Thyron Pharmaceuticals

Unlocking the potential of Thyroid Hormone Mimetics in severe diseases

Paul Fonteyne and Naftali Kaminski MD
Thyroid Hormones: Role in Critical Diseases

- critical to homeostasis of the normal alveolus, surfactant secretion and alveolar fluid reabsorption.
- protective in sepsis and hyperoxia models of ARDS in rodents
- supplementing results in antifibrotic effects in the lung and other organs
- concerns for systemic toxicity - heart, skeletal muscle, GI
- In humans, hypothyroidism is associated with poor prognosis in critically-ill patients, diabetic nephropathy, idiopathic pulmonary fibrosis
Our Solution: Sobetirome

- A clinical-stage orally-available small molecule
  - Well-characterized thyroid hormone receptor-β agonist
  - Tested in 65 human subjects so far
  - Well-tolerated in wide dose range for up to 28 days with no dose-limiting toxicities

- The opportunity:
  - Open IND and clinical data package with Right of Reference (Kaminski)
  - Yale has filed 2 patents for IPF, ARDS (methods of use; formulation; application; dosage)
First Indication and Rationale: Idiopathic Pulmonary Fibrosis (IPF)

- Idiopathic Pulmonary Fibrosis (IPF) prevalence US approx. 190,000 (Orphan)
- Standard of Care: Ofev (Boehringer-Ingelheim) or Esbriet (Roche), oral medicines, combined expected 2021 sales >$2.4 Billion (US); significant tolerability and safety concerns result in low treatment and adherence.
- Our Indication: develop sobetirome into an effective, safer, better tolerated, inhaled medicine for pulmonary fibrosis patients.
- Rapid path to clinic (based upon open IND) due to vast toxicology and human safety available on this compound.
- Extensive Preclinical data (in-vitro, in-vivo & ex-vivo) established in the Kaminski lab at Yale
Sobetirome Resolves Established Pulmonary Fibrosis in multiple models:

- **In-Vitro** - improved epithelial and fibroblast mitochondrial function
- **In-Vivo** - reversal of fibrosis in widely accepted animal models of Disease
- **Ex-Vivo** - human tissues (lung slices)
  - collagen content
  - fibrotic gene expression

Yu et al. Nature Medicine 2018
Assembled Experienced Team to lead Thyron Pharmaceuticals

- Scientific Founder: Naftali Kaminski MD (Yale)
- Startup CEO: Paul Fonteyne (ex CEO Boehringer-Ingelheim USA)
- Startup COO: Timm Crowder PhD (21 years inhalation development experience, Glaxo, Spyryx, Aerami)
- Board Members: David Scheer (serial entrepreneur in life sciences, Viropharma, Achillion, and many others); Stephen Bloch MD (GP, Canaan Partners); Peter Farina PhD (ex SVP R&D Boehringer-Ingelheim)
Our Focus: Development Planning for Sobetirome

- Optimization of route of administration and formulation
- Optimization of PK and dosing regimen for inhalation
- Toxicology (change in route of administration to inhalation)
- Most efficient and de-risked clinical trial strategy
- Role of sobetirome in ARDS?
Getting to Know Thyron Pharmaceuticals Inc.

- Thyron Pharmaceuticals Inc. founded April 2021.
- Over the next few months, we are going to meet with investors and strategic partners to discuss the development of sobetirome in severe diseases.

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