Background

YPL-001 is an oral dosage form of the extract from the plant Sprediaella used in traditional Asian medicine to treat respiratory inflammatory conditions including chronic obstructive pulmonary disease (COPD). This botanical drug product is a mixture of two identified active indoles and other related compounds. Biological activity is considered to be from the mixture and not from one component.

Preclinical Results:
- YPL-001 inhibited neutrophil accumulation in bronchoalveolar lavage (BAL) fluid and several pro-inflammatory cytokines and chemokines (including interleukin-6) and activated the nuclear factor erythroid-derived-2-like 2 (Nrf2). Antioxidant pathway.
- YPL-001 may down-regulate neutrophil influx and production of tumor necrosis factor alpha (TNF-a) and production of inflammatory cytokines (IL-6, chemokine ligand-1 (CXCL-1), and macrophage inflammatory protein-2 (MIP-2)).

Pharmacokinetics:
- Oral doses of YLP-001 are rapidly absorbed and cleared rapidly from plasma, with mean t1/2 < 2.5 hours.
- YVP and picroside II, the main active indoles of YPL-001, are rapidly absorbed and cleared rapidly from plasma.

Methods

Study Timeline:
- Oral doses of YLP-001 or placebo (BID) from Days 1 to 56.
- Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 5 and QD on Day 56 AM.
- Treatment B: Single oral dose of YPL-001 160 mg and Placebo
- Treatment C: Multiple oral doses of placebo BID on Days 1 -5 and QD on Day 56 AM.

Objectives and Hypothesis

Objectives:
- To assess the safety and tolerability of YPL-001 versus placebo administered for 8 weeks in moderate to severe COPD patients (n=61).
- To determine the effect of YPL-001 on COPD respiratory symptoms.
- To evaluate the pharmacokinetics and pharmacodynamics of YPL-001.

Hypothesis: YPL-001 will improve respiratory symptoms in patients without any significant AEs.

Exploratory objectives were to assess BAL and blood inflammatory biomarkers, symptom measurements, quality of life (QoL) scores, and verpiroside and picroside II pharmacokinetics (PK) plasma profiles after YPL-001 BID.

Results

All 61 subjects were included in the safety analyses and there were 61 subjects included in PK, PD and symptom measurement analysis.

Primary Objectives:
- There were no discorable treatment-related or time-related changes in the laboratory, vital signs (including pulse, oxygen, ECG, or physical examination abnormalities).
- The safety analysis included all 61 treated patients.
- 10 AEs were reported in 5 patients overall 20% (5 patients in the YPL-001 80 mg group, 16% in the YPL-001 160 mg group, and 70% in the placebo group).

Secondary Objectives:
- There were no discorable treatment differences in DAS24 (erythroid-derived-2)-like 2 (Nrf2) anti-oxidative activity (Duke Activity Status Index [DASI]) scores.

Exploratory Objectives:
- Symptoms: No apparent treatment-related changes in FEV1, PEF, and FEV1/FVC.
- QoL: All QoL scores were unchanged from baseline (BDI, TDI, and CAT).
- Spirometry: Mean PEF values in patients receiving YPL-001 increased from 250-260 L/min at baseline to 275-290 L/min following 8 weeks of treatment whereas patients who received placebo saw a difference of less than 3%, from 241 L/min to 240 L/min.

Conclusion

Observed data are consistent with the historical use of this herbal product in traditional Asian medicine for treatment of inflammatory diseases of the respiratory tract including COPD and provide a basis to consider future studies at higher doses and longer duration.

Clinical Research supported by Thung Pharmaceuticals Ltd., IL, and Dental Korea.