Table S1. Analysis of the effects of varying clinical scenarios for GEE models fitted individually for each of the type of preclinical evidence[a]

	Scenario 7		Scenario 6		Scenario 5		Scenario 4		Scenario 3		Scenario 2	
Preclinical evidence	**Odds ratio (95% Wald CI)**	**Wald p-value**	**Odds ratio (95% Wald CI)**	**Wald p-value**	**Odds ratio (95% Wald CI)**	**Wald p-value**	**Odds ratio (95% Wald CI)**	**Wald p-value**	**Odds ratio (95% Wald CI)**	**Wald p-value**	**Odds ratio (95% Wald CI)**	**Wald p-value**
Primary human cells	13.08	<0.001	6.45	<0.001	4.35	<0.001	3.20	<0.001	1.87	<0.001	1.20	0.050
Primary human cells, mouse model in 2 years	13.13	<0.001	6.78	<0.001	5.22	<0.001	3.19	<0.001	1.72	<0.001	1.14	0.129
Good mouse model	14.64	<0.001	7.85	<0.001	5.12	<0.001	3.35	<0.001	1.23	0.365	1.00	1.000
Poor mouse model	14.08	<0.001	8.76	<0.001	5.52	<0.001	3.38	<0.001	1.78	<0.001	1.00	1.000
Good mouse model, large animal study would delay trial by 3 years	14.91	<0.001	10.57	<0.001	6.43	<0.001	4.35	<0.001	1.93	<0.001	0.95	0.655
Large animal model	14.45	<0.001	7.60	<0.001	4.08	<0.001	2.60	0.004	0.49	0.092	0.25	0.326
Good mouse model, data from related phase I trial without adverse events	13.61	<0.001	7.50	<0.001	5.47	<0.001	1.71	0.160	0.83	0.564	0.83	0.316
Good mouse model, data from related phase I trial with low frequency adverse events	23.52	<0.001	14.59	<0.001	6.34	<0.001	3.98	<0.001	1.58	0.034	1.00	1.000

[a]For each of the types of preclinical evidence, odds ratios are expressed as the likelihood that support for a hypothetical trial was associated with a change in clinical scenario, relative to the scenario where there was no available treatment and death occurred in infancy.

Table S2. Analysis of the effects of varying preclinical evidence for GEE models fitted individually for each clinical scenario[a]

	Large animal model		Good mouse model with data from related phase I without adverse events		Good mouse model		Good mouse model with data from related phase I with low frequency adverse events		Good mouse model, large animal study would delay trial by 3 years		Poor mouse model		Primary human cells	
Clinical Scenario	**Odds ratio (95% Wald CI)**	**Wald p-value**	**Odds ratio (95% Wald CI)**	**Wald p-value**	**Odds ratio (95% Wald CI)**	**Wald p-value**	**Odds ratio (95% Wald CI)**	**Wald p-value**	**Odds ratio (95% Wald CI)**	**Wald p-value**	**Odds ratio (95% Wald CI)**	**Wald p-value**	**Odds ratio (95% Wald CI)**	**Wald p-value**
Scenario 1	29.37	<0.001	19.32	<0.001	7.27	<0.001	7.84	<0.001	4.97	<0.001	3.38	<0.001	1.24	0.004
Scenario 2	136.32	<0.001	26.55	<0.001	8.27	<0.001	8.92	<0.001	5.98	<0.001	3.85	<0.001	1.17	0.013
Scenario 3	102.31	<0.001	40.13	<0.001	10.19	<0.001	8.54	<0.001	4.43	<0.001	3.28	<0.001	1.14	0.129
Scenario 4	36.02	<0.001	36.02	<0.001	6.92	<0.001	6.28	<0.001	3.64	<0.001	3.19	<0.001	1.23	0.106
Scenario 5	37.90	<0.001	18.43	<0.001	7.40	<0.001	6.45	<0.001	4.03	<0.001	3.20	<0.001	1.49	0.002
Scenario 6	26.21	<0.001	17.46	<0.001	6.27	<0.001	3.64	<0.001	3.19	<0.001	2.62	<0.001	1.30	0.056
Scenario 7	26.66	<0.001	18.63	<0.001	6.51	<0.001	4.38	<0.001	4.38	<0.001	3.16	<0.001	1.24	0.081

[a]For each of the clinical scenarios, odds ratios are expressed as the likelihood that support for a hypothetical trial was associated with a change in type of preclinical evidence, relative to the evidence generated in a cell culture model where a mouse model could be generated within two years.