PRANA BIOTECHNOLOGY LTD
Form 6-K
January 07, 2019

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER PURSUANT TO RULE 13a-16 OR

15d-16 UNDER THE SECURITIES EXCHANGE ACT OF 1934

For the month of January 2019

Prana Biotechnology Limited

(Name of Registrant)

Level 3, 460 Bourke Street, Melbourne, VIC 3000, Australia

(Address of Principal Executive Office)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F x Form 40-F ¨

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): __

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): __

Indicate by check mark whether by furnishing the information contained in this Form, the registrant is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes ¨ No x

If "Yes" is marked, indicate below the file number assigned to the registrant in connection with Rule 12g3-2(b): 82- _____

This Form 6-K is being incorporated by reference into the Registrant's Registration Statements on Form F-3 (File No. 333-199783) and Form S-8 (File No. 333-153669).

PRANA BIOTECHNOLOGY LIMITED

6-K Items

1. Investor presentation - Biotech Showcase

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

PRANA
BIOTECHNOLOGY
LIMITED
(Registrant)

By: /s/ Geoffrey Kempler
Geoffrey Kempler,
Executive Chairman

January 7, 2019

1 January 2019 Treatment of Neurological Disorders David Stamler, MD Chief Medical Officer and SVP, Clinical Development

Targeting Proteins in Neurodegeneration 2 PBT2 (1 st generation) • Mechanism of action: Zn and Cu ionophore • Originally developed for neurological indications by targeting extracellular protein • Evaluating non - neurological indications for further development PBT434 (2 nd generation) • Targets intracellular proteins with established function: - synuclein, tau • Mechanism of action: Effluxes labile Fe • Reduces - synuclein accumulation in transgenic animal models of PD and MSA MSA

Current Focus 3 Novel Drug Candidate PBT434 • Targets key proteins implicated in neurodegeneration of Parkinson’s disease and atypical parkinsonism • Distinct scaffold and biological profile compared to PBT2 Strong Research and Development • U.S. development team with proven track record • Innovative discovery program • Long standing collaborations with Harvard and Florey Institute of Neuroscience and Mental Health Multiple Indication Opportunity • PBT434 active in models of Parkinson’s disease and atypical parkinsonism including orphan diseases such as Multiple System Atrophy (MSA) Trading information: ASX: PBT Nasdaq: PRAN Share price: US$1.72 Valuation: US$19M Cash: ~A$23M Approximate cash on completion of initial securities purchase agreement with Life BIosciences

US - based development team with strong drug development experience and FDA approvals Margaret Bradbury, Ph.D. VP, Nonclinical Development Previously Non - Clinical leadership at Auspex/ Teva. At Teva, l ed non - clinical development of several neuroscience programs . At Auspex Pharmaceuticals, led strategic planning and program management in Huntin g ton Disease chorea from IND through NDA filing. 4 James Kerr VP, Chemistry, Manufacturing and controls Previously CMC leadership at Auspe x / Teva . Senior member of leadership team responsible for budget managme nt and operational direction of CMC team. Prior to Auspex, was Senior Director, CovX Operations at Pfizer WRD. David Stamler, M.D. Chief Medical Officer & Senior VP, Clinical Development Former VP, Clinical Development and Therapeutic Head, Movement Disorders, Teva Pharmaceuticals and Chief Medical Officer, Auspex Pharmaceuticals. Part of Teva's US$3.5 billion acquisition of Auspex . Led development of AUSTEDO (deutetrabenazine) for treatment of Huntington disease (approved by FDA - April 2017) and tardive dyskinesia, also in 2017. Cynthia Wong, M.P.H. Senior Director, Clinical Operations Previously Clinical Operations leadership at Auspex/Teva . At Auspex, led clinical trial activities for the registration study of AUSTEDO in Huntin g ton Disease chorea . Prior to Auspex, led Phase 1 - 3 studies, including registration studies for marketing approval for Quillichew ER, Esbriet and Infergen . CONFIDENTIAL

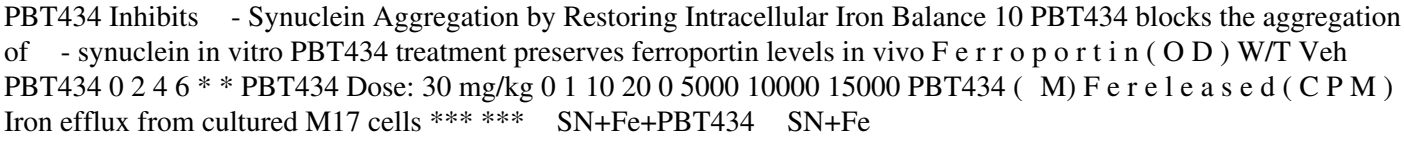
Investment Thesis • Alpha ( ) - synuclein is an intracellular protein critical for neurotransmission • - synulein accumulates and aggregates in many neurodegenerative diseases and is implicated in pathology • PBT434 blocks - synuclein accumulation and aggregation, preserves neurons and improves function in animal models of synucleinopathy (Parkinson's disease, MSA) • PBT434 also prevents tau accumulation and improves function in animal models of tauopathy • Link between increased brain iron and the synucleinopathies • Phase 2 data with a related compound supports proof of concept • Clear development path for symptomatic therapy in atypical parkinsonism • Current symptomatic therapy has limited benefit • Potential path for disease modifying therapy 5 PBT434 is an excellent drug candidate for treating neurodegenerative diseases

PBT434: Promising Drug Profile • Good CNS penetration based on low molecular weight and lipophilicity • Brain concentrations 2 to 3 fold higher than plasma • Straightforward synthetic process with demonstrated ability to make kg amounts of GMP material • Benign safety profile in GLP toxicology studies • Non - toxic dose exceeds efficacious dose by >10 - fold based on allometric scaling • Phase 1 in Healthy volunteers ongoing 6 N N O R R R OH R

Importance of - Synuclein • - Synuclein is an intracellular protein, abundantly expressed in the brain • Critical for normal function of neurons • Soluble, in highest concentration at presynaptic nerve endings • Key regulatory protein involved in neurotransmission • Enables neurotransmitter release by facilitating synaptic vesicle fusion to pre - synaptic membrane 7 MAb to - synuclein stains red

- Synuclein is an Important Disease Target Strong genetic and pathological link to disease 8 “Collectively these data strongly suggest that alpha synuclein is a potentially important and novel target of candidate neuroprotective therapies. Several different therapeutic strategies designed to clear or prevent the formation of toxic forms of - synuclein are currently being investigated in the laboratory, and clinical trials have already begun.” https://www.michaeljfox.org/research/priority - area - detail.php?alpha - synuclein AstraZeneca and Takeda establish collaboration to develop and commercialise MEDI1341 for Parkinson’s disease 29 August 2017

- Synuclein as Target for PBT434 • - synuclein fibrillizes readily • Factors regulating its production and conformation are relevant to disease pathogenesis and treatment • Homeostasis of iron is disrupted in PD and atypical parkinsonism • - synuclein is highly conserved in vertebrates but only humans develop synucleinopathy • Human - synuclein mRNA contains an Iron responsive element Lee and Trojanowski , 2006 • The iron responsive element (IRE) of - synuclein is a 5' - untranslated region of mRNA predicted to form a single RNA stem loop • The stem loop shows striking similarity to the 5' - UTRs of mRNAs encoding ferritin and ferroportin from Friedlich , Tanzi, et al. 2007


PBT434 Inhibits - Synuclein Aggregation by Restoring Intracellular Iron Balance 10 PBT434 blocks the aggregation of - synuclein in vitro PBT434 treatment preserves ferroportin levels in vivo F e r r o p o r t i n (O D) W/T Veh PBT434 0 2 4 6 * * PBT434 Dose: 30 mg/kg 0 1 10 20 0 5000 10000 15000 PBT434 (M) F e r e l e a s e d (C P M) Iron efflux from cultured M17 cells *** *** SN+Fe+PBT434 SN+Fe

11 Fe Fe Native, unfolded protein Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Aggregation of fibrillar protein Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe Fe H 2 O 2 Fe OH • Cell Death N N O R R O R R Fe Ferroportin Fe Fe Fe Fe Fe Fe Fe Fe Alpha - synuclein Pathology and PBT434 Mechanism of Action Iron Chaperone, reducing - synuclein accumulation, aggregation and preserving neurons Transferrin Normal Iron trafficking Cytoplasm Extracellular Accumulation H 2 O 2 Fe Ineffective autophagy NH 2 HO HO Dopamine PBT434 exports Fe from cell Oxidative Stress

PBT434 Lowers - Synuclein , Prevents Neuronal Death and Improves Motor Function Transgenic Animal Model (hA53T) of Parkinson’s Disease 12 Preserves neurons in S. nigra T o t a l S N p c n e u r o n s W/T Vehicle PBT434 0 4000 8000 ** Finkelstein et al. Acta Neuropath Comm (2017) 5:53 - Synuclein aggregation Treatment randomly allocated • 4 - 8 months of age • 30 mg/kg/day (via feed) Assessments done in blinded manner h A 5 3 T - s y n Vehicle PBT434 0 2 4 6 ** Foot Clasping % C l a s p i n g Vehicle PBT434 0 50 100 **

Strategy Supported by Proof of Concept with Deferiprone 6 month placebo controlled data in Parkinson’s disease patients 13 S. nigra Brain Iron by MRI Motor Function – UPDRS III Devos et al. Antiox . and Redox Signaling. 2014; 21: 195 DFP PBO DFP PBO S. nigra Improvement Deferiprone • Indicated for Treatment of Iron Overload • Black Box for neutropenia and agranucloctyosis • Iron Binding Affinity Kd =10 - 36 Reducing excess iron associated with improved motor function Worsening

PBT434 has Optimal Iron Binding Affinity for Efficacy and Safety 14 Agent/Protein Kd for Fe 3+ - Synuclein 10 - 5 PBT434 10 - 10 Ferritin 10 - 22 Transferrin 10 - 23 Deferiprone 10 - 36 Davies et al. PLoS ONE. 2011; 6; 1; e15814. doi.org/10.1371/journal.pone.0015814 Aisen P and Listowsky I. Ann Rev Biochem 1980 49: 357 - 393 Aisen P, Leibman A, Zweier J. J Biol Chem. 1978; 253:1930 - 1937 Kline MA and Orvig C. Clin Chem (1992); 38: 562 - 565 Stronger binding

Link Between Iron and Severity of PD 15 Gotz et al. Ann N.Y. Acad Sci. 2004 However, biochemical studies have reported increased iron content in the nigra in PD, 2 - 4 with the changes most marked in severe disease (PD) 5 Martin, et al. Neurology 2008;70:1411 – 1417 Iron concentrations increase with disease severity

Brain Iron Increased in Parkinson’s Disease Patients 16 Substantia nigra (T) Substantia nigra (pc) Cerebellum n = 24 n = 13 nmol iron/g of human brain n = 9 n = 7 * n = 3 n = 8 * 0 10000 20000 30000 And in Multiple System Atrophy Patients Cerebral cortex Caudate nucleus Putamen (M) Putamen (L) Globus pallidus (M) Globus pallidus (L) Substantia nigra (T) Cerebellum n = 11 n = 8 n = 8 n = 8 n = 9 n = 8 n = 12 n = 8 n = 11 n = 8 * nmol iron/g of human brain n = 9 n = 6 * 0 10000 20000 30000 n = 10 n = 8 * n = 10 n = 8 * Healthy Patients Dexter . Brain.1991;114 Langkammer . PLoS ONE 11(9): e0162460. 2016 Specialized MRI Technique (QSM) to Non - invasively Quantify Brain Iron (PD Patient)

Multiple System Atrophy A form of Atypical Parkinsonism • Rapidly progressive neurodegenerative disorder leading to severe disability and impairment in quality of life • Sporadic, typically presents in 50s to 60s • Orphan Indication: Prevalence ~ 5 per 100,000 in the U.S. • Characterized by a variable combination of • Parkinsonism, which responds poorly to levodopa • Cerebellar impairments: impaired gait and speaking • Autonomic failure: Orthostatic hypotension, bladder dysfunction, erectile dysfunction, constipation • MSA patients have neuron loss in multiple brain regions • The hallmark of MSA is the accumulation of - synuclein within neurons and glial support cells 17 Halliday 2015, based on Brain 2015: 138; 2293 – 2309

PBT434 reduces Alpha - synuclein and Lowers Glial Cell Inclusions Transgenic Mouse Model (PLP) - - SYN of MSA 18 - Synuclein Treatment: Randomly allocated, 4 months, 30 mg/kg/day or Vehicle (Veh) Data presented are for animals at 16 mo age Vehicle PBT434 0.0 0.1 0.2 0.3 0.4 R a t i o t o P o n c e a u ** Oligomeric Vehicle PBT434 0.0 0.2 0.4 0.6 0.8 R e l a t i v e t o T o t a l P r o t e i n ** Aggregated Vehicle PBT434 0 1000 2000 3000 4000 N u m b e r o f G C I *** SNpc Vehicle PBT434 0 5000 10000 15000 N u m b e r o f G C I ** Pontine Nucleus Glial Cell Inclusions

PBT434 Preserves Neurons and Improves Motor Function Transgenic Mouse Model (PLP) - - SYN of MSA 19 Treatment: Randomly allocated, 4 months, 30 mg/kg/day or Vehicle Vehicle PBT434 0 2 4 6 8 T i m e t o d e s c e n d t h e P o l e (s) * Pole Test after 4 months treatment 30 mg/kg at 16 months Vehicle PBT434 0 10 20 30 40 T i m e o n t h e r o d (s) ** Rotarod after 4 months treatment 30 mg/kg/day at 20 months W/T Veh PBT434 2000 3000 4000 5000 6000 T o t a l N S N p c n e u r o n s P=0.001 S. Nigra Neurons at 16 months

Brain Iron is also Increased in Tauopathies 20

Progressive Supranuclear Palsy (PSP) A form of Atypical Parkinsonism 21 Cerebral cortex Caudate nucleus Putamen (T) Substantia nigra (T) Cerebellum n = 13 n = 11 n = 14 n = 11 n = 13 n = 11 n = 12 n = 7 nmol iron/g of human brain n = 8 n = 7 * 0 10000 20000 30000 * Healthy Patients Dexter et al . Brain. 1 991;114:1953. Brain Iron increased compared to Healthy controls

PBT434 in an Animal Model of Acute Oxidative Stress 22 Total SNpc neurons 0 1 3 10 30 80 C 0 3000 6000 T o t a l S N p c n e u r o n s PBT434 (mg/kg) *** *** * * Pole test 0 1 3 10 30 80 C 0 6 12 T i m e (s e c s) PBT434 (mg/kg) ** * For - synuclein, lipid peroxidation: PBT434 dose 30 mg/kg/d † Treatment randomly allocated, assessors blinded *P<0.05, **P<0.01, ***P<0.001 PBT434 preserves neurons, improves motor function and reduces - Synuclein accumulation and oxidative stress in the MPTP mouse MPTP mouse model • MPTP is a potent inhibitor of complex 1 of the mitochondrial electron transport chain • Significant neuron loss in SNpc and motor impairment • Rapid and sustained elevation of iron in the SNpc • Causes acute elevation in ROS and oxidative damage • PBT434 or vehicle treatment † started 1 day after toxin administration - Synuclein Lipid peroxidation VEH PBT434 0 100 200 300 400 8 - I s o p r o s t a n e (% U L) *

Development Milestones • Phase 1 Completion 1H ‘19 • Initiate LT toxicology 1H ‘19 • Initiate Phase 2 planning study 1H ‘19 • Initial Patient study start 2020 23

Preliminary Market Assessment (U.S. only) $1 - 1.7B potential commercial opportunity for PBT434 in MSA and PSP* • Severely debilitating, fatal illnesses with no current treatments are ripe for new entrants targeting what may be the actual cause of the disease, even if only motor symptom endpoints Substantial Unmet Need • PBT434 likely to be used in combination with symptomatic treatments and alpha - synuclein antibodies given it works differently and targets different aspects of MSA and PSP Non - Competitive Landscape • Given similar efficacy, clinicians will likely prefer PBT434's once or twice daily oral administration vs. the monthly IV infusions or injections required for any alpha - synuclein or tau antibodies that come to market Ease of Use • Inhibition of iron - mediated protein accumulation and aggregation is a novel mechanism of action that may ultimately prove in clinical practice to impact more than motor symptoms Unique MOA *Additional market research required to validate preliminary opportunity assessment. CONFIDENTIAL 24

Summary • PBT434 is an excellent drug candidate to prevent alpha - synuclein aggregation and reduce oxidative stress by targeting intracellular reactive iron • Brain iron pathologically increased in Parkinson’s disease and atypical parkinsonism • PBT434 has demonstrated efficacy in various animal models of neurodegeneration and has been shown to prevent acute oxidative damage in vivo • Multiple indication opportunity, with potential for treating PD and atypical parkinsonism such as Multiple System Atrophy, an orphan disease • Significant commercial opportunity given limited treatment options which target underlying cause of disease CONFIDENTIAL 25