Neurotech to Pursue a Targeted Global Partnering Strategy and Registration-Directed Initiatives in Australia

Highlights:

- **Neurotech to secure one or more strategic partnerships for NTI164 in the United States, Europe and certain Asian territories to support clinical, regulatory development, manufacturing and future market launches**
- **Pursue multiple registrations of NTI164 in Australia, including leveraging the provisional registration pathway via the TGA, based on strong clinical evidence and safety to date**
- **The Australian market represents a significant annual opportunity for NTI164**
- **Complete FDA IND-enabling studies relating to toxicity (commenced) and human pharmacokinetic trials (set to commence)**
- **Secure an FDA IND approval for NTI164 clinical trials in at least one neurological disorder (Rett Syndrome, ASD, PANDAS/PANS)**
- **Execution of strategy expected to deliver significant value and reduce financial/clinical/regulatory risks for Neurotech shareholders**

Neurotech International Limited (ASX: NTI) ('**Neurotech**', '**NTI**' or '**the Company**') a clinical-stage biopharmaceutical development company focused predominately on paediatric neurological disorders, is pleased to announce the Company will focus its operating and financial resources towards several initiatives relating to global partnering for NTI164 (the Company's broad spectrum cannabinoid drug therapy) and a focussed approach to securing registration of NTI164 in Australia initially via the provisional registration pathway unique to Australia's Therapeutic Drug Administration (TGA).

Dr Thomas Duthy, Executive Director of Neurotech International said *"The strategy announced today reflects our core focus to date on generating conclusive clinical evidence pertaining to the efficacy and safety of NTI164 for paediatric neurological patients with persistent or progressive neuroinflammation where standard therapies are urgently needed or lacking altogether. We believe Neurotech is now in a strong position to leverage our robust clinical data, accompanying intellectual property, manufacturing expertise and ongoing regulatory initiatives to deliver significant value to our shareholders moving forward through a combination of global corporate development through partnering, while in parallel leveraging our domestic expertise here in Australia with timely regulatory submissions initially for our orphan disease franchise."*

Dr Duthy continued *"We believe now is the right time to pursue an active strategy for our unique paediatric neurological franchise which consists of two rare (orphan) diseases with limited or no treatment options and autism with many patients where approved therapies are restrictive (non-enabling), have negative side-effects and are therefore not generally considered as effective front line treatments. We note that during 2023, at least 49 deals were announced involving rare neurological diseases, with disclosed values totalling US$13.2 billion.*[1] *As a Board, we are fully committed to this strategy and are positioning the business to achieve these stated goals as quickly as possible and within our balance sheet capability with $11.6 million in cash as at 30 June 2024."*

[1] https://www.nature.com/articles/d43747-023-00128-7

Strategic Partnering

Neurotech is committed to securing one or more strategic partnerships for NTI164 in the United States (US), Europe and certain Asian territories (e.g. Japan). Such partner(s) will have the necessary financial resources and experience in late-stage drug development, clinical trials, and commercialisation. Prospective partners will be responsible for all costs of development and commercialisation of NTI164 outside of Australia.

These partnerships may take the form of licensing transactions, equity-based investment(s) or M&A. As discussed, Neurotech is operating in an exciting area of development for pharma companies seeking exposure to rare neurological diseases. A partnership will minimise the financial, clinical and regulatory risks for Neurotech shareholders in these markets.

This strategy, if successful, will allow Neurotech to focus its financial resources and expertise towards registration of NTI164 in Australia, where the Company intends to maintain 100% commercial ownership of NTI164 in the Australian market. The Company believes there is a large opportunity for NTI164 for all three neurological disorders where Neurotech has generated solid clinical evidence to date.

Build-out of Intellectual Property (IP)

Since Mid-2022, Neurotech has invested into developing a defendable 'Asset Moat' around NTI164. This has involved generating clinical evidence of safety and effectiveness and securing PCT patent applications that seek both composition of matter, combinations and methods of treatment claims. These patent applications if granted with provide protection until at least 2041.

Neurotech is now able to manufacture drug product in a controlled semi outdoor environment (polytunnel) irrespective of seasonal conditions which provides year-round continuity of supply across multiple sites to support clinical and future commercial activities. Neurotech has developed significant know how and expertise to ensure stable plant genetics which in turn has meant the development of a well-defined Standard Operating Protocol (SOP) that is fully transferable to new manufacturing partners and ensures Neurotech operates according to the highest standards of drug manufacture and supply.

Neurotech is in the process of establishing a fully integrated, GMP-compliant process for NTI164 and in addition, has established proprietary processes for extraction, fractionation, isolation and analytical chromatographic methods for product composition, control and release of NTI164.

The Company recently lodged its first Orphan Drug Designation (ODD) request for PANDAS/PANS with the US Food and Drug Administration (FDA). Further ODDs filings are planned for the US and Europe for Rett Syndrome and PANDAS/PANS in Europe. If granted an ODD provides 7 and 10 years market exclusivity in the US and Europe, respectively.

Complete Pre-Clinical Toxicology and Human Pharmacokinetic (PK) Studies

US FDA Investigational New Drug Application (IND)-enabling studies include *in vitro* and *in vivo* assessments that help define the pharmacological and toxicological properties of NTI164 in significant detail. Although Neurotech has developed solid human clinical data in patients across three neurological disorders, these standard assessments are a requirement to support all future regulatory initiatives including clinical trials in the US/Europe and future product registrations, including for provisional registration in Australia. The Company aims to complete the necessary pre-clinical toxicology and human pharmacokinetic (PK) trials in line with FDA, TGA and European Medicines Agency (EMA) standards for NTI164 before the end of Q1 CY2025. The Company has commenced and will complete the toxicology work from existing cash reserves following on from the capital raise completed in April 2024 and planning for the PK study is well advanced (also funded from existing cash).

FDA IND Approval / EMA CTA Approval for a Paediatric Clinical Trial

Subject to the completion of the necessary IND-enabling studies, Neurotech aims to file for, and secure an FDA IND as well as European Medicines Agency (EMA) approval in 1H CY2025 for at least one paediatric clinical trial. For Europe, the Company intends to file a Clinical Trial Application (CTA) utilising the centralised Clinical Trials Information System (CTIS) that enables sponsors to apply for clinical trial authorisation in up to 30 European countries with a single online application (process takes a minimum of 60 days).

For PANDAS/PANS and Rett Syndrome, the Company believes a well-designed, Phase III clinical trial may be sufficient to potentially qualify NTI164 for registration in the US and Europe. The proposed clinical trial protocol will be integral to a pre-IND meeting to be sought with the FDA. As previously indicated, Neurotech aims to have partnered the NTI164 program prior to the actual commencement of a Phase III clinical trial in the US/Europe.

Provisional Registration Pathway – Australia

Following a pre-submission meeting with the TGA, Neurotech has further explored with its advisors a means to accelerate the commercialisation of NTI164 in Australia. Subject to the satisfactory completion of the necessary pre-clinical toxicology and PK studies, Neurotech intends to commit to the provisional registration pathway for NTI164 initially for either PANDAS/PANS or Rett Syndrome (i.e. the orphan disease franchise) based on the long clinical evidence accumulated to date. In the Company's view, both are serious disorders necessitating and supporting an accelerated approach to commercialisation (i.e. via a provisional pathway).

As previously disclosed, a provisional approval pathway allows sponsors to apply for time-limited provisional registration on the Australian Register of Therapeutic Goods (ARTG). It provides access to certain promising new medicines where the TGA has made an assessment that early availability of the treatment outweighs the risk inherent in the fact that additional data is still required. If granted, a provisional registration can save up to two years of development and a provisionally registered prescription medicine may be able to receive reimbursement via the Pharmaceutical Benefits Scheme (PBS) through a Category 1 filing and based on a positive recommendation from the Pharmaceutical Benefits Advisory Committee (PBAC).

Neurotech expects to formalise a pre-submission meeting with TGA in Q2 CY2025 to discuss the planned provisional determination application and subsequent submission for provisional registration. The provisional determination process is expected to complete in 2H CY2025 with Neurotech (on success) intending to file for provisional registration also in the 2H CY2025. The TGA registration process takes approximately 220 working days from submission.

The Australian Market Total Addressable Market Opportunity is Significant

Neurotech has undertaken some further analysis of the market opportunity in Australia, based on the three neurological disorders where there is clinical evidence of benefit and very acceptable safety.

Since the introduction of the National Disability Insurance Scheme (NDIS) there has been significant data available to assess the number of autism patients (with Neurotech estimating 90-95% classified as Level II (requiring substantial support) and Level III (requiring very substantial support) receiving payment under the NDIS.[2] This equates to 169,000 Level II/III autism recipients aged (0-18) under the NDIS receiving on average $35,300 in annual payments for their disorder, with patient growth of 12% and payment growth of 7% annually.

[2] https://dataresearch.ndis.gov.au/reports-and-analyses/participant-dashboards/autism

Although the NDIS does not fund or subsidise medicines (i.e. the PBS), the annual payment reflects the necessary cost of support services to be more independent and engage socially and economically. Neurotech believes NTI164 has shown in ASD patients via its multiple clinical trials to improve children's lives in a similar manner. In the 12 months to March 2024, the Company believes the NDIS has paid $5.9 billion to Level II/Level III ASD children.

Neurotech believes there are approximately 1,000 paediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS) / paediatric acute neuropsychiatric disorders (PANS), collectively (PANDAS/PANS) children in Australia who may benefit from NTI164 treatment based on published incidence data and approximate duration of the disorder in children. There are no approved PANDAS/PANS treatments available in Australia. For moderate to severe PANDAS/PANS in Australia, Intravenous Immunoglobulin (IVIG) is used sporadically off-label, although evidence is somewhat lacking for benefit and durability.[3] A monthly IVIG infusion in these patients can equate to approximately $100,000 per annum.

Neurotech estimates there are approximately 380 Rett Syndrome patients in Australia with no approved therapies. Accordingly, the estimated annual addressable market in dollar terms is not available through lack of precedent drug availability to assess the potential threshold to pay. In the US, there is a single approved drug called DAYBUE™ (trofinetide) that can cost up to US$1,000 per day per patient and is reimbursed. Indirectly, Trikafta® a new medication for children with cystic fibrosis (a serious rare disease) is approved by the TGA and listed on the PBS and would ordinarily cost ~$250,000 per annum ($31.60 per prescription on the PBS). There are approximately 1,600 children with cystic fibrosis in Australia, which is classified as an orphan disease like Rett Syndrome.

Neurological Disorder	Est. Number of Patients	Potential Threshold to Pay Per Annum	Est. Annual Total Addressable Market
Autism (Level II/III)	169,000[1]	$35,300[2]	$5.9 billion
PANDAS/PANS	1,000[3]	$100,000[4]	$100 million
Rett Syndrome	380[5]	N/A | US$0.36m (in US only)[6]	N/A[6]

* See end of ASX release for footnote information N/A – not available

In conclusion, Neurotech will direct its efforts to obtaining multiple registrations for NTI164 in Australia, with an initial focus on provisional registration applications for its orphan disease, given the severity of illness and lack of approved treatments.

To defray the financial and clinical risk internationally, Neurotech intends to enter into a strategic partnership with one or more pharma/biotech companies with a focus on paediatric neurological disorders / orphan diseases.

Authority
This announcement has been authorised for release by the Board of Neurotech International Limited.

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[3] https://www.criteria.blood.gov.au/MedicalCondition/View/2683

About Neurotech

Neurotech International Limited (ASX:NTI)) is a clinical-stage biopharmaceutical development company focused predominately on paediatric neurological disorders with a broad-spectrum oral cannabinoid drug therapy called NTI164. Neurotech has completed a Phase II/III randomised, double-blind, placebo-controlled clinical trial in Autism Spectrum Disorder (ASD) with clinically meaningful and statistically significant benefits reported across a number of clinically-validated measures and excellent safety. In addition, Neurotech has completed and reported statistically significant and clinically meaningful Phase I/II trials in ASD and Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Paediatric Acute-Onset Neuropsychiatric Syndrome (PANS), collectively PANDAS/PANS along with Rett Syndrome. Neurotech has received human ethics committee clearance for a Phase I/II clinical trial in spastic cerebral palsy.

For more information about Neurotech please visit http://www.neurotechinternational.com.

About NTI164

NTI164 is a proprietary drug formulation derived from a unique cannabis strain with low THC (M<0.3%) and a novel combination of cannabinoids including CBDA, CBC, CBDP, CBDB and CBN. NTI164 has been exclusively licenced for neurological applications globally. Pre-clinical studies have demonstrated a potent anti-proliferative, anti-oxidative, anti-inflammatory and neuro-protective effects in human neuronal and microglial cells. NTI164 is being developed as a therapeutic drug product for a range of neurological disorders in children where neuroinflammation is involved.

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1. National Disability Insurance Scheme (NDIS) ASD Participants as at 31 March 2024 (232,646 total patients, of which 177,596 are aged 0-18 years), assumes 95% are Level II/III (automatic recipients). Average payment at 31 March 2024 was $35,300
2. Based on the average annual government payment for ASD National Disability Insurance Scheme Participants for support services as at 31 March 2024
3. Based on *Wald ER et al (2023) Estimate of the incidence of PANDAS and PANS in 3 primary care populations. Front Pediatr. 2023.* Incidence of 3-12 year olds of 1/11,765 and calculated from 5.7m children <18 yrs in Australia and average duration of disease lasting 3 years in 35% of cases *(Murphy et al, (2010) Clinical factors associated with Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections (PANDAS). Journal of Pediatrics, 160(4),*
4. Based on IVIG used off-label for PANDAS/PANS moderate to severely ill children. 2g/kg per month at $60 per gram See: https://www.blood.gov.au/blood-products/national-product-price-list
5. Based on midpoint of prevalence data of 1/10,000-1/15,000 females between 5-18 years using 2022 population data that 18.4% of 26m Australians are 5-19 years. https://brainfoundation.org.au/disorders/rett-syndrome/
6. N/A – not available. DAYBUE™ (trofinetide) estimated costs of up to US$1,000 per day and approved in the US only and no comparison exists in Australia that is currently reimbursed or used off-label for Rett.