1 TITLE PAGE

EVALUATION OF SAFETY AND PHARMACODYNAMICS OF OP0201 COMPARED TO PLACEBO IN HEALTHY ADULTS

Study Drug:	OP0201
Indication Studied:	Eustachian tube function
Study Design:	Single-center, randomized, double-blind, placebo-controlled, single-dose, cross-over clinical study
Sponsor:	Novus Therapeutics, Inc 19900 MacArthur Blvd, Suite 550 Irvine, CA 92612 (949) 238-8090
Protocol Number:	OP0201-C-001
EudraCT Number:	2016-003667-19
Clinical Development Phase:	1
Study Initiation Date:	04 Feb 2019
Study Completion Date:	07 Mar 2019
Principal Investigator:	Prof. Dr. Jens Peter Klußmann
Sponsor Signatory:	Janak A. Patel, MD 19900 MacArthur Blvd, Suite 550 Irvine, CA 92612 (949) 238-8090 jpatel@novustherapeutics.com
Version:	Final
Date of Report:	14 Oct 2019

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

CONFIDENTIAL

Part of or all the information in this report may be unpublished material. Accordingly, this report should be treated confidentially and restricted to its intended use. Should any portion of this unpublished material be desired for purposes of publication, authorization must be obtained from Novus Therapeutics, Inc.

2 SYNOPSIS

NAME OF THE SPONSOR: Novus Therapeutics, Inc.	
NAME OF FINISHED PRODUCT: OP0201	
NAME OF ACTIVE INGREDIENT: dipalmitoylphosphatidylcholine (DPPC) and cholesteryl palmitate (CP)	
Title of Study: Evaluation of Safety and Pharmacodynamics of OP0201 Compared to Placebo in Healthy Adults	
Principal Coordinating Investigator: Prof. Dr. Jens Peter Klußmann	
Study Center: Department of Otorhinolaryngology, Head, and Neck Surgery, University of Cologne	
Publication(s) (reference): None	
Study Period: First subject first visit: 08 Feb 2019 Last subject last visit: 07 Mar 2019	**Phase of Development**: 1
Objectives: The primary objective of this study was: • To assess the safety and tolerability of a single intranasal dose of OP0201 compared to a single intranasal dose of placebo in healthy adults. The secondary objectives of this study were: • To assess pharmacodynamics of the Eustachian tube (ET) following a single intranasal dose of OP0201 compared to a single intranasal dose of placebo in healthy adults. • To explore whether a single intranasal dose of OP0201 compared to a single intranasal dose of placebo modulates ear pain during the hypobaric/hyperbaric atmospheric pressure chamber assessment in healthy adults.	
Methodology: This was a randomized, double-blind, placebo-controlled, cross-over trial designed to evaluate the safety, tolerability, and pharmacodynamics of the ET and potential effect	

in modulating ear pain of a single intranasal dose of OP0201 compared to a single intranasal dose of placebo in healthy adults.

A total of 17 healthy subjects were randomized (OP0201-placebo N = 9; placebo-OP0201 N = 8). Each subject participated in the trial for up to 5 weeks and had up to 3 in-clinic visits and 2 telephone follow-up visits. There was a screening period of up to 28 days, with a randomization visit on Day 1 where subjects were randomly assigned to receive a single masked dose of intranasal OP0201 containing a total of 20 mg OP0201 or placebo. The trial site staff administered the study treatment to each subject as 4 consecutive sprays at a time into each nare so that a total of eight sprays (4 per nare) were administered. On Day 8, subjects returned to the trial site for the cross-over visit where they received the opposite masked treatment administered in the same way. Subjects remained in the clinic for the duration of approximately 4 to 6 hours at each visit.

Safety was assessed by clinical monitoring and included a general physical examination, an ear, nose, and throat examination that included otoscopy, nose and epipharynx endoscopy, tympanogram, clinical laboratory tests (hematology, biochemistry, and urinalysis), triplicate12-lead electrocardiogram (ECG), vital signs (pulse rate, respiratory rate, blood pressure, temperature), and spontaneous adverse event (AE) reporting.

Pharmacodynamics of OP0201 on ET function were assessed by continuous tympanic impedance measures using a single-person hypobaric/hyperbaric atmospheric pressure chamber. Subjects were exposed to atmospheric pressure changes induced by a hypobaric/hyperbaric protocol lasting a total of 4.5 minutes per each pressure chamber assessment.

An exploratory efficacy assessment of OP0201's effect on modulation of ear pain during the hypobaric/hyperbaric atmospheric pressure chamber protocol was evaluated. During the conduct of the hypobaric/hyperbaric atmospheric pressure chamber protocol, subjects rated the worst pain they felt in the right ear, and separately in the left ear using a whole number Numeric Rating Scale ranging from 0 (no pain) to 10 (worst pain imaginable).

Number of Subjects (Planned and Analyzed):

Planned:16 subjects, 8 subjects per sequence
Actual: 17 subjects, OP0201-Placebo N = 9 and Placebo-OP0201 N = 8
Completed: 17 subjects, OP0201-Placebo N = 9 and Placebo-OP0201 N = 8
Analyzed: 17 subjects, OP0201-Placebo N = 9 and Placebo-OP0201 N = 8

Main Criteria for Inclusion: Male and female subjects 18 to 50 years of age with a body mass index 18 to 30 kg/m^2 and minimum body weight of 50 kg at the time of informed consent. Subjects were considered healthy with no history or presence of significant medical condition or

clinically significant abnormal finding on screening assessments as determined by the investigator. Subjects were required to refrain from immersing their ears in water while in the study. Females of childbearing potential were required to have a negative urine pregnancy test at Screening and Baseline. Subjects were eligible for enrolment if they met all inclusion criteria and none of the exclusion criteria and signed a written Informed Consent Form.

Test Product, Dose, Mode of Administration, and Batch Number:

OP0201: DPPC + CP (approximately 20:1 weight/weight) suspended in propellant (hydrofluoroalkane-134a [HFA-134a])
Dose: 20 mg (4 sprays per nare, each 0.1 mL spray contained 2.5 mg OP0201)
Batch Number: 0002-062

Duration of Treatment: Subjects received a single dose of OP0201 or OP0201 Placebo at the Day 1 visit, followed by an approximately 1-week washout. Subjects then received a single dose of the opposite treatment at the Day 8 cross-over visit.

Reference Therapy, Dose, Mode of Administration, and Batch Number:

Placebo: Propellant (HFA-134a) only
Dose: 0 mg (4 sprays per nare, each 0.1 mL spray contained 0 mg OP0201)
Batch Number: 0002-060

Safety Results:

Subject Disposition:

A total of 17 subjects were enrolled in the study (OP0201-Placebo N = 9; Placebo-OP0201 N = 8); all 17 (100%) enrolled subjects completed the study.

Safety Results:

Overall, 15 (88.2%) subjects reported a treatment-emergent adverse event (TEAE) during the study. A total of 14/17 (82.4%) placebo-treated subjects and 12/17 (70.6%) OP0201-treated subjects reported 1 or more TEAEs. In the Placebo-OP0201 sequence, 7 (87.5%) subjects reported a TEAE in Period 1 (ie, following placebo) and 6 (75%) subjects reported a TEAE in Period 2 (ie, following OP0201). In the OP0201-Placebo sequence, 6 (66.7%) subjects reported a TEAE in Period 1 (ie, following OP0201) and 7 (77.8%) subjects reported a TEAE in Period 2 (ie, following placebo). A total of 4 placebo-treated subjects and a total of 3 OP0201-treated subjects reported TEAEs that were considered treatment-related. The most common system organ class category for TEAEs was ear and labyrinth disorders (14 [82.4%] subjects overall). Overall, the most commonly reported TEAEs were ear pain (12 [70.6%] subjects), tympanic membrane

(TM) hyperemia (7 [41.2%] subjects), TM disorder (5 [29.4%] subjects), headache (5 [29.4%] subjects), and nasal discomfort (3 [17.6%] subjects). TEAEs reported by more than 2 subjects and at a frequency greater than placebo include TM hyperemia and TM disorder. All reported TEAEs were of mild severity except for ear pain. Across all subjects, moderate ear pain was reported by 2 (11.8%) subjects and severe ear pain was reported by 1 (5.9%) subject; these events were considered unrelated to the study treatment. The incidence of pre-treatment AEs was similar across both treatment sequences. Non-TEAEs were reported by subjects in both treatment sequences in Period 1. No subject had an AE leading to withdrawal from study treatment. No death or other SAE occurred during this study.

No clinically important findings for other safety assessments including clinical laboratory parameters, vital signs, otoscopy, nasal and epipharynx endoscopy, tympanograms or electrocardiograms (ECGs) were observed.

Conclusion:

The primary objective of the study was met. This study demonstrated that a single 20 mg dose of intranasal OP0201 is safe and tolerable when administered to healthy adults.

Date of Report: Final, 14 Oct 2019

