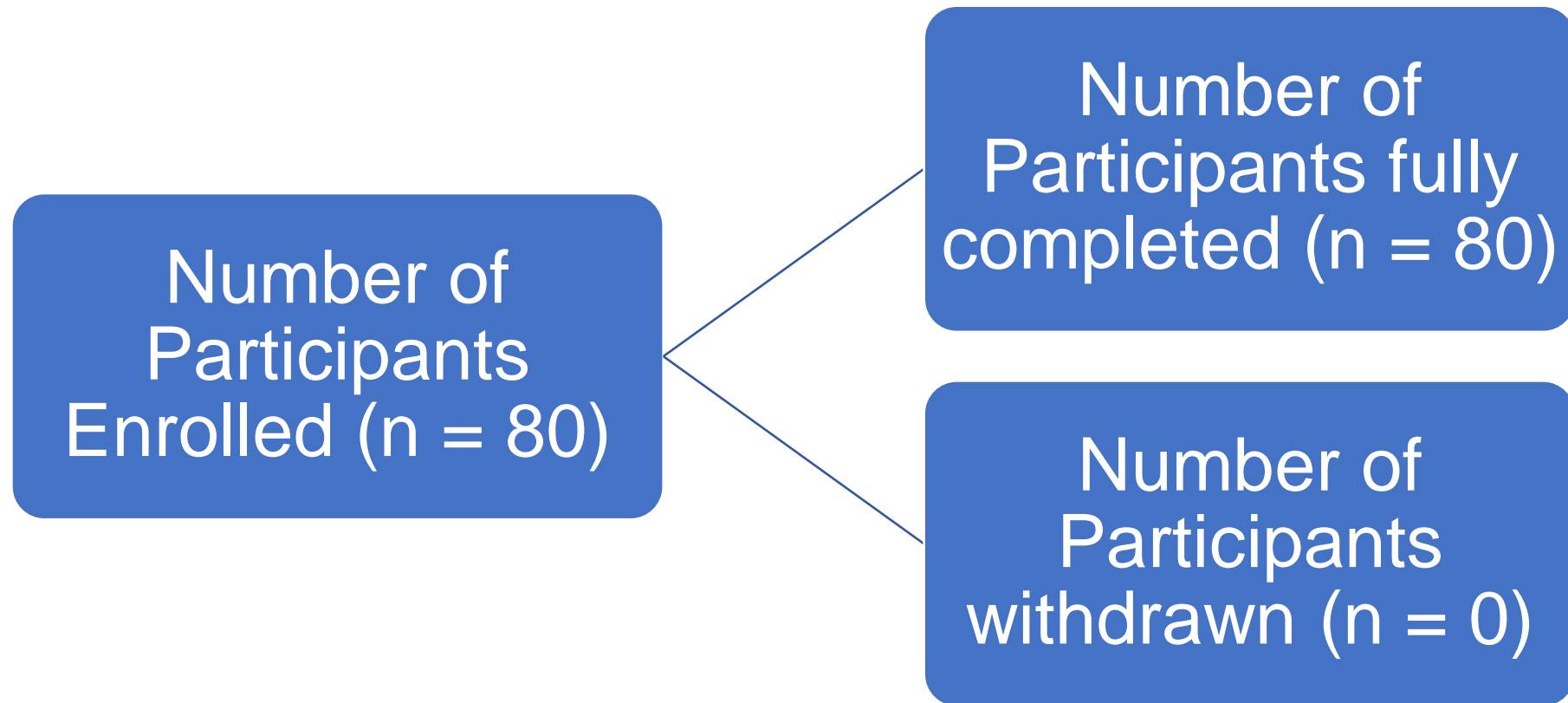


**Participant Flow**

**Demographics and Baseline Characteristics (Safety Analysis Set)**

Characteristics	Cohorts					
	Pooled Placebo <sup>a</sup>	A1	A2	A3	A4	A5
	Placebo Single Dose IV/SC	GS-0272 2.3 mg Single IV Dose	GS-0272 7.0 mg Single IV Dose	GS-0272 21 mg Single IV Dose	GS-0272 50 mg Single IV Dose	GS-0272 100 mg Single IV Dose
Age (years)						
N	20	6	6	6	6	6
Mean (SD)	40 (13.5)	46 (12.4)	30 (10.0)	35 (7.8)	46 (9.0)	36 (12.3)
Median	39	41	29	35	47	32
Q1, Q3	30, 51	36, 61	26, 30	31, 43	38, 52	29, 45
Min, max	19, 62	36, 63	19, 49	24, 44	34, 58	22, 56
Sex at birth						
Male	17 (85.0%)	6 (100.0%)	5 (83.3%)	6 (100.0%)	5 (83.3%)	6 (100.0%)
Female	3 (15.0%)	0	1 (16.7%)	0	1 (16.7%)	0
Race						
Asian	0	1 (16.7%)	1 (16.7%)	0	0	0
Black or African American	0	0	1 (16.7%)	0	0	1 (16.7%)
White	20 (100.0%)	5 (83.3%)	4 (66.7%)	5 (83.3%)	6 (100.0%)	5 (83.3%)
Other	0	0	0	0	0	0
Mixed	0	0	0	1 (16.7%)	0	0

Characteristics	Cohorts					
	Pooled Placebo <sup>a</sup>	A1	A2	A3	A4	A5
	Placebo Single Dose IV/SC	GS-0272 2.3 mg Single IV Dose	GS-0272 7.0 mg Single IV Dose	GS-0272 21 mg Single IV Dose	GS-0272 50 mg Single IV Dose	GS-0272 100 mg Single IV Dose
Ethnicity						
Not Hispanic or Latino	20 (100.0%)	6 (100.0%)	6 (100.0%)	6 (100.0%)	6 (100.0%)	6 (100.0%)
Hispanic or Latino	0	0	0	0	0	0
Weight (kg)						
N	20	6	6	6	6	6
Mean (SD)	83.3 (16.01)	78.1 (10.70)	85.0 (12.93)	79.5 (8.66)	81.7 (7.99)	80.3 (10.98)
Median	79.2	75.1	86.0	80.7	84.8	81.0
Q1, Q3	71.4, 97.7	68.5, 88.3	71.7, 97.5	73.5, 81.6	72.9, 87.7	71.7, 91.1
Min, max	59.0, 111.5	68.3, 93.0	68.9, 99.7	67.4, 93.1	70.7, 89.1	65.1, 92.1
Height (cm)						
N	20	6	6	6	6	6
Mean (SD)	177.2 (10.79)	174.5 (5.09)	177.2 (12.22)	176.7 (7.47)	172.8 (4.79)	176.5 (3.62)
Median	178.0	173.5	179.5	179.5	173.0	177.5
Q1, Q3	171.0, 185.5	170.0, 180.0	169.0, 187.0	170.0, 182.0	171.0, 176.0	175.0, 179.0
Min, max	156.0, 194.0	169.0, 181.0	158.0, 190.0	165.0, 184.0	165.0, 179.0	170.0, 180.0

Characteristics	Cohorts					
	Pooled Placebo <sup>a</sup>	A1	A2	A3	A4	A5
	Placebo Single Dose IV/SC	GS-0272 2.3 mg Single IV Dose	GS-0272 7.0 mg Single IV Dose	GS-0272 21 mg Single IV Dose	GS-0272 50 mg Single IV Dose	GS-0272 100 mg Single IV Dose
Body mass index (kg/m <sup>2</sup> )						
N	20	6	6	6	6	6
Mean (SD)	26.3 (2.93)	25.6 (3.29)	27.0 (1.85)	25.5 (2.91)	27.3 (2.11)	25.8 (3.84)
Median	26.6	25.9	27.6	25.3	27.8	26.7
Q1, Q3	24.3, 28.9	23.6, 28.7	25.1, 27.9	24.4, 27.5	25.7, 28.8	22.1, 29.4
Min, max	19.7, 30.5	20.9, 28.8	24.3, 29.2	21.0, 29.6	24.2, 29.6	20.3, 29.7
Smoking history						
Ex-smoker	3 (15.0%)	1 (16.7%)	2 (33.3%)	3 (50.0%)	1 (16.7%)	1 (16.7%)
Never smoked	17 (85.0%)	5 (83.3%)	4 (66.7%)	3 (50.0%)	5 (83.3%)	5 (83.3%)
Smoker	0	0	0	0	0	0

	Cohorts					
	A6	A7	A8	A9	A10	Overall GS-0272
	GS-0272 200 mg Single IV Dose (N = 6)	GS-0272 20 mg Single SC Dose (N = 6)	GS-0272 200 mg Single SC Dose (N = 6)	GS-0272 400 mg Single IV Dose (N = 6)	GS-0272 800 mg Single IV Dose (N = 6)	GS-0272 Single Dose IV/SC (N = 60)
<b>Continued</b>						
Age (years)						
N	6	6	6	6	6	60
Mean (SD)	39 (10.5)	40 (9.9)	47 (9.9)	45 (12.8)	34 (11.3)	40 (11.4)
Median	37	38	51	46	34	38
Q1, Q3	36, 39	32, 48	47, 54	34, 54	24, 36	31, 49
Min, max	26, 58	30, 55	28, 54	27, 60	23, 54	19, 63
Sex at birth						
Male	6 (100.0%)	5 (83.3%)	6 (100.0%)	6 (100.0%)	6 (100.0%)	57 (95.0%)
Female	0	1 (16.7%)	0	0	0	3 (5.0%)
Race						
Asian	0	0	0	1 (16.7%)	0	3 (5.0%)
Black or African American	0	0	0	0	0	2 (3.3%)
White	6 (100.0%)	6 (100.0%)	6 (100.0%)	4 (66.7%)	6 (100.0%)	53 (88.3%)
Other	0	0	0	1 (16.7%)	0	1 (1.7%)
Mixed	0	0	0	0	0	1 (1.7%)
Ethnicity						
Not Hispanic or Latino	6 (100.0%)	6 (100.0%)	6 (100.0%)	5 (83.3%)	6 (100.0%)	59 (98.3%)
Hispanic or Latino	0	0	0	1 (16.7%)	0	1 (1.7%)
Weight (kg)						
N	6	6	6	6	6	60
Mean (SD)	81.8 (11.64)	91.5 (16.23)	84.5 (10.20)	84.4 (11.23)	85.2 (11.29)	83.2 (11.10)
Median	81.8	88.5	84.1	85.3	84.6	82.5
Q1, Q3	71.3, 92.9	79.1, 99.1	75.1, 93.7	82.3, 93.7	80.9, 88.2	73.5, 91.6
Min, max	66.9, 96.4	74.5, 119.1	73.5, 96.5	64.4, 95.7	69.2, 103.6	64.4, 119.1

	Cohorts					
	A6	A7	A8	A9	A10	Overall GS-0272
	GS-0272 200 mg Single IV Dose (N = 6)	GS-0272 20 mg Single SC Dose (N = 6)	GS-0272 200 mg Single SC Dose (N = 6)	GS-0272 400 mg Single IV Dose (N = 6)	GS-0272 800 mg Single IV Dose (N = 6)	GS-0272 Single Dose IV/SC (N = 60)
<b>Continued</b>						
<b>Height (cm)</b>						
N	6	6	6	6	6	60
Mean (SD)	178.2 (10.23)	181.7 (12.08)	177.7 (5.50)	178.5 (13.52)	179.7 (5.79)	177.3 (8.39)
Median	178.5	180.0	181.0	177.0	180.0	177.5
Q1, Q3	168.0, 184.0	177.0, 189.0	174.0, 181.0	171.0, 192.0	175.0, 185.0	171.5, 181.5
Min, max	167.0, 193.0	164.0, 200.0	168.0, 181.0	159.0, 195.0	172.0, 186.0	158.0, 200.0
<b>Body mass index (kg/m<sup>2</sup>)</b>						
N	6	6	6	6	6	60
Mean (SD)	26.0 (4.30)	27.5 (1.82)	26.7 (2.50)	26.4 (1.25)	26.3 (2.60)	26.4 (2.66)
Median	28.0	27.7	27.1	26.2	25.9	27.0
Q1, Q3	22.1, 28.8	26.9, 28.6	25.7, 28.6	25.4, 27.4	23.9, 28.8	24.8, 28.7
Min, max	19.1, 29.7	24.4, 29.8	22.4, 29.5	25.2, 28.1	23.4, 29.9	19.1, 29.9
<b>Smoking history</b>						
Ex-smoker	4 (66.7%)	1 (16.7%)	2 (33.3%)	1 (16.7%)	2 (33.3%)	18 (30.0%)
Never smoked	2 (33.3%)	5 (83.3%)	4 (66.7%)	5 (83.3%)	3 (50.0%)	41 (68.3%)
Smoker	0	0	0	0	1 (16.7%)	1 (1.7%)

IV = intravenous; max = maximum; min = minimum; Q1 = first quartile; Q3 = third quartile; SC = subcutaneous, SD = standard deviation

a Pooled group of participants who received placebo in Cohorts A1 to A10.

Age (in years) was collected at the time of informed consent.

Denominator for percentage was the Safety Analysis Set.

Body mass index (kg/m<sup>2</sup>) = (Weight [kg]/Height [cm]<sup>2</sup>) × 10,000

Source: [Table 15.8.3.1](#)

## Outcome Measures

**Table 9. MB272-001: GS-0272 Mean (%CV) Serum PK Parameters Following Single IV Doses: Cohorts A1 to A6 (2.3-200 mg), A9 (400 mg), and A10 (800 mg) (PK Analysis Set)**

GS-0272 PK Parameter Mean (%CV)	Cohorts							
	A1	A2	A3	A4	A5	A6	A9	A10
	GS-0272 2.3 mg IV (N = 6)	GS-0272 7.0 mg IV (N = 6)	GS-0272 21 mg IV (N = 6)	GS-0272 50 mg IV (N = 6)	GS-0272 100 mg IV (N = 6)	GS-0272 200 mg IV (N = 6)	GS-0272 400 mg IV (N = 6)	GS-0272 800 mg IV (N = 6)
C <sub>max</sub> (µg/mL)	0.471 (23.6)	1.89 (20.5)	5.33 (15.8)	14.6 (10.7)	25.9 (9.77)	57.1 (13.5)	121 (21.2)	181 (14.4)
T <sub>max</sub> (h) <sup>a</sup>	1.50 (1.00, 2.00)	2.00 (1.00, 4.00)	1.00 (0.500, 1.00)	2.00 (1.00, 4.00)	2.00 (1.00, 8.00)	0.750 (0.500, 2.00)	1.50 (1.00, 2.00)	0.750 (0.500, 2.00)
AUC <sub>last</sub> (h•µg/mL)	17.2 (28.4)	152 (29.7)	756 (14.3)	2750 (19.5)	5810 (29.8)	15,500 (21.0)	33,100 (20.8)	63,100 (32.1)
AUC <sub>inf</sub> (h•µg/mL)	19.1 (29.2)	159 (26.6)	760 (14.3)	2770 (19.0)	5830 (29.6)	15,500 (21.2)	33,500 (21.7)	68,100 (35.9)
AUC <sub>exp</sub> (%)	9.60 (28.3)	4.82 (126)	0.536 (35.0)	1.10 (121)	0.451 (81.8)	0.279 (153)	1.14 (85.8)	5.99 (97.4)
C <sub>last</sub> (µg/mL)	0.0490 (33.5)	0.0856 (113)	0.0351 (36.4)	0.148 (104)	0.103 (64.6)	0.138 (130)	0.954 (87.2)	5.73 (85.8)
t <sub>1/2</sub> (h) <sup>a</sup>	25.3 (24.4, 29.0)	51.9 (43.4, 61.1)	77.4 (73.6, 92.0)	122 (108, 129)	181 (98.7, 193)	163 (141, 183)	274 (214, 324)	376 (287, 695)
CL (mL/h)	132 (36.6)	46.1 (19.5)	28.1 (13.1)	18.6 (19.0)	18.2 (24.5)	13.5 (27.1)	12.4 (20.4)	13.2 (38.8)
V <sub>z</sub> (mL)	4730 (22.6)	3520 (26.9)	3250 (5.13)	3340 (20.8)	3940 (25.1)	3340 (26.5)	4620 (17.8)	7760 (29.3)

%CV = percentage coefficient of variation; IV = intravenous; PK = pharmacokinetic(s); Q1 = first quartile; Q3 = third quartile

<sup>a</sup> Median (Q1, Q3).

N represents the number of participants in the PK Analysis Set for each treatment.

Means presented are unadjusted arithmetic means.

Source: [Table 15.10.1.1.4.1](#)

**Table 10. MB272-001: GS-0272 Mean (%CV) Serum PK Parameters Following Single SC Doses (Cohorts A7 20 mg and A8 200 mg) (PK Analysis Set)**

GS-0272 PK Parameter Mean (%CV)	Cohorts	
	A7	A8
	GS-0272 20 mg SC (N = 6)	GS-0272 200 mg SC (N = 6)
$C_{max}$ (µg/mL)	0.538 (62.5)	11.5 (31.3)
$T_{max}$ (h) <sup>a</sup>	168 (168, 168)	168 (72.0, 336)
$AUC_{last}$ (h•µg/mL)	149 (63.3)	8260 (47.5)
$AUC_{inf}$ (h•µg/mL)	178 (42.7)	8450 (49.1)
$AUC_{exp}$ (%)	1.71 (70.6)	1.96 (83.1)
$C_{last}$ (µg/mL)	0.0375 (114)	0.479 (96.5)
$t_{1/2}$ (h) <sup>a</sup>	76.9 (75.0, 85.4)	222 (162, 234)
CL/F (mL/h)	154 (82.5)	28.0 (42.1)
$V_z/F$ (mL)	19,900 (104)	8420 (25.0)

%CV = percentage coefficient of variation; PK = pharmacokinetic(s); Q1 = first quartile; Q3 = third quartile; SC = subcutaneous  
 a Median (Q1, Q3).

N represents the number of participants in the PK Analysis Set for each treatment.

Means presented are unadjusted arithmetic means.

Source: [Table 15.10.1.1.4.2.](#)



**Table 11. MB272-001: Summary of Overall Immunogenicity Results (Immunogenicity Analysis Set)**

	Cohorts											
	Pooled placebo <sup>a</sup>	A1	A2	A3	A4	A5	A6	A7	A8	A9	A10	Total (N = 80)
	Placebo Single Dose IV/SC (N = 20)	2.3 mg GS-0272 Single IV Dose (N = 6)	7.0 mg GS-0272 Single IV Dose (N = 6)	21 mg GS-0272 Single IV Dose (N = 6)	50 mg GS-0272 Single IV Dose (N = 6)	100 mg GS-0272 Single IV Dose (N = 6)	200 mg GS-0272 Single IV Dose (N = 6)	20 mg GS-0272 Single SC Dose (N = 6)	200 mg GS-0272 Single SC Dose (N = 6)	400 mg GS-0272 Single IV Dose (N = 6)	800 mg GS-0272 Single IV Dose (N = 6)	
Evaluable for ADA Prevalence <sup>b</sup>	20	6	6	6	6	6	6	6	6	6	6	80
Any ADA Positive (ADA prevalence)	0	0	0	0	1 (16.7%)	0	0	0	0	1 (16.7%)	3 (50.0%)	5 (6.3%)
ADA positive at postbaseline	0	0	0	0	1 (16.7%)	0	0	0	0	1 (16.7%)	3 (50.0%)	5 (6.3%)
ADA positive at baseline and postbaseline	0	0	0	0	0	0	0	0	0	0	0	0
Evaluable for ADA Incidence <sup>c</sup>	20	6	6	6	6	6	6	6	6	6	6	80
ADA negative (no treatment-emergent ADA)	20 (100.0%)	6 (100.0%)	6 (100.0%)	6 (100.0%)	5 (83.3%)	6 (100.0%)	6 (100.0%)	0	0	5 (83.3%)	3 (50.0%)	75 (93.8%)
Treatment-emergent ADA positive (ADA incidence)	0	0	0	0	1 (16.7%)	0	0	0	0	1 (16.7%)	3 (50.0%)	5 (6.3%)
Treatment-induced ADA	0	0	0	0	1 (16.7%)	0	0	0	0	1 (16.7%)	3 (50.0%)	5 (6.3%)
Transient positive	0	0	0	0	0	0	0	0	0	0	0	0
Persistent positive	0	0	0	0	1 (16.7%)	0	0	0	0	1 (16.7%)	3 (50.0%)	5 (6.3%)

ADA = antidrug antibody; IV = intravenous; SC = subcutaneous

a Pooled group of participants who received placebo in Cohorts A1 to A10.

b With reportable ADA result any time.

c With nonmissing baseline ADA result and reportable postbaseline ADA result.

Treatment-induced ADA: ADA positive at postbaseline and negative or missing at baseline. Persistent positive ADA: treatment-induced ADA detected at 2 or more time points where the first and last ADA-positive sample were separated by  $\geq 16$  weeks or at the last postbaseline assessment.

Transient positive ADA: treatment-induced ADA that did not meet the definition of persistent positive ADA.

Treatment-emergent ADA: treatment-induced ADA.

Source: [Table 15.10.1.7.1](#)

### Adverse Events

Overall, 40 of 80 participants (50.0%) had at least 1 AE across all cohorts in the study. The incidence of AEs was comparable between the treatments: GS-0272 IV (24 of 48 participants [50.0%]), GS-0272 SC (7 of 12 participants [58.3%]), and placebo IV or SC (9 of 20 participants [45.0%]). No severe AEs were reported in any of the treatment cohorts. Of the 80 participants, 1 participant in Cohort A2 (who received a single dose of GS-0272 7.0 mg IV) experienced an SAE of right ankle fracture, which was reported during the poststudy follow-up period (approximately 2 months following dosing). No AEs or SAEs were considered related to the study drug. No deaths were reported in this study. An overall summary of AEs reported in the IV and SC cohorts is presented in Table 12.

**Table 12. MB272-001: Overall Summary of Adverse Events (Safety Analysis Set)**

	Cohorts					
	Pooled Placebo <sup>a</sup>	A1	A2	A3	A4	A5
	Placebo Single Dose IV/SC (N = 20)	GS-0272 2.3 mg Single IV Dose (N = 6)	GS-0272 7.0 mg Single IV Dose (N = 6)	GS-0272 21 mg Single IV Dose (N = 6)	GS-0272 50 mg Single IV Dose (N = 6)	GS-0272 100 mg Single IV Dose (N = 6)
AE	9 (45.0%)	3 (50.0%)	5 (83.3%)	4 (66.7%)	3 (50.0%)	2 (33.3%)
Severe AE	0	0	0	0	0	0
Moderate AE	3 (15.0%)	1 (16.7%)	4 (66.7%)	3 (50.0%)	3 (50.0%)	0
AE related to study drug	0	0	0	0	0	0
AE related to study drug with Grade 3 or higher	0	0	0	0	0	0
AE related to study drug with Grade 2 or higher	0	0	0	0	0	0
SAE	0	0	1 (16.7%)	0	0	0
SAE related to study drug	0	0	0	0	0	0
Death	0	0	0	0	0	0

(Continued)	Cohorts							
	A6	A7	A8	A9	A10	Overall GS-0272		
	GS-0272 200 mg Single IV Dose (N = 6)	GS-0272 20 mg Single SC Dose (N = 6)	GS-0272 200 mg Single SC Dose (N = 6)	GS-0272 400 mg Single IV Dose (N = 6)	GS-0272 800 mg Single IV Dose (N = 6)	GS-0272 Single Dose IV/SC (N = 60)	Single Dose IV (N = 48)	Single Dose SC (N = 12)
AE	2 (33.3%)	6 (100.0%)	1 (16.7%)	2 (33.3%)	3 (50.0%)	31 (51.7%)	24 (50.0%)	7 (58.3%)
Severe AE	0	0	0	0	0	0	0	0
Moderate AE	0	1 (16.7%)	1 (16.7%)	1 (16.7%)	2 (33.3%)	16 (26.7%)	14 (29.2%)	2 (16.7%)
AE related to study drug	0	0	0	0	0	0	0	0
AE related to study drug with Grade 3 or higher	0	0	0	0	0	0	0	0
AE related to study drug with Grade 2 or higher	0	0	0	0	0	0	0	0
SAE	0	0	0	0	0	1 (1.7%)	1 (2.1%)	0
SAE related to study drug	0	0	0	0	0	0	0	0
Death	0	0	0	0	0	0	0	0

AE = adverse event; IV = intravenous; MedDRA = Medical Dictionary for Regulatory Activities; SAE = serious adverse event; SC = subcutaneous

a Pooled group of participants who received placebo in Cohorts A1 to A10.

Adverse events were coded according to MedDRA Version 27.0.

Treatment-emergent events were defined as any AEs with an onset date on or after the study drug start date.

Source: [Table 15.11.2.1.1](#)

**Table 13. MB272-001: Adverse Events by Preferred Term (Safety Analysis Set)**

[illegible]

[illegible]

[illegible]

(Continued)		
	<b>Overall GS-0272 Single Dose IV (N = 48)</b>	<b>Overall GS-0272 Single Dose SC (N = 12)</b>
Number (%) of participants with any treatment-emergent adverse events	24 (50.0%)	7 (58.3%)
Upper respiratory tract infection	6 (12.5%)	3 (25.0%)
Headache	6 (12.5%)	0
Pain in extremity	3 (6.3%)	0
Toothache	3 (6.3%)	0
Back pain	1 (2.1%)	1 (8.3%)
Arthralgia	1 (2.1%)	1 (8.3%)
Dizziness	2 (4.2%)	0
Gastroenteritis	1 (2.1%)	1 (8.3%)
Influenza like illness	2 (4.2%)	0
Nausea	1 (2.1%)	0
SARS-COV-2 test positive	0	1 (8.3%)
Vomiting	1 (2.1%)	0
Abdominal discomfort	1 (2.1%)	0
Ankle fracture	1 (2.1%)	0
Anxiety	1 (2.1%)	0
Atrial fibrillation	1 (2.1%)	0
COVID-19	1 (2.1%)	0
Catheter site pain	1 (2.1%)	0
Cough	1 (2.1%)	0
Eye contusion	1 (2.1%)	0
Face injury	1 (2.1%)	0
Gout	1 (2.1%)	0
Hypoaesthesia	1 (2.1%)	0

(Continued)	Overall GS-0272 Single Dose IV (N = 48)	Overall GS-0272 Single Dose SC (N = 12)
Ligament sprain	0	1 (8.3%)
Neck pain	1 (2.1%)	0
Oropharyngeal pain	1 (2.1%)	0
Panic attack	1 (2.1%)	0
Procedural pain	1 (2.1%)	0
Pruritus	1 (2.1%)	0
Skin laceration	0	1 (8.3%)
Blood creatine phosphokinase increased	0	0
Pain in jaw	0	0
Rhinorrhoea	0	0
Skin abrasion	0	0
Transaminases increased	0	0
Wheezing	0	0

AE = adverse event; COVID-19 = coronavirus disease 2019; IV = intravenous; MedDRA = Medical Dictionary for Regulatory activities; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SC = subcutaneous

a Pooled group of participants who received placebo in Cohorts A1 to A10.

Adverse events were coded according to MedDRA Version 27.0.

Treatment-emergent events were defined as any AEs with an onset date on or after the study drug start date.

Multiple AEs were counted only once per participant for each preferred term.

Preferred terms were presented by descending order of the total frequencies.

Source: [Table 15.11.2.1.3](#)