
<th></th>
<th>Pitt Street Research</th>
<th>Bell Potter</th>
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<tbody>
<tr>
<td>Total value</td>
<td>A$428m</td>
<td>A$234m</td>
</tr>
<tr>
<td>Total value per share</td>
<td>A$4.17</td>
<td>A$2.28</td>
</tr>
<tr>
<td>Value of Rett and Fragile X in North America</td>
<td>A$351m</td>
<td>A$236m</td>
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<tr>
<td>Value of potential Priority Review Voucher</td>
<td>A$19m</td>
<td>nil</td>
</tr>
<tr>
<td>Value of Rett and Fragile X outside North America</td>
<td>A$53m</td>
<td>nil</td>
</tr>
<tr>
<td>Value of NNZ-2591</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Probability of US marketing authorisation for Rett</td>
<td>71%</td>
<td>40%</td>
</tr>
<tr>
<td>Probability of US marketing authorisation for Fragile X</td>
<td>38%</td>
<td>25%</td>
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<tr>
<td>Peak annual US sales for Rett</td>
<td>US$1.2B</td>
<td>US$0.9B</td>
</tr>
<tr>
<td>Peak annual US sales for Fragile X</td>
<td>US$1.4B</td>
<td>US$1.5B</td>
</tr>
<tr>
<td>Cost of capital</td>
<td>15.3%</td>
<td>16.2%</td>
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</table>

Disclaimer: Neuren does not endorse, confirm, or express a view as to the accuracy of the valuations.
About Neuren

Neuren Pharmaceuticals Limited (Neuren) is a biopharmaceutical company developing new therapies for neurodevelopmental and neurodegenerative disorders and brain injury. Neuren has completed Phase 2 development of 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. In addition, Neuren is advancing the pre-clinical development of its second drug candidate NNZ-2591.

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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.