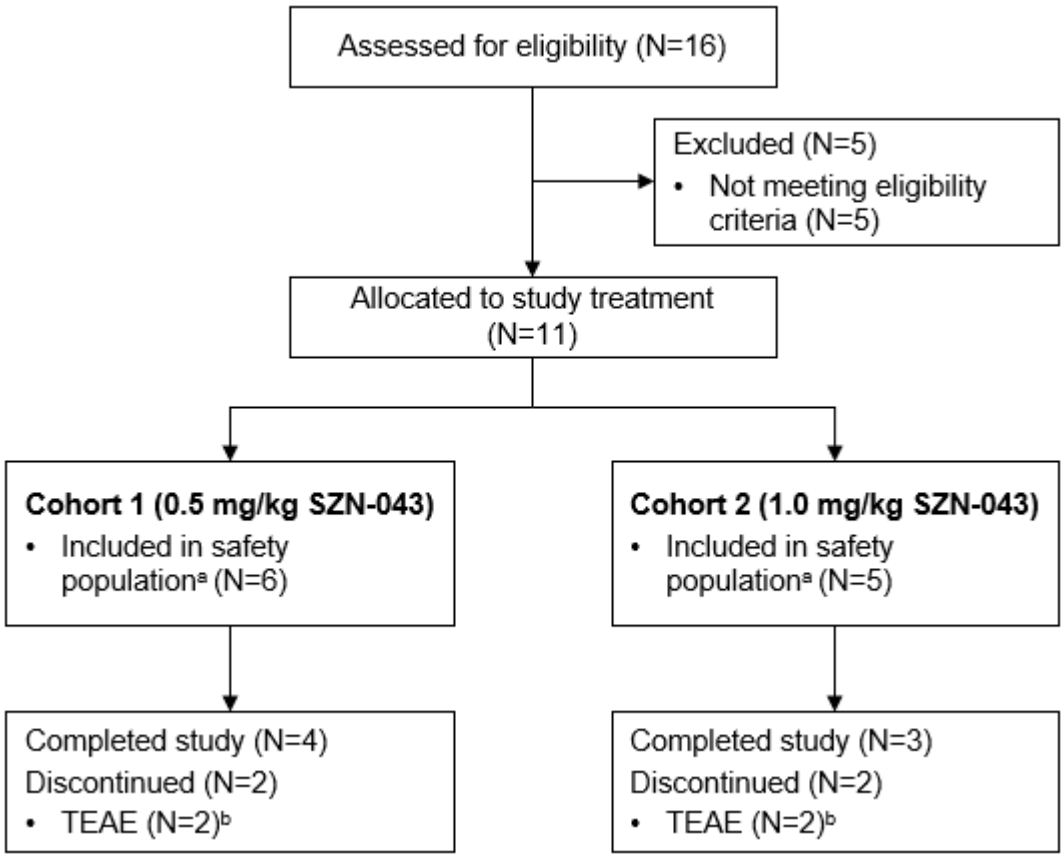
BASICS RESULTS SUMMARY

Study Title:	A Phase 1b multiple ascending dose study to assess the safety, tolerability, and pharmacokinetics of SZN-043 in participants with severe alcohol-associated hepatitis
Brief Title:	A Phase 1b study evaluating safety and pharmacokinetics of SZN-043 in participants with severe alcohol-associated hepatitis
Study Number:	CL-0043-1002
Study Phase:	Phase 1b
Compound:	SZN-043
Indication:	Severe alcohol-associated hepatitis
Study Sponsor:	Surrozen Operating, Inc. 171 Oyster Point Blvd, Suite 400 South San Francisco, CA 94080
Study Dates	09 May 2024 to 17 March 2026

PARTICIPANT FLOW

Figure 1. Participant Disposition



Abbreviations: TEAE = treatment-emergent adverse event.
[a] Includes all participants who received any amount of study drug.
[b] Reported TEAE that resulted in a fatal outcome prior to completion of the study (see Table 7 for details).

BASELINE CHARACTERISTICS

Table 1. Participant Demographics (Safety Population)

	Cohort 1 (0.5 mg/kg SZN-043) (N=6)	Cohort 2 (1.0 mg/kg SZN-043) (N=5)	Total (N=11)
Age (years)			
Mean (SD)	49.7 (7.81)	51.0 (4.30)	50.3 (6.20)
Median (min, max)	49.0 (39, 59)	53.0 (44, 55)	50.0 (39, 59)
Sex at birth, n (%)			
Male	3 (50.0%)	4 (80.0%)	7 (63.6%)
Female	3 (50.0%)	1 (20.0%)	4 (36.4%)
Of childbearing potential[a]			
Yes	3 (100%)	0	3 (75.0%)
No	0	1 (100%)	1 (25.0%)
Post-menopausal[a]			
Yes	0	1 (100%)	1 (25.0%)
No	3 (100%)	0	3 (75.0%)
Ethnicity, n (%)			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	6 (100%)	5 (100%)	11 (100%)
Not reported/unknown	0	0	0
Race, n (%)			
American Indian or Alaska native	0	0	0
Asian	0	0	0
Black or African American	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0
White	6 (100%)	5 (100%)	11 (100%)
Other	0	0	0
Not reported/unknown	0	0	0

Abbreviations: max = maximum; min = minimum; SD = standard deviation.
[a] Percentages are based on number of females within their respective cohort.

OUTCOME MEASURES

Change from Baseline in Alcohol-associated Hepatitis Disease Progression

Efficacy data are summarised in Tables 2–4.

Table 2. Survival Status (Intent to Treat Population)

	Cohort 1 (0.5 mg/kg SZN-043) (N=6)	Cohort 2 (1.0 mg/kg SZN-043) (N=5)	Total (N=11)
Survival status, n (%)			
Alive at Day 28	6 (100%)	3 (60.0%)	9 (81.8%)
Alive at Day 60	4 (66.7%)	3 (60.0%)	7 (63.6%)
Alive at Day 90	4 (66.7%)	3 (60.0%)	7 (63.6%)

Table 3. Mean MELD Scores (Intent to Treat Population)

	MELD Score							
	Day -1	**Day 4**	**Day 7**	**Day 14**	**Day 18**	**Day 28**	**Day 60**	**EOS**
Cohort 1 (N=6)								
n[a]	5	4	4	5	3	6	3	4
Mean[b]	26.2	25.3	26.5	27.2	22.7	22.5	11.0	12.5
Cohort 2 (N=5)								
n[a]	4	5	5	0	5	2	2	3
Mean[b]	28.3	27.6	27.2	N/A	23.4	20.5	14.5	14

Abbreviations: EOS = end of study; MELD = model for end-stage liver disease; N/A = not applicable.
[a] Number of participants with available measurement at each time point.
[b] Calculated based on the total number of participants with an available measurement at each time point.

Table 4. Lille Scores (Intent to Treat Population)

	Lille Score[a]			Alive (Y/N)	Steroid use (Y/N)
Participant	**Day 0**	**Day 4**	**Day 7**		
Cohort 1					
1	N/A	N/A	N/A	Y	Y
2	0.276	0.221	0.221	Y	Y
3	0.822	0.544	0.552	N (CVA, Day 33)	Y
4	0.472	0.415	0.220	Y	N
5	0.710	0.452	0.510	Y	N
6	0.324	0.131	0.162	N (sepsis, Day 55)	N
Cohort 2					
7	0.382	0.182	0.077	Y	Y
8	0.460	0.334	0.234	Y	N
9	0.173	0.162	0.092	N (variceal bleed, Day 19)	N
10	0.655	0.301	0.249	Y	Y
11	0.495	0.248	0.049	N (acute aspiration event, Day 22)	N

Abbreviations: CVA = cerebrovascular accident; N = no; Y = yes.
[a] The Lille model score ranges from 0 to 1. A Lille score of <0.45 indicates a greater treatment response and survivability at Day 90 while a score of >0.45 indicates a poorer treatment response and lessened survivability at Day 90.

Change from Baseline in Measures of Liver Function

Overall, decreases from baseline were observed for bilirubin, alanine aminotransferase, aspartate aminotransferase and gamma-glutamyl transferase at the end of the study.

Serum Pharmacokinetic Parameters

Table 5. Serum PK Parameters Following a Single IV Infusion of SZN-043 in Participants with Severe Alcohol-Associated Hepatitis on Day 0

PK parameter (units)[a]	Cohort 1 (0.5 mg/kg SZN-043) (N=6)	Cohort 2 (1.0 mg/kg SZN-043) (N=5)
$AUC_{0\text{-last}}$ (h*ng/mL)	37100 (146.8)	112000 (48.2)
$AUC_{0\text{-inf}}$ (h*ng/mL)	49000 (146.4)[c]	113000 (48.4)
C_{max} (ng/mL)	7299.38 (30.1)	14751.6 (15.0)
T_{max}[b] (h)	0.43 (0.42, 0.43)	0.65 (0.58, 0.98)
$t_{1/2}$ (h)	12.3 (143.7)[c]	16.2 (46.5)
CL (L/h)	3.55 (108.7)[c]	0.957 (62.5)
V_z (L)	22.9 (68.7)[c]	17.2 (22.1)

Abbreviations: $AUC_{0\text{-inf}}$ = area under the plasma concentration-time curve from zero to infinity; AUC_{last} = area under the plasma concentration-time curve up to the last quantifiable timepoint; CL = total drug clearance from plasma; C_{max} = maximum plasma concentration; CV% = coefficient of variation; max = maximum; min = minimum; n = number of participants with evaluable data; $t_{1/2}$ = half-life; T_{max} = time to maximum plasma concentration; V_z = apparent volume of distribution.
[a] Arithmetic mean (arithmetic CV%).
[b] Median (min, max).
[c] n = 5.

Immunogenicity

At baseline, 8 participants (72.7%) tested negative for anti-drug antibodies (ADAs) for SZN-043, while 3 participants (27.3%) tested positive for ADAs (all in Cohort 2). After dosing, 4 participants tested positive for ADAs: 1 participant (9.1%) in Cohort 1 and 3 participants (27.3%) in Cohort 2. In one participant, reactivity to the RSPO2 domain of SZN-043 was still detectable, but declining, at ~15 months after dosing stopped. There were no treatment-emergent adverse events (TEAEs) related to immunogenicity recorded in any of the participants.

ADVERSE EVENTS

Safety data are summarised in Tables 6–7.

Table 6. Summary of Treatment-Emergent Adverse Events (TEAEs) (Safety Population)

	Cohort 1 (0.5 mg/kg SZN-043) (N=6)	**Cohort 2 (1.0 mg/kg SZN-043) (N=5)**	**Total (N=11)**
Total number of TEAEs	37	17	54
Number (%) of participants reporting at least one TEAE	6 (100%)	5 (100%)	11 (100%)
TEAE related to study drug[a]	0	0	0
TEAE related to study procedure[a]	1 (16.7%)	0	1 (9.1%)
TEAE leading to premature withdrawal from the study	2 (33.3%)	2 (40.0%)	4 (36.4%)
TEAEs by SOC and PT[b]			
Infections and infestations	**4 (66.7%)**	**4 (80.0%)**	**8 (72.7%)**
Pneumonia	2 (33.3%)	1 (20.0%)	3 (27.3%)
Spontaneous bacterial peritonitis	2 (33.3%)	0	2 (18.2%)
Cellulitis	1 (16.7%)	0	1 (9.1%)
Gastroenteritis	0	1 (20.0%)	1 (9.1%)
Influenza	0	1 (20.0%)	1 (9.1%)
Sepsis	1 (16.7%)	0	1 (9.1%)
Upper respiratory tract infection	0	1 (20.0%)	1 (9.1%)
Gastrointestinal disorders	**3 (50.0%)**	**3 (60.0%)**	**6 (54.5%)**
Haemorrhoidal haemorrhage	2 (33.3%)	1 (20.0%)	3 (27.3%)
Ascites	2 (33.3%)	0	2 (18.2%)
Abdominal pain	0	1 (20.0%)	1 (9.1%)
Constipation	1 (16.7%)	0	1 (9.1%)
Gastroesophageal haemorrhage	0	1 (20.0%)	1 (9.1%)
Nausea	0	1 (20.0%)	1 (9.1%)
Rectal haemorrhage	1 (16.7%)	0	1 (9.1%)
Renal and urinary disorders	**3 (50.0%)**	**2 (40.0%)**	**5 (45.5%)**
Acute kidney injury	1 (16.7%)	2 (40.0%)	3 (27.3%)
Renal impairment	2 (33.3%)	0	2 (18.2%)
Metabolism and nutrition disorders	**3 (50.0%)**	**1 (20.0%)**	**4 (36.4%)**
Hyperglycaemia	2 (33.3%)	0	2 (18.2%)

	Cohort 1 (0.5 mg/kg SZN-043) (N=6)	Cohort 2 (1.0 mg/kg SZN-043) (N=5)	Total (N=11)
Hypophosphataemia	1 (16.7%)	1 (20.0%)	2 (18.2%)
Hypocalcaemia	1 (16.7%)	0	1 (9.1%)
Hypokalaemia	0	1 (20.0%)	1 (9.1%)
General disorders and administration site conditions	**1 (16.7%)**	**1 (20.0%)**	**2 (18.2%)**
Fatigue	0	1 (20.0%)	1 (9.1%)
Multiple organ dysfunction syndrome	1 (16.7%)	0	1 (9.1%)
Hepatobiliary disorders	**2 (33.3%)**	**0**	**2 (18.2%)**
Hepatic cirrhosis	2 (33.3%)	0	2 (18.2%)
Alcoholic liver disease	1 (16.7%)	0	1 (9.1%)
Injury, poisoning and procedural complications	**2 (33.3%)**	**0**	**2 (18.2%)**
Fall	2 (33.3%)	0	2 (18.2%)
Nervous system disorders	**1 (16.7%)**	**1 (20.0%)**	**2 (18.2%)**
Hepatic encephalopathy	1 (16.7%)	1 (20.0%)	2 (18.2%)
Cerebrovascular accident	1 (16.7%)	0	1 (9.1%)
Respiratory, thoracic and mediastinal disorders	**1 (16.7%)**	**1 (20.0%)**	**2 (18.2%)**
Aspiration	0	1 (20.0%)	1 (9.1%)
Pulmonary oedema	1 (16.7%)	0	1 (9.1%)
Skin and subcutaneous tissue disorders	**1 (16.7%)**	**1 (20.0%)**	**2 (18.2%)**
Penile ulceration	0	1 (20.0%)	1 (9.1%)
Pruritus	1 (16.7%)	0	1 (9.1%)
Investigations	**1 (16.7%)**	**0**	**1 (9.1%)**
C-reactive protein increased	1 (16.7%)	0	1 (9.1%)
Gamma-glutamyl transferase increased	1 (16.7%)	0	1 (9.1%)
Liver function test abnormal	1 (16.7%)	0	1 (9.1%)
Musculoskeletal and connective tissue disorders	**1 (16.7%)**	**0**	**1 (9.1%)**
Joint effusion	1 (16.7%)	0	1 (9.1%)
Psychiatric disorders	**1 (16.7%)**	**0**	**1 (9.1%)**
Insomnia	1 (16.7%)	0	1 (9.1%)

	Cohort 1 (0.5 mg/kg SZN-043) (N=6)	Cohort 2 (1.0 mg/kg SZN-043) (N=5)	Total (N=11)
Vascular disorders	**1 (16.7%)**	**0**	**1 (9.1%)**
Thrombophlebitis	1 (16.7%)	0	1 (9.1%)

Abbreviations: MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; SOC = system organ class; TEAE = treatment-emergent adverse event.
[a] Participants reporting more than one adverse event are counted only once using the closest relationship to study drug. Not related events include those with relationship reported as “Unlikely” or “Not Related”, related events include those with relationship to study drug reported as “Possibly” “Probable,” or “Definite”.
[b] Adverse events were coded to SOC and PT using MedDRA, version 27.1. At each level of summarisation (any event, SOC, and PT), participants reporting more than one adverse event are counted only once.

Table 7. Summary of Treatment-Emergent Serious Adverse Events (TESAEs) (Safety Population)

	Cohort 1 (0.5 mg/kg SZN-043) (N=6)	Cohort 2 (1.0 mg/kg SZN-043) (N=5)	Total (N=11)
Total number of TESAEs	13	5	18
Number (%) of participants reporting at least one TESAE	4 (66.7%)	4 (80.0%)	8 (72.7%)
TESAE related to study drug[a]	0	0	0
TESAE related to study procedure[a]	0	0	0
TESAE leading to hospitalisation[b]	4 (66.7%)	3 (60.0%)	7 (63.6%)
TESAE causing death[b,c]	2 (33.3%)	2 (40.0%)	4 (36.4%)
TESAEs by SOC and PT[d]			
Gastrointestinal disorders	**2 (33.3%)**	**1 (20.0%)**	**3 (27.3%)**
Ascites	1 (16.7%)	0	1 (9.1%)
Gastroesophageal haemorrhage	0	1 (20.0%)	1 (9.1%)
Haemorrhoidal haemorrhage	1 (16.7%)	0	1 (9.1%)
Infections and infestations	**2 (33.3%)**	**1 (20.0%)**	**3 (27.3%)**
Pneumonia	2 (33.3%)	0	2 (18.2%)
Influenza	0	1 (20.0%)	1 (9.1%)
Sepsis	1 (16.7%)	0	1 (9.1%)
Spontaneous bacterial peritonitis	1 (16.7%)	0	1 (9.1%)
Renal and urinary disorders	**2 (33.3%)**	**1 (20.0%)**	**3 (27.3%)**
Acute kidney injury	1 (16.7%)	1 (20.0%)	2 (18.2%)
Renal impairment	1 (16.7%)	0	1 (9.1%)
Hepatobiliary disorders	**2 (33.3%)**	**0**	**2 (18.2%)**
Hepatic cirrhosis	2 (33.3%)	0	2 (18.2%)

	Cohort 1 (0.5 mg/kg SZN-043) (N=6)	Cohort 2 (1.0 mg/kg SZN-043) (N=5)	Total (N=11)
Alcoholic liver disease	1 (16.7%)	0	1 (9.1%)
General disorders and administration site conditions	**1 (16.7%)**	**0**	**1 (9.1%)**
Multiple organ dysfunction syndrome	1 (16.7%)	0	1 (9.1%)
Nervous system disorders	**1 (16.7%)**	**0**	**1 (9.1%)**
Cerebrovascular accident	1 (16.7%)	0	1 (9.1%)
Respiratory, thoracic and mediastinal disorders	**0**	**1 (20.0%)**	**1 (9.1%)**
Aspiration	0	1 (20.0%)	1 (9.1%)
Skin and subcutaneous tissue disorders	**0**	**1 (20.0%)**	**1 (9.1%)**
Penile ulceration	0	1 (20.0%)	1 (9.1%)

Abbreviations: MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; SOC = system organ class; TESAE = treatment-emergent serious adverse event.
[a] Participants reporting more than one adverse event are counted only once using the closest relationship to study drug. Not related events include those with relationship reported as “Unlikely” or “Not Related”, related events include those with relationship to study drug reported as “Possibly” “Probable,” or “Definite”.
[b] Only collected for serious adverse events.
[c] Refers to the 4 participants who experienced TESAEs causing death (primary cause of death for each participant was reported as variceal bleed; acute aspiration event; presumed stroke secondary to severe alcohol-associated hepatitis, hepato-renal syndrome and hospital acquired pneumonia; and sepsis and decompensation). Other than these 4 participants, there were no additional TESAEs that led to premature withdrawal from the study.
[d] Adverse events were coded to SOC and PT using MedDRA, version 27.1. At each level of summarisation (any event, SOC, and PT), participants reporting more than one adverse event are counted only once.