Clinical trial results:
A two part, Phase IIa, randomized, placebo-controlled study to investigate the safety, tolerability, pharmacokinetics, pharmacodynamics, and clinical efficacy of oral danirixin (GSK1325756) in symptomatic COPD subjects with mild to moderate airflow limitation at risk for exacerbations

Summary

EudraCT number	2013-003510-41
Trial protocol	DE
Global end of trial date	29 August 2016

Results information

Result version number	v2 (current)
This version publication date	23 July 2017
First version publication date	20 April 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	200163

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Main objective of the trial: Primary-Part A & Part B: To evaluate the safety and tolerability of danirixin compared with placebo in symptomatic COPD subjects with mild to moderate airflow limitation
Primary -Part A: To characterize the pharmacokinetics of danirixin in symptomatic COPD subjects with mild to moderate airflow limitation
Primary-Part B: To characterize the effect of danirixin compared with placebo on the incidence and severity of respiratory symptoms and COPD exacerbations in symptomatic COPD subjects with mild to moderate airflow limitation

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 February 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 90
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	102
EEA total number of subjects	90

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	68
From 65 to 84 years	34

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a 2 part study. In Part A, an open label, single arm, participants (par.) received danrixin 50 milligrams (mg) twice daily (BID) for 2 weeks. In Part B, a randomized (1:1), double-blind (sponsor unblinded) placebo controlled on top of standard of care study, par. received DNX 75 mg BID in one arm and placebo in the other arm for 52 weeks.

Pre-assignment

Screening details:

A total of 19 par. in Part A were screened (10 failed) and 9 were randomized in a 2-week treatment period (TP) followed by a follow-up visit (FU) at 7- 14 days after last dose. A total of 127 par. in Part B were screened (34 failed) and 93 were randomized in a 52-week TP followed by a FU at 14- 28 days after last dose of the study.

Period 1

Period 1 title	Ovarall period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received one tablet of placebo twice daily with food and water for 52 weeks. It was administered on top of the participant’s current standard of care. Participants were permitted to continue taking inhaled maintenance medications. Rescue medications for acute symptoms were also permitted (e.g. short acting bronchodilators).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received one tablet of placebo twice daily for 52 weeks in Part B of the study

Arm title	DNX 75 mg

Arm description:

Participants received one immediate release tablet of danirixin (DNX) 75 mg BID with food and water for 52 weeks. It was administered on top of the participant’s current standard of care. Participants were permitted to continue taking inhaled maintenance medications. Rescue medications for acute symptoms were also permitted (e.g. short acting bronchodilators).

Arm type	Experimental
Investigational medicinal product name	Danirixin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received one immediate release tablet of danirixin 75 mg twice daily for 52 weeks in Part B of the study.

Number of subjects in period 1[1]	Placebo	DNX 75 mg
Started	48	45
Completed	38	37
Not completed	10	8
Consent withdrawn by subject	3	3
Physician decision	-	1
Adverse event, non-fatal	5	3
Protocol deviation	2	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 19 par. in Part A were screened (10 failed) and 9 were randomized in a 2-week treatment period (TP) followed by a follow-up visit (FU) at 7- 14 days after last dose. A total of 127 par. in Part B were screened (34 failed) and 93 were randomized in a 52-week TP followed by a FU at 14- 28 days after last dose of the study.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received one tablet of placebo twice daily with food and water for 52 weeks. It was administered on top of the participant's current standard of care. Participants were permitted to continue taking inhaled maintenance medications. Rescue medications for acute symptoms were also permitted (e.g. short acting bronchodilators).	
Reporting group title	DNX 75 mg
Reporting group description:	
Participants received one immediate release tablet of danirixin (DNX) 75 mg BID with food and water for 52 weeks. It was administered on top of the participant's current standard of care. Participants were permitted to continue taking inhaled maintenance medications. Rescue medications for acute symptoms were also permitted (e.g. short acting bronchodilators).	

Reporting group values	Placebo	DNX 75 mg	Total
Number of subjects	48	45	93
Age categorical Units: Subjects			
Age continuous			
Data for Part B is presented.			
Units: years			
arithmetic mean	58.8	62.4	
standard deviation	± 7.32	± 6.91	-
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	25	23	48
Male	23	22	45
Race/Ethnicity, Customized Units: Subjects			
African American/African Heritage	1	0	1
White - White/Caucasian/European Heritage	47	45	92

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received one tablet of placebo twice daily with food and water for 52 weeks. It was administered on top of the participant's current standard of care. Participants were permitted to continue taking inhaled maintenance medications. Rescue medications for acute symptoms were also permitted (e.g. short acting bronchodilators).

Reporting group title	DNX 75 mg

Reporting group description:

Participants received one immediate release tablet of danirixin (DNX) 75 mg BID with food and water for 52 weeks. It was administered on top of the participant's current standard of care. Participants were permitted to continue taking inhaled maintenance medications. Rescue medications for acute symptoms were also permitted (e.g. short acting bronchodilators).

Subject analysis set title	DNX 50 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received one immediate release tablet of danirixin (DNX) 50 mg BID with food and water for 2 weeks. Participants were permitted to continue taking inhaled maintenance medications. Rescue medications for acute symptoms were also permitted (e.g. short acting bronchodilators).

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received one tablet of placebo twice daily with food and water for 52 weeks. It was administered on top of the participant's current standard of care. Participants were permitted to continue taking inhaled maintenance medications. Rescue medications for acute symptoms were also permitted (e.g. short acting bronchodilators).

Subject analysis set title	DNX 75 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received one immediate release tablet of danirixin (DNX) 75 mg BID with food and water for 52 weeks. It was administered on top of the participant's current standard of care. Participants were permitted to continue taking inhaled maintenance medications. Rescue medications for acute symptoms were also permitted (e.g. short acting bronchodilators).

Primary: Number of participants with any adverse event (AE) and, serious adverse event (SAE) in Part A

End point title	Number of participants with any adverse event (AE) and, serious adverse event (SAE) in Part A[1]

End point description:

An AE is any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention, events associated with liver injury and impaired liver function were categorized as SAE. Participants with any AE or SAE were summarized. Participants with AE or SAE occurrences >= 5 percent were summarized. All Subjects Population comprised of all participants who were screened and for whom a record existed on the study database.

End point type	Primary

End point timeframe:

Up to Day 28 in Part A

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	DNX 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	9[2]			
Units: Participants				
AE	5			
SAEs	1			

Notes:

[2] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any AE and SAE in Part B

End point title	Number of participants with any AE and SAE in Part B[3]

End point description:

An AE is any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention, events associated with liver injury and impaired liver function were categorized as SAE. Participants with AE or SAE occurrences >= 5 percent were summarized.

End point type	Primary

End point timeframe:

Up to Day 392 in Part B

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[4]	45[5]		
Units: Participants				
AE	25	25		
SAEs	10	10		

Notes:

[4] - All Subjects Population

[5] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate, respiratory rate and body temperature abnormalities of potential clinical importance in Part A

End point title	Number of participants with systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate, respiratory rate and body temperature abnormalities of potential clinical importance in Part A[6]

End point description:

Vital signs including SBP, DBP, pulse rate, respiratory rate and body temperature were taken on Day 1 pre-dose and on Day 14 and at Follow-up (Day 21 to 28) in Part A. Measurements were obtained in a semi-supine/ supine position after 5 minutes rest. The mean of replicate assessments at any given time point was used as the value for that time point. SBP <90 or >160 millimeter of mercury (mmHg); DBP <40 or >110 mmHg, pulse rate <35 or >120 beats per minute (bpm) and respiratory rate <8 or >30 breaths per minute were considered as values of potential clinical importance and were presented as 'High' or 'Low' values. Intent-to-Treat (ITT) Population comprised of all randomized par. who received at least one dose of study medication.

End point type	Primary

End point timeframe:

Up to Day 28 in Part A

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	DNX 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	9[7]			
Units: Participants				
SBP, Day 14, low	0			
SBP, Day 14, high	2			
DBP, Day 14, low	0			
DBP, Day 14, high	1			

Notes:

[7] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate and respiratory rate abnormalities of potential clinical importance in Part B

End point title	Number of participants with systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate and respiratory rate abnormalities of potential clinical importance in Part B[8]

End point description:

Vital signs including SBP, DBP, pulse rate and respiratory rate were taken on Day 1 pre-dose and on Day 28, 56, 112, 168, 280, 364 and at Follow-up (Day 378 to 392) in Part B. Measurements were obtained in a semi-supine/ supine position after 5 minutes rest. The mean of replicate assessments at any given time point was used as the value for that time point. SBP <90 or >160 mmHg, DBP <40 or >110 mmHg, pulse rate <35 or >120 bpm and respiratory rate <8 or >30 breaths per minute were considered as values of potential clinical importance and were presented as 'High' or 'Low' values. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Primary

End point timeframe:

Up to Day 392 in Part B

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[9]	45[10]		
Units: Participants				
SBP, Day 1, low, n=48, 45	0	0		
SBP, Day 1, high, n=48, 45	0	2		
SBP, Day 28, low, n=47, 44	0	0		
SBP, Day 28, high, n=47, 44	0	3		
SBP, Day 56, low, n=46, 41	0	0		
SBP, Day 56, high, n=46, 41	2	2		
SBP, Day 112, low, n=46, 40	0	0		
SBP, Day 112, high, n=46, 40	3	2		
SBP, Day 168, low, n=44, 39	0	0		
SBP, Day 168, high, n=44, 39	2	3		
SBP, Day 280, low, n=39, 37	1	0		
SBP, Day 280, high, n=39, 37	2	2		
SBP, Day 364, low, n=39, 37	0	0		
SBP, Day 364, high, n=39, 37	1	4		
DBP, Day 280, low, n=39, 37	0	0		
DBP, Day 280, high, n=39, 37	1	0		
Respiratory rate, Day 1, low, n=48, 45	1	0		
Respiratory rate, Day 1, high, n=48, 45	1	0		
Respiratory rate, Day 56, low, n=46, 41	0	0		
Respiratory rate, Day 56, high, n=46, 41	2	0		
Respiratory rate, Day 112, low, n=46, 40	1	0		
Respiratory rate, Day 112, high, n=46, 40	0	0		
Respiratory rate, Day 168, low, n=44, 39	0	0		
Respiratory rate, Day 168, high, n=44, 39	0	1		

Notes:

[9] - ITT Population

[10] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with abnormal 12-lead electrocardiogram (ECG) in Part A

End point title	Number of participants with abnormal 12-lead electrocardiogram (ECG) in Part A[11]

End point description:

12-lead ECG was taken on Day 1 pre-dose and on Follow-up visit (Day 21 to 28) in Part A using an ECG machine. Triplicate reading were taken on Day 1 pre-dose. Participants with abnormal-clinically not significant (NCS) and abnormal-clinically significant (CS) findings were sumarized.

End point type	Primary

End point timeframe:

Up to Day 28 in Part A

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	DNX 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	9[12]			
Units: Participants				
Abnormal-NCS, Day 1, pre-dose	3			
Abnormal-CS, Day 1, pre-dose	0			
Abnormal-NCS, Day 1, pre-dose 2	2			
Abnormal-CS, Day 1, pre-dose 2	0			
Abnormal-NCS, Day 1, pre-dose 3	2			
Abnormal-CS, Day 1, pre-dose 3	0			

Notes:

[12] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with abnormal 12-lead ECG in Part B

End point title	Number of participants with abnormal 12-lead ECG in Part B[13]

End point description:

12-lead ECG was taken on Day 1 pre-dose and on Day 28, 168 and at Follow-up (Day 378 to 392) in Part B using an ECG machine. Participants with abnormal-NCS and abnormal-CS findings were sumarized. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Primary

End point timeframe:

Up to Day 392 in Part B

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[14]	45[15]		
Units: Participants				
Abnormal-NCS, Day 28, n=47, 44	20	16		
Abnormal-CS, Day 28, n=47, 44	0	1		
Abnormal-NCS, Day 168, n=44, 38	15	11		
Abnormal-CS, Day 168, n=44, 38	0	0		

Notes:

[14] - ITT Population

[15] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with hematology values of potential clinical importance in Part A

End point title	Number of participants with hematology values of potential clinical importance in Part A[16]

End point description:

Blood samples were collected at Screening and Day 14 in Part A to evaluate hematology parameters which included hemoglobin, hematocrit, basophils, eosinophils, lymphocytes, monocytes, neutrophils, mean corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), red blood cell (RBC) count, white blood cell (WBC) count, platelet count and reticulocyte count. Hematology values of potential clinical importance were presented as 'High' or 'Low' values based on the reference laboratory standards.

End point type	Primary

End point timeframe:

Up to Day 28 in Part A

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	DNX 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	9[17]			
Units: Participants				
RBC count, Day 14, low	1			
Category title 2. RBC count, Day 14, high	0			

Notes:

[17] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with hematology values of potential clinical importance in Part B

End point title	Number of participants with hematology values of potential clinical importance in Part B[18]

End point description:

Blood samples were collected at Screening and on Day 28, 168, and 364 in Part B to evaluate hematology parameters which included hemoglobin, hematocrit, basophils, eosinophils, lymphocytes, monocytes, neutrophils, MCHC, MCH, MCV, RBC count, WBC count, platelet count and reticulocyte count. Hematology values of potential clinical importance were presented as 'High' or 'Low' values based on the reference laboratory standards. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Primary

End point timeframe:

Up to Day 392 in Part B

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[19]	45[20]		
Units: Participants				
Platelet count, Day 28, low, n=46, 43	0	1		
Platelet count, Day 28, high, n=46, 43	0	0		
RBC count, Day 28, low, n=46, 43	0	1		
RBC count, Day 28, high, n=46, 43	0	0		
Platelet count, Day 168, low, n=43, 38	0	1		
Platelet count, Day 168, high, n=43, 38	1	0		
RBC count, Day 168, low, n=44, 38	2	1		
RBC count, Day 168, high, n=44, 38	0	0		
WBC count, Day 168, low, n=44, 38	0	0		
WBC count, Day 168, high, n=44, 38	1	0		
Platelet count, Day 364, low, n=39, 36	0	1		
Platelet count, Day 364, high, n=39, 36	0	0		
RBC count, Day 364, low, n=39, 36	2	1		
RBC count, Day 364, high, n=39, 36	0	0		

Notes:

[19] - ITT Population

[20] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with clinical chemistry values of potential clinical importance in Part A

End point title	Number of participants with clinical chemistry values of potential clinical importance in Part A[21]

End point description:

Blood samples were collected at Screening and Day 14 in Part A to evaluate clinical chemistry parameters which included alanine aminotransferase (ALT), albumin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), total bilirubin, calcium, bicarbonate, chloride, creatinine, direct bilirubin, gamma glutamyl transferase (GGT), glucose, potassium, total protein, sodium, blood urea nitrogen (BUN) and uric acid. Additional liver monitoring chemistry (ALT, AST, ALP and total and direct bilirubin) was done on Day 1 pre-dose. Clinical chemistry values of potential clinical importance were presented as 'High' or 'Low' values based on the reference laboratory standards.

End point type	Primary

End point timeframe:

Up to Day 28 in Part A

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	DNX 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	9[22]			
Units: Participants				
GGT, Day 14, low	0			
GGT, Day 14, high	2			
Uric acid, Day 14, low	0			
Uric acid, Day 14, high	8			

Notes:
[22] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with clinical chemistry values of potential clinical importance in Part B

End point title	Number of participants with clinical chemistry values of potential clinical importance in Part B[23]

End point description:

Blood samples were collected at Screening and on Day 28, 168 and 364 in Part B to evaluate clinical chemistry parameters which included ALT, albumin, ALP, AST, total bilirubin, calcium, bicarbonate, chloride, creatinine, direct bilirubin, GGT, glucose, potassium, total protein, sodium, BUN and uric acid. Additional liver monitoring chemistry (ALT, AST, ALP and total and direct bilirubin) was done on Day 14, 56, 84, 224 and 280. Clinical chemistry values of potential clinical importance were presented as 'High' or 'Low' values based on the reference laboratory standards. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Primary

End point timeframe:

Up to Day 392 in Part B

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[24]	45[25]		
Units: Participants				
Creatinine, Day 28, low, n=47, 44	0	0		
Creatinine, Day 28, high, n=47, 44	0	1		
GGT, Day 28, low, n=47, 44	0	0		
GGT, Day 28, high, n=47, 44	7	3		
Uric acid, Day 28, low, n=47, 44	0	0		
Uric acid, Day 28, high, n=47, 44	47	44		
ALP, Day 84, low, n=46, 40	0	0		
ALP, Day 84, high, n=46, 40	0	1		
ALT, Day 84, low, n=46, 40	0	0		
ALT, Day 84, high, n=46, 40	0	1		
AST, Day 84, low, n=46, 40	0	0		
AST, Day 84, high, n=46, 40	0	1		
GGT, Day 168, low, n=43, 39	0	0		
GGT, Day 168, high, n=43, 39	5	1		
Uric acid, Day 168, low, n=43, 39	0	0		
Uric acid, Day 168, high, n=43, 39	43	39		
Direct bilirubin, Day 364, low, n=39, 37	0	0		
Direct bilirubin, Day 364, high, n=39, 37	1	0		
Total bilirubin, Day 364, low, n=39, 37	0	0		

Total bilirubin, Day 364, high, n=39, 37	1	0		
GGT, Day 364, low, n=39, 37	0	0		
GGT, Day 364, high, n=39, 37	5	1		
Uric acid, Day 364, low, n=39, 37	0	0		
Uric acid, Day 364, high, n=39, 37	39	37		

Notes:

[24] - ITT Population

[25] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with urinalysis dipstick results in Part A

End point title	Number of participants with urinalysis dipstick results in Part

End point description:

Test strip urinalysis was done for glucose, ketones, occult blood and protein at Screening and Day 14 in Part A. Results were presented as negative, trace, 1+, 2+ and 3+ for glucose, ketones, occult blood and protein. Urine microscopic examination was done if urine blood or protein was found abnormal. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

Up to Day 28 in Part A

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	DNX 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	9[27]			
Units: Participants				
Occult blood, Day 14, negative, n=9	9			
Glucose, Day 14, negative, n=9	9			
Ketones, Day 14, negative, n=9	9			
Protein, Day 14, 1+, n=9	1			
Protein, Day 14, negative, n=9	8			
Urine microscopy-RBC, Day 14, not seen, n=1	1			
Urine microscopy-WBC, Day 14, not seen, n=1	1			

Notes:

[27] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with urinalysis dipstick results in Part B

End point title	Number of participants with urinalysis dipstick results in Part

End point description:

Test strip urinalysis was done for glucose, ketones, occult blood and protein at Screening and on Day 28, 168, 224 and 364 in Part B. Results were presented as negative, trace, 1+, 2+ and 3+ for glucose, ketones, occult blood and protein. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Primary

End point timeframe:

Up to Day 392 in Part B

Notes:

[28] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[29]	45[30]		
Units: Participants				
Occult blood, Day 28, trace, n=47, 44	0	2		
Occult blood, Day 28, 1+, n=47, 44	3	0		
Occult blood, Day 28, negative, n=47, 44	44	42		
Glucose, Day 28, trace, n=47, 44	0	1		
Glucose, Day 28, 1+, n=47, 44	1	0		
Glucose, Day 28, 3+, n=47, 44	0	2		
Glucose, Day 28, negative, n=47, 44	46	41		
Ketones, Day 28, trace, n=47, 44	3	2		
Ketones, Day 28, negative, n=47, 44	44	42		
Protein, Day 28, trace, n=47, 44	2	1		
Protein, Day 28, 1+, n=47, 44	2	2		
Protein, Day 28, negative, n=47, 44	43	41		
Occult blood, Day 168, trace, n=42, 36	3	2		
Occult blood, Day 168, 1+, n=42, 36	1	1		
Occult blood, Day 168, 3+, n=42, 36	1	0		
Occult blood, Day 168, negative, n=42, 36	37	33		
Glucose, Day 168, 2+, n=42, 36	1	0		
Glucose, Day 168, negative, n=42, 36	41	36		
Ketones, Day 168, trace, n=42, 36	3	0		
Ketones, Day 168, negative, n=42, 36	39	36		
Protein, Day 168, trace, n=42, 36	2	1		
Protein, Day 168, 1+, n=42, 36	1	2		
Protein, Day 168, 2+, n=42, 36	1	0		
Protein, Day 168, negative, n=42, 36	38	33		
Occult blood, Day 224, negative, n=1, 0	1	0		
Glucose, Day 224, negative, n=1, 0	1	0		
Ketones, Day 224, negative, n=1, 0	1	0		
Protein, Day 224, negative, n=1, 0	1	0		
Occult blood, Day 364, trace, n=38, 36	3	2		
Occult blood, Day 364, 1+, n=38, 36	2	1		
Occult blood, Day 364, negative, n=38, 36	33	33		
Glucose, Day 364, trace, n=38, 36	1	0		
Glucose, Day 364, 2+, n=38, 36	1	0		
Glucose, Day 364, negative, n=38, 36	36	36		

Ketones, Day 364, trace, n=38, 36	3	0		
Ketones, Day 364, negative, n=38, 36	35	36		
Protein, Day 364, trace, n=38, 36	3	0		
Protein, Day 364, 1+, n=38, 36	1	2		
Protein, Day 364, 2+, n=38, 36	1	1		
Protein, Day 364, negative, n=38, 36	33	33		

Notes:

[29] - ITT Population

[30] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urine power of hydrogen (pH) at Day 14 in Part A

End point title	Change from Baseline in urine power of hydrogen (pH) at Day 14 in Part A[31]

End point description:

Urinalysis including urine pH was done at Screening and Day 14 in Part A. Baseline was considered as the measurement obtained at Screening (Day -1). The change from Baseline was calculated by subtracting the Baseline values from the individual post-randomization values.

End point type	Primary

End point timeframe:

Up to Day 28 in Part A

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	DNX 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	9[32]			
Units: pH				
arithmetic mean (standard deviation)	-0.06 (± 1.488)			

Notes:

[32] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urine pH in Part B

End point title	Change from Baseline in urine pH in Part B[33]

End point description:

Urinalysis including urine pH was done at Screening and on Day 28, 168 and 364 in Part B. Baseline was considered as the measurement obtained at Screening (Day -1). The change from Baseline was calculated by subtracting the Baseline values from the individual post-randomization values. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Primary

End point timeframe:

Up to Day 392 in Part B

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[34]	45[35]		
Units: pH				
arithmetic mean (standard deviation)				
Day 28, n=45, 43	-0.17 (± 0.648)	-0.1 (± 0.552)		
Day 168, n=40, 35	-0.18 (± 0.694)	-0.13 (± 0.751)		
Day 364, n=36, 35	-0.29 (± 0.731)	-0.07 (± 0.768)		

Notes:

[34] - ITT Population

[35] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urine specific gravity of urine in Part A

End point title	Change from Baseline in urine specific gravity of urine in Part

End point description:

Urinalysis including urine specific gravity was done at Screening and Day 14 in Part A. Baseline was considered as the measurement obtained at Screening (Day -1). The change from Baseline was calculated by subtracting the Baseline values from the individual post-randomization values.

End point type	Primary

End point timeframe:

Up to Day 28 in Part A

Notes:

[36] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	DNX 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	9[37]			
Units: Urine specific gravity				
arithmetic mean (standard deviation)	-0.0008 (± 0.00817)			

Notes:

[37] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urine specific gravity of urine in Part B

End point title	Change from Baseline in urine specific gravity of urine in Part B

	[38]

End point description:

Urinalysis including urine specific gravity was done at Screening and on Day 28, 168 and 364 in Part B. Baseline was considered as the measurement obtained at Screening (Day -1). The change from Baseline was calculated by subtracting the Baseline values from the individual post-randomization values.

End point type	Primary

End point timeframe:

Up to Day 392 in Part B

Notes:

[38] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[39]	45[40]		
Units: Urine specific gravity				
arithmetic mean (standard deviation)				
Day 28, n=45, 43	-0.0011 (± 0.00643)	-0.0008 (± 0.00536)		
Day 168, n=40, 35	-0.0012 (± 0.00771)	-0.0002 (± 0.00748)		
Day 364, n=36, 35	0.0004 (± 0.00569)	0.0013 (± 0.00561)		

Notes:

[39] - ITT Population

[40] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) at the indicated time points in Part A

End point title	Change from Baseline in forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) at the indicated time points in Part A[41]

End point description:

FEV1 measures how much air a person can exhale during a forced breath in 1 second. FVC is the total amount of air exhaled during the FEV test. FEV1 and FVC were performed at Screening and on Day 1, 14 and at Follow-up visit (Day 21 to 28). FEV1 and FVC assessments at each time point (post-bronchodilator) were taken in triplicate. The maximum of the triplicate assessments were used. Baseline was considered as the measurement obtained at Day 1 pre-dose. The change from Baseline was calculated by subtracting the Baseline values from the individual post-randomization values.

End point type	Primary

End point timeframe:

Up to Day 28 in Part A

Notes:

[41] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	DNX 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	9[42]			
Units: Liter				
arithmetic mean (standard deviation)				
FEV1, Day 14	0.0978 (± 0.10378)			
FVC, Day 14	0.2233 (± 0.25407)			

Notes:

[42] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in FEV1 and FVC at the indicated time points in Part B

End point title	Change from Baseline in FEV1 and FVC at the indicated time points in Part B

End point description:

FEV1 and FVC were performed at Screening and on Day 1, 28, 56, 112, 168, 280, 364 and at Follow-up (Day 378 to 392) in Part B. FEV1 and FVC assessments at each time point (post-bronchodilator) were taken in triplicate. The maximum of the triplicate assessments were used. Baseline was considered as the measurement obtained at Day 1 pre-dose. The change from Baseline was calculated by subtracting the Baseline values from the individual post-randomization values. Statistical analysis was performed using a repeated measures mixed effects model in a Bayesian framework. The estimate of the treatment difference and corresponding 95 percent credible interval was constructed for the difference between danirixin and placebo for each visit. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Primary

End point timeframe:

Up to Day 392 in Part B

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[43]	45[44]		
Units: Liter				
arithmetic mean (standard deviation)				
FEV1, Day 28, n=47, 44	-0.018 (± 0.2049)	0.048 (± 0.1433)		
FEV1, Day 56, n=46, 41	0.048 (± 0.3377)	0.017 (± 0.1633)		
FEV1, Day 112, n=45, 39	0.011 (± 0.2431)	0.088 (± 0.3044)		
FEV1, Day 168, n=44, 39	0.018 (± 0.2944)	0.015 (± 0.2129)		
FEV1, Day 280, n=39, 37	-0.012 (± 0.33)	0.043 (± 0.231)		
FEV1, Day 364, n=39, 37	-0.009 (± 0.2746)	0.028 (± 0.2988)		
FVC, Day 28, n=47, 44	0.027 (± 0.3407)	0.022 (± 0.2845)		

FVC, Day 56, n=46, 41	0.046 (± 0.4344)	0.036 (± 0.2706)		
FVC, Day 112, n=45, 39	0.024 (± 0.4195)	0.014 (± 0.3714)		
FVC, Day 168, n=44, 39	-0.061 (± 0.3956)	-0.005 (± 0.3301)		
FVC, Day 280, n=39, 37	-0.02 (± 0.5966)	0.041 (± 0.4271)		
FVC, Day 364, n=39, 37	-0.021 (± 0.429)	0.008 (± 0.419)		

Notes:

[43] - ITT Population

[44] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

FEV1, Day 28. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[45]
P-value	= 0.87 [46]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.18
Variability estimate	Standard deviation
Dispersion value	0.06

Notes:

[45] - P-value is actually a posterior probability.

[46] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0 L is presented.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

FEV1, Day 28. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[47]
P-value	= 0.78 [48]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.18
Variability estimate	Standard deviation
Dispersion value	0.06

Notes:

[47] - P-value is actually a posterior probability.

[48] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.02 L is presented.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

FEV1, Day 28. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.67 [49]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.18
Variability estimate	Standard deviation
Dispersion value	0.06

Notes:

[49] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.04 L is presented.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

FEV1, Day 28. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[50]
P-value	= 0.52 [51]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.18
Variability estimate	Standard deviation
Dispersion value	0.06

Notes:

[50] - P-value is actually a posterior probability.

[51] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.06 L is presented.

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

FEV1, Day 28. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[52]
P-value	= 0.39 [53]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.18
Variability estimate	Standard deviation
Dispersion value	0.06

Notes:

[52] - P-value is actually a posterior probability.

[53] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.08 L is presented.

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

FEV1, Day 28. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[54]
P-value	= 0.26 [55]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.18
Variability estimate	Standard deviation
Dispersion value	0.06

Notes:

[54] - P-value is actually a posterior probability.

[55] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.10 L is presented.

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

FEV1, Day 56. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.31 [56]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.09
Variability estimate	Standard deviation
Dispersion value	0.07

Notes:

[56] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0 L is presented.

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

FEV1, Day 56. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.22 [57]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.09
Variability estimate	Standard deviation
Dispersion value	0.07

Notes:

[57] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.02 L is presented.

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

FEV1, Day 56. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.14 [58]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.09
Variability estimate	Standard deviation
Dispersion value	0.07

Notes:

[58] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.04 L is presented.

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

FEV1, Day 56. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.09 [59]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.09
Variability estimate	Standard deviation
Dispersion value	0.07

Notes:

[59] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.06 L is presented.

Statistical analysis title	Statistical analysis 11

Statistical analysis description:

FEV1, Day 56. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[60]
P-value	= 0.05 [61]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.04

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.09
Variability estimate	Standard deviation
Dispersion value	0.07

Notes:

[60] - P-value is actually a posterior probability.

[61] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.08 L is presented.

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

FEV1, Day 56. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[62]
P-value	= 0.03 [63]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.09
Variability estimate	Standard deviation
Dispersion value	0.07

Notes:

[62] - P-value is actually a posterior probability.

[63] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.10 L is presented.

Statistical analysis title	Statistical analysis 13

Statistical analysis description:

FEV1, Day 112. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[64]
P-value	= 0.85 [65]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.23
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[64] - P-value is actually a posterior probability.

[65] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0 L is presented.

Statistical analysis title	Statistical analysis 14

Statistical analysis description:

FEV1, Day 112. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[66]
P-value	= 0.79 [67]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.23
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[66] - P-value is actually a posterior probability.

[67] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.02 L is presented.

Statistical analysis title	Statistical analysis 15

Statistical analysis description:

FEV1, Day 112. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[68]
P-value	= 0.71 [69]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.23
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[68] - P-value is actually a posterior probability.

[69] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.04 L is presented.

Statistical analysis title	Statistical analysis 16

Statistical analysis description:	
FEV1, Day 112. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[70]
P-value	= 0.61 [71]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.23
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[70] - P-value is actually a posterior probability.

[71] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.06 L is presented.

Statistical analysis title	Statistical analysis 17
Statistical analysis description:	
FEV1, Day 112. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[72]
P-value	= 0.51 [73]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.23
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[72] - P-value is actually a posterior probability.

[73] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.08 L is presented.

Statistical analysis title	Statistical analysis 18
Statistical analysis description:	
FEV1, Day 112. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	DNX 75 mg v Placebo

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[74]
P-value	= 0.41 [75]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.23
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[74] - P-value is actually a posterior probability.

[75] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.10 L is presented.

Statistical analysis title	Statistical analysis 19

Statistical analysis description:

FEV1, Day 168. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[76]
P-value	= 0.47 [77]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.14
Variability estimate	Standard deviation
Dispersion value	0.07

Notes:

[76] - P-value is actually a posterior probability.

[77] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0 L is presented.

Statistical analysis title	Statistical analysis 20

Statistical analysis description:

FEV1, Day 168. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[78]
P-value	= 0.36 [79]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.14
Variability estimate	Standard deviation
Dispersion value	0.07

Notes:

[78] - P-value is actually a posterior probability.

[79] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.02 L is presented.

Statistical analysis title	Statistical analysis 21

Statistical analysis description:

FEV1, Day 168. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[80]
P-value	= 0.26 [81]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.14
Variability estimate	Standard deviation
Dispersion value	0.07

Notes:

[80] - P-value is actually a posterior probability.

[81] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.04 L is presented.

Statistical analysis title	Statistical analysis 22

Statistical analysis description:

FEV1, Day 168. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[82]
P-value	= 0.19 [83]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.14
Variability estimate	Standard deviation
Dispersion value	0.07

Notes:

[82] - P-value is actually a posterior probability.

[83] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.06 L is presented.

Statistical analysis title	Statistical analysis 23

Statistical analysis description:

FEV1, Day 168. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[84]
P-value	= 0.13 [85]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.14
Variability estimate	Standard deviation
Dispersion value	0.07

Notes:

[84] - P-value is actually a posterior probability.

[85] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.08 L is presented.

Statistical analysis title	Statistical analysis 24

Statistical analysis description:

FEV1, Day 168. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[86]
P-value	= 0.09 [87]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.14
Variability estimate	Standard deviation
Dispersion value	0.07

Notes:

[86] - P-value is actually a posterior probability.

[87] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.10 L is presented.

Statistical analysis title	Statistical analysis 25

Statistical analysis description:

FEV1, Day 280. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[88]
P-value	= 0.78 [89]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[88] - P-value is actually a posterior probability.

[89] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0 L is presented.

Statistical analysis title	Statistical analysis 26

Statistical analysis description:

FEV1, Day 280. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[90]
P-value	= 0.69 [91]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[90] - P-value is actually a posterior probability.

[91] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.02 L is presented.

Statistical analysis title	Statistical analysis 27

Statistical analysis description:

FEV1, Day 280. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[92]
P-value	= 0.59 [93]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[92] - P-value is actually a posterior probability.

[93] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.04 L is presented.

Statistical analysis title	Statistical analysis 28

Statistical analysis description:

FEV1, Day 280. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[94]
P-value	= 0.5 [95]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[94] - P-value is actually a posterior probability.

[95] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.06 L is presented.

Statistical analysis title	Statistical analysis 29

Statistical analysis description:

FEV1, Day 280. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[96]
P-value	= 0.39 [97]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[96] - P-value is actually a posterior probability.

[97] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.08 L is presented.

Statistical analysis title	Statistical analysis 30

Statistical analysis description:

FEV1, Day 280. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[98]
P-value	= 0.3 [99]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[98] - P-value is actually a posterior probability.

[99] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.10 L is presented.

Statistical analysis title	Statistical analysis 31

Statistical analysis description:

FEV1, Day 364. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[100]
P-value	= 0.68 [101]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[100] - P-value is actually a posterior probability.

[101] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0 L is presented.

Statistical analysis title	Statistical analysis 32

Statistical analysis description:

FEV1, Day 364. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[102]
P-value	= 0.59 [103]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[102] - P-value is actually a posterior probability.

[103] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.02 L is presented.

Statistical analysis title	Statistical analysis 33

Statistical analysis description:

FEV1, Day 364. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[104]
P-value	= 0.5 [105]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[104] - P-value is actually a posterior probability.

[105] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.04 L is presented.

Statistical analysis title	Statistical analysis 34

Statistical analysis description:	
FEV1, Day 364. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[106]
P-value	= 0.4 [107]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[106] - P-value is actually a posterior probability.

[107] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.06 L is presented.

Statistical analysis title	Statistical analysis 35
Statistical analysis description:	
FEV1, Day 364. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[108]
P-value	= 0.3 [109]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[108] - P-value is actually a posterior probability.

[109] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.08 L is presented.

Statistical analysis title	Statistical analysis 36
Statistical analysis description:	
FEV1, Day 364. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	DNX 75 mg v Placebo

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[110]
P-value	= 0.22 [111]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[110] - P-value is actually a posterior probability.

[111] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.10 L is presented.

Statistical analysis title	Statistical analysis 37

Statistical analysis description:

FVC, Day 28. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[112]
P-value	= 0.41 [113]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.13
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[112] - P-value is actually a posterior probability.

[113] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0 L is presented.

Statistical analysis title	Statistical analysis 38

Statistical analysis description:

FVC, Day 28. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[114]
P-value	= 0.32 [115]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.13
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[114] - P-value is actually a posterior probability.

[115] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.02 L is presented.

Statistical analysis title	Statistical analysis 39

Statistical analysis description:

FVC, Day 28. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[116]
P-value	= 0.24 [117]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.13
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[116] - P-value is actually a posterior probability.

[117] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.04 L is presented.

Statistical analysis title	Statistical analysis 40

Statistical analysis description:

FVC, Day 28. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[118]
P-value	= 0.16 [119]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.13
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[118] - P-value is actually a posterior probability.

[119] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.06 L is presented.

Statistical analysis title	Statistical analysis 41

Statistical analysis description:

FVC, Day 28. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.11 [120]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.13
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[120] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.08 L is presented.

Statistical analysis title	Statistical analysis 42

Statistical analysis description:

FVC, Day 28. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[121]
P-value	= 0.07 [122]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.13
Variability estimate	Standard deviation
Dispersion value	0.08

Notes:

[121] - P-value is actually a posterior probability.

[122] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.10 L is presented.

Statistical analysis title	Statistical analysis 43

Statistical analysis description:

FVC, Day 56. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[123]
P-value	= 0.41 [124]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.15
Variability estimate	Standard deviation
Dispersion value	0.09

Notes:

[123] - P-value is actually a posterior probability.

[124] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0 L is presented.

Statistical analysis title	Statistical analysis 44

Statistical analysis description:

FVC, Day 56. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[125]
P-value	= 0.32 [126]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.15
Variability estimate	Standard deviation
Dispersion value	0.09

Notes:

[125] - P-value is actually a posterior probability.

[126] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.02 L is presented.

Statistical analysis title	Statistical analysis 45

Statistical analysis description:

FVC, Day 56. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[127]
P-value	= 0.25 [128]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.15
Variability estimate	Standard deviation
Dispersion value	0.09

Notes:

[127] - P-value is actually a posterior probability.

[128] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.04 L is presented.

Statistical analysis title	Statistical analysis 46

Statistical analysis description:

FVC, Day 56. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[129]
P-value	= 0.18 [130]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.15
Variability estimate	Standard deviation
Dispersion value	0.09

Notes:

[129] - P-value is actually a posterior probability.

[130] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.06 L is presented.

Statistical analysis title	Statistical analysis 47

Statistical analysis description:

FVC, Day 56. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[131]
P-value	= 0.12 [132]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.15
Variability estimate	Standard deviation
Dispersion value	0.09

Notes:

[131] - P-value is actually a posterior probability.

[132] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.08 L is presented.

Statistical analysis title	Statistical analysis 48

Statistical analysis description:

FVC, Day 56. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[133]
P-value	= 0.07 [134]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.15
Variability estimate	Standard deviation
Dispersion value	0.09

Notes:

[133] - P-value is actually a posterior probability.

[134] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.10 L is presented.

Statistical analysis title	Statistical analysis 49

Statistical analysis description:

FVC, Day 112. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[135]
P-value	= 0.45 [136]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.17
Variability estimate	Standard deviation
Dispersion value	0.1

Notes:

[135] - P-value is actually a posterior probability.

[136] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0 L is presented.

Statistical analysis title	Statistical analysis 50

Statistical analysis description:

FVC, Day 112. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.37 [137]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.17
Variability estimate	Standard deviation
Dispersion value	0.1

Notes:

[137] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.02 L is presented.

Statistical analysis title	Statistical analysis 51

Statistical analysis description:

FVC, Day 112. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[138]
P-value	= 0.3 [139]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.17
Variability estimate	Standard deviation
Dispersion value	0.1

Notes:

[138] - P-value is actually a posterior probability.

[139] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.04 L is presented.

Statistical analysis title	Statistical analysis 52

Statistical analysis description:

FVC, Day 112. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[140]
P-value	= 0.22 [141]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.17
Variability estimate	Standard deviation
Dispersion value	0.1

Notes:

[140] - P-value is actually a posterior probability.

[141] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.06 L is presented.

Statistical analysis title	Statistical analysis 53

Statistical analysis description:

FVC, Day 112. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[142]
P-value	= 0.17 [143]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.17
Variability estimate	Standard deviation
Dispersion value	0.1

Notes:

[142] - P-value is actually a posterior probability.

[143] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.08 L is presented.

Statistical analysis title	Statistical analysis 54

Statistical analysis description:

FVC, Day 112. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[144]
P-value	= 0.12 [145]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.17
Variability estimate	Standard deviation
Dispersion value	0.1

Notes:

[144] - P-value is actually a posterior probability.

[145] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.10 L is presented.

Statistical analysis title	Statistical analysis 55

Statistical analysis description:

FVC, Day 168. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[146]
P-value	= 0.72 [147]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.24
Variability estimate	Standard deviation
Dispersion value	0.09

Notes:

[146] - P-value is actually a posterior probability.

[147] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0 L is presented.

Statistical analysis title	Statistical analysis 56

Statistical analysis description:

FVC, Day 168. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[148]
P-value	= 0.65 [149]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.24
Variability estimate	Standard deviation
Dispersion value	0.09

Notes:

[148] - P-value is actually a posterior probability.

[149] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.02 L is presented.

Statistical analysis title	Statistical analysis 57

Statistical analysis description:

FVC, Day 168. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[150]
P-value	= 0.57 [151]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.24
Variability estimate	Standard deviation
Dispersion value	0.09

Notes:

[150] - P-value is actually a posterior probability.

[151] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.04 L is presented.

Statistical analysis title	Statistical analysis 58

Statistical analysis description:

FVC, Day 168. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[152]
P-value	= 0.48 [153]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.24
Variability estimate	Standard deviation
Dispersion value	0.09

Notes:

[152] - P-value is actually a posterior probability.

[153] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.06 L is presented.

Statistical analysis title	Statistical analysis 59

Statistical analysis description:

FVC, Day 168. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[154]
P-value	= 0.39 [155]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.24
Variability estimate	Standard deviation
Dispersion value	0.09

Notes:

[154] - P-value is actually a posterior probability.

[155] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.08 L is presented.

Statistical analysis title	Statistical analysis 60

Statistical analysis description:

FVC, Day 168. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[156]
P-value	= 0.3 [157]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.24
Variability estimate	Standard deviation
Dispersion value	0.09

Notes:

[156] - P-value is actually a posterior probability.

[157] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.10 L is presented.

Statistical analysis title	Statistical analysis 61

Statistical analysis description:	
FVC, Day 280. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[158]
P-value	= 0.76 [159]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.32
Variability estimate	Standard deviation
Dispersion value	0.12

Notes:

[158] - P-value is actually a posterior probability.

[159] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0 L is presented.

Statistical analysis title	Statistical analysis 62
Statistical analysis description:	
FVC, Day 280. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[160]
P-value	= 0.71 [161]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.32
Variability estimate	Standard deviation
Dispersion value	0.12

Notes:

[160] - P-value is actually a posterior probability.

[161] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.02 L is presented.

Statistical analysis title	Statistical analysis 63
Statistical analysis description:	
FVC, Day 280. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	DNX 75 mg v Placebo

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[162]
P-value	= 0.65 [163]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.32
Variability estimate	Standard deviation
Dispersion value	0.12

Notes:

[162] - P-value is actually a posterior probability.

[163] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.04 L is presented.

Statistical analysis title	Statistical analysis 64

Statistical analysis description:

FVC, Day 280. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[164]
P-value	= 0.59 [165]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.32
Variability estimate	Standard deviation
Dispersion value	0.12

Notes:

[164] - P-value is actually a posterior probability.

[165] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.06 L is presented.

Statistical analysis title	Statistical analysis 65

Statistical analysis description:

FVC, Day 280. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[166]
P-value	= 0.53 [167]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.32
Variability estimate	Standard deviation
Dispersion value	0.12

Notes:

[166] - P-value is actually a posterior probability.

[167] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.08 L is presented.

Statistical analysis title	Statistical analysis 66

Statistical analysis description:

FVC, Day 280. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[168]
P-value	= 0.46 [169]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.32
Variability estimate	Standard deviation
Dispersion value	0.12

Notes:

[168] - P-value is actually a posterior probability.

[169] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.10 L is presented.

Statistical analysis title	Statistical analysis 67

Statistical analysis description:

FVC, Day 364. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[170]
P-value	= 0.68 [171]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.28
Variability estimate	Standard deviation
Dispersion value	0.11

Notes:

[170] - P-value is actually a posterior probability.

[171] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0 L is presented.

Statistical analysis title	Statistical analysis 68

Statistical analysis description:

FVC, Day 364. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[172]
P-value	= 0.61 [173]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.28
Variability estimate	Standard deviation
Dispersion value	0.11

Notes:

[172] - P-value is actually a posterior probability.

[173] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.02 L is presented.

Statistical analysis title	Statistical analysis 69

Statistical analysis description:

FVC, Day 364. Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[174]
P-value	= 0.55 [175]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.28
Variability estimate	Standard deviation
Dispersion value	0.11

Notes:

[174] - P-value is actually a posterior probability.

[175] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.04 L is presented.

Statistical analysis title	Statistical analysis 70

Statistical analysis description:	
FVC, Day 364. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[176]
P-value	= 0.46 [177]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.28
Variability estimate	Standard deviation
Dispersion value	0.11

Notes:

[176] - P-value is actually a posterior probability.

[177] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.06 L is presented.

Statistical analysis title	Statistical analysis 71
Statistical analysis description:	
FVC, Day 364. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[178]
P-value	= 0.4 [179]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.28
Variability estimate	Standard deviation
Dispersion value	0.11

Notes:

[178] - P-value is actually a posterior probability.

[179] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.08 L is presented.

Statistical analysis title	Statistical analysis 72
Statistical analysis description:	
FVC, Day 364. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	DNX 75 mg v Placebo

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[180]
P-value	= 0.33 [181]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.28
Variability estimate	Standard deviation
Dispersion value	0.11

Notes:

[180] - P-value is actually a posterior probability.

[181] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is greater than 0.10 L is presented.

Primary: Maximum observed plasma concentration (Cmax) of danirixin in Part A

End point title	Maximum observed plasma concentration (Cmax) of danirixin in Part A[182]

End point description:

Cmax of danirixin was derived from the Pharmacokinetics (PK) samples collected at pre-dose and at 0.5, 1, 2, 4, 6, 8, 10 and 12 hour post-dose on Day 1 and Day 14 in Part A. PK analysis of danirixin was conducted by non-compartmental methods. PK Concenteration Population comprised of par. in the ITT Population and who had provided at least one on-treatment blood sample for determination of danirixin concentration.

End point type	Primary

End point timeframe:

Pre-dose and at 0.5, 1, 2, 4, 6, 8, 10 and 12 hour post-dose on Day 1 and Day 14 in Part A

Notes:

[182] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	DNX 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	9[183]			
Units: Nanogram per milliliter (ng/mL)				
geometric mean (confidence interval 95%)				
Day 1 dose	397.785 (222.166 to 712.229)			
Day 14 dose	512.576 (350.162 to 750.324)			

Notes:

[183] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: Time of occurrence of Cmax (Tmax) of danirixin in Part A

End point title	Time of occurrence of Cmax (Tmax) of danirixin in Part A[184]

End point description:

Tmax of danirixin was derived from the PK samples collected at pre-dose and at 0.5, 1, 2, 4, 6, 8, 10 and 12 hour post-dose on Day 1 and Day 14 in Part A. PK analysis of danirixin was conducted by non-compartmental methods.

End point type	Primary

End point timeframe:

Pre-dose and at 0.5, 1, 2, 4, 6, 8, 10 and 12 hour post-dose on Day 1 and Day 14 in Part A

Notes:

[184] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	DNX 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	9[185]			
Units: Hour				
median (full range (min-max))				
Day 1 dose	1.017 (0.98 to 4)			
Day 14 dose	2 (0.35 to 4.02)			

Notes:

[185] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: Area under the blood concentration-time curve (AUC) over dosing interval (AUC[0-12]) of danirixin in Part A

End point title	Area under the blood concentration-time curve (AUC) over dosing interval (AUC[0-12]) of danirixin in Part A[186]

End point description:

AUC (0-12) of danirixin was derived from the PK samples collected at pre-dose and at 0.5, 1, 2, 4, 6, 8, 10 and 12 hour post-dose on Day 1 and Day 14 in Part A. PK analysis of danirixin was conducted by non-compartmental methods. A Bayesian random effects model was performed adjusting for the trial as a random effect. A non-informative normal prior distribution was used. Point estimates and corresponding 90 percent credible intervals were constructed.

End point type	Primary

End point timeframe:

Pre-dose and at 0.5, 1, 2, 4, 6, 8, 10 and 12 hour post-dose on Day 1 and Day 14 in Part A

Notes:

[186] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	DNX 50 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	9[187]			
Units: Hour*ng/mL				
geometric mean (confidence interval 95%)				
Day 1 dose	2203.522 (1303.851 to 3723.976)			
Day 14 dose	2838.526 (1907.863 to 4223.171)			

Notes:

[187] - PK Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of health care resource utilization (HCRU) defined COPD exacerbations per year in Part B

End point title	Number of health care resource utilization (HCRU) defined COPD exacerbations per year in Part B

End point description:

HCRU COPD exacerbations are defined as moderate or severe exacerbations based on requirement of new prescription antibiotics or oral corticosteroids, hospitalization or emergency room visits for management of COPD exacerbation. For par. with less than 364 days on-treatment, the annual exacerbation rate was imputed as the number of recorded on-treatment exacerbations, divided by the number of 4-week treatment period intervals for which the par. was in the study, multiplied by 13. For par. with 364 or more days on-treatment, the annual exacerbation rate was calculated as the number of recorded exacerbations between study days 1 and 364. Statistical analysis was done using a Bayesian Cox model, assuming a negative binomial distribution for the underlying exacerbation rate. The exacerbation rates along with the ratio (danirixin/placebo), were estimated and corresponding 95 percent credible intervals were produced using non-informative priors. 1 par. was excluded from the analysis.

End point type	Primary

End point timeframe:

Up to Day 392 in Part B

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[188]	20[189]		
Units: Exacerbations per year				
arithmetic mean (standard deviation)	2.9 (± 3.13)	3.2 (± 5.82)		

Notes:

[188] - ITT Population

[189] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority[190]
P-value	= 0.013 [191]
Method	Bayesian Cox analysis
Parameter estimate	Posterior mean difference
Point estimate	2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	4.43
Variability estimate	Standard deviation
Dispersion value	0.977

Notes:

[190] - P-value is actually a posterior probability.

[191] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 1.0 is presented.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority[192]
P-value	= 0.006 [193]
Method	Bayesian Cox analysis
Parameter estimate	Posterior mean difference
Point estimate	2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	4.43
Variability estimate	Standard deviation
Dispersion value	0.977

Notes:

[192] - P-value is actually a posterior probability.

[193] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0.9 is presented.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo

Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority[194]
P-value	= 0.003 [195]
Method	Bayesian Cox analysis
Parameter estimate	Posterior mean difference
Point estimate	2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	4.43
Variability estimate	Standard deviation
Dispersion value	0.977

Notes:

[194] - P-value is actually a posterior probability.

[195] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0.8 is presented.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority[196]
P-value	= 0.001 [197]
Method	Bayesian Cox analysis
Parameter estimate	Posterior mean difference
Point estimate	2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	4.43
Variability estimate	Standard deviation
Dispersion value	0.977

Notes:

[196] - P-value is actually a posterior probability.

[197] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0.7 is presented.

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Data presented are for 95% equal-tailed credible intervals

Comparison groups	DNX 75 mg v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority[198]
P-value	< 0.001 [199]
Method	Bayesian Cox analysis
Parameter estimate	Posterior mean difference
Point estimate	2.48

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	4.43
Variability estimate	Standard deviation
Dispersion value	0.977

Notes:

[198] - P-value is actually a posterior probability.

[199] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0.6 is presented.

Primary: Monthly weighted means of exacerbations of chronic pulmonary disease tool-respiratory symptoms (EXACT-RS) total score in Part B

End point title	Monthly weighted means of exacerbations of chronic pulmonary disease tool-respiratory symptoms (EXACT-RS) total score in Part B

End point description:

EXACT-RS is a tool which consists of 11 items from the 14 item EXACT- patient reported outcomes (EXACT-PRO) instrument, intended to capture information related to the respiratory symptoms of COPD, i.e. breathlessness, cough, sputum production, chest congestion and chest tightness. The EXACT-RS has a scoring range of 0-40, higher scores indicate more severe symptoms. A par. had at least 10 days of diary data in any month to contribute a non-missing weighted mean AUC of daily values; otherwise the weighted mean for that month were considered missing. A mixed effects model in a Bayesian framework with repeated measures were performed on the EXACT-RS monthly weighted mean AUC data. The posterior mean and corresponding 95 percent credible interval were calculated. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Primary

End point timeframe:

Up to Day 392 in Part B

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[200]	45[201]		
Units: Score on a scale				
arithmetic mean (standard deviation)				
EXACT-RS, 1 month, n=48,45	12.4 (± 5.86)	11.8 (± 5.87)		
EXACT-RS, 2 month, n=47,44	12.5 (± 6.67)	11.6 (± 6.31)		
EXACT-RS, 3 month, n=46,41	12.5 (± 7.03)	10.5 (± 6.33)		
EXACT-RS, 4 month, n=46,41	12.4 (± 6.97)	10.6 (± 6.61)		
EXACT-RS, 5 month, n=46,40	12 (± 7.12)	10.6 (± 6.65)		
EXACT-RS, 6 month, n=44,39	12.4 (± 7.34)	10.4 (± 6.14)		
EXACT-RS, 7 month, n=44,39	12.3 (± 7.16)	10.3 (± 6.48)		
EXACT-RS, 8 month, n=43,39	12.4 (± 7.3)	10.3 (± 6.93)		
EXACT-RS, 9 month, n=40,38	12.2 (± 6.98)	10.7 (± 7.08)		
EXACT-RS, 10 month, n=39,38	13 (± 7.14)	10.3 (± 7.09)		
EXACT-RS, 11 month, n=39,37	12.2 (± 7.23)	10.5 (± 6.91)		
EXACT-RS, 12 month, n=39,37	12.5 (± 7.08)	10.5 (± 7.12)		

Notes:

[200] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
EXACT-RS, 1 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[202]
P-value	= 0.6 [203]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.81
upper limit	2.17
Variability estimate	Standard deviation
Dispersion value	1.29

Notes:

[202] - P-value is actually a posterior probability.

[203] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
EXACT-RS, 2 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[204]
P-value	= 0.65 [205]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.11
upper limit	2.37
Variability estimate	Standard deviation
Dispersion value	1.42

Notes:

[204] - P-value is actually a posterior probability.

[205] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

EXACT-RS, 3 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[206]
P-value	= 0.83 [207]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.43
upper limit	1.45
Variability estimate	Standard deviation
Dispersion value	1.52

Notes:

[206] - P-value is actually a posterior probability.

[207] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

EXACT-RS, 4 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[208]
P-value	= 0.78 [209]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.07
upper limit	1.9
Variability estimate	Standard deviation
Dispersion value	1.53

Notes:

[208] - P-value is actually a posterior probability.

[209] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 5

Statistical analysis description:	
EXACT-RS, 5 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[210]
P-value	= 0.73 [211]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.82
upper limit	2.28
Variability estimate	Standard deviation
Dispersion value	1.56

Notes:

[210] - P-value is actually a posterior probability.

[211] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 6
Statistical analysis description:	
EXACT-RS, 6 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[212]
P-value	= 0.72 [213]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.01
upper limit	2.26
Variability estimate	Standard deviation
Dispersion value	1.58

Notes:

[212] - P-value is actually a posterior probability.

[213] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 7
Statistical analysis description:	
EXACT-RS, 7 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[214]
P-value	= 0.73 [215]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.15
upper limit	2.09
Variability estimate	Standard deviation
Dispersion value	1.58

Notes:

[214] - P-value is actually a posterior probability.

[215] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

EXACT-RS, 8 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[216]
P-value	= 0.81 [217]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.71
upper limit	1.76
Variability estimate	Standard deviation
Dispersion value	1.69

Notes:

[216] - P-value is actually a posterior probability.

[217] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

EXACT-RS, 9 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[218]
P-value	= 0.76 [219]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.23

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.66
upper limit	2.22
Variability estimate	Standard deviation
Dispersion value	1.75

Notes:

[218] - P-value is actually a posterior probability.

[219] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

EXACT-RS, 10 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[220]
P-value	= 0.91 [221]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-2.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.66
upper limit	0.99
Variability estimate	Standard deviation
Dispersion value	1.74

Notes:

[220] - P-value is actually a posterior probability.

[221] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 11

Statistical analysis description:

EXACT-RS, 11 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[222]
P-value	= 0.71 [223]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.73
upper limit	2.13
Variability estimate	Standard deviation
Dispersion value	1.73

Notes:

[222] - P-value is actually a posterior probability.

[223] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

EXACT-RS, 12 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[224]
P-value	= 0.78 [225]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.77
upper limit	2.04
Variability estimate	Standard deviation
Dispersion value	1.74

Notes:

[224] - P-value is actually a posterior probability.

[225] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Secondary: Cmax of danirixin in Part B

End point title	Cmax of danirixin in Part B

End point description:

Cmax of danirixin was derived from the PK samples collected at pre-dose and at 0.5, 1, 2, 4, 6, 8, 10 and 12 hour post-dose on Day 1 and Day 364; and at pre-dose and 2 hours on Day 28, 56 and 168 in Part B. PK analysis of danirixin was conducted by non-compartmental methods. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Pre-dose and at 0.5, 1, 2, 4, 6, 8, 10 and 12 hour post-dose on Day 1 and Day 364; and at pre-dose and 2 hours on Day 28, 56 and 168 in Part B

End point values	DNX 75 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	45[226]			
Units: ng/mL				
geometric mean (confidence interval 95%)				
Day 1 dose, n=44	517.784 (388.207 to 690.612)			

Day 364 dose, n=36	756.391 (554.011 to 1032.7)			

Notes:

[226] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of danirixin in Part B

End point title	Tmax of danirixin in Part B

End point description:

Tmax of danirixin was derived from the PK samples collected at pre-dose and at 0.5, 1, 2, 4, 6, 8, 10 and 12 hour post-dose on Day 1 and Day 364; and at pre-dose and 2 hours on Day 28, 56 and 168 in Part B. PK analysis of danirixin was conducted by non-compartmental methods. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Pre-dose and at 0.5, 1, 2, 4, 6, 8, 10 and 12 hour post-dose on Day 1 and Day 364; and at pre-dose and 2 hours on Day 28, 56 and 168 in Part B

End point values	DNX 75 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	45[227]			
Units: Hour				
median (full range (min-max))				
Day 1 dose, n=44 Day 364 dose, n=36	2 (0.48 to 6) 1.1 (0.5 to 10)			

Notes:

[227] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: AUC(0-12) of danirixin in Part B

End point title	AUC(0-12) of danirixin in Part B

End point description:

AUC (0-12) of danirixin was derived from the PK samples collected at pre-dose and at 0.5, 1, 2, 4, 6, 8, 10 and 12 hour post-dose on Day 1 and Day 364; and at pre-dose and 2 hours on Day 28, 56 and 168 in Part B. PK analysis of danirixin was conducted by non-compartmental methods. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Pre-dose and at 0.5, 1, 2, 4, 6, 8, 10 and 12 hour post-dose on Day 1 and Day 364; and at pre-dose and 2 hours on Day 28, 56 and 168 in Part B

End point values	DNX 75 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	45[228]			
Units: Hour*ng/mL				
geometric mean (confidence interval 95%)				
Day 1 dose, n=44	2388.303 (1834.42 to 3109.425)			
Day 364 dose, n=36	4366.995 (3254.122 to 5860.458)			

Notes:

[228] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of EXACT-PRO exacerbations per year in Part B

End point title	Number of EXACT-PRO exacerbations per year in Part B

End point description:

EXACT-PRO is a 14 item patient reported outcome instrument designed to capture information on the occurrence, frequency, severity, and duration of COPD exacerbations. The total score for EXACT-PRO ranges from 0-100, higher scores indicate more severe symptoms. For par. with less than 364 days on-treatment, the annual exacerbation rate was imputed as the number of recorded on-treatment exacerbations, divided by the number of 4-week treatment period intervals for which the par. was in the study, multiplied by 13. For par. with 364 or more days on-treatment, the annual exacerbation rate was calculated as the number of recorded exacerbations between study days 1 and 364. Statistical analysis was done using a Bayesian Cox model, assuming a negative binomial distribution for the underlying exacerbation rate. The exacerbation rates and the ratio (danirixin/placebo), were estimated and 95 percent credible intervals were produced using non-informative priors. 1 par. was excluded from analysis.

End point type	Secondary

End point timeframe:

Up to Day 392 in Part B

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27[229]	28[230]		
Units: Exacerbations per year				
arithmetic mean (standard deviation)	3.6 (± 2.75)	3.3 (± 3.47)		

Notes:

[229] - ITT Population

[230] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority[231]
P-value	= 0.278 [232]
Method	Bayesian Cox analysis
Parameter estimate	Posterior mean difference
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.63
Variability estimate	Standard deviation
Dispersion value	0.242

Notes:

[231] - P-value is actually a posterior probability.

[232] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 1.0 is presented.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority[233]
P-value	= 0.138 [234]
Method	Bayesian Cox analysis
Parameter estimate	Posterior mean difference
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.63
Variability estimate	Standard deviation
Dispersion value	0.242

Notes:

[233] - P-value is actually a posterior probability.

[234] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0.9 is presented.

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority[235]
P-value	= 0.05 [236]
Method	Bayesian Cox analysis
Parameter estimate	Posterior mean difference
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.63
Variability estimate	Standard deviation
Dispersion value	0.242

Notes:

[235] - P-value is actually a posterior probability.

[236] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0.8 is presented.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority[237]
P-value	= 0.011 [238]
Method	Bayesian Cox analysis
Parameter estimate	Posterior mean difference
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.63
Variability estimate	Standard deviation
Dispersion value	0.242

Notes:

[237] - P-value is actually a posterior probability.

[238] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0.7 is presented.

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority[239]
P-value	= 0.002 [240]
Method	Bayesian Cox analysis
Parameter estimate	Posterior mean difference
Point estimate	1.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.63
Variability estimate	Standard deviation
Dispersion value	0.242

Notes:

[239] - P-value is actually a posterior probability.

[240] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0.6 is presented.

Secondary: Monthly weighted means of exacerbations of EXACT-PRO total score in Part B

End point title	Monthly weighted means of exacerbations of EXACT-PRO total score in Part B

End point description:

EXACT-PRO is a 14 item patient reported outcome instrument designed to capture information on the occurrence, frequency, severity, and duration of COPD exacerbations. The total score for EXACT-PRO ranges from 0-100, higher scores indicate more severe symptoms. A par. had at least 10 days of diary data in any month to contribute a non-missing weighted mean AUC of daily values; otherwise the weighted mean for that month were considered missing. A mixed effects model in a Bayesian framework with repeated measures were performed on the EXACT-PRO monthly weighted mean AUC data. The posterior mean and corresponding 95 percent credible interval were calculated. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Day 392 in Part B

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[241]	45[242]		
Units: Score on a scale				
arithmetic mean (standard deviation)				
EXACT-PRO, 1 month, n=48,45	36.5 (± 9.53)	35.5 (± 9.81)		
EXACT-PRO, 2 month, n=47,44	36.5 (± 10.77)	35.3 (± 10.69)		
EXACT-PRO, 3 month, n=46,41	36.4 (± 11.23)	33.6 (± 10.84)		
EXACT-PRO, 4 month, n=46,41	36.4 (± 11.35)	33.9 (± 10.91)		
EXACT-PRO, 5 month, n=46,40	35.9 (± 11.84)	33.8 (± 11.28)		
EXACT-PRO, 6 month, n=44,39	36.8 (± 11.58)	33.8 (± 10.75)		
EXACT-PRO, 7 month, n=44,39	36.5 (± 11.61)	33.3 (± 11.15)		
EXACT-PRO, 8 month, n=43,38	36.5 (± 11.82)	33.7 (± 11.73)		
EXACT-PRO, 9 month, n=40,36	36.3 (± 11.25)	35.2 (± 11.22)		
EXACT-PRO, 10 month, n=39,37	37.4 (± 11.71)	33.7 (± 12.2)		
EXACT-PRO, 11 month, n=39,36	36 (± 11.87)	34.6 (± 11.49)		
EXACT-PRO, 12 month, n=39,35	36.7 (± 11.57)	35 (± 11.28)		

Notes:

[241] - ITT Population

[242] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
EXACT-PRO, 1 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[243]
P-value	= 0.62 [244]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.55
upper limit	3.23
Variability estimate	Standard deviation
Dispersion value	2.04

Notes:

[243] - P-value is actually a posterior probability.

[244] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
EXACT-PRO, 2 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[245]
P-value	= 0.64 [246]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.03
upper limit	3.6
Variability estimate	Standard deviation
Dispersion value	2.21

Notes:

[245] - P-value is actually a posterior probability.

[246] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
EXACT-PRO, 3 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[247]
P-value	= 0.81 [248]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	2.27
Variability estimate	Standard deviation
Dispersion value	2.29

Notes:

[247] - P-value is actually a posterior probability.

[248] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

EXACT-PRO, 4 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[249]
P-value	= 0.77 [250]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.92
upper limit	3.07
Variability estimate	Standard deviation
Dispersion value	2.31

Notes:

[249] - P-value is actually a posterior probability.

[250] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

EXACT-PRO, 5 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[251]
P-value	= 0.71 [252]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	3.55
Variability estimate	Standard deviation
Dispersion value	2.4

Notes:

[251] - P-value is actually a posterior probability.

[252] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

EXACT-PRO, 6 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[253]
P-value	= 0.7 [254]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.46
upper limit	3.05
Variability estimate	Standard deviation
Dispersion value	2.42

Notes:

[253] - P-value is actually a posterior probability.

[254] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

EXACT-PRO, 7 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[255]
P-value	= 0.74 [256]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.75
upper limit	2.9
Variability estimate	Standard deviation
Dispersion value	2.45

Notes:

[255] - P-value is actually a posterior probability.

[256] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

EXACT-PRO, 8 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[257]
P-value	= 0.79 [258]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.93
upper limit	3.3
Variability estimate	Standard deviation
Dispersion value	2.63

Notes:

[257] - P-value is actually a posterior probability.

[258] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

EXACT-PRO, 9 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[259]
P-value	= 0.77 [260]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.04
upper limit	3.18
Variability estimate	Standard deviation
Dispersion value	2.63

Notes:

[259] - P-value is actually a posterior probability.

[260] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 10

Statistical analysis description:	
EXACT-PRO, 10 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[261]
P-value	= 0.9 [262]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-3.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.74
upper limit	1.87
Variability estimate	Standard deviation
Dispersion value	2.72

Notes:

[261] - P-value is actually a posterior probability.

[262] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 11
Statistical analysis description:	
EXACT-PRO, 11 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[263]
P-value	= 0.66 [264]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	4.2
Variability estimate	Standard deviation
Dispersion value	2.72

Notes:

[263] - P-value is actually a posterior probability.

[264] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 13
Statistical analysis description:	
EXACT-PRO, 1 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[265]
P-value	= 0.43 [266]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.55
upper limit	3.23
Variability estimate	Standard deviation
Dispersion value	2.04

Notes:

[265] - P-value is actually a posterior probability.

[266] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

EXACT-PRO, 12 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[267]
P-value	= 0.74 [268]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.91
upper limit	3.45
Variability estimate	Standard deviation
Dispersion value	2.7

Notes:

[267] - P-value is actually a posterior probability.

[268] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 14

Statistical analysis description:

EXACT-PRO, 2 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[269]
P-value	= 0.45 [270]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.72

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.03
upper limit	3.6
Variability estimate	Standard deviation
Dispersion value	2.21

Notes:

[269] - P-value is actually a posterior probability.

[270] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 16

Statistical analysis description:

EXACT-PRO, 4 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[271]
P-value	= 0.62 [272]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.92
upper limit	3.07
Variability estimate	Standard deviation
Dispersion value	2.31

Notes:

[271] - P-value is actually a posterior probability.

[272] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 15

Statistical analysis description:

EXACT-PRO, 3 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[273]
P-value	= 0.67 [274]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	2.27
Variability estimate	Standard deviation
Dispersion value	2.29

Notes:

[273] - P-value is actually a posterior probability.

[274] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 17

Statistical analysis description:

EXACT-PRO, 5 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[275]
P-value	= 0.55 [276]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	3.55
Variability estimate	Standard deviation
Dispersion value	2.4

Notes:

[275] - P-value is actually a posterior probability.

[276] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 18

Statistical analysis description:

EXACT-PRO, 6 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[277]
P-value	= 0.55 [278]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.46
upper limit	3.05
Variability estimate	Standard deviation
Dispersion value	2.42

Notes:

[277] - P-value is actually a posterior probability.

[278] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 19

Statistical analysis description:	
EXACT-PRO, 7 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[279]
P-value	= 0.59 [280]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.75
upper limit	2.9
Variability estimate	Standard deviation
Dispersion value	2.45

Notes:

[279] - P-value is actually a posterior probability.

[280] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 20
Statistical analysis description:	
EXACT-PRO, 8 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[281]
P-value	= 0.65 [282]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.93
upper limit	3.3
Variability estimate	Standard deviation
Dispersion value	2.63

Notes:

[281] - P-value is actually a posterior probability.

[282] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 22
Statistical analysis description:	
EXACT-PRO, 10 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[283]
P-value	= 0.81 [284]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-3.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.74
upper limit	1.87
Variability estimate	Standard deviation
Dispersion value	2.72

Notes:

[283] - P-value is actually a posterior probability.

[284] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 21

Statistical analysis description:

EXACT-PRO, 9 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[285]
P-value	= 0.63 [286]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.04
upper limit	3.18
Variability estimate	Standard deviation
Dispersion value	2.63

Notes:

[285] - P-value is actually a posterior probability.

[286] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 23

Statistical analysis description:

EXACT-PRO, 11 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[287]
P-value	= 0.52 [288]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.16

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	4.2
Variability estimate	Standard deviation
Dispersion value	2.72

Notes:

[287] - P-value is actually a posterior probability.

[288] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 24

Statistical analysis description:

EXACT-PRO, 12 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[289]
P-value	= 0.6 [290]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.91
upper limit	3.45
Variability estimate	Standard deviation
Dispersion value	2.7

Notes:

[289] - P-value is actually a posterior probability.

[290] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 25

Statistical analysis description:

EXACT-PRO, 1 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[291]
P-value	= 0.24 [292]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.55
upper limit	3.23
Variability estimate	Standard deviation
Dispersion value	2.04

Notes:

[291] - P-value is actually a posterior probability.

[292] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -2 is presented.

Statistical analysis title	Statistical analysis 26

Statistical analysis description:

EXACT-PRO, 2 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[293]
P-value	= 0.28 [294]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.03
upper limit	3.6
Variability estimate	Standard deviation
Dispersion value	2.21

Notes:

[293] - P-value is actually a posterior probability.

[294] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -2 is presented.

Statistical analysis title	Statistical analysis 28

Statistical analysis description:

EXACT-PRO, 4 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[295]
P-value	= 0.43 [296]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.92
upper limit	3.07
Variability estimate	Standard deviation
Dispersion value	2.31

Notes:

[295] - P-value is actually a posterior probability.

[296] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -2 is presented.

Statistical analysis title	Statistical analysis 27

Statistical analysis description:

EXACT-PRO, 3 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[297]
P-value	= 0.5 [298]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	2.27
Variability estimate	Standard deviation
Dispersion value	2.29

Notes:

[297] - P-value is actually a posterior probability.

[298] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -2 is presented.

Statistical analysis title	Statistical analysis 29

Statistical analysis description:

EXACT-PRO, 5 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[299]
P-value	= 0.37 [300]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	3.55
Variability estimate	Standard deviation
Dispersion value	2.4

Notes:

[299] - P-value is actually a posterior probability.

[300] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -2 is presented.

Statistical analysis title	Statistical analysis 30

Statistical analysis description:

EXACT-PRO, 6 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[301]
P-value	= 0.38 [302]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.46
upper limit	3.05
Variability estimate	Standard deviation
Dispersion value	2.42

Notes:

[301] - P-value is actually a posterior probability.

[302] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -2 is presented.

Statistical analysis title	Statistical analysis 32

Statistical analysis description:

EXACT-PRO, 8 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[303]
P-value	= 0.51 [304]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.93
upper limit	3.3
Variability estimate	Standard deviation
Dispersion value	2.63

Notes:

[303] - P-value is actually a posterior probability.

[304] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -2 is presented.

Statistical analysis title	Statistical analysis 31

Statistical analysis description:

EXACT-PRO, 7 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[305]
P-value	= 0.43 [306]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.75
upper limit	2.9
Variability estimate	Standard deviation
Dispersion value	2.45

Notes:

[305] - P-value is actually a posterior probability.

[306] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -2 is presented.

Statistical analysis title	Statistical analysis 33

Statistical analysis description:

EXACT-PRO, 9 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[307]
P-value	= 0.5 [308]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.04
upper limit	3.18
Variability estimate	Standard deviation
Dispersion value	2.63

Notes:

[307] - P-value is actually a posterior probability.

[308] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -2 is presented.

Statistical analysis title	Statistical analysis 35

Statistical analysis description:

EXACT-PRO, 11 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[309]
P-value	= 0.38 [310]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	4.2
Variability estimate	Standard deviation
Dispersion value	2.72

Notes:

[309] - P-value is actually a posterior probability.

[310] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -2 is presented.

Statistical analysis title	Statistical analysis 34

Statistical analysis description:

EXACT-PRO, 10 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[311]
P-value	= 0.7 [312]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-3.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.74
upper limit	1.87
Variability estimate	Standard deviation
Dispersion value	2.72

Notes:

[311] - P-value is actually a posterior probability.

[312] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -2 is presented.

Statistical analysis title	Statistical analysis 36

Statistical analysis description:

EXACT-PRO, 12 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[313]
P-value	= 0.45 [314]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.91
upper limit	3.45
Variability estimate	Standard deviation
Dispersion value	2.7

Notes:

[313] - P-value is actually a posterior probability.

[314] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -2 is presented.

Statistical analysis title	Statistical analysis 37

Statistical analysis description:

EXACT-PRO, 1 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[315]
P-value	= 0.11 [316]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.55
upper limit	3.23
Variability estimate	Standard deviation
Dispersion value	2.04

Notes:

[315] - P-value is actually a posterior probability.

[316] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -3 is presented.

Statistical analysis title	Statistical analysis 38

Statistical analysis description:

EXACT-PRO, 2 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[317]
P-value	= 0.15 [318]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.03
upper limit	3.6
Variability estimate	Standard deviation
Dispersion value	2.21

Notes:

[317] - P-value is actually a posterior probability.

[318] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -3 is presented.

Statistical analysis title	Statistical analysis 39

Statistical analysis description:

EXACT-PRO, 3 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[319]
P-value	= 0.32 [320]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	2.27
Variability estimate	Standard deviation
Dispersion value	2.29

Notes:

[319] - P-value is actually a posterior probability.

[320] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -3 is presented.

Statistical analysis title	Statistical analysis 41

Statistical analysis description:

EXACT-PRO, 5 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[321]
P-value	= 0.23 [322]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	3.55
Variability estimate	Standard deviation
Dispersion value	2.4

Notes:

[321] - P-value is actually a posterior probability.

[322] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -3 is presented.

Statistical analysis title	Statistical analysis 40

Statistical analysis description:

EXACT-PRO, 4 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[323]
P-value	= 0.28 [324]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.64

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.92
upper limit	3.07
Variability estimate	Standard deviation
Dispersion value	2.31

Notes:

[323] - P-value is actually a posterior probability.

[324] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -3 is presented.

Statistical analysis title	Statistical analysis 42

Statistical analysis description:

EXACT-PRO, 6 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[325]
P-value	= 0.24 [326]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.46
upper limit	3.05
Variability estimate	Standard deviation
Dispersion value	2.42

Notes:

[325] - P-value is actually a posterior probability.

[326] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -3 is presented.

Statistical analysis title	Statistical analysis 43

Statistical analysis description:

EXACT-PRO, 7 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[327]
P-value	= 0.29 [328]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.75
upper limit	2.9
Variability estimate	Standard deviation
Dispersion value	2.45

Notes:

[327] - P-value is actually a posterior probability.

[328] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -3 is presented.

Statistical analysis title	Statistical analysis 44

Statistical analysis description:

EXACT-PRO, 8 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[329]
P-value	= 0.36 [330]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.93
upper limit	3.3
Variability estimate	Standard deviation
Dispersion value	2.63

Notes:

[329] - P-value is actually a posterior probability.

[330] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -3 is presented.

Statistical analysis title	Statistical analysis 45

Statistical analysis description:

EXACT-PRO, 9 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[331]
P-value	= 0.35 [332]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.04
upper limit	3.18
Variability estimate	Standard deviation
Dispersion value	2.63

Notes:

[331] - P-value is actually a posterior probability.

[332] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -3 is presented.

Statistical analysis title	Statistical analysis 46

Statistical analysis description:

EXACT-PRO, 10 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[333]
P-value	= 0.57 [334]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-3.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.74
upper limit	1.87
Variability estimate	Standard deviation
Dispersion value	2.72

Notes:

[333] - P-value is actually a posterior probability.

[334] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -3 is presented.

Statistical analysis title	Statistical analysis 48

Statistical analysis description:

EXACT-PRO, 12 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[335]
P-value	= 0.32 [336]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.91
upper limit	3.45
Variability estimate	Standard deviation
Dispersion value	2.7

Notes:

[335] - P-value is actually a posterior probability.

[336] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -3 is presented.

Statistical analysis title	Statistical analysis 47

Statistical analysis description:

EXACT-PRO, 11 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[337]
P-value	= 0.25 [338]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	4.2
Variability estimate	Standard deviation
Dispersion value	2.72

Notes:

[337] - P-value is actually a posterior probability.

[338] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -3 is presented.

Secondary: Time to first HCRU COPD exacerbation in Part B

End point title	Time to first HCRU COPD exacerbation in Part B

End point description:

HCRU COPD exacerbations are defined as moderate or severe exacerbations based on requirement of new prescription antibiotics or oral corticosteroids, hospitalization or emergency room visits for management of COPD exacerbation. The time to the first on-treatment HRCU exacerbation were summarized by treatment group. It was analyzed using a Bayesian Cox proportional hazards model. The hazard ratio for the danirixin vs. placebo comparison, along with 95 percent credible interval, was derived, with terms for treatment group, smoking status and country. Posterior probabilities of the ratio of the percentage of par. with an HCRU exacerbation, adjusted for time to first exacerbation, in the danirixin group relative to the placebo group were calculated. 1 par. was excluded from analysis.

End point type	Secondary

End point timeframe:

Up to Day 392 in Part B

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[339]	20[340]		
Units: Days				
arithmetic mean (standard deviation)	166.3 (± 97.97)	172.7 (± 89.66)		

Notes:

[339] - ITT Population

[340] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.477 [341]
Method	Bayesian analysis
Parameter estimate	Hazard ratio (HR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.82

Notes:

[341] - Posterior probability that the treatment ratio (DNX 75 mg/ placebo) is less than 1.0 is presented.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.343 [342]
Method	Bayesian analysis
Parameter estimate	Hazard ratio (HR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.82

Notes:

[342] - Posterior probability that the treatment ratio (DNX 75 mg/ placebo) is less than 0.9 is presented.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.221 [343]
Method	Bayesian analysis
Parameter estimate	Hazard ratio (HR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.82

Notes:

[343] - Posterior probability that the treatment ratio (DNX 75 mg/ placebo) is less than 0.8 is presented.

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.116 [344]
Method	Bayesian analysis
Parameter estimate	Hazard ratio (HR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.82

Notes:

[344] - Posterior probability that the treatment ratio (DNX 75 mg/ placebo) is less than 0.7 is presented.

Statistical analysis title	Statistical analysis 5
Statistical analysis description:	
Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.052 [345]
Method	Bayesian analysis
Parameter estimate	Hazard ratio (HR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.82

Notes:

[345] - Posterior probability that the treatment ratio (DNX 75 mg/ placebo) is less than 0.6 is presented.

Secondary: Time to first EXACT-PRO event in Part B

End point title	Time to first EXACT-PRO event in Part B

End point description:

The hazard ratio for the DNX versus placebo comparison, along with 95% credible interval and posterior probability was derived and a Bayesian Cox proportional hazards model was used for statistical analysis. The analysis was performed on ITT Population. One participant was excluded from analysis.

End point type	Secondary

End point timeframe:

Up to Day 392 in Part B

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27[346]	28[347]		
Units: Days				
arithmetic mean (standard deviation)	101 (± 100.18)	114.7 (± 91.16)		

Notes:

[346] - ITT Population

[347] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.212 [348]
Method	Bayesian Cox analysis
Parameter estimate	Hazard ratio (HR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	2.11

Notes:

[348] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 1.0 is presented.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.111 [349]
Method	Bayesian Cox analysis
Parameter estimate	Hazard ratio (HR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	2.11

Notes:

[349] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0.9 is presented.

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.049 [350]
Method	Bayesian Cox analysis
Parameter estimate	Hazard ratio (HR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	2.11

Notes:

[350] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0.8 is presented.

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.012 [351]
Method	Bayesian Cox analysis
Parameter estimate	Hazard ratio (HR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	2.11

Notes:

[351] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0.7 is presented.

Statistical analysis title	Statistical analysis 5
Statistical analysis description:	
Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.001 [352]
Method	Bayesian Cox analysis
Parameter estimate	Hazard ratio (HR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	2.11

Notes:

[352] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0.6 is presented.

Secondary: Assessment of duration of EXACT-PRO events in Part B

End point title	Assessment of duration of EXACT-PRO events in Part B

End point description:

Duration is the length of time in days from onset to recovery. It was calculated as the difference in days between day of onset and day of recovery. Onset of event was identified as either an increase in EXACT-PRO score of >=12 points above the par. current mean Baseline for 2 consecutive days, with Day 1 of the 2 days serving as Day 1 onset of the event, or an increase of >=9 points above the par. current mean Baseline for 3 consecutive days, with Day 1 of the 3 days serving as Day 1 onset of the event. Duration was 3-day rolling average was used, which was initiated on Day 1 of onset and ended on Day 1 of Recovery. Recovery was defined as the first day in which par. experienced a persistent, sustained improvement in their condition i.e. decrease in the rolling average EXACT-PRO total score >=9 point from the maximum observed value (highest rolling average EXACT-PRO total score observed the first 14 days of the event) during the first 14 days of an event that is sustained for 7 days.

End point type	Secondary

End point timeframe:

Up to Day 392 in Part B

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	45[353]	48[354]		
Units: Days				
arithmetic mean (standard deviation)	33.7 (± 65.4)	31.5 (± 59.27)		

Notes:

[353] - ITT Population

[354] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of severity of EXACT-PRO events in Part B

End point title	Assessment of severity of EXACT-PRO events in Part B

End point description:

EXACT-PRO tool was used to measure severity of COPD exacerbations in participants. Severity was indicated by the maximum EXACT-PRO total score during the course of event (from day of onset to day of recovery).

End point type	Secondary
End point timeframe:	
Up to Day 392 in Part B	

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	45[355]	48[356]		
Units: Score on a scale				
arithmetic mean (standard deviation)	48.8 (± 13.22)	49.7 (± 12.63)		

Notes:

[355] - ITT Population

[356] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Monthly weighted means of EXACT-RS domain scores in Part B

End point title	Monthly weighted means of EXACT-RS domain scores in Part B

End point description:

EXACT-RS is a tool which consists of 11 items from the 14 item EXACT-PRO instrument, intended to capture information related to the respiratory symptoms of COPD. EXACT-RS domains included breathlessness, cough and chest symptoms. The EXACT-RS has a scoring range of 0-40, higher scores indicate more severe symptoms. A par. had at least 10 days of diary data in any month to contribute a non-missing weighted mean AUC of daily values; otherwise the weighted mean for that month were considered missing. A mixed effects model in a Bayesian framework with repeated measures were performed. The posterior mean and corresponding 95 percent credible interval were calculated. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary
End point timeframe:	
Up to Day 392 in Part B	

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[357]	45[358]		
Units: Score on a scale				
arithmetic mean (standard deviation)				
EXACT-RS-breath, 1 month, n=48,45	6 (± 3.4)	5.5 (± 3.59)		
EXACT-RS-breath, 2 month, n=47,44	6.3 (± 3.77)	5.5 (± 3.83)		
EXACT-RS-breath, 3 month, n=46,41	6 (± 3.79)	5 (± 3.75)		
EXACT-RS-breath, 4 month, n=46,41	6 (± 3.91)	5 (± 3.86)		
EXACT-RS-breath, 5 month, n=46,40	5.8 (± 4.05)	5 (± 3.94)		
EXACT-RS-breath, 6 month, n=44,39	6 (± 4.11)	4.8 (± 3.73)		
EXACT-RS-breath, 7 month, n=44,39	5.9 (± 4.17)	4.6 (± 3.83)		
EXACT-RS-breath, 8 month, n=43,39	5.9 (± 3.93)	4.9 (± 3.91)		
EXACT-RS-breath, 9 month, n=40,38	5.8 (± 3.87)	5.1 (± 4.05)		
EXACT-RS-breath, 10 month, n=39,38	6.1 (± 3.95)	4.8 (± 4.12)		

EXACT-RS-breath, 11 month, n=39,37	5.8 (± 3.96)	5 (± 4.15)		
EXACT-RS-breath, 12 month, n=39,37	5.9 (± 3.9)	4.9 (± 4.19)		
EXACT-RS-chest, 1 month, n=48,45	2.6 (± 1.69)	2.5 (± 1.59)		
EXACT-RS-chest, 2 month, n=47,44	2.7 (± 1.94)	2.4 (± 1.76)		
EXACT-RS-chest, 3 month, n=46,41	2.9 (± 2.13)	2.2 (± 1.85)		
EXACT-RS-chest, 4 month, n=46,41	2.8 (± 2.04)	2.3 (± 1.9)		
EXACT-RS-chest, 5 month, n=46,40	2.8 (± 2.08)	2.3 (± 1.87)		
EXACT-RS-chest, 6 month, n=44,39	2.9 (± 2.2)	2.3 (± 1.67)		
EXACT-RS-chest, 7 month, n=44,39	2.8 (± 2.16)	2.2 (± 1.74)		
EXACT-RS-chest, 8 month, n=43,39	2.9 (± 2.27)	2.3 (± 1.91)		
EXACT-RS-chest, 9 month, n=40,38	2.9 (± 2.23)	2.4 (± 1.87)		
EXACT-RS-chest, 10 month, n=39,38	3.1 (± 2.21)	2.2 (± 1.86)		
EXACT-RS-chest, 11 month, n=39,37	3 (± 2.35)	2.3 (± 1.78)		
EXACT-RS-chest, 12 month, n=39,37	3 (± 2.31)	2.4 (± 1.83)		
EXACT-RS-cough, 1 month, n=48,45	3.8 (± 1.5)	3.8 (± 1.32)		
EXACT-RS-cough, 2 month, n=47,44	3.5 (± 1.8)	3.7 (± 1.42)		
EXACT-RS-cough, 3 month, n=46,41	3.6 (± 1.87)	3.3 (± 1.55)		
EXACT-RS-cough, 4 month, n=46,41	3.6 (± 1.79)	3.3 (± 1.57)		
EXACT-RS-cough, 5 month, n=46,40	3.4 (± 1.76)	3.3 (± 1.58)		
EXACT-RS-cough, 6 month, n=44,39	3.5 (± 1.76)	3.4 (± 1.54)		
EXACT-RS-cough, 7 month, n=44,39	3.6 (± 1.58)	3.4 (± 1.72)		
EXACT-RS-cough, 8 month, n=43,39	3.6 (± 1.74)	3.2 (± 1.82)		
EXACT-RS-cough, 9 month, n=40,38	3.5 (± 1.72)	3.3 (± 1.83)		
EXACT-RS-cough, 10 month, n=39,38	3.8 (± 1.91)	3.2 (± 1.82)		
EXACT-RS-cough, 11 month, n=39,37	3.5 (± 1.88)	3.3 (± 1.75)		
EXACT-RS-cough, 12 month, n=39,37	3.6 (± 1.91)	3.2 (± 1.7)		

Notes:

[357] - ITT Population

[358] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
EXACT-RS-breath, 1 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[359]
P-value	= 0.64 [360]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.53
upper limit	1.25
Variability estimate	Standard deviation
Dispersion value	0.72

Notes:

[359] - P-value is actually a posterior probability.

[360] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

EXACT-RS-breath, 2 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[361]
P-value	= 0.75 [362]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.91
upper limit	1.1
Variability estimate	Standard deviation
Dispersion value	0.78

Notes:

[361] - P-value is actually a posterior probability.

[362] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

EXACT-RS-breath, 3 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[363]
P-value	= 0.77 [364]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.09
upper limit	0.98
Variability estimate	Standard deviation
Dispersion value	0.8

Notes:

[363] - P-value is actually a posterior probability.

[364] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:	
EXACT-RS-breath, 4 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[365]
P-value	= 0.74 [366]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.23
upper limit	0.87
Variability estimate	Standard deviation
Dispersion value	0.81

Notes:

[365] - P-value is actually a posterior probability.

[366] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 5
Statistical analysis description:	
EXACT-RS-breath, 5 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[367]
P-value	= 0.67 [368]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.88
upper limit	1.27
Variability estimate	Standard deviation
Dispersion value	0.83

Notes:

[367] - Posterior mean difference

[368] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 6
Statistical analysis description:	
EXACT-RS-breath, 6 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[369]
P-value	= 0.69 [370]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.99
upper limit	1.26
Variability estimate	Standard deviation
Dispersion value	0.86

Notes:

[369] - P-value is actually a posterior probability.

[370] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

EXACT-RS-breath, 7 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[371]
P-value	= 0.72 [372]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	1.08
Variability estimate	Standard deviation
Dispersion value	0.85

Notes:

[371] - Posterior mean difference

[372] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

EXACT-RS-breath, 8 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[373]
P-value	= 0.71 [374]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.11
upper limit	1.14
Variability estimate	Standard deviation
Dispersion value	0.87

Notes:

[373] - P-value is actually a posterior probability.

[374] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

EXACT-RS-breath, 9 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[375]
P-value	= 0.66 [376]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.14
upper limit	1.23
Variability estimate	Standard deviation
Dispersion value	0.88

Notes:

[375] - P-value is actually a posterior probability.

[376] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

EXACT-RS-breath, 10 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[377]
P-value	= 0.84 [378]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.71
upper limit	0.69
Variability estimate	Standard deviation
Dispersion value	0.89

Notes:

[377] - P-value is actually a posterior probability.

[378] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 11

Statistical analysis description:

EXACT-RS-breath, 11 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[379]
P-value	= 0.65 [380]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.15
upper limit	1.41
Variability estimate	Standard deviation
Dispersion value	0.91

Notes:

[379] - P-value is actually a posterior probability.

[380] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

EXACT-RS-breath, 12 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[381]
P-value	= 0.71 [382]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.36
upper limit	1.13
Variability estimate	Standard deviation
Dispersion value	0.9

Notes:

[381] - P-value is actually a posterior probability.

[382] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 13

Statistical analysis description:	
EXACT-RS-breath, 1 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[383]
P-value	= 0.13 [384]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.53
upper limit	1.25
Variability estimate	Standard deviation
Dispersion value	0.72

Notes:

[383] - P-value is actually a posterior probability.

[384] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 14
Statistical analysis description:	
EXACT-RS-breath, 2 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[385]
P-value	= 0.27 [386]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.91
upper limit	1.1
Variability estimate	Standard deviation
Dispersion value	0.78

Notes:

[385] - P-value is actually a posterior probability.

[386] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 15
Statistical analysis description:	
EXACT-RS-breath, 3 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[387]
P-value	= 0.31 [388]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.09
upper limit	0.98
Variability estimate	Standard deviation
Dispersion value	0.8

Notes:

[387] - P-value is actually a posterior probability.

[388] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 16

Statistical analysis description:

EXACT-RS-breath, 4 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[389]
P-value	= 0.29 [390]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.23
upper limit	0.87
Variability estimate	Standard deviation
Dispersion value	0.81

Notes:

[389] - P-value is actually a posterior probability.

[390] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 17

Statistical analysis description:

EXACT-RS-breath, 5 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[391]
P-value	= 0.23 [392]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.36

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.88
upper limit	1.27
Variability estimate	Standard deviation
Dispersion value	0.83

Notes:

[391] - P-value is actually a posterior probability.

[392] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 18

Statistical analysis description:

EXACT-RS-breath, 6 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[393]
P-value	= 0.26 [394]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.99
upper limit	1.26
Variability estimate	Standard deviation
Dispersion value	0.86

Notes:

[393] - P-value is actually a posterior probability.

[394] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 19

Statistical analysis description:

EXACT-RS-breath, 7 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[395]
P-value	= 0.28 [396]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	1.08
Variability estimate	Standard deviation
Dispersion value	0.85

Notes:

[395] - P-value is actually a posterior probability.

[396] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 20

Statistical analysis description:

EXACT-RS-breath, 8 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[397]
P-value	= 0.29 [398]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.11
upper limit	1.14
Variability estimate	Standard deviation
Dispersion value	0.87

Notes:

[397] - P-value is actually a posterior probability.

[398] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 21

Statistical analysis description:

EXACT-RS-breath, 9 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[399]
P-value	= 0.23 [400]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.14
upper limit	1.23
Variability estimate	Standard deviation
Dispersion value	0.88

Notes:

[399] - P-value is actually a posterior probability.

[400] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 22

Statistical analysis description:	
EXACT-RS-breath, 10 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[401]
P-value	= 0.45 [402]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.71
upper limit	0.69
Variability estimate	Standard deviation
Dispersion value	0.89

Notes:

[401] - P-value is actually a posterior probability.

[402] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 23
Statistical analysis description:	
EXACT-RS-breath, 11 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[403]
P-value	= 0.24 [404]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.15
upper limit	1.41
Variability estimate	Standard deviation
Dispersion value	0.91

Notes:

[403] - P-value is actually a posterior probability.

[404] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 24
Statistical analysis description:	
EXACT-RS-breath, 12 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[405]
P-value	= 0.28 [406]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.36
upper limit	1.13
Variability estimate	Standard deviation
Dispersion value	0.9

Notes:

[405] - P-value is actually a posterior probability.

[406] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 25

Statistical analysis description:

EXACT-RS-breath, 1 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[407]
P-value	= 0.26 [408]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.53
upper limit	1.25
Variability estimate	Standard deviation
Dispersion value	0.72

Notes:

[407] - P-value is actually a posterior probability.

[408] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 26

Statistical analysis description:

EXACT-RS-breath, 2 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[409]
P-value	= 0.41 [410]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.53

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.91
upper limit	1.1
Variability estimate	Standard deviation
Dispersion value	0.78

Notes:

[409] - P-value is actually a posterior probability.

[410] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 27

Statistical analysis description:

EXACT-RS-breath, 3 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[411]
P-value	= 0.46 [412]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.09
upper limit	0.98
Variability estimate	Standard deviation
Dispersion value	0.8

Notes:

[411] - P-value is actually a posterior probability.

[412] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 28

Statistical analysis description:

EXACT-RS-breath, 4 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[413]
P-value	= 0.43 [414]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.23
upper limit	0.87
Variability estimate	Standard deviation
Dispersion value	0.81

Notes:

[413] - P-value is actually a posterior probability.

[414] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 29

Statistical analysis description:

EXACT-RS-breath, 5 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[415]
P-value	= 0.36 [416]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.88
upper limit	1.27
Variability estimate	Standard deviation
Dispersion value	0.83

Notes:

[415] - P-value is actually a posterior probability.

[416] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 30

Statistical analysis description:

EXACT-RS-breath, 6 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[417]
P-value	= 0.39 [418]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.99
upper limit	1.26
Variability estimate	Standard deviation
Dispersion value	0.86

Notes:

[417] - P-value is actually a posterior probability.

[418] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 31

Statistical analysis description:	
EXACT-RS-breath, 7 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[419]
P-value	= 0.42 [420]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	1.08
Variability estimate	Standard deviation
Dispersion value	0.85

Notes:

[419] - P-value is actually a posterior probability.

[420] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 32
Statistical analysis description:	
EXACT-RS-breath, 8 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[421]
P-value	= 0.42 [422]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.11
upper limit	1.14
Variability estimate	Standard deviation
Dispersion value	0.87

Notes:

[421] - P-value is actually a posterior probability.

[422] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 33
Statistical analysis description:	
EXACT-RS-breath, 9 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[423]
P-value	= 0.35 [424]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.14
upper limit	1.23
Variability estimate	Standard deviation
Dispersion value	0.88

Notes:

[423] - P-value is actually a posterior probability.

[424] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 34

Statistical analysis description:

EXACT-RS-breath, 10 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[425]
P-value	= 0.58 [426]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.71
upper limit	0.69
Variability estimate	Standard deviation
Dispersion value	0.89

Notes:

[425] - P-value is actually a posterior probability.

[426] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 35

Statistical analysis description:

EXACT-RS-breath, 11 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[427]
P-value	= 0.36 [428]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.36

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.15
upper limit	1.41
Variability estimate	Standard deviation
Dispersion value	0.91

Notes:

[427] - P-value is actually a posterior probability.

[428] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 36

Statistical analysis description:

EXACT-RS-breath, 12 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[429]
P-value	= 0.41 [430]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.36
upper limit	1.13
Variability estimate	Standard deviation
Dispersion value	0.9

Notes:

[429] - P-value is actually a posterior probability.

[430] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 37

Statistical analysis description:

EXACT-RS-chest, 1 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[431]
P-value	= 0.66 [432]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	0.52
Variability estimate	Standard deviation
Dispersion value	0.35

Notes:

[431] - P-value is actually a posterior probability.

[432] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 38

Statistical analysis description:

EXACT-RS-chest, 2 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[433]
P-value	= 0.66 [434]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	0.55
Variability estimate	Standard deviation
Dispersion value	0.39

Notes:

[433] - P-value is actually a posterior probability.

[434] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 39

Statistical analysis description:

EXACT-RS-chest, 3 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[435]
P-value	= 0.91 [436]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.46
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.43

Notes:

[435] - P-value is actually a posterior probability.

[436] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 40

Statistical analysis description:	
EXACT-RS-chest, 4 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[437]
P-value	= 0.79 [438]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.16
upper limit	0.44
Variability estimate	Standard deviation
Dispersion value	0.41

Notes:

[437] - P-value is actually a posterior probability.

[438] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 41
Statistical analysis description:	
EXACT-RS-chest, 5 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[439]
P-value	= 0.84 [440]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	0.41
Variability estimate	Standard deviation
Dispersion value	0.42

Notes:

[439] - P-value is actually a posterior probability.

[440] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 42
Statistical analysis description:	
EXACT-RS-chest, 6 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[441]
P-value	= 0.81 [442]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	0.47
Variability estimate	Standard deviation
Dispersion value	0.44

Notes:

[441] - P-value is actually a posterior probability.

[442] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 43

Statistical analysis description:

EXACT-RS-chest, 7 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[443]
P-value	= 0.76 [444]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.14
upper limit	0.56
Variability estimate	Standard deviation
Dispersion value	0.44

Notes:

[443] - P-value is actually a posterior probability.

[444] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 44

Statistical analysis description:

EXACT-RS-chest, 8 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[445]
P-value	= 0.84 [446]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.48

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.43
upper limit	0.43
Variability estimate	Standard deviation
Dispersion value	0.48

Notes:

[445] - P-value is actually a posterior probability.

[446] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 45

Statistical analysis description:

EXACT-RS-chest, 9 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[447]
P-value	= 0.83 [448]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	0.38
Variability estimate	Standard deviation
Dispersion value	0.49

Notes:

[447] - P-value is actually a posterior probability.

[448] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 46

Statistical analysis description:

EXACT-RS-chest, 10 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[449]
P-value	= 0.94 [450]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.49

Notes:

[449] - P-value is actually a posterior probability.

[450] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 47

Statistical analysis description:

EXACT-RS-chest, 11 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[451]
P-value	= 0.84 [452]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.45
upper limit	0.48
Variability estimate	Standard deviation
Dispersion value	0.5

Notes:

[451] - P-value is actually a posterior probability.

[452] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 48

Statistical analysis description:

EXACT-RS-chest, 12 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[453]
P-value	= 0.81 [454]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.36
upper limit	0.55
Variability estimate	Standard deviation
Dispersion value	0.5

Notes:

[453] - P-value is actually a posterior probability.

[454] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 49

Statistical analysis description:	
EXACT-RS-chest, 1 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[455]
P-value	= 0.01 [456]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	0.52
Variability estimate	Standard deviation
Dispersion value	0.35

Notes:

[455] - P-value is actually a posterior probability.

[456] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 50
Statistical analysis description:	
EXACT-RS-chest, 2 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[457]
P-value	= 0.02 [458]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	0.55
Variability estimate	Standard deviation
Dispersion value	0.39

Notes:

[457] - P-value is actually a posterior probability.

[458] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 51
Statistical analysis description:	
EXACT-RS-chest, 3 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[459]
P-value	= 0.15 [460]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.46
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.43

Notes:

[459] - P-value is actually a posterior probability.

[460] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 52

Statistical analysis description:

EXACT-RS-chest, 4 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[461]
P-value	= 0.05 [462]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.16
upper limit	0.44
Variability estimate	Standard deviation
Dispersion value	0.41

Notes:

[461] - P-value is actually a posterior probability.

[462] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 53

Statistical analysis description:

EXACT-RS-chest, 5 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[463]
P-value	= 0.08 [464]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	0.41
Variability estimate	Standard deviation
Dispersion value	0.42

Notes:

[463] - P-value is actually a posterior probability.

[464] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 54

Statistical analysis description:

EXACT-RS-chest, 6 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[465]
P-value	= 0.08 [466]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	0.47
Variability estimate	Standard deviation
Dispersion value	0.44

Notes:

[465] - P-value is actually a posterior probability.

[466] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 55

Statistical analysis description:

EXACT-RS-chest, 7 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[467]
P-value	= 0.06 [468]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.14
upper limit	0.56
Variability estimate	Standard deviation
Dispersion value	0.44

Notes:

[467] - P-value is actually a posterior probability.

[468] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 56

Statistical analysis description:

EXACT-RS-chest, 8 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[469]
P-value	= 0.14 [470]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.43
upper limit	0.43
Variability estimate	Standard deviation
Dispersion value	0.48

Notes:

[469] - P-value is actually a posterior probability.

[470] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 57

Statistical analysis description:

EXACT-RS-chest, 9 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[471]
P-value	= 0.14 [472]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	0.38
Variability estimate	Standard deviation
Dispersion value	0.49

Notes:

[471] - P-value is actually a posterior probability.

[472] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 58

Statistical analysis description:	
EXACT-RS-chest, 10 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[473]
P-value	= 0.29 [474]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.49

Notes:

[473] - P-value is actually a posterior probability.

[474] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 59
Statistical analysis description:	
EXACT-RS-chest, 11 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[475]
P-value	= 0.15 [476]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.45
upper limit	0.48
Variability estimate	Standard deviation
Dispersion value	0.5

Notes:

[475] - P-value is actually a posterior probability.

[476] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 60
Statistical analysis description:	
EXACT-RS-chest, 12 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[477]
P-value	= 0.13 [478]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.36
upper limit	0.55
Variability estimate	Standard deviation
Dispersion value	0.5

Notes:

[477] - P-value is actually a posterior probability.

[478] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -1 is presented.

Statistical analysis title	Statistical analysis 61

Statistical analysis description:

EXACT-RS-chest, 1 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[479]
P-value	= 0.06 [480]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	0.52
Variability estimate	Standard deviation
Dispersion value	0.35

Notes:

[479] - P-value is actually a posterior probability.

[480] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 62

Statistical analysis description:

EXACT-RS-chest, 2 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[481]
P-value	= 0.09 [482]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.17

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	0.55
Variability estimate	Standard deviation
Dispersion value	0.39

Notes:

[481] - P-value is actually a posterior probability.

[482] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 63

Statistical analysis description:

EXACT-RS-chest, 3 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[483]
P-value	= 0.37 [484]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.46
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.43

Notes:

[483] - P-value is actually a posterior probability.

[484] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 64

Statistical analysis description:

EXACT-RS-chest, 4 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[485]
P-value	= 0.18 [486]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.16
upper limit	0.44
Variability estimate	Standard deviation
Dispersion value	0.41

Notes:

[485] - P-value is actually a posterior probability.

[486] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 65

Statistical analysis description:

EXACT-RS-chest, 5 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[487]
P-value	= 0.24 [488]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	0.41
Variability estimate	Standard deviation
Dispersion value	0.42

Notes:

[487] - P-value is actually a posterior probability.

[488] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 66

Statistical analysis description:

EXACT-RS-chest, 6 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[489]
P-value	= 0.24 [490]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	0.47
Variability estimate	Standard deviation
Dispersion value	0.44

Notes:

[489] - P-value is actually a posterior probability.

[490] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 67

Statistical analysis description:	
EXACT-RS-chest, 7 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[491]
P-value	= 0.19 [492]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.14
upper limit	0.56
Variability estimate	Standard deviation
Dispersion value	0.44

Notes:

[491] - P-value is actually a posterior probability.

[492] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 68
Statistical analysis description:	
EXACT-RS-chest, 8 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[493]
P-value	= 0.32 [494]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.43
upper limit	0.43
Variability estimate	Standard deviation
Dispersion value	0.48

Notes:

[493] - P-value is actually a posterior probability.

[494] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 69
Statistical analysis description:	
EXACT-RS-chest, 9 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[495]
P-value	= 0.32 [496]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	0.38
Variability estimate	Standard deviation
Dispersion value	0.49

Notes:

[495] - P-value is actually a posterior probability.

[496] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 70

Statistical analysis description:

EXACT-RS-chest, 10 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[497]
P-value	= 0.52 [498]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	0.2
Variability estimate	Standard deviation
Dispersion value	0.49

Notes:

[497] - P-value is actually a posterior probability.

[498] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 71

Statistical analysis description:

EXACT-RS-chest, 11 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[499]
P-value	= 0.33 [500]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.49

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.45
upper limit	0.48
Variability estimate	Standard deviation
Dispersion value	0.5

Notes:

[499] - P-value is actually a posterior probability.

[500] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 72

Statistical analysis description:

EXACT-RS-chest, 12 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[501]
P-value	= 0.29 [502]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.36
upper limit	0.55
Variability estimate	Standard deviation
Dispersion value	0.5

Notes:

[501] - P-value is actually a posterior probability.

[502] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 73

Statistical analysis description:

EXACT-RS-cough, 1 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[503]
P-value	= 0.43 [504]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	0.62
Variability estimate	Standard deviation
Dispersion value	0.31

Notes:

[503] - P-value is actually a posterior probability.

[504] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 74

Statistical analysis description:

EXACT-RS-cough, 2 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[505]
P-value	= 0.29 [506]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.85
Variability estimate	Standard deviation
Dispersion value	0.35

Notes:

[505] - P-value is actually a posterior probability.

[506] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 75

Statistical analysis description:

EXACT-RS-cough, 3 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[507]
P-value	= 0.7 [508]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	0.52
Variability estimate	Standard deviation
Dispersion value	0.38

Notes:

[507] - P-value is actually a posterior probability.

[508] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 76

Statistical analysis description:	
EXACT-RS-cough, 4 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[509]
P-value	= 0.71 [510]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	0.5
Variability estimate	Standard deviation
Dispersion value	0.37

Notes:

[509] - P-value is actually a posterior probability.

[510] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 77
Statistical analysis description:	
EXACT-RS-cough, 5 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[511]
P-value	= 0.61 [512]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	0.61
Variability estimate	Standard deviation
Dispersion value	0.37

Notes:

[511] - P-value is actually a posterior probability.

[512] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 78
Statistical analysis description:	
EXACT-RS-cough, 6 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[513]
P-value	= 0.48 [514]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	0.69
Variability estimate	Standard deviation
Dispersion value	0.36

Notes:

[513] - P-value is actually a posterior probability.

[514] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 79

Statistical analysis description:

EXACT-RS-cough, 7 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[515]
P-value	= 0.58 [516]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.62
Variability estimate	Standard deviation
Dispersion value	0.36

Notes:

[515] - P-value is actually a posterior probability.

[516] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 80

Statistical analysis description:

EXACT-RS-cough, 8 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[517]
P-value	= 0.83 [518]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	0.43
Variability estimate	Standard deviation
Dispersion value	0.4

Notes:

[517] - P-value is actually a posterior probability.

[518] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 81

Statistical analysis description:

EXACT-RS-cough, 9 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[519]
P-value	= 0.74 [520]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	0.52
Variability estimate	Standard deviation
Dispersion value	0.41

Notes:

[519] - P-value is actually a posterior probability.

[520] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 82

Statistical analysis description:

EXACT-RS-cough, 10 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[521]
P-value	= 0.89 [522]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.29
Variability estimate	Standard deviation
Dispersion value	0.43

Notes:

[521] - P-value is actually a posterior probability.

[522] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 83

Statistical analysis description:

EXACT-RS-cough, 11 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[523]
P-value	= 0.59 [524]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	0.69
Variability estimate	Standard deviation
Dispersion value	0.41

Notes:

[523] - P-value is actually a posterior probability.

[524] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 84

Statistical analysis description:

EXACT-RS-cough, 12 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[525]
P-value	= 0.77 [526]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	0.54
Variability estimate	Standard deviation
Dispersion value	0.42

Notes:

[525] - P-value is actually a posterior probability.

[526] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than 0 is presented.

Statistical analysis title	Statistical analysis 85

Statistical analysis description:	
EXACT-RS-cough, 1 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[527]
P-value	= 0.01 [528]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	0.62
Variability estimate	Standard deviation
Dispersion value	0.31

Notes:

[527] - P-value is actually a posterior probability.

[528] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 86
Statistical analysis description:	
EXACT-RS-cough, 2 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[529]
P-value	= 0.01 [530]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.85
Variability estimate	Standard deviation
Dispersion value	0.35

Notes:

[529] - P-value is actually a posterior probability.

[530] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 87
Statistical analysis description:	
EXACT-RS-cough, 3 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[531]
P-value	= 0.09 [532]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	0.52
Variability estimate	Standard deviation
Dispersion value	0.38

Notes:

[531] - P-value is actually a posterior probability.

[532] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 88

Statistical analysis description:

EXACT-RS-cough, 4 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[533]
P-value	= 0.09 [534]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	0.5
Variability estimate	Standard deviation
Dispersion value	0.37

Notes:

[533] - P-value is actually a posterior probability.

[534] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 89

Statistical analysis description:

EXACT-RS-cough, 5 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[535]
P-value	= 0.05 [536]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	0.61
Variability estimate	Standard deviation
Dispersion value	0.37

Notes:

[535] - P-value is actually a posterior probability.

[536] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 90

Statistical analysis description:

EXACT-RS-cough, 6 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[537]
P-value	= 0.02 [538]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	0.69
Variability estimate	Standard deviation
Dispersion value	0.36

Notes:

[537] - P-value is actually a posterior probability.

[538] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 91

Statistical analysis description:

EXACT-RS-cough, 7 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[539]
P-value	= 0.04 [540]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.62
Variability estimate	Standard deviation
Dispersion value	0.36

Notes:

[539] - P-value is actually a posterior probability.

[540] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 92

Statistical analysis description:

EXACT-RS-cough, 8 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[541]
P-value	= 0.22 [542]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	0.43
Variability estimate	Standard deviation
Dispersion value	0.4

Notes:

[541] - P-value is actually a posterior probability.

[542] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 93

Statistical analysis description:

EXACT-RS-cough, 9 month. Data presented are for 95% equal-tailed credible intervals

Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[543]
P-value	= 0.14 [544]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	0.52
Variability estimate	Standard deviation
Dispersion value	0.41

Notes:

[543] - P-value is actually a posterior probability.

[544] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 94

Statistical analysis description:	
EXACT-RS-cough, 10 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[545]
P-value	= 0.36 [546]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.29
Variability estimate	Standard deviation
Dispersion value	0.43

Notes:

[545] - P-value is actually a posterior probability.

[546] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 95
Statistical analysis description:	
EXACT-RS-cough, 11 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[547]
P-value	= 0.07 [548]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	0.69
Variability estimate	Standard deviation
Dispersion value	0.41

Notes:

[547] - P-value is actually a posterior probability.

[548] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Statistical analysis title	Statistical analysis 96
Statistical analysis description:	
EXACT-RS-cough, 12 month. Data presented are for 95% equal-tailed credible intervals	
Comparison groups	Placebo v DNX 75 mg

Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[549]
P-value	= 0.17 [550]
Method	Bayesian analysis
Parameter estimate	Posterior mean difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	0.54
Variability estimate	Standard deviation
Dispersion value	0.42

Notes:

[549] - P-value is actually a posterior probability.

[550] - Posterior probability that the treatment difference (DNX 75 mg-placebo) is less than -0.7 is presented.

Secondary: Change from Baseline for COPD assessment test (CAT) at the indicated time points in Part B

End point title	Change from Baseline for COPD assessment test (CAT) at the indicated time points in Part B

End point description:

The CAT is a validated, 8 item questionnaire which has been developed designed to measure overall COPD-related health status for the initial assessment and longitudinal follow up of par. with COPD. Participants completed each question by rating their experience on a 6 point scale ranging from 0 (no impairment) to 5 (maximum impairment) with a total scoring range of 0 - 40. CAT was assessed at Baseline (Day 1), Day 28, Day 112, Day 168, Day 280 and Day 364 where Baseline was considered as score on Day 1. The change from Baseline was calculated by subtracting the Baseline values from the individual post-randomization values. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Day 392 in Part B

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[551]	45[552]		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 28; n= 43, 37	-0.6 (± 5.19)	-0.7 (± 7)		
Day 112; n= 44, 39	-0.5 (± 5.53)	-1 (± 9.5)		
Day 168; n= 43, 37	-0.8 (± 5.72)	-1.5 (± 9.11)		
Day 280; n= 36, 35	-0.6 (± 6.02)	-1.2 (± 9.59)		
Day 364; n= 38, 34	0.7 (± 5.78)	-2.1 (± 8.77)		

Notes:

[551] - ITT Population

[552] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with physician's global assessment (PGA) readings in Part B

End point title	Number of participants with physician's global assessment (PGA) readings in Part B

End point description:

The PGA is a single item clinician reported outcome measure assessing the overall severity of COPD. Physicians rated disease severity on a four point scale ranging from 1-4 (1=mild, 2=moderate, 3=severe, 4=very severe) at Week 0, 4, 8, 16, 24, 40 and 52. Baseline was considered as score on Day 1. A categorical summary of PGA is presented by treatment and visit.Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Day 392 in Part B

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[553]	45[554]		
Units: Participants				
Baseline; mild; n= 47, 43	5	2		
Baseline; moderate; n= 47, 43	35	37		
Baseline; severe; n= 47, 43	7	4		
Baseline; very severe; n= 47, 43	0	0		
Week 4; mild; n= 44, 39	10	8		
Week 4; moderate; n= 44, 39	28	27		
Week 4; severe; n= 44, 39	6	3		
Week 4; very severe; n= 44, 39	0	1		
Week 8; mild; n= 44, 40	10	8		
Week 8; moderate; n= 44, 40	31	30		
Week 8; severe; n= 44, 40	3	2		
Week 8; very severe; n= 44, 40	0	0		
Week 16; mild; n= 46, 40	12	6		
Week 16; moderate; n= 46, 40	29	32		
Week 16; severe; n= 46, 40	5	2		
Week 16; very severe; n= 46, 40	0	0		
Week 24; mild; n= 44, 38	8	9		
Week 24; moderate; n= 44, 38	32	25		
Week 24; severe; n= 44, 38	4	4		
Week 24; very severe; n= 44, 38	0	0		
Week 40; mild; n= 37, 36	4	6		
Week 40; moderate; n= 37, 36	30	28		
Week 40; severe; n= 37, 36	3	2		
Week 40; very severe; n= 37, 36	0	0		
Week 52; mild; n= 39, 36	7	11		
Week 52; n= moderate; n= 39, 36	28	24		
Week 52; severe; n= 39, 36	4	1		
Week 52; very severe; n= 39, 36	0	0		

Notes:
[553] - ITT Population
[554] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with patient global rating of severity (PGRS) score in Part B

End point title	Number of participants with patient global rating of severity (PGRS) score in Part B

End point description:

PGRS is a single global question and was asked to participants to rate their COPD severity on a four point scale ranging from 1-4 (1=mild, 2=moderate, 3=severe, 4=very severe). Participants completed PGRS at Week 0, 4, 8, 16, 24, 40 and 52. Baseline was considered as score on Day 1. A categorical summary of PGRS is presented by treatment and visit.Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Day 392 in Part B

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[555]	45[556]		
Units: Participants				
Baseline; mild; n= 47, 43	10	6		
Baseline; moderate; n= 47, 43	21	29		
Baseline; severe; n= 47, 43	15	8		
Baseline; very severe; n= 47, 43	1	0		
Week 4; mild; n= 44, 39	7	7		
Week 4; moderate; n= 44, 39	27	27		
Week 4; severe; n= 44, 39	10	4		
Week 4; very severe; n= 44, 39	0	1		
Week 8; mild; n= 44, 40	4	7		
Week 8; moderate; n= 44, 40	32	29		
Week 8; severe; n= 44, 40	7	4		
Week 8; very severe; n= 44, 40	1	0		
Week 16; mild; n= 45, 40	6	8		
Week 16; moderate; n= 45, 40	28	26		
Week 16; severe; n= 45, 40	11	6		
Week 16; very severe; n= 45, 40	0	0		
Week 24; mild; n= 44, 38	6	9		
Week 24; moderate; n= 44, 38	31	23		
Week 24; severe; n= 44, 38	7	6		
Week 24; very severe; n= 44, 38	0	0		
Week 40; mild; n= 37, 36	7	9		
Week 40; moderate; n= 37, 36	21	21		

Week 40; severe; n= 37, 36	9	6		
Week 40; very severe; n= 37, 36	0	0		
Week 52; mild; n= 39, 36	6	7		
Week 52; n= moderate; n= 39, 36	24	23		
Week 52; severe; n= 39, 36	9	6		
Week 52; very severe; n= 39, 36	0	0		

Notes:

[555] - ITT Population

[556] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with patient global impression of change (PGIC)score in Part B

End point title	Number of participants with patient global impression of change (PGIC)score in Part B

End point description:

Participants completed a PGIC questions at Week 4, 8, 16, 24, 40 and 52. Response options were on a 7 point Likert scale ranging from much better to much worse. PGIC was re-coded from a categorical to numerical value prior to analysis as: much worse = -3, worse = -2, slightly worse = -1, no change = 0, slightly better = 1, better = 2, much better = 3.A categorical summary of PGIC is presented by treatment and visit.Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Day 392 in Part B

End point values	Placebo	DNX 75 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[557]	45[558]		
Units: Participants				
Week 4; much worse; n= 44, 39	0	1		
Week 4; worse; n= 44, 39	1	4		
Week 4; slightly worse; n= 44, 39	1	0		
Week 4; no change; n= 44, 39	18	17		
Week 4; slightly better; n= 44, 39	15	12		
Week 4; better; n= 44, 39	9	4		
Week 4; much better; n= 44, 39	0	1		
Week 8; much worse; n= 44, 39	1	0		
Week 8; worse; n= 44, 39	1	1		
Week 8; slightly worse; n= 44, 39	6	5		
Week 8; no change; n= 44, 39	16	18		
Week 8; slightly better; n= 44, 39	15	10		
Week 8; better; n= 44, 39	4	4		
Week 8; much better; n= 44, 39	1	1		
Week 16; much worse; n= 45, 40	0	1		
Week 16; worse; n= 45, 40	0	1		
Week 16; slightly worse; n= 45, 40	0	3		
Week 16; no change; n= 45, 40	21	17		

Week 16; slightly better; n= 45, 40	20	13		
Week 16; better; n= 45, 40	3	2		
Week 16; much better; n= 45, 40	1	3		
Week 24; much worse; n= 44, 38	0	1		
Week 4; worse; n= 44, 38	1	2		
Week 24; slightly worse; n= 44, 38	3	3		
Week 24; no change; n= 44, 38	15	13		
Week 24; slightly better; n= 44, 38	16	9		
Week 24; better; n= 44, 38	8	8		
Week 24; much better; n= 44, 38	1	2		
Week 40; much worse; n= 37, 36	0	0		
Week 40; worse; n= 37, 36	2	1		
Week 40; slightly worse; n= 37, 36	3	7		
Week 40; no change; n=37, 36	9	12		
Week 40; slightly better; n=37, 36	14	7		
Week 40; better; n= 37, 36	7	7		
Week 40; much better; n= 37, 36	2	2		
Week 52; much worse; n= 39, 35	0	1		
Week 52; worse; n= 39, 35	1	0		
Week 52; slightly worse; n= 39, 35	3	7		
Week 52; no change; n= 39, 35	14	15		
Week 52; slightly better; n= 39, 35	9	4		
Week 52; better; n= 39, 35	11	5		
Week 52; much better; n= 39, 35	1	3		

Notes:

[557] - ITT Population

[558] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of the study treatment up to Day 28 in Part A and up to Day 392 in Part B.

Adverse event reporting additional description:

On treatment SAEs and non-serious AEs were reported for the All Subjects Population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	DNX 50 mg

Reporting group description:

Participants received one immediate release tablet of danirixin (DNX) 50 mg BID with food and water for 2 weeks. Participants were permitted to continue taking inhaled maintenance medications. Rescue medications for acute symptoms were also permitted (e.g. short acting bronchodilators).

Reporting group title	DNX 75 mg

Reporting group description:

Participants received one immediate release tablet of danirixin (DNX) 75 mg BID with food and water for 52 weeks. It was administered on top of the participant's current standard of care. Participants were permitted to continue taking inhaled maintenance medications. Rescue medications for acute symptoms were also permitted (e.g. short acting bronchodilators).

Reporting group title	Placebo

Reporting group description:

Participants received one tablet of placebo twice daily with food and water for 52 weeks. It was administered on top of the participant's current standard of care. Participants were permitted to continue taking inhaled maintenance medications. Rescue medications for acute symptoms were also permitted (e.g. short acting bronchodilators).

Serious adverse events	DNX 50 mg	DNX 75 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)	10 / 45 (22.22%)	10 / 48 (20.83%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gallbladder adenoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer			

subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 9 (0.00%)	2 / 45 (4.44%)	4 / 48 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 5	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord leukoplakia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood sodium decreased			

subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device loosening			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Coronary artery stenosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis sclerosing			

subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	3 / 48 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis infective			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obesity			
subjects affected / exposed	0 / 9 (0.00%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	DNX 50 mg	DNX 75 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 9 (55.56%)	25 / 45 (55.56%)	25 / 48 (52.08%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 9 (11.11%)	4 / 45 (8.89%)	4 / 48 (8.33%)
occurrences (all)	1	5	5
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 9 (11.11%)	3 / 45 (6.67%)	0 / 48 (0.00%)
occurrences (all)	1	3	0

Malaise			
subjects affected / exposed	1 / 9 (11.11%)	0 / 45 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 9 (11.11%)	1 / 45 (2.22%)	2 / 48 (4.17%)
occurrences (all)	1	1	3
Abdominal pain upper			
subjects affected / exposed	0 / 9 (0.00%)	0 / 45 (0.00%)	3 / 48 (6.25%)
occurrences (all)	0	0	5
Diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)	4 / 45 (8.89%)	8 / 48 (16.67%)
occurrences (all)	0	4	8
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 9 (11.11%)	5 / 45 (11.11%)	3 / 48 (6.25%)
occurrences (all)	1	6	4
Hyperhidrosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 45 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	1 / 9 (11.11%)	1 / 45 (2.22%)	0 / 48 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 9 (0.00%)	5 / 45 (11.11%)	0 / 48 (0.00%)
occurrences (all)	0	5	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 9 (11.11%)	13 / 45 (28.89%)	16 / 48 (33.33%)
occurrences (all)	1	14	28
Cystitis			
subjects affected / exposed	0 / 9 (0.00%)	5 / 45 (11.11%)	3 / 48 (6.25%)
occurrences (all)	0	8	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 July 2014	Amendment included changes to fibrinogen inclusion criteria; addition of macrolide exclusion criteria; addition of screen failure data collection; addition of COPD exacerbation or pneumonia confirmation criteria. Also included are several minor clarifications. In appendix 4 the study questionnaires and diary were added for reference purposes
08 October 2014	Amendment included changes to the age inclusion criteria and supplemental information on requirements for participants receiving oxygen therapy.
05 August 2015	Amendment included a change which allow data from the interim analysis for EXACT-RS to be externally disclosed prior to study end or release of the clinical pharmacology study report (CPSR). The scope of the exit interview expanded to include study sites in Germany in addition to the United States. Stopping of recruitment prior to reaching the estimated approximate number of participants to be enrolled in Part B was also addressed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported