Table 1: Schedule of Events

Visit	Screening	Randomization[a]	Treatment Period			Final Visit/ET[c]
			1st eligible HAE attack[b]	2nd eligible HAE attack[b]	3rd eligible HAE attack[b]	
In-clinic[d]	X	X				X
TeleVisit[e]			X	X	X	
Informed Consent/Assent[f]	X					
Eligibility Assessment	X	X				
HAE Diagnostic Lab Test[g]	X					
Medical History[h]	X					
12-lead ECG[i]	X					X
Demographics[j]	X					
Physical Examination[k]	X					X
Vital Signs[l]	X					X
Safety Laboratory[m]	X					X
Pregnancy Test[n]	X					X
Randomize patient in RTSM		X				
Patient diary training	X	X				
Patient diary retraining			X	X	X	
Conventional on-demand treatment washout[o]			◄———	———	———►	
Dose[p]			X	X	X	
IMP dispensing/return/accountability[q]		X				X
PGI-S[r]			X	X	X	
PGI-C[r]			X	X	X	
VAS[r]			X	X	X	
GA-NRS[r]			X	X	X	
Concomitant Medication Review	◄———	———	———	———	———►	

Visit	Screening	Randomization[a]	Treatment Period			Final Visit/ET[c]
			1st eligible HAE attack[b]	2nd eligible HAE attack[b]	3rd eligible HAE attack[b]	
Adverse Event Review[s]	◄	———	———	———	———	►

Abbreviations: C1-INH=C1-esterase inhibitor; ECG=electrocardiogram; eDiary=electronic diary; ET=Early Termination; GA-NRS= General Anxiety – Numeric Rating Scale; HAE=hereditary angioedema; IMP=investigational medicinal product; PGI-C=patient global impression of change; PGI-S=patient global impression of severity; RTSM=Randomization Trial Supply Management System; VAS=visual analog scale.

a Randomization to occur within 4 weeks of the Screening Visit. The Randomization Visit may be a televisit or an in-clinic visit.

b For each of the 3 eligible HAE attacks, a televisit will occur by the next working day after the completion of the patient diary (visit window: +1 week). A televisit must occur before treating the next eligible attack.

c Once 3 HAE attacks have been treated with IMP, or upon patient ET, the patient should return to the clinic for the final visit as soon as possible within 1 week of completing all patient diary assessments. Whenever possible this visit should be completed prior to starting any new medication or treatment.

d If an in-clinic visit cannot be conducted (e.g. in the event of a pandemic or other reason that prevents the patient from attending in-clinic visits), home health visits will be used to perform these visits. Information captured during a home health visit will mirror that captured during an in-clinic visit.

e A televisit can be conducted via a telephone call or via an interactive audio/video system.

f Consent and assent may be collected through e-consent if allowed through country and site regulations.

g Diagnostic testing must be available for patients without genetic confirmation of HAE type I or II.

h Medical history includes any relevant previous and concurrent diseases, HAE disease history including the attack history and corresponding treatment for the past 3 months; therapies and supplements taken within the past 4 weeks; and previous participation in interventional clinical trials in the past 4 weeks.

i ECG to be recorded after patient has rested supine for at least 5 minutes.

j Demographics: Year of birth; height (meters [m]; without shoes); weight (kilograms [kg]); race and ethnicity (if allowed); and sex.

k Complete physical examination at Screening only, all others will be symptom directed. In the case of a home health visit, the home healthcare nurse will conduct an abbreviated physical examination, and the Investigator will conduct the symptom-directed physical examination via televisit.

l Vital signs include pulse rate, respiratory rate, and systolic and diastolic blood pressure after patient has been resting at least 5 minutes.

m Laboratory assessments, including C1-INH functional level, performed by a central laboratory; repeat laboratory assessments may be performed.

n Serum pregnancy test will be performed on females of childbearing potential at Screening and at the Final/ET visit.

o If a patient takes conventional on-demand treatment during the trial, a 48-hour washout period is required prior to the subsequent dosing with IMP.

p Eligible attacks should be treated with IMP as soon as possible after recognition of the start of the attack. A minimum 48-hour washout period is required between each eligible attack and last dose of IMP or conventional on-demand treatment. After the first dose of IMP and prior to the second dose or conventional on-demand treatment, patients will be required to call a designated Study Call Center to be reminded of the repeat dosing criteria. The Call Center staff will remind patients of the rules for re-dosing and the eDiary assessment requirements.

q Arrangements will be made to dispense the assigned IMP. The IMP will be shipped to the patient via a courier service or will be dispensed at the trial clinic as required by local regulations or per the site's local practice, as described in the Pharmacy Manual. Confirmation of dosing compliance will be performed at each of the HAE attack televisits. All unused IMP and packaging will be returned at the in-clinic Final Visit/ET Visit. If the Final Visit/ET Visit is performed by Home Health, arrangements will be made to return any unused IMP and packaging via courier.

r Patients will complete timed assessments of HAE attack symptoms through 48 hours following first dose of IMP. Patient assessments will be performed as outlined in Table S1.

s Adverse events recorded from the first dose of KVD900 or placebo up to and including to Final Visit/ET. Serious AEs recorded from the time of signing the informed consent up to and including the Final Visit/ET.