**Product Type**
Small molecule drug candidate – repurpose or NCE

**Indication/ROA**
Obesity – intra-nasal (reformulation existing drug) or oral NCE

**Target/MoA**
A hypothalamic protein tyrosine phosphatase (PTP) ‘switch’, regulated by glucocorticoids (GC), modulates insulin sensitivity and weight loss. CNS-targeted blocking of TCPTP (via GC-receptor antagonism) resets arcuate nucleus (ARC) neurons to insulin, increases energy expenditure and white adipose tissue (WAT) browning leading to weight loss. Combined with targeting PTP1B to re-sensitize ARC neurons to leptin, this represses feeding and leads to synergistic and sustained weight loss and improved glucose metabolism.

**Development Stage**
Targets validated through intra-nasal administration of TCPTP inhibitor (or GC antagonist) and PTP1B inhibitor; in preclinical efficacy studies; re-profile existing marketed drugs/drug candidates for i.n. delivery.

**Brief Description & Differentiation**
Central targeting of the hypothalamic PTPs is a new approach to increase insulin and leptin signalling, increase WAT browning and energy expenditure and repress feeding for the treatment of metabolic disease and obesity. Inhibiting TCPTP and PTP1B in ARC neurons is highly efficacious in promoting weight loss in obesity and improving glucose metabolism, even without lifestyle modifications.

**Research Team**
Prof Tony Tiganis (Monash BioMedicine Discovery Institute)

**Intellectual Property**
PCT/AU2018/050588 - METHODS AND COMPOSITIONS FOR THE TREATMENT OF OBESITY

**Key Publications**

**Future**
Re-profile TCPTP and PTP1B inhibitors for i.n. administration and formal preclinical studies

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**Key Data**
Monash researchers have identified a novel hypothalamic PTP switch linking GC to insulin receptor signalling.
- Elevated ARC PTP1B & TCPTP promote cellular leptin & insulin resistance.
- Elevated ARC PTP1B & TCPTP contribute to the maintenance of obesity, systemic insulin resistance & hyperglycemia.
- Intranasal delivery of TCPTP (via GC antagonist) increases WAT browning and energy expenditure while PTP1B inhibitor represses feeding to promote weight loss and improve glucose metabolism in obesity.

**Figure 1:** Once daily Intranasal Delivery of TCPTP and PTP1B inhibitors promotes weight loss in DIO

**Figure 2:** Once daily Intranasal Delivery of TCPTP and PTP1B inhibitors promotes weight loss in DIO