# *NTP42*, an antagonist of the thromboxane receptor, attenuates experimentally-induced pulmonary arterial hypertension

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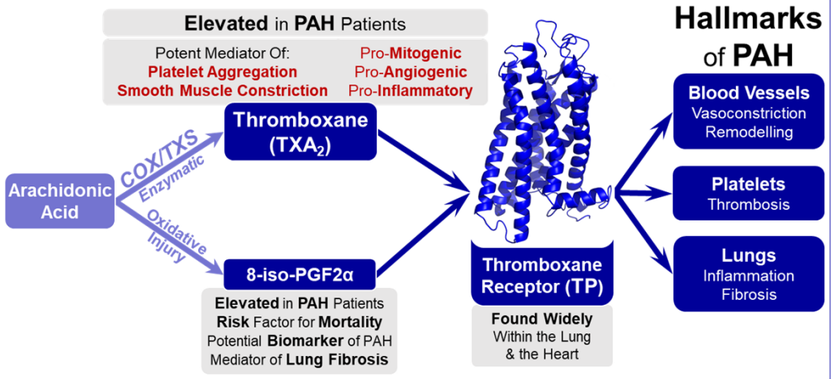
## Background & Aims

***NTP42*** is a **novel antagonist** of the thromboxane (TX)$A_2$ receptor (TP), currently in development for the treatment of pulmonary arterial hypertension (PAH).

### The **TP** is a **Key Driver** of **PAH**




Mechanistically, **TP antagonists should treat many of the hallmarks of PAH**, including inhibiting the excessive vasoconstriction and pulmonary artery remodelling, *in situ* thrombosis, fibrosis and inflammation.

***NTP42*** has been confirmed to display **potent antagonist** activity; it also has excellent target **specificity**, **pharmacokinetic & drug safety/toxicology profiles**.

The ***aim*** of this study was to investigate the **efficacy of *NTP42*** in a monocrotaline (MCT)-induced PAH model in rats (Wistar Kyoto), comparing its effects to the standard-of-care (SoC) drugs Sildenafil and Selexipag.

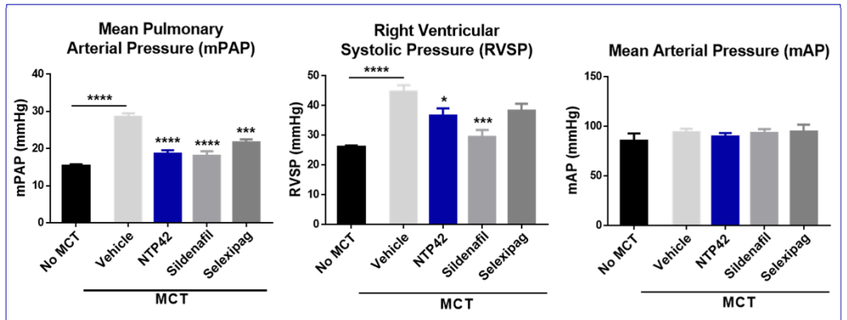
## Methods

PAH was induced by bolus injection of 60 mg/kg MCT (s.c). Rats were randomly assigned to 5 groups: (1) No MCT; (2) MCT Only; (3) MCT+*NTP42* (0.25 mg/kg PO, BID); (4) MCT+Sildenafil (50 mg/kg PO,BID); (5) MCT+Selexipag (1 mg/kg PO, BID), where treatment was initiated 24hr post-MCT & was continued for 28 days.

## Results

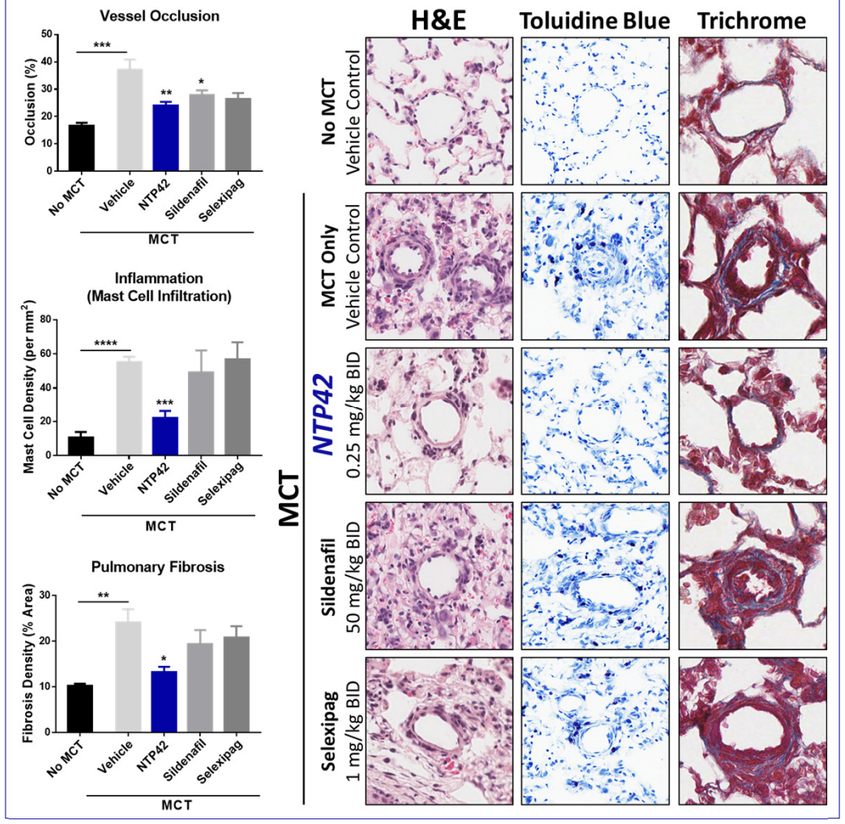
### Pulmonary & Cardiac Haemodynamics

- ***NTP42*** **reduced the severity of MCT-induced PAH** as determined from hemodynamic measurements, including reductions in mean pulmonary arterial pressure (mPAP) and right systolic ventricular pressure (RSVP).
- ***NTP42*** (0.25 mg/kg BID) was at least comparable to the SoC drugs Sildenafil (50 mg/kg BID) or Selexipag (1 mg/kg BID) in these effects.
- ***NTP42*** or the SoC drugs had **no effect on systemic arterial pressure** (mAP).



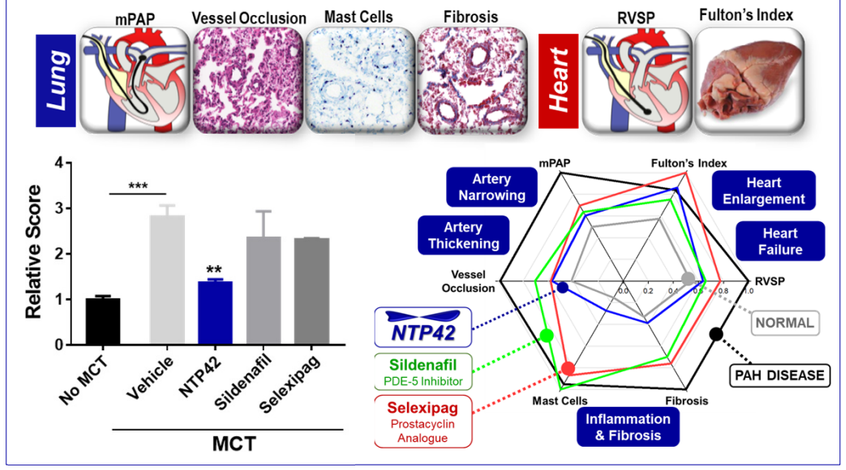

### Pulmonary Histology

- ***NTP42*** was **superior to the SoC** drugs Sildenafil or Selexipag in significantly **reducing pulmonary vascular remodeling** in the MCT-treated animals. Notably *NTP42-treated* animals displayed remarkedly similar histology to the sham (No MCT) control animals across all morphometric parameters analyzed.
- ***NTP42***, unlike the SoCs, was **the only drug therapy** that significantly reduced pulmonary inflammation (mast cell infiltration) and pulmonary fibrosis.

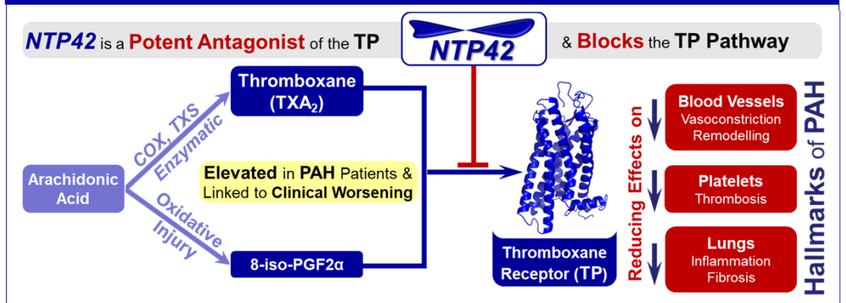



### Multiparameter Disease Efficacy

A **multiparameter score** of key PAH disease indices, *incl*. mPAP, RVSP, Fulton's index, vessel remodelling, inflammation & fibrosis, shows that ***NTP42*** **has significant treatment benefits,** and is superior to the SoCs Sildenafil & Selexipag.




## Conclusions




This study shows that ***NTP42***, through its antagonism of TP signaling, **alleviates PAH pathophysiology** and, therefore, represents a **novel therapeutic drug & target pathway** displaying marked **benefits over existing SoC therapies**.

## About ATXA Therapeutics Limited

- Headquartered in Dublin, Ireland, ATXA Therapeutics Ltd is a drug-development company developing novel, *first-in-class* small molecule drugs to the TP. Spun out from UCD, it has pipeline of TP antagonists, incl. *NTP42*, protected by 9 granted in the US (7) & Europe (2).
- In 2018, ATXA secured Orphan Designation from both the EMA and the FDA for its lead drug ***NTP42*** for its primary target disease indication PAH.
- During 2018, ATXA was successful in winning €2.5 million in grant aid from the EU Horizon 2020 SME Instrument funding scheme. This project, dubbed *PAH-HOPE*, will fast-track ATXA's ***NTP42*** into clinical development in the disease indication PAH.

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PAH HOPE

This project received funding from the European Union Horizon 2020 research and innovation programme under Grant Agreement No 822258.