Supplementary File

Supplementary Table 1 Outcome assessments in the phase 3 study and open-label extension

	Phase 3 Study							Open-label extension				
Week	**BL**	**12a**	**24a**	**36a**	**48a**	**72a**	**96a**	**0b**	**12b**	**24b**	**36b**	**48b**
Clinical laboratory tests of efficacy												
Fasting serum phosphate	X	X	X	X	X	X	X	X	X	X	X	X
Phosphate reabsorption (TmP/GFR)	X	X	X		X	X	X	X	X	X	X	X
Serum 1,25 dihydroxyvitamin D	X				X	X	X	X	X	X	X	X
Patient-reported outcomes												
WOMAC	X	X	X	X	X	X	X	X	X	X	X	X
BPI-SF	X	X	X	X	X	X	X	X	X	X	X	X
BFI	X	X	X	X	X	X	X	X	X	X	X	X
Ambulatory function												
6MWT	X	X	X	X	X	X	X	X	X	X	X	X
Pain medication use (participant diaries)	X	X	X	X	X			X	X	X	X	X

BFI, Brief Fatigue Inventory; BL, baseline; BPI-SF, Brief Pain Inventory short-form; 6MWT, 6-Minute Walk Test; TmP/GFR, ratio of tubular maximum reabsorption rate to glomerular filtration rate; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary Table 2 Burosumab Dose in the Open-label Extension Study Population (n=31)

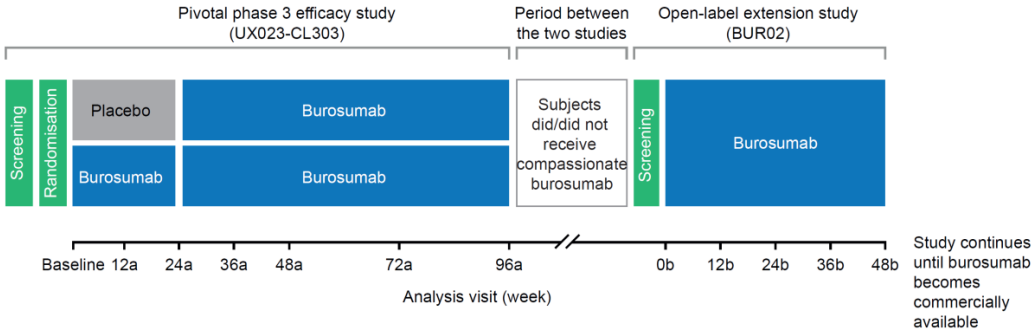
Study	Week	*n*	Mean (SD) mg/kg	Range mg/kg
Phase 3 study	Baseline	15	1.0 (0.06)	0.9–1.1
	12a[a]	15	1.0 (0.07)	0.9–1.1
	24a	31	1.0 (0.07)	0.8–1.2
	36a	31	1.0 (0.08)	0.9–1.2
	48a	30	1.0 (0.09)	0.1–1.2
	72a	30	1.0 (0.08)	1.8–1.1
	96a	30	1.0 (0.08)	0.5–1.1
Open-label extension	0b	31	1.0 (0.11)	0.9–1.5
	12b	31	1.0 (0.11)	0.9–1.5
	24b	31	1.0 (0.11)	0.9–1.5
	36b	31	1.0 (0.11)	0.8–1.5
	48b	31	1.0 (0.14)	0.8–1.5
Randomized double-blind treatment period; participants were randomized 1:1 to burosumab or placebo.				

Supplementary Table 3 Pain medication use reported in participants' diaries (n=31)

Study	Week	Any pain medication n (%)	Opioid n (%)
Phase 3 study	Baseline	25 (80.6)	8 (25.8)
	12a	22 (71.0)	5 (16.1)
	24a	21 (67.7)	6 (19.4)
	36a	23 (74.2)	7 (22.6)
	48a	21 (67.7)	5 (16.1)
Open-label extension	0b	16 (51.6)	6 (19.4)
	12b	8 (25.8)	2 (6.5)
	24b	20 (64.5)	7 (22.6)
	36b	12 (38.7)	2 (6.5)
	48b	15 (48.4)	4 (12.9)

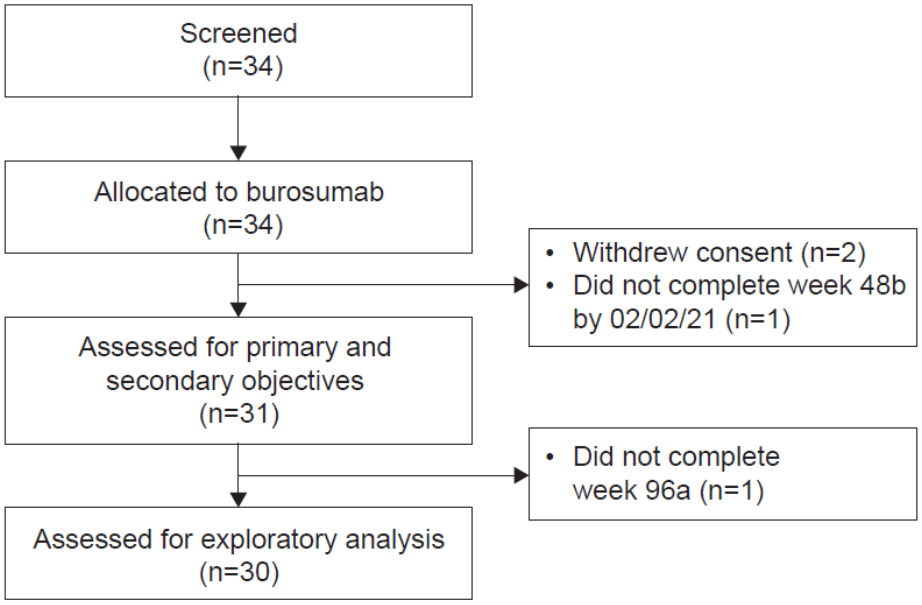
Pain medication use was not collected in weeks 72a and 96a.

Supplementary Figure 1 Treatment and randomization in the phase 3 study and open-label extension



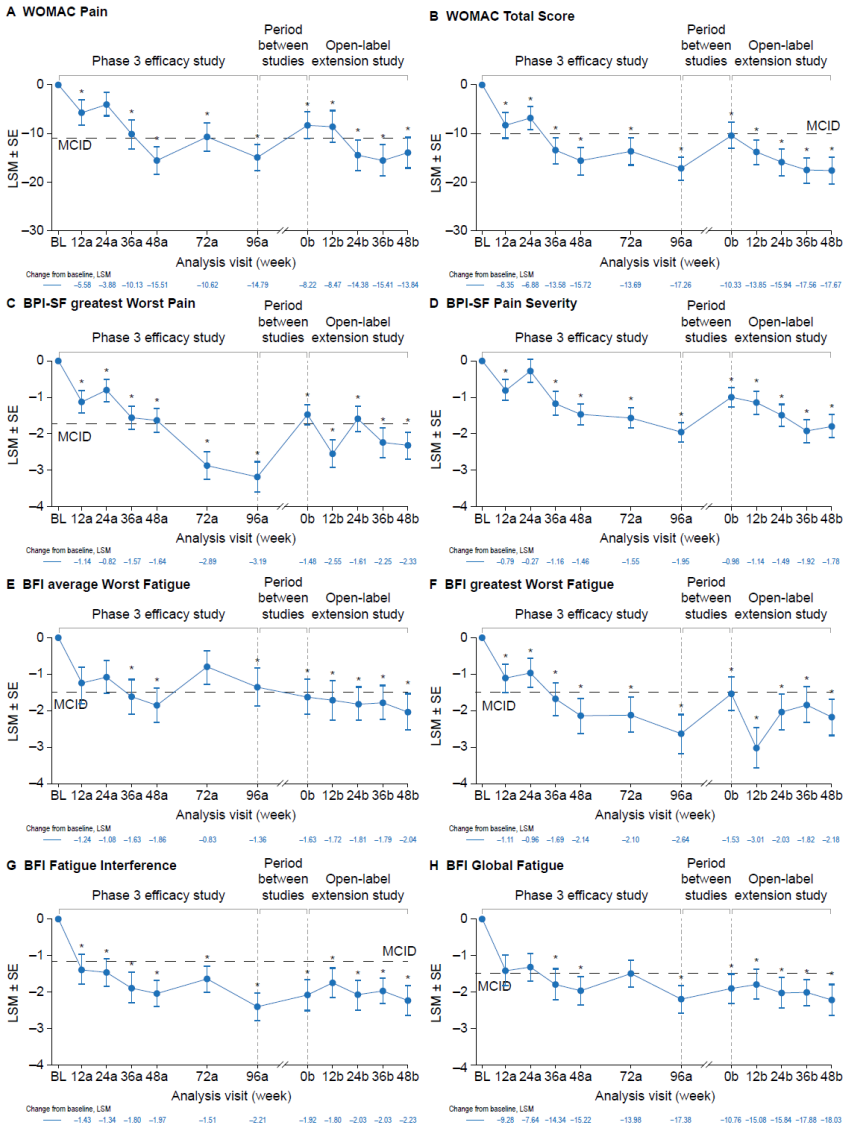
Analysis visits in the phase 3 study and open-label extension study are suffixed a and b, respectively.
The phase 3 efficacy study (UX023-CL303) comprised a 24 week placebo-controlled treatment period (baseline to week 24a) followed by a treatment continuation period during which all participants received open-label burosumab (weeks 24a–96a). Week 0b is the open-label extension study baseline.

Supplementary Figure 2 Flow of patients through the phase 3 and open label extension studies



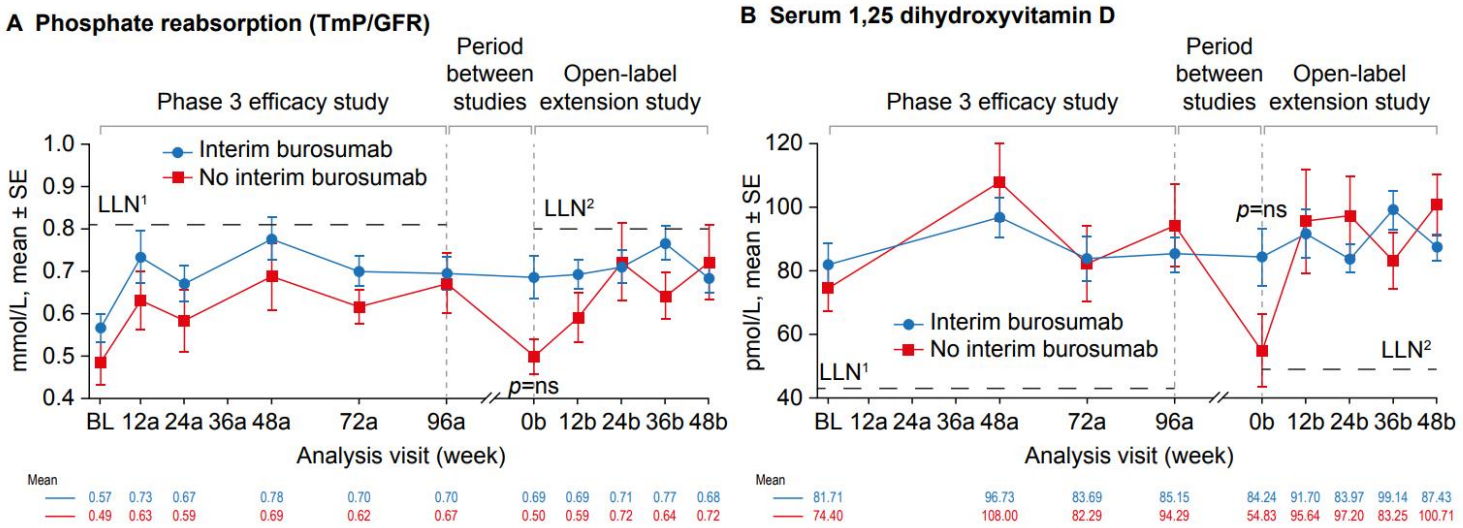
Week 96a is the end of the randomized study; week 48b is the end of the open-label extension.

Supplementary Figure 3 Effect of burosumab maintenance on additional PRO endpoints



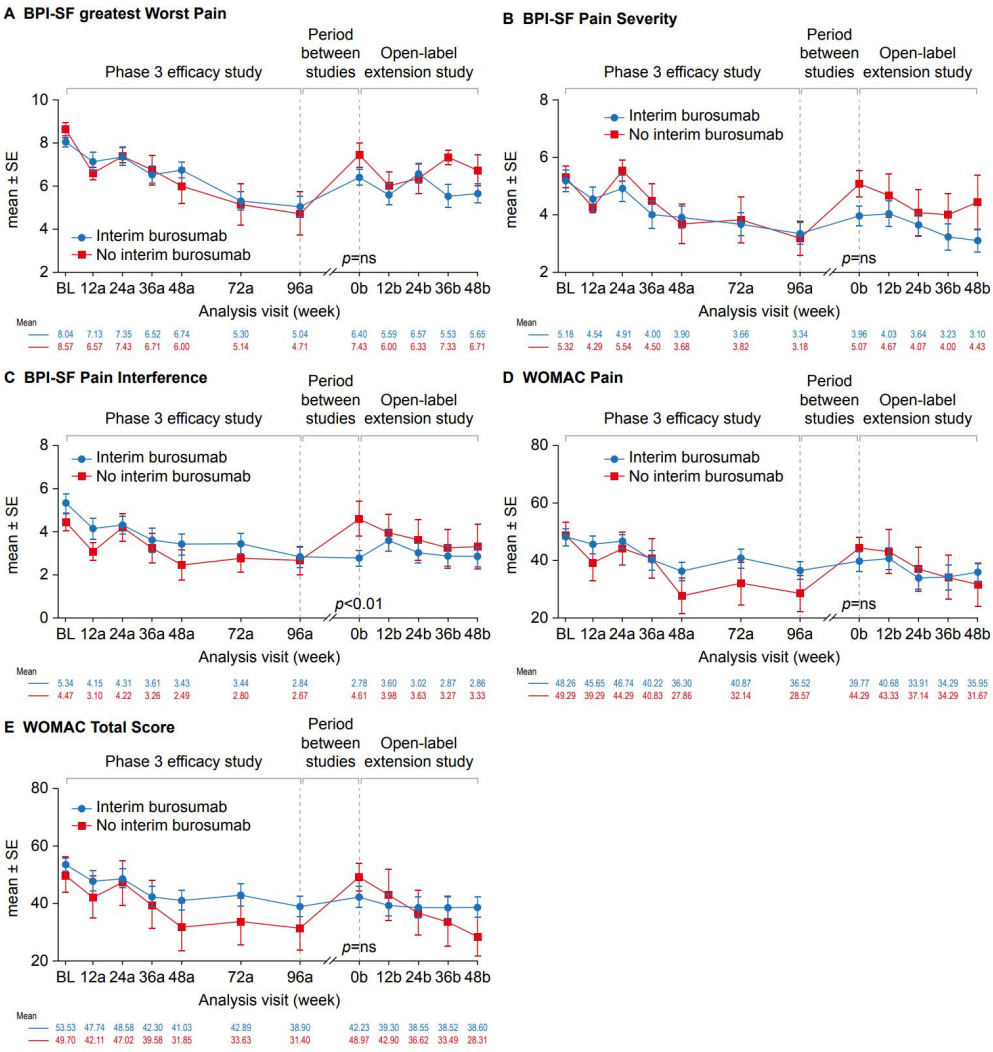
Data available for 31 participants at BL, 28 at week 48b for WOMAC, 27 at week 48b for BPI-SF and BFI
Analysis weeks in the phase 3 study and open-label extension are indicated by 'a' and 'b' suffixes, respectively
A decrease in WOMAC, BPI-SF and BFI score indicates improvement
BPI-SF and BFI data were captured at a single site visit and were not completed as part of a patient diary at weeks 72a and 96a
*p < 0.05 for LSM change from BL (generalized estimating equation repeated-measures analysis)
BFI, Brief Fatigue Inventory; BL, baseline; BPI-SF, Brief Pain Inventory short-form; LSM, least squares mean; MCID, minimum clinically important difference; SE, standard error; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary Figure4 Effect of burosumab treatment interruption on additional clinical laboratory tests of efficacy



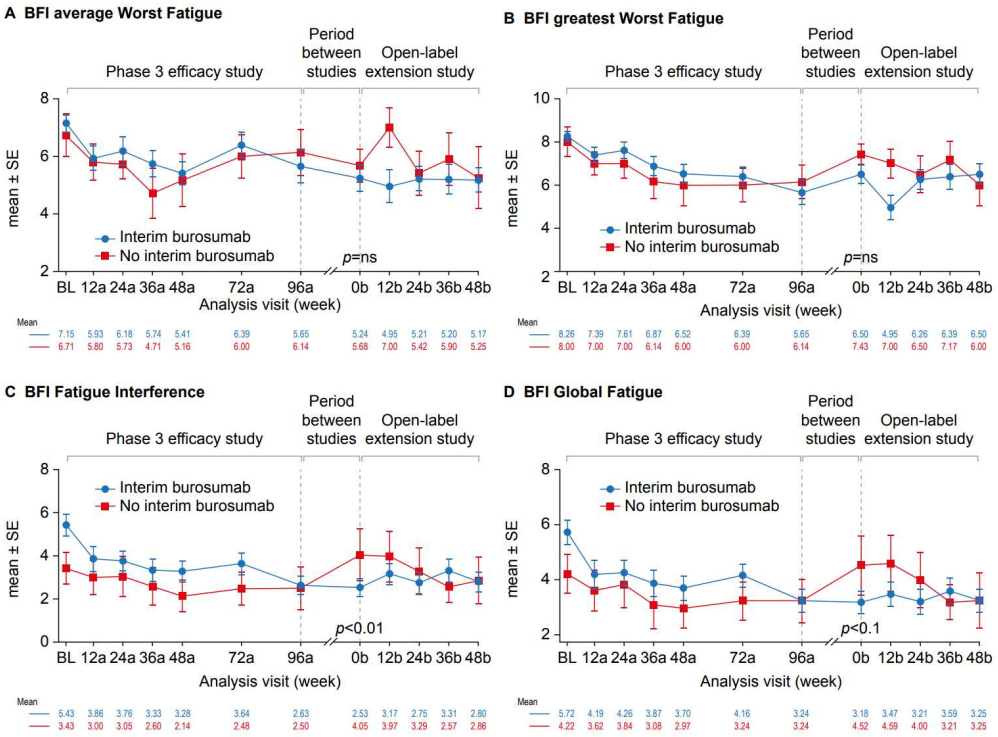
Interim burosumab, n=23; no interim burosumab, n=7
Analysis weeks in the phase 3 study and open-label extension are indicated by 'a' and 'b' suffixes, respectively
Samples from the two studies were measured at different central laboratories, with different LLN values for 1,25 dihydroxyvitamin D (43 pmol/L in the phase 3 study [LLN^1]; 48 pmol/L in the open-label extension [LLN^2]) and TmP/GFR (0.81 and 0.80–1.00 mmol/L).
p values are for the difference between the groups at week 0b (Fischer's exact test); $p < 0.05$ was considered significant. There was no significant difference between the groups at study baseline.
For serum 1,25 dihydroxyvitamin D, 29% of the interim burosumab group but none of the no interim burosumab group had values≥ LLN at the start of the open-label extension period (not significant). For phosphate reabsorption (TmP/GFR), 83% of the interim burosumab group and 43% of the no interim burosumab group had values ≥LLN at the start of the open-label extension period (not significant).
BL, baseline; LLN, lower limit of normal range; TmP/GFR, ratio of tubular maximum reabsorption rate to glomerular filtration rate

Supplementary Figure5 Effect of burosumab treatment interruption on additional BPI-SF and WOMAC endpoints



Interim burosumab, n=23; no interim burosumab, n=7
Analysis weeks in the phase 3 study and open-label extension are indicated by 'a' and 'b' suffixes, respectively
Decrease in WOMAC and BPI-SF scores indicates improvement
BPI-SF data were captured at a single site visit and were not completed as part of a patient diary at weeks 72a and 96a
p values are for the difference between the groups tested using the Mann–Whitney U test) $p < 0.05$ was considered significant. There was no significant difference between the groups at study baseline.
BL, baseline; BPI-SF, Brief Pain Inventory short-form; SE, standard error; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary Figure 6 Effect of burosumab treatment interruption on additional BFI endpoints



Interim burosumab, n=23; no interim burosumab, n=7
Analysis weeks in the phase 3 study and open-label extension are indicated by 'a' and 'b' suffixes, respectively
Decrease in BFI scores indicates improvement
BFI data were captured at a single site visit and were not completed as part of a patient diary at weeks 72a and 96a
p values are for the difference between the groups tested using the Mann–Whitney U test; $p < 0.05$ was considered significant. There was no significant difference between the groups at study baseline.
BFI, Brief Fatigue Inventory; BL, baseline; SE, standard error