Study Results

Participant Flow

Recruitment Details	A total of 45 participants were enrolled between 09 Nov 2021 and 28 Feb 2023 at a total of three clinical sites in the Netherlands (2 sites) and the United Kingdom (1 site).
Pre-assignment Details	For the single ascending dose (SAD) part, a total of 118 potentially eligible participants were screened, and 42 of these participants were included in the study. For the multiple ascending dose (MAD) part, a total of 11 potentially eligible participants were screened, and 3 of these participants were included in the study.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a subcutaneous (SC) injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: Pooled Placebo	Healthy participants received a single dose of placebo matching INS-3001 administered as a SC injection on Day 1 of the study within each SAD cohort.
MAD: INS-3001 25 mg	Participants with moderate aortic valve stenosis (AVS) received multiple 25 mg doses of INS-3001 administered as a SC injection once daily (qd) on Day 1 to Day 14 of the study.
MAD: Pooled Placebo	Participants with moderate AVS received multiple doses of placebo matching INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Overall Study

Number of Participants Who:	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Started Study	3	3	6	6	6	6
Received INS-3001 or Placebo	3	3	6	6	6	6
Completed Study	3	3	6	6	6	6
Did Not Complete Study	0	0	0	0	0	0
Reason for Discontinuation:						
Adverse Event	0	0	0	0	0	0

Number of Participants Who:	SAD: Pooled Placebo	MAD: INS-3001 25 mg	MAD: Pooled Placebo
Started Study	12	1	2
Received INS-3001 or Placebo	12	1	2
Completed Study	12	1	1
Did Not Complete Study	0	0	1
Reason for Discontinuation:			
Adverse Event	0	0	1

Baseline Characteristics

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: Pooled Placebo	Healthy participants received a single dose of placebo matching INS-3001 administered as a SC injection on Day 1 of the study within each SAD cohort.
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.
MAD: Pooled Placebo	Participants with moderate AVS received multiple doses of placebo matching INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Baseline Measures

		SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants		3	3	6	6	6	6
Age, Categorical Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
	<=18 years	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Between 18 and 65 years	3 (100%)	3 (100%)	6 (100%)	6 (100%)	6 (100%)	6 (100%)
	>=65 years	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sex: Female, Male Measure Count of	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants

		SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Type: Participants Unit of measure: participants	Female	0 (0%)	1 (33.33%)	0 (0%)	0 (0%)	0 (0%)	2 (33.33%)
	Male	3 (100%)	2 (66.67%)	6 (100%)	6 (100%)	6 (100%)	4 (66.67%)
Ethnicity (NIH/ OMB) Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
	Hispanic or Latino	0 (0%)	0 (0%)	1 (16.67%)	0 (0%)	1 (16.67%)	0 (0%)
	Not Hispanic or Latino	3 (100%)	3 (100%)	5 (83.33%)	6 (100%)	5 (83.33%)	6 (100%)
	Unknown or Not Reported	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Race (NIH/OMB) Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
	American Indian or Alaska Native	0 (0%)	0 (0%)	1 (16.67%)	0 (0%)	1 (16.67%)	0 (0%)
	Asian	0 (0%)	0 (0%)	0 (0%)	1 (16.67%)	0 (0%)	0 (0%)
	Native Hawaiian or Other Pacific Islander	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Black or African American	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	White	3 (100%)	3 (100%)	5 (83.33%)	5 (83.33%)	5 (83.33%)	5 (83.33%)
	More than one race	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (16.67%)
	Unknown or Not Reported	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

		SAD: Pooled Placebo	MAD: INS-3001 25 mg	MAD: Pooled Placebo	Total
Overall Number of Participants		12	1	2	45
Age, Categorical Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	12 participants	1 participant	2 participants	45 participants
	<=18 years	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Between 18 and 65 years	12 (100%)	0 (0%)	0 (0%)	42 (93.33%)
	>=65 years	0 (0%)	1 (100%)	2 (100%)	3 (6.67%)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	12 participants	1 participant	2 participants	45 participants
	Female	1 (8.33%)	0 (0%)	0 (0%)	4 (8.89%)
	Male	11 (91.67%)	1 (100%)	2 (100%)	41 (91.11%)
Ethnicity (NIH/ OMB) Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	12 participants	1 participant	2 participants	45 participants
	Hispanic or Latino	0 (0%)	0 (0%)	0 (0%)	2 (4.44%)
	Not Hispanic or Latino	12 (100%)	1 (100%)	0 (0%)	41 (91.11%)
	Unknown or Not Reported	0 (0%)	0 (0%)	2 (100%)	2 (4.44%)
Race (NIH/OMB) Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	12 participants	1 participant	2 participants	45 participants
	American Indian or Alaska Native	0 (0%)	0 (0%)	0 (0%)	2 (4.44%)
	Asian	1 (8.33%)	0 (0%)	0 (0%)	2 (4.44%)

		SAD: Pooled Placebo	MAD: INS-3001 25 mg	MAD: Pooled Placebo	Total
	Native Hawaiian or Other Pacific Islander	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Black or African American	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	White	11 (91.67%)	1 (100%)	1 (50%)	39 (86.67%)
	More than one race	0 (0%)	0 (0%)	0 (0%)	1 (2.22%)
	Unknown or Not Reported	0 (0%)	0 (0%)	1 (50%)	1 (2.22%)

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE)
Measure Description	A TEAE was defined as any event not present prior to the first administration of the study drug or any event already present that worsened in either severity or frequency following exposure to the study drug. Any clinically significant observations in the results of clinical laboratory, vital signs, 12-lead electrocardiograms (ECGs), continuous cardiac monitoring (telemetry; SAD part only) physical examinations, or injection site assessments, as determined by the Investigator, were recorded as TEAEs.
Time Frame	SAD: Day 1 to Day 24; MAD: Day 1 to Day 37

Analysis Population Description

Safety Analysis Set: Included all randomized participants who received at least 1 dose of INS-3001 or placebo.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

	Description
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: Pooled Placebo	Healthy participants received a single dose of placebo matching INS-3001 administered as a SC injection on Day 1 of the study within each SAD cohort.
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.
MAD: Pooled Placebo	Participants with moderate AVS received multiple doses of placebo matching INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed	3	3	6	6	6	6
Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE) Measure Type: Count of Participants Unit of measure: participants	0 (0%)	1 (33.33%)	3 (50%)	3 (50%)	6 (100%)	5 (83.33%)

	SAD: Pooled Placebo	MAD: INS-3001 25 mg	MAD: Pooled Placebo
Overall Number of Participants Analyzed	12	1	2

	SAD: Pooled Placebo	MAD: INS-3001 25 mg	MAD: Pooled Placebo
Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE) Measure Type: Count of Participants Unit of measure: participants	4 (33.33%)	1 (100%)	2 (100%)

2. Secondary Outcome Measure:

Measure Title	SAD Only: Serum Concentration of INS-3001
Measure Description	Blood samples of 4 mL were taken via an indwelling intravenous (IV) catheter or by direct venipuncture into heparin tubes. For calculation of descriptive statistics, below quantification level (BQL) values are set 1/2 lower limit of quantification (LLOQ) according to the statistical analysis plan (SAP).
Time Frame	Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose

Analysis Population Description

Pharmacokinetic (PK) Analysis Set: Included all randomized participants in SAD part of the study who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

Measured Values

		SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed		3	3	6	6	6	6
SAD Only: Serum Concentration of INS-3001 Mean (Standard Deviation) Unit of measure: ng/mL	[Not specified]						
Pre-dose	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
		NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]
0.5 Hours Post-dose	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
		53.0 (4.44)	112 (22.3)	785 (236)	1213 (550)	931 (355)	1468 (607)
0.75 Hours Post-dose	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
		54.8 (4.00)	157 (34.0)	844 (231)	1514 (685)	1392 (488)	2377 (858)
1 Hour Post-dose	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
		49.8 (4.95)	170 (28.2)	895 (217)	1705 (657)	1910 (703)	3165 (895)
1.5 Hours Post-dose	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
		32.5 (3.18)	173 (29.3)	785 (165)	1777 (473)	2512 (800)	4622 (1066)
2 Hours Post-dose	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
		21.9 (1.41)	151 (23.6)	634 (126)	1492 (279)	2687 (645)	5430 (1265)
3 Hours Post-dose	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
		8.10 (0.471)	93.6 (27.0)	320 (55.0)	790 (135)	2033 (240)	5160 (1874)
4 Hours Post-dose	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
		NA (NA) [1]	55.5 (21.8)	168 (43.6)	414 (93.7)	1225 (232)	3540 (1653)
6 Hours Post-dose	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
		NA (NA) [1]	15.9 (7.41)	49.2 (16.8)	128 (46.6)	415 (120)	1160 (577)
8 Hours Post-dose	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants

		SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
		NA (NA) [1]	5.94 (3.24)	19.2 (6.23)	51.6 (21.9)	139 (36.1)	423 (229)
12 Hours Post-dose	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
		NA (NA) [1]	NA (NA) [1]	7.34 (1.16)	16.0 (2.48)	34.2 (4.40)	91.4 (48.5)
24 Hours Post-dose	Number Analyzed	3 participants	3 participants	6 participants	6 participants	6 participants	6 participants
		NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	8.74 (1.26)	15.1 (5.70)
36 Hours Post-dose	Number Analyzed	3 participants	3 participants	6 participants	5 participants	6 participants	6 participants
		NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	4.44 (1.56)	9.00 (2.70)
48 Hours Post-dose	Number Analyzed	3 participants	3 participants	6 participants	5 participants	6 participants	6 participants
		NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]

[1] Data not available as INS-3001 concentration was below the LLOQ.

3. Secondary Outcome Measure:

Measure Title	MAD Only: Serum Concentration of INS-3001
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes. For calculation of descriptive statistics, BQL values are set 1/2 LLOQ according to the SAP.
Time Frame	Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, and 12 hours post-dose; Days 2, 3 and 8: Pre-dose; Day 14: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, and 48 hours post-dose

Analysis Population Description

PK Analysis Set: Included all randomized participants in MAD part of the study who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	MAD: INS-3001 25 mg
Overall Number of Participants Analyzed	1
MAD Only: Serum Concentration of INS-3001 Mean (Standard Deviation) Unit of measure: ng/mL	
Day 1: Pre-dose	NA (NA) [1]
Day 1: 0.5 Hours Post-dose	248 (NA) [2]
Day 1: 0.75 Hours Post-dose	367 (NA) [2]
Day 1: 1 Hour Post-dose	357 (NA) [2]
Day 1: 1.5 Hours Post-dose	702 (NA) [2]
Day 1: 2 Hours Post-dose	442 (NA) [2]
Day 1: 3 Hours Post-dose	269 (NA) [2]
Day 1: 4 Hours Post-dose	185 (NA) [2]
Day 1: 6 Hours Post-dose	76.9 (NA) [2]
Day 1: 8 Hours Post-dose	25.2 (NA) [2]
Day 1: 12 Hours Post-dose	5.82 (NA) [2]
Day 2: Pre-dose	NA (NA) [1]
Day 3: Pre-dose	NA (NA) [1]
Day 8: Pre-dose	NA (NA) [1]
Day 14: Pre-dose	5.65 (NA) [2]
Day 14: 0.5 Hours Post-dose	271 (NA) [2]
Day 14: 0.75 Hours Post-dose	448 (NA) [2]
Day 14: 1 Hour Post-dose	512 (NA) [2]
Day 14: 1.5 Hours Post-dose	618 (NA) [2]

	MAD: INS-3001 25 mg
Day 14: 2 Hours Post-dose	456 (NA) [2]
Day 14: 3 Hours Post-dose	329 (NA) [2]
Day 14: 4 Hours Post-dose	178 (NA) [2]
Day 14: 6 Hours Post-dose	71.8 (NA) [2]
Day 14: 8 Hours Post-dose	34.1 (NA) [2]
Day 14: 12 Hours Post-dose	13.1 (NA) [2]
Day 14: 24 Hours Post-dose	NA (NA) [1]
Day 14: 48 Hours Post-dose	NA (NA) [1]

[1] Data not available as INS-3001 concentration was below the LLOQ.
[2] Standard deviation not available as only 1 participant had data collected.

4. Secondary Outcome Measure:

Measure Title	MAD Only: Trough Plasma Concentration (Ctrough) of INS-3001
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes. Ctrough was defined as the pre-dose plasma concentration on Days 2, 3, 8 and 14.
Time Frame	Days 2, 3, 8, and 14: Pre-dose

Analysis Population Description

PK Analysis Set: Included all randomized participants in MAD part of the study who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	MAD: INS-3001 25 mg
Overall Number of Participants Analyzed	1

	MAD: INS-3001 25 mg
MAD Only: Trough Plasma Concentration (Ctrough) of INS-3001 Mean (Standard Deviation) Unit of measure: ng/mL	
Day 2: Pre-dose	NA (NA) [1]
Day 3: Pre-dose	NA (NA) [1]
Day 8: Pre-dose	NA (NA) [1]
Day 14: Pre-dose	5.65 (NA) [2]

[1] Data not available as INS-3001 concentration was below the LLOQ.
[2] Standard deviation not available as only 1 participant had data collected.

5. Secondary Outcome Measure:

Measure Title	Maximum Plasma Concentration (Cmax) of INS-3001
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes. Cmax was defined as the observed peak analyte concentration obtained directly from the experimental data without interpolation, expressed in concentration units.
Time Frame	SAD - Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose. MAD - Day 1 and Day 14: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 48, and 168 (Day 14 only) hours post-dose.

Analysis Population Description

PK Analysis Set: Included all randomized participants who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

	Description
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed	3	3	6	6	6	6
Maximum Plasma Concentration (Cmax) of INS-3001 Mean (Standard Deviation) Unit of measure: ng/mL						
Day 1	54.8 (4.00)	177 (32.0)	911 (200)	1862 (549)	2757 (633)	5868 (1325)
Day 14	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]

[1] Data was not collected on Day 14 for participants in the SAD part of the study.

	MAD: INS-3001 25 mg
Overall Number of Participants Analyzed	1
Maximum Plasma Concentration (Cmax) of INS-3001 Mean (Standard Deviation) Unit of measure: ng/mL	
Day 1	702 (NA) [1]
Day 14	618 (NA) [2]

[1] Standard deviation not available as only 1 participant had data collected.
[2] Data was not collected on Day 14 for participants in the SAD part of the study.

Statistical Analysis 1 for Maximum Plasma Concentration (Cmax) of INS-3001

Statistical Analysis Overview	Comparison Group Selection	SAD: INS-3001 1 mg, SAD: INS-3001 5 mg, SAD: INS-3001 25 mg, SAD: INS-3001 50 mg, SAD: INS-3001 100 mg, SAD: INS-3001 200 mg
	Comments	Power Model Analysis
	Type of Statistical Test	Other
	Comments	Dose proportionality for INS-3001 was explored using a power model on log transformed PK parameters across the 1 mg to 200 mg dose range. Model: log(PK) = slope*log(dose) + intercept + error.

Method of Estimation	Estimation Parameter	Slope
	Estimated Value	0.889
	Confidence Interval	(2-Sided) 95% 0.831 to 0.946
	Estimation Comments	[Not specified]

6. Secondary Outcome Measure:

Measure Title	Time to Cmax (Tmax) of INS-3001
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes. Tmax was defined as the first observed time to reach peak analyte concentration obtained directly from the experimental data without interpolation, expressed in time units.
Time Frame	SAD - Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose. MAD - Day 1 and Day 14: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 48, and 168 (Day 14 only) hours post-dose.

Analysis Population Description

PK Analysis Set: Included all randomized participants who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

	Description
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed	3	3	6	6	6	6
Time to Cmax (Tmax) of INS-3001 Median (Full Range) Unit of measure: hours						
Day 1	0.75 (0.73 to 0.75)	1.00 (1.00 to 1.50)	1.00 (0.75 to 1.50)	1.50 (0.77 to 2.00)	2.01 (1.50 to 3.03)	2.50 (1.50 to 3.02)
Day 14	NA (NA to NA) [1]	NA (NA to NA) [1]	NA (NA to NA) [1]	NA (NA to NA) [1]	NA (NA to NA) [1]	NA (NA to NA) [1]

[1] Data was not collected on Day 14 for participants in the SAD part of the study.

	MAD: INS-3001 25 mg
Overall Number of Participants Analyzed	1

	MAD: INS-3001 25 mg
Time to Cmax (Tmax) of INS-3001 Median (Full Range) Unit of measure: hours	
Day 1	1.50 (1.50 to 1.50)
Day 14	1.48 (1.48 to 1.48)

7. Secondary Outcome Measure:

Measure Title	Time of Last Measurable Observed Concentration (Tlast) of INS-3001
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes.
Time Frame	SAD - Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose. MAD - Day 14: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 48, and 168 hours post-dose.

Analysis Population Description

PK Analysis Set: Included all randomized participants who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

	Description
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed	3	3	6	6	6	6
Time of Last Measurable Observed Concentration (Tlast) of INS-3001 Median (Full Range) Unit of measure: hours	3.00 (3.00 to 3.03)	8.02 (6.00 to 8.02)	12.00 (12.00 to 12.00)	12.00 (12.00 to 24.03)	36.00 (24.02 to 36.07)	36.00 (36.00 to 48.00)

	MAD: INS-3001 25 mg
Overall Number of Participants Analyzed	1
Time of Last Measurable Observed Concentration (Tlast) of INS-3001 Median (Full Range) Unit of measure: hours	11.98 (11.98 to 11.98)

8. Secondary Outcome Measure:

Measure Title	Apparent Terminal Half-Life (t1/2) of INS-3001
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes. Calculated as: Ln (2) (0.693)/kel, where kel represents the elimination rate constant.
Time Frame	SAD - Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose MAD - Day 14: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 48, and 168 hours post-dose.

Analysis Population Description

PK Analysis Set: Included all randomized participants who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed	3	3	6	6	6	6
Apparent Terminal Half-Life (t1/2) of INS-3001 Mean (Standard Deviation) Unit of measure: hours	0.751 (0.0777)	1.18 (0.266)	2.36 (0.329)	3.32 (2.11)	7.40 (2.30)	10.7 (3.89)

	MAD: INS-3001 25 mg
Overall Number of Participants Analyzed	1

	MAD: INS-3001 25 mg
Apparent Terminal Half-Life (t1/2) of INS-3001 Mean (Standard Deviation) Unit of measure: hours	2.48 (NA) [1]

[1] Standard deviation not available as only 1 participant had data collected.

9. Secondary Outcome Measure:

Measure Title	MAD Only: Effective Terminal Phase Half-life of INS-3001 Based on the Degree of Area Under the Plasma Concentration-time Curve (AUC) Accumulation (t1/2 Eff AUC)
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes.
Time Frame	Day 14: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 48, and 168 hours post-dose

Analysis Population Description

PK Analysis Set: Included all randomized participants in MAD part of the study who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	MAD: INS-3001 25 mg
Overall Number of Participants Analyzed	1
MAD Only: Effective Terminal Phase Half-life of INS-3001 Based on the Degree of Area Under the Plasma Concentration-time Curve (AUC) Accumulation (t1/2 Eff AUC) Mean (Standard Deviation) Unit of measure: hours	6.84 (NA) [1]

[1] Standard deviation not available as only 1 participant had data collected.

10. Secondary Outcome Measure:

Measure Title	SAD Only: AUC of INS-3001 From Time 0 to Tmax (AUC0-t)
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes.
Time Frame	Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose

Analysis Population Description

PK Analysis Set: Included all randomized participants in SAD part of the study who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

Measured Values

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed	3	3	6	6	6	6
SAD Only: AUC of INS-3001 From Time 0 to Tmax (AUC0-t) Mean (Standard Deviation) Unit of measure: h#ng/mL	87.2 (6.62)	544 (75.6)	2389 (406)	5219 (950)	9882 (1188)	22845 (6929)

Statistical Analysis 1 for SAD Only: AUC of INS-3001 From Time 0 to Tmax (AUC0-t)

Statistical Analysis Overview	Comparison Group Selection	SAD: INS-3001 1 mg, SAD: INS-3001 5 mg, SAD: INS-3001 25 mg, SAD: INS-3001 50 mg, SAD: INS-3001 100 mg, SAD: INS-3001 200 mg
	Comments	Power Model Analysis
	Type of Statistical Test	Other
	Comments	Dose proportionality for INS-3001 was explored using a power model on log transformed PK parameters across the 1 mg to 200 mg dose range. Model: log(PK) = slope*log(dose) + intercept + error.

Method of Estimation	Estimation Parameter	Slope
	Estimated Value	1.028
	Confidence Interval	(2-Sided) 95% 0.986 to 1.070
	Estimation Comments	[Not specified]

11. Secondary Outcome Measure:

Measure Title	SAD Only: AUC of INS-3001 From Time 0 (Dosing) Extrapolated to Infinity (AUC0-inf)
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes. Calculated as: AUC0 inf=AUC0 t+Clast/kel where Clast is the last observed quantifiable concentration.
Time Frame	Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose

Analysis Population Description

PK Analysis Set: Included all randomized participants in SAD part of the study who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

	Description
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

Measured Values

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed	3	3	6	6	6	6
SAD Only: AUC of INS-3001 From Time 0 (Dosing) Extrapolated to Infinity (AUC0-inf) Mean (Standard Deviation) Unit of measure: h#ng/mL	96.0 (5.66)	557 (74.4)	2413 (405)	5264 (949)	9946 (1195)	22964 (6976)

Statistical Analysis 1 for SAD Only: AUC of INS-3001 From Time 0 (Dosing) Extrapolated to Infinity (AUC0-inf)

Statistical Analysis Overview	Comparison Group Selection	SAD: INS-3001 1 mg, SAD: INS-3001 5 mg, SAD: INS-3001 25 mg, SAD: INS-3001 50 mg, SAD: INS-3001 100 mg, SAD: INS-3001 200 mg
	Comments	Power Model Analysis
	Type of Statistical Test	Other
	Comments	Dose proportionality for INS-3001 was explored using a power model on log transformed PK parameters across the 1 mg to 200 mg dose range. Model: log(PK) = slope*log(dose) + intercept + error.

Method of Estimation	Estimation Parameter	Slope
	Estimated Value	1.014
	Confidence Interval	(2-Sided) 95% 0.972 to 1.056
	Estimation Comments	[Not specified]

12. Secondary Outcome Measure:

Measure Title	MAD Only: AUC of INS-3001 Over a Dosing Interval Tau (AUC0-tau)
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes.
Time Frame	Day 1 and Day 14: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12 and 24 hours post-dose

Analysis Population Description

PK Analysis Set: Included all randomized participants in MAD part of the study who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	MAD: INS-3001 25 mg
Overall Number of Participants Analyzed	1
MAD Only: AUC of INS-3001 Over a Dosing Interval Tau (AUC0-tau) Mean (Standard Deviation) Unit of measure: h*ng/mL	
Day 1	1763 (NA) [1]
Day 14	1933 (NA) [1]

[1] Standard deviation not available as only 1 participant had data collected.

13. Secondary Outcome Measure:

Measure Title	SAD Only: Apparent Oral Clearance (CL/F) of INS-3001
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes. Calculated as: dose/AUC0-inf.
Time Frame	Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose

Analysis Population Description

PK Analysis Set: Included all randomized participants in SAD part of the study who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

Measured Values

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed	3	3	6	6	6	6
SAD Only: Apparent Oral Clearance (CL/F) of INS-3001 Mean (Standard Deviation) Unit of measure: L/h	10.4 (0.609)	9.08 (1.15)	10.6 (1.74)	9.75 (1.69)	10.2 (1.21)	9.28 (2.29)

14. Secondary Outcome Measure:

Measure Title	MAD Only: Apparent Oral Clearance at Steady State (CLss/F) of INS-3001
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes. Calculated as: dose/AUC0-tau.
Time Frame	Day 14: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 48, and 168 hours post-dose

Analysis Population Description

PK Analysis Set: Included all randomized participants in MAD part of the study who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	MAD: INS-3001 25 mg
Overall Number of Participants Analyzed	1
MAD Only: Apparent Oral Clearance at Steady State (CLss/F) of INS-3001 Mean (Standard Deviation) Unit of measure: L/h	12.9 (NA) [1]

[1] Standard deviation not available as only 1 participant had data collected.

15. Secondary Outcome Measure:

Measure Title	Apparent Volume of Distribution of INS-3001 at Terminal Phase (Vz/F)
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes. Calculated as (CL/F)/kel (Day 1) or as (CLss/F)/kel (Day 14).
Time Frame	SAD - Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose. MAD - Day 14: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 48, and 168 hours post-dose.

Analysis Population Description

PK Analysis Set: Included all randomized participants who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

	Description
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed	3	3	6	6	6	6
Apparent Volume of Distribution of INS-3001 at Terminal Phase (Vz/F) Mean (Standard Deviation) Unit of measure: Liters	11.3 (1.78)	15.4 (3.74)	36.2 (8.26)	44.1 (23.7)	106 (28.1)	133 (19.0)

	MAD: INS-3001 25 mg
Overall Number of Participants Analyzed	1
Apparent Volume of Distribution of INS-3001 at Terminal Phase (Vz/F) Mean (Standard Deviation) Unit of measure: Liters	46.4 (NA) [1]

[1] Standard deviation not available as only 1 participant had data collected.

16. Secondary Outcome Measure:

Measure Title	MAD Only: Accumulation Ratio (Rac) of INS-3001 of Day 14 Versus Day 1
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes.
Time Frame	Day 14: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 48, and 168 hours post-dose

Analysis Population Description

PK Analysis Set: Included all randomized participants in MAD part of the study who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	MAD: INS-3001 25 mg
Overall Number of Participants Analyzed	1
MAD Only: Accumulation Ratio (Rac) of INS-3001 of Day 14 Versus Day 1 Mean (Standard Deviation) Unit of measure: Ratio	1.10 (NA) [1]

[1] Standard deviation not available as only 1 participant had data collected.

17. Secondary Outcome Measure:

Measure Title	Dose Normalized Cmax (Cmax/Dose) of INS-3001
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes. Cmax was defined as the observed peak analyte concentration obtained directly from the experimental data without interpolation, expressed in concentration units.
Time Frame	SAD - Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose. MAD - Day 1 and Day 14: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 48, and 168 (Day 14 only) hours post-dose.

Analysis Population Description

PK Analysis Set: Included all randomized participants who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed	3	3	6	6	6	6
Dose Normalized Cmax (Cmax/Dose) of INS-3001 Mean (Standard Deviation) Unit of measure: ng/mL/mg						
Day 1	54.8 (4.00)	35.4 (6.41)	36.4 (8.01)	37.2 (11.0)	27.6 (6.33)	29.3 (6.62)
Day 14	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]

[1] Data was only collected on Day 14 for participants in MAD part of the study.

	MAD: INS-3001 25 mg
Overall Number of Participants Analyzed	1

	MAD: INS-3001 25 mg
Dose Normalized Cmax (Cmax/Dose) of INS-3001 Mean (Standard Deviation) Unit of measure: ng/mL/mg	
Day 1	28.1 (NA) [1]
Day 14	24.7 (NA) [1]

[1] Standard deviation not available as only 1 participant had data collected.

18. Secondary Outcome Measure:

Measure Title	SAD Only: Dose Normalized AUC0-t (AUC0-t/Dose) of INS-3001
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes.
Time Frame	Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose

Analysis Population Description

PK Analysis Set: Included all randomized participants in SAD part of the study who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

Measured Values

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed	3	3	6	6	6	6
SAD Only: Dose Normalized AUC0-t (AUC0-t/Dose) of INS-3001 Mean (Standard Deviation) Unit of measure: h#ng/mL/mg	87.2 (6.62)	109 (15.1)	95.5 (16.3)	104 (19.0)	98.8 (11.9)	114 (34.6)

19. Secondary Outcome Measure:

Measure Title	SAD Only: Dose Normalized AUC0-inf (AUC0-inf/Dose) of INS-3001
Measure Description	Blood samples of 4 mL were taken via an indwelling IV catheter or by direct venipuncture into heparin tubes. AUC0-inf was calculated as: AUC0 inf=AUC0 t+Clast/kel where Clast is the last observed quantifiable concentration.
Time Frame	Day 1: Pre-dose and 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose

Analysis Population Description

PK Analysis Set: Included all randomized participants in SAD part of the study who received at least 1 dose of INS-3001 and provided sufficient bioanalytical assessment results to calculate reliable estimates of the PK parameters.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

	Description
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

Measured Values

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg
Overall Number of Participants Analyzed	3	3	6	6	6	6
SAD Only: Dose Normalized AUC0-inf (AUC0-inf/ Dose) of INS-3001 Mean (Standard Deviation) Unit of measure: h#ng/mL/mg	96.0 (5.66)	111 (14.9)	96.5 (16.2)	105 (19.0)	99.5 (11.9)	115 (34.9)

20. Secondary Outcome Measure:

Measure Title	MAD Only: Aortic Valve 18F-sodium Fluoride (NaF) Uptake
Measure Description	Aortic valve 18F-NaF uptake was determined by the tissue to background ratio (TBR) derived from 18F-NaF-positron emission tomography (PET) scans. An 18F-NaF-PET scan was performed approximately 60 minutes after IV injection of 125 megabecquerel (MBq) 18F-NaF.
Time Frame	24 hours prior to dosing on Day 1 and 2.5 hours post-dose on Day 14.

Analysis Population Description

Randomized Set: Included all participants in MAD part of the study who were assigned a randomization number in the study and had available data.

Reporting Groups

	Description
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.
MAD: Pooled Placebo	Participants with moderate AVS received multiple doses of placebo matching INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

Measured Values

		MAD: INS-3001 25 mg	MAD: Pooled Placebo
Overall Number of Participants Analyzed		1	2
MAD Only: Aortic Valve 18F-sodium Fluoride (NaF) Uptake Median (Full Range) Unit of measure: ratio	[Not specified]		
24 Hours Prior to Dosing on Day 1: Mean TBR	Number Analyzed	1 participant	2 participants
		1.83 (1.83 to 1.83)	1.75 (1.74 to 1.76)
24 Hours Prior to Dosing on Day 1: Maximum TBR	Number Analyzed	1 participant	2 participants
		3.10 (3.10 to 3.10)	2.35 (2.21 to 2.50)
Day 14 - 2.5 Hours Post-dose: Mean TBR	Number Analyzed	1 participant	1 participant
		1.70 (1.70 to 1.70)	1.83 (1.83 to 1.83)
Day 14 - 2.5 Hours Post-dose: Maximum TBR	Number Analyzed	1 participant	1 participant
		2.94 (2.94 to 2.94)	2.16 (2.16 to 2.16)

Reported Adverse Events

Time Frame	SAD: Day 1 to Day 24; MAD: Day 1 to Day 37
Adverse Event Reporting Description	A TEAE was defined as any event not present prior to the first administration of the study drug or any event already present that worsened in either severity or frequency following exposure to the study drug.

Reporting Groups

	Description
SAD: INS-3001 1 mg	Healthy participants received a single 1 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.

	Description
SAD: INS-3001 5 mg	Healthy participants received a single 5 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 25 mg	Healthy participants received a single 25 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 50 mg	Healthy participants received a single 50 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 100 mg	Healthy participants received a single 100 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: INS-3001 200 mg	Healthy participants received a single 200 mg dose of INS-3001 administered as a SC injection on Day 1 of the study.
SAD: Pooled Placebo	Healthy participants received a single dose of placebo matching INS-3001 administered as a SC injection on Day 1 of the study within each SAD cohort.
MAD: INS-3001 25 mg	Participants with moderate AVS received multiple 25 mg doses of INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.
MAD: Pooled Placebo	Participants with moderate AVS received multiple doses of placebo matching INS-3001 administered as a SC injection qd on Day 1 to Day 14 of the study.

All-Cause Mortality

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg
	Participants Affected/ Participants at Risk (%)	Participants Affected/ Participants at Risk (%)	Participants Affected/ Participants at Risk (%)	Participants Affected/ Participants at Risk (%)
Total All-Cause Mortality	0/3 (0%)	0/3 (0%)	0/6 (0%)	0/6 (0%)

	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg	SAD: Pooled Placebo	MAD: INS-3001 25 mg
	Participants Affected/ Participants at Risk (%)	Participants Affected/ Participants at Risk (%)	Participants Affected/ Participants at Risk (%)	Participants Affected/ Participants at Risk (%)
Total All-Cause Mortality	0/6 (0%)	0/6 (0%)	0/12 (0%)	0/1 (0%)

	MAD: Pooled Placebo
	Participants Affected/ Participants at Risk (%)
Total All-Cause Mortality	0/2 (0%)

Serious Adverse Events

	SAD: INS-3001 1 mg	SAD: INS-3001 5 mg	SAD: INS-3001 25 mg	SAD: INS-3001 50 mg
	Participants Affected/ Participants at Risk (%)	Participants Affected/ Participants at Risk (%)	Participants Affected/ Participants at Risk (%)	Participants Affected/ Participants at Risk (%)
Total	0/3 (0%)	0/3 (0%)	0/6 (0%)	0/6 (0%)

	SAD: INS-3001 100 mg	SAD: INS-3001 200 mg	SAD: Pooled Placebo	MAD: INS-3001 25 mg
	Participants Affected/ Participants at Risk (%)	Participants Affected/ Participants at Risk (%)	Participants Affected/ Participants at Risk (%)	Participants Affected/ Participants at Risk (%)
Total	0/6 (0%)	0/6 (0%)	0/12 (0%)	0/1 (0%)

	MAD: Pooled Placebo
	Participants Affected/ Participants at Risk (%)
Total	0/2 (0%)

Other (Non-Serious) Adverse Events

Frequency Threshold Above Which Other (Non-Serious) Adverse Events are Reported: 0%

	SAD: INS-3001 1 mg		SAD: INS-3001 5 mg		SAD: INS-3001 25 mg		SAD: INS-3001 50 mg	
	Participants Affected/ Participants at Risk (%)	# Events	Participants Affected/ Participants at Risk (%)	# Events	Participants Affected/ Participants at Risk (%)	# Events	Participants Affected/ Participants at Risk (%)	# Events
Total	0/3 (0%)	0	1/3 (33.33%)	1	3/6 (50%)	4	3/6 (50%)	5
Cardiac disorders								
Atrial fibrillation [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Palpitations [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Sinus tachycardia [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Gastrointestinal disorders								
Abdominal Pain [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Abdominal distension [1,2]	0/3 (0%)	0	1/3 (33.33%)	1	0/6 (0%)	0	0/6 (0%)	0

Diarrhea [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Dry mouth [1,2]	0/3 (0%)	0	0/3 (0%)	0	1/6 (16.67%)	1	0/6 (0%)	0
Lip dry [1,2]	0/3 (0%)	0	0/3 (0%)	0	1/6 (16.67%)	1	0/6 (0%)	0
Toothache [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
General disorders								
Asthenia [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Catheter site pain [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	1/6 (16.67%)	1
Chest pain [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Fatigue [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Injection site bruising [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Injection site erythema [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	1/6 (16.67%)	1
Injection site inflammation [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Injection site pain [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Non-cardiac chest pain [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Infections and infestations								
Nasopharyngitis [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Rhinitis [1,2]	0/3 (0%)	0	0/3 (0%)	0	1/6 (16.67%)	1	0/6 (0%)	0
Viral upper respiratory tract infection [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Injury, poisoning and procedural complications								
Contusion [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Thermal burn [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	1/6 (16.67%)	1
Investigations								
SARS-CoV-2 test positive [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	1/6 (16.67%)	1

	SAD: INS-3001 1 mg		SAD: INS-3001 5 mg		SAD: INS-3001 25 mg		SAD: INS-3001 50 mg	
	Participants Affected/ Participants at Risk (%)	# Events	Participants Affected/ Participants at Risk (%)	# Events	Participants Affected/ Participants at Risk (%)	# Events	Participants Affected/ Participants at Risk (%)	# Events
Metabolism and nutrition disorders								
Vitamin D deficiency [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Musculoskeletal and connective tissue disorders								
Back pain [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Muscle twitching [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Myalgia [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Nervous system disorders								
Dizziness [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0
Headache [1,2]	0/3 (0%)	0	0/3 (0%)	0	1/6 (16.67%)	1	1/6 (16.67%)	1
Presyncope [1,2]	0/3 (0%)	0	0/3 (0%)	0	0/6 (0%)	0	0/6 (0%)	0

[1] Indicates events were collected by systematic assessment.
[2] Term from vocabulary, MedDRA (24.0)

	SAD: INS-3001 100 mg		SAD: INS-3001 200 mg		SAD: Pooled Placebo		MAD: INS-3001 25 mg	
	Participants Affected/ Participants at Risk (%)	# Events	Participants Affected/ Participants at Risk (%)	# Events	Participants Affected/ Participants at Risk (%)	# Events	Participants Affected/ Participants at Risk (%)	# Events
Total	6/6 (100%)	14	5/6 (83.33%)	12	4/12 (33.33%)	6	1/1 (100%)	15
Cardiac disorders								
Atrial fibrillation [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Palpitations [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Sinus tachycardia [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Gastrointestinal disorders								
Abdominal Pain [1,2]	1/6 (16.67%)	1	0/6 (0%)	0	1/12 (8.33%)	1	0/1 (0%)	0

Abdominal distension [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Diarrhea [1,2]	1/6 (16.67%)	1	0/6 (0%)	0	1/12 (8.33%)	1	0/1 (0%)	0
Dry mouth [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Lip dry [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Toothache [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
General disorders								
Asthenia [1,2]	0/6 (0%)	0	0/6 (0%)	0	1/12 (8.33%)	1	0/1 (0%)	0
Catheter site pain [1,2]	0/6 (0%)	0	0/6 (0%)	0	1/12 (8.33%)	1	0/1 (0%)	0
Chest pain [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Fatigue [1,2]	0/6 (0%)	0	1/6 (16.67%)	1	0/12 (0%)	0	0/1 (0%)	0
Injection site bruising [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	1/1 (100%)	1
Injection site erythema [1,2]	4/6 (66.67%)	4	4/6 (66.67%)	4	0/12 (0%)	0	1/1 (100%)	10
Injection site inflammation [1,2]	1/6 (16.67%)	1	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Injection site pain [1,2]	3/6 (50%)	3	5/6 (83.33%)	5	0/12 (0%)	0	1/1 (100%)	1
Non-cardiac chest pain [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Infections and infestations								
Nasopharyngitis [1,2]	0/6 (0%)	0	0/6 (0%)	0	1/12 (8.33%)	1	0/1 (0%)	0
Rhinitis [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Viral upper respiratory tract infection [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	1/1 (100%)	1
Injury, poisoning and procedural complications								
Contusion [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	1/1 (100%)	1
Thermal burn [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Investigations								

	SAD: INS-3001 100 mg		SAD: INS-3001 200 mg		SAD: Pooled Placebo		MAD: INS-3001 25 mg	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
SARS-CoV-2 test positive [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Metabolism and nutrition disorders								
Vitamin D deficiency [1,2]	0/6 (0%)	0	0/6 (0%)	0	0/12 (0%)	0	1/1 (100%)	1
Musculoskeletal and connective tissue disorders								
Back pain [1,2]	0/6 (0%)	0	1/6 (16.67%)	1	0/12 (0%)	0	0/1 (0%)	0
Muscle twitching [1,2]	1/6 (16.67%)	1	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Myalgia [1,2]	0/6 (0%)	0	1/6 (16.67%)	1	0/12 (0%)	0	0/1 (0%)	0
Nervous system disorders								
Dizziness [1,2]	1/6 (16.67%)	1	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Headache [1,2]	2/6 (33.33%)	2	0/6 (0%)	0	0/12 (0%)	0	0/1 (0%)	0
Presyncope [1,2]	0/6 (0%)	0	0/6 (0%)	0	1/12 (8.33%)	1	0/1 (0%)	0

[1] Indicates events were collected by systematic assessment.
[2] Term from vocabulary, MedDRA (24.0)

	MAD: Pooled Placebo	
	Participants Affected/ Participants at Risk (%)	# Events
Total	2/2 (100%)	10
Cardiac disorders		
Atrial fibrillation [1,2]	2/2 (100%)	2
Palpitations [1,2]	1/2 (50%)	1
Sinus tachycardia [1,2]	1/2 (50%)	1
Gastrointestinal disorders		
Abdominal Pain [1,2]	1/2 (50%)	1

Abdominal distension [1,2]	0/2 (0%)	0
Diarrhea [1,2]	0/2 (0%)	0
Dry mouth [1,2]	0/2 (0%)	0
Lip dry [1,2]	0/2 (0%)	0
Toothache [1,2]	1/2 (50%)	1
General disorders		
Asthenia [1,2]	0/2 (0%)	0
Catheter site pain [1,2]	0/2 (0%)	0
Chest pain [1,2]	1/2 (50%)	2
Fatigue [1,2]	1/2 (50%)	1
Injection site bruising [1,2]	0/2 (0%)	0
Injection site erythema [1,2]	0/2 (0%)	0
Injection site inflammation [1,2]	0/2 (0%)	0
Injection site pain [1,2]	1/2 (50%)	1
Non-cardiac chest pain [1,2]	1/2 (50%)	1
Infections and infestations		
Nasopharyngitis [1,2]	0/2 (0%)	0
Rhinitis [1,2]	0/2 (0%)	0
Viral upper respiratory tract infection [1,2]	0/2 (0%)	0
Injury, poisoning and procedural complications		
Contusion [1,2]	0/2 (0%)	0
Thermal burn [1,2]	0/2 (0%)	0
Investigations		
SARS-CoV-2 test positive [1,2]	0/2 (0%)	0

	MAD: Pooled Placebo	
	Participants Affected/ Participants at Risk (%)	# Events
Metabolism and nutrition disorders		
Vitamin D deficiency [1,2]	0/2 (0%)	0
Musculoskeletal and connective tissue disorders		
Back pain [1,2]	0/2 (0%)	0
Muscle twitching [1,2]	0/2 (0%)	0
Myalgia [1,2]	0/2 (0%)	0
Nervous system disorders		
Dizziness [1,2]	0/2 (0%)	0
Headache [1,2]	0/2 (0%)	0
Presyncope [1,2]	0/2 (0%)	0

[1] Indicates events were collected by systematic assessment.
[2] Term from vocabulary, MedDRA (24.0)

Limitations and Caveats

During execution of the MAD part, preliminary findings from ongoing long-term toxicology studies in animals showed certain toxicity signals. As a precautionary measure and in order to allow full analysis, evaluation, and discussion of the toxicity findings, the current clinical study was put on temporary halt, after which the Sponsor decided to terminate the study. The trial was not ended early because of safety concerns for participants in this trial.