

# XYnapse Therapeutics Pty Ltd

A spin off company from Hudson Institute of Medical Research seeking capital investment to fund the development of novel Parkinson's disease therapies.

Taking a novel approach to developing treatments for Parkinson's disease, our team have identified a male-specific factor that may underlie the sex-based bias of Parkinson's and influence development of disease in men. We are now developing this finding into a therapeutic approach using proprietary targeted antisense oligonucleotides.

## Summary

Parkinson's disease (PD) is a chronic, debilitating neurological condition, altering co-ordination and movement. It results from progressive degeneration of cells in part of the brain, the substantia nigra. These nigral cells produce dopamine, which is needed for smooth, controlled movements. The loss of these cells and resulting decreased dopamine levels causes many of the symptoms of PD.

The cause of PD is unknown, likely a combination of environmental and genetic factors; a strong risk factor is being male, with more men than women diagnosed (nearly 2:1). Disease severity can also be greater in males and these sex-based differences are also observed in animal models of PD. Hence, a male-specific factor may contribute to PD.

The Hudson Institute team has found that a male-only gene called SRY may underlie the sex-based bias in PD, and influence development of disease in men. They have found levels of SRY are abnormally high in multiple models of PD. Reducing SRY levels in these models mitigates dopamine cell loss and motor symptoms, suggesting a novel treatment strategy to halt or slow PD.

Our researchers have designed proprietary antisense oligonucleotides (ASO) as a gene therapy approach targeting SRY, and initial work in animal models has demonstrated this is highly therapeutic. The team are developing this therapeutic to reduce the burden of PD in men, who are disproportionately affected. Representing a move towards individualised precision-based medicine, this novel approach may lead to new insights to improve overall PD patient care.

## Development pathway

After successful demonstration of the approach in *in vivo* rodent models, our team are now developing this approach further with an initial focus on use in male PD patients with late-stage disease. With a defined R&D plan in place, our team are optimising the human-specific ASO product as part of a strong preclinical program leading to planned first-in-patient Phase 1b clinical trials.

## Applications

There is no cure for PD, and the treatments currently available focus on reduction of symptoms. This includes supportive treatments such as physiotherapy, dopamine-regulating medication, and surgery. These treatments do not change disease progression. There are no therapeutics currently on the market that halt or reverse the brain cell death associated with PD.

Our SRY ASO approach aims to reduce or halt nigral cell death and therefore reduce or prevent the worsening of motor symptoms. ASOs are in clinical development for other neurological diseases, demonstrating the modality can be safe and effective.

## Commercial Opportunity

XYnapse Therapeutics Pty Ltd, is an early stage biotechnology company spun-out from the Hudson Institute and is focused on development of an antisense oligonucleotide therapy targeting SRY for men with PD. The opportunity is structured to maximize non-diluting tax rebates and government incentives for R&D active Australian businesses.

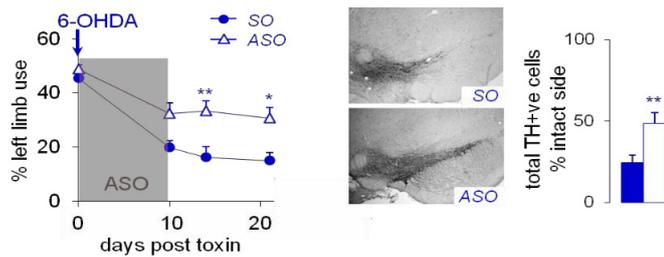
## Global Market Opportunity

Target market: men with late-stage Parkinson's disease.

An estimated 10 million people worldwide are living with PD; 1 million of these in the USA. PD affects men disproportionately to women, around 1.5-2:1. The cost of PD in the US alone is estimated at nearly \$25 billion per year (Parkinson's Foundation). There is a key need for novel therapeutics to ease the burden of this disease worldwide.

A rising disease prevalence due to an aging global population is expected to increase the market for PD therapeutics. The market is expected to shift away from a focus on symptom relief to neuroprotective and disease-modifying approaches (Visiongain).

## Key data



Antisense oligonucleotide treatment significantly improved motor function (A) and diminished dopamine cell loss (B) in the 6-OHDA-induced model of Parkinson's disease. 6-OHDA, 6-hydroxydopamine toxin; ASO, antisense oligonucleotide (SRY treatment); SO, sense oligonucleotide (control) treatment.

## Team

Driving this project are Hudson-based researchers, Professor Vincent Harley, PhD and Dr Joohyung Lee, PhD. This partnership combines Professor Harley's internationally-recognised expertise in SRY (co-discovered role of SRY in the brain) with Dr Lee's extensive experience in Parkinson's disease research (expert in preclinical models demonstrating the link between SRY and PD).

Informing the clinical program is Professor Terence O'Brien, MBBS MD FRACP FRCPE FAHMS FAES, The Van Cleef Roet Professor of Medicine (Neurology) and Head, Departments of Neuroscience and Medicine, Monash University and Director of Neurology, Alfred Health. Professor Dominic Thyagarajan MBBS MD FRACP also joins the team as an established, experienced clinician-researcher.

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## IP position

Hudson Institute is sole owner of two patent applications covering SRY ASOs and their use in neurological diseases, including Parkinson's disease:

1. WO2016164977A1 (priority date 15 April 2015)
2. Australian Prov. Pat. No. AU2017903933 (priority date 28 September 2017)

## Hudson Institute of Medical Research

Hudson Institute is a leading independent Australian medical research institute located in the heart of the Monash Health Translation Precinct in Clayton, Victoria. Our specialist centres bring together the finest professionals in Australian science and medicine to conduct basic and translational research in the areas of:

- Cancer
- Endocrinology and metabolism
- Fetal, infant and child health
- Immunology and infectious diseases
- Reproductive health and biology
- Women's health

Opportunities for collaboration and partnership

Partnership opportunities include:

- Therapeutics, including oncology and gene therapy
- Reproductive, women's and children's health

- Regenerative medicine
- Infectious disease, inflammation and immunology
- Diagnostics and biomarkers

Hudson can facilitate access to:

- Unique pre-clinical models and research tools
- Platform technologies and clinical trials centre
- A Research Service Provider – Hudson is registered with AusIndustry to provide contract R&D services

Key Indicators

- 230 research staff trained nationally and internationally
- 51 research laboratories
- > 275 publications annually
- 140 HDR students
- 2 start-up companies