Study Title: A phase I, open-label, parallel-group study to investigate the pharmacokinetics, pharmacodynamics, safety, and tolerability of a single subcutaneous administration of RO7434656 in healthy adult chinese participants

Study Arms:

RO7434656 40 mg	Participants received RO7434656, 40 milligrams (mg), as a single subcutaneously (SC) dose, on Day 1, followed by a 90-day observation period.
RO7434656 70 mg	Participants received RO7434656, 70 mg, as a single SC dose, on Day 1, followed by a 90-day observation period.

Participant Flow:

Table 1: Participant Flow (ITT Population)

Category	RO7434656 40 mg	RO7434656 70 mg
Started	7	7
Completed	7	6
Not Completed	0	1
Reasons for Not Completed		
Withdrawal by Participant	0	1

Baseline Characteristics:

Table 2: Baseline Characteristics (ITT Population)

Variable	Statistics	RO7434656 40 mg (N=7)	RO7434656 70 mg (N=7)	All Participants (N=14)
Age (years)	**n**	7	7	14
	Mean	31.0	29.0	30.0
	Standard Deviation (SD)	8.1	7.3	7.5
Gender (participants)	**Female n (%)**	3 (42.9%)	2 (28.6%)	5 (35.7%)
	Male n (%)	4 (57.1%)	5 (71.4%)	9 (64.3%)

Outcome Measures:

Primary Outcome Measures:

1. Plasma Concentrations of RO7434656

Timeframe: Pre-dose and Post-dose at 0.5 hours (hr), 1 hr, 1.5 hr, 2 hr, 3 hr, 4 hr, 6 hr, 8 hr, 12 hr on Day 1; Post-dose at 26 hr, 36 hr, and Days 3, 4, 8, 15, 22, 30, 50, 70, and 90

Analysis Population Description: Pharmacokinetic (PK) analysis population included all participants who had received any dose of factor B antisense oligonucleotide (FB ASO) given as study drug, had at least one post-dose PK sample that was evaluable, and had no major protocol deviations that would impact the PK results. Number analyzed is the number of participants with data available for analysis at the specified timepoint.

Unit of Measurement: nanograms per milliliter (ng/mL)

Table 3: Plasma concentrations of RO7434656

		RO7434656 40 mg		**RO7434656 70 mg**	
	Number of Participants Analyzed:	7 Participants		7 Participants	
	Category	**Geometric Mean**	**Geometric Coefficient of Variation**	**Geometric Mean**	**Geometric Coefficient of Variation**
Pre-dose, Day 1	Number Analyzed:	7 Participants		7 Participants	
		NA	NA	NA	NA
		Geometric mean and geometric coefficient of variation were not estimable because all samples were below the limit of quantification (BLQ).		Geometric mean and geometric coefficient of variation were not estimable because all samples were BLQ.	
0.5hr Post-dose, Day 1	Number Analyzed:	7 Participants		7 Participants	
		117	41.3	183	40.7

1 hr Post-dose, Day 1	Number Analyzed:	7 Participants		7 Participants	
		150	37.0	236	29.9
1.5 hr Post-dose, Day 1	Number Analyzed:	7 Participants		7 Participants	
		142	56.0	227	28.6
2 h Post-dose, Day 1	Number Analyzed:	7 Participants		7 Participants	
		162	43.3	247	27.4
3 h Post-dose, Day 1	Number Analyzed:	7 Participants		7 Participants	
		117	45.0	166	30.1
4 h Post-dose, Day 1	Number Analyzed:	7 Participants		7 Participants	
		122	43.6	208	34.8
6 h Post-dose, Day 1	Number Analyzed:	7 Participants		7 Participants	
		102	33.2	196	34.9

8 h Post-dose, Day 1	Number Analyzed:	7 Participants		7 Participants	
		90.4	31.3	188	28.8
12 h Post-dose, Day 1	Number Analyzed:	7 Participants		7 Participants	
		43.8	15.6	135	35.9
24 hr Postdose	Number Analyzed:	7 Participants		7 Participants	
		3.60	76.1	12.0	72.0
36 hr Post-dose	Number Analyzed:	7 Participants		7 Participants	
		1.27	45.8	3.79	33.5
Post-dose, Day 3	Number Analyzed:	7 Participants		7 Participants	
		0.819	32.0	1.87	28.1
Post-dose, Day 4	Number Analyzed:	7 Participants		7 Participants	
		0.560	36.1	1.15	23.0
Post-dose, Day 8	Number Analyzed:	7 Participants		7 Participants	

		0.485	20.6	0.880	20.4
Post-dose, Day 15	Number Analyzed:	7 Participants		7 Participants	
		0.388	26.8	0.683	22.4
Post-dose, Day 22	Number Analyzed:	7 Participants		7 Participants	
		0.367	44.8	0.613	21.9
Post-dose, Day 30	Number Analyzed:	7 Participants		7 Participants	
		0.337	51.2	0.559	26.1
Post-dose, Day 50	Number Analyzed:	7 Participants		6 Participants	
		0.279	46.3	0.450	29.3
Post-dose, Day 70	Number Analyzed:	6 Participants		7 Participants	
		0.201	33.7	0.298	17.6
Post-dose, Day 90	Number Analyzed:	6 Participants		6 Participants	
		0.216	33.6	0.212	26.1

2. Maximum Plasma Concentration (Cmax) of RO7434656

Timeframe: Pre-dose and Post-dose at 0.5 hours (hr), 1 hr, 1.5 hr, 2 hr, 3 hr, 4 hr, 6 hr, 8 hr, 12 hr on Day 1; Post-dose at 26 hr, 36 hr, and Days 3, 4, 8, 15, 22, 30, 50, 70, and 90

Analysis Population Description: PK analysis population included all participants who had received any dose of FB ASO given as study drug, had at least one post-dose PK sample that was evaluable, and had no major protocol deviations that would impact the PK results.

Unit of Measurement: ng/mL

Table 4: Cmax of RO7434656

	RO7434656 40 mg		**RO7434656 70 mg**	
Number of Participants Analyzed:	7 Participants		7 Participants	
Category	**Geometric Mean**	**Geometric Coefficient of Variation**	**Geometric Mean**	**Geometric Coefficient of Variation**
Number Analyzed:	7 Participants		7 Participants	
	172	44.8	279	29.4

3. Time to Maximum Plasma Concentration (Tmax) of RO7434656

Timeframe: Pre-dose and Post-dose at 0.5 hours (hr), 1 hr, 1.5 hr, 2 hr, 3 hr, 4 hr, 6 hr, 8 hr, 12 hr on Day 1; Post-dose at 26 hr, 36 hr, and Days 3, 4, 8, 15, 22, 30, 50, 70, and 90

Analysis Population Description: PK analysis population included all participants who had received any dose of FB ASO given as study drug, had at least one post-dose PK sample that was evaluable, and had no major protocol deviations that would impact the PK results.

Unit of Measurement: hours

Table 5: Tmax of RO7434656

	RO7434656 40 mg	**RO7434656 70 mg**

Number of Participants Analyzed:	7 Participants			7 Participants		
Category	**Median**	**Minimum**	**Maximum**	**Median**	**Minimum**	**Maximum**
Number Analyzed:	7 Participants			7 Participants		
	2	1	6	1	0.5	8

4. Area Under the Plasma Concentration-time Curve From Zero to 24 Hours Post-dose (AUC0-24hr) of RO7434656

Timeframe: Pre-dose and Post-dose at 0.5 hours (hr), 1 hr, 1.5 hr, 2 hr, 3 hr, 4 hr, 6 hr, 8 hr, 12 hr and 24 hrs

Analysis Population Description: PK analysis population included all participants who had received any dose of FB ASO given as study drug, had at least one post-dose PK sample that was evaluable, and had no major protocol deviations that would impact the PK results.

Unit of Measurement: hours-nanogram per milliliter (hr*ng/mL)

Table 6: AUC0-24hr of RO7434656

	RO7434656 40 mg		**RO7434656 70 mg**	
Number of Participants Analyzed:	7 Participants		7 Participants	
Category	**Geometric Mean**	**Geometric Coefficient of Variation**	**Geometric Mean**	**Geometric Coefficient of Variation**
Number Analyzed:	7 Participants		7 Participants	
	1410	21.9	2880	23.8

5. Elimination Half-life (t1/2) of RO7434656

Timeframe: Pre-dose and Post-dose at 0.5 hours (hr), 1 hr, 1.5 hr, 2 hr, 3 hr, 4 hr, 6 hr, 8 hr, 12 hr on Day 1; Post-dose at 26 hr, 36 hr, and Days 3, 4, 8, 15, 22, 30, 50, 70, and 90

Analysis Population Description: The PK analysis population included all participants who had received any dose of FB ASO given as study drug, had at least one post-dose PK sample that was evaluable, and had no major protocol deviations that would impact the PK results. Overall number analyzed is the number of participants with data available for analysis.

Unit of Measurement: days

Table 7: t1/2 of RO7434656

	RO7434656 40 mg			**RO7434656 70 mg**		
Number of Participants Analyzed:	6 Participants			7 Participants		
Category	**Median**	**Minimum**	**Maximum**	**Median**	**Minimum**	**Maximum**
Number Analyzed:	6 Participants			7 Participants		
	47.9	45.6	50.6	46.6	27.4	48.7

Secondary Outcome Measures:

6. Percent Change From Baseline of Plasma Factor B (FB) Levels Following SC Administration of RO7434656

Timeframe: Baseline, Days 2, 4, 8, 15, 22, 30, 50, 70, and 90

Analysis Population Description: Pharmacodynamic (PD) analysis population included all participants who had a pre-dose measurement and at least one evaluable PD measurement after administration of the investigational product. Number analyzed is the number of participants with data available for analysis at specified timepoints.

Unit of Measurement: percent change

Table 8: Percent Change From Baseline of Plasma FB Levels Following SC Administration of RO7434656

		RO7434656 40 mg		RO7434656 70 mg	
Number of Participants Analyzed:		7 Participants		7 Participants	
	Category	**Mean**	**Standard Deviation**	**Mean**	**Standard Deviation**
Change at Day 2	Number Analyzed:	7 Participants		7 Participants	
		-2.32	6.26	3.29	7.85
Change at Day 4	Number Analyzed:	7 Participants		7 Participants	
		-6.80	18.98	-8.41	12.29
Change at Day 8	Number Analyzed:	7 Participants		7 Participants	
		-32.79	13.18	-41.42	11.83
Change at Day 15	Number Analyzed:	7 Participants		7 Participants	
		-44.20	13.22	-60.20	11.48
Change at Day 22	Number Analyzed:	7 Participants		7 Participants	
		-49.37	7.72	-65.78	8.88
Change at Day 30	Number Analyzed:	7 Participants		7 Participants	
		-48.51	13.36	-63.52	15.22
Change at Day 50	Number Analyzed:	7 Participants		6 Participants	
		-41.61	10.62	-56.63	14.44

Change at Day 70	Number Analyzed:	7 Participants		7 Participants	
		-32.88	13.37	-44.03	13.58
Change at Day 90	Number Analyzed:	7 Participants		6 Participants	
		-23.12	13.73	-33.62	11.43

7. Number of Participants With Treatment-emergent Adverse Events (TEAEs)

Timeframe: Up to 90 days

Analysis Population Description: Safety analysis set (SAS) included all randomized participants who had received any amount of study drug, with participants grouped and analyzed according to the treatment that they actually received.

Unit of Measurement: participants

Table 9: Number of Participants With TEAEs

	RO7434656 40 mg	**RO7434656 70 mg**
Number of Participants Analyzed:	7 Participants	7 Participants
Category	**Count of Participants**	**Count of Participants**
Number Analyzed:	7 Participants	7 Participants
	5	4

8. Number of Participants With Alanine Aminotransferase (ALT) > 3 × Upper Limit of Normal

Timeframe: Up to 90 days

Analysis Population Description: SAS included all randomized participants who had received any amount of study drug, with participants grouped and analyzed according to the treatment that they actually received.

Unit of Measurement: participants

Table 10: Number of Participants With ALT > 3 × Upper Limit of Normal

	RO7434656 40 mg	**RO7434656 70 mg**
Number of Participants Analyzed:	7 Participants	7 Participants
Category	**Count of Participants**	**Count of Participants**
Number Analyzed:	7 Participants	7 Participants
	0	0

9. Number of Participants With Meningococcal and Pneumococcal Infections

Timeframe: Up to 90 days

Analysis Population Description:SAS included all randomized participants who had received any amount of study drug, with participants grouped and analyzed according to the treatment that they actually received.

Unit of Measurement: participants

Table 11: Number of Participants With Meningococcal and Pneumococcal Infections

	RO7434656 40 mg	**RO7434656 70 mg**
Number of Participants Analyzed:	7 Participants	7 Participants
Category	**Count of Participants**	**Count of Participants**
Number Analyzed:	7 Participants	7 Participants
	0	0

10. Number of Participants With Injection-site Reactions

Timeframe: Up to 90 days

Analysis Population Description: SAS included all randomized participants who had received any amount of study drug, with participants grouped and analyzed according to the treatment that they actually received.

Unit of Measurement: participants

Table 12: Number of Participants With Injection-site Reactions

	RO7434656 40 mg	**RO7434656 70 mg**
Number of Participants Analyzed:	7 Participants	7 Participants
Category	**Count of Participants**	**Count of Participants**
Number Analyzed:	7 Participants	7 Participants
	0	1

Adverse Events:

Table 13: Adverse Events (AEs)

Body System or Organ Class Dictionary-Derived Term	**RO7434656 40 mg (N=7)**	**RO7434656 70 mg (N=7)**
Total number of participants with at least one AE	5 (71.4%)	4 (57.1%)
Investigations ● Blood triglycerides increased ● Alanine aminotransferase increased ● Blood creatine phosphokinase increased ● Aspartate aminotransferase increased ● Blood uric acid increased ● C-reactive protein increased	 2 (28.6%) 0 2 (28.6%) 0 1 (14.3%) 1 (14.3%)	 1 (14.3%) 2 (28.6%) 0 1 (14.3%) 0 0
Infections and infestations ● Upper respiratory tract infection	2 (28.6%)	1 (14.3%)
Gastrointestinal disorders ● Diarrhoea	1 (14.3%)	0
General disorders and administration site conditions ● Injection site reaction	0	1 (14.3%)