CLINICAL STUDY PROTOCOL

Title: A Phase 2 Multiple Dose Study to Evaluate the Efficacy and Safety of PUL-042 Inhalation Solution in Reducing the Infection Rate and Progression to COVID-19 in Adults Exposed to SARS-CoV-2

Protocol Number:	PUL-042-501
IND Number/Version:	148628/v.1.60 (29 January 2021)
Investigational Product:	PUL-042 Inhalation Solution
IND Applicant and Sponsor:	Pulmotect, Inc. 3900 Essex Lane, Suite 575 Houston, TX 77027 USA
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Investigational Site:	Multicenter
Principal Monitor:	Colin Broom, MD Pulmotect, Inc. 3900 Essex Lane, Suite 575 Houston, TX 77027

_____ _____
Signature Date

INVESTIGATOR'S SIGNATURE

I agree to abide by all the provisions set forth in this attached protocol. I also understand that these materials contain confidential information belonging to Pulmotect, Inc. Except as may be otherwise agreed to in writing, I agree to hold such information in confidence and not to disclose it to others (except where required by applicable law) nor use it for unauthorized purposes. In the event of actual or suspected breach of this obligation, Pulmotect, Inc. should be promptly notified.

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Printed Name of Investigator

_____

Signature of Investigator

_____

Date

PROCEDURES IN CASE OF EMERGENCY

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4. LIST OF ABBREVIATIONS

The following abbreviations are used in this study protocol.

Abbreviation or specialist term	Explanation
AE	adverse event
ANC	absolute neutrophil count
CFR	Code of Federal Regulations
COVID-19	Disease caused by infection with SARS-CoV-2
DSMB	Data and Safety Monitoring Board
eCRF	electronic case report form
EDC	electronic data capture
FDA	Food and Drug Administration
FEV1	forced expiratory volume in 1 second
FVC	Forced Vital Capacity
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IRB	Institutional Review Board
MERS	Disease caused by infection with MERS-CoV
ODN	ODN M362
OHRP	Office for Human Research Protections
Pam2	Pam2CSK4
PUL-042	drug product consisting of a 4:1 molar ratio of Pam2:ODN; Inhalation Solution
Pulmotect	Pulmotect, Inc.
RNA	ribonucleic acid
SAE	serious adverse event
SAP	statistical analysis plan
SARS	Disease caused by infection with SARS-CoV
SARS-CoV-2	Coronavirus causing COVID-19
SWFI	sterile water for injection
TLR	Toll-like receptor
USP	United States Pharmacopeia
WHO	World Health Organization

5. BACKGROUND

This protocol is being conducted under a COVID-19 specific IND filed with the Division of Pulmonary, Allergy and Critical Care of the FDA and is intended to provide preliminary data on the efficacy and safety of PUL-042 in reducing the infection rate and progression to COVID-19 in adult subjects exposed to SARS-CoV-2. Evaluation of these data will determine the feasibility of advancing to Phase 3 clinical development to pursue an NDA filing and the potential for Emergency Use Authorization.

This section includes a brief summary of the rationale for clinical investigation of PUL-042 and a summary of the nonclinical data available on PUL-042. More detailed information can be found in the Investigator's Brochure.

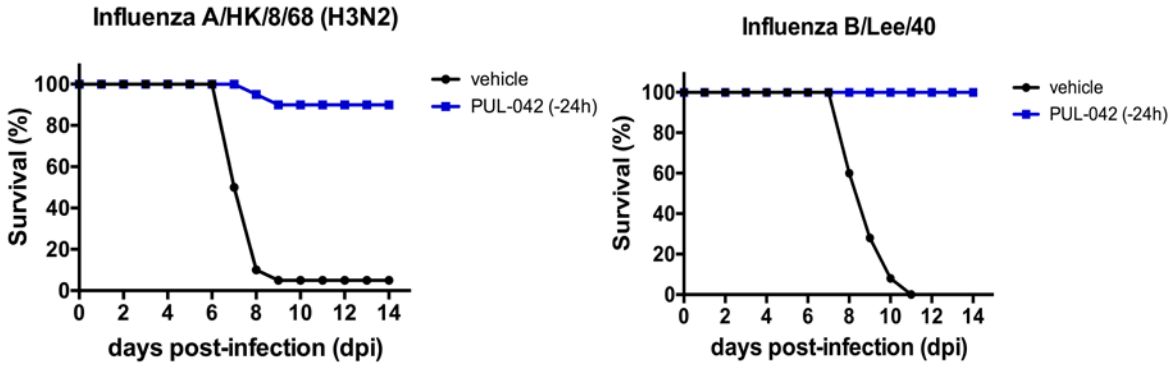
5.1. Introduction

Respiratory infection can be caused by a variety of pathogenic organisms including bacteria, fungi, and viruses and is one of the leading causes of death worldwide[1]. Even in developed countries, respiratory infection continues to be the leading cause of death from infection and a serious complication for patients being treated for other diseases. The threat of respiratory infections is elevated when there is a decreased level of host resistance such as in immunosuppressed individuals and when there is an increased level of pathogen exposure such as in the case of bioterror attacks and biowarfare or epidemics and pandemics such as the current COVID-19 pandemic.

Pulmotect, Inc. (Pulmotect) has developed a novel therapeutic to stimulate innate immunity in the lungs that may provide protection against lower respiratory tract infection. The technology platform is a direct result of basic research conducted by Pulmotect's founders on the mechanisms of microbial resistance in the lung epithelium[2,3,4,5,6]. PUL-042 is a combination of two synthetic molecules, a lipopeptide (Pam2CSK4 acetate [Pam2]) and a phosphorothioate oligodeoxynucleotide (ODN M362 sodium [ODN]) that act synergistically as agonists of Toll-like receptors (TLR)2/6 and TLR9, respectively. The response is primarily localized and specific to the site of administration. In animal studies, inhalation treatment with PUL-042 results in increased survival rates after respiratory exposure to a broad spectrum of pathogens including Gram-positive and Gram-negative bacteria (including three Class A bioterror agents), the fungus *Aspergillus fumigatus*, and viral pathogens.

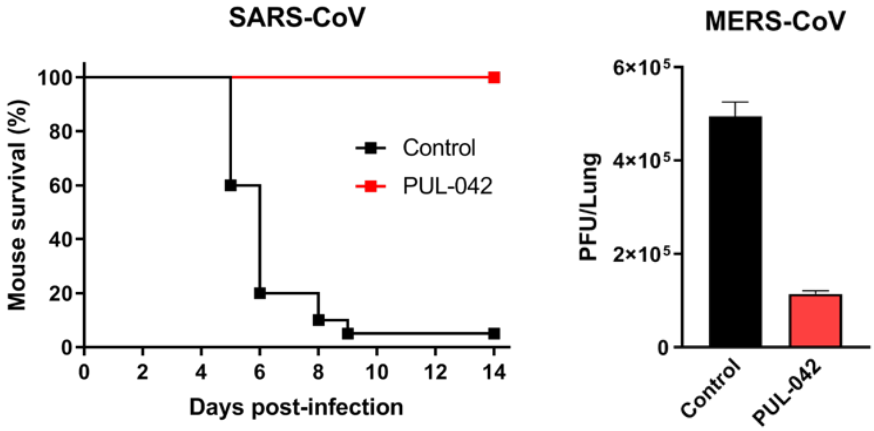
The activity of PUL-042 has been evaluated in animal models against a range of viruses as a single agent[7] and in combination with existing anti-viral drugs, including oseltamivir against influenza H3N2 for successful treatment at more advanced stages of infection[8].

Figure 1: Pretreatment with PUL-042 has been demonstrated to protect mice against Influenza A and B



Antiviral activity has also been demonstrated against coronavirus strains. In unpublished experiments conducted at the University of Texas Medical Branch at Galveston (UTMB) a single inhaled dose of PUL-042 was shown to protect mice from SARS-CoV, and significantly reduced the amount of virus in the lungs after infection with MERS-CoV virus (Figure 2). The antiviral activity of PUL-042 therefore has the potential for the prevention of infection with the SARS-CoV-2 virus.

Figure 2: Pretreatment with PUL-042 has been demonstrated to protect mice against SARS-CoV and MERS-CoV

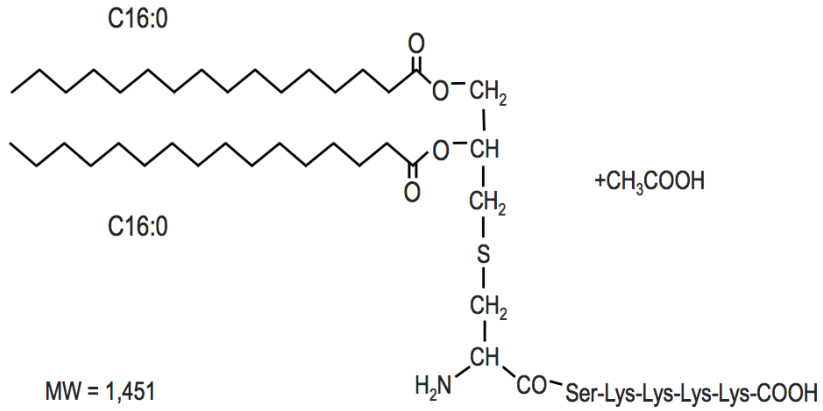


5.2. Chemical Name and Structure

The investigational product, PUL-042 Inhalation Solution, is a combination of Pam2 and ODN. Pam2 is a synthetic 6-amino acid lipopeptide as an acetate salt, and ODN is a synthetic 25-base, single-stranded oligonucleotide that contains unmethylated CpG dinucleotides with a phosphorothioate backbone as a sodium salt. The structure of Pam2 and nucleotide sequence of ODN are shown in Figure 3.

Figure 3: Structure and Nucleotide Sequence of PUL-042 Components Pam2 and ODN

Pam2



C = carbon; H = hydrogen; O = oxygen; S = sulfur; Ser = serine, Lys = lysine; MW = molecular weight

ODN

5′–TCG TCG TCG TTC GAA CGA CGT TGA T–3′ M.W.: 8,049.5
(single-stranded, nuclease-resistant phosphorothioate oligodeoxynucleotides)

5.3. Nonclinical Studies

The nonclinical pharmacology, pharmacokinetics, and toxicology of PUL-042 are described in detail in the Investigator's Brochure.

5.4. Clinical Studies

The initial phase 1 study of PUL-042 Inhalation Solution (PUL-042-001) "A Randomized, Double-Blind, Placebo-Controlled, Ascending Dose Study to Assess the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of PUL-042 Inhalation Solution in Healthy Subjects" has been completed. Subjects were administered a single dose of PUL-042 Inhalation Solution by nebulization. A total of 4 mL of a solution of PUL-042 at increasing concentrations was administered using sterile water for injection (SWFI) as the diluent.

Review of the data from the PUL-042-001 study indicated that there was a potential pharmacodynamic effect indicated by a rise in the absolute neutrophil count (ANC) as measured at 4 hours post dose in subjects treated with PUL-042 Inhalation Solution compared to placebo. The ANC was at or near baseline levels when measured again at 24 hours post dose. All values were within the normal range at the 24-hour time point. The neutrophil response was confirmed in sheep and mice, and furthermore was shown to be dose dependent in mice. The time course of that response has been further explored in subjects in the study PUL-042-003 "A Randomized, Open-label, Crossover Study to Assess the Safety, Tolerability and Pharmacodynamics of PUL-042 Inhalation Solution in Healthy Subjects and the Effect of Pretreatment with Cromolyn Sodium or Albuterol Sulfate".

A similar potential pharmacodynamic effect was seen in the spirometry data (specifically the forced expiratory volume in 1 second [FEV1]) from PUL-042-001, likely due to the effect of PUL-042 on the bronchial airways. A dose-dependent decrease in FEV1 was seen with a nadir at approximately 30 minutes post-dose in subjects treated with PUL-042 Inhalation Solution. There was no comparable decline observed with placebo. These measurements were largely within the 12% change from baseline accepted as normal variability. This was followed by a recovery to near baseline levels at 24 hours post dose. Over the course of 7 days, the mean FEV1 was within 0-5% of the baseline value, with the subjects who received higher doses of PUL-042 showing a larger mean decrease in FEV1. None of the decreases in FEV1 were accompanied by signs of respiratory distress or a drop in oxygen saturation. None of the FEV1 results in the PUL-042 inhalation treated groups were statistically different from placebo after the 30-minute time point. The MTD delivered as a single dose was established as 40.6 μg Pam2 : 59.5 μg ODN in PUL-042-001.

A second phase 1 study (PUL-042-003) has been completed. PUL-042-003 was a randomized, open-label, cross-over study to determine the safety and tolerability of PUL-042 Inhalation Solution and to explore the effect of pretreatment with either cromolyn sodium or albuterol sulfate. The primary objective of this study was to determine the safety and tolerability in healthy normal subjects of single or repeated doses of PUL-042 in SWFI. Exploratory objectives include determining whether ANC was an indicator of biological activity and to determine 1) the duration of local biological activity in the bronchial airways by serial FEV1 measurements, 2) whether the administration of cromolyn sodium prior to the administration of PUL-042 had an effect on the FEV1 response, and 3) whether the administration of albuterol prior to the administration of PUL-042 had an effect on the FEV1 response.

In protocol PUL-042-003, the first cohort of 8 subjects (cohort 1) received a dose of 20.3 μg Pam2 : 29.8 μg ODN (1/2 the single-dose MTD of PUL-042) with or without pretreatment with cromolyn sodium (4 each). Subjects were then crossed over to the alternative treatment after a 2-week follow-up period and an additional 2-week washout period.

A similar design was used for the second cohort (8 subjects) with PUL-042 +/- albuterol sulfate. The second cohort of subjects received a total dose of 40.6 μg Pam2 : 59.5 μg ODN as two doses over 3 days (1 dose on Day 1 and 1 dose on Day 3) and a total dose of 81.2 μg Pam2 : 119 μg ODN as four doses over 32 days (1 dose each on Day 1, Day 3, Day 29 and Day 32).

Results from PUL-042-003 showed no clinically significant abnormalities or changes from baseline for vital signs, electrocardiography, pulse oximetry, physical examination, or safety laboratory assessments.

In general, FEV1 results were consistent with those seen in PUL-042-001 with an early onset decrease in FEV1 in some subjects that spontaneously reversed to near baseline levels over several minutes to hours. In the PUL-042-001 study, a small decrease in average FEV1 was also observed 7 days post-treatment (the last observation in that study) compared to the pre-dose baseline. A similar pattern was observed through 7 days post-treatment in PUL-042-003. Observations at later time points showed sporadic decreases in FEV1 values, but longer-term follow-up measurements of FEV1 gave results comparable to the initial pre-dose baseline values. As in study PUL-042-001, none of the decreases in FEV1 were accompanied by signs of respiratory distress or a drop in oxygen saturation. Pre-treatment with cromolyn sodium or albuterol sulfate had no significant effect on the short lasting FEV1 decreases observed following administration of PUL-042.

Currently there is an ongoing Phase 2 study, PUL-042-402 (A Phase 2, Single-Center, Double-Blind, Placebo-Controlled Study of PUL-042 Inhalation Solution in Rhinovirus-induced Symptoms in Current Smokers with GOLD Stage 0 COPD), that is evaluating the effects of PUL-042 on peak lower respiratory symptoms and safety in subjects with an experimentally induced rhinovirus infection with laboratory human rhinovirus strain HRV A16.

Subjects are dosed with PUL-042 (20.3 μg Pam2 : 29.8 μg ODN [50 μg PUL-042]) or placebo 24 hours prior to viral inoculation and again 48 hours post inoculation. The subjects are then followed for 6 weeks. To date, 19 of the planned 24 subjects have completed the study and data from 18 subjects reviewed by the Data Safety Monitoring Board (DSMB). The DSMB approved enrolling 6 additional subjects based on the data from these subjects. The study has been suspended due to the COVID-19 pandemic but, is anticipated to re-start in Q4 2020. The study remains blinded to treatment related efficacy and safety. There have been no Serious Adverse Events reported and no apparent safety concerns with PUL-042 administration following a respiratory viral infection.

5.5. Dosing

The dose selected is based on the results of PUL-042-001, a single ascending dose study to determine the maximum tolerated dose of PUL-042 in healthy volunteers, PUL-042-003, an open-label crossover study to investigate the effects of pretreatment with cromolyn sodium or albuterol sulfate on the safety, tolerability, and pharmacodynamics of PUL-042 administered to healthy volunteers, and PUL-042-402 an ongoing double-blind study of PUL-042 in a COPD rhinovirus challenge model.

Based on the results of these studies, the dose level of PUL-042 Inhalation Solution in the current study will be 20.3 μg Pam2 : 29.8 μg ODN/mL (50 μg PUL-042 [this is the same dose level currently used in the ongoing viral challenge study]). A total of up to 4 doses will be administered over a 10 day period for a total dose of 81.2 μg Pam2 : 119.2 μg ODN.

Doses of PUL-042 or placebo will be prepared by an unblinded pharmacist and administered to the subject within 4 hours of preparation. Further details will be supplied in a pharmacy manual.

Doses will be administered via nebulization to deliver 4 mL using a PARI Sprint nebulizer equipped with a filter valve to prevent aerosol generation. The nebulizer will be operated until all drug is delivered. Each nebulizer will be dedicated to each subject during participation in the study. A new filter pad will be used in the filter valve for each administration of PUL-042. A nose clip will be used during the nebulization procedure.

Despite the use of the above nebulization equipment health care professionals should wear appropriate personal protective equipment and observe the procedure from a distance of at least six feet or preferably from another room until after nebulization has been completed.

6. STUDY OBJECTIVES

6.1. Primary Objective

To determine the efficacy of PUL-042 Inhalation Solution in the prevention of viral infection with SARS-CoV-2 and progression to COVID-19 in subjects: 1) who have repeated exposure to individuals with SARS-CoV-2 infection, and 2) are asymptomatic at enrollment.

The primary endpoint is the severity of COVID-19 as measured by the maximum difference from the baseline value in the Ordinal Scale for Clinical Improvement within 28 days from the start of experimental therapy.

6.2. Secondary Objective

To determine the difference in incidence of SARS-CoV-2 infection 28 days from the start of experimental therapy in subjects who test negative for SARS-CoV-2 at the pre-treatment visit

To determine the difference in incidence of SARS-CoV-2 infection 14 days from the start of experimental therapy in subjects who test negative for SARS-CoV-2 at the pre-treatment visit

To compare the severity of COVID-19 within 14 days from the start of experimental therapy

To compare the severity of COVID-19 within 28 days from the start of experimental therapy

To assess the requirement for ICU admission within 28 days from the start of experimental therapy

To assess the requirement for mechanical ventilation within 28 days from the start of experimental therapy

To assess mortality within 28 days from the start of experimental therapy

To determine the tolerability of PUL-042 Inhalation Solution in this population

7. INVESTIGATIONAL PLAN

7.1. Overall Study Design

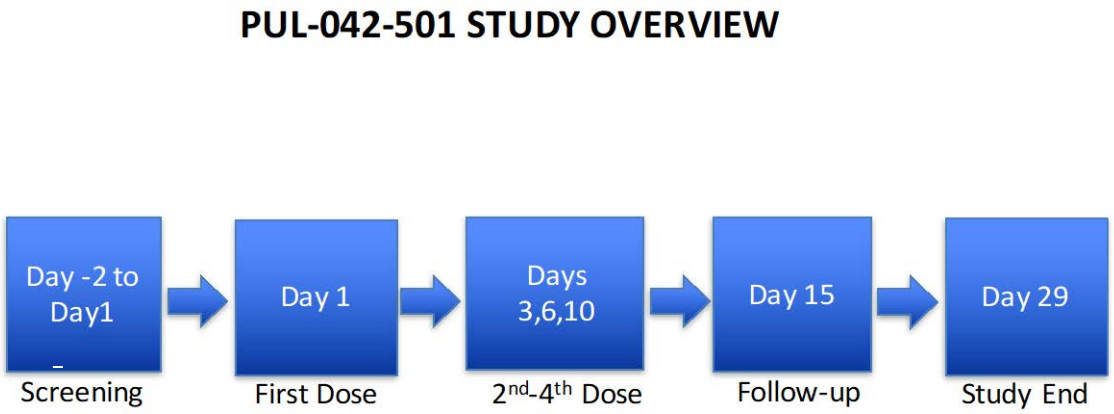
This will be a double-blind trial. A total of 200 subjects randomized 1:1 (PUL-042 Inhalation Solution: placebo) will be enrolled in the trial.

Doses will be administered via nebulization with a PARI sprint nebulizer. All subjects will receive up to 4 doses of PUL-042 Inhalation Solution or placebo over 10 days (Days 1, 3, 6, and 10).

Note: There is no Day 0 in this study.

An overview of the study design is presented in Figure 4.

Figure 4 Study Design



7.2. Subject Selection

7.2.1. Inclusion Criteria

Subjects aged 18 years or older must fulfill all of the following inclusion criteria to be eligible for the study:

1. Subjects must have recent exposure to SARS-CoV-2 (such as repeated or extensive exposure to an infected individual(s) or cohabiting with a SARS-CoV-2 positive individual).
2. Subjects must be 50 years or older if the exposure is due to cohabitation.
3. Subjects must be free of clinical signs or symptoms of a potential COVID-19 diagnosis (Ordinal Scale for Clinical Improvement score of 0) with a SARS-CoV-2 infection symptom score (fever, cough, shortness of breath, and fatigue) of 0 in each category.
4. Spirometry (forced expiratory volume in one second FEV_1 and forced vital capacity [FVC]) ≥70% of predicted value.
5. If female, the subject must be surgically sterile or ≥ 1 year postmenopausal. If of child-bearing potential (including being < 1years postmenopausal) and, if participating in sexual activity that may

lead to pregnancy, the subject agrees to use an effective dual method of birth control (acceptable methods include intrauterine device, spermicide, barrier, male partner surgical sterilization, and hormonal contraception) during the study and through 30 days after completion of the study.

6. If female, must not be pregnant, plan to become pregnant, or nurse a child during the study and through 30 days after completion of the study. A pregnancy test must be negative at the Screening Visit, prior to dosing on Day 1.
7. If male, must be surgically sterile or, if not surgically sterile and if participating in sexual activities that may lead to pregnancy, be willing to practice two effective methods of birth control (acceptable methods include barrier, spermicide, or female partner surgical sterilization) during the study and through 30 days after completion of the study.
8. Ability to understand and give informed consent.

7.2.2. Exclusion Criteria

Subjects will be excluded if they fulfill any of the following exclusion criteria:

1. Previous infection with SARS-CoV-2.
2. Receipt of any vaccine for the prevention of COVID-19 (single or multiple doses).
3. A SARS-CoV-2 infection symptom score greater than 0 in any of the 4 catergories (fever, cough, shortness of breath or fatigue) at the time of screening (Ordinal Scale for Clinical Improvement score of 0).
4. Known history of chronic pulmonary disease (e.g., asthma [including atopic asthma, exercise-induced asthma, or asthma triggered by respiratory infection], chronic pulmonary disease, pulmonary fibrosis, COPD), pulmonary hypertension, or heart failure.
5. Any condition which, in the opinion of the Principal Investigator, would prevent full participation in this trial or would interfere with the evaluation of the trial endpoints.

7.3. Study Integrity

This will be a double-blind study randomized 1:1 PUL-042 Inhalation Solution: placebo.

7.4. Number of Subjects

Approximately 200 subjects (100 Pul-042 Inhalation Solution: 100 placebo) will be enrolled.

7.5. Number of Study Sites

There will be up to 20 study centers.

7.6. Duration of Subject Participation

Subjects will participate for approximately 28 days.

7.7. Schedule of Study Activities

The schedule of events is presented in Table 1.

Table 1: Schedule of Events

Event	Screening	Dose 1[a]	Dose 2, 3, 4 [a]	Follow-up/Early Discontinuation from Study	Study Completion
	V1	V2	V3, 4, 5	V6	V7
	Day -2 to Day 1	Day 1[b]	Days 3, 6, 10	Day 15	Day 29
Informed consent	X				
Medical history	X				
Pregnancy test[c]	X			X	X
Physical exam	X	X	X	X	
Vital signs[d]	X	X	X	X	
Spirometry[e]	X	X	X		
Symptom score[f]	X	X	X	X	X
SARS-CoV-2 test[g]		X		X	X
Study drug administration[h]		X	X		
Adverse events	X	X	X	X	X
Concomitant medications	X	X	X	X	X
Ordinal Scale for Clinical Improvement	X	X	X	X	X
Randomization	X				

[a] Vital signs, adverse events, and concomitant medications will be assessed prior to administration of study medication and also at 30 minutes post-dose.
[b] There is no Day 0 in this study
[c] Urine pregnancy test or serum pregnancy test if women are of child-bearing potential. If urine pregnancy test is positive, a serum pregnancy test must be done. Pregnancy test is required for Early Discontinuation, not Day 15.
[d] Vital signs will include body temperature, blood pressure measurements, heart rate, and respiratory rate.
[e] Spirometry will be done at screening to document eligibility. On days of dosing, spirometry will be done pre-dose and at 30 minutes (±15) minutes post-dose. If the FEV1 is reduced > 10% compared to the pre-dose baseline the FEV1 should be repeated as clinically indicated
[f] SARS-CoV-2 symptoms will be assessed at each visit according to the Symptom Score
[g] SARS-CoV-2 testing will be performed pre-dose on Day 1 (Visit 2), Day 15 (Visit 6) and at Day 29 (Visit 7). Additional testing should be conducted at any point during the study when clinical symptoms are suggestive of potential COVID-19.
[h] Study drug administration must be done by a health care professional

7.8. Subject Participation

Subjects will be followed for the duration of the entire study (28 days) to assess the incidence of SARS-CoV-2 infection and progession to COVID-19. The following are general guidelines for study conduct:

- Subjects, including those in whom dosing is discontinued for any reason should complete all visits as outlined in the protocol.
- Subjects who test positive for SARS-CoV-2 during the study, prior to the completion of the dosing regimen, may continue to receive additional doses of study drug up to Day 10 if treatment continues to be well tolerated at the discretion of the Principal Investigator. Subjects who withdraw from dosing should complete the Early Discontinuation Visit and complete the assessments on Day 29.

7.9. Study Day -2 to Day 1 (Screening)

The following assessments will be conducted prior to performing any study-specific procedures:

- Informed consent: The subject will sign an informed consent form approved by the governing Institutional Review Board (IRB) or Ethics Committee.

Once the informed consent is obtained, the following will be conducted as part of Screening to document subject eligibility for the study.

- Medical history (including documentation of exposure to SARS-CoV-2)
- Physical examination (including height and weight)
- Vital signs
- Spirometry
- Serum pregnancy test or urine test (if urine test is positive, a serum test must be conducted)
- SARS- CoV-2 infection symptom score
- Concomitant medication assessment
- Ordinal Scale for Clinical Improvement
- Randomization to study treatment
- Adverse event (AE) assessment (AE collection starts at the time the time of randomization to study treatment and is continuous throughout the study until 28 days after receiving study drug)

7.10. Study Day 1

7.10.1. Day 1 (Pre-dose)

Assessments conducted during Screening do not have to be repeated if done on Day 1.

The following should be obtained prior to dosing.

- Physical examination

- Vital signs
- Spirometry
- Nasopharyngeal or oropharyngeal sample for SARS-CoV-2 testing
- Adverse event assessment
- Concomitant medication assessment
- SARS- CoV-2 infection symptom score
- Ordinal Scale for Clinical Improvement

7.10.2. Day 1 (Study Drug Administration)

Dosing

PUL-042 administration must be supervised by a health care professional. PUL-042 will be administered via a PARI Sprint nebulizer equipped with a filter valve to prevent aerosol generation. A nose clip will be used during the nebulization procedure. All doses will be administered as a constant volume (4 mL) via nebulization; the nebulizer will be operated until all drug has been delivered. All of the following time points are defined relative to the completion of dosing (T_0).

Post-Dose Guidelines

In previous studies with healthy volunteers, some subjects have demonstrated a transient decrease in lung function, usually asymptomatic. To date, subjects have recovered to at or near baseline lung function values without the administration of rescue medication. However, if after administration of PUL-042 Inhalation Solution there are clinical symptoms (increased respiratory rate, cough, shortness of breath) of decreased lung function, albuterol (salbtuamol) can be administered.

Following dosing, if a reduction of FEV1 >10% relative to pre-treatment is recorded, the subject should have the FEV1 measurement repeated as clinically indicated. If a reduction of FEV1 >12% relative to pre-treatment is recorded at 4 hours, the subject must be reviewed by the Principal Investigator prior to further dosing. If a reduction of FEV1 >12% relative to pre-treatment persists for up to 4 hours and is associated with clinical symptoms over this period, no further investigational treatment should be administered. Albuterol (salbutamol) may be given to symptomatic subjects at the discretion of the investigator.

If a reduction of FEV1 >20% relative to pre-treatment is recorded, no further investigational treatment should be administered to that subject.

7.10.3. Day 1 (T_0 +30 minutes [±15 minutes])

- Vital signs
- Spirometry
- Adverse event assessment
- Concomitant medication assessment

7.11. Study Days 3, 6, and 10 (Study Drug Administration)

All procedures should occur ±1 day from the scheduled Study Day.

7.11.1. Pre-dose

On Days 3, 6, and 10 the following dosing guideline should be observed prior to dose administration:

- At Investigator discretion, dosing can be HELD or STOPPED at any time for safety reasons.

The following should be obtained prior to dosing.

- Physical examination
- Vital signs
- Spirometry
- Adverse event assessment
- Concomitant medication assessment
- SARS- CoV-2 infection symptom score
- Ordinal Scale for Clinical Improvement

7.11.2. Days 3, 6, and 10 (Study Drug Administration)

Dosing

PUL-042 administration must be supervised by a health care professional. PUL-042 will be administered via a PARI Sprint nebulizer equipped with a filter valve to prevent aerosol generation. A nose clip will be used during the nebulization procedure. All doses will be administered as a constant volume (4 mL) via nebulization; the nebulizer will be operated until all drug has been delivered. All of the following time points are defined relative to the completion of dosing (T_0).

Note: Missed doses should not be replaced

Post-Dose Guidelines

In previous studies with healthy volunteers, some subjects have demonstrated a transient decrease in lung function, usually asymptomatic. To date, subjects have recovered to at or near baseline lung function values without the administration of rescue medication. However, if after administration of PUL-042 Inhalation Solution there are clinical symptoms (increased respiratory rate, cough, shortness of breath) of decreased lung function, albuterol (salbutamol) can be administered.

Following dosing, if a reduction of FEV1 >10% relative to pre-treatment is recorded, the subject should have the FEV1 measurement repeated as clinically indicated. If a reduction of FEV1 >12% relative to pre-treatment is recorded at 4 hours, the subject must be reviewed by the Principal Investigator prior to further dosing. If a reduction of FEV1 >12% relative to pre-treatment persists for up to 4 hours and is associated with clinical symptoms over this period, no further investigational treatment should be administered. Albuterol (salbutamol) may be given to symptomatic subjects at the discretion of the investigator.

If a reduction of FEV1 >20% relative to pre-treatment is recorded, no further investigational treatment should be administered to that subject.

7.11.3. Days 3, 6, and 10 (T_0 +30 minutes [±15 minutes])

- Vital signs
- Spirometry
- Adverse event assessment
- Concomitant medication assessment

7.12. Study Day 15 (Follow-up)

Assessments should occur within +1 day of target Study Day.

The following assessments will be conducted:

- Physical examination
- Vital signs
- Nasaopharyngeal or oropharyngeal sample for SARS-CoV-2 testing
- Adverse event assessment
- Concomitant medication assessment
- SARS- CoV-2 infection symptom score
- Ordinal Scale for Clinical Improvement

7.13. Early Discontinuation from Dosing and Study Withdrawal

Subjects who have received at least one dose of investigational treatment and are discontinued from dosing should continue to the final assessment at Day 29 according to the schedule of events specified for pre-dose assessments. There will be no post-dose assessments for these subjects.

Should the subject's study participation end prior to the completion of Study Day 15, the following assessments will be conducted as soon as possible after the decision to withdraw from the study is made.

- Physical examination
- Vital signs
- Serum pregnancy test or urine test (if urine test is positive, a serum test must be conducted)
- Nasaopharyngeal or oropharyngeal sample for SARS-CoV-2 testing
- Adverse event assessment
- Concomitant medication assessment

- SARS- CoV-2 infection symptom score
- Ordinal Scale for Clinical Improvement

7.14. Study Completion Day 29

Assessments should occur within +2 days of target Study Day.

- Serum pregnancy test or urine test (if urine test is positive, a serum test must be conducted)
- SARS- CoV-2 Symptom Score
- Adverse event assessment
- Concomitant medication assessment
- Ordinal Scale for Clincal Improvement
- Nasaopharyngeal or oropharyngeal sample for SARS-CoV-2 testing

8. CLINICAL EVALUATIONS AND PROCEDURES

8.1. Medical History

Medical history will include significant medical conditions, surgical history, and all medications, both prescription and nonprescription, taken within 14 days prior to screening. Exposure to SARS-CoV-2 infected individuals or patients with COVID-19 will be documented.

8.2. SARS-CoV-2 Infection Assessment

Ordinal Scale for Clinical Improvement: A nine point scale will be used to assess the severity of COVID-19 which has been derived from the draft scale proposed by WHO.[9]

The following table will be used to assess symptoms due to SARS-CoV-2 infection:

Table 2: SARS-CoV-2 Infection Symptom Score

Symptom	**Score (0-3)**
Cough	
Shortness of breath or difficulty breathing	
Muscle aches or fatigue	
	Score (0-4)
Fever	

Symptom Scores (Cough, Shortness of breath or difficulty breathing, Muscle aches or fatigue)

0- None

1- Mild (occasional or not bothersome)

2- Moderate (frequent or bothersome)

3- Severe (interferes with daily activities)

Note: Fever will be scored based on temperature recorded as part of vital signs and graded according to the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials:

- 0 No Fever
- 1- Mild 38.0-38.4°C/100.4-101.1°F
- 2-Moderate 38.5-38.9°C/101.2-102.0°F
- 3-Severe 39.0-40.0°C/102.1-104.0°F
- 4-Life Threatening > 40.0°C/>104.0°F

8.3. Physical Examination and Vital Signs

A qualified medical person will perform a physical examination at all indicated visits.

- Physical examination: general appearance, head, eyes, ears, nose, throat, neck, cardiovascular, lungs, abdomen, lymph nodes, extremities, neurological, skin, musculoskeletal, and other.
- Vital signs will include body temperature, blood pressure, heart rate, and respiratory rate.

8.4. SARS-CoV-2 Testing

All testing associated with the conduct of the study will be conducted at a central laboratory designated by the Sponsor. At every sampling time point, a nasopharyngeal swab or an oropharyngeal swab will be taken. Directions for specimen collection, handling and transport will be provided in the Laboratory Manual.

8.5. Spirometry

American Thoracic Society or British Thoracic Society guidelines should be followed in the conduct of spirometry assessments performed at screening.

9. DESCRIPTION OF STUDY TREATMENT

9.1. Placebo

Sterile saline for inhalation will be used as the placebo.

9.2. PUL-042 Inhalation Solution

Additional information concerning PUL-042 including receipt, storage, preparation, and time windows for preparation and subject administration will be provided in the Pharmacy Manual.

The teratogenic effects of PUL-042 are unknown.

9.2.1. PUL-042

The investigational product, PUL-042 Inhalation Solution, is a combination of Pam2CSK4 acetate and ODN M362 sodium (4:1 molar ratio [Pam2:ODN]). PUL-042 is formulated as a solution in SWFI, USP, with no other excipients, at a pH of 5 to 8. Pam2 is a synthetic 6-amino acid lipopeptide, and ODN is a synthetic 25-base, single-stranded phosphorothioate oligodeoxynucleotide. The structure of Pam2 and the nucleotide sequence of ODN are shown in Section 5.2 (Figure 3).

The investigational product components (Pam2CSK4 and ODN M362 sodium) are manufactured by: Albany Molecular Research (Glasgow) Ltd. Todd Campus, West of Scotland Science Park, Acre Road, Glasgow G20 0XA, UK.

9.3. Packaging and Labeling

PUL-042 will be packaged as separate component solutions of Pam2 and ODN in 5-mL Type I sterile glass vials or 2-mL Type I sterile glass vials, sealed with a rubber injection stopper and an aluminum tear-off overseal. PUL-042 components will be manufactured, labeled, and packaged under Good Manufacturing Practice guidelines. Sterile saline for inhalation will be supplied by the investigative site.

9.4. Shipment and Storage

Individual components of PUL-042, Pam2 Solution and ODN Solution, are stored frozen (-20 ±5°C) at the drug distribution center and will be shipped to the site on dry ice.

Cartons containing 5-mL or 2-mL glass vials of individual PUL-042 components (Pam2 and ODN) will be sent to the clinical study site pharmacy. The study drug components will be stored frozen (-20 ±5°C) at the study site until ready for use.

9.5. Preparation and Administration

The pharmacist at the clinical site will be responsible for the preparation of the appropriate concentration of PUL-042 by dilution of the components of PUL-042 in SWFI. Specific instructions will be provided for the preparation of PUL-042 Inhalation Solution in the Pharmacy Manual. PUL-042 Inhalation Solution must be administered within 4 hours of preparation.

10. CONCOMITANT MEDICATIONS, TREATMENTS, AND PROCEDURES

All concomitant medications, including prescription and nonprescription over-the-counter drugs, vitamins, or nutritional supplements, taken during the 14 days prior to screening or while a participant is on study will be recorded in the electronic case report form (eCRF). Documentation will include start and stop dates and reasons for use.

Any diagnostic, therapeutic, or surgical procedures performed during the study period will be documented.

11. STUDY WITHDRAWAL

11.1. Study Termination

The entire study may be terminated at any point based on the evaluation of the study or development program by Pulmotect. A Data Safety Monitoring Board (DSMB) will review unblinded data on the first 40 subjects then again at 80 subjects and 120 subjects with additional ad hoc reviews at the request of the DSMB. The DSMB can also request that study enrollment be paused at any time should enrollment be faster than anticpated such that adequate safety review is not able to occur between the specified review meetings.

11.2. Subject Withdrawal/Lost to Follow-up

Subjects who are discontinued from dosing during the study and have received at least one dose of investigational treatment must be followed to Day 29 according to the schedule of events specified above for pre-dose assessments. There will be no post-dose assessments for these subjects.

Subjects will be free to withdraw from the study at any time without giving a reason. Subjects will be considered withdrawn from the study in the event of any of the following reasons:

- Withdrawal of the subject's consent for any reason.
- Subject lost to follow-up prior to the Study Day 29 assessments.

In the event a subject withdraws from the study for any reason, the Investigator must notify Pulmotect as soon as possible and complete the applicable eCRF pages. An effort should be made to capture the reason(s) for withdrawal.

Subjects that withdraw should complete the Early Discontinuation assessments as soon as possible.

A subject is considered lost to follow-up after 3 documented attempts to contact the subject without success.

Subjects who withdraw after the start of study drug administration will not be replaced.

12. ADVERSE EVENTS

Adverse events will be described and graded according to the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials.

Symptoms and events associated with SARS-CoV-2 infection will be scored as per the SARS-CoV-2 infection symptom score (Table 2) and the Ordinal Scale for Clinical Improvement (Table 4). These findings should not be reported as Adverse Events.

12.1. Definitions

Adverse Event (AE)

An AE is any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related.

An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

An abnormal laboratory value will be considered an AE if it qualifies as such based on the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials.

Throughout the course of the study, every effort should be made to remain alert to possible AEs. Subjects should be encouraged to report AEs spontaneously or in response to general, nondirected questioning.

With the occurrence of an AE, the primary concern is the safety of the subject. Appropriate management of the AE should always be the first priority.

Suspected Adverse Reaction

Defined as any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of IND safety reporting "reasonable possibility" means there is evidence to suggest a causal relationship between the drug and the adverse event. Suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any adverse event caused by the drug.

Life-Threating Adverse Event or Life-Threatening Suspected Adverse Reaction

An adverse event or suspected adverse reaction is considered "life-threatening" if, in the view of either the investigator or sponsor, its occurrence places the patient or subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form might have caused death.

Serious Adverse Event (SAE) or Serious Suspected Adverse Reaction

The terms "serious" and "severe" are not synonymous. Adverse events classified as "serious" have defined regulatory requirements. Those classified as "severe" do not have defined regulatory requirements unless they are also classified as "serious".

The term "severe" is often used to describe the intensity of a specific event (as in mild, moderate, or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache).

An AE is classified as "serious" based on the criteria outlined below. Seriousness (not severity) defines the regulatory reporting obligations.

An adverse event or suspected adverse reaction is considered "serious" if in the view of either the investigator or sponsor, it results in any of the following outcomes:

- Death
- A life-threatening adverse event
- In-patient hospitalization or prolongation of existing hospitalization
- Persistent or significant incapacity or substantial disruption to conduct normal life functions
- A congenital anomaly/birth defect
- Intervention to prevent any one of the other outcomes listed above (based on medical judgment)

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based on appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above. Examples of such medical events are allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias, convulsions that do not result in in-patient hospitalization, or the development of drug dependency or drug abuse.

Unexpected Adverse Event or Unexpected Suspected Adverse Reaction

An AE or suspected adverse reaction is considered "unexpected" if it is not listed in the Investigator's Brochure or is not listed in the Investigator's Brochure at the specificity and severity observed.

Serious and Unexpected Adverse Event or Suspected Adverse Reaction

Any AE or suspected adverse reaction that occurs during the subject's participation in the study that meets the criteria for both serious and unexpected as defined above is considered a serious and unexpected AE or suspected adverse reaction.

12.2. Adverse Event Reporting Period

The AE reporting period for this study is continuous and begins at the time of randomization to study treatment and ends on Study Day 29.

In addition, any known untoward event that occurs subsequent to the AE reporting period that the Investigator assesses as related to the investigational medication should also be reported as an AE.

All AEs (both serious and nonserious) must be followed until resolution or until a stable clinical endpoint is reached. All measures required for AE management and the ultimate outcome of the AE must be recorded in the source documentation and in the eCRF.

12.3. Treatment Emergent Adverse Events

Treatment-emergent AEs are defined as those that begin or worsen after the start of study drug administration.

12.4. Recording of AEs

All AEs will be documented in the appropriate section of the eCRF.

NOTE: Symptoms and events associated with SARS-CoV-2 infection will be scored as per the SARS-CoV-2 infection symptom score (Table 2) and the Ordinal Scale for Clinical Improvement (Table 4). These findings should not be reported as Adverse Events.

In the event that the electronic data capture (EDC) system cannot be accessed and a SAE or serious suspected adverse reaction has occurred, a paper SAE report form will be available to be completed and faxed or emailed to the Sponsor or their designee.

The following will be recorded for each AE in the eCRF:

- A description of the AE in medical terms. Whenever possible, a diagnosis should be given when signs and symptoms are due to common etiology (e.g., cough, runny nose, sneezing, sore throat, and head congestion should be reported as “upper respiratory infection”)
- Start date
- Stop date
- The severity (i.e., grade) as assessed by the Investigator according to the definitions in the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials. If the AE is not specifically listed in the reference above, the following grades should be used:
    - Grade 1 Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
    - Grade 2 Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL (Activities of Daily Living)
    - Grade 3 Severe or medically significant but not immediately life threatening; hospitalizaton or prolongation of hospitalization indicated; disabling; limiting self-care ADL
    - Grade 4 Life-threatening consequences; urgent intervention indicated
    - Grade 5 Death related to AE
- The causal relationship to study drug as assessed by the Investigator; the decisive factor in the documentation is the temporal relation between the AE and the study drug.
- Action(s) taken (e.g., study drug administration interrupted, study drug not administered, none, unknown).
- The outcome (e.g., recovered/resolved, not recovered/not resolved, recovering/resolving, recovered/resolved with sequelae, fatal, unknown).

- Whether it caused the subject to discontinue the study.

If in any 1 subject the same AE occurs on several occasions (unless the AE is continuous and of stable grade), the AE in question will be documented and assessed at each occurrence.

Should a pregnancy of a female participant or a partner of a male participant occur, it must be reported and recorded in the eCRF. Pregnancy in itself is not regarded as an AE unless there is suspicion that an investigational product may have interfered with the effectiveness of a contraceptive medication.

The outcome of all pregnancies (spontaneous miscarriage, elective termination, normal birth, or congenital abnormality) must be followed up and documented even if the subject was discontinued from the study.

All reports of congenital abnormalities/birth defects are SAEs. Spontaneous miscarriages should also be reported and handled as SAEs. Elective abortions without complications should not be handled as AEs.

12.5. Assessing Relationships of AE to Study Drug

The Investigator must record his/her opinion concerning the relationship of the AE to study therapy on the AE eCRF. Table 3 provides guidance for assigning relationship to the study drug.

Table 3: Relationship of Adverse Event to the Administration of the Study Drug

Unrelated	There is not a temporal relationship to study drug or there is a reasonable causal relationship between another drug, concurrent disease, or circumstance and the AE. *The AE is clearly not related to study drug.*
Unlikely	There is a temporal relationship to study drug, but there is not a reasonable causal relationship between the study drug and the AE. *The AE is doubtfully related to study drug.*
Possibly	There is a reasonable causal relationship between the study drug and the AE. *The AE may be related to study drug.*
Probably	There is a reasonable causal relationship between the study drug and the AE. *The AE is likely related to the study drug*.
Definitely	There is a causal relationship between the study drug and the AE. *The AE is clearly related to the study drug.*

12.6. Reporting Serious or Unexpected AEs

Any SAE or serious suspected adverse reaction that occurs during the course of the study will be reported **within 24 hours after the site becomes aware of the event.**

All SAE reporting will adhere to the United States Code of Federal Regulations (CFR), specifically 21 CFR 312.32 for Investigational New Drugs, and applicable local regulations. The Investigator will notify the governing IRB or Ethics Committee of any SAEs and safety reports per IRB or Ethics Committee reporting requirements.

12.7. Follow-up of Adverse Events

All AEs (both serious and non-serious) should be followed until resolution or until a stable clinical endpoint is reached. All measures required for AE management and the ultimate outcome of the AE must be recorded in the source document and the eCRF.

Any SAE or serious suspected adverse reaction follow-up information requested should be provided in a timely manner. The additional information may include copies of hospital reports, autopsy reports, or other relevant documents.

13. STATISTICAL METHODS

13.1. Sample Size Determination

The trial size of 200 subjects (100 PUL-042 inhalation solution: 100 placebo) was chosen based on clinical considerations. The rates of infection to adequately estimate a sample size for a statistically significant result are unknown.

Enrolled subjects will be randomized with equal probability to receive blinded treatment consisting of either PUL-042 or placebo.

13.2. Subject Populations

Intent to Treat Population (ITT)

The ITT population will include all randomized subjects who receive at least one dose of experimental treatment (i.e., PUL-042 or Placebo)

The ITT population will be the primary data source used to address the primary study efficacy objectives

Modified Intention to Treat (MITT)

The MITT population will include all randomized subjects who receive at least one dose of experimental treatment (i.e., PUL-042 or Placebo) and are negative for SARS-CoV-2 infection at the time of administration of the first dose.

Safety Population

The Safety population is the ITT population defined as all randomized subjects who have received at least one dose of experimental treatment. The Safety population will be the data source used to evaluate the safety and tolerability of experimental treatment for this study.

13.3. Primary Objective

To determine the efficacy of PUL-042 Inhalation Solution in the prevention of viral infection with SARS-CoV-2 and progression to COVID-19 in subjects: 1) who have repeated exposure to individuals with SARS-COV-2 infection and 2) who are asymptomatic at enrollment.

The primary endpoint is the severity of COVID-19 as measured by the maximum difference from the baseline value in the Ordinal Scale for Clinical Improvement within 28 days from the start of experimental therapy. The Ordinal Scale for Clinical Improvement is a 9-point scale that measures disease severity at a given point in time. Notably, a score of 0 indicates that an individual is infection-free. The difference in scores obtained at different times provides a quantitative assessment of the incidence of infection and change in disease severity over that time interval. The change in severity between the placebo- and actively-treated groups will be analyzed by a linear statistical model adjusting for the main effect of randomized treatment and other relevant covariates (e.g., age, baseline OSCI Score, and presence of comorbidities). Because the statistical properties of these score differences might not conform to the theoretical requirements of this procedure, a Wilcoxon Rank-Sum (nonparametric) test may also be used to analyze the main effect of treatment. Full details of the planned analysis will be included in the Statistical Analysis Plan that will be developed for this study.

The Ordinal Scale for Clinical Improvement to be used in this study is derived from a draft scale proposed by the World Health Organization[9] for clinical improvement as presented below in Table 4:

Table 4: Ordinal Scale for Clinical Improvement (Derived from draft WHO scale)

Descriptor	Score
No clinical or virological evidence of infection	0
Infected but no limitation of activities	1
Limitation of activities	2
Hospitalized not requiring oxygen therapy (SpO2 > 93% on room air)	3
Oxygen by mask or nasal prongs	4
Non-invasive ventilation or high-flow oxygen	5
Intubation and mechanical ventilation	6
Ventilation + additional organ support- pressors, RRT, ECMO	7
Death	8

It is possible that medically justified treatment and or procedures cannot be implemented due to the unavailability of equipment (e.g., scarcity of ventilators). In such cases, the data recorded in the eCRF should reflect the prescribed circumstances rather than the reality. For example, if clinical evaluation of a patient indicates the need for mechanical ventilation when no ventilator is available, that patient should be scored as 6 – "Intubation and mechanical ventilation" not as a lower score on the Ordinal Scale for Clinical Improvement.

13.4. Secondary Objectives

To determine the difference in incidence of SARS-CoV-2 infection 28 days from the start of experimental therapy in subjects who test negative for SARS-CoV-2 at the pre-treatment visit

To determine the difference in incidence of SARS-CoV-2 infection 14 days from the start of experimental therapy in subjects who test negative for SARS-CoV-2 at the pre-treatment visit (MITT)

To compare the severity of COVID-19 within 14 days from the start of experimental therapy (ITT)

To compare the severity of COVID-19 within 28 days from the start of experimental therapy (ITT)

To assess the requirement for ICU admission within 28 days from the start of experimental therapy (ITT)

To assess the requirement for mechanical ventilation within 28 days from the start of experimental therapy (ITT)

To assess mortality within 28 days from the start of experimental therapy (ITT)

To determine the tolerability of PUL-042 Inhalation Solution in this population (ITT population)

13.5. Safety Analysis

A comprehensive statistical analysis plan (SAP) will be finalized prior to unblinding of the study results. The SAP may modify the plans outlined in the protocol; however, any major modifications of planned analyses will be reflected in a protocol amendment. Safety data will be presented in tabular and/or graphical format and summarized descriptively, if appropriate.

Adverse events will be described and graded according to the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials.

Treatment-emergent AEs, vital signs, physical examinations, clinical laboratory data, lung function tests, and noncompliance will be reviewed on an ongoing basis during the study to evaluate the safety of the subjects.

14. ADMINISTRATION OF THE STUDY

14.1. Regulatory Considerations

This study will be conducted in compliance with the protocol, International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines, and the applicable local regulatory requirements. This study will be conducted in accordance with the ethical principles that originate in the Declaration of Helsinki and ICH Guidelines for GCP.

Study protocols and informed consent forms will be approved by the appropriate IRB or Ethics Committee prior to initiation of the study. All subjects will sign an informed consent form prior to any study-specific procedures. The study will be monitored for regulatory and protocol compliance by a study monitor selected by Pulmotect.

14.2. Institutional Review Board (IRB)/Ethics Committee

The Investigator must submit the final protocol and proposed informed consent document to an IRB/ethics committee that complies with the ICH GCP. The IRB/ethics committee will provide the Investigator with a written decision regarding the conduct of the study and a copy of the document will be forwarded to the Sponsor. The study will not be initiated and subjects will not be enrolled until the appropriate documentation of IRB/ethics committee approval of the study protocol and the informed consent form has been received.

Substantive modifications to the protocol must be submitted to the IRB/ethics committee for approval. Administrative changes to the protocol, such as revisions for clarification that do not affect the conduct of the study or increase the risk to the subject, should be submitted to the IRB/ethics committee for informational purposes; formal approval is not required.

The Investigator must also submit any written information that will be given to the study subjects, as well any subject recruitment material, to the IRB/ethics committee for approval prior to use.

The Investigator will make appropriate and timely reports to the IRB/ethics committee as required by applicable government regulations and IRB/ethics committee policy. In addition to progress reports, all known information regarding SAEs will be reported per IRB/ethics committee requirements.

It is the Investigator's obligation to provide the Sponsor with copies of all study-related correspondence with the IRB/ethics committee in a timely fashion and to retain the originals as part of the Site Regulatory File. The Site Regulatory File will be made available as requested for monitoring or quality assurance review during site audits and to governmental regulatory representatives as required.

14.3. Subject Information and Informed Consent

Written informed consent must be obtained from each subject in accordance with the ICH GCP. Informed consent must be obtained prior to performing any study-specific procedures. The consent form that is used must be approved by both the reviewing IRB/ethics committee and Pulmotect.

The subject and the individual explaining the study will sign the current IRB/ethics committee-approved version of the consent form. A copy of the signed consent form will be given to the subject. The date that consent was obtained will be recorded on the eCRF as well as in the subject's source documents.

A copy of each version of the informed consent form that has been approved by the IRB/ethics committee will be provided to the Sponsor. Care should be taken that the current approved version of the consent form is provided to the subject for review and signature. It is possible that in some cases an updated consent form will contain significant information that will require a previously enrolled subject to sign the updated consent form. Original signed consent forms must be in the Site Regulatory File and be available for review by authorized individuals.

A sample consent form is provided in Section 15.

14.4. Data Safety Monitoring Board

An external DSMB will be used to evaluate safety of the study in an ongoing manner. There will be three voting members. None of the voting members will have any affiliation with Pulmotect, Inc. A full description of the membership, role, and responsibilities of the DSMB will be finalized prior to the start of the study, and will be provided in the DSMB charter. The DSMB will evaluate safety at regular intervals including early in the trial.

The DSMB chair has the ability to pause study enrollment at any point during the study for any reason including rapid enrollment which could hinder the DSMB's ability to review the safety of PUL-042 Inhalation Solution in a timely manner relative to overall enrollment. The first evaluation will be done after 40 subjects have completed dosing. Unless the DSMB recommends to the contrary, enrollment will be allowed to continue until 80 patients have completed dosing. Enrollment beyond 80 subjects will require formal DSMB review of the data from the first 40 subjects to have been completed with explicit approval to continue enrollment beyond 80 subjects. Subsequent evaluations will occur at 120 patients with further ad hoc meetings at the discretion of the DSMB.

One potential recommendation of the DSMB is to stop the study due to safety concerns. Any imbalance in the incidence of AEs between placebo and active treatment is to be further reviewed by the DSMB taking into account the totality of evidence in order to render a recommendation to the sponsor regarding study continuation. As specified in the DSMB charter the formal review of data will take place at each meeting of the DSMB after 40, 80 and 120 subjects have completed dosing. Ad hoc meetings can also be called.

As a further effort to ensure the safety of PUL-042, a stopping rule that is based only on mortality will be employed. This rule will be implemented if there is a high probability of excess mortality risk among patients randomized to PUL-042. The following hierarchical analysis of mortality will be performed after 50% of subjects have been enrolled (50/group) and followed up for 28 days from the start of investigational therapy:

1) Based on blinded data, if no more than 3 deaths have occurred during the study this analysis will not be conducted due to the lack of evidence of increased mortality risk attributable to PUL-042.

If more than 3 deaths occur:

2) The Unblinded statistician will evaluate unblinded mortality data to determine the treatment specific death rate (i.e., $D_{Tx} = Deaths_{Tx} / N_{Tx}$; Tx = Active or Placebo).
3) If the difference, Δ, in treatment-specific death rates (i.e., $\Delta = D_{Active} - D_{Placebo}$) is greater than 7.5%, the DSMB will further review the totality of evidence and render a recommendation to the sponsor regarding study continuation.

Characteristics of this rule are as follows:

Assuming that the true underlying control arm mortality rate is 5% and using a normal approximation when comparing proportions, the probability of stopping is approximately:

- 90% if the true underlying mortality rate attributable to PUL-042 is 25%.
- 62% if the true underlying mortality rate attributable to PUL-042 is 15%.
- only 11% if the true underlying mortality rate attributable to PUL-042 is 5% (equal to the assumed true underlying control arm mortality rate)

14.5. Adherence to the Protocol

The study shall be conducted as described in this protocol except for an emergency situation in which proper care of the subject requires immediate alternative intervention. This protocol refers to the protocol as provided by Pulmotect and approved by both the IRB/ethics committee and submitted to the FDA as part of the Investigational New Drug Application that is in effect. While FDA regulations permit the protocol to be amended, this must be done in accordance with the provisions agreed upon in Section 14.6.

Any material deviation from study procedures (identified by site personnel or monitor) will be documented. Major subject-level deviations will be captured on the protocol deviation form in the eCRF. A list of protocol deviations will be compiled and reviewed by the Principal Investigator and Sponsor to identify major and minor deviations periodically using the following criteria:

Major – A serious breach of protocol and GCP compliance, which may also impact subject safety or study endpoints. Examples include (but are not limited to):

- Violation of inclusion/exclusion criteria
- Dose calculation error
- Failure to collect primary endpoint data

Minor – An administrative breach of protocol procedure that has minimal impact on regulatory compliance, subject safety, or study endpoints. Examples include (but are not limited to):

- Visits conducted out of established timeframes
- Dose timing out of established timeframes
- Missing selected laboratory panel parameters

14.6. Protocol Modifications

The Investigator will not modify this protocol without obtaining the concurrence of Pulmotect. All protocol amendments will be issued by Pulmotect, and must be signed and dated by the Investigator prior to implementation of the amendment. Pulmotect will submit protocol modifications to regulatory agencies as required by 21 CFR 312.30. The Investigator is responsible for notifying the IRB/ethics committee of changes. Any changes that potentially affect subject safety or significantly alter the conduct of the study (e.g., changes to inclusion or exclusion criteria, study drug dosage, study procedures, etc.) must have written approval prior to implementation.

Note: The IRB/ethics committee may require the informed consent form be revised to reflect the study revisions.

In situations requiring a departure from the protocol for a subject that has been enrolled appropriately, the Investigator or other physician in attendance will contact Pulmotect by telephone. If possible, this contact will occur before implementing any departure from the protocol. In all cases, contact must be made as soon as possible in order to discuss the situation and agree on an appropriate course of action. The source documents must reflect any departure from the protocol and be transcribed into the eCRF. The investigator is responsible for notifying the IRB/ethics committee of any departures from the protocol.

No requests for a waiver from the specified inclusion/exclusion criteria will be granted.

14.7. Data Collection

Study data will be entered into an EDC system (eCRFs). Subject screening information will be recorded by the study site. The following will be the minimum captured: initials, subject personal identification number, date of screening, and enrollment status.

Data collected through the completion of experimental procedures required by this protocol will be recorded in the subject's source documentation. These data will then be transcribed into the eCRF.

All required study data will be entered into the eCRFs provided by Pulmotect. All study data should be entered into the eCRF as soon as possible after collection. All information in the eCRFs must be supported by original data in the subject’s medical records. All medical records, laboratory printouts, notes made by the physician, and other materials such as x-rays will be considered source data and must be available for inspection by Pulmotect, its designees, or regulatory authorities.

Appropriate training of the study site will be conducted prior to study initiation to assist with making entries and corrections to data entered into an eCRF. The Investigator remains responsible for the accuracy and adequacy of all data entered into the eCRFs (EDC system).

Data will be monitored as described in Section 14.9. Data entered into eCRFs will be reviewed and compared with source documents by monitors that are adequately trained using the EDC system.

Upon further data processing, queries may be generated and sent electronically to the Investigator for clarification or correction. The Investigator or designee will address any queries and provide resolution within the EDC system.

The eCRF will be signed (electronically) by the Investigator after review (date and time will be captured in the eCRF audit trail). After completion of the study, completed eCRFs will be electronically transferred to Pulmotect and/or designee and stored in the archives according to the data management plan. Once the eCRFs are signed by the Investigator, the data manager will lock the eCRFs for data analysis.

14.8. Maintaining Records

A Site Regulatory Binder must be maintained at the investigative site and will contain the documents identified in the list of Essential Documents according to ICH GCP, including a signed Investigator Agreement. Pulmotect, or its designee, will provide a Site Regulatory Binder to the site.

According to the United States Federal Regulations (21 CFR 312.57[c]), all records and reports related to this clinical study must be retained by the Investigator for at least 2 years after approval of a marketing application and until there are no pending or contemplated marketing applications or until at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. Pulmotect will inform the Investigator as to when these documents no longer need to be retained. These documents must be stored in a secure archive and be available in the event of a regulatory audit.

Study records that must be retained in the Site Regulatory Binder (or the Pharmacy Manual, if appropriate) may include, but are not necessarily limited to: study personnel identification, designation and signature list, subject screening records, subject roster (names omitted), protocol and any amendments or administrative changes, product disposition records, essential documents identified in ICH GCP guidelines, correspondence, laboratory accreditations, and normal laboratory ranges. The site must keep the binder current and available along with relevant subject charts and study reports for review by the Sponsor, IRB/Ethics Commitee, FDA, and/or local regulatory authorities.

14.9. Monitoring, Auditing, and Inspecting

Pulmotect or its designee will monitor all aspects of the study with respect to current GCP and standard operating procedures for compliance with applicable regulations and to ensure that the rights of subjects are protected. Pulmotect or a designee (e.g., clinical research organization) will assure the accuracy of the data and the selection of a qualified Investigator and appropriate study center. The protocol procedures will be reviewed with the Investigator and associated personnel prior to study initiation and during periodic monitoring visits. Pulmotect or a designee will review eCRFs for accuracy and completeness during on-site monitoring visits. Discrepancies will be resolved with the Investigator or designee as appropriate.

Remote monitoring may be conducted as required to identify trends and issues, evaluate enrollment status, query status, data quality, AEs, etc.

Pulmotect or its designees will monitor the study using the following methods:

- Frequent telephone contacts
- Periodic site visits
- Review of original subject records, eCRFs, drug accountability and storage, and general study documentation

To ensure the study can be adequately monitored, the Investigator will cooperate in providing Pulmotect, or Pulmotect's designee, with direct access to all study source documents (e.g., subject charts and study files) and responding to inquiries that may arise as a result of the document review.

Review of these documents will usually occur during a routine monitoring visit but may also be required during a visit by a quality assurance auditor. The Investigator will also provide direct access to these records to regulatory representatives if and when requested. Pulmotect reserves the right to terminate the study if access to source documentation of work performed in this study is denied to the Pulmotect, its designee, or regulatory representatives.

14.10. Confidentiality

The anonymity of subjects participating in this study must be maintained. Subjects will be identified by their assigned number and their initials in all written communications between the Investigator and Pulmotect, or Pulmotect's designee. Documents that are not submitted to Pulmotect and that identify the subject (e.g., signed informed consent, source documents/charts) will be made available to Pulmotect or regulatory authorities for inspections, but will be maintained in confidence.

All study-related information provided by Pulmotect to the Investigator and not previously published, including but not limited to the active study agent identity, the Investigator's Brochure, the study protocol, verbal and written communication, eCRFs, assay methods, and scientific data, will be considered confidential. In addition, all information developed during the conduct of the clinical investigation of the study agent is also considered confidential. Neither the Investigator nor any of his/her employees or agents shall disclose or use this information for any purpose other than the performance of the clinical study. Such information shall remain the confidential and proprietary property of Pulmotect, and disclosure to others will be limited to other physicians who are conducting studies with the same active study agent, the IRB/ethics committee, and the applicable regulatory authorities, except by prior written permission of Pulmotect or its agents. At such time that information becomes widely and publicly available through no fault of the Investigator, the obligation of nondisclosure toward that particular information will cease.

15. SAMPLE INFORMED CONSENT

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Study Title: A Phase 2 Multiple Dose Study to Evaluate the Efficacy and Safety of PUL-042 Inhalation Solution in Reducing the Infection Rate and Progession to COVID-19 in Adults Exposed to SARS-CoV-2

RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

WHAT SHOULD I KNOW ABOUT THIS RESEARCH?

- Someone will explain this research to you.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you do not take part, it will not be held against you.
- You can take part now and later drop out, and it will not be held against you
- If you do not understand, ask questions.
- Ask all the questions you want before you decide.

HOW LONG WILL I BE IN THIS RESEARCH?

We expect that your taking part in this research will last for approximately 28 days. Your study doctor will inform you of how long you will be in the study and when study visits are required.

WHY IS THIS RESEARCH BEING DONE?

The purpose of this research is try to see whether an experimental drug, PUL-042 Inhalation Solution (PUL-042), is effective in preventing infection with the COVID-19 virus (SARS-CoV-2) and reducing the severity of COVID-19 illness in particpants who become infected.

WHAT HAPPENS TO ME IF I AGREE TO TAKE PART IN THIS RESEARCH?

If you decide to take part in this research study, you will take the experimental drug, PUL-042 Inhalation Solution (PUL-042) or a placebo 4 times over a 10 day period. The study visits may involve collection of mouth/nasal swabs in addition to completion of physical examination, vital signs and lung function tests. Urine samples or blood samples will be required for females of child bearing potential.

COULD BEING IN THIS RESEARCH HURT ME?

The most important risks or discomforts that you may expect from taking part in this research may include irritation of the airways resulting in symptoms such as cough and tightness of the chest.

WILL BEING IN THIS RESEARCH BENEFIT ME?

There is no guarantee that you will receive personal benefit from participating in this study. The information gathered during this study could help develop treatments to prevent or reduce illness from SARS-CoV-2 virus infection in other patients.

WHAT OTHER CHOICES DO I HAVE BESIDES TAKING PART IN THIS RESEARCH?

You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. The treatment being tested in this study is intended to be given in addition to any standard treatment needed, not as a replacement or alternative. If you choose not to take part, you will still receive the standard treatment that you would normally receive.

You are being asked to take part in this study because you have have had docoumented exposure to the SARS-CoV-2 virus.

DESCRIPTION OF RESEARCH

1. PURPOSE OF STUDY

This study will try to see whether an experimental drug, PUL-042 Inhalation Solution (PUL-042), is effective in preventing COVID-19 infection or reducing the severity of COVID-19 illness in participants who have been exposed to SARS-CoV-2, but have no documented infection of the virus at the time of enrollment.

2. DESCRIPTION OF STUDY

This is an investigational study. PUL-042 has not yet been approved by the U.S. Food and Drug Administration (FDA) or other Regulatory Authority to treat any medical condition and is not available for sale to the public or to be prescribed by a doctor. PUL-042 is a combination of two molecules (called Pam2 and ODN for short) mixed in sterile water. Previous studies in animals have shown that PUL-042 may help tissues in the lungs to resist infections better.

PUL-042 will be given through a nebulizer. This is a machine that uses a small motor to turn liquid into a mist, like a humidifier, so that you can breathe the drug into your lungs. You breathe in the mist through a plastic tube or facemask. Using a nebulizer is not painful or uncomfortable and is a common method of giving drugs during asthma attacks. It will take around 10 minutes to breathe in all of the study drug.

A total of up to approximately 200 participants will be enrolled in this study, all at up to 20 centers. Participants in the study will receive either PUL-042 or a placebo (an inactive agent that appears

identical to PUL-042). There is a 50% chance you will receive PUL-042 (like flipping a coin). Neither you or your doctor will know if you receive PUL-042 or placebo. However, your study doctor can find out which study group you are in if there is an emergency. All study procedures will be provided free of charge. If you decide to participate in this study, you will have assessments done over the course of approximately 28 days. The assessments performed at each Study Day are described below.

Study Day -2 to Study Day 1

- You will read this informed consent document and discuss any questions you have with the study staff. No other parts of this study will be performed until all your questions have been answered and you have signed this form, indicating that you want to take part in the study.
- The study doctor will collect information about your overall health and medical history, including documenting your exposure to SARS-CoV-2. You will be asked by study staff whether you have been diagnosed with COVID-19 illness.
- A physical examination will be performed.
- Your vital signs (blood pressure, pulse, temperature, and breathing rate) will be measured
- Your lung function will be measured by having you blow into a tube
- Women who can become pregnant will take a serum or urine pregnancy test. If a urine test is positive, the results will be confirmed with a blood pregnancy test. If you are pregnant, you will not be allowed to participate in the study.
- You will be asked about any recent health issues and medications you are taking.

Study Day 1

- A physical examination will be performed.
- Your vital signs (blood pressure, pulse, temperature, and breathing rate) will be measured
- Your lung function will be measured by having you blow into a tube
- A specimen will be taken by inserting a swab into your nasal passage or from the back of your mouth in order to test for the SARS-CoV-2 virus
- You will be asked about any recent health issues and medications you have taken.
- **You will be given the study treatment (PUL-042 or placebo) through the nebulizer.**
- Your vital signs (blood pressure, pulse, temperature, and breathing rate) and your lung function (by having you blow into a tube) will be measured at 30 minutes after you finish taking taking PUL-042.

If you are confirmed to have a SARS-CoV-2 infection at any time during the course of the study, you may continue to recieve further doses of PUL-042 if treatment has been well tolerated and at the discretion of the Principal Investigator.

Study Day 3

- A physical examination will be performed.
- Your vital signs (blood pressure, pulse, temperature, and breathing rate) will be measured.
- Your lung function will be measured by having you blow into a tube
- You will be asked about any recent health issues and medications you have taken since the assessment.
- **You will be given the study treatment (PUL-042 or placebo) through the nebulizer.**
- Your vital signs (blood pressure, pulse, temperature, and breathing rate) and your lung function (by having you blow into a tube) will be measured at 30 minutes after you finish taking PUL-042.

Study Day 6

Study Day 6 will have the same procedures as Study Day 3

Study Day 10

Study Day 10 will have the same procedures as Study Day 3.

Study Day 15

- A physical examination will be performed.
- Your vital signs (blood pressure, pulse, temperature, and breathing rate) will be measured.
- A specimen will be taken by inserting a swab into your nasal passage or from the back of your mouth in order to test for the SARS-CoV-2 virus.You will be asked about any recent health issues and medications you are taking.

Study Day 29

- You will be asked about any recent health issues and medications you are taking.
- A specimen will be taken by inserting a swab into your nasal passage or from the back of your mouth in order to test for the SARS-CoV-2 virus A
- Women who can become pregnant will take a urine pregnancy test. If the test is positive, the results will be confirmed with a blood pregnancy test.

This visit will end your participation in the study.

If dosing with experimental treatment is discontinued for any reason, you will be asked to complete all scheduled pre-treatment procedures but, will not receive further treatments or post-treatment measurements. It is still important that you complete all scheduled visits up to the Study Day 29 assessment.

If you withdraw from the study for any other reasons you will need to complete an Early Discontinuation Vist that will have the same procedures as Study Day 15 with the addition that women who can become pregnant will take a urine pregnancy test. If the test is positive, the results will be confirmed with a blood pregnancy test

3. RISKS, SIDE EFFECTS, AND DISCOMFORTS TO PARTICIPANTS

Two previous studies in humans have been completed in which 49 people received PUL-042. The side effects noted in these 49 participants that were considered at least possibly related to PUL-042 administration included:

- a potential short term decrease in the ability of the lungs to transfer gas from inhaled air to red blood cells in 14 of 33 participants
- a short term increase in the number of white blood cells in 12 participants
- a short term decrease in the amount of air that can be forced out after a deep breath in 14 participants
- increased mucus in the nose or throat in 2 participants
- cough in 4 participants
- productive cough in 1 participant
- increased mucus in the lungs in 1 participant
- phlegm production in 1 participant
- aches in 1 participant
- chills in 1 participant
- viral symptoms in 1 participant
- chest pain, chest tightness, chest heaviness in 1 participant

Most of these side effects were mild and none were considered serious. As with any investigational study, the current study may involve unpredictable risks to the participants.

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn.

You may be asked questions about your medical history that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns about this, you are encouraged to contact your doctor or the study chairperson.

Pregnancy-Related Risks
Because taking part in this study can result in risks to an unborn or breastfeeding baby, you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications

If you are female, you must either have gone through menopause (at least one year since your last period) or be surgically sterilized (had a hysterectomy or your tubes tied). If you are capable of becoming pregnant and, if participating in sexual activity that may lead to pregnancy, you agree to use an effective dual method of birth control (acceptable methods include intrauterine device, spermicide, barrier, male partner surgical sterilization, and hormonal contraception) during the study and through 30 days after completion of the study.

If male, you must be surgically sterile (vasectomy) or, if not surgically sterile and if participating in sexual activities that may lead to pregnancy, you must be willing to practice two effective methods of birth control (acceptable methods include barrier, spermicide, or female partner surgical sterilization) during the study and through 30 days after completion of the study.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away. Getting pregnant may result in your removal from this study.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

If a pregnancy occurs during the study, you or your partner will be asked to report on the course of the pregnancy and birth of the child.

4. WHAT ARE MY RESPONSIBILITIES AS A RESEARCH PARTICIPANT

If you decide to participate in this medical research study, these are your responsibilities:

- Report all symptoms, side effects, injuries or medical treatments to your study doctor right away. Your safety depends on the prompt description of what you experience in the study. The quality of the safety information also depends on your prompt reporting.
- Attend all study visits.
- Report all medicines (including health supplements) taken. Safety and data quality depends telling your study doctor about everything you take.

Follow your study doctor's instructions about medicines and procedures you need to treat side effects.

5. POTENTIAL BENEFITS

There may be no medical benefits for you in this study. The information gathered during this study could help develop treatments to prevent or reduce the severity of COVID-19 illness in other patients.

6. ALTERNATIVE PROCEDURES OR TREATMENTS

You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. The treatment being tested in this study is intended to be given in addition to any standard treatment needed, not as a replacement or alternative. If you choose not to take part, you will still receive the standard treatment that you would normally receive.

7. WHAT ABOUT CONFIDENTIALITY?

Your medical records will remain confidential. While you are part of the study, you may be asked that the investigators communicate with your other doctors.

For your protection and safety, your medical records may be reviewed by:

- The sponsor of this trial, Pulmotect or their designees
- The Institutional Review Board, or Ethics Committee (the agency that oversees human research at the Institution)
- The US Food and Drug Administration (FDA) or other Regulatory Authority
- Department of Health and Human Services (DHHS [US only])
- Department of Defense (US only)
- The Office for Human Research Protections (OHRP), the agency that oversees human research in the US (US only).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Website at any time.

Absolute confidentiality cannot be guaranteed because of the need to give information to these parties. The results of this research study may be presented at meetings or in publications. Your name or identity will not be used for publication or publicity purposes.

Your name or the names of other participants will not be revealed in any data collected by the Sponsor. The United States Food and Drug Administration (FDA), Research Ethics Boards (REB), Institutional Review Boards (IRB), the Sponsor, or designee, or agents, may inspect and copy your medical records (without disclosing your identity) relating to this study. The results of this study will be reported to the FDA, and to other regulatory agencies. Absolute confidentiality cannot be guaranteed because of the need to give information to these parties.

You have the right to see and copy your personal health information related to the research study to request information, rectification, erasure, restriction of your personal data processing as long as the study doctor holds the information or research institution. However, for the scientific validity of the study, you will not be able to review some of the study information until after the study has been completed.

8. REMOTE MONITORING

We will keep your study records private and confidential. Certain people may need to see your study records. By law, anyone who looks at your records must keep them completely confidential.

Due to the nature of this study, the sponsor of this study and affiliated contract research organization will not be able to review your study data while at your medical facility. The reviewing of your data may be required to be performed from an outside location.

If you sign and date this document, you give permission to the study's Sponsor (Pulmotect) or their designee who have been contracted to help in the conduct the study and the review of your data to use or disclose (release) your health information electronically outside of the clinical study site in a manner that is intended to protect the confidentiality of your data. In preparing copies of your medical records to be released electronically, the clinical study site staff will "de-identify"

the records, removing any directly identifiable data such as your name, initials, medical record number and full date of birth. The records will only be identifiable using the study number assigned to you by the study site. The disclosure is specific to this clinical study.

The only people who will be allowed to see these records are:

- The research team, including the study doctors and research staff, research nurses, and all other research staff as well as other doctors involved in your care.
- Certain government and university staff who need to know more about the study. For example, individuals who provide oversight on this study may need to look at your records. This is done to make sure that we are doing the study in the right way. They also need to make sure that we are protecting your rights and your safety.
- Any agency of the country, state, provincial, or local government that regulates this research. This includes, Food and Drug Administration (FDA), State and Local Health Departments, the Department of Health and Human Services (DHHS), Department of Defense (DOD), and the Office for Human Research Protection (OHRP), European Medicines Agency (EMA)
- Institutional Review Board (IRB) and its related staff who have oversight responsibilities for this study and other offices who oversee this research.
- The sponsors of this study and any affiliated contract research organization.

The health information that we may use or disclose (release) for this research study may include:

- All information in a medical record
- Results of physical examinations
- Medical history
- Lab tests
- Health information related your Covid-19 infection

9. ADDITIONAL INFORMATION

You may ask the study chair any questions you have about this study. You may contact the study chair, Dr. *XX*, at *XXX-XXXX*. You may also contact the Chair of the Institutional Review Board or Ethics Committee (a committee that reviews research studies) at xxxxx with any questions that you have regarding this study and your rights as a study participant.

Your participation in this research study is strictly voluntary. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits.

If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated.

The study doctor or the Sponsor may remove you from the study without your consent for any of the following reasons:

- if it appears to be medically harmful to you,
- if you fail to follow directions for participating in the study,
- if it is discovered you do not meet the study requirements,
- at the discretion of the study doctor,
- if the study is canceled,
- or if you become pregnant.

If your participation in this study is stopped for any reason, you will be asked to complete the early discontinuation study procedures for your safety. An Early Discontinuation study visit, will be scheduled.

You will be asked to complete the assessments at Study Day 29.

If you agree to be in this study, you will be given a signed and dated copy of this consent form.

This study or your participation in it may be changed or stopped at any time by the study chair, Pulmotect, Inc., the U.S. Food and Drug Administration (FDA) or other Regulatory Authority, the Office for Human Research Protections (OHRP - a regulatory agency that oversees research in humans), or the IRB/Ethic Committee.

You will be informed of any new findings that might affect your willingness to continue taking part in the study.

The institution conducting the study may benefit from your participation and/or what is learned in this study.

This study is supported by Pulmotect, Inc. with funding from the Department of Defense.

In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s). If you have any questions about this, you may call the IRB.

10. STUDY COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, the institution's health providers will provide medical care. Pulmotect may pay for the treatment of the injury or illness. The institution cannot determine at this time what you may be reimbursed for. A financial counselor will be made available to you after the injury or illness is reported. You may also contact the Chair of the IRB or Ethics Committee at XXX-XXXX with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

A new public health declaration, called the Public Readiness and Emergency Preparedness Declaration (PREP), was issued by the Department of Health and Human Services on March 10,

2020. This declaration limits the legal rights of a subject participating in a COVID-19 clinical study that uses a drug, device or vaccine designed to treat, diagnose, cure or prevent COVID-19. This includes the study treatment, PUL-042 used in this study. Participants using PUL-042 in this study will have limits on their right to sue the manufacturers, the study sponsor, healthcare providers and others for significant injuries and adverse reactions.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

11. AUTHORIZATION FOR USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

A. During the course of this study, the research team will be collecting and using your protected health information. This information may include personal identifying information about you (such as your name, race, date of birth, gender, city, and zip code), your medical history, study schedule, and the results of any of your tests, therapies, and/or procedures. The purpose of collecting and sharing this information is to learn about how the study procedures may affect the disease and any study-related side effects. Your doctor and the research team may share your study information with the parties named in Section D below.

B. Signing this consent and authorization form is optional However, if you refuse to provide authorization to use and disclose your protected health information for this study, you will not be able to participate in this research study.

C. The institution will take appropriate steps to keep your protected health information private when possible, and it will be protected according to state and federal law. However, there is no guarantee that your information will remain confidential, and it may be re-disclosed at some point. Federal agencies (such as the FDA, other Regulatory Agencies, Office for Human Research Protections (OHRP)), Pulmotect or its designee, and the IRB/Ethics Committee might view or receive your record in order to collect data and/or meet legal, ethical, research, and safety-related obligations.

D. Your protected health information may be shared with the following parties:

- Pulmotect, Inc. (and/or any future sponsors of the study) and its designees

- CTI Clinical Trial & Consulting, a company Pulmotect has hired to help run this study and analyze its results
- Department of Defense (US)
- Federal agencies that require reporting of clinical study data (such as the FDA and OHRP)
- The governing IRB/Ethics Committee
- Officials of the institution
- Clinical study monitors who verify the accuracy of the information
- Individuals with medical backgrounds who determine the effect that the study procedures may have on the disease
- Individuals who put all the study information together in report form

E. There is no expiration date for the use of your protected health information. In California and any other state that requires an expiration date, the Authorization will expire 50 years after you sign and date this authorization document. You may withdraw your authorization to share your protected health information at any time in writing. Instructions on how to do this can be found in XXXXXXX. You may contact the IRB/Ethics Committee questions. If you withdraw your authorization, you will be removed from the study and the study chair and staff will no longer use or disclose your protected health information in connection with this study, unless the study chair or staff needs to use or disclose some of your research-related protected health information to preserve the scientific value of the study. Data collected about you up to the time you withdrew will be used and included in the data analysis. The parties listed in Section D above may use and disclose any study data that were collected before you canceled your authorization.

CONSENT/AUTHORIZATION
(Adult Participants Only)

I understand the information in this consent form. I have had a chance to read the consent form for this study or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give XXXX permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

WITNESS TO CONSENT
I was present during the explanation of the research to be performed under Protocol PUL-042-501.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN) DATE

A witness signature is only required for vulnerable adult participants.

PERSON OBTAINING CONSENT

I have discussed this clinical research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
SIGNATURE of Person Authorized to Obtain Consent DATE

16. REFERENCES

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