Statistical Analysis Plan

A Randomized, Double-Blind, Placebo Controlled, Multicenter Phase 2a Study to Assess Safety, Daily Respiratory Symptoms, Pharmacokinetics, and Biomarker Variations after Administration of either YPL-001, or Placebo in Patients with Moderate-to-Severe Chronic Obstructive Pulmonary Disease

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Statistical Analysis Plan Signature Page

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1. INTRODUCTION

The following analysis plan provides the framework for the summarization of the data from this study. The Statistical Analysis Pan (SAP) may change due to unforeseen circumstances. Any changes made after the unblinding or locking of the database will be documented in the clinical study report (CSR). Please note that the header for this page will be the one used for the main body of the CSR.

Any additional exploratory analyses not addressed within this SAP and/or driven by the data, or requested by Yungjin Pharm. CO., LTD., will be considered out of scope and must be approved, by Yungjin Pharm. CO., LTD., and must be described in the CSR.

2. OBJECTIVES AND ENDPOINTS

2.1 Objectives

Primary Objective: To assess the safety and tolerability of two multiple oral YPL-001 dose levels versus placebo in moderate to severe chronic obstructive pulmonary disease (COPD) patients.

Secondary Objective: To assess the number and magnitude of daily respiratory symptoms of two multiple oral YPL-001 dose levels versus placebo in moderate to severe COPD patients.

Exploratory Objectives: To evaluate the following in moderate to severe COPD patients:

1. To assess BAL epithelial brushings for YPL-001 component levels.
2. To compare BAL samples for total cell count (cells/mL) macrophages, lymphocytes, neutrophils, and eosinophils as a percentage of total cells; neutrophil, macrophage, lymphocyte, and eosinophil counts as absolute inflammatory cell numbers in YPL-001 groups versus placebo group.
3. To compare BAL samples for TNF-α, IL-1β, IL-4, IL-5, IL-6, IL-8, IL-13, MPO, neutrophil elastase, MCP-1, and MMP-9 in YPL-001 groups versus placebo group.
4. To compare blood inflammatory markers (total and differential cell counts as absolute and percentage for neutrophils, monocytes, eosinophils and lymphocytes) and concentrations of CRP, fibrinogen, TNF-α, IL-1β, IL-4, IL-5, IL-6, IL-8, IL-13, MCP-1, and MMP-9 in YPL-001 groups versus placebo group.
5. To compare spirometric functions (FEV_1, FVC, FEV_1/FVC, and IC) in YPL-001 groups versus placebo group.

6. To compare patient reported outcomes (BDI/TDI, CAT) in YPL-001 groups versus placebo group.
7. To assess verproside and picroside II concentration in plasma and BAL and verproside and picroside II PK in plasma following multiple oral doses administration of two YPL-001 dose levels.

2.2 Endpoints

Primary Endpoint: The number and severity of treatment-emergent adverse events (TEAEs) following multiple oral doses of YPL-001 or placebo.

Secondary Endpoint: The number of symptom free days and overall symptom burden following multiple oral doses of YPL-001 or placebo, assessed by measuring:

- daily peak expiratory flow (PEF);
- major (e.g., estimated sputum quality (e.g., color, consistency) and quantity) and minor (e.g., cough, wheeze, sore throat, nasal congestion, discharge, and body temperature above 100°F) symptoms of COPD exacerbation;
- dyspnea (using the Modified Borg Dyspnea Scale);
- activity (using the Duke Activity Status Index [DASI]).

Exploratory Endpoints:

1. YPL-001 component levels in epithelial brushings;
2. BAL biomarkers following multiple oral doses of YPL-001 or placebo, measuring:
    - total cell count (cells/mL) of macrophages, lymphocytes, neutrophils, and eosinophils as a percentage of total cells
    - total cell count (cells/mL) of neutrophils, macrophages, lymphocytes, and eosinophils as absolute inflammatory cell numbers
    - concentrations of TNF-α, IL-1β, IL-4, IL-5, IL-6, IL-8, IL-13, MPO, neutrophil elastase, MCP-1, and MMP-9.
3. Blood biomarkers following multiple oral doses of YPL-001 or placebo, measuring:
    - inflammatory markers (total and differential cell counts as absolute and percentage for neutrophils, monocytes, eosinophils, and lymphocytes)

- concentrations of CRP, fibrinogen, TNF-α, IL-1β, IL-4, IL-5, IL-6, IL-8, IL-13, MCP-1, and MMP-9.

4. Pulmonary function results (spirometry) following multiple oral doses of YPL-001 or placebo.
5. Quality of life scores using the BDI/TDI, CAT questionnaires.
6. Concentrations and PK of verproside and picroside II in plasma following multiple oral doses of YPL-001.
7. Concentrations of verproside and picroside II in BAL following multiple oral doses of YPL-001.

3. STUDY DESIGN

This is a Phase 2a, proof-of-concept, multicenter, randomized, double-blind, double-dummy, 3-treatment, parallel study, with low and high YPL-001 doses (80 mg and 160 mg twice daily [BID]) and a placebo control, in moderate to severe COPD male and female patients.

Sixty (60) patients will be enrolled and randomized into 3 treatment groups (20 patients per group). Patients will participate only once. An approximately equal number of current and ex-smokers will be enrolled in the study.

Screening of patients will occur within 14 days of Day 1 (inclusive) of the Run-in Period.

Following screening, eligible patients will discontinue non-permitted respiratory drugs and enter a 14 ± 2 days Run-in Period during which patients will be given albuterol taken on an as required basis and daily tiotropium 18 μg to be administered at home. They will record their daily symptoms in an electronic diary (e-diary) throughout the Run-in Period.

Patients will return to the clinical research unit (CRU) in the morning of Day -3 to -1 for Check-in of the Treatment Period to confirm their eligibility and undergo Check-in scheduled study procedures. Patients will return to the CRU on the morning of Day 1 to be randomized and receive one of the 3 treatments and undergo all scheduled study procedures. Patients will return on the morning of Days 15 (± 2 days), 29 (± 2 days), 43 (± 2 days), 54 (± 1 day) , and 56 of the Treatment Period for study drug administration and procedures. Prior to each release from the CRU, patients will receive sufficient doses to be self-administered at home until the next morning visit at the CRU. Patients will continue recording their daily symptoms via the e-diary throughout the Treatment Period.

YLP-001 and placebo will be administered approximately every 12 hours under fasting conditions.

Patients will remain ambulatory or seated upright for 1 hour following each study medication administration.

Safety and tolerability will be assessed throughout the study through physical examinations, vital signs, pulse oximetry, electrocardiograms (ECGs), clinical laboratory tests, and adverse events (AEs).

Assessment of respiratory symptoms and symptom burden in YPL-001 and placebo treatments will be performed daily through patient self-report of PEF, major and minor symptoms of COPD exacerbation, dyspnea, and activity.

Spirometry measurement, quality of life assessments, BAL, and blood samples will be collected for the pharmacodynamic (PD) assessment of YPL-001 and placebo treatments.

Serial blood samples will also be collected for PK assessment of verproside and picroside II in plasma and BAL.

The CRU will attempt to contact patients using their standard procedures approximately 14 days after the last study drug administration to determine if any AE has occurred since the last dose of study drug.

The planned length of participation in the study for each patient is approximately 12 weeks (from Run-in through follow-up).

4. ANALYSIS POPULATIONS

4.1 Analysis Populations

Safety population: All available data for patients who received at least one dose of the investigational product (i.e., YPL-001) or placebo. Safety data for all discontinued patients will be included in this set for the time points for which their data are available.

Symptom monitoring population: All available data for patients who received at least one dose of the investigational product (i.e., YPL-001) or placebo. Symptom monitoring data for all discontinued patients will be included in this set for the time points for which their data are available.

PK population: All patients receiving at least one dose of YPL-001 and having at least one measurable plasma concentration of verproside and picroside II.

PK per-protocol population: All protocol-compliant patients who received all scheduled doses of YPL-001 and have sufficient samples collected to determine PK parameters from plasma concentrations of verproside and picroside II on at least one of the two PK days (Days 1 and 54 (±1 day) or 56).

PD population: All patients who received at least one dose of YPL-001 or placebo and provide at least one post-baseline PD measurement.

PD per-protocol population: All protocol-compliant patients who received all scheduled doses ofYPL-001 or placebo and have measurable PD data.

PK/PD population: All patients who received at least one dose of YPL-001 and having any measurable concentration of verproside and picroside II and measurable PD data will be included in the PK/PD relationship assessment, as applicable.

4.2 Preliminary Data and Interim Analysis

No formal interim analysis is planned for this study.

5. TREATMENT DESCRIPTIONS

5.1 Study Treatments

YPL-001 will be supplied as 80 mg tablets for oral administration.

Placebo will be supplied as YPL-001 80 mg matching placebo tablets for oral administration.

Treatments A, B, and C are described as follows:

Treatment A: Multiple oral YPL-001 80 mg doses (1 x 80 mg tablet + 1 x 1 YPL-001 80 mg matching placebo tablet) will be administered approximately every 12 hours under fasting conditions for 55 consecutive days.*

Treatment B: Multiple oral YPL-001 160 mg doses (2 x 80 mg tablets) will be administered approximately every 12 hours under fasting conditions for 55 consecutive days.*

Treatment C: Multiple oral matching placebo (2 x 1 YPL-001 80 mg matching placebo tablets) will be administered approximately every 12 hours under fasting conditions for 55 consecutive days.*

* Patients following up to Amendment version 5 of protocol also received a morning dose on Day 56

In the tables, figures, and listings (TFLs) (PK, PD, and safety), treatments will be referred to as:

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55.

Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55.

Treatment C: Multiple oral doses of placebo BID on Days 1 – 55.

Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

In the text of the CSR, treatments will be referred to as Treatments A, B and C or as 80 mg YPL-001, 160 mg YPL-001, and placebo, respectively.

The finished product will be referred to in the CSR as YPL-001 or placebo. The active ingredient will be referred to in the CSR as verproside and picroside II.

5.2 Other Treatments

Tiotropium (Spiriva® HandiHaler®) will be supplied as 18 µg capsules for inhalation.

Albuterol will be supplied as 100 µg albuterol base (1 actuation = 100 µg albuterol base) for oral inhalation. Albuterol may be administered via a nebulizer or a metered-dose inhaler.

During the Run-in Period, multiple oral inhalation of tiotropium (Spiriva® HandiHaler®) 18 µg capsule will be administered QD every morning for 14 ± 2 days. Albuterol will be administered on an as needed basis.

In treatments A to C, one tiotropium (Spiriva® HandiHaler®) 18 µg capsule will also be administered QD every morning prior to study drugs administration. Albuterol will be administered on an as needed basis.

6. SYMPTOM MONITORING ANALYSIS

The following section is organized based on the secondary endpoints in Section 2.2.

6.1 Measurements, Collection Schedule, and Analysis

When readings are not performed in the CRU, patients will record their daily symptoms in their e-diary prior to each dose from Day 1 of the Run-in Period through the Treatment Period. Patients will return the e-diary device on Day 56 (or prior to early termination) to CRU.

The following symptoms will be monitored daily by all patients:

Peak Expiratory Flow: Three (3) PEF measurements will be made at each time point. PEF measurements and their change from baseline will be summarized by treatment and time point of collection. Baseline is Day 1 predose measurement.

Symptoms of COPD Exacerbation: Major (estimated sputum quality [color and consistency] and quantity) and minor (cough, wheeze, sore throat, nasal congestion, nasal discharge, and body temperature above 100°F) symptoms of COPD exacerbation and their change from baseline will be listed and presented descriptively. Baseline is Day 1 predose measurement.

Dyspnea: Severity level of patient's dyspnea will be assessed via the Modified Borg Dyspnea Scale (0 to 10; where 0 corresponds the absence sensation of dyspnea and 10 corresponds to maximum possible sensation of dyspnea). The Modified Borg Dyspnea Scale scores will be listed and presented descriptively.

Activity: Patient's functional capacity and activity status will be assessed via the DASI 12-item questionnaire. The final score ranges between 0 and 58.2 points. The higher the score, the better the functional capacity. DASI scores will be listed and presented descriptively.

Additional analysis may be performed if deemed appropriate.

6.2 Data Summarization and Presentation

Symptom free days and overall symptom burden will be evaluated and compared across treatment groups. Secondary outcome analysis will be based on treatment actually received by patients. Quantitative data will be summarized by treatment group using descriptive statistics including sample size (N), arithmetic mean, standard deviation (SD), coefficient of variation (CV%), median, minimum, and maximum. Frequency counts will be compiled for classification of qualitative data, when appropriate. Descriptive statistics and frequency counts will be generated using SAS® Version 9.3 (or higher).

7. PHARMACODYNAMICS ANALYSIS

The following sub-sections are organized based on exploratory endpoints 1 to 5 in Section 2.2.

7.1 Biomarkers and Quality of Life Assessments

7.1.1 Measurements, Collection Schedule, and Analysis

7.1.1.1 Biomarkers in Bronchoalveolar Lavage Samples

BAL samples for PD assessments of biomarkers will be collected at baseline at Check-in and on Day 55 or 56 of the Treatment Period.

BAL (lavage material) will be performed in the right middle or lower lobe. BAL cell pellet and supernatant will be kept cooled until processed or stored as indicated in the laboratory manual to be provided as a separate document.

Samples must be protected from UV light during collection, processing, and storage.

Biomarkers assessments in BAL include:

- White blood cell (WBC) count (cells/mL) and differential (including macrophages, lymphocytes, neutrophils, and eosinophils) will be expressed as

raw counts and % change from baseline and as a percent (%) of WBC for each differential.

WBC and differential in BAL will be determined using a differential stain (blood smear; microscopic examination with manual differential WBC count) at the local Investigator sites.

- Concentrations of TNF-α, IL-1β, IL-4, IL-5, IL-6, IL-8, IL-13, MPO, neutrophil elastase, MCP-1, and MMP-9 will be expressed as raw and % change from baseline levels. Baseline is defined as Check-in of the Treatment Period level and is patient specific.

  The concentrations of MPO, neutrophil elastase, MMP-9 will be determined using enzyme-linked immunosorbent assay (ELISA) assays and the rest of BAL inflammatory markers will be determined using Luminex® assays. All assays are validated with respect to accuracy, precision, linearity, sensitivity, and specificity at Temple University School of Medicine (Philadelphia, Pennsylvania, USA).

7.1.1.2 Biomarkers in Blood

Blood samples for PD assessments of biomarkers will be collected in pre-chilled evacuated tubes containing K_2EDTA at screening, on Days 1 and 54 (± 1) or Day 56 of the Treatment Period prior to dosing (predose) and at 1 hour postdose. In addition, predose samples will be collected on Days 15 (± 2), 29 (± 2), and 43 (± 2) of the Treatment Period.

Biomarker assessments include:

- WBC counts and differential (including monocytes, lymphocytes, neutrophils, and eosinophils) will be expressed as raw counts, % change from baseline, and as % of WBC for each differential.

  WBC and differential counts in blood will be determined using a differential stain (blood smear; microscopic examination with manual differential WBC count) at the local Investigator sites.

- Concentrations of CRP, fibrinogen, TNF-α, IL-1β, IL-4, IL-5, IL-6, IL-8, IL-13, MCP-1, and MMP-9 will be expressed as raw and % change from baseline levels. Baseline is defined as the predose time point at Check-in of the Treatment Period level and is patient specific.

  The concentrations of MMP-9 will be determined using an ELISA assay and the rest of blood inflammatory markers will be determined using Luminex® assays. All assays are validated with respect to accuracy, precision, linearity, sensitivity,

and specificity at Temple University School of Medicine (Philadelphia, Pennsylvania, USA).

7.1.1.3 Pulmonary Function Biomarkers

Spirometry measures for assessment of the pulmonary function will be taken pre- and post-bronchodilator (albuterol) administration at Screening (baseline), at Check-in, on Days 15 (± 2), 29 (± 2), 43 (± 2), and 55 or 56 (predose) of the Treatment Period, and prior to early termination, if applicable.

Pulmonary function measurements include the following parameters below:

- FEV1;
- FVC;
- FEV1/FVC;
- IC.

Short and long acting β2-agonist and anticholinergic bronchodilators agents will be withheld approximately 4 and 24 hours, respectively, before each pre-bronchodilator spirometry.

At screening, baseline pre-bronchodilator spirometry will be performed (prior to albuterol administration) for a minimum of 3 times and a maximum of 8 times in order to obtain 3 manoeuvers with FEV1 values within 150 mL of each other, using the manoeuver with the highest value of FEV1 and FVC as the basis for comparison.

Patients shall receive 4 inhalations of albuterol, (100 μg/inhalation), for a total dose of 400 μg via metered-dose inhaler using a spacer. Within approximately 20 to 30 minutes after albuterol administration, the baseline post-bronchodilator spirometry will be performed.

Assessment of FEV1 stability will take place:

1. Prior to Day 1 dosing of the Treatment Period (Check-in measurement): Predose FEV1 is defined as the time-point prior to Day 1 dosing in the Treatment Period and will be performed pre- and post-bronchodilator administration. Predose FEV1 will be compared to the corresponding baseline measurement. If the best FEV1 measurement at predose at Check-in of the Treatment Period has declined by greater than 20% from the best FEV1 at screening, the visit may be rescheduled up to 3 times, at the discretion of the Investigator.

2. Following Day 1 dosing: At all other spirometry time point, measurements will be performed once. If the value shows a difference of greater than 150 mL

decline than the best FEV1 value collected predose at Check-in, up to 3 measures will be performed.

Consideration should be given, if a patient experiences any change in post Day 1 dose FEV1 from the Day 1 predose FEV1 value (measured following dosing with albuterol) equal to or greater than 20 % and should alert the PI to consider whether individual patients should continue to dose.

Pre- and post-bronchodilator change in activity by time point will be calculated relative to the pre- and post-bronchodilator baseline activity. Baseline is defined as Screening and is patient specific.

7.1.1.4 Quality of Life Assessments

Baseline Dyspnea Index/Transition Dyspnea Index (BDI/TDI):

BDI/TDI has 3 domains (functional impairment, magnitude of task and magnitude of effort) with the values added for a combined focal score.

Dyspnea will be assessed at Check-in of the Treatment Period (considered as the baseline) using the BDI score. The BDI scores range from 0 (very severe impairment) to 4 (no impairment) for each domain with the baseline focal score consisting of the sum of each domain (0 to 12).

Dyspnea throughout the study will be assessed at predose on Days 15 (± 2), 29 (± 2), 43 (± 2), and 54 (± 1) or Day 56 of the Treatment Period using the TDI score. The change from baseline (BDI score) is measured by the TDI score which ranges from -3 (major deterioration) to +3 (major improvement) for each domain with the TDI focal score consisting in the sum of each domain (-9 to +9).

COPD Assessment Test (CAT):

Overall impact of a patient's condition (i.e., COPD) on their life will be assessed. The CAT questionnaire will be completed by patients at Check-in of the Treatment Period, and at predose on Days 15 (± 2), 29 (± 2), 43 (± 2), 54 (± 1) or Day 56. CAT score range from 0 (no impact on daily activities) to 40 (very high impact on daily activity).

7.1.2 Data Summarization and Presentation

Descriptive statistics will be generated using SAS® Version 9.3 (or higher) for the actual values (raw) and relative values (% change from baseline or total) as specified above for each type of biomarker variable. When applicable, the PD biomarkers (BAL, blood, pulmonary function) will be summarized by treatment group and time point using descriptive statistics including sample size (N), arithmetic mean, standard deviation (SD), coefficient of variation (CV%), median, minimum, and maximum.

Figures will be created to display mean measure, level or activity value as a function of time on linear plots with and without SD, as appropriate.

The quality of life parameters reported from the BDI/TDI and CAT questionnaires will be listed and presented descriptively using SAS® Version 9.3 (or higher)

Additional analysis may be performed if deemed appropriate.

8. PHARMACOKINETIC ANALYSIS

This following section is organized based on the exploratory endpoints 6 and 7 in Section 2.2.

8.1 Measurements and Collection Schedule

8.1.1 Blood Sample Collection

PK blood samples for the determination of plasma verproside and picroside II concentrations will be collected in 4 mL pre-chilled evacuated tubes containing K_2EDTA on Days 1 and 54 (± 1) or Day 56 of the Treatment Period prior to dosing (predose) and at 0.167, 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 8, 10, and 12 hours postdose. In addition, predose samples will be collected on Days 15 (± 2), 29 (± 2) and, 43 (± 2) of the Treatment Period.

The sampling schedule and/or collection intervals may be modified based on the results as the study progresses.

Samples must be protected from UV light during collection, processing, and storage.

8.1.1.1 Handling of Time Deviation

For verproside and picroside II PK blood samples, the actual sampling times will be assessed as available.

All concentration data will be included in the calculation of the PK parameters and the individual concentration-time plots (based on actual sample times), as well as in the mean concentration-time plots (based on nominal sample times); however, if there are any significant deviations (i.e., the actual sample time is closer to the next nominal time point than the intended nominal time point), concentration data may be excluded from mean concentration-time plots (based on nominal sample times). However if there are any significant time deviations that are judged to compromise the integrity of the PK results, the PK data for those patients will be handled as described in Section 8.5.1.

8.1.2 Bronchoalveolar Sample Collection

Epithelial brushings samples for the determination verproside and picroside II concentrations will be collected at baseline at Check-in and on Day 55 or 56

The brushings (cellular material) will be collected from each of 4 quadrants of visible subsegments of the right middle or lower lobe. The brushings cell pellet will be stored at -70°C until processed or stored as indicated in the laboratory manual to be provided as a separate document.

Samples must be protected from UV light during collection, processing, and storage.

8.2 Bioanalytical Method

Plasma concentrations of verproside and picroside II will be determined using the bioanalytical method SOP (EDT) methods validated with respect to accuracy, precision, linearity, sensitivity, and specificity at Celerion, Lincoln, Nebraska, USA.

The validated analytical range (lower limit of quantitation [LLOQ] – upper limit of quantitation [ULOQ]) for verproside and picroside II is 50.0 – 20 000 pg/mL.

8.3 Investigational Product and PK Analyte Information

YPL-001 is a botanical drug substance containing a mixture of iridoids from the aerial parts of the plant Speedwell (*Pseudolysimachion rotundum var. subintegrum*). The principal pharmaceutically-active ingredient in YPL-001 is verproside, an iridoid. YPL-001 contains additional iridoids in lesser relative amounts.

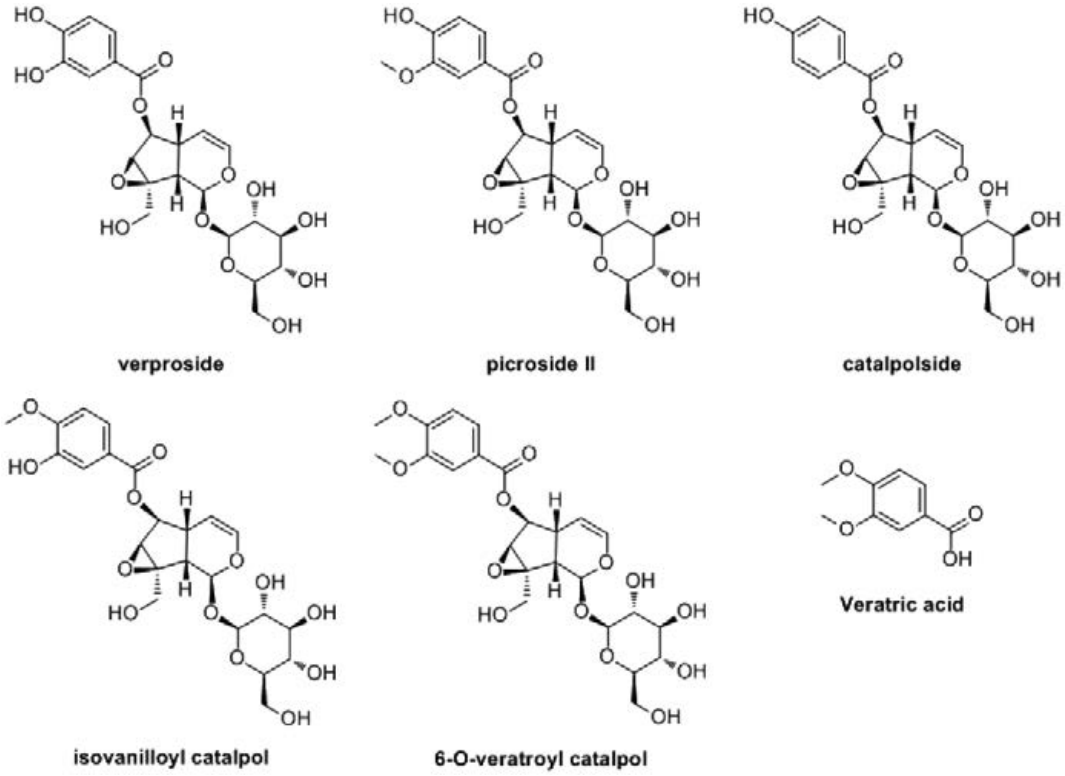
Molecular formulae and the molecular masses of the six constituents of YPL-001 are provided in Table 1.

Table 1 Principle Active Constituents in YPL-001

Generic Name	Molecular Formula	Molecular Weight (g/mol)
Verproside	$C_{22}H_{26}O_{13}$	498.43
Picroside II	$C_{23}H_{28}O_{13}$	512.46
Catalpolside	$C_{22}H_{26}O_{12}$	482.43
Isovanilloyl catalpol	$C_{23}H_{28}O_{13}$	512.46
6-*O*-veratroylcatalpol	$C_{24}H_{28}O_{13}$	526.17
Veratric acid	$C_9H_{10}O_4$	182.17

The structure of verproside and related congeners are provided in Figure 1.

Figure 1 Structure of Verproside and Related Active Compounds in YPL-001



Note that only plasma and BAL verproside and picroside II concentrations are planned for analysis in this current study. However, other components of YPL-001 and its metabolites may also be analyzed, if required. If metabolite data are available, metabolite to parent ratios may be calculated for $AUC_{0\text{-}t}$, AUC_{τ}, and C_{max_ss}.

Any dose dependent PK parameters such as clearance and volume of distribution will need adjustment for the content of verproside in the YPL-001 dose. Verproside content is 28.96 and 57.92 mg for the 80 and 160 mg YPL-001 dose levels, respectively.

8.4 Pharmacokinetic Concentrations

Plasma and BAL concentrations of verproside and picroside II will be determined at the collection times and per the bioanalytic method described in Section 8.1 and Section 8.2, respectively. Plasma concentrations of verproside and picroside II will be used for the calculation of the plasma verproside and picroside II PK parameters. BAL concentrations of verproside and picroside II will be reported, but no PK parameters will be calculated.

8.5 Noncompartmental Pharmacokinetic Analysis and Parameter Calculation

8.5.1 Plasma Pharmacokinetic Parameters

The appropriate noncompartmental PK parameters will be calculated from the plasma verproside and picroside II concentration-time data following administration of YLP-001 on Days 1 and 54 (± 1) or Day 56, as well as predose concentrations in morning of Days 15 (± 2), 29 (± 2), 43 (± 2), and 54 (± 1) or Day 56 using Phoenix® WinNonlin® Version 6.3 or higher. All PK parameters included in the protocol are listed in Table 2 below, and are defined as appropriate for study design. Other PK parameters may be calculated if deemed appropriate and requested by the sponsor and agreed upon by Celerion.

Table 2 Noncompartmental Pharmacokinetic Parameters to be Calculated

Following a Single Dose of YLP-001 - Day 1			
Parameter	**Label to be Used in Post-Text Tables**	**Definition**	**Method of Determination**
AUC_{0-12}	AUC0-12	Area under the drug concentration-time curve (AUC) from time zero to 12 hours.	Calculated using the Linear Trapezoidal with Linear Interpolation Method. May be extrapolated using the terminal elimination rate constant (k_{el}), if last measurable concentration (C_t) occurs prior to 12 hours postdose.
AUC_{0-t}	AUC0-t	AUC from time zero to time t, where t is the time of the C_t. This parameter will be reported only if plasma concentrations fall below the lower limit of quantitation before the last time point prior to the evening drug administration on Day 1 for at least one patient. Otherwise, only AUC_{0-12} will be reported.	Calculated using the Linear Trapezoidal with Linear Interpolation Method.
AUC_{0-inf}	AUCinf	AUC from time 0 extrapolated to infinity.	Calculated as: $AUC_{0-t} + C_t/k_{el}$
C_{max}	Cmax	Maximum observed drug concentration.	Taken directly from bioanalytical data.

Following a Single Dose of YLP-001 - Day 1			
Parameter	**Label to be Used in Post-Text Tables**	**Definition**	**Method of Determination**
t_{max}	tmax	Time of the maximum drug concentration (obtained without interpolation).	Observed
k_{el}	kel	Apparent first-order terminal elimination rate constant, which represents the fraction of drug eliminated per unit time.	Calculated from a semi-log plot of the plasma concentration versus time curve, calculated by linear least-squares regression analysis using the maximum number of points in the terminal log linear phase (e.g., three or more non-zero plasma concentrations).
$t_{½}$	t½	Apparent first-order elimination half-life.	Calculated as: $\ln(2)/k_{el}$
CL/F	CL/F	Apparent total plasma clearance after extravascular administration (verproside only).	Calculated as: $Dose/AUC_{0\text{-}inf}$
V_Z/F	Vz/F	Apparent volume of distribution during the terminal elimination phase after extravascular administration (verproside only).	Calculated as: $Dose/(k_{el} \times AUC_{0\text{-}inf})$

Following Multiple Doses of YLP-001 - Day 54 (± 1) or Day 56			
Parameter	**Label to be Used in Tables**	**Definition**	**Method of Determination**
AUC_{τ}	AUCtau	AUC over the final 12-hour dosing interval (τ) at steady state (e.g., 0-12 hours).	Calculated using the Linear Trapezoidal with Linear Interpolation Method. May be extrapolated using the k_{el}, if C_t occurs prior to 12 hours postdose.
AUC_{0-t}	AUC0-t	AUC from time zero to time t, where t is the time of the C_t.	Calculated using the Linear Trapezoidal with Linear Interpolation Method.
C_{max_ss}	Cmax_ss	Maximum observed plasma concentration during a dosing interval at steady state.	Taken directly from bioanalytical data.
C_{min_ss}	Cmin,ss	Minimum observed/measured non-zero concentration during a dosing interval at steady state.	Taken directly from bioanalytical data.
t_{max_ss}	tmax_ss	Time to reach C_{max_ss} (obtained without interpolation).	Observed
C_{trough}	Ctrough	Plasma concentration observed at the end of a dosing interval at steady state. Presented as predose in the morning Days 15 (± 2), 29 (± 2), 43 (± 2), and 54 (± 2) (following PM dosing on Days 14 (± 2), 28 (± 2), 42 (± 2), and 54 (± 1) or 56, respectively).	Taken directly from bioanalytical data.
C_{avg_ss}	Cavg_ss	Average plasma concentration at steady state.	Calculated as: AUC_{τ}/τ
%Fluc	%Fluc	Percent peak-to-trough fluctuation at steady-state.	Calculated as: $(C_{max\_ss} - C_{min\_ss})/C_{avg\_ss} \times 100$
Swing	Swing	Percent swing at steady-state.	Calculated as: $(C_{max\_ss} - C_{min\_ss})/C_{min\_ss} \times 100$

Following Multiple Doses of YLP-001 - Day 54 (± 1) or Day 56			
Parameter	**Label to be Used in Tables**	**Definition**	**Method of Determination**
k_{el}	kel	Apparent first-order terminal elimination rate constant, which represents the fraction of drug eliminated per unit time.	Calculated from a semi-log plot of the plasma concentration versus time curve, calculated by linear least-squares regression analysis using the maximum number of points in the terminal log linear phase (e.g., three or more non-zero plasma concentrations).
$t_{½}$	t½	Apparent first-order elimination half-life.	Calculated as: $\ln(2)/k_{el}$
CL_{ss}/F	CLss/F	Total body clearance estimated at steady-state after oral administration (verproside only).	Calculated as: $Dose/AUC_{\tau}$
$R_{A,AUC}$	RA,AUC	Accumulation ratio	Calculated as: AUC_{τ} / AUC_{0-12} (on Day 1) If AUC_{0-12} on Day 1 or AUC_{τ} on Day 54 (± 1) or 56 cannot be calculated for a patient, then no $R_{A,AUC}$ value will be presented for that patient.
V_{z_ss}/F	Vz,ss/F	Apparent volume of distribution at steady state.	Calculated as: $(CL_{ss}/F)/k_{el}$

For the calculation of the PK parameters that depended on the dose (CL/F, V_Z/F, CL_{ss}/F, and V_{z_ss}/F) verproside content is 28.96 and 57.92 mg for the 80 and 160 mg YPL-001 dose levels, respectively.

Actual sample times will be used in the calculations. Patients for whom there are insufficient data to calculate the PK parameters (at least 3 consecutive measurable concentrations) will be included in the concentration tables only and excluded from the pharmacokinetic and statistical analyses.

For the calculation of the PK parameters, plasma concentrations below the limit of quantitation (BLQ) prior to the first quantifiable concentration will be set to 0.00 and plasma concentrations BLQ after the first quantifiable concentration will be treated as missing.

Plasma verproside and picroside II C_{trough} concentrations will be presented. Although C_{trough} concentrations are related to the PM dose given on Days 14 (± 2), 28 (± 2), 42 (± 2), and 53 (± 2), they will be labeled and referred with in the TFLs as AM predose time point on Days 15 (± 2), 29 (± 2), 43 (± 2), and 54 (± 1) or Day 56.

For the calculation of summary statistics and PK parameters, BLQ plasma concentrations will generally be set to 0 prior to the first quantifiable concentration on each study day and to missing thereafter. Based on the reported mean $t_{½}$ of plasma verproside and picroside II following the BID administration of 80 mg YLP-001 in a previous multiple ascending dose (MAD) study in healthy subjects, C_{trough} that are BLQ may be expected in this study. Therefore, C_{trough} BLQ concentrations measured at predose on Days 15 (± 2), 29 (± 2), 43 (± 2), and 54 (± 1) or Day 56 will be set to 0 for the calculations of summary statistics and PK parameters.

The k_{el} will be determined using linear regressions composed of least 3 data points. The k_{el} will not be assigned if 1) the terminal elimination phase is not apparent, 2) if t_{max} is one of the 3 last data points, or 3) if the R^2 value is less than 0.8. For the analysis on Day 1, the k_{el} will only be reported if the $t_{½}$ of verproside or picroside II can be appropriately estimated from a 12-hour sampling period following dosing. In cases where the k_{el} interval is not assigned, the values of $AUC_{0\text{-inf}}$, $t_{½}$, CL/F, V_z/F, AUC_{τ}, CL_{ss}/F, V_{z_ss}/F, and $R_{A,AUC}$, as applicable, are considered not calculable and will not be reported. Wherever the resulting $t_{½}$ is more than half as long as the sampling interval, the k_{el} values and associated parameters ($AUC_{0\text{-inf}}$, $t_{½}$, CL/F, V_z/F, AUC_{τ}, CL_{ss}/F, V_{z_ss}/F, and $R_{A,AUC}$ as applicable) may not be presented as judged appropriate and in accordance wih Celerion SOPs.

All available data will be included in the concentration and PK parameter tables to the extent possible. Patients will be excluded from the PK population if they significantly violate a protocol inclusion or exclusion criteria, deviate significantly from the protocol, or if data are unavailable or incomplete, which may influence the PK analysis.

Except if otherwise specified, available concentration and PK data of each patient will be included in the summary statistics and statistical comparisons for PK parameters.

Data from patients who experience emesis within 1.5 hours following YPL-001 dosing (i.e., a period of time equal to 2 times the estimated t_{max} of verproside and picroside II) during the PK sampling periods (i.e., after AM dosing on Days 1 or 54 [± 1] or Day 56, as appropriate) may be excluded from the summary statistics for the given day and from the statistical comparison of PK parameters.

Any patient or data excluded from the PK analysis, summary statistics or statistical analysis will be identified, along with their reason for exclusion, in the CSR.

8.6 Data Summarization and Presentation

All plasma and BAL verproside and picroside II concentrations and plasma PK parameters descriptive statistics will be generated using SAS® Version 9.3 or higher.

Plasma and BAL concentrations of verproside and picroside II will be presented with the same level of precision as received from the bioanalytical laboratory. Summary statistics, including N, arithmetic mean, SD, CV%, median, minimum, and maximum will be calculated for all nominal concentration time points. The plasma and BAL concentrations of verproside and picroside II will be tabulated by treatment and listed by nominal sample time (Day/hour) and patient for all patients in the PK population. Patients included in the PK population but excluded from the PK per-protocol population will be included in the concentration table listings, but will be excluded from the summary statistics and noted as such in the tables. All BLQ values will be presented as "BLQ" in the concentration table listings and footnoted accordingly. For the calculation of summary statistics, BLQ concentrations will be treated as missing or 0 per defined in Section 8.5.1.

The level of precision for each verproside and picroside II plasma PK parameter will be determined based on the output values, except for C parameters (i.e., C_{max}, C_{max_ss}, C_{min_ss}, C_{avg_ss}, and C_{trough}) which will be presented with the same precision as the concentrations. For instance, t_{max}, t_{last}, $t_{½}$, %Fluc, and Swing and may be presented with 2-3 decimals and AUCs, k_{el}, CL/F, V_z/F, CL_{ss}/F, and V_{z_ss}/F with 3-5 significant digits. Summary statistics, including N, arithmetic mean (mean), SD, CV%, median, minimum, maximum will be calculated for all verproside and picroside II PK parameters. In addition, geometric means (geo. mean) and geometric CV% (geo. CV%) will be presented for all C and AUC parameters. PK parameters will be tabulated by treatment and listed by patient and parameter for all patients in the PK population. Patients included in the PK population but excluded from the PK per-protocol population will be included in the PK parameter table listings, but will be excluded from the summary statistics and noted as such in the tables.

The level of precision for the summary statistics on plasma and BAL concentrations and plasma PK parameters will be the following:

- N: integer
- Minimum/Maximum: same precision as the individual values
- Mean/Median/Geo. Mean: 1 more level of precision than the individual values
- SD: 1 more level of precision than AM/median
- CV% and Geo.CV%: 1 decimal place.

Arithmetic mean and individual plasma verproside and picroside II concentrations versus time profiles on Days 1 and 54 (± 1) or Day 56 will be presented on the same plot and on linear and semi-log scales. Arithmetic mean and individual plasma verproside and picroside II C_{trough} versus time profiles will be presented on a different

plot than for Days 1 and 54 (± 1) or Day 56 and on a linear scale. Linear mean plots will be presented with and without SD and semi-log mean plots without SD.

Steady-state will be assessed by visual inspection of predose plasma C_{trough} values on Days 15 (± 2), 29 (± 2), 43 (± 2), and 54 (± 1) or Day 56 following multiple oral dose administration of YPL-001. C_{trough} values will be summarized by nominal day (i.e., 15, 29, 43, and 54), and footnotes may be included as necessary to clarify actual sampling day windows. Additional summaries and plots by actual day may be presented if deemed appropriate (e.g., significant trends observed) and requested by the Sponsor.

8.7 Statistical Analysis of Pharmacokinetic Parameters

An estimate of the relative systemic exposure after multiple dose administration of YLP-001 using plasma verproside and picroside II AUC_{τ}, $AUC_{0\text{-}t}$, and C_{max_ss} on Day 54 (± 1) or Day 56 will be performed by dose-normalized (to 80 mg YLP-001) ratio analysis (i.e., parameter values for 160 mg versus parameter values for 80 mg; Treatment B Versus Treatment A), expressing the geometric mean ratio (GMR) and 90% confidence interval (CI) of the GMR.

The ANOVA analysis will be performed using the following SAS® code:

```
PROC MIXED;
CLASS TREATMENT SUBJECT;
MODEL PK_PARAMETER = TREATMENT;
ESTIMATE "B vs A" TREATMENT -1 1  / cl alpha=0.1 e;
LSMEANS TREATMENT / cl;
```

Note: Parameters will be dose-normalized to 80 mg YLP-001, prior to analysis.

Additional analyses may be performed as deemed necessary upon review of the data and/or upon Sponsor's request.

9. PHARMACOKINETIC/PHARMACODYNAMIC RELATIONSHIP

There are no PK/PD analyses planned at this time. The PK/PD relationship(s) may be explored (e.g., graphically using scatter plots and an appropriate regression model), upon Sponsor's request.

10. SAFETY

No inferential statistics are to be performed for safety analysis.

The following are descriptions of the summary tables that will be created to assess safety. Table shells are also provided in Section 11. In the summary tables, N will be presented without decimal, minimum/maximum in same precision as in the database, mean/median in one more decimal than minimum/maximum, and SD in one more decimal than mean/median.

Where individual data points are missing because of dropouts or other reasons, the data will be summarized based on reduced denominators.

When change from baseline is calculated, baseline is the last schedule assessment before dosing, also including rechecks and unscheduled assessments, whichever is later. Rechecks, unscheduled assessments and early termination measurements taken after first dosing will not be used in the summarization.

10.1 Subject Discontinuation

Frequency counts will be tabulated by treatment and total for the number of subjects who were dosed, the number of subjects who completed, and the number of subjects who discontinued early, along with the reason for discontinuation. Individual patient's treatment along with their study completion status and date will be provided in a listing.

10.2 Demographics

Descriptive statistics (N, mean, SD, minimum, median, and maximum) will be calculated for continuous demographic variables (age, weight, height, and body mass index [BMI]) and frequency counts will be tabulated for categorical demographic variables (gender, race, and ethnicity) by treatment and total.

10.3 Exposure to Study Drug

For each treatment, exposure to study drug will be summarized through frequency count (number of patients) and percentage by AM/PM of each study day for each scheduled dose.

10.4 Adverse Events

Adverse events will be coded with MedDRA dictionary version 18.0.

A treatment-emergent adverse event (TEAE) is defined as an AE that is starting or worsening at the time of or after study drug administration. All AEs collected by the clinics and recorded in the CRF are captured in the database and will be listed in by-patient data listings. Only TEAEs will be summarized in the report. Data will be summarized by SOC and preferred term.

Summary tables will include the number and the percentage of patients reporting the TEAE and percentage of patients dosed, the number of TEAEs and the percentage of total TEAEs. These results will be summarized by treatment and total. The number of patients reporting each TEAE and number of TEAEs will also be summarized by treatment, severity, and relationship to treatment.

A by-patient AE data listing, including verbatim term, preferred term, treatment, severity, outcome, and relationship to treatment, will be provided.

10.5 Clinical Laboratory Tests (Serum Chemistry, Hematology, Urinalysis)

Clinical laboratory assessments (serum chemistry, hematology, and urinalysis) will be performed at screening, Check-in, Day 29 (± 2), and Day 55 or Day 56 or early termination.

Descriptive statistics (N, mean, SD, median, minimum, and maximum) will be reported for numeric clinical laboratory results and change-from-baseline values by treatment and time point of collection. Baseline value will be the Check-in value and is the last non-missing measurement prior to dosing. Postdose recheck values will not be used for calculation of descriptive statistics. Shift tables describing out-of-range shifts from baseline (in frequency counts) will be created. Out-of-normal-range and clinically significant laboratory values will be listed by patient. Early termination record will be excluded from the summary. All laboratory results will be listed in by-patient data listings. Because clinical laboratory test results will come from multiple sites with different reference ranges, out-of-range tables and shift tables will still use original units for presentation. For mean and mean change summary tables, the results and ranges will be converted to SI units for presentation. In the lab listings, both original units and SI units will be presented.

10.6 Vital Signs and Pulse Oximetry

Vital signs include systolic and diastolic blood pressure, pulse rate, respiratory rate, and body temperature. They will be measured at screening, Check-in, predose and 1, 2, 6 hours postdose of Day 1, Days 15 (± 2), 29 (± 2), 43 (± 2), and predose and 1, 2, 6, 12 hours postdose of Day 55 or Day 56 or early termination. Pulse oximetry will be measured at screening, Check-in, and Day 55 or Day 56 or early termination. All vital signs and pulse oximetry results will be presented in a by-patient listing.

Descriptive statistics (N, mean, SD, median, minimum, and maximum) will be provided for vital sign variables and change from baseline at each assessment time point by treatment. Baseline value will be the Day 1 predose value and is the last observation, including rechecks, obtained prior to dosing. For pulse oximetry, baseline value will be the Check-in value and is the last observation, including rechecks, obtained prior to dosing. For the purposes of summary statistics calculations, recheck values will not be used in the determination of postdose values. Early termination record will be excluded from the summary.

10.7 12-lead Electrocardiogram

Twelve-lead ECGs will be performed at screening, Check-in, Day 29 (± 2), and Day 55 or Day 56 or early termination. All ECG results will be presented in a by-patient data listing.

Descriptive statistics (N, mean, SD, median, minimum, and maximum) will be provided for ECG variables (HR, PR, QRS, QT, and QTcB [Bazett's correction]) and

change from baseline at each assessment time point by treatment. Baseline value will be the Check-in value and is the last observation, including rechecks, obtained prior to dosing. For the purposes of summary statistics calculations, recheck values will not be used in the determination of postdose values. ECG results will also be classified as normal, abnormal, not clinically significant (ANCS), and abnormal, clinically significant (ACS). A normal-abnormal shift table will be created to describe shifts from predose baseline for postdose time points. Early termination record will be excluded from the summary.

10.8 Concomitant Medications

Concomitant medications will be coded with the WHO Drug Dictionary 01MAR2015 version and presented in the data listings.

10.9 Physical Examination

Physical examination will occur at screening, Check-in, Day 29, and Day 55 or Day 56 early termination. Abnormal physical examination findings at screening will be reported as medical history. Any clinically significant changes compared to screening will be recorded as an AE.

10.10 Medical History

Medical history will be listed by patient.

11. SUMMARY TABLES AND FIGURES

Summary tables and figures are numbered following the International Conference on Harmonization (ICH) structure but may be renumbered as appropriate during the compilation of the tables and figures for the CSR. Please note that all Symptom Monitoring, PD, PK, PK/PD (if applicable), and Safety summary tables and figures will be generated using SAS® Version 9.3 or higher.

The following are lists of TFLs numbers and titles that will be included within the CSR.

11.1 In-text Summary Tables and Figures

The following is a list of table and figure titles that will be included in the text of the CSR. Tables and figures will be numbered appropriately during compilation of the CSR.

Section 10:

Table 10-1 Disposition Summary by Treatment

Section 11 (Symptom Monitoring, PD, PK, PK/PD (if applicable):

Note to programmer: the following list of in-text tables and figures may be modified and numbering adjusted.

Symptom Monitoring

Pharmacodynamics

11.2 Section 14 Summary Tables and Figures

The following is a list of table and figure titles that will be included in Section 14 of the CSR.

14.1 Demographic Data Summary Tables

Table 14.1.1 Disposition of Patients

Table 14.1.2 Demographic Summary

Table 14.1.3 Summary of Exposure to Study Drug

14.2 Symptom Monitoring, Pharmacodynamic, Pharmacokinetic, and Pharmacokinetic/Pharmacodynamic (if applicable) Data Summary Tables and Figures

Note to programmer: the following list of tables and figures may be modified and numbering adjusted.

Symptom Monitoring

14.2.1 Symptom Monitoring Tables

PEF

Table 14.2.1.1 Summary and Change From Baseline of Main Peak Expiratory Flow (PEF) Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Symptoms of COPD Exacerbation

Table 14.2.1.2 Categorical Summary of Sputum Quantity, Color, and Consistency for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Table 14.2.1.3 Categorical Summary of Cough, Wheeze, Sore Throat, Nasal Congestion, Nasal Discharge, and Body Temperature Above 100°F for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Table 14.2.1.4 Categorical Summary of Symptom Score for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Table 14.2.1.5 Summary and Change From Baseline of Symptom Score for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral

YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Dyspnea

Table 14.2.1.6 Categorical Summary of Modified Borg Dyspnea Scale Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Table 14.2.1.7 Summary and Change From Baseline of Modified Borg Dyspnea Scale Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Activity

Table 14.2.1.8 Categorical Summary of 12-Item Questionnaire of Duke Activity Status Index (DASI) Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Table 14.2.1.9 Summary and Change From Baseline of Calculated Score from 12-Item Questionnaire of Duke Activity Status Index (DASI) Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Pharmacodynamics

14.2.2 Pharmacodynamic Tables

BAL Biomarkers

Table 14.2.2.1 Summary of BAL WBC Counts and Differential Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Raw, % Change from Baseline, and % of WBC)

Table 14.2.2.2 Summary of BAL Inflammatory Marker Concentrations Following Multiple Oral YPL 001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Table 14.2.2.3 Summary of BAL Inflammatory Marker Concentration Changes Following Multiple Oral YPL 001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Raw and % Change from Baseline)

Blood Biomarkers

Table 14.2.2.4 Summary of Blood WBC Counts and Differential Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Raw and % of WBC)

	(COPD) Assessment Test (CAT) Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)
Table 14.2.2.16	Categorical Summary of Level of Sleepiness and Level of Energy from Chronic Obstructive Pulmonary Disease (COPD) Assessment Test (CAT) Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)
Table 14.2.2.17	Summary and Change From Baseline of Individual Score (0 – 5) and Total Score (0 – 40) from Chronic Obstructive Pulmonary Disease (COPD) Assessment Test (CAT) Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

14.2.3 Pharmacodynamic Figures

Note to programmer: For all the following figures, the biomarker type will be included at the top of each graph. This will be used by the clinical pharmacologist to construct multi-panel in-text figures.

BAL Biomarkers

No figures are planned.

Blood Biomarkers

Note: where necessary, samples on Day 54 (± 1) or Day 56 will be presented as Day 54 with a footnote indicating this is Day 54 (± 1) or Day 56.

Inflammatory Cells –% Change from Baselines Versus Time

Figure 14.2.3.1	Mean (SD) Blood WBC Counts Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)
Figure 14.2.3.2	Mean Blood WBC Counts Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)
Figure 14.2.3.3	Mean (SD) Blood Monocyte Counts Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)
Figure 14.2.3.4	Mean Blood Monocyte Counts Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.5 Mean (SD) Blood Lymphocyte Counts Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.6 Mean Blood Lymphocyte Counts Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.7 Mean (SD) Blood Neutrophil Counts Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.8 Mean Blood Neutrophil Counts Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.9 Mean (SD) Blood Eosinophil Counts Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.10 Mean Blood Eosinophil Counts Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Biomarkers – % Change from Baseline Versus Time

Figure 14.2.3.11 Mean (SD) Blood CRP Concentration Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.12 Mean Blood CRP Concentration Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.13 Mean (SD) Blood Fibrinogen Concentration Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.14 Mean Blood Fibrinogen Concentration Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.25 Mean (SD) Blood IL-8 Concentration Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.26 Mean Blood IL-8 Concentration Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.27 Mean (SD) Blood IL-13 Concentration Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.28 Mean Blood IL-13 Concentration Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.29 Mean (SD) Blood MCP-1 Concentration Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.30 Mean Blood MCP-1 Concentration Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.31 Mean (SD) Blood MMP-9 Concentration Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Figure 14.2.3.32 Mean Blood MMP-9 Concentration Changes from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Pulmonary Function Measurement

Note: where necessary, samples on Day 55 or 56 will be presented as Day 56 with a footnote indicating this is Day 55 or 56.

% Change from Baseline Versus Time

Figure 14.2.3.33 Mean (SD) FEV1 Pre- and Post-Bronchodilator Change in Activity from Baseline Versus Time Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Linear Scale)

Quality of Life

No figures are planned.

Pharmacokinetics

14.2.4 Pharmacokinetic Tables

14.2.4.1 Plasma Verproside Tables

11.3 Section 16 Data Listings

Note: Hepatitis and HIV results that are provided by the clinical laboratory will not be presented in subject data listings and will not be included in any database transfer.

Data listings are numbered following the ICH structure but may be renumbered as appropriate during the compilation of the tables and figures for the CSR. The following is a list of appendix numbers and titles that will be included as data listings.

16.1. Study Information

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

16.2. Subject Data Listings

16.2.1. Subject Discontinuation

Appendix 16.2.1 Study Completion/Early Termination

16.2.2. Protocol Deviations

Appendix 16.2.2 Protocol Deviations

16.2.3. Patients Excluded From the Pharmacodymanic and Pharmacokinetic Analyses

Appendix 16.2.3 Patients Excluded from the Pharmacodynamic and Pharmacokinetic Analyses

Note: Appendices 16.2.2 and 16.2.3 are generated in Microsoft® Word® for inclusion in the CSR.

16.2.4. Demographic Data

Appendix 16.2.4.1 Subject Information
Appendix 16.2.4.2 Demographics
Appendix 16.2.4.3 Physical Examination
Appendix 16.2.4.4 Chest X-Ray
Appendix 16.2.4.5 Medical History
Appendix 16.2.4.6 Substance Use

16.2.5. Compliance and Drug Concentration Data

Appendix 16.2.5.1 Subject Eligibility
Appendix 16.2.5.2 Study Drug Administration
Appendix 16.2.5.3 Drug Accountability
Appendix 16.2.5.4 Tiotropium and Albuterol Administration
Appendix 16.2.5.5.1 Bronchoscopy and BAL Biomarkers (I of II)

Appendix 16.2.5.5.2 Bronchoscopy and BAL Biomarkers (II of II)
Appendix 16.2.5.6 Blood Biomarker Samples
Appendix 16.2.5.7 Pharmacokinetic Sampling
Appendix 16.2.5.8 Prior and Concomitant Medications

16.2.6. Individual Symptom Monitoring, Pharmacodynamic, Pharmacokinetic, and Response Data

Note to programmer: the following list of listings may be modified and numbering adjusted.

16.2.6.1 Symptom Monitoring

Appendix 16.2.6.1.1 Peak Expiratory Flow and Breathlessness (Modified Borg Dyspnea Scale)
Appendix 16.2.6.1.2 Symptoms of COPD Exacerbation (I of II)
Appendix 16.2.6.1.3 Symptoms of COPD Exacerbation (II of II)
Appendix 16.2.6.1.4 Duke Activity Status Index (DASI) Scores

16.2.6.2 Pharmacodynamics

Appendix 16.2.6.2.1 BAL Inflammatory Cells Counts
Appendix 16.2.6.2.2 BAL Inflammatory Marker Concentrations
Appendix 16.2.6.2.3 Blood Inflammatory Cells
Appendix 16.2.6.2.4 Blood Inflammatory Marker Concentrations
Appendix 16.2.6.2.5 Individual Blood WBC Counts Changes from Baseline Versus Time Following Single and Multiple Oral YPL-001 Doses or Placebo in COPD Patients (Linear Scale)
Appendix 16.2.6.2.6 Individual Blood Monocyte Counts Changes from Baseline Versus Time Following Single and Multiple Oral YPL-001 Doses or Placebo in COPD Patients (Linear Scale)
Appendix 16.2.6.2.7 Individual Blood Lymphocyte Counts Changes from Baseline Versus Time Following Single and Multiple Oral YPL-001 Doses or Placebo in COPD Patients (Linear Scale)
Appendix 16.2.6.2.8 Individual Blood Neutrophil Counts Changes from Baseline Versus Time Following Single and Multiple Oral YPL-001 Doses or Placebo in COPD Patients (Linear Scale)
Appendix 16.2.6.2.9 Individual Blood Eosinophil Counts Changes from Baseline Versus Time Following Single and Multiple

Appendix 16.2.8.7	Vital Signs
Appendix 16.2.8.8	12-Lead Electrocardiogram
Appendix 16.2.8.9	Telephone Contact

12. TABLE SHELLS

The following table shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the tables that will be presented and included in the final report.

12.1 In-text Table Shells

Note to programmer: Formatting and content of PK and PD in-text tables may be modified based on provided data.

Table 10-1 Disposition Summary by Treatment

Disposition	Treatment A YPL-001 80 mg	Treatment B YPL-001 160 mg	Treatment C Placebo	Total
Dosed	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Completed Study	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Dropped from Study	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Adverse Event	X (X%)	X (X%)	X (X%)	X (X%)
Protocol Deviation	X (X%)	X (X%)	X (X%)	X (X%)
Other	X (X%)	X (X%)	X (X%)	X (X%)
Etc.	X (X%)	X (X%)	X (X%)	X (X%)

Percentage is based on number of patients dosed in a given dose.

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.1.1 and Appendix 16.2.1

Table 11-1 Summary and Change From Baseline of Main Peak Expiratory Flow (PEF) Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients

Day	Main Peak Expiratory Flow (L/min)					
	Treatment A YPL-001 80 mg		Treatment B YPL-001 160 mg		Treatment C Placebo	
	Result	Change from Baseline	Result	Change from Baseline	Result	Change from Baseline
1	XXX± XXX (N=X)	NA	XXX± XXX (N=X)	NA	XXX± XXX (N=X)	NA
2	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
3	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
4	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
5	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
< >	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)

Presented as arithmetic mean ± SD, baseline is Day 1.

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.1.1

Table 11-2.1 Summary of Sputum Quantity for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients

Day	Sputum Quantity					
	Treatment A YPL-001 80 mg		Treatment B YPL-001 160 mg		Treatment C Placebo	
	Less than 1 tbs	1 tbs or more	Less than 1 tbs	1 tbs or more	Less than 1 tbs	1 tbs or more
1	XX % (N=X)	XX % (N=X)	XX % (N=X)	XX % (N=X)	XX % (N=X)	XX % (N=X)
2	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
3	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
4	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
5	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
< >	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)

Less than 1 tbs includes none and less than 1 tbs.
1 tbs or more includes 1 tbs or more and greater than ¼ cup.
Percentage is based on number of patients in the binary arrangement.

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.1.2

Table 11-2.2 Summary of Sputum Color for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients

Day	Sputum Color					
	Treatment A YPL-001 80 mg		Treatment B YPL-001 160 mg		Treatment C Placebo	
	White	Not White	White	Not White	White	Not White
1	XX % (N=X)	XX % (N=X)	XX % (N=X)	XX % (N=X)	XX % (N=X)	XX % (N=X)
2	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
3	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
4	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
5	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
< >	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)

Not white includes yellow, green, and brown colors.
Percentage is based on number of patients in the binary arrangement.

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.1.2

Table 11-2.3 Summary of Sputum Consistency for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients

Day	Sputum Consistency					
	Treatment A YPL-001 80 mg		Treatment B YPL-001 160 mg		Treatment C Placebo	
	Watery	Not Watery	Watery	Not Watery	Watery	Not Watery
1	XX % (N=X)	XX % (N=X)	XX % (N=X)	XX % (N=X)	XX % (N=X)	XX % (N=X)
2	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
3	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
4	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
5	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
< >	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)

Not watery includes thin and thick consistency.
Percentage is based on number of patients in the binary arrangement.

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.1.2

Table 11-3.1 Categorical Summary of Symptom Score for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients

Day	Treatment	N	Symptom Score of COPD Symptoms							
			0	0.5	1	1.5	2	2.5	3	3.5
1	A	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
2	A	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
< >	< >	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)

Symptom severity score: Normal (0-0.5), Mild (1-1.5), Moderate (2-2.5), Severe (3-3.5)

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.1.4

Table 11-3.2 Summary and Change From Baseline of Symptom Severity Score for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients

Day	Symptom Severity Score					
	Treatment A YPL-001 80 mg		Treatment B YPL-001 160 mg		Treatment C Placebo	
	Result	Change from Baseline	Result	Change from Baseline	Result	Change from Baseline
1	XXX± XXX (N=X)	NA	XXX± XXX (N=X)	NA	XXX± XXX (N=X)	NA
2	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
3	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
4	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
5	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
< >	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)

Presented as arithmetic mean scores ± SD, baseline is Day 1.
Symptom severity score: Normal (0-0.5), Mild (1-1.5), Moderate (2-2.5), Severe (3-3.5)

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.1.5

Table 11-4 Summary and Change From Baseline of Modified Borg Dyspnea Scale Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients

Day	Breathlessness Indicator					
	Treatment A YPL-001 80 mg		Treatment B YPL-001 160 mg		Treatment C Placebo	
	Result	Change from Baseline	Result	Change from Baseline	Result	Change from Baseline
1	XXX± XXX (N=X)	NA	XXX± XXX (N=X)	NA	XXX± XXX (N=X)	NA
2	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
3	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
4	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
5	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
< >	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)

Presented as arithmetic mean scores ± SD, baseline is Day 1.
Breathlessness score: None (0), very mild (0.5), less mild (1), mild (2), more mild (3), less moderate (4), moderate (5), more moderate (6), less severe (7), severe (8), more severe (9), extreme (10)

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.1.7

Table 11-5 Summary and Change From Baseline of Calculated Score from 12-Item Questionnaire of Duke Activity Status Index (DASI) Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients

Day	DASI Score					
	Treatment A YPL-001 80 mg		Treatment B YPL-001 160 mg		Treatment C Placebo	
	Result	Change from Baseline	Result	Change from Baseline	Result	Change from Baseline
1	XXX± XXX (N=X)	NA	XXX± XXX (N=X)	NA	XXX± XXX (N=X)	NA
2	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
3	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
4	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
5	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
< >	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)

Presented as arithmetic mean ± SD, baseline is Day 1.
DASI score ranged from 0 to 58.2

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.1.9

Table 11-6 Summary of BAL WBC and Differential Following Multiple Oral YPL 001 Doses of 80 mg and 160 mg and Placebo in COPD Patients – Day 55 or Day 56 (% Change from Baseline)

BAL Inflammatory Cell	% Change from Baseline		
	Treatment A YPL-001 80 mg	Treatment B YPL-001 160 mg	Treatment C Placebo
WBC	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
Macrophage	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
Lymphocyte	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
Neutrophil	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)
Eosinophil	XX ± XX (N=X)	XX ± XX (N=X)	XX ± XX (N=X)

Presented as arithmetic mean ± SD, baseline is at Check-in.
WBC = White blood cell

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.2.1

Table 11-7 Summary of BAL Inflammatory Marker Concentration Changes Following Multiple Oral YPL 001 Doses of 80 mg and 160 mg and Placebo in COPD Patients –Day 55 or Day 56 (% Change from Baseline)

BAL Inflammatory Biomarkers	% Change from Baseline		
	Treatment A YPL-001 80 mg	Treatment B YPL-001 160 mg	Treatment C Placebo
TNF-α	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
IL-1β	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
IL-4	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
IL-5	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
IL-6	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
IL-8	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
IL-13	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
MPO	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
Neutrophil Elastase	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
MCP-1	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
MMP-9	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)

Presented as arithmetic mean ± SD, baseline is at Check-in.

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.2.3

Table 11-8 Summary and Change From Baseline of Pre-Bronchodilator Spirometric Functions Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients

Parameter/Day	Actual Value					
	Treatment A YPL-001 80 mg		Treatment B YPL-001 160 mg		Treatment C Placebo	
	Result	Change from Baseline	Result	Change from Baseline	Result	Change from Baseline
FEV_1 (L)/Screen	XXX± XXX (N=X)	NA	XXX± XXX (N=X)	NA	XXX± XXX (N=X)	NA
Check-in	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
15 (± 2)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
29 (± 2)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
43 (± 2)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
55 or 56	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)

Presented as arithmetic mean ± SD, baseline is at Screening.
FEV_1 (L) = forced expiratory volume in one second, FVC (L) = forced vital capacity, IC (L) = inspiratory capacity

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.2.7

Programmer note: Present FEV_1, FVC, FEV_1/FVC, and IC.
If space is limiting, Day "55 or 56" may be presented as "56" with a footnote indicating "Day 55 or 56".

Table 11-9 Change From Baseline of Combined Focal Score (-9 – +9) from Transition Dyspnea Index (TDI) Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients

Day	Combined Focal Score (-9 – +9)		
	Treatment A YPL-001 80 mg	**Treatment B YPL-001 160 mg**	**Treatment C Placebo**
15 (± 2)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
29 (± 2)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
43 (± 2)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
54 (± 1) or 56	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)

Presented as arithmetic mean ± SD
TDI has 3 domains (functional impairment, magnitude of task, and magnitude of effort).
The change from baseline is measured by the TDI score which ranges from -3 (major deterioration) to +3 (major improvement) for each domain with the TDI focal score consisting in the sum of each domain (-9 to +9).

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.2.12

Programmer note: If space is limiting, Day "54 (± 1) or 56" may be presented as Day "54" with a footnote indicating this is "Day 54 (± 1) or 56".

Table 11-10 Summary and Change From Baseline of Total Score (0 – 40) from Chronic Obstructive Pulmonary Disease (COPD) Assessment Test (CAT) Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients

Day	CAT Total Score					
	Treatment A YPL-001 80 mg		Treatment B YPL-001 160 mg		Treatment C Placebo	
	Result	Change from Baseline	Result	Change from Baseline	Result	Change from Baseline
Check-in	XXX± XXX (N=X)	NA	XXX± XXX (N=X)	NA	XXX± XXX (N=X)	NA
15 (± 2)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
29 (± 2)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
43 (± 2)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)
54 (± 1) or 56	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)	XXX± XXX (N=X)

Presented as arithmetic mean ± SD, baseline is at Check-in.
CAT items are Cough, Mucus Production, Chest Tightness, Breathlessness, Activities, Confidence, Sleepiness, and Energy. Each has 0 to 5 scores so total has 0 to 40 scores (higher score indicates worse symptom).

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.2.17

Programmer note: If space is limiting, Day "54 (± 1) or 56" may be presented as Day "54" with a footnote indicating this is "Day 54 (± 1) or 56".

Note that in-text Tables 11-12, -15, and -16 will be in a similar format as for Table 11-11:

Table 11-11 Summary of Plasma Verproside Pharmacokinetic Parameters Following Single Oral YPL-001 Doses of 80 mg and 160 mg in COPD Patients – Day 1

Verproside Pharmacokinetic Parameters	Treatment A YPL-001 80 mg	Treatment B YPL-001 160 mg
$AUC_{0\text{-}12}$ (pg*hr/mL)[a]	XXX (XXX) (N=X)	XXX (XXX) (N=X)
$AUC_{0\text{-}t}$ (pg*hr/mL)[a]	XXX (XXX) (N=X)	XXX (XXX) (N=X)
$AUC_{0\text{-}inf}$ (pg*hr/mL)[a]	XXX (XXX) (N=X)	XXX (XXX) (N=X)
C_{max} (pg/mL)[a]	XX (XX) (N=X)	XXX (XXX) (N=X)
t_{max} (hr)[b]	XXX (XXX, XXX) (N=X)	XXX (XXX, XXX) (N=X)
t_{last} (hr)[b]	XXX (XXX, XXX) (N=X)	XXX (XXX, XXX) (N=X)
k_{el} (1/hr)[c]	XXX± XXX (N=X)	XXX± XXX (N=X)
$t_{½}$ (hr)[c]	XXX± XXX (N=X)	XXX± XXX (N=X)
CL/F (L/hr)[c]	XXX± XXX (N=X)	XXX± XXX (N=X)
V_z/F (L)[c]	XXX± XXX (N=X)	XXX± XXX (N=X)
$R_{A,AUC}$[c]	XXX± XXX (N=X)	XXX± XXX (N=X)

[a]: Presented as geo. mean (geo. CV%)
[b]: Presented as median (minimum, maximum)
[c]: Presented as arithmetic mean ± SD

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Tables 14.2.4.1.3 and 14.2.4.1.5

Note to Programmer: For verproside and picroside II tables on Day 54 (± 1) or 56 the PK parameters will be: AUC_{τ}, $AUC_{0\text{-}t}$, C_{max_ss}, t_{max_ss}, C_{min_ss}, t_{last}, $C_{trough,}$ C_{avg_ss}, %Fluc, Swing, k_{el}, $t_{½}$, CL_{ss}/F, $V_{z\_ss/F}$, and $R_{A,AUC.}$Note that in-text Table 11-17 will be in a similar format as for Table 11-13:

Table 11-13 Statistical Comparisons of Dose-Normalized Plasma Verproside Pharmacokinetic Parameters Following Multiple Oral YPL-001 Doses of 160 mg Versus Multiple Oral YPL-001 Doses of 80 mg and in COPD Patients – Day 54 (± 1) or Day 56 (Treatment B Versus Treatment A)

Verproside Pharmacokinetic Parameter	Geometric LSM		Geometric Mean Ratio (%)	90% Confidence Intervals
	Treatment B (test, N=X)	Treatment A (reference, N=X)		
AUC_{τ} (pg*hr/mL)	XX	XX	XX	XX – XX
$AUC_{0\text{-}t}$ (pg*hr/mL)	XX	XX	XX	XX – XX
C_{max_ss} (pg/mL)	XX	XX	XX	XX – XX

Parameters were dose-normalized (to 80 mg YLP-001) and ln-transformed prior to analysis.
Geometric least square means (LSMs) were calculated by exponentiating the LSM from the ANOVA.
% Geometric Mean Ratio = 100 × (test/reference)
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.4.1.8

Note that in-text Table 11-18 will be in a similar format as for Table 11-14:

Table 11-14 Epithelial Brushing Verproside Concentrations Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg in COPD Patients – Baseline and Day 55 or 56 (Treatments A and B)

Time	Verproside Concentration (pg/mL)	
	Treatment A YPL-001 80 mg (N=X)	**Treatment B YPL-001 160 mg (N=X)**
Check-in (Baseline)	XXX ±XXX	XXX ± XXX
Day 55 or 56	XXX ± XXX	XXX ± XXX

Presented as arithmetic mean ± SD

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Source: Table 14.2.4.3.1

Table 12-1 Incidence of Treatment-Emergent Adverse Events

Adverse Events*	Treatment A YPL-001 80 mg	Treatment B YPL-001 160 mg	Treatment C Placebo	Total
Number of Patients Dosed	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Number of Patients With Adverse Events	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
System Organ Class 1	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.
*Adverse events are coded using MedDRA® Version 18.0.

Source: Table 14.3.1.1

Programmer note: Present TEAEs ordered by decreasing frequency of SOC and then preferred term in the Total column.

12.2 Post-text Table Shells

Note to programmer: Formatting and content of post-text tables may be modified based on provided data.

Table 14.1.1 Disposition of Subjects

	Treatment			
Disposition	A	B	C	Total
Dosed	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Completed Study	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Dropped from Study	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Reason 1	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Reason 2	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Reason 3	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
etc.				

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas prg/stsas/tab tab-programname.sas DDMMMYYYY HH:MM

Table 14.1.2 Demographic Summary

Trait		Treatment A	Treatment B	Treatment C	Total
Gender	XXXXX	X (X %)	X (X %)	X (X %)	X (X %)
Race	XXXXX	X (X %)	X (X %)	X (X %)	X (X %)
Ethnicity	XXXXXXX	X (X %)	X (X %)	X (X %)	X (X %)
Age	N	XX.X	XX.X	XX.X	XX.X
	Mean	XX.X	XX.X	XX.X	XX.X
	SD	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X
	Minimum	XX.X	XX.X	XX.X	XX.X
	Maximum	XX.X	XX.X	XX.X	XX.X
Height (cm)	N	XX.X	XX.X	XX.X	XX.X
	Mean	XX.X	XX.X	XX.X	XX.X
	SD	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X
	Minimum	XX.X	XX.X	XX.X	XX.X
	Maximum	XX.X	XX.X	XX.X	XX.X
Weight (kg)	N	XX.X	XX.X	XX.X	XX.X
	Mean	XX.X	XX.X	XX.X	XX.X
	SD	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X
	Minimum	XX.X	XX.X	XX.X	XX.X
	Maximum	XX.X	XX.X	XX.X	XX.X
BMI (kg/m^2)	N	XX.X	XX.X	XX.X	XX.X
	Mean	XX.X	XX.X	XX.X	XX.X
	SD	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X
	Minimum	XX.X	XX.X	XX.X	XX.X
	Maximum	XX.X	XX.X	XX.X	XX.X

BMI = Body Mass Index
Weight at screening is used for summarization.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.
Program: /AAXXXXX/ECR/sas prg/stsas/tab tab-programname.sas DDMMMYYYY HH:MM

Table 14.1.3 Summary of Exposure to Study Drug

	Treatment		
Study Day	A (N=XX)	B (N=XX)	C (N=XX)
1 AM	X (%)	X (%)	X (%)
1 PM	X (%)	X (%)	X (%)
2 AM	X (%)	X (%)	X (%)
2 PM	X (%)	X (%)	X (%)
3 AM	X (%)	X (%)	X (%)
3 PM	X (%)	X (%)	X (%)
4 AM	X (%)	X (%)	X (%)
4 PM	X (%)	X (%)	X (%)
5 AM	X (%)	X (%)	X (%)
5 PM	X (%)	X (%)	X (%)
6 AM	X (%)	X (%)	X (%)
6 PM	X (%)	X (%)	X (%)
7 AM	X (%)	X (%)	X (%)
7 PM	X (%)	X (%)	X (%)
8 AM	X (%)	X (%)	X (%)
8 PM	X (%)	X (%)	X (%)
9 AM	X (%)	X (%)	X (%)
9 PM	X (%)	X (%)	X (%)
10 AM	X (%)	X (%)	X (%)
10 PM	X (%)	X (%)	X (%)
< >	< >	< >	< >

Number of subjects dosed by day with percentage is based on total number of subjects dosed in each treatment.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Symptom Monitoring

Table 14.2.1.1 Summary and Change From Baseline of Main Peak Expiratory Flow (PEF) Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

		Treatment A		Treatment B		Treatment C	
		Result	Change From Baseline	Result	Change From Baseline	Result	Change From Baseline
Day	Summary Statistic	(N = XX)	(N = XX)	(N = XX)	(N = XX)	(N = XX)	(N = XX)
1	N	XX		XX		XX	
	Mean	XX.X		XX.X		XX.X	
	SD	XX.XX		XX.XX		XX.XX	
	CV%	XX.X		XX.X		XX.X	
	Median	XX.X		XX.X		XX.X	
	Minimum	XX		XX		XX	
	Maximum	XX		XX		XX	
2	N	XX	XX	XX	XX	XX	XX
	Mean	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	Minimum	XX	-XX	XX	-XX	XX	-XX
	Maximum	XX	XX	XX	XX	XX	XX
	P-Value (Within)		X.XXX		X.XXX		X.XXX
	P-Value (Between)		X.XXX		X.XXX		

Main peak expiratory flow (L/min) = Highest of the three peak flow recordings
Baseline is Day 1 predose measurement.
P-value (Within) came from Wilcoxon Signed Rank Test, P-value (Between) came from Wilcoxon Rank Sum Test: A vs C and B vs C
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.1.2 Categorical Summary of Sputum Quantity, Color, and Consistency for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

		Sputum Quantity					Sputum Color					Sputum Consistency			
Day	Treatment	N	0	< 1 t	>= 1 t	> ¼ c	N	White	Yellow	Green	Brown	N	Watery	Thin	Thick
1	A	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX	X (X%)	X (X%)	X (X%)	XX (XX%)	XX	XX (XX%)	X (X%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	XX	X (XX%)	X (XX%)	X (X%)	X (X%)	XX	X (XX%)	X (X%)	X (X%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (X%)	X (X%)	X (X%)
2	A	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	XX	X (XX%)	XX (XX%)	X (X%)	X (X%)	XX	X (X%)	X (X%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (X%)	X (X%)	X (X%)
	C	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX	X (XX%)	X (X%)	X (X%)	XX (XX%)	XX	X (X%)	X (X%)	X (X%)

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Sputum Quantity: 0 = None, < 1 t = Less than 1 tbs, >= 1 t = 1 tbs or more, > ¼ c = Greater than ¼ cup
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.1.3 Categorical Summary of Cough, Wheeze, Sore Throat, Nasal Congestion, Nasal Discharge, and Body Temperature Above 100°F for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

		Cough		Wheeze		Sore Throat		Nasal Congestion		Nasal Discharge		Body Temperature Above 100°F	
Day	Treat-ment	N	Yes	N	Yes	N	Yes	N	Yes	N	Yes	N	Yes
1	A	XX	XX (XX%)	XX	XX (XX%)	XX	XX (XX%)	XX	XX (XX%)	XX	XX (XX%)	XX	XX (XX%)
	B	XX	X (XX%)	XX	X (XX%)	XX	X (XX%)	XX	X (XX%)	XX	X (XX%)	XX	X (XX%)
	C	XX	X (XX%)	XX	X (XX%)	XX	X (XX%)	XX	X (XX%)	XX	X (XX%)	XX	X (XX%)
2	A	XX	X (X%)	XX	X (X%)	XX	X (X%)	XX	X (X%)	XX	X (X%)	XX	X (X%)
	B	XX	X (XX%)	XX	X (XX%)	XX	X (XX%)	XX	X (XX%)	XX	X (XX%)	XX	X (XX%)
	C	XX	XX (XX%)	XX	XX (XX%)	XX	XX (XX%)	XX	XX (XX%)	XX	XX (XX%)	XX	XX (XX%)

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Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.1.4 Categorical Summary of Symptom Score for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

			Symptom Score of COPD Symptoms							
Day	Treat-ment	N	0	0.5	1	1.5	2	2.5	3	3.5
1	A	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	X (X%)	X (X%)	X (X%)	XX (XX%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (XX%)	X (X%)	X (X%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
2	A	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	C	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	X (X%)	XX (XX%)

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Severity of symptom scores: Normal (0 - 0.5), Mild(1 - 1.5), Moderate(2 - 2.5), Severe(3 - 3.5)
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 - 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 - 55
Treatment C: Multiple oral doses of placebo BID on Days 1 - 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.1.5 Summary and Change From Baseline of Symptom Score for Symptoms of Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

		Treatment A		Treatment B		Treatment C	
		Result	Change From Baseline	Result	Change From Baseline	Result	Change From Baseline
Day	Summary Statistic	(N = XX)	(N = XX)	(N = XX)	(N = XX)	(N = XX)	(N = XX)
1	N	XX		XX		XX	
	Mean	XX.X		XX.X		XX.X	
	SD	XX.XX		XX.XX		XX.XX	
	CV%	XX.X		XX.X		XX.X	
	Median	XX.X		XX.X		XX.X	
	Minimum	XX		XX		XX	
	Maximum	XX		XX		XX	
2	N	XX	XX	XX	XX	XX	XX
	Mean	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	Minimum	XX	-XX	XX	-XX	XX	-XX
	Maximum	XX	XX	XX	XX	XX	XX
	P-Value (Within)		X.XXX		X.XXX		X.XXX
	P-Value (Between)		X.XXX		X.XXX		

Baseline is Day 1 predose measurement.
Severity of symptom scores: Normal (0 - 0.5), Mild(1 - 1.5), Moderate(2 - 2.5), Severe(3 - 3.5)
P-value (Within) came from Wilcoxon Signed Rank Test, P-value (Between) came from Wilcoxon Rank Sum Test: A vs C and B vs C
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.1.6 Categorical Summary of Modified Borg Dyspnea Scale Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Day	Treatment	N	Number Indicator of Breathlessness 0	0.5	1	2	3	4	5	6	7	8	9	10
1	A	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	X (X%)	X (X%)	X (X%)	XX (XX%)	XX (XX%)	X (X%)	X (X%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (XX%)	X (X%)	X (X%)	X (XX%)	X (X%)	X (X%)	X (X%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (X%)	X (X%)	X (X%)
2	A	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (X%)	X (X%)	X (X%)
	C	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	X (X%)	X (X%)	X (X%)

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0 = None, 0.5 = Very Mild, 1 = Less Mild, 2 = Mild, 3 = More Mild, 4 = Less Moderate, 5 = Moderate, 6 = More Moderate, 7 = Less Severe, 8 = Severe, 9 = More Severe, 10 = Extreme
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.1.7 Summary and Change From Baseline of Modified Borg Dyspnea Scale Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

		Treatment A		Treatment B		Treatment C	
		Result	Change From Baseline	Result	Change From Baseline	Result	Change From Baseline
Day	Summary Statistic	(N = XX)	(N = XX)	(N = XX)	(N = XX)	(N = XX)	(N = XX)
1	N	XX		XX		XX	
	Mean	XX.X		XX.X		XX.X	
	SD	XX.XX		XX.XX		XX.XX	
	CV%	XX.X		XX.X		XX.X	
	Median	XX.X		XX.X		XX.X	
	Minimum	XX		XX		XX	
	Maximum	XX		XX		XX	
2	N	XX	XX	XX	XX	XX	XX
	Mean	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	Minimum	XX	-XX	XX	-XX	XX	-XX
	Maximum	XX	XX	XX	XX	XX	XX
	P-Value (Within)		X.XXX		X.XXX		X.XXX
	P-Value (Between)		X.XXX		X.XXX		

Baseline is Day 1 predose measurement.
P-value (Within) came from Wilcoxon Signed Rank Test, P-value (Between) came from Wilcoxon Rank Sum Test: A vs C and B vs C
Modified Borg Dyspnea Scale: 0 = None, 0.5 = Very Mild, 1 = Less Mild, 2 = Mild, 3 = More Mild, 4 = Less Moderate, 5 = Moderate, 6 = More Moderate, 7 = Less Severe, 8 = Severe, 9 = More Severe, 10 = Extreme
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.1.8 Categorical Summary of 12-Item Questionnaire of Duke Activity Status Index (DASI) Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

			DASI 12-Item Questionnaire											
Day	Treat-ment	N	1	2	3	4	5	6	7	8	9	10	11	12
1	A	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	X (X%)	X (X%)	X (X%)	XX (XX%)	XX (XX%)	X (X%)	X (X%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (XX%)	X (X%)	X (X%)	X (XX%)	X (X%)	X (X%)	X (X%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (X%)	X (X%)	X (X%)
2	A	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (X%)	X (X%)	X (X%)
	C	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	X (X%)	X (X%)	X (X%)

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1. Able to take care of yourself that is eating, dressing, bathing, or using the toilet yet?
2. Able to walk indoors, such as around the house?
3. Able to walk a block or 2 on level ground?
4. Able to climb a flight of stairs or walk up a hill without stopping?
5. Able to run a short distance?
6. Able to do light work around the house like dusting or washing dishes?
7. Able to do moderate work around the house like vacuuming, sweeping floors or carrying in the groceries?
8. Able to do heavy work around the house like scrubbing floors, or lifting or moving heavy furniture?
9. Able to do yard work like raking leaves, weeding, or pushing a power mower yet?
10. Are you having sexual relations?
11. Able to participate in moderate recreational activities like golf, bowling, dancing, double tennis, or throwing a baseball or football yet?
12. Are you able to participate in strenuous sports like swimming, singles tennis, football, basketball, or skiing?

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 - 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 - 55
Treatment C: Multiple oral doses of placebo BID on Days 1 - 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.1.9 Summary and Change From Baseline of Calculated Score from 12-Item Questionnaire of Duke Activity Status Index (DASI) Recorded in the e-Diary Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

		Treatment A		Treatment B		Treatment C	
		Result	Change From Baseline	Result	Change From Baseline	Result	Change From Baseline
Day	Summary Statistic	(N = XX)	(N = XX)	(N = XX)	(N = XX)	(N = XX)	(N = XX)
1	N	XX		XX		XX	
	Mean	XX.X		XX.X		XX.X	
	SD	XX.XX		XX.XX		XX.XX	
	CV%	XX.X		XX.X		XX.X	
	Median	XX.X		XX.X		XX.X	
	Minimum	XX		XX		XX	
	Maximum	XX		XX		XX	
2	N	XX	XX	XX	XX	XX	XX
	Mean	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	Minimum	XX	-XX	XX	-XX	XX	-XX
	Maximum	XX	XX	XX	XX	XX	XX
	P-Value (Within)		X.XXX		X.XXX		X.XXX
	P-Value (Between)		X.XXX		X.XXX		

Baseline is Day 1 predose measurement.
Score ranges between 0 and 58.2 points.
P-value (Within) came from Wilcoxon Signed Rank Test, P-value (Between) came from Wilcoxon Rank Sum Test: A vs C and B vs C
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Pharmacodynamics

Inflammatory Cell Counts in BAL and Blood

Note: Tables 14.2.2.1 and 14.2.2.4 will be in a similar format:

Table 14.2.2.1 Summary of BAL WBC Counts Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C) (Raw, % Change from Baseline, and % of WBC)

			Raw			% Change from Baseline			% of WBC		
			Treatment			Treatment			Treatment		
Measurement	Time Point	Statistic	A	B	C	A	B	C	A	B	C
WBC (units)	<Check-in>	N	X	X	X	X	X	X	NA	NA	NA
		Mean	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	NA	NA	NA
		SD	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	NA	NA	NA
		CV%	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	NA	NA	NA
		Median	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	NA	NA	NA
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	NA	NA	NA
		Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	NA	NA	NA
<Cell type> (units)	<Day 55 or 56>	N	X	X	X	X	X	X	X	X	X
		Mean	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		SD	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
		CV%	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
		Median	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 - 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 - 55
Treatment C: Multiple oral doses of placebo BID on Days 1 - 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.
NA = Not applicable
. = Value missing or not reportable

Programmers note: For the list of time point refer to Section 7.1.1.1 and 7.1.1.2
Differential cells include macropaghes, lymphocytes, neutrophils, and eosinophils
Program: /CAXXXXX/XXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Inflammatory Markers in BAL and Blood

Note: Tables 14.2.2.2 and 14.2.2.5 and will be in a similar format:

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Table 14.2.2.5 Summary of Blood Inflammatory Marker Concentrations Following Multiple Oral YPL 001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

			Treatment		
Measurement	Time Point	Statistic	A	B	C
IL-X (units)	<Screen, Day X predose> (Baseline)>	N	X	X	X
		Mean	X.XXX	X.XXX	X.XXX
		SD	X.XXXX	X.XXXX	X.XXXX
		CV%	X.XXXX	X.XXXX	X.XXXX
		Median	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX
		Maximum	X.XX	X.XX	X.XX
IL-X (units)	<Day X+/-X 1 Hr postdose or Predose>	N	X	X	X
		Mean	X.XXX	X.XXX	X.XXX
		SD	X.XXXX	X.XXXX	X.XXXX
		CV%	X.XXXX	X.XXXX	X.XXXX
		Median	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX
		Maximum	X.XX	X.XX	X.XX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.
. = Value missing or not reportable

Programmers note:
Add separation (table break) between each marker type as well as the marker type name at the top of the table.
For the list of time point for each table refer to Sections 7.1.1.1 and 7.1.1.2
Biomarkers types include : BAL: TNF-α, IL 1β, IL-4, IL-5, IL-6, IL-8, IL-13, MPO, neutrophil elastase, MCP-1, and MMP-9
Blood: CRP, fibrinogen, TNF-α, IL-1β, IL-4, IL-5, IL-6, IL-8, IL 13, MCP-1, and MMP-9
Program: /AAXXXXX/XXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Note: Tables 14.2.2.3 and 14.2.2.6 and will be in a similar format:

Table 14.2.2.6 Summary of Blood Inflammatory Marker Concentration Changes Following Multiple Oral YPL 001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A – C) (Raw and % Change from Baseline)

			Change From Baseline			% Change from Baseline		
			Treatment			Treatment		
Measurement	Time Point	Statistic	A	B	C	A	B	C
IL-X (units)	<Day X 1 Hr postdose or predose>	N	X	X	X	X	X	X
		Mean	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		SD	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
		CV%	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
		Median	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
IL-X (units)	<Day X+/-X 1 Hr postdose or predose>	N	X	X	X	X	X	X
		Mean	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		SD	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
		CV%	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
		Median	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.
. = Value missing or not reportable

Programmers note:
Add separation (table break) between each marker type as well as the marker type name at the top of the table.
For the list of time point for each table refer to Sections 7.1.1.1 and 7.1.1.2
Biomarkers types include : BAL: TNF-α, IL 1β, IL-4, IL-5, IL-6, IL-8, IL-13, MPO, neutrophil elastase, MCP-1, and MMP-9
Blood: CRP, fibrinogen, TNF-α, IL-1β, IL-4, IL-5, IL-6, IL-8, IL 13, MCP-1, and MMP-9

Program: /AAXXXXX/XXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Pulmonary Function Biomarkers

Note: Tables 14.2.2.7, 14.2.2.8, and 14.2.2.9 and will be in a similar format:

Table 14.2.2.7 Summary of Spirometric Functions Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Actual Results, Treatments A - C)

Parameter (Unit) (Pre/ Post/ Change)	Day	Summary Statistic	Treatment A Result (N = XX)	Treatment A Change From Baseline (N = XX)	Treatment B Result (N = XX)	Treatment B Change From Baseline (N = XX)	Treatment C Result (N = XX)	Treatment C Change From Baseline (N = XX)
FEV1 (L)								
Pre^	Screen	N	XX		XX		XX	
		Mean	XX.X		XX.X		XX.X	
		SD	XX.XX		XX.XX		XX.XX	
		CV%	XX.X		XX.X		XX.X	
		Median	XX.X		XX.X		XX.X	
		Minimum	XX		XX		XX	
		Maximum	XX		XX		XX	
Post^		N	XX		XX		XX	
		Mean	XX.X		XX.X		XX.X	
		SD	XX.XX		XX.XX		XX.XX	
		CV%	XX.X		XX.X		XX.X	
		Median	XX.X		XX.X		XX.X	
		Minimum	XX		XX		XX	
		Maximum	XX		XX		XX	
Change^		N	XX		XX		XX	
		Mean	XX.X		XX.X		XX.X	
		SD	XX.XX		XX.XX		XX.XX	
		CV%	XX.X		XX.X		XX.X	
		Median	XX.X		XX.X		XX.X	
		Minimum	XX		XX		XX	
		Maximum	XX		XX		XX	
Pre^	Check-in	N	XX	XX	XX	XX	XX	XX
		Mean	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
		SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		Median	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X

	Minimum	XX	-XX	XX	-XX	XX	-XX
	Maximum	XX	XX	XX	XX	XX	XX
	P-Value (Within)		X.XXX		X.XXX		X.XXX
	P-Value (Between)		X.XXX		X.XXX		
Post^	N	XX	XX	XX	XX	XX	XX
	Mean	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	Minimum	XX	-XX	XX	-XX	XX	-XX
	Maximum	XX	XX	XX	XX	XX	XX
	P-Value (Within)		X.XXX		X.XXX		X.XXX
	P-Value (Between)		X.XXX		X.XXX		
Change^	N	XX	XX	XX	XX	XX	XX
	Mean	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	Minimum	XX	-XX	XX	-XX	XX	-XX
	Maximum	XX	XX	XX	XX	XX	XX
	P-Value (Within)		X.XXX		X.XXX		X.XXX
	P-Value (Between)		X.XXX		X.XXX		
Pre^ 15+/-2	N	XX	XX	XX	XX	XX	XX
	Mean	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	Minimum	XX	-XX	XX	-XX	XX	-XX
	Maximum	XX	XX	XX	XX	XX	XX
	P-Value (Within)		X.XXX		X.XXX		X.XXX
	P-Value (Between)		X.XXX		X.XXX		
Post^	N	XX	XX	XX	XX	XX	XX
	Mean	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
	Minimum	XX	-XX	XX	-XX	XX	-XX
	Maximum	XX	XX	XX	XX	XX	XX
	P-Value (Within)		X.XXX		X.XXX		X.XXX
	P-Value (Between)		X.XXX		X.XXX		
Change^	N	XX	XX	XX	XX	XX	XX
	Mean	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X

SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
Minimum	XX	-XX	XX	-XX	XX	-XX
Maximum	XX	XX	XX	XX	XX	XX
P-Value (Within)		X.XXX		X.XXX		X.XXX
P-Value (Between)		X.XXX		X.XXX		

< > < > < >

FEV1 = forced expiratory volume in one second, FVC = forced vital capacity, IC = inspiratory capacity
^ Pre- and Post-Bronchodilator, Change = Post- minus Pre-
Baseline is screening measurement.
P-value (Within) came from Wilcoxon Signed Rank Test, P-value (Between) came from Wilcoxon Rank Sum Test: A vs C and B vs C
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Programmers note:
Measurments to include are FEV1 (L), FVC (L), FEV1/FVC (%), and IC (L).
Postdose time points are Day 15+/-2, 29+/-2, 43+/-2, and 55 or 56.
If space is limiting, Day “55 or 56” may be presented as “56” with a footnote indicating “Day 55 or 56”.

Program: /AAXXXXX/XXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Quality of Life

Table 14.2.2.10 Categorical Summary of Baseline Dyspnea Index (BDI) at Check-in by Treatment Assignment of Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Treatment		N	Grade 4	Grade 3	Grade 2	Grade 1	Grade 0	Amount Uncertain	Unknown	Impaired for Reasons Other than Shortness of Breath
A	Functional Impairment	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Magnitude of Task	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Magnitude of Effort	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
B	Functional Impairment	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Magnitude of Task	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Magnitude of Effort	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
C	Functional Impairment	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Magnitude of Task	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Magnitude of Effort	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)

Functional Impairment: Grade 4 = No Impairment, Grade 3 = Slight Impairment, Grade 2 = Moderate Impairment, Grade 1 = Severe Impairment, Grade 0 = Very Severe Impairment
Magnitude of Task: Grade 4 = Extraordinary, Grade 3 = Major, Grade 2 = Moderate, Grade 1 = Light, Grade 0 = No Task
Magnitude of Effort: Grade 4 = Extraordinary, Grade 3 = Major, Grade 2 = Moderate, Grade 1 = Light, Grade 0 = No Effort
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.2.11 Categorical Summary of Transition Dyspnea Index (TDI) Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

Day	Treat-ment	Change of Grade From Check-in	N	-3	-2	-1	0	+1	+2	+3	Further Impairment for Reasons Other than Shortness of Breath
15+/-2	A	Functional Impairment	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
		Magnitude of Task	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
		Magnitude of Effort	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	B	Functional Impairment	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
		Magnitude of Task	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
		Magnitude of Effort	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	C	Functional Impairment	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
		Magnitude of Task	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
		Magnitude of Effort	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)

-3 = Major Deterioration, -2 = Moderate Deterioration, -1 = Minor Deterioration, 0 = No Change, +1 = Minor Improvement, +2 = Moderate Improvement, +3 = Major Improvement
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Programmers note:
Time points are Day 15+/-2, 29+/-2, 43+/-2, and 54+/-1 or 56.
If space is limiting, Day "54+/-1 or 56" may be presented as Day "54" with a footnote indicating this is "Day 54+/-1 or 56".

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.2.12 Change From Baseline of Combined Focal Score (-9 – +9) from Transition Dyspnea Index (TDI) Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A – C)

Day	Summary Statistic	Treatment A (N = XX)	Treatment B (N = XX)	Treatment C (N = XX)
15+/-2	N	XX	XX	XX
	Mean	-X.X	-X.X	-X.X
	SD	XX.XX	XX.XX	XX.XX
	CV%	XX.X	XX.X	XX.X
	Median	-X.X	-X.X	-X.X
	Minimum	-XX	-XX	-XX
	Maximum	XX	XX	XX
	P-Value (Between)	X.XXX	X.XXX	
29+/-2	N	XX	XX	XX
	Mean	-X.X	-X.X	-X.X
	SD	XX.XX	XX.XX	XX.XX
	CV%	XX.X	XX.X	XX.X
	Median	-X.X	-X.X	-X.X
	Minimum	-XX	-XX	-XX
	Maximum	XX	XX	XX
	P-Value (Between)	X.XXX	X.XXX	

TDI has 3 domains (functional impairment, magnitude of task, and magnitude of effort).
The change from baseline is measured by the TDI score which ranges from -3 (major deterioration) to +3 (major improvement) for each domain with the TDI focal score consisting in the sum of each domain (-9 to +9).
P-value (Between) came from Wilcoxon Rank Sum Test: A vs C and B vs C
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Programmers note:
Time points are Day 15+/-2, 29+/-2, 43+/-2, and 54+/-1 or 56.
If space is limiting, Day "54+/-1 or 56" may be presented as Day "54" with a footnote indicating this is "Day 54+/-1 or 56".

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.2.13 Categorical Summary of Cough and Mucus Production from Chronic Obstructive Pulmonary Disease (COPD) Assessment Test (CAT) Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

		Cough							Mucus Production						
Day	Treatment	N	0	1	2	3	4	5	N	0	1	2	3	4	5
CI^	A	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
15*	A	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
29*	A	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	C	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
54#	A	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	C	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)

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^ CI = Check-in
* Nominal +/-2 days
# Day 54+/1 or Day 56
Cough: 0 = I never cough, 5 = I cough all the time
Mucus Production: 0 = I have no phlegm (mucus) in my chest at all, 5 = My chest is completely full of phlegm (mucus)
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 - 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 - 55
Treatment C: Multiple oral doses of placebo BID on Days 1 - 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.2.14 Categorical Summary of Chest Tightness and Breathlessness from Chronic Obstructive Pulmonary Disease (COPD) Assessment Test (CAT) Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

		Chest Tightness							Breathlessness						
Day	Treatment	N	0	1	2	3	4	5	N	0	1	2	3	4	5
CI^	A	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
15*	A	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
29*	A	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	C	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
54#	A	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	C	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)

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^ CI = Check-in
* Nominal +/-2 days
# Day 54+/1 or Day 56
Chest Tightness: 0 = My chest does not feel tight at all, 5 = My chest feels very tight
Breathlessness: 0 = When I walk up a hill or one flight of stairs I am not breathless, 5 = When I walk up a hill or one flight of stairs I am very breathless
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 - 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 - 55
Treatment C: Multiple oral doses of placebo BID on Days 1 - 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.2.15 Categorical Summary of Level of Activities and Level of Confidence from Chronic Obstructive Pulmonary Disease (COPD) Assessment Test (CAT) Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

		Level of Activities							Level of Confidence						
Day	Treatment	N	0	1	2	3	4	5	N	0	1	2	3	4	5
CI^	A	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
15*	A	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
29*	A	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	C	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
54#	A	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	C	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)

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^ CI = Check=in
* Nominal +/-2 days
# Day 54+/1 or Day 56
Level of Activities: 0 = I am not limited doing any activities at home, 5 = I am very limited doing activities at home
Level of Confidence: 0 = I am confident leaving my home despite my lung condition, 5 = I am not at all confident leaving my home because of my lung condition
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 - 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 - 55
Treatment C: Multiple oral doses of placebo BID on Days 1 - 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.2.16 Categorical Summary of Level of Sleepiness and Level of Energy from Chronic Obstructive Pulmonary Disease (COPD) Assessment Test (CAT) Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

		Level of Sleepiness							Level of Energy						
Day	Treatment	N	0	1	2	3	4	5	N	0	1	2	3	4	5
CI^	A	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
15*	A	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	X (X%)	XX (XX%)	X (X%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)	XX	X (XX%)	X (XX%)	X (XX%)	X (X%)	X (XX%)	X (X%)
	C	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
29*	A	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	C	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
54#	A	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)	XX	XX (XX%)	X (X%)	X (X%)	XX (XX%)	X (X%)	XX (XX%)
	B	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	XX	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	C	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)

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^ CI = Check-in
* Nominal +/-2 days
# Day 54+/1 or Day 56
Level of Sleepiness: 0 = I sleep soundly, 5 = I don't sleep soundly because of my lung condition
Level of Energy: 0 = I have lots of energy, 5 = I have no energy at all
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 - 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 - 55
Treatment C: Multiple oral doses of placebo BID on Days 1 - 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.2.17 Summary and Change From Baseline of Individual Score (0 – 5) and Total Score (0 – 40) from Chronic Obstructive Pulmonary Disease (COPD) Assessment Test (CAT) Following Multiple Oral YPL-001 Doses of 80 mg and 160 mg and Placebo in COPD Patients (Treatments A - C)

			Treatment A		Treatment B		Treatment C	
CAT Item	Day	Summary Statistic	Result (N = XX)	Change From Baseline (N = XX)	Result (N = XX)	Change From Baseline (N = XX)	Result (N = XX)	Change From Baseline (N = XX)
Cough	Check-in	N	XX		XX		XX	
		Mean	XX.X		XX.X		XX.X	
		SD	XX.XX		XX.XX		XX.XX	
		CV%	XX.X		XX.X		XX.X	
		Median	XX.X		XX.X		XX.X	
		Minimum	XX		XX		XX	
		Maximum	XX		XX		XX	
	15+/-2	N	XX	XX	XX	XX	XX	XX
		Mean	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
		SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		Median	XX.X	-X.X	XX.X	-X.X	XX.X	-X.X
		Minimum	XX	-XX	XX	-XX	XX	-XX
		Maximum	XX	XX	XX	XX	XX	XX
		P-Value (Within)		X.XXX		X.XXX		X.XXX
		P-Value (Between)		X.XXX		X.XXX		

Baseline is Check-in measurement.
P-value (Within) came from Wilcoxon Signed Rank Test, P-value (Between) came from Wilcoxon Rank Sum Test: A vs C and B vs C
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Programmers note: CAT items are Cough, Mucus Production, Chest Tightness, Breathlessness, Activities, Confidence, Sleepiness, Energy, and Total score.
For the "Day 54+/1 or Day 56" time point (if space is limiting), this may be presented as Day "54" with a footnote indicating this is "Day 54+/1 or 56".

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Pharmacokinetics

Note: Tables 14.2.4.1.1 - 2, 14.2.4.2.1 – 2 (plasma), 14.2.4.3.1, and 14.2.4.4.1 (epithelial brushing) will be in a similar format:

Table 14.2.4.1.1 Plasma Verproside Concentrations (pg/mL) Following Single and Multiple Oral YPL-001 Doses of 80 mg in COPD Patients - Days 1 to 54 (+/- 1) or Day 56 (Treatment A)

	Sample Times (Day / hr)										
Subject	Day X					- Day X --		Day XX	Day XX	------Day XX---	
Number	XX	XX	XX	XX	XX	XX	XX	Predose	Predose	XX	XX
XXXX	BLQ	XX	XX	XX	XX	XX	XX	BLQ	XX	XX	XX
XXXX	BLQ	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
XXXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
N	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
Mean	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
SD	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
CV%	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
Median	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
Maximum	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
Minimum	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX

Footnotes to include, as appropriate:
For the calculation of summary statistics and pharmacokinetic parameters, values on Days 1 and 54+/-2 that are below the lower limit of quantitation (BLQ) of 50.0 pg/mL are treated as 0.00 before the first quantifiable concentration on each study day and as missing elsewhere. In addition, predose BLQ values on Days 15+/-2 to 56 were set to 0.00.
. = Value missing or not reportable

Programmer Note:
PK Time points are listed in Sections 8.1.1 and 8.1.2 of this SAP.
Please see text in Section 8.6 for description of significant figures/decimals to be used for descriptive statistics.

Program : /AAXXXXX/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Note: Tables 14.2.4.1.3 - 6 (verproside) and 14.2.4.2.3 - 6 (picroside II) will be in a similar format:

Table 14.2.4.1.3 Plasma Verproside Pharmacokinetic Parameters Following a Single Oral YPL-001 Dose of 80 mg in COPD Patients - Day 1 (Treatment A)

	Parameters							
Subject Number	Param (units)	Param (units)	Param (units)	Param (units)	Param (units)	Param (units)	Param (units)	Param (units)
XX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
XX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
XX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
N	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX
Mean	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX
SD	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX
CV%	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX
Median	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX
Minimum	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX
Maximum	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX
Geom. Mean	XXXX	NC	XXXX	NC	NC	XXXX	NC	NC
Geo. CV%	XXXX	NC	XXXX	NC	NC	XXXX	NC	NC

NC = Not calculated.
. = Value missing or not reportable.

Programmers note:
Geo. Mean and Geo. CV% will be calculated for C and AUC parameters only.
Please refer to Section 8.5.1 for list of pharmacokinetic parameters on each study day. Significant figures/decimals to be used for PK parameters will be specified by the PKist upon review of the data. Please refer to Section 8.6 for description of significant figures/decimals to be used for descriptive statistics.

Program : /AAXXXXX/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Note: Tables 14.2.4.1.7 and 14.2.4.2.7 and will be in a similar format:

Table 14.2.4.1.7 Intervals (Hours) Used for Determination of Plasma Verproside kel Values Following Single and Multiple Oral YPL-001 Doses of 80 mg and 160 mg - Days 1 to 54 (+/- 1) or Day 56(Treatments A and B)

Day 1

Subject Number	Treatment A Interval	Treatment A R^2	Treatment A N	Treatment B Interval	Treatment B R^2	Treatment B N
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X

Day 54+/-1 or Day 56

Subject Number	Treatment A Interval	Treatment A R^2	Treatment A N	Treatment B Interval	Treatment B R^2	Treatment B N
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X
XX	X.X - XX.X	X.XXX	X	X.X - XX.X	X.XXX	X

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.
R^2 = Square of the correlation coefficient of the linear regression
N = Number of points used in kel calculation
. = Value missing or not reportable

Note: Tables 14.2.4.1.8 and 14.2.4.2.8 and will be in a similar format:

Table 14.2.4.1.8 Statistical Comparisons of Dose-Normalized Plasma Verproside Pharmacokinetic Parameters Following Multiple Oral YPL-001 Doses of 160 mg Versus Multiple Oral YPL-001 Doses of 80 mg and in COPD Patients – Day 54 (+/- 1) or Day 56 (Treatment B Versus Treatment A)

	Geometric LSM			
Parameter	Treatment B	Treatment A	Geometric Mean Ratio (%)	90% CI
Param1 (unit)	X.XXX	X.XXX	XX.XX	XXX.XX – XXX.XX
Param2 (unit)	X.XXX	X.XXX	XX.XX	XXX.XX – XXX.XX
Param3 (unit)	X.XXX	X.XXX	XX.XX	XXX.XX – XXX.XX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Parameters were dose-normalized (to 80 mg YLP-001) and ln-transformed prior to analysis.
Geometric least-squares means (LSMs) were calculated by exponentiating the LSM from the ANOVA.
% Geometric Mean Ratio = 100 x (test/reference)
CI = Confidence interval

Program: /AAXXXXX/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.3.1.1 Treatment-Emergent Adverse Event Frequency by Treatment - Number of Patients Reporting Events (% of Patients Dosed)

	Treatment			
Adverse Event*	A	B	C	Total
Number of Patients Dosed	X (XXX %)	X (XXX %)	X (XXX %)	X (XXX %)
Number of Patients With AEs	X (XX %)	X (XX %)	X (XX %)	X (XX %)
Number of Patients Without AEs	X (XX %)	X (XX %)	X (XX %)	X (XX %)
System Organ Class 1	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 1	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 2	X (X %)	X (X %)	X (X %)	X (XX %)
System Organ Class 2	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 1	X (X %)	X (X %)	X (X %)	X (XX %)
System Organ Class 3	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 1	X (XX %)	X (XX %)	X (XX %)	X (XX %)
System Organ Class 4	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 1	X (X %)	X (X %)	X (X %)	X (XX %)
System Organ Class 5	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 1	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 2	X (X %)	X (X %)	X (X %)	X (XX %)
etc.				

* Adverse events are classified according to MedDRA Version 18.0.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/SAS_PRG/STSAS/TAB DDMMMYYYY XX:XX

Table 14.3.1.2 Treatment-Emergent Adverse Event Frequency by Treatment - Number of Adverse Events (% of Total Adverse Events)

	Treatment			
Adverse Event*	A	B	C	Total
Number of AEs	X (XXX %)	X (XXX %)	X (XXX %)	X (XXX %)
System Organ Class 1	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 1	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 2	X (X %)	X (X %)	X (X %)	X (XX %)
System Organ Class 2	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 1	X (X %)	X (X %)	X (X %)	X (XX %)
System Organ Class 3	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 1	X (XX %)	X (XX %)	X (XX %)	X (XX %)
System Organ Class 4	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 1	X (X %)	X (X %)	X (X %)	X (XX %)
System Organ Class 5	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 1	X (X %)	X (X %)	X (X %)	X (XX %)
Preferred term 2	X (X %)	X (X %)	X (X %)	X (XX %)
etc.				

* Adverse events are classified according to MedDRA Version 18.0.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/SAS_PRG/STSAS/TAB DDMMMYYYY XX:XX

Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Drug - Number of Patients Reporting Events

Adverse Event*	Treat-ment	Number of Patients With Adverse Events	Severity			Relationship to Drug				
			Mild	Moderate	Severe	Unrelated	Unlikely	Possible	Probable	Definte
Anxiety	C	X	X	X	X	X	X	X	X	X
	A	X	X	X	X	X	X	X	X	X
Chest discomfort	B	X	X	X	X	X	X	X	X	X
Dry mouth	A	X	X	X	X	X	X	X	X	X
Headache	B	X	X	X	X	X	X	X	X	X
Nausea	B	X	X	X	X	X	X	X	X	X
Nervousness	B	X	X	X	X	X	X	X	X	X
Pharyngolaryngeal pain	C	X	X	X	X	X	X	X	X	X
A		X	X	X	X	X	X	X	X	X
B		X	X	X	X	X	X	X	X	X
C		X	X	X	X	X	X	X	X	X
Total		X	X	X	X	X	X	X	X	X

* Adverse events are classified according to MedDRA Version 18.0.
When a patient experienced the same AE at more than one level of severity,the patient was counted once under the highest severity level.
When a patient experienced the same AE at more than one level of drug relationship, the patient was counted once under the closest relationship to study drug.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Programmers note: If Life-Threatening or Fatal severity is present, please add this.

Program: /AAXXXXX/ECR/SAS_PRG/STSAS/TAB DDMMMYYYY XX:XX

Table 14.3.1.4 Treatment-Emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Drug - Number of Adverse Events

Adverse Event*	Treat-ment	Number of Adverse Events	Severity			Relationship to Drug				
			Mild	Moderate	Severe	Unrelated	Unlikely	Possible	Probable	Definte
Anxiety	C	X	X	X	X	X	X	X	X	X
	A	X	X	X	X	X	X	X	X	X
Chest discomfort	B	X	X	X	X	X	X	X	X	X
Dry mouth	A	X	X	X	X	X	X	X	X	X
Headache	B	X	X	X	X	X	X	X	X	X
Nausea	B	X	X	X	X	X	X	X	X	X
Nervousness	B	X	X	X	X	X	X	X	X	X
Pharyngolaryngeal pain	C	X	X	X	X	X	X	X	X	X
A		X	X	X	X	X	X	X	X	X
B		X	X	X	X	X	X	X	X	X
C		X	X	X	X	X	X	X	X	X
Total		X	X	X	X	X	X	X	X	X

* Adverse events are classified according to MedDRA Version 18.0.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 - 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 - 55
Treatment C: Multiple oral doses of placebo BID on Days 1 - 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Programmers note: If Life-Threatening or Fatal severity is present, please add this.

Program: /AAXXXXX/ECR/SAS_PRG/STSAS/TAB DDMMMYYYY XX:XX

Table 14.3.2 Serious Adverse Event

Subject Number	Treat-ment	Age/ Gender	Adverse Event (Preferred Term*)	Date/Time of Onset	Date/Time of Resolved	Severity	Relation to Study Drug	Action Taken	Other Action	Outcome
X	A	XX/X	XXXXXXXXXXXXXXX	DDMMMYYYY/HH:MM	DDMMMYYYY/HH:MM	Mild	Probable	XXXXXXXXX	XXXXXXXX	Recovered/ Resolved

Note: * Adverse events are classified according to MedDRA Version 18.0.

NOTE: If no SAE occurred, in the middle of this table, a sentence, “No serious adverse event was reported.” will be added.

Program : /AAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Note: Tables 14.3.4.2 - 14.3.4.3 will appear similar to Table 14.3.4.1

Table 14.3.4.1 Out-of-Range Values and Recheck Results – Serum Chemistry

Subject Number	Age/ Gender	Visit Name	Visit Date	Treat-ment	Collection Date	Collection Time	Parameter	Reference Range (Unit)	Result Flag	Reference Range (SI Unit)	Result (SI Unit)	Comments
X	XX/X	Screening	DDMMMYYYY	X	DDMMMYYYY	HH:MM	XXXXXXXXXXXXX	XX – XX (unit)	XX HN	XX – XX (unit)	XX	XXXXXXXXXXXXX
		XXXX	DDMMMYYYY		DDMMMYYYY	HH:MM	XXXXXXXXXXXXX	XX – XX (unit)	XX LY	XX – XX (unit)	XX	XXXXXXXXXXXXX

Abnormal Flag: H = Above Reference Range, L = Below Reference Range
Clinical Significance: N = Not Clinically Significant, Y = Clinically Significant
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas prg/stsas/tab tab-programname.sas DDMMMYYYY HH:MM

Note: Tables 14.3.5.3 and 14.3.5.5 will appear similar to Table 14.3.5.1

Table 14.3.5.1 Clinical Laboratory Summary and Change From Check-in – Serum Chemistry

				Treatment			Change From Check-in		
Laboratory Test	Range	Day	Statistic	A	B	C	A	B	C
XXXXXXXXXX (X)	X-X	Screen	N	X.XX	X.XX	X.XX			
			Mean	X.XX	X.XX	X.XX			
			SD	X.XX	X.XX	X.XX			
			Median	X.XX	X.XX	X.XX			
			Minimum	X.XX	X.XX	X.XX			
			Maximum	X.XX	X.XX	X.XX			
		Check-in	N	X.XX	X.XX	X.XX			
			Mean	X.XX	X.XX	X.XX			
			SD	X.XX	X.XX	X.XX			
			Median	X.XX	X.XX	X.XX			
			Minimum	X.XX	X.XX	X.XX			
			Maximum	X.XX	X.XX	X.XX			
		29+/-2	N	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Median	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		54+/-2	N	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Median	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX

Baseline is Check-in measurement.
Early termination records are excluded from the summary.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas prg/stsas/tab tab-programname.sas DDMMMYYYY HH:MM

Note: Table 14.3.5.4 will appear similar to Table 14.3.5.2

Table 14.3.5. 2 Clinical Laboratory Shift From Check-in – Serum Chemistry

			Baseline L			Baseline N			Baseline H		
			Postdose			Postdose			Postdose		
Laboratory Test	Treatment	Day	L	N	H	L	N	H	L	N	H
XXXXXXX XXXXXXXXXXXXXXX	A	29+/-2	X	X	X	X	X	X	X	X	X
		54+/-2	X	X	X	X	X	X	X	X	X
	B	29+/-2	X	X	X	X	X	X	X	X	X
		54+/-2	X	X	X	X	X	X	X	X	X
	C	29+/-2	X	X	X	X	X	X	X	X	X

L = Below Normal Range, N = Within Normal Range, H = Above Normal Range.
Baseline is Check-in measurement.
Early termination records are excluded from the summary.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas prg/stsas/tab tab-programname.sas DDMMMYYYY HH:MM

Table 14.3.5.6 Clinical Laboratory Shift From Check-in – Urinalysis

			Baseline O		Baseline N	
			Postdose		Postdose	
Laboratory Test	Treatment	Day	O	N	O	N
XXXXXXX XXXXXXXXXXXXXXX	A	29+/-2	X	X	X	X
		54+/-2	X	X	X	X
	B	29+/-2	X	X	X	X
		54+/-2	X	X	X	X
	C	29+/-2	X	X	X	X
		54+/-2	X	X	X	X

O = Outside of Normal Range, N = Within Normal Range.
Baseline is Check-in measurement.
Early termination records are excluded from the summary.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas prg/stsas/tab tab-programname.sas DDMMMYYYY HH:MM

Table 14.3.5.7 Vital Sign Summary and Change From Day 1 Predose

				Treatment			Change From Day 1 Predose		
Measurement	Day	Hour^	Statistic	A	B	C	A	B	C
Systolic BP (mm Hg)	Screen		N	X.XX	X.XX	X.XX			
			Mean	X.XX	X.XX	X.XX			
			SD	X.XX	X.XX	X.XX			
			Median	X.XX	X.XX	X.XX			
			Minimum	X.XX	X.XX	X.XX			
			Maximum	X.XX	X.XX	X.XX			
	Check-in		N	X.XX	X.XX	X.XX			
			Mean	X.XX	X.XX	X.XX			
			SD	X.XX	X.XX	X.XX			
			Median	X.XX	X.XX	X.XX			
			Minimum	X.XX	X.XX	X.XX			
			Maximum	X.XX	X.XX	X.XX			
	1	0	N	X.XX	X.XX	X.XX			
			Mean	X.XX	X.XX	X.XX			
			SD	X.XX	X.XX	X.XX			
			Median	X.XX	X.XX	X.XX			
			Minimum	X.XX	X.XX	X.XX			
			Maximum	X.XX	X.XX	X.XX			
	1	1	N	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Median	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX

Hour 0 represents predose of that day.
Baseline is the last predose timepoint. Early termination records are excluded from the summary.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.
<Programmer note: Day 1 at 2 and 6 hours postdose, Days 15+/-2, 29+/-2, 43+/-2, and Day 54+/-2 at 0 hour predose and at 1, 2, 6, and 12 hours postdose, and end-of-treatment will also be presented.>
Program: /AAXXXXX/ECR/sas prg/stsas/tab tab-programname.sas DDMMMYYYY HH:MM

Table 14.3.5.8 Pulse Oximetry Summary and Change From Check-in

			Treatment			Change From Check-in		
Measurement	Day	Statistic	A	B	C	A	B	C
Oxygen Saturation (%)	Screen	N	X.XX	X.XX	X.XX			
		Mean	X.XX	X.XX	X.XX			
		SD	X.XX	X.XX	X.XX			
		Median	X.XX	X.XX	X.XX			
		Minimum	X.XX	X.XX	X.XX			
		Maximum	X.XX	X.XX	X.XX			
	Check-in	N	X.XX	X.XX	X.XX			
		Mean	X.XX	X.XX	X.XX			
		SD	X.XX	X.XX	X.XX			
		Median	X.XX	X.XX	X.XX			
		Minimum	X.XX	X.XX	X.XX			
		Maximum	X.XX	X.XX	X.XX			
	54+/-2	N	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Median	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX

Baseline is Check-in measurement.
Early termination records are excluded from the summary.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas prg/stsas/tab tab-programname.sas DDMMMYYYY HH:MM

Table 14.3.5.9 12-Lead Electrocardiogram Summary and Change From Check-in

			Treatment			Change From Check-in		
Measurement	Day	Statistic	A	B	C	A	B	C
Heart Rate (bpm)	Screen	N	X.XX	X.XX	X.XX			
		Mean	X.XX	X.XX	X.XX			
		SD	X.XX	X.XX	X.XX			
		Median	X.XX	X.XX	X.XX			
		Minimum	X.XX	X.XX	X.XX			
		Maximum	X.XX	X.XX	X.XX			
	Check-in	N	X.XX	X.XX	X.XX			
		Mean	X.XX	X.XX	X.XX			
		SD	X.XX	X.XX	X.XX			
		Median	X.XX	X.XX	X.XX			
		Minimum	X.XX	X.XX	X.XX			
		Maximum	X.XX	X.XX	X.XX			
	29+/-2	N	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Median	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	54+/-2	N	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Mean	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Median	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Maximum	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX

Baseline is Check-in measurement.
Early termination records are excluded from the summary.
QTcB = QT corrected for heart rate using Bazett's Correction
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.
<Programmer note: ECG includes heart rate, PR, QRS, QT, and QTcB. >
Program: /AAXXXXX/ECR/sas prg/stsas/tab tab-programname.sas DDMMMYYYY HH:MM

Table 14.3.5.10 12-Lead Electrocardiogram Shift From Check-in

		Predose=Normal			Predose=ANCS			Predose=ACS		
		Postdose			Postdose			Postdose		
Treatment	Day	Normal	ANCS	ACS	Normal	ANCS	ACS	Normal	ANCS	ACS
A	29+/-2	X	X	X	X	X	X	X	X	X
	54+/-2	X	X	X	X	X	X	X	X	X
B	29+/-2	X	X	X	X	X	X	X	X	X
	54+/-2	X	X	X	X	X	X	X	X	X
C	29+/-2	X	X	X	X	X	X	X	X	X
	54+/-2	X	X	X	X	X	X	X	X	X

ANCS = Abnormal, Not Clinically Significant, ACS = Abnormal, Clinically Significant
Baseline is Check-in measurement.
Early termination records are excluded from the summary.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas prg/stsas/tab tab-programname.sas DDMMMYYYY HH:MM

13. LISTING SHELLS

The following listing shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the listings that will be presented and included in the final report.

Note to programmer: Formatting and content of listings may be modified based on provided data.

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

Site	Laboratory Group	Test Name	Gender	Age Category	Reference Range	Unit
XXXXX	Serum Chemistry	Test Name	<>	<>	XX – XX	units
		Test Name	<>	<>	XX – XX	units
		Test Name	<>	<>	XX – XX	units
		Test Name	<>	<>	XX – XX	units
		Test Name	<>	<>	XX – XX	units
		Test Name	<>	<>	XX – XX	units
	Hematology	Test Name	<>	<>	XX – XX	units
		Test Name	<>	<>	XX – XX	units
		Test Name	<>	<>	XX – XX	units
		Test Name	<>	<>	XX – XX	units
		Test Name	<>	<>	XX – XX	units

<similar for remaining Laboratory Groups and Test Names>

Program: /AAXXXXX/ECR/sas_prg/stsas/lis LIS_PROGRAMNAME.SAS DDMMMYYYY HH:MM

Appendix 16.2.1 Study Completion/Early Termination

Subject Number	Site	Treatment	Visit Name	Visit Date	Completed Study?	Reason for Discontinuation	Specify	Date of Completion or Discontinuation
XXXX	XXXX	X	XXXX	DDMMMYYYY	Yes			DDMMMYYYY

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.1 Subject Information

Subject Number	Site Number	Treatment	Informed/ Reconsent Consent Date	Protocol Amendment/ Reconsent Version No.	Subject Caption	Active?	Enrolled?	Dropped?	Enrolled Date	Randomization Number	Randomization Date	Registration Date
XXXX	XXXX	X	DDMMMYYYY/ DDMMMYYYY	XX/ XX	XXX	XXX	XXX	XXX	DDMMMYYYY	XX	DDMMMYYYY	DDMMMYYYY

Protocol amendment number indicates the version that the subject consented under.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.2 Demographics

Subject Number	Treatment	Visit Name	Visit Date	Date Of Birth	Age (yrs)	Gender	Ethnicity	Primary Race	Height (cm)	Weight (kg)	BMI (kg/m^2)
X	A	Screening	DDMMMYYYY	DDMMMYYYY	XX	XXXX	XXXXXXXXXX	XXXXXXXXX	XX.X	XXX.X	XX.XX
X	B	Screening	DDMMMYYYY	DDMMMYYYY	XX	XXXX	XXXXXXXXXX	XXXXXXXXX	XX.X	XXX.X	XX.XX
X	C	Screening	DDMMMYYYY	DDMMMYYYY	XX	XXXX	XXXXXXXXXX	XXXXXXXXX	XX.X	XXX.X	XX.XX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.3 Physical Examination

Subject Number	Treat-ment	Visit Name	Date of Examination	Was Physical Examination Performed?	If No, Specify	Body System	Result	Abnormal Fingings	Clinically Significant?
X	X	X	DDMMMYYYY	Yes		XXXXXXXXX	Abnormal	XXXXXXXXXX	No

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.4 Chest X-Ray

Subject Number	Treatment	Visit Name	Visit Date	Date of Chest X-Ray	Abnormalities Found?	Specify
X	X	XXXXXXX	DDMMMYYYY	DDMMMYYYY	Yes	

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.5 Medical History

Subject Number	Treatment	Visit Name	Visit Date	Any Past and/or Concomitant Disease or Past Surgeries?	Medical History Number	Reported/ Preferred Term	Date Onset	Date End	Ongoing?
X	X	Screening	DDMMMYYYY	Yes	XX	XXXXXXXXXX/ XXXXXXXXXX	DDMMMYYYY	DDMMMYYYY	YES

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.6 Substance Use

Subject Number	Treatment	Visit Name	Visit Date	Ever Used Cigarettes?	Amount of Cigarettes (Unit)	Frequency of Cigarettes	Start Date	End Date	Duration of Cigarette Use (Unit)	Number of Pack-Year
X	X	Screening	DDMMMYYYY	Current	XXXXXXXX (XX)	XXXXXXXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXX (XX)	XX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1 Subject Eligibility

Subject Number	Treat-ment	Visit Name	Did subject meet all eligibility criteria?	Crieterion Not Met
X	X	X	No	EXCLUSION X

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.2 Study Drug Administration

Subject Number	Treatment	Visit		Took Study Treatment?	Dose 1		Dose 2		Kit Number		
		Name	Date		Date	Time	Date	Time	1	2	3
X	X	XXX	DDMMMYYYY	Yes	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XXX	XXX	XXX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.3 Drug Accountability

Subject Number	Treatment	Visit		Dispensed			Returned			Tablets Taken	Tablets Missed
		Name	Date	Day	Date	Tablets	Day	Date	Tablets		
X	X	XXX	DDMMMYYYY	XXX	DDMMMYYYY	XX	XXX	DDMMMYYYY	XX	XX	XX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.4 Tiotropium and Albuterol Administration

Subject Number	Treatment	Visit		Take Tiotropium?	Last Tiotropium Dose		Take Albuterol?	Last Albuterol Dose	
		Name	Date		Date	Time		Date	Time
X	X	XXX	DDMMMYYYY	Yes	DDMMMYYYY	HH:MM	Yes	DDMMMYYYY	HH:MM

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.5.1 Bronchoscopy and BAL Biomarkers (I of II)

Subject Number	Treatment	Visit Name	Visit Date	Bronchoscopy Performed?	Date Performed	Time Performed	BAL Sample Collected?	Date of Collection	Time of Collection	Bronchial Brushings Performed?	Date Performed
X	X	XXXXXXXXX	DDMMMYYYY	Yes	DDMMMYYYY	HH:MM	Yes	DDMMMYYYY	HH:MM	Yes	DDMMMYYYY

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.5.2 Bronchoscopy and BAL Biomarkers (II of II)

Subject Number	Treatment	Visit Name	Visit Date	Macrophages cells/mL)	Neutrophages (cells/mL)	Eosinophages (cells/mL)	Lymphocytes (cells/mL)	Macrophages (%)	Neutrophages (%)	Eosinophages (%)	Lymphocytes (%)
X	X	XXXXXXXXX	DDMMMYYYY	XXX	XXX	XXX	XXX	XX	XX	XX	XX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:

Appendix 16.2.5.6 Blood Biomarker Samples

Subject Number	Treatment	Visit Name	Visit Date	Biomarker Blood Sample Collected?	Planned Time Point	Date of Collection	PD Time of Collection	Fibrinogen Date/Time of Collection	Result (Unit)	CRP Date/Time of Collection	Result (Unit)
X	X	XXXXXXXXX	DDMMMYYYY	Yes	XX	DDMMMYYYY	HH:MM	DDMMMYYYY/ HH:MM	XXXX (XX)	DDMMMYYYY/ HH:MM	XXXX (XX)

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.7 Pharmacokinetic Sampling

Subject Number	Treatment	Visit Name	Visit Date	Planned Time Point	Sample Collected?	Date of Collection	Time of Collection
X	X	XXX	DDMMMYYYY	XX	Yes	DDMMMYYYY	HH:MM

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.8 Prior and Concomitant Medications

Subject Number	Treatment	Medication (WHO* Term)	Indication	AE ID	MH ID	Dose/ Unit	Freq.	Route	Start Date	End Date	Ongoing?
X	X	ACETAMINOPHEN (ACETAMINOPHEN)	< >	XX	XX	XX mg	Once	Oral	DDMMMYYYY	DDMMMYYYY	No

Concomitant medications are coded with WHO Dictionary Version 01MAR2015.
Freq. = Frequency, AE = Adverse Event, MH = Medical History, ID = Identification
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.1.1 Peak Expiratory Flow and Breathlessness (Modified Borg Dyspnea Scale)

Subject Number	Treatment	Day	Assessment		Peak Flow				Breathlessness (Modified Borg Dyspnea Scale)
			Date	Time	First	Second	Third	Main	
X	X	XX	DDMMMYYYY	HH:MM	XX	XX	XX	XX	0.5, very mild

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.1.2 Symptoms of COPD Exacerbation (I of II)

Subject Number	Treatment	Day	Assessment		Sputum		
			Date	Time	Quantity	Color	Consistency
X	X	XX	DDMMMYYYY	HH:MM	less than 1 tbs.	White	Watery

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.1.3 Symptoms of COPD Exacerbation (II of II)

Subject Number	Treatment	Day	Assessment Date	Assessment Time	Cough	Wheeze	Sore Throat	Nasal Congestion	Nasal Discharge	Body Temperature Above 100°F	Symptm Score	Symptm Severity
X	X	XX	DDMMMYYYY	HH:MM	Yes	Yes	Yes	Yes	Yes	Yes	3.5	Severe

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.1.4 Duke Activity Status Index (DASI) Scores

Subject Number	Treatment	Day	Assessment Date	Assessment Time	DASI 12-Item Questionnaire 1	2	3	4	5	6	7	8	9	10	11	12	DASI Score
X	X	XX	DDMMMYYYY	HH:MM	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	XX

1. Able to take care of yourself that is eating, dressing, bathing, or using the toilet yet?
2. Able to walk indoors, such as around the house?
3. Able to walk a block or 2 on level ground?
4. Able to climb a flight of stairs or walk up a hill without stopping?
5. Able to run a short distance?
6. Able to do light work around the house like dusting or washing dishes?
7. Able to do moderate work around the house like vacuuming, sweeping floors or carrying in the groceries?
8. Able to do heavy work around the house like scrubbing floors, or lifting or moving heavy furniture?
9. Able to do yard work like raking leaves, weeding, or pushing a power mower yet?
10. Are you having sexual relations?
11. Able to participate in moderate recreational activities like golf, bowling, dancing, double tennis, or throwing a baseball or football yet?
12. Are you able to participate in strenuous sports like swimming, singles tennis, football, basketball, or skiing?

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

All listings of PD measures in blood and BAL, Appendices 16.2.6.2.1 to 16.2.6.2.4, will have the following format:

Page 1 of X

Appendix 16.2.6.1.2.X < >

Subject Number	Treat-ment	Visit	Day	Collection Date	Time	Parameter1 < Range> (Unit)	Parameter2 < Range> (Unit)	Parameter3 < Range> (Unit)	Parameter4 < Range> (Unit)	Parameter5 < Range> (Unit)
XXXXXX	X	Predose	1	DDMMMYYYY	XX:XX	XXXXX.XX	X.XX	X.XX	XXXX.XX	XXX.XX
		X.X hrs postdose	X	DDMMMYYYY	XX:XX	XXXX.XX	XX.XX	X.XX	XXXX.XX	XX.XX
		X hrs postdose	X	DDMMMYYYY	XX:XX	XXXX.XX	X.XX	X.XX	XXXX.XX	XX.XX
		X hrs postdose	X	DDMMMYYYY	XX:XX	XXXX.XX	X.XX	X.XX	XXXX.XX	XX.XX
		XX hrs postdose	X	DDMMMYYYY	XX:XX	XXXXX.XX	X.XX	X.XX	XXXX.XX	XX.XX
		XX hrs postdose	X	DDMMMYYYY	XX:XX	XXXX.XX	X.XX	X.XX	XXXX.XX	XX.XX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.2.22 Baseline Dyspnea Index

Subject Number	Treatment	Visit Name	Visit Date	Date of Assessment	Functional Impairment	Magnitude of Task	Magnitude of Effort
X	X	Screening	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.2.23 Transition Dyspnea Index

Subject Number	Treatment	Visit Name	Visit Date	Planned Time Point	Date of Assessment	Change in Functional Impairment	Change in Magnitude of Task	Change in Magnitude of Effort
X	X	Screening	DDMMMYYYY	XX	DDMMMYYYY	XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.2.24 Pulmonary Function Test (Spirometry)

Subject Number	Treatment	Visit Name	Visit Date	Planned Time Point	Pulmonary Function Test Performed?	Assessment Date	Assessment Time	Pre/ Post/ Change^	Test Type	Result Actual	Result Predicted	Result Percent (%)
X	X	XXX	DDMMMYYYY	XX	Yes	DDMMMYYYY	HH:MM	Pre	FVC (L)	XX	XX	XX
									FEV1(L)	XX	XX	XX
									FEV1/FVC	XX	XX	XX
									IC (L)	XX	XX	XX

FEV1 = forced expiratory volume in one second, FVC = forced vital capacity, IC = inspiratory capacity, L = liter
^ Pre- and Post-Bronchodilator, Change = Post- minus Pre-
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Programmers note: Please calculate Change and present this as the 3rd category.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.2.25 Change from Baseline in Pulmonary Function Test (Spirometry)

Subject Number	Treatment	Visit Name	Visit Date	Planned Time Point	Pre/ Post/ Change^	Test Type	Baseline Actual	Baseline Predicted	Baseline Percent (%)	Test Type	Change from Baseline Actual	Change from Baseline Predicted	Change from Baseline Percent (%)
X	X	XXX	DDMMMYYYY	XX	Pre	FVC (L)	XX	XX	XX	FVC (L)	XX	XX	XX
						FEV1(L)	XX	XX	XX	FEV1(L)	XX	XX	XX
						FEV1/FVC	XX	XX	XX	FEV1/FVC	XX	XX	XX
						IC (L)	XX	XX	XX	IC (L)	XX	XX	XX

FEV1 = forced expiratory volume in one second, FVC = forced vital capacity, IC = inspiratory capacity
^ Pre- and Post-Bronchodilator, Change = Post- minus Pre-
Baseline is Check-in measurement.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.2.26 COPD Assessment Test

Subject Number	Treat-ment	Visit Name/ Date	Planned Time Point	Date of Assessment	Rate Cough (0-5)	Rate Mucus Production (0-5)	Rate Chest Tightness (0-5)	Rate Breath-lessness (0-5)	Rate Level of Activities (0-5)	Rate Level of Confidence (0-5)	Rate Level of Sleepiness (0-5)	Rate Level of Energy (0-5)	Total Score
X	X	XXXX/ DDMMMYYYY	XX	DDMMMYYYY	X	X	X	X	X	X	X	X	XX

Cough: 0 = I never cough, 5 = I cough all the time
Mucus Production: 0 = I have no phlegm (mucus) in my chest at all, 5 = My chest is completely full of phlegm (mucus)
Chest Tightness: 0 = My chest does not feel tight at all, 5 = My chest feels very tight
Breathlessness: 0 = When I walk up a hill or one flight of stairs I am not breathless, 5 = When I walk up a hill or one flight of stairs I am very breathless
Level of Activities: 0 = I am not limited doing any activities at home, 5 = I am very limited doing any activities at home
Level of Confidence: 0 = I am confident leaving my home despite my lung condition, 5 = I am not at all confident leaving my home because of my lung condition
Level of Sleepiness: 0 = I sleep soundly, 5 = I don't sleep soundly because of my lung condition
Level of Energy: 0 = I have lots of energy, 5 = I have no energy at all
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.1 Adverse Events (I of III)

Subject Number	Treatment	AE Number	TE?^	Adverse Event	Preferred Term*	Time From Dose (DD:HH:MM)	Start Date	Start Time	End Date	End Time	Duration (DD:HH:MM)	Ongoing?
X	X	X	Yes	XXXXXXXXXXXX	XXXXXXXXXXXX	XX:XX:XX	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XX:XX:XX	XXXX

^ = Abbreviation for treatment-emergent, * = Adverse events are classified according to MedDRA Version 18.0.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.2 Adverse Events (II of III)

Subject Number	Treatment	Adverse Event	Start Date	Start Time	Severity	Outcome	Relationship to Study drug	Action Taken With Study Drug	Other Action
X	X	XXXXXXXXX	DDMMMYYYY	XX:XX	Mild	Recovered/ Resolved	XXXXXXXX	XXXXXXXXX	XXXXXXXX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.3 Adverse Events (III of III)

Subject Number	Treatment	Adverse Event	Start Date	Start Time	Serious	Serious Criteria * 1	2	3	4	5	6
X	X	XXXXXXXXX	DDMMMYYYY	XX:XX	YES	XXX	XXX	XXX	XXX	XXX	XXX

Only subjects who reported adverse events during the study were included in the listing.
* Serious Criteria: 1 = Death, 2 = Life Threatening, 3 = Initial or Prolonged Hospitalization
4 = Persistent or Significant Disability or Incapacity, 5 = Congenital Anomaly or Birth Defect
6 = Other Serious or Important Medical Events
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.4 Adverse Event Non-Drug Therapy

Subject Number	Treatment	Adverse Event	Start Therapy Date	Start Therapy Time	Stop Therapy Date	Stop Therapy Time	Description
X	X	DRY LIPS	DDMMMYYYY	XX:XX	DDMMMYYYY	XX:XX	PETROLEUM JELLY

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.5 Adverse Event Preferred Term Classification

Subject Number	Treatment	Adverse Event	Preferred Term*	System Organ Class	Start Date	Start Time
X	X	XXXXXXX XXXXX XXXX XXXXXX	XXXXXXXXXX XXXXXXX	XXXXXXXXXXXXXXXXXXXX	DDMMMYYYY	XX:XX

* Adverse events are classified according to MedDRA Version 18.0.
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Note: Appendices 16.2.8.2 and 16.2.8.3 will have the following format.

Appendix 16.2.8.1 Clinical Laboratory Report - Serum Chemistry

Subject Number	Age/ Gender	Visit Name	Visit Date	Treat-ment	Collection Date	Collection Time	Parameter	Reference Range (Unit)	Result Flag	Reference Range (SI Unit)	Result (SI Unit)	Comments
X	XX/X	Screening	DDMMMYYYY	X	DDMMMYYYY	HH:MM	XXXXXXXXXXXXX	XX - XX (unit)	XX HN	XX - XX (unit)	XX	XXXXXXXXXXXXX
		XXXX	DDMMMYYYY		DDMMMYYYY	HH:MM	XXXXXXXXXXXXX	XX - XX (unit)	XX LY	XX - XX (unit)	XX	XXXXXXXXXXXXX

Abnormal Flag: H = Above Reference Range, L = Below Reference Range
Clinical Significance: N = Not Clinically Significant, Y = Clinically Significant
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 - 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 - 55
Treatment C: Multiple oral doses of placebo BID on Days 1 - 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.4 Urine Alcohol and Drug Screen

Subject Number	Visit Name	Visit Date	Treatment	Was the Lab Sample Collected?	Planned Time Point	Date of Collection	Test	Result
X	Screening	DDMMMYYYY	X	XXXXXXX	XX	DDMMMYYYY	XXXXXXX	NEGATIVE

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.5 Pregnancy Test

Subject Number	Visit Name	Visit Date	Treatment	Was the Pregnancy Test Done?	Reason for Not Done	Test Type	Date of Collection	Result
X	Screening	DDMMMYYYY	X	XXX	XXXX	XXXXXX	DDMMMYYYY	NEGATIVE

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.6 Serology

Subject Number	Visit Name	Visit Date	Treatment	Sample Collected?	Date of Collection	Hepatitis B Result	Hepatitis C Result	HIV Result
X	Screening	DDMMMYYYY	X	Yes	DDMMMYYYY	XXXXXX	XXXXXX	XXXXXX

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.7 Vital Signs

Subject Number	Treatment	Visit Name	Visit Date	Planned Time Point	Date	Time	Test	Blood Pressure (mmHg) Systolic/Diastolic	Heart Rate (bpm)	Respiration (rpm)	Temperature (°C)	Oxygen Saturation (%)	Weight (kg)
X	X	Screening	DDMMMYYYY	XXXXXXXX	DDMMMYYYY	HH:MM	XXXX	XXX/ XX	XX	XX	XX.X	XX	XXX.X
		XXXXX	DDMMMYYYY	XXXXXXXX	DDMMMYYYY	HH:MM							XXX.X
			DDMMMYYYY	XXXXXXXX	DDMMMYYYY	HH:MM		XXX/ XX	XX	XX			

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.8 12-Lead Electrocardiogram

Subject Number	Treatment	Visit Name	Visit Date	Planned Time Point	Assessment Date	Assessment Time	ECG Result	Heart Rate (bpm)	PR (msec)	RR (msec)	QRS (msec)	QT (msec)	QTcB* (msec)	If Abnormal, Specify
X	X	Screening	DDMMMYYYY	XXXXXX	DDMMMYYYY	HH:MM	XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	
		XXXXX	DDMMMYYYY	XXXXXX	DDMMMYYYY	HH:MM	XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	

* QTcB = QT corrected for heart rate using Bazett's Correction
Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.9 Telephone Contact

Subject Number	Treatment	Was Subject Contacted?	Reason Subject Not Contacted	Date of Contact
X	X	Yes	XXXXXXXXXX	DDMMMYYYY

Treatment A: Multiple oral doses of YPL-001 80 mg BID on Days 1 – 55
Treatment B: Multiple oral doses of YPL-001 160 mg BID on Days 1 – 55
Treatment C: Multiple oral doses of placebo BID on Days 1 – 55
Note: Patients following up to Amendment version 5 of the protocol also received a morning dose on Day 56.

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM