ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: July 31, 2021

ClinicalTrials.gov ID: NCT03979638

Study Identification

Unique Protocol ID:	BUS-P2-01
Brief Title:	A Dose Escalation Study of BLU-5937 in Unexplained or Refractory Chronic Cough (RELIEF)
Official Title:	A Randomized, Double-Blind, Placebo-Controlled, Crossover, Dose Escalation Study of BLU-5937 in Subjects With Unexplained or Refractory Chronic Cough (RELIEF)
Secondary IDs:	2019-000375-16 [EudraCT Number]

Study Status

Record Verification:	April 2020
Overall Status:	Terminated [Trial was terminated due to the impact of the COVID-19 on trial activities. 68 patients with refractory chronic cough were enrolled with 52 completing treatment]
Study Start:	July 10, 2019 [Actual]
Primary Completion:	April 23, 2020 [Actual]
Study Completion:	April 23, 2020 [Actual]

Sponsor/Collaborators

Sponsor:	Bellus Health Inc
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:	Yes

U.S. FDA-regulated Device:	No
U.S. FDA IND/IDE:	Yes
IND/IDE Information:	FDA Center: CDER IND/IDE Number: 142905 Serial Number: 0000 Has Expanded Access: No
Human Subjects Review:	Board Status: Approved Approval Number: Pro00034378 Board Name: Advarra Board Affiliation: Independent Phone: 410.884.2900 Email: advarra.admin@advarra.com Address:
Data Monitoring:	No
FDA Regulated Intervention:	Yes
Section 801 Clinical Trial:	Yes

Study Description

Brief Summary:	This is a multi-center, randomized, double-blind, placebo-controlled, crossover, dose escalation study of BLU-5937 in subjects with unexplained or refractory chronic cough
Detailed Description:	This study will have two 16-day treatment periods (four escalating doses or matching placebo at four days interval) separated by a 10 to 14-day washout period. There will be a 14-day follow-up period.

Conditions

Conditions:	Chronic Refractory Cough
Keywords:	Unexplained or refractory chronic cough, P2X3 antagonists

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2

Interventional Study Model:	Crossover Assignment Two-arm, Two-Period, crossover assignment
Number of Arms:	2
Masking:	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Allocation:	Randomized
Enrollment:	68 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: BLU-5937 oral tablet BID Randomized crossover design of 4 different doses (25, 50, 100, 200 mg BID) of BLU-5937 tablets to be administered orally BID	Drug: BLU-5937 Four escalating doses of BLU-5937 administered BID over the course of the study
Placebo Comparator: Placebo oral tablet BID Randomized crossover design of matching placebo tablets to be administered orally BID	Drug: Placebo Matching placebo for BLU-5937

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	80 Years
Sex:	All
Gender Based:	No
Accepts Healthy Volunteers:	No
Criteria:	Inclusion Criteria:

- Unexplained or refractory chronic cough for at least one year
- Chest radiograph or CT thorax within the last 60 months not demonstrating any abnormality considered to be significantly contributing to the chronic cough
- Cough count of ≥ 10 per hour (Awake Cough Count) at Screening
- Score of ≥ 40mm on the Cough Severity VAS at Screening
- Women of child-bearing potential must have a negative serum pregnancy test at Screening
- Women of child-bearing potential must use a highly effective contraception method from Screening through the Follow-Up Visit

- Male subjects and their partners of child-bearing potential must use 2 methods of acceptable birth control

Exclusion Criteria:

- Current smoker or individuals who have given up smoking within the past 6 months, or those with >20 pack-year smoking history
- Diagnosis of COPD, bronchiectasis, idiopathic pulmonary fibrosis
- Treatment with an ACE-inhibitor as the potential cause of a subject's cough, or requiring treatment with an ACE-inhibitor during the study, or within 12 weeks prior to the Screening Visit
- FEV1/FVC < 60%
- History of upper respiratory tract infection or recent significant change in pulmonary status within 4 weeks of the Baseline Visit
- History of concurrent malignancy or recurrence of malignancy within 2 years prior to Screening
- History of a diagnosis of drug or alcohol dependency or abuse within the last 3 years
- Clinically significant abnormal electrocardiogram (ECG) or laboratory tests at Screening
- Other severe, acute, or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with trial participation or investigational product administration or may interfere with the interpretation of trial results

Contacts/Locations

Central Contact Person: Laurent Harvey, M.Sc.
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Study Officials: Jacky Smith, MD, Ph.D.
Study Principal Investigator
University of Manchester

Locations: **United States, California**
Allergy & Asthma Associates of Santa Clara Valley
San Jose, California, United States, 95117

United States, Florida
Centre for Cough
Largo, Florida, United States, 33778

United States, Texas
Diagnostics Research Group
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United Kingdom

Belfast City Hospital
Belfast, United Kingdom, BT9 7BL

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Royal Brompton Hospital
London, United Kingdom, SW3 6HP

King's College Hospital
London, United Kingdom, SE5 9RS

Manchester Clinical Research Facility
Manchester, United Kingdom, M23 9LT

North Tyneside General Hospital
North Shields, United Kingdom, NE29 8NH

Prince Phillip Hospital
Llanelli, United Kingdom, SA14 8QF

United States, North Carolina
Clinical Research of Gastonia
Gastonia, North Carolina, United States, 20854

United States, Wisconsin
Allergy Asthma & Sinus Center
Greenfield, Wisconsin, United States, 53228

United States, South Carolina
National Allergy & Asthma Research
Charleston, South Carolina, United States, 29420

United States, California
Allergy Associates Medical Group Inc.
San Diego, California, United States, 92108

United States, Minnesota
Clinical Research Institute
Minneapolis, Minnesota, United States, 55402

IPDSharing

Plan to Share IPD:

References

Citations:

Links:

Available IPD/Information:

Documents

Study Protocol and Statistical Analysis Plan
Document Date: September 26, 2019
Uploaded: 07/05/2021 10:17

Study Results

Participant Flow

Recruitment Details	Participants were recruited at 16 clinical trial sites in the United-Kingdom and in United States.
Pre-assignment Details	A total of 68 participants were randomized to receive the study drug (BLU-5937) followed by placebo (33 participants) or placebo followed by the study drug (35 participants).

Reporting Groups

	Description
BLU-5937 > Placebo	Randomized crossover design of 4 different doses (25, 50, 100, 200 mg BID) of BLU-5937 tablets to be administered orally BID BLU-5937: Four escalating doses of BLU-5937 administered BID over the course of the study followed by matching Placebo
Placebo > BLU-5937	Randomized crossover design of matching placebo tablets to be administered orally BID Placebo: Matching placebo for BLU-5937 follow by four escalating doses of BLU-5937

Period 1

	BLU-5937 > Placebo	Placebo > BLU-5937
Started	33	35
Completed	26	28
Not Completed	7	7
Physician Decision	1	1
Withdrawal by Subject	4	3
Study terminated by Sponsor	1	3
Protocol Violation	1	0

Period 2

	BLU-5937 > Placebo	Placebo > BLU-5937
Started	26	28
Completed	25	27
Not Completed	1	1
Study terminated by Sponsor	1	1

Baseline Characteristics

Baseline Analysis Population Description

The baseline analysis population consisted of all randomized participants who have received at least 1 dose of study drug.

Reporting Groups

	Description
BLU-5937 > Placebo	Randomized crossover design of 4 different doses (25, 50, 100, 200 mg BID) of BLU-5937 tablets to be administered orally BID BLU-5937: Four escalating doses of BLU-5937 administered BID over the course of the study followed by matching Placebo

	Description
Placebo > BLU-5937	Randomized crossover design of matching placebo tablets to be administered orally BID Placebo: Matching placebo for BLU-5937 followed by four escalating doses of BLU-5937

Baseline Measures

		BLU-5937 > Placebo	Placebo > BLU-5937	Total
Overall Number of Participants		33	35	68
Age, Continuous Mean (Standard Deviation) Unit of measure: years	Number Analyzed	33 participants	35 participants	68 participants
		64.3 (11.49)	63.7 (9.70)	64.0 (10.53)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	33 participants	35 participants	68 participants
	Female	28 84.85%	30 85.71%	58 85.29%
	Male	5 15.15%	5 14.29%	10 14.71%
Ethnicity (NIH/OMB) Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	33 participants	35 participants	68 participants
	Hispanic or Latino	2 6.06%	1 2.86%	3 4.41%
	Not Hispanic or Latino	29 87.88%	34 97.14%	63 92.65%
	Unknown or Not Reported	2 6.06%	0 0%	2 2.94%
Race (NIH/OMB) Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	33 participants	35 participants	68 participants
	American Indian or Alaska Native	0 0%	0 0%	0 0%
	Asian	0 0%	0 0%	0 0%

		BLU-5937 > Placebo	Placebo > BLU-5937	Total
	Native Hawaiian or Other Pacific Islander	0 0%	1 2.86%	1 1.47%
	Black or African American	0 0%	1 2.86%	1 1.47%
	White	33 100%	33 94.29%	66 97.06%
	More than one race	0 0%	0 0%	0 0%
	Unknown or Not Reported	0 0%	0 0%	0 0%

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change in Awake Objective Cough Frequency on Log-transformed Scale
Measure Description	Change in awake cough frequency (average hourly cough frequency while the subject is awake) evaluated using the VitaloJAK cough monitor with 24-hour sound recordings collected
Time Frame	Period 1: baseline (Day 0) and 24 hours after Day 4, 8, 12, 16 doses ; Period 2: baseline (Day 30) and 24 hours after Day 34, 38, 42, 46 doses

Analysis Population Description

Analysis population consisted of all randomized subjects who took at least one dose of study drug and provided at least one baseline and at least one post-baseline cough frequency measurement

Reporting Groups

	Description
BLU-5937 - 25 mg	BLU-5937 25 mg tablet administered orally BID for 4 days
Placebo Comparator - 25 mg	Matching Placebo for BLU-5937 administered orally BID for 4 days
BLU-5937 - 50 mg	BLU-5937 50 mg tablet administered orally BID for 4 days
Placebo Comparator - 50 mg	Matching Placebo for BLU-5937 administered orally BID for 4 days

	Description
BLU-5937 - 100 mg	BLU-5937 100 mg tablet administered orally BID for 4 days
Placebo Comparator - 100 mg	Matching Placebo for BLU-5937 administered orally BID for 4 days
BLU-5937 - 200 mg	BLU-5937 200 mg tablet administered orally BID for 4 days
Placebo Comparator - 200 mg	Matching Placebo for BLU-5937 administered orally BID for 4 days

Measured Values

	BLU-5937 - 25 mg	Placebo Comparator - 25 mg	BLU-5937 - 50 mg	Placebo Comparator - 50 mg	BLU-5937 - 100 mg	Placebo Comparator - 100 mg
Overall Number of Participants Analyzed	60	59	59	58	56	58
Change in Awake Objective Cough Frequency on Log-transformed Scale Least Squares Mean (95% Confidence Interval) Unit of measure: Log coughs/hour	-0.19 (-0.29 to -0.08)	-0.07 (-0.19 to 0.05)	-0.20 (-0.32 to -0.08)	-0.14 (-0.26 to -0.01)	-0.25 (-0.40 to -0.09)	-0.17 (-0.30 to -0.04)

	BLU-5937 - 200 mg	Placebo Comparator - 200 mg
Overall Number of Participants Analyzed	58	58
Change in Awake Objective Cough Frequency on Log-transformed Scale Least Squares Mean (95% Confidence Interval) Unit of measure: Log coughs/hour	-0.33 (-0.49 to -0.17)	-0.14 (-0.29 to 0.00)

Statistical Analysis 1 for Change in Awake Objective Cough Frequency on Log-transformed Scale

Statistical Analysis Overview	Comparison Group Selection	BLU-5937 - 25 mg, Placebo Comparator - 25 mg
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1424
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	Intention To Treat (ITT), statistical analysis follows a Mixed Model which uses log-transformation

Method of Estimation	Estimation Parameter	Other [Estimated percent change]
	Estimated Value	-10.8
	Confidence Interval	(2-Sided) 95% -23.5 to 4.0
	Estimation Comments	Percent change difference between BLU-5937 and placebo was estimated by 100 x [e^diff - 1] where 'e' = exponent of difference; and 'diff' = the treatment mean difference from mixed model of change from baseline based on log-transformed data.

Statistical Analysis 2 for Change in Awake Objective Cough Frequency on Log-transformed Scale

Statistical Analysis Overview	Comparison Group Selection	BLU-5937 - 50 mg, Placebo Comparator - 50 mg
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4602
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	Intention To Treat (ITT), statistical analysis follows a Mixed Model which uses log-transformation

Method of Estimation	Estimation Parameter	Other [Estimated percent change]
	Estimated Value	-6.1
	Confidence Interval	(2-Sided) 95% -20.8 to 11.2
	Estimation Comments	Percent change difference between BLU-5937 and placebo was estimated by 100 x [e^diff - 1] where 'e' = exponent of difference; and 'diff' = the treatment mean difference from mixed model of change from baseline based on log-transformed data.

Statistical Analysis 3 for Change in Awake Objective Cough Frequency on Log-transformed Scale

Statistical Analysis Overview	Comparison Group Selection	BLU-5937 - 100 mg, Placebo Comparator - 100 mg
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4181
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	Intention To Treat (ITT), statistical analysis follows a Mixed Model which uses log-transformation
Method of Estimation	Estimation Parameter	Other [Estimated percent change]
	Estimated Value	-7.8
	Confidence Interval	(2-Sided) 95% -24.4 to 12.5
	Estimation Comments	Percent change difference between BLU-5937 and placebo was estimated by 100 x [e^diff - 1] where 'e' = exponent of difference; and 'diff' = the treatment mean difference from mixed model of change from baseline based on log-transformed data.

Statistical Analysis 4 for Change in Awake Objective Cough Frequency on Log-transformed Scale

Statistical Analysis Overview	Comparison Group Selection	BLU-5937 - 200 mg, Placebo Comparator - 200 mg
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0855
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	Intention To Treat (ITT), statistical analysis follows a Mixed Model which uses log-transformation
Method of Estimation	Estimation Parameter	Other [Estimated percent change]
	Estimated Value	-16.7
	Confidence Interval	(2-Sided) 95%

		-32.3 to 2.6
	Estimation Comments	Percent change difference between BLU-5937 and placebo was estimated by 100 x [e^diff - 1] where 'e' = exponent of difference; and 'diff' = the treatment mean difference from mixed model of change from baseline based on log-transformed data.

2. Other Pre-specified Outcome Measure:

Measure Title	Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = 20 Coughs/Hour at Baseline
Measure Description	Change in awake cough frequency (average hourly cough frequency while the subject is awake) in the a pre-specified subgroup of participants with awake cough frequency > or = 20 coughs/hour at baseline evaluated using the VitaloJAK cough monitor with 24-hour sound recordings collected
Time Frame	Period 1: baseline (Day 0) and 24 hours after Day 4, 8, 12, 16 doses ; Period 2: baseline (Day 30) and 24 hours after Day 34, 38, 42, 46 doses

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
BLU-5937 - 25 mg	BLU-5937 25 mg tablet administered orally BID for 4 days
Placebo Comparator - 25 mg	Matching Placebo for BLU-5937 administered orally BID for 4 days
BLU-5937 - 50 mg	BLU-5937 50 mg tablet administered orally BID for 4 days
Placebo Comparator - 50 mg	Matching Placebo for BLU-5937 administered orally BID for 4 days
BLU-5937 - 100 mg	BLU-5937 100 mg tablet administered orally BID for 4 days
Placebo Comparator - 100 mg	Matching Placebo for BLU-5937 administered orally BID for 4 days
BLU-5937 - 200 mg	BLU-5937 200 mg tablet administered orally BID for 4 days
Placebo Comparator - 200 mg	Matching Placebo for BLU-5937 administered orally BID for 4 days

Measured Values

	BLU-5937 - 25 mg	Placebo Comparator - 25 mg	BLU-5937 - 50 mg	Placebo Comparator - 50 mg	BLU-5937 - 100 mg	Placebo Comparator - 100 mg
Overall Number of Participants Analyzed	46	46	45	46	44	47

	BLU-5937 - 25 mg	Placebo Comparator - 25 mg	BLU-5937 - 50 mg	Placebo Comparator - 50 mg	BLU-5937 - 100 mg	Placebo Comparator - 100 mg
Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = 20 Coughs/Hour at Baseline Least Squares Mean (95% Confidence Interval) Unit of measure: Log coughs/hour	-0.23 (-0.34 to -0.11)	0.00 (-0.09 to 0.10)	-0.29 (-0.42 to -0.15)	-0.09 (-0.21 to 0.03)	-0.33 (-0.51 to -0.16)	-0.12 (-0.25 to 0.01)

	BLU-5937 - 200 mg	Placebo Comparator - 200 mg
Overall Number of Participants Analyzed	45	46
Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = 20 Coughs/Hour at Baseline Least Squares Mean (95% Confidence Interval) Unit of measure: Log coughs/hour	-0.41 (-0.58 to -0.24)	-0.09 (-0.23 to 0.05)

Statistical Analysis 1 for Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = 20 Coughs/Hour at Baseline

Statistical Analysis Overview	Comparison Group Selection	BLU-5937 - 25 mg, Placebo Comparator - 25 mg
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0010
	Comments	[Not specified]
	Method	Mixed Models Analysis

	Comments	Intention To Treat (ITT), statistical analysis follows a Mixed Model which uses log-transformation

Method of Estimation	Estimation Parameter	Other [Estimated percent change]
	Estimated Value	-20.3
	Confidence Interval	(2-Sided) 95% -29.9 to -9.5
	Estimation Comments	Percent change difference between BLU-5937 and placebo was estimated by 100 x [e^diff - 1] where 'e' = exponent of difference; and 'diff' = the treatment mean difference from mixed model of change from baseline based on log-transformed data.

Statistical Analysis 2 for Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = 20 Coughs/Hour at Baseline

Statistical Analysis Overview	Comparison Group Selection	BLU-5937 - 50 mg, Placebo Comparator - 50 mg
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0186
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	Intention To Treat (ITT), statistical analysis follows a Mixed Model which uses log-transformation

Method of Estimation	Estimation Parameter	Other [Estimated percent change]
	Estimated Value	-17.7
	Confidence Interval	(2-Sided) 95% -29.9 to -3.3
	Estimation Comments	Percent change difference between BLU-5937 and placebo was estimated by 100 x [e^diff - 1] where 'e' = exponent of difference; and 'diff' = the treatment mean difference from mixed model of change from baseline based on log-transformed data.

Statistical Analysis 3 for Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = 20 Coughs/Hour at Baseline

Statistical Analysis Overview	Comparison Group Selection	BLU-5937 - 100 mg, Placebo Comparator - 100 mg
	Comments	[Not specified]

	Type of Statistical Test	Superiority
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0320
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	Intention To Treat (ITT), statistical analysis follows a Mixed Model which uses log-transformation

Method of Estimation	Estimation Parameter	Other [Estimated percent change]
	Estimated Value	-19.4
	Confidence Interval	(2-Sided) 95% -33.9 to -1.9
	Estimation Comments	Percent change difference between BLU-5937 and placebo was estimated by 100 x [e^diff - 1] where 'e' = exponent of difference; and 'diff' = the treatment mean difference from mixed model of change from baseline based on log-transformed data.

Statistical Analysis 4 for Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = 20 Coughs/Hour at Baseline

Statistical Analysis Overview	Comparison Group Selection	BLU-5937 - 200 mg, Placebo Comparator - 200 mg
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0026
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	Intention To Treat (ITT), statistical analysis follows a Mixed Model which uses log-transformation

Method of Estimation	Estimation Parameter	Other [Estimated percent change]
	Estimated Value	-27.0
	Confidence Interval	(2-Sided) 95% -40.3 to -10.8

	Estimation Comments	Percent change difference between BLU-5937 and placebo was estimated by 100 x [e^diff - 1] where 'e' = exponent of difference; and 'diff' = the treatment mean difference from mixed model of change from baseline based on log-transformed data.

3. Other Pre-specified Outcome Measure:

Measure Title	Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = Median (32.4 Coughs/Hour) at Baseline
Measure Description	Change in awake cough frequency (average hourly cough frequency while the subject is awake) in the a pre-specified subgroup of participants with awake cough frequency > or = median (32.4 coughs/hour) at baseline evaluated using the VitaloJAK cough monitor with 24-hour sound recordings collected
Time Frame	Period 1: baseline (Day 0) and 24 hours after Day 4, 8, 12,16 doses ; Period 2: baseline (Day 30) and 24 hours after Day 34, 38, 42, 46 doses

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
BLU-5937 - 25 mg	BLU-5937 25 mg tablet administered orally BID for 4 days
Placebo Comparator - 25 mg	Matching Placebo for BLU-5937 administered orally BID for 4 days
BLU-5937 - 50 mg	BLU-5937 50 mg tablet administered orally BID for 4 days
Placebo Comparator - 50 mg	Matching Placebo for BLU-5937 administered orally BID for 4 days
BLU-5937 - 100 mg	BLU-5937 100 mg tablet administered orally BID for 4 days
Placebo Comparator - 100 mg	Matching Placebo for BLU-5937 administered orally BID for 4 days
BLU-5937 - 200 mg	BLU-5937 200 mg tablet administered orally BID for 4 days
Placebo Comparator - 200 mg	Matching Placebo for BLU-5937 administered orally BID for 4 days

Measured Values

	BLU-5937 - 25 mg	Placebo Comparator - 25 mg	BLU-5937 - 50 mg	Placebo Comparator - 50 mg	BLU-5937 - 100 mg	Placebo Comparator - 100 mg
Overall Number of Participants Analyzed	28	30	28	31	27	31

	BLU-5937 - 25 mg	Placebo Comparator - 25 mg	BLU-5937 - 50 mg	Placebo Comparator - 50 mg	BLU-5937 - 100 mg	Placebo Comparator - 100 mg
Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = Median (32.4 Coughs/Hour) at Baseline Least Squares Mean (95% Confidence Interval) Unit of measure: Log coughs/hour	-0.31 (-0.45 to -0.18)	0.02 (-0.11 to 0.15)	-0.42 (-0.55 to -0.28)	-0.08 (-0.22 to 0.05)	-0.44 (-0.60 to -0.27)	-0.09 (-0.24 to 0.06)

	BLU-5937 - 200 mg	Placebo Comparator - 200 mg
Overall Number of Participants Analyzed	28	31
Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = Median (32.4 Coughs/Hour) at Baseline Least Squares Mean (95% Confidence Interval) Unit of measure: Log coughs/hour	-0.49 (-0.68 to -0.31)	-0.10 (-0.24 to 0.03)

Statistical Analysis 1 for Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = Median (32.4 Coughs/Hour) at Baseline

Statistical Analysis Overview	Comparison Group Selection	BLU-5937 - 25 mg, Placebo Comparator - 25 mg
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0005
	Comments	[Not specified]
	Method	Mixed Models Analysis

	Comments	Intention To Treat (ITT), statistical analysis follows a Mixed Model which uses log-transformation

Method of Estimation	Estimation Parameter	Other [Estimated percent change]
	Estimated Value	-28.1
	Confidence Interval	(2-Sided) 95% -39.5 to -14.5
	Estimation Comments	Percent change difference between BLU-5937 and placebo was estimated by 100 x [e^diff - 1] where 'e' = exponent of difference; and 'diff' = the treatment mean difference from mixed model of change from baseline based on log-transformed data.

Statistical Analysis 2 for Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = Median (32.4 Coughs/Hour) at Baseline

Statistical Analysis Overview	Comparison Group Selection	BLU-5937 - 50 mg, Placebo Comparator - 50 mg
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0003
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	Intention To Treat (ITT), statistical analysis follows a Mixed Model which uses log-transformation

Method of Estimation	Estimation Parameter	Other [Estimated percent change]
	Estimated Value	-28.4
	Confidence Interval	(2-Sided) 95% -39.7 to -15.0
	Estimation Comments	Percent change difference between BLU-5937 and placebo was estimated by 100 x [e^diff - 1] where 'e' = exponent of difference; and 'diff' = the treatment mean difference from mixed model of change from baseline based on log-transformed data.

Statistical Analysis 3 for Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = Median (32.4 Coughs/Hour) at Baseline

Statistical Analysis Overview	Comparison Group Selection	BLU-5937 - 100 mg, Placebo Comparator - 100 mg
	Comments	[Not specified]

	Type of Statistical Test	Superiority
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0014
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	Intention To Treat (ITT), statistical analysis follows a Mixed Model which uses log-transformation

Method of Estimation	Estimation Parameter	Other [Estimated percent change]
	Estimated Value	-29.5
	Confidence Interval	(2-Sided) 95% -42.7 to -13.2
	Estimation Comments	Percent change difference between BLU-5937 and placebo was estimated by 100 x [e^diff - 1] where 'e' = exponent of difference; and 'diff' = the treatment mean difference from mixed model of change from baseline based on log-transformed data.

Statistical Analysis 4 for Change in Awake Cough Frequency on Log-transformed Scale in the Subgroup of Participants With Awake Cough Frequency > or = Median (32.4 Coughs/Hour) at Baseline

Statistical Analysis Overview	Comparison Group Selection	BLU-5937 - 200 mg, Placebo Comparator - 200 mg
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0006
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	Intention To Treat (ITT), statistical analysis follows a Mixed Model which uses log-transformation

Method of Estimation	Estimation Parameter	Other [Estimated percent change]
	Estimated Value	-32.4
	Confidence Interval	(2-Sided) 95% -45.3 to -16.4

	Estimation Comments	Percent change difference between BLU-5937 and placebo was estimated by 100 x [e^diff - 1] where 'e' = exponent of difference; and 'diff' = the treatment mean difference from mixed model of change from baseline based on log-transformed data.

Reported Adverse Events

Time Frame	All-cause mortality and Adverse Event data collection is up to 11 weeks
Adverse Event Reporting Description	Analysis population consisted of all randomized participants who received at least 1 dose of study drug

Reporting Groups

	Description
BLU-5937 - 25 mg	BLU-5937 25 mg tablet administered orally BID for 4 days
BLU-5937 - 50 mg	BLU-5937 50 mg tablet administered orally BID for 4 days
BLU-5937 - 100 mg	BLU-5937 100 mg tablet administered orally BID for 4 days
BLU-5937 - 200 mg	BLU-5937 200 mg tablet administered orally BID for 4 days
Placebo	Matching Placebo for BLU-5937 administered orally BID for 4 days

All-Cause Mortality

	BLU-5937 - 25 mg		BLU-5937 - 50 mg		BLU-5937 - 100 mg		BLU-5937 - 200 mg		Placebo	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total All-Cause Mortality	0/61 (0%)		0/61 (0%)		0/60 (0%)		0/58 (0%)		0/61 (0%)	

Serious Adverse Events

	BLU-5937 - 25 mg		BLU-5937 - 50 mg		BLU-5937 - 100 mg		BLU-5937 - 200 mg		Placebo	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	0/61 (0%)		0/61 (0%)		0/60 (0%)		0/58 (0%)		1/61 (1.64%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)										
colorectal cancer [A] [1] *	/61		/61		/60		/58		1/61 (1.64%)	1

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA v23.0

[1] colorectal cancer considered as not related to study drug was reported approximately 6 months after the last dose of study medication.

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	BLU-5937 - 25 mg		BLU-5937 - 50 mg		BLU-5937 - 100 mg		BLU-5937 - 200 mg		Placebo	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	10/61 (16.39%)		14/61 (22.95%)		15/60 (25%)		10/58 (17.24%)		19/61 (31.15%)	
Gastrointestinal disorders										
Diarrhoea [A] *	1/61 (1.64%)	1	1/61 (1.64%)	1	1/60 (1.67%)	1	0/58 (0%)	0	3/61 (4.92%)	3
Infections and infestations										
Upper respiratory tract infection [A] *	2/61 (3.28%)	2	4/61 (6.56%)	4	4/60 (6.67%)	4	3/58 (5.17%)	3	3/61 (4.92%)	3
Musculoskeletal and connective tissue disorders										
Back pain [A] *	2/61 (3.28%)	2	3/61 (4.92%)	3	2/60 (3.33%)	2	1/58 (1.72%)	1	6/61 (9.84%)	6
Nervous system disorders										
Dizziness [A] *	3/61 (4.92%)	3	4/61 (6.56%)	4	3/60 (5%)	3	2/58 (3.45%)	2	2/61 (3.28%)	2
Dysgeusia [A] *	3/61 (4.92%)	3	5/61 (8.2%)	5	5/60 (8.33%)	5	4/58 (6.9%)	4	2/61 (3.28%)	2
Headache [A] *	3/61 (4.92%)	3	2/61 (3.28%)	2	4/60 (6.67%)	4	3/58 (5.17%)	3	7/61 (11.48%)	7

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA v23.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

No data collected as part of this study will be utilized in any written work, including publications, without the written consent of sponsor.

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