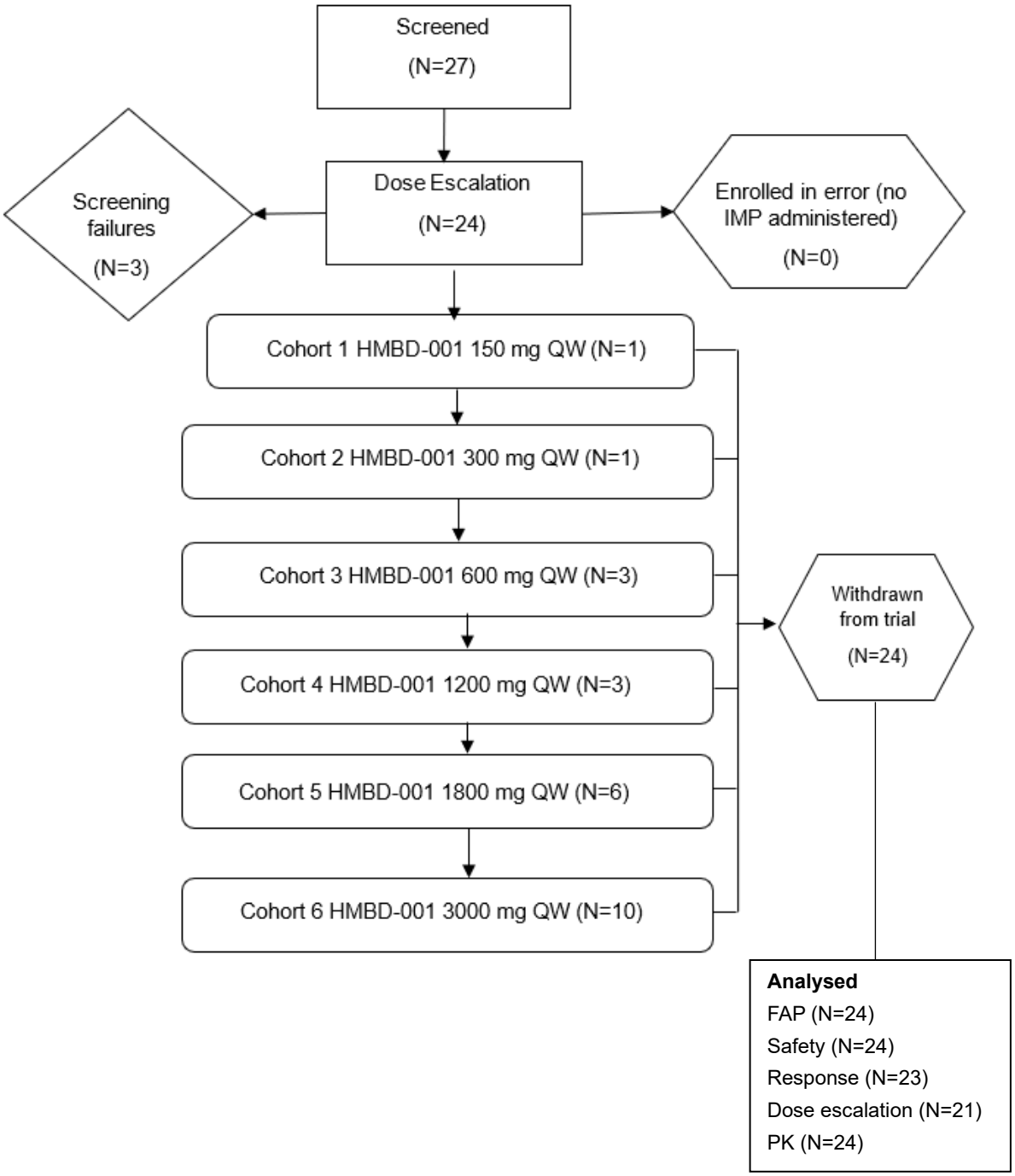
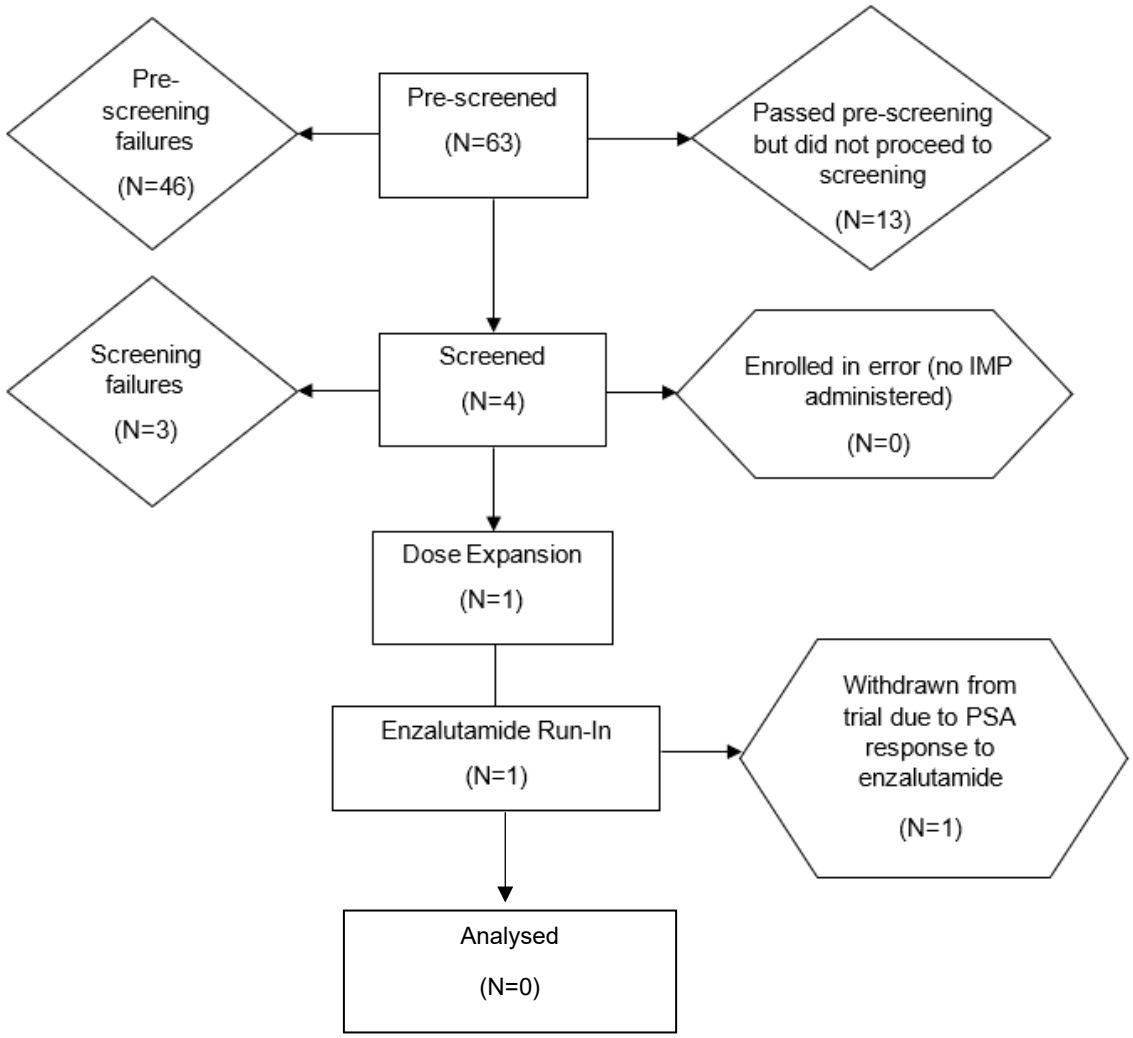
PARTICIPANT FLOW
Patient Disposition for the Dose Escalation Phase (Part A) of Trial CRUKD/22/002



Abbreviations: FAP=Full Analysis Population; IMP=investigational medicinal product; N=number of patients in the (treatment) group; PK=pharmacokinetic; QW=once weekly.

Patient Disposition for the Dose Expansion Phase (Part B) of Trial CRUKD/22/002



Abbreviations: IMP=investigational medicinal product; N=number of patients in the (treatment) group; PSA=prostate-specific antigen.
No patient received HMBD-001 in Part B Arm 1.

BASELINE CHARACTERISTICS (FULL ANALYSIS POPULATION)

Part A - Demographics and Baseline Characteristics (Full Analysis Population)

Characteristic	All Patients (N=24) n (%)	HMBD-001 150 mg QW (N=1) n (%)	HMBD-001 300 mg QW (N=1) n (%)	HMBD-001 600 mg QW (N=3) n (%)	HMBD-001 1200 mg QW (N=3) n (%)	HMBD-001 1800 mg QW (N=6) n (%)	HMBD-001 3000 mg QW (N=10) n (%)
Sex (n [%])							
Male	15 (62.5)	1 (100.0)	0	2 (66.7)	2 (66.7)	6 (100.0)	4 (40.0)
Female	9 (37.5)	0	1 (100.0)	1 (33.3)	1 (33.3)	0	6 (60.0)
Ethnicity (n [%])							
White	20 (83.3)	0	1 (100.0)	2 (66.7)	3 (100.0)	5 (83.3)	9 (90.0)
Mixed/Multiple ethnic groups	1 (4.2)	0	0	0	0	1 (16.7)	0
Asian/Asian British	0	0	0	0	0	0	0
Black/African/ Caribbean/Black British	0	0	0	0	0	0	0
Other ethnic group	1 (4.2)	0	0	0	0	0	1 (10.0)
Prefer not to say	0	0	0	0	0	0	0
Unknown	2 (8.3)	1 (100.0)	0	1 (33.3)	0	0	0
Age (Years)							
n	24	1	1	3	3	6	10
Mean	64.9	83.0	74.0	68.7	61.7	63.5	62.8
Median	64.5	83.0	74.0	70.0	63.0	62.5	64.5
Min	45	83	74	64	54	54	45
Max	83	83	74	72	68	75	78

CRUKD/22/002, HMBD-001 Basic Results Summary for ISRCTN

https://www.isrctn.com/ISRCTN62918594

Part A - Demographics and Baseline Characteristics (Full Analysis Population)

Characteristic	All Patients (N=24) n (%)	HMBD-001 150 mg QW (N=1) n (%)	HMBD-001 300 mg QW (N=1) n (%)	HMBD-001 600 mg QW (N=3) n (%)	HMBD-001 1200 mg QW (N=3) n (%)	HMBD-001 1800 mg QW (N=6) n (%)	HMBD-001 3000 mg QW (N=10) n (%)
Weight (kg)							
n	24	1	1	3	3	6	10
Mean	77.65	78.30	58.60	75.20	75.50	79.93	79.49
Median	77.25	78.30	58.60	72.70	75.30	77.25	82.65
Min	47.4	78.3	58.6	54.9	72.0	63.9	47.4
Max	108.2	78.3	58.6	98.0	79.2	97.2	108.2
ECOG performance status (n [%])							
0	8 (33.3)	0	0	1 (33.3)	1 (33.3)	1 (16.7)	5 (50.0)
1	16 (66.7)	1 (100.0)	1 (100.0)	2 (66.7)	2 (66.7)	5 (83.3)	5 (50.0)

Abbreviations: ECOG=Eastern Cooperative Oncology Group; max=maximum; min=minimum; n=number of patients in analysis for a continuous variable and number of patients per category for a categoric variable; N=number of patients in the treatment group; QW=once weekly.
One patient presented in HMBD-001 150 mg QW dose increased to 300 mg QW on Cycle 1 Day 15.
One patient presented in HMBD-001 300 mg QW dose increased to 600 mg QW on Cycle 1 Day 15.

OUTCOME MEASURES

PRIMARY OUTCOME MEASURES

Number of Patients who Experienced Dose Limiting Toxicities (DLTs) (Part A)

Part A – Dose Limiting Toxicities (Dose Escalation Population)

	All Patients (N=21)	HMBD-001 150 mg QW (N=1)	HMBD-001 300 mg QW (N=1)	HMBD-01 600 mg QW (N=3)	HMBD-001 1200 mg QW N=2)	HMBD-001 1800 mg QW (N=5)	HMBD-001 3000 mg QW (N=9)
Number of dose limiting toxicities	0	0	0	0	0	0	0

Abbreviations: N=number of patients evaluable for dose limiting toxicities; QW=once weekly.
One patient presented in HMBD-001 150 mg QW dose increased to 300 mg QW on Cycle 1 Day 15.
One patient presented in HMBD-001 300 mg QW dose increased to 600 mg QW on Cycle 1 Day 15.

Number of Adverse Events (AEs) by Arm Considered to be At Least Possibly Related to HMBD-001 (Part A)

Part A – Treatment-Emergent Adverse Events Related to HMBD-001 by System Order Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	All Patients (N=24)		HMBD-001 150 mg QW (N=1)		HMBD-001 300 mg QW (N=1)		HMBD-001 600 mg QW (N=3)		HMBD-001 1200 mg QW (N=3)		HMBD-001 1800 mg QW (N=6)		HMBD-001 3000 mg QW (N=10)	
	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events
Gastrointestinal disorders	**20 (83.3)**	**50**	**1 (100.0)**	**2**	**0**	**0**	**2 (66.7)**	**6**	**3 (100.0)**	**5**	**4 (66.7)**	**14**	**10 (100.0)**	**23**
Angular cheilitis	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Anorectal discomfort	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Cheilitis	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Diarrhoea	19 (79.2)	31	1 (100.0)	2	0	0	2 (66.7)	6	3 (100.0)	4	4 (66.7)	8	9 (90.0)	11
Dyspepsia	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Nausea	8 (33.3)	9	0	0	0	0	0	0	1 (33.3)	1	2 (33.3)	3	5 (50.0)	5
Oral pain	1 (4.2)	1	0	0	0	0	0	0	0	0	1 (16.7)	1	0	0
Rectal haemorrhage	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Stomatitis	3 (12.5)	3	0	0	0	0	0	0	0	0	1 (16.7)	1	2 (20.0)	2
Vomiting	1 (4.2)	1	0	0	0	0	0	0	0	0	1 (16.7)	1	0	0

Part A – Treatment-Emergent Adverse Events Related to HMBD-001 by System Order Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	All Patients (N=24)		HMBD-001 150 mg QW (N=1)		HMBD-001 300 mg QW (N=1)		HMBD-001 600 mg QW (N=3)		HMBD-001 1200 mg QW (N=3)		HMBD-001 1800 mg QW (N=6)		HMBD-001 3000 mg QW (N=10)	
	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events
General disorders and administration site conditions	**8 (33.3)**	**9**	**0**	**0**	**0**	**0**	**2 (66.7)**	**2**	**1 (33.3)**	**2**	**2 (33.3)**	**2**	**3 (30.0)**	**3**
Fatigue	5 (20.8)	5	0	0	0	0	0	0	1 (33.3)	1	2 (33.3)	2	2 (20.0)	2
Mucosal inflammation	3 (12.5)	3	0	0	0	0	1 (33.3)	1	1 (33.3)	1	0	0	1 (10.0)	1
Pyrexia	1 (4.2)	1	0	0	0	0	1 (33.3)	1	0	0	0	0	0	0
Skin and subcutaneous tissue disorders	**7 (29.2)**	**12**	**0**	**0**	**0**	**0**	**1 (33.3)**	**2**	**0**	**0**	**0**	**0**	**6 (60.0)**	**10**
Alopecia	1 (4.2)	1	0	0	0	0	1 (33.3)	1	0	0	0	0	0	0
Dermatitis acneiform	2 (8.3)	2	0	0	0	0	0	0	0	0	0	0	2 (20.0)	2
Dry skin	2 (8.3)	2	0	0	0	0	1 (33.3)	1	0	0	0	0	1 (10.0)	1
Madarosis	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Pruritus	2 (8.3)	2	0	0	0	0	0	0	0	0	0	0	2 (20.0)	2
Rash maculo-papular	2 (8.3)	3	0	0	0	0	0	0	0	0	0	0	2 (20.0)	3
Skin ulcer	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1

Part A – Treatment-Emergent Adverse Events Related to HMBD-001 by System Order Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	All Patients (N=24)		HMBD-001 150 mg QW (N=1)		HMBD-001 300 mg QW (N=1)		HMBD-001 600 mg QW (N=3)		HMBD-001 1200 mg QW (N=3)		HMBD-001 1800 mg QW (N=6)		HMBD-001 3000 mg QW (N=10)	
	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events
Investigations	**6 (25.0)**	**8**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (33.3)**	**1**	**1 (16.7)**	**1**	**4 (40.0)**	**6**
Alanine aminotransferase increased	1 (4.2)	2	0	0	0	0	0	0	0	0	0	0	1 (10.0)	2
Amylase increased	1 (4.2)	2	0	0	0	0	0	0	0	0	0	0	1 (10.0)	2
Blood alkaline phosphatase increased	1 (4.2)	1	0	0	0	0	0	0	1 (33.3)	1	0	0	0	0
Blood creatinine increased	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Lymphocyte count decreased	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Troponin increased	1 (4.2)	1	0	0	0	0	0	0	0	0	1 (16.7)	1	0	0
Metabolism and nutrition disorders	**6 (25.0)**	**6**	**1 (100.0)**	**1**	**0**	**0**	**0**	**0**	**1 (33.3)**	**1**	**2 (33.3)**	**2**	**2 (20.0)**	**2**
Decreased appetite	3 (12.5)	3	0	0	0	0	0	0	1 (33.3)	1	1 (16.7)	1	1 (10.0)	1
Hypokalaemia	1 (4.2)	1	1 (100.0)	1	0	0	0	0	0	0	0	0	0	0
Hypomagnesaemia	2 (8.3)	2	0	0	0	0	0	0	0	0	1 (16.7)	1	1 (10.0)	1

Part A – Treatment-Emergent Adverse Events Related to HMBD-001 by System Order Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	All Patients (N=24)		HMBD-001 150 mg QW (N=1)		HMBD-001 300 mg QW (N=1)		HMBD-001 600 mg QW (N=3)		HMBD-001 1200 mg QW (N=3)		HMBD-001 1800 mg QW (N=6)		HMBD-001 3000 mg QW (N=10)	
	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events
Injury, poisoning and procedural complications	**5 (20.8)**	**7**	**0**	**0**	**1 (100.0)**	**1**	**1 (33.3)**	**2**	**1 (33.3)**	**1**	**0**	**0**	**2 (20.0)**	**3**
Gastrointestinal stoma complication	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Infusion related reaction	4 (16.7)	6	0	0	1 (100.0)	1	1 (33.3)	2	1 (33.3)	1	0	0	1 (10.0)	2
Nervous system disorders	**4 (16.7)**	**5**	**1 (100.0)**	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (16.7)**	**1**	**2 (20.0)**	**2**
Dysgeusia	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Headache	1 (4.2)	1	1 (100.0)	1	0	0	0	0	0	0	0	0	0	0
Hypoaesthesia	1 (4.2)	1	1 (100.0)	1	0	0	0	0	0	0	0	0	0	0
Lethargy	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Taste disorder	1 (4.2)	1	0	0	0	0	0	0	0	0	1 (16.7)	1	0	0
Blood and lymphatic system disorders	**2 (8.3)**	**3**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**2 (20.0)**	**3**
Anaemia	2 (8.3)	2	0	0	0	0	0	0	0	0	0	0	2 (20.0)	2
Neutropenia	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1

Part A – Treatment-Emergent Adverse Events Related to HMBD-001 by System Order Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	All Patients (N=24)		HMBD-001 150 mg QW (N=1)		HMBD-001 300 mg QW (N=1)		HMBD-001 600 mg QW (N=3)		HMBD-001 1200 mg QW (N=3)		HMBD-001 1800 mg QW (N=6)		HMBD-001 3000 mg QW (N=10)	
	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events
Infections and infestations	**2 (8.3)**	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**2 (20.0)**	**2**
Gastroenteritis	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Paronychia	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Musculoskeletal and connective tissue disorders	**2 (8.3)**	**2**	**1 (100.0)**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (10.0)**	**1**
Muscle spasms	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Muscular weakness	1 (4.2)	1	1 (100.0)	1	0	0	0	0	0	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders	**2 (8.3)**	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**2 (33.3)**	**2**	**0**	**0**
Cough	1 (4.2)	1	0	0	0	0	0	0	0	0	1 (16.7)	1	0	0
Epistaxis	1 (4.2)	1	0	0	0	0	0	0	0	0	1 (16.7)	1	0	0
Eye disorders	**1 (4.2)**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (10.0)**	**1**
Eyelids pruritus	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1

CRUKD/22/002, HMBD-001 Basic Results Summary for ISRCTN

https://www.isrctn.com/ISRCTN62918594

Part A – Treatment-Emergent Adverse Events Related to HMBD-001 by System Order Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	All Patients (N=24)		HMBD-001 150 mg QW (N=1)		HMBD-001 300 mg QW (N=1)		HMBD-001 600 mg QW (N=3)		HMBD-001 1200 mg QW (N=3)		HMBD-001 1800 mg QW (N=6)		HMBD-001 3000 mg QW (N=10)	
	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events
Renal and urinary disorders	**1 (4.2)**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (10.0)**	**1**
Proteinuria	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1

Abbreviations: AE=adverse event; MedDRA=Medical Dictionary for Regulatory Activities v28.0; n=number of patients in the category; N=number of patients in the treatment group; QW=once weekly.
Patients are only counted once per category, irrespective of the number of occurrences.
Only includes treatment-emergent AEs, defined as any AE that worsened or onset after the first day of HMBD-001.
Related to HMBD-001 includes all AEs that are considered possibly, probably, or highly probably related to HMBD-001 as assessed by the Investigator.
One patient presented in HMBD-001 150 mg QW dose increased to 300 mg QW on Cycle 1 Day 15.
One patient presented in HMBD-001 300 mg QW dose increased to 600 mg QW on Cycle 1 Day 15.

Number of Grade 3, 4 and 5 AEs by Arm Considered to be At Least Possibly Related to HMBD-001 (Part A)

Part A – Treatment-Emergent Adverse Events of CTCAE Grade ≥3 Related to HMBD-001 by System Order Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	All Patients (N=24)		HMBD-001 150 mg QW (N=1)		HMBD-001 300 mg QW (N=1)		HMBD-001 600 mg QW (N=3)		HMBD-001 1200 mg QW (N=3)		HMBD-001 1800 mg QW (N=6)		HMBD-001 3000 mg QW (N=10)	
	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events
Any	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Abbreviations: AE=adverse event; CTCAE=Common Terminology Criteria for Adverse Events v5.0; MedDRA=Medical Dictionary for Regulatory Activities v28.0; n=number of patients in the category; N=number of patients in the treatment group; QW=once weekly.
Patients are only counted once per category, irrespective of the number of occurrences.
Only includes treatment-emergent AEs, defined as any AE that worsened or onset after the first day of HMBD-001.
Related to HMBD-001 includes all AEs that are considered possibly, probably, or highly probably related to HMBD-001 as assessed by the Investigator.
One patient presented in HMBD-001 150 mg QW dose increased to 300 mg QW on Cycle 1 Day 15.
One patient presented in HMBD-001 300 mg QW dose increased to 600 mg QW on Cycle 1 Day 15.

Number of Patients who Experienced DLTs, Number of AEs by Arm Considered to be At Least Possibly Related to HMBD-001, Number of Grade 3, 4 and 5 AEs by Arm Considered to be At Least Possibly Related to HMBD-001 and Overall Response Rate (ORR) within Six Cycles of HMBD-001 (Part B Arm 1)

These outcome measures were not analysed as recruitment was halted before any patient received HMBD-001 in Part B of the trial, due to a strategic decision not related to safety.

SECONDARY OUTCOME MEASURES - EFFICACY

ORR Within Six Cycles of HMBD-001, ORR Within 8 and 16 weeks of Commencing HMBD-001 and Disease Control Rate Within Six Cycles of HMBD-001 (Part A)

Part A - Summary of Overall Response and Disease Control Data (Response Population)

	All Patients (N=23) n (%)	HMBD-001 150 mg QW (N=1) n (%)	HMBD-001 300 mg QW (N=1) n (%)	HMBD-01 600 mg QW (N=3) n (%)	HMBD-001 1200 mg QW (N=3) n (%)	HMBD-001 1800 mg QW (N=6) n (%)	HMBD-001 3000 mg QW (N=9) n (%)
Overall response rate within six cycles of HMBD-001	1 (4.3)	0	0	0	0	0	1 (11.1)
Overall response rate within 8 weeks of commencing HMBD-001	1 (4.3)	0	0	0	0	0	1 (11.1)
Overall response rate within 16 weeks of commencing HMBD-001	1 (4.3)	0	0	0	0	0	1 (11.1)
Disease control rate within six cycles of HMBD-001 [a]	10 (43.5)	1 (100)	0	1 (33.3)	1 (33.3)	2 (33.3)	5 (5.5)

Abbreviations: N=number of patients in the treatment group; n=number of patients in the category; QW=once weekly.
One patient presented in HMBD-001 150 mg QW dose increased to 300 mg QW on Cycle 1 Day 15.
One patient presented in HMBD-001 300 mg QW dose increased to 600 mg QW on Cycle 1 Day 15.
[a] A patient was defined to have reached disease control within six cycles if they had a best overall response of complete response, partial response or stable disease per Response Evaluation Criteria in Solid Tumour Version 1.1 and/or Prostate Cancer Working Group 3 as applicable.

Duration of Response and Duration of Clinical Benefit (Part A)

Part A – Summary of Durations of Response and Clinical Benefit (Response Population, Responders Only)

	All Patients (n=1)	HMBD-001 150 mg QW (n=0)	HMBD-001 300 mg QW (n=0)	HMBD-01 600 mg QW (n=0)	HMBD-001 1200 mg QW (n=0)	HMBD-001 1800 mg QW (n=0)	HMBD-001 3000 mg QW (n=1)
Duration of response (days)	227	0	0	0	0	0	227
Duration of clinical benefit (days)	276	0	0	0	0	0	256

Abbreviations: n=number of responders; QW=once weekly.
One patient presented in HMBD-001 150 mg QW dose increased to 300 mg QW on Cycle 1 Day 15.
One patient presented in HMBD-001 300 mg QW dose increased to 600 mg QW on Cycle 1 Day 15.

ORR Within 8 and 16 weeks of Commencing HMBD-001, Disease Control Rate Within Six cycles of HMBD-001, Duration of Response, Duration of Clinical Benefit, Progression Free Survival and Overall Survival (Part B Arm 1)

These outcome measures were not analysed as recruitment was halted before any patient received HMBD-001 in Part B of the trial, due to a strategic decision not related to safety.

SECONDARY OUTCOME MEASURES - PHARMACOKINETICS

Maximum Observed Serum Concentration (C_{max}), Minimum Observed Serum Concentration (C_{min}), Area Under the Serum Concentration-Time Curve (AUC), Terminal Elimination Half-Life ($T_{½}$), Steady State Volume of Distribution in Serum (V_{ss}) and Total Body Clearance (CL) of HMBD-001 (Part A)

Part A - Pharmacokinetic Parameters on Cycle 1 Day 1 (Pharmacokinetic Population)

Parameter	Statistic	Cohort						
		Overall	HMBD-001 150 mg QW [a]	HMBD-001 300 mg QW [a]	HMBD-001 600 mg QW	HMBD-001 1200 mg QW	HMBD-001 1800 mg QW	HMBD-001 3000 mg QW
C_{max} (ng/mL)	n	24	1	1	3	3	6	10
	Min	33.0	33.0	98.3	113.9	252.0	351.5	359.7
	Max	977.5	ND	ND	177.2	364.8	495.2	977.5
	Median	406.0	ND	ND	119.9	271.9	406.0	707.2
	Geometric mean	358.5	ND	ND	134.3	292.4	408.8	683.4
	Geometric SD	2.3	ND	ND	1.3	1.2	1.1	1.4
	Geometric CV%	99.9	ND	ND	24.5	19.7	13.9	33.9
	Arithmetic mean	460.6	ND	ND	137.0	296.2	412.1	715.1
	Arithmetic SD	280.0	ND	ND	34.9	60.2	57.8	212.2
C_{trough} (ng/mL) [b,c]	n	24	1	1	3	3	6	10
	Min	11.0	11.0	25.6	47.4	142.3	124.8	129.5
	Max	448.9	ND	ND	82.1	155.1	235.8	448.9
	Median	155.8	ND	ND	58.6	147.7	147.2	246.8
	Geometric mean	138.2	ND	ND	61.1	148.3	154.8	246.0
	Geometric SD	2.3	ND	ND	1.3	1.0	1.3	1.5
	Geometric CV%	102.0	ND	ND	28.2	4.3	23.9	39.5
	Arithmetic mean	176.9	ND	ND	62.7	148.4	158.6	262.3
	Arithmetic SD	107.2	ND	ND	17.7	6.4	41.2	98.9

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Part A - Pharmacokinetic Parameters on Cycle 1 Day 1 (Pharmacokinetic Population)

Parameter	Statistic	Cohort						
		Overall	HMBD-001 150 mg QW [a]	HMBD-001 300 mg QW [a]	HMBD-001 600 mg QW	HMBD-001 1200 mg QW	HMBD-001 1800 mg QW	HMBD-001 3000 mg QW
AUC (µg/mL.h)	n	24	1	1	3	3	6	10
	Min	4499.0	4499.0	11822.0	21390.0	68413.0	69488.0	57513.0
	Max	261197.0	ND	ND	39163.0	82059.0	126024.0	261197.0
	Median	76364.5	ND	ND	27199.0	80825.0	72937.0	119750.0
	Geometric mean	69849.2	ND	ND	28349.6	76842.9	79616.5	129229.2
	Geometric SD	2.5	ND	ND	1.4	1.1	1.3	1.6
	Geometric CV%	116.0	ND	ND	31.2	10.1	23.2	51.5
	Arithmetic mean	94008.8	ND	ND	29250.7	77099.0	81590.2	143130.1
	Arithmetic SD	64668.1	ND	ND	9062.4	7547.6	22018.7	66852.3
T½ (h)	n	24	1	1	3	3	6	10
	Min	95.1	107.5	138.7	135.6	144.8	95.1	122.5
	Max	363.6	ND	ND	164.6	244.4	213.2	363.6
	Median	161.8	ND	ND	158.6	226.8	164.7	173.9
	Arithmetic mean	177.2	ND	ND	152.9	205.3	160.4	197.0
	Arithmetic SD	61.8	ND	ND	15.3	53.2	38.9	80.4

Part A - Pharmacokinetic Parameters on Cycle 1 Day 1 (Pharmacokinetic Population)

Parameter	Statistic	Cohort						
		Overall	HMBD-001 150 mg QW [a]	HMBD-001 300 mg QW [a]	HMBD-001 600 mg QW	HMBD-001 1200 mg QW	HMBD-001 1800 mg QW	HMBD-001 3000 mg QW
CL (mL/h)	n	24	1	1	3	3	6	10
	Min	11.5	33.3	25.4	15.3	14.6	14.3	11.5
	Max	52.2	ND	ND	28.1	17.5	25.9	52.2
	Median	24.5	ND	ND	22.1	14.8	24.7	25.1
	Arithmetic mean	23.7	ND	ND	21.8	15.6	23.1	25.8
	Arithmetic SD	9.3	ND	ND	6.4	1.6	4.4	12.8
V_{ss} (L)	n	24	1	1	3	3	6	10
	Min	3.4	5.4	5.0	3.6	3.7	3.4	4.0
	Max	9.2	ND	ND	5.5	5	6.3	9.2
	Median	5.1	ND	ND	5.1	4.8	5.2	6.1
	Arithmetic mean	5.5	ND	ND	4.7	4.5	5.1	6.2
	Arithmetic SD	1.4	ND	ND	1.0	0.7	1.1	1.7

Abbreviations: AUC=area under the curve; CL=clearance; C_{max}=maximum observed serum concentration; C_{trough}=trough serum concentration; CV%=coefficient of variation; n=number of patients assessed; max=maximum; min=minimum; ND=not done; SD=standard deviation; $T_{½}$=terminal half-life; T_{max}=time to reach maximum concentration; V_{ss}=volume of distribution at steady state.

[a] *For 150 mg and 300 mg single-patient cohorts, there is only one value shown in the min statistics row.*

[b] *Trough serum concentration (C_{trough}) was used to define the C_{min}.*

[c] *C_{trough} for Cycle 1 Day 1 dosing was measured pre-dose at Cycle 1 Day 8.*

C_{max}, C_{min}, AUC, $T_{½}$, V_{ss} and CL of HMBD-001 (Part B Arm 1)

These outcome measures were not analysed as recruitment was halted before any patient received HMBD-001 in Part B of the trial, due to a strategic decision not related to safety.

ADVERSE EVENTS SUMMARIES: Dose Escalation Phase

Part A – Treatment-Emergent Serious Adverse Events by System Order Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	All Patients (N=24)		HMBD-001 150 mg QW (N=1)		HMBD-001 300 mg QW (N=1)		HMBD-001 600 mg QW (N=3)		HMBD-001 1200 mg QW (N=3)		HMBD-001 1800 mg QW (N=6)		HMBD-001 3000 mg QW (N=10)	
	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events
Infections and infestations	**3 (12.5)**	**4**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (33.3)**	**1**	**1 (16.7)**	**1**	**1 (10.0)**	**2**
Lower respiratory tract infection	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Pneumonia	1 (4.2)	1	0	0	0	0	0	0	0	0	1 (16.7)	1	0	0
Prostatic abscess	1 (4.2)	1	0	0	0	0	0	0	1 (33.3)	1	0	0	0	0
Urinary tract infection	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Gastrointestinal disorders	**1 (4.2)**	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (33.3)**	**2**	**0**	**0**	**0**	**0**
Small intestinal obstruction	1 (4.2)	2	0	0	0	0	0	0	1 (33.3)	2	0	0	0	0
Hepatobiliary disorders	**1 (4.2)**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (10.0)**	**1**
Hepatorenal syndrome	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Investigations	**1 (4.2)**	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (10.0)**	**2**
Blood bilirubin increased	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1
Blood creatinine increased	1 (4.2)	1	0	0	0	0	0	0	0	0	0	0	1 (10.0)	1

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Part A – Treatment-Emergent Serious Adverse Events by System Order Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	All Patients (N=24)		HMBD-001 150 mg QW (N=1)		HMBD-001 300 mg QW (N=1)		HMBD-001 600 mg QW (N=3)		HMBD-001 1200 mg QW (N=3)		HMBD-001 1800 mg QW (N=6)		HMBD-001 3000 mg QW (N=10)	
	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events
Renal and urinary disorders	**1 (4.2)**	**1**	**0**	**0**	**0**	**0**	**1 (33.3)**	**1**	**0**	**0**	**0**	**0**	**0**	**0**
Acute kidney injury	1 (4.2)	1	0	0	0	0	1 (33.3)	1	0	0	0	0	0	0

Abbreviations: AE=adverse event; MedDRA=Medical Dictionary for Regulatory Activities v28.0; n=number of patients in the category; N=number of patients in the treatment group; QW=once weekly.
Patients are only counted once per category, irrespective of the number of occurrences.
Only includes treatment-emergent AEs, defined as any AE that worsened or onset after the first day of HMBD-001.
One patient presented in HMBD-001 150 mg QW dose increased to 300 mg QW on Cycle 1 Day 15.
One patient presented in HMBD-001 300 mg QW dose increased to 600 mg QW on Cycle 1 Day 15.

CRUKD/22/002, HMBD-001 Basic Results Summary for ISRCTN

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Part A – Treatment-Emergent Non-Serious Adverse Events Reported in ≥10% of Patients by System Order Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	All Patients (N=24)		HMBD-001 150 mg QW (N=1)		HMBD-001 300 mg QW (N=1)		HMBD-001 600 mg QW (N=3)		HMBD-001 1200 mg QW (N=3)		HMBD-001 1800 mg QW (N=6)		HMBD-001 3000 mg QW (N=10)	
	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events
Gastrointestinal disorders	**22 (91.7)**	**69**	**1 (100.0)**	**2**	**1 (100.0)**	**1**	**2 (66.7)**	**7**	**3 (100.0)**	**7**	**5 (83.3)**	**19**	**10 (100.0)**	**33**
Diarrhoea	19 (79.2)	32	1 (100.0)	2	0	0	2 (66.7)	6	3 (100.0)	4	4 (66.7)	8	9 (90.0)	12
Nausea	10 (41.7)	12	0	0	0	0	0	0	2 (66.7)	2	2 (33.3)	3	6 (60.0)	7
Abdominal pain	4 (16.7)	4	0	0	1 (100.0)	1	0	0	0	0	1 (16.7)	1	2 (20.0)	2
Dyspepsia	4 (16.7)	4	0	0	0	0	0	0	0	0	1 (16.7)	1	3 (30.0)	3
Stomatitis	3 (12.5)	3	0	0	0	0	0	0	0	0	1 (16.7)	1	2 (20.0)	2
General disorders and administration site conditions	**14 (58.3)**	**17**	**0**	**0**	**1 (100.0)**	**1**	**3 (100.0)**	**4**	**1 (33.3)**	**2**	**4 (66.7)**	**4**	**5 (50.0)**	**6**
Fatigue	8 (33.3)	8	0	0	0	0	1 (33.3)	1	1 (33.3)	1	3 (50.0)	3	3 (30.0)	3
Mucosal inflammation	4 (16.7)	4	0	0	0	0	1 (33.3)	1	1 (33.3)	1	0	0	2 (20.0)	2
Pyrexia	1 (4.2)	1	0	0	0	0	1 (33.3)	1	0	0	0	0	0	0
Metabolism and nutrition disorders	**12 (50.0)**	**12**	**1 (100.0)**	**1**	**0**	**0**	**2 (66.7)**	**2**	**1 (33.3)**	**1**	**3 (50.0)**	**3**	**5 (50.0)**	**5**
Decreased appetite	5 (20.8)	5	0	0	0	0	1 (33.3)	1	1 (33.3)	1	1 (16.7)	1	2 (20.0)	2

Part A – Treatment-Emergent Non-Serious Adverse Events Reported in ≥10% of Patients by System Order Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	All Patients (N=24)		HMBD-001 150 mg QW (N=1)		HMBD-001 300 mg QW (N=1)		HMBD-001 600 mg QW (N=3)		HMBD-001 1200 mg QW (N=3)		HMBD-001 1800 mg QW (N=6)		HMBD-001 3000 mg QW (N=10)	
	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events
Hypomagnesaemia	3 (12.5)	3	0	0	0	0	0	0	0	0	1 (16.7)	1	2 (20.0)	2
Investigations	**10 (41.7)**	**22**	**0**	**0**	**0**	**0**	**1 (33.3)**	**3**	**1 (33.3)**	**2**	**4 (66.7)**	**7**	**4 (40.0)**	**10**
Blood creatinine increased	4 (16.7)	4	0	0	0	0	0	0	1 (33.3)	1	1 (16.7)	1	2 (20.0)	2
Alanine aminotransferase increased	3 (12.5)	4	0	0	0	0	1 (33.3)	1	0	0	0	0	2 (20.0)	3
Aspartate aminotransferase increased	3 (12.5)	3	0	0	0	0	1 (33.3)	1	0	0	0	0	2 (20.0)	2
Skin and subcutaneous tissue disorders	**10 (41.7)**	**17**	**0**	**0**	**1 (100.0)**	**1**	**1 (33.3)**	**2**	**1 (33.3)**	**1**	**1 (16.7)**	**1**	**6 (60.0)**	**12**
Dry skin	3 (12.5)	3	0	0	0	0	1 (33.3)	1	1 (33.3)	1	0	0	1 (10.0)	1
Pruritus	3 (12.5)	3	0	0	1 (100.0)	1	0	0	0	0	0	0	2 (20.0)	2
Blood and lymphatic system disorders	**10 (41.7)**	**16**	**0**	**0**	**1 (100.0)**	**4**	**1 (33.3)**	**1**	**1 (33.3)**	**2**	**2 (33.3)**	**2**	**5 (50.0)**	**7**
Anaemia	10 (41.7)	12	0	0	1 (100.0)	1	1 (33.3)	1	1 (33.3)	2	2 (33.3)	2	5 (50.0)	6
Infections and infestations	**9 (37.5)**	**10**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (33.3)**	**1**	**2 (33.3)**	**2**	**6 (60.0)**	**7**
Upper respiratory tract infection	3 (12.5)	3	0	0	0	0	0	0	0	0	0	0	3 (30.0)	3

Part A – Treatment-Emergent Non-Serious Adverse Events Reported in ≥10% of Patients by System Order Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	All Patients (N=24)		HMBD-001 150 mg QW (N=1)		HMBD-001 300 mg QW (N=1)		HMBD-001 600 mg QW (N=3)		HMBD-001 1200 mg QW (N=3)		HMBD-001 1800 mg QW (N=6)		HMBD-001 3000 mg QW (N=10)	
	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events	n (%)	No. of Events
Musculoskeletal and connective tissue disorders	**6 (25.0)**	**12**	**1 (100.0)**	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (16.7)**	**3**	**4 (40.0)**	**7**
Arthralgia	3 (12.5)	3	1 (100.0)	1	0	0	0	0	0	0	0	0	2 (20.0)	2
Injury, poisoning and procedural complications	**6 (25.0)**	**8**	**0**	**0**	**1 (100.0)**	**1**	**1 (33.3)**	**2**	**1 (33.3)**	**1**	**0**	**0**	**3 (30.0)**	**4**
Infusion related reaction	4 (16.7)	6	0	0	1 (100.0)	1	1 (33.3)	2	1 (33.3)	1	0	0	1 (10.0)	2
Respiratory, thoracic and mediastinal disorders	**6 (25.0)**	**10**	**0**	**0**	**0**	**0**	**1 (33.3)**	**1**	**1 (33.3)**	**1**	**3 (50.0)**	**6**	**1 (10.0)**	**2**
Nervous system disorders	**5 (20.8)**	**6**	**1 (100.0)**	**2**	**0**	**0**	**1 (33.3)**	**1**	**0**	**0**	**1 (16.7)**	**1**	**2 (20.0)**	**2**
Reproductive system and breast disorders	**3 (12.5)**	**4**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (16.7)**	**1**	**2 (20.0)**	**3**

Abbreviations: AE=adverse event; MedDRA=Medical Dictionary for Regulatory Activities v28.0; n=number of patients in the category; N=number of patients in the treatment group; QW=once weekly.
Patients are only counted once per category, irrespective of the number of occurrences.
Only includes treatment-emergent AEs, defined as any AE that worsened or onset after the first day of HMBD-001.
One patient presented in HMBD-001 150 mg QW dose increased to 300 mg QW on Cycle 1 Day 15.
One patient presented in HMBD-001 300 mg QW dose increased to 600 mg QW on Cycle 1 Day 15.

ADVERSE EVENTS SUMMARIES: Dose Expansion Phase (PART B ARM 1)

AE summaries were not generated for the dose expansion phase as recruitment was halted before any patient received HMBD-001 in Part B of the trial, due to a strategic decision not related to safety.