Paradigm Biopharmaceuticals Ltd (ASX:PAR)

Respiratory Product

Rhinosul®: a non-steroidal Th2 cytokine (IL-4, IL-5 and IL-13) antagonist for treatment of Allergic Rhinitis

Partnership Opportunity:

Phase 2a clinical trial complete and product has compelling advantages for the Allergic Rhinitis market.

The current market for Allergic Rhinitis (AR) is dominated by anti-histamines and nasal corticosteroids with market surveys highlighting patient dissatisfaction and the need for effective therapy. Rhinosul, which contains the active pentosan polysulfate sodium (PPS) has both mast cell stabilizing properties (blocking histamine release from mast cells) and anti-inflammatory properties without the potential side-effects of anti-histamine and steroids. Paradigm believes its product can meet market needs that are not effectively managed by current nasal sprays.

- Strong need for more effective treatment options
  - More than 50% of patients are dissatisfied with current medication and 60% have said they would be interested in new treatments
  - Long term use of corticosteroids proven to be harmful to certain sufferers.
- Allergic Rhinitis associated with growing economic burden.
- A product with the capacity to be a fast-moving consumer good with a pharmaceutical margin
  - Clear need for safer, superior and cheaper treatments.

Scientific basis supporting Rhinosul as a treatment for Allergic Rhinitis

- PPS is a potent Th2 cytokine-binding molecule targeting the cytokines IL-4, IL-5 and IL-13 with biological neutralization capacity and broad anti-inflammatory effects (Sanden et al, Immunity, Inflammation and Disease; 2017 DOI: 10.1002/iid3.164).
- After OVA challenge in Guinea pig model of Allergic Rhinitis, total leukocyte, eosinophil and neutrophil numbers in the nasal lavage fluid were equally inhibited by PPS and budesonide (Astra Zeneca Rhinocort).
- PPS significantly reduces allergen-induced plasma extravasation and influx of leukocytes into the nasal cavity.

PPS has a powerful dose dependent inhibitory effect on mast cell release of histamine which is more potent than di-sodium cromoglycate (cromolyn) (Chiang et al, J Urol. 2000 Dec;164(6):2119-25).

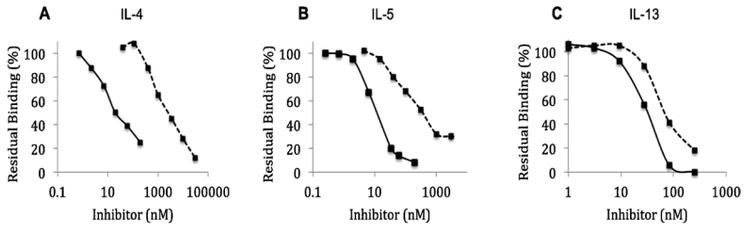
- PPS is potentially a first-in-class, non-steroidal intranasal spray to treat the acute and chronic phases of allergic rhinitis.

GMP Manufacturing and Clinical development program

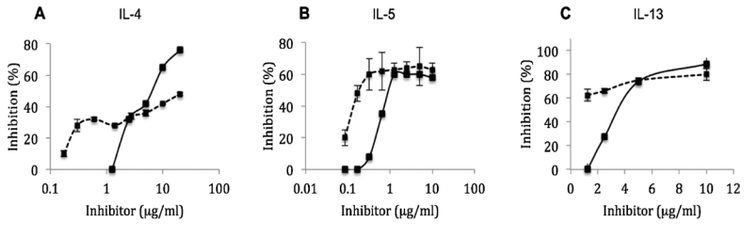
- Rhinosul is presented as a metered-dose nasal spray – developmental formulation manufactured in Europe under cGMP using world leading device technology.
- Rhinosul contains the active (pentosan polysulfate sodium (PPS)) – safety and tolerability of PPS in humans is well established.
- Intranasal preclinical toxicology study (Charles River Laboratories, USA) – complete.
- Intranasal safety and tolerability in Phase 1 clinical trial n= 20 healthy subjects, (1:1) Randomised double, blinded placebo controlled clinical trial – complete.
- Phase 2a clinical trial examining safety and efficacy of Rhinosul in 40 Allergic Rhinitis subjects: Randomized, double blind, placebo-controlled, cross-over design – 'on study' period completed, with successful recruitment of 40 subjects to meet the recruitment target. Results anticipated in June/July 2017.

Scientific and Preclinical data demonstrating efficacy of PPS in allergic rhinitis therapy (Sanden et al 2017)

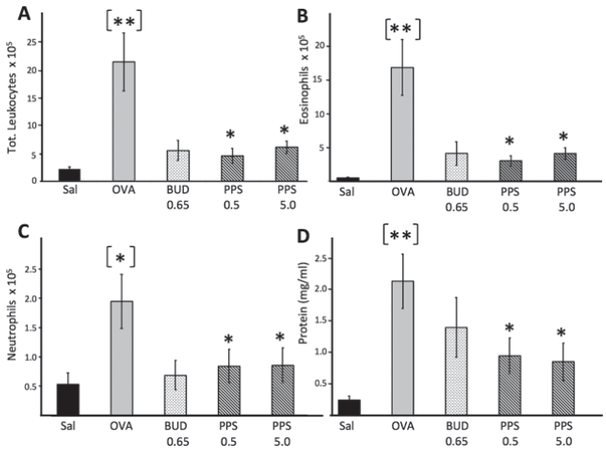
Molecular interactions and binding of PPS (solid line) and heparin (dashed line) to Th2 cytokines as revealed by surface plasmon resonance (SPR) methodology.

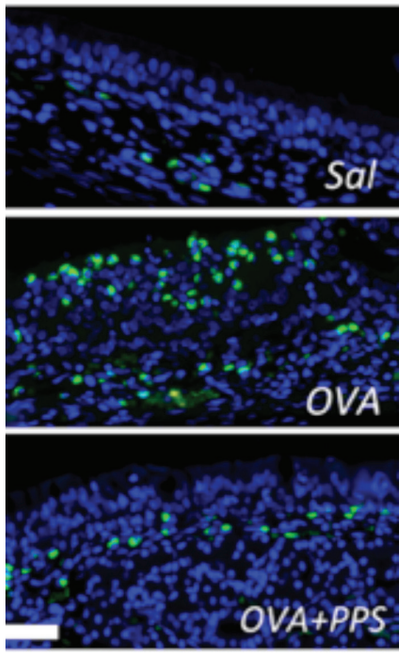


Dose–response curves of the capacity of PPS (solid line) and heparin (dashed line) to inhibit cytokine-dependent cell proliferation in vitro.



Capacity of PPS and budesonide to reduce allergen-induced influx of nasal lumen leukocytes (A–C) and plasma extravasation (D).





Impact of PPS and budesonide on histological nasal tissue parameters during the allergic late phase reaction

(Image of Fluorochrome–stained eosinophils)