Appendix Table 1: Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
1. 18 years of age or older 2. Diagnosis of Larsen grade II or III knee osteoarthritis 3. Pain during everyday work 4. Negative treatment results with other products 5. No anti-inflammatory treatment or analgesic for two weeks 6. Erythrocyte sedimentation rate value less than 40 mm 7. Rheumatoid factor less than 1:160	1. Unreliable patients 2. Patients free from pain

Appendix Table 2: Patient-assessed efficacy outcomes.

Outcome	Timepoint	Mean (SEM)		P-value between groups
		Hylan G-F 20	Placebo	
Weightbearing pain (VAS)	Baseline (Week 0)	65 (4)	70 (4)	NS
	Week 1	10 (3)	5 (3)	NS
	Week 2	31 (4)	19 (4)	0.0447
	Week 3	43 (5)	25 (5)	0.0136
	Week 8	51 (4)	24 (4)	0.0001
	Week 12	54 (4)	27 (4)	0.0001
Night pain (VAS)	Baseline (Week 0)	30 (7)	33 (7)	NS
	Week 1	8 (3)	4 (3)	NS
	Week 2	16 (4)	13 (4)	NS
	Week 3	23 (5)	16 (5)	NS
	Week 8	27 (6)	16 (6)	NS
	Week 12	27 (6)	18 (6)	NS
Improvement of most painful knee movement (VAS)	Week 1	45 (5)	24 (5)	0.0091
	Week 2	56 (6)	29 (6)	0.0043
	Week 3	71 (7)	41 (7)	0.0041
	Week 8	88 (7)	42 (7)	0.0001
	Week 12	88 (6)	38 (7)	0.0001
Overall assessment of arthritic pain (VAS)	Week 1	34 (7)	19 (7)	NS
	Week 2	57 (7)	33 (7)	0.0212
	Week 3	79 (6)	51 (6)	0.0034
	Week 8	90 (7)	48 (7)	0.0002
	Week 12	91 (7)	43 (7)	0.0001

NS, not significant; SEM, standard error of the mean; VAS, visual analogue scale.
Baseline (week 0) values represent absolute scores. Follow-up values represent improvements from baseline.

Appendix Table 3: Evaluator-assessed efficacy outcomes.

Outcome	Timepoint	Mean (SEM)		P-value between groups
		Hylan G-F 20	Placebo	
Weightbearing pain (VAS)	Baseline (Week 0)	65 (3)	66 (3)	NS
	Week 1	15 (3)	8 (3)	NS
	Week 2	29 (4)	17 (4)	0.0418
	Week 3	41 (5)	22 (5)	0.0069
	Week 8	52 (4)	20 (4)	0.0001
	Week 12	55 (4)	20 (4)	0.0001
	Week 26	42 (6)	21 (6)	0.0180
Night pain (VAS)	Baseline (Week 0)	26 (6)	30 (6)	NS
	Week 1	11 (3)	1 (3)	0.0203
	Week 2	18 (4)	6 (4)	NS
	Week 3	22 (5)	11 (5)	NS
	Week 8	24 (5)	12 (5)	NS
	Week 12	24 (5)	12 (5)	NS
	Week 26	23 (6)	15 (6)	NS
Decrease of activity (VAS)	Baseline (Week 0)	58 (6)	52 (6)	NS
	Week 1	12 (3)	1 (3)	0.0164
	Week 2	29 (4)	9 (4)	0.0035
	Week 3	39 (4)	14 (4)	0.0004
	Week 8	48 (4)	14 (4)	0.0001
	Week 12	49 (5)	11 (5)	0.0001
	Week 26	44 (7)	7 (7)	0.0004
Overall assessment of clinical condition (VAS)	Week 1	44 (5)	40 (5)	NS
	Week 2	58 (5)	41 (5)	0.0309
	Week 3	74 (5)	48 (5)	0.0010
	Week 8	85 (7)	42 (7)	0.0002
	Week 12	86 (7)	40 (7)	0.0001
Inactivity stiffness, time until the first rest period	Baseline (Week 0)	189 (38)	143 (38)	NS
	Week 1	-9 (11)	8 (11)	NS
	Week 2	33 (23)	28 (20)	NS
	Week 3	13 (39)	52 (27)	NS
	Week 8	75 (60)	39 (36)	NS
	Week 12	20 (63)	31 (33)	NS
	Week 26	120 (91)	8 (41)	NS
Inactivity stiffness, length of rest period	Baseline (Week 0)	21 (4)	20 (4)	NS
	Week 1	1 (1)	3 (1)	NS
	Week 2	5 (3)	5 (3)	NS
	Week 3	17 (6)	7 (4)	NS
	Week 8	13 (7)	7 (4)	NS
	Week 12	17 (9)	7 (5)	NS

Outcome	Timepoint	Mean (SEM)		P-value between groups
		Hylan G-F 20	Placebo	
	Week 26	20 (16)	-1 (7)	NS
Inactivity stiffness, number of rest periods per day	Baseline (Week 0)	3 (1)	4 (1)	NS
	Week 1	0.5 (0.2)	0.2 (0.2)	NS
	Week 2	1.5 (0.5)	0.5 (0.4)	NS
	Week 3	2.4 (0.6)	0.9 (0.4)	NS
	Week 8	3.3 (0.8)	0.5 (0.5)	0.0145
	Week 12	2.0 (0.7)	0.5 (0.4)	NS
	Week 26	2.0 (1.5)	0.4 (0.7)	NS

NS, not significant; SEM, standard error of the mean; VAS, visual analogue scale.
Baseline (week 0) values represent absolute scores. Follow-up values represent improvements from baseline.

Appendix Table 4: Proportion of patients with >50% improvement on patient-assessed efficacy outcomes.

Outcome	Timepoint	Proportion with >50% improvement		P-value between groups
		Hylan G-F 20	Placebo	
Weightbearing pain (VAS)	Week 1	7%	0%	NS
	Week 2	33%	0%	0.012
	Week 3	73%	33%	0.008
	Week 8	87%	33%	0.002
	Week 12	87%	33%	0.003
Night pain (VAS)	Week 1	14%	20%	NS
	Week 2	43%	40%	NS
	Week 3	64%	53%	NS
	Week 8	64%	47%	NS
	Week 12	64%	54%	NS
Improvement of most painful knee movement (VAS)	Week 1	13%	0%	0.006
	Week 2	47%	13%	0.007
	Week 3	73%	33%	0.009
	Week 8	100%	33%	0.001
	Week 12	100%	33%	0.001
Overall assessment of arthritic pain (VAS)	Week 1	13%	13%	NS
	Week 2	53%	20%	0.040
	Week 3	93%	53%	0.014
	Week 8	100%	47%	0.002
	Week 12	100%	47%	0.002

NS, not significant; VAS, visual analogue scale.

Appendix Table 5: Proportion of patients with >50% improvement on evaluator-assessed efficacy outcomes.

Outcome	Timepoint	Proportion with >50% improvement		P-value between groups
		Hylan G-F 20	Placebo	
Weightbearing pain (VAS)	Week 1	13%	7%	NS
	Week 2	33%	13%	NS
	Week 3	73%	33%	0.006
	Week 8	100%	33%	<0.0001
	Week 12	100%	27%	<0.0001
	Week 26	60%	40%	0.066
Night pain (VAS)	Week 1	20%	0%	0.038
	Week 2	47%	20%	NS
	Week 3	53%	47%	NS
	Week 8	60%	47%	NS
	Week 12	53%	47%	NS
	Week 26	60%	53%	NS
Decrease of activity (VAS)	Week 1	13%	0%	0.0160
	Week 2	33%	0%	0.0180
	Week 3	67%	20%	0.006
	Week 8	87%	27%	<0.0001
	Week 12	87%	27%	<0.0001
	Week 26	80%	33%	0.001
Overall assessment of clinical condition (VAS)	Week 1	20%	13%	NS
	Week 2	60%	27%	0.048
	Week 3	93%	27%	<0.0001
	Week 8	100%	40%	0.001
	Week 12	100%	47%	0.002

NS, not significant; VAS, visual analogue scale.