SUPPLEMENTARY APPENDIX

Eligibility Criteria

Consent

1. Patients or their legally authorized representative must voluntarily **sign and date an informed consent**, approved by an independent ethics committee/institutional review board, prior to the initiation of any screening or study-specific procedures.

Demographic and Laboratory Assessments

2. Adult **male or female**, at least 18 years old.
3. **Laboratory values** meeting the following criteria within the screening period prior to the first dose of study drug:
   - Serum alanine transaminase <2 × upper limit of normal
   - Estimated glomerular filtration rate by simplified four-variable modification of diet in renal disease formula >40 mL/min/1.73 m^2
   - Total white blood cell count >3000/µL
   - Absolute neutrophil count >1500/µL
   - Platelet count >100,000/µL
   - Absolute lymphocyte count >800/µL
   - Hemoglobin >10 g/dL

Disease Activity

4. Diagnosis of rheumatoid arthritis (RA) for ≥3 months based on the 2010 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for RA.
5. Patient meets the following minimum disease activity criteria:
   - ≥6 swollen joints (based on 66 joint counts) and ≥6 tender joints (based on 68 joint counts) at screening and baseline visits, and high-sensitivity C-reactive protein ≥3 mg/L (central laboratory) at screening visit.

Patient History

6. No history of any of the following cardiovascular conditions:
   - Moderate to severe congestive heart failure (New York Heart Association Class III or IV).
   - Recent history (within past 6 months) of cerebrovascular accident, myocardial infarction, and/or coronary stenting.
   - Uncontrolled hypertension as defined by a persistent systolic blood pressure (BP).
   - >160 mmHg or diastolic BP >100 mmHg. For patients with known hypertension, the patient's BP must be stable for at least 4 weeks on current, stable anti-hypertensive medications.
   - Prior unprovoked deep vein thrombosis or pulmonary embolism (ie, any spontaneous event not directly attributable to trauma or vascular instrumentation).

- Any other condition which, in the opinion of the investigator, would put the patient at risk by participating in the protocol.

7. No history of any arthritis with onset prior to age 17 years or current diagnosis of inflammatory joint disease other than RA (including but not limited to gout, systemic lupus erythematosus, psoriatic arthritis, axial spondyloarthritis including ankylosing spondylitis and non-radiographic axial spondyloarthritis, reactive arthritis, overlap connective tissue diseases, scleroderma, polymyositis, dermatomyositis, fibromyalgia [currently with active symptoms], or any arthritis with onset prior to age 17 years). Current diagnosis of secondary Sjogren's Syndrome is permitted.
8. Must not have been treated with intra-articular, intramuscular, intravenous, trigger point or tender point, intra-bursa, or intra-tendon sheath corticosteroids in the preceding 8 weeks prior to the first dose of study drug.
9. Must not have been treated with any investigational drug within 30 days or five half-lives of the drug (whichever is longer) prior to the first dose of study drug or is currently enrolled in another clinical study.
10. Females must not be pregnant, breastfeeding, or considering becoming pregnant during the study or for approximately 30 days after the last dose of study drug.
11. For all females of childbearing potential: a **negative serum pregnancy test** at the screening visit and a negative urine pregnancy test at baseline prior to the first dose of study drug.
12. Female patients of childbearing potential must practice at least one protocol-specified **method of birth control** that is effective from study day 1 through at least 30 days. Female patients of non-childbearing potential do not need to use birth control.
13. Must not have any active or recurrent viral infection that, based on the investigator's clinical assessment, makes the patient an unsuitable candidate for the study, including hepatitis B virus (HBV) or hepatitis C virus (HCV), recurrent or disseminated (even a single episode) herpes zoster, disseminated (even a single episode) herpes simplex, or HIV. Active HBV, HCV, and HIV are defined as:
14. HBV: Hepatitis B surface antigen positive or, for hepatitis B core antibody positive patients, detection of HBV DNA by PCR
    - HCV: HCV RNA detectable in any patient with anti-HCV antibody
    - HIV: Confirmed positive anti-HIV antibody test
15. Must not have active tuberculosis (TB) or meets TB exclusionary parameters (defined as the presence of active TB or latent TB not adequately treated as per protocol requirements). Canada only: Must not have active TB or untreated or inadequately treated latent TB
    - Must not have evidence of active TB defined in this study as the following:
        - Documented by a positive purified protein derivative test (≥5 mm induration between approximately 48 and 72 hours after application, regardless of vaccination history) and/or medical history, clinical features, and abnormal chest x-ray at screening consistent with active TB
    - The QuantiFERON®-TB Gold test or T SPOT.*TB* test (as available and if compliant with local TB guidelines) may be used instead of the purified protein derivative (PPD) test. Patients are excluded from the study if the test is not negative and there is clinical evidence of active TB
    - Must not have evidence of untreated/inadequately or inappropriately treated latent TB, defined in this study as the following:
        - Documented to have a positive PPD test (≥5 mm induration between approximately 48 and 72 hours after application, regardless of vaccination history), no clinical features consistent with active TB, and a chest x-ray with no evidence of active TB at screening; or

- PPD test is positive, and the patient has no medical history or chest x-ray findings consistent with active TB, the patient may have a QuantiFERON-TB Gold test or T SPOT.*TB* test (as available and if compliant with local TB guidelines). If the test results are not negative, the patient will be considered to have latent TB (for purposes of this study); or
- QuantiFERON®-TB Gold test or T SPOT.*TB* test (as available and if compliant with local TB guidelines) may be used instead of the PPD test. If the test results are positive, the patient will be considered to have latent TB. If the test is not negative, the test may be repeated once within approximately 2 weeks of the initial value. If the repeat test results are again not negative, the patient will be considered to have latent TB (for purposes of this study)

16. Must not have used known strong cytochrome P450 (CYP)3A or CYP1A2 inhibitors or strong CYP3A or CYP1A2 inducers from screening through the end of the study.
17. Must not have had receipt of any live vaccine within 4 weeks prior to the first dose of study drug or expected need of live vaccination during study participation including at least 4 weeks after the last dose of oral study drug.
18. Must not have a history of any malignancy except for successfully treated non-melanoma skin cancer or localized carcinoma in situ of the cervix.
19. Must not have a history of clinically significant (per Investigator's judgment) drug or alcohol abuse within the last 6 months.
20. Must not have a history of gastrointestinal perforation (other than appendicitis or penetrating injury), diverticulitis or significantly increased risk for gastrointestinal perforation per Investigator judgment.
21. Must not have any conditions that could interfere with drug absorption including but not limited to short bowel syndrome.
22. Must not be a recipient of an organ transplant.
23. Must not have history of clinically significant medical conditions or any other reason that in the opinion of the investigator would interfere with the patient's participation in this study or would make the patient an unsuitable candidate to receive study drug.
24. Must not have had an active infection(s) requiring treatment with parenteral anti-infectives within 30 days, or oral anti-infectives within 14 days prior to the first dose of study drug.
25. Must not have a history of an allergic reaction or significant sensitivity to constituents of the study drugs (and its excipients) and/or other products in the same class.

Concomitant Medications

26. Patients must have been treated for ≥3 months with ≥1 biologic disease-modifying antirheumatic drug (bDMARD) therapy but continue to exhibit active RA or had to discontinue due to intolerability or toxicity, irrespective of treatment duration.
27. Patients must have been receiving conventional synthetic disease-modifying antirheumatic drug (csDMARD) therapy ≥3 months and on a stable dose for ≥4 weeks prior to the first dose of study drug.
    - The following csDMARDs are allowed (stable dose for ≥4 weeks prior to the first dose of study drug): oral or parenteral methotrexate (MTX) (7·5 to 25 mg/week), sulfasalazine (≤3000 mg/day), hydroxychloroquine (≤400 mg/day), chloroquine (≤250 mg/day), and leflunomide (≤20 mg/day).
    - A combination of up to two background csDMARDs is allowed EXCEPT the combination of MTX and leflunomide.
28. Dose of non-steroidal anti-inflammatory drugs and acetaminophen/paracetamol must have been at a stable dose ≥1 week prior to the first dose of study drug; oral corticosteroids (equivalent to

prednisone ≤ 10 mg/day) or inhaled corticosteroids for stable medical conditions are allowed but must have been at a stable dose ≥4 weeks prior to the first dose of study drug.

29. Patients must have discontinued all bDMARDs prior to the first dose of study drug. The washout period for bDMARDs prior to the first dose of study drug is specified below or should be at least five times the mean terminal elimination half-life of a drug:
    - ≥4 weeks for etanercept, adalimumab, infliximab, certolizumab, golimumab, tocilizumab, and abatacept
    - ≥1 year for rituximab OR ≥6 months if B cells have returned to pretreatment level or normal reference range (central laboratory) if pretreatment levels are not available (B cell testing may be completed at screening if indicated).
30. Patients must have discontinued all high-potency opiates at least 1 week and oral traditional Chinese medicine for at least 4 weeks prior to the first dose of study drug.
31. Patient must not have prior exposure to any JAK inhibitor for longer than 2 weeks (including but not limited to upadacitinib, tofacitinib, baricitinib, and filgotinib). A washout period of ≥30 days is required for any JAK inhibitor prior to the first dose of study drug.

Dose-Response Modelling for Elsubrutinib

The dose-response relationship among elsubrutinib dose groups and the placebo group was characterized for the primary endpoint using the Multiple Comparison Procedure – Modeling (MCP-Mod) method (Pinheiro 2006, Bretz 2005). The response based on the primary analysis was used, and ADDPLAN DF software was used to perform the MCP-Mod analyses. The posterior mean (SD) for placebo group (i.e., with historical borrowing) was used as primary analysis. The data directly from MMRM for placebo was also analysed as sensitivity analysis.

A set of 6 pre-specified standardized candidate dose-response models, as described in the Table below were utilized to examine the dose-response relationship. A statistically significant dose-response relationship would be declared if at least one model was identified by the MCP-Mod method to be statistically significant at $\alpha = 0.1$ two-sided. The fitted dose-response curves were generated for all statistically significant models along with confidence bands. The minimum effective dose (MED) was identified for each statistically significant model based on the pre-specified clinical meaningful target of –0.88. The weighted MED across all significant models was calculated, with weight being inverse of model AIC.

Table: **Candidate models.**

Model	$f(d, \theta)$ d = dose, θ = Model Parameters	$f^0(d, \theta)$ Standardized Model	Initial Value(s) for Parameter(s)
Linear	$E_0 + \delta d$	d	NA
Exponential	$E_0 + E_1\left[exp\left(\frac{d}{\delta}\right) - 1\right]$	$exp\left(\frac{d}{\delta}\right) - 1$	$\delta = 20$
Logistic	$E_0 + \frac{E_{max}}{1 + exp\left(\frac{ED_{50} - d}{\delta}\right)}$	$\frac{1}{1 + exp\left(\frac{ED_{50} - d}{\delta}\right)}$	$ED_{50} = 5$, $\delta = 10$
EMax	$E_0 + \frac{E_{max} d}{ED_{50} + d}$	$\frac{d}{ED_{50} + d}$	$ED_{50} = 5$
sigEMax	$E_0 + \frac{E_{max} d^h}{{ED_{50}}^h + d^h}$	$\frac{d^h}{{ED_{50}}^h + d^h}$	$ED_{50} = 5$, $h = 2$
Quadratic	$E_0 + \beta_1 d + \beta_2 d^2$	$d + \frac{\beta_2}{\lvert\beta_1\rvert} d^2$	$\delta = -0.01$

Steps of MCPMod:

1. Choose a candidate set of *S* models as in Table 1.
2. Compute the optimum contrast for each model.
3. Use contrast test to find the significant *T* models while preserving FWER.
4. Use AIC criteria to find the most significant model from the significant *T* models found from Step 3.

5. Use the model found from Step 4 to fit observed data from the study and make inference (e.g., to find Minimum Effective Dose (MED) or the dose achieving certain amount of maximum effect), or use all significant models to make inference about the weighted target dose of interest.

Supplemental Table 1: **Change from baseline in DAS28 (CRP) at week 12 by BMI subgroups at week 12[a,b]**

	n	LSM change (90% CI)	Difference vs placebo LSM (90% CI)
DAS28 CRP (BMI <25 kg/m^2)			
Placebo	3	–2·17 (–3·61, –0·73)	–
ABBV-599	11	–2·87 (–3·62, –2·12)	–0·70 (–2·30, 0·90)
ELS 60 mg	6	–0·42 (–1·39, 0·54)	1·75 (0·04, 3·45)
ELS 20 mg	4	–0·31 (–1·53, 0·92)	1·86 (–0·05, 3·78)
ELS 5 mg	11	–1·72 (–2·42, –1·01)	0·46 (–1·13, 2·04)
UPA 15 mg	9	–3·50 (–4·31, –2·68)	–1·33 (–2·99, 0·33)
DAS28 CRP (BMI ≥25 kg/m^2)			
Placebo	15	–0·94 (–1·48, –0·40)	–
ABBV-599	43	–2·46 (–2·79, –2·14)	–1·52 (–2·15, –0·90)
ELS 60 mg	29	–1·73 (–2·12, –1·33)	–0·78 (–1·45, –0·12)
ELS 20 mg	25	–1·44 (–1·85, –1·03)	–0·50 (–1·17, 0·18)
ELS 5 mg	23	–1·14 (–1·57, –0·71)	–0·20 (–0·88, 0·49)
UPA 15 mg	28	–2·70 (–3·10, –2·29)	–1·76 (–2·42, –1·09)

BMI=body mass index; DAS28 CRP=disease activity score 28 based on C-reactive protein; ELS=elsubrutinib; LSM=least-squares mean; UPA=upadacitinib.

[a]Based on patients with non-missing baseline and ≥1 post-baseline value.
[b]Baseline is defined as the last non-missing value prior to the first dose of study drug.
[C]P values are based on a mixed-effect model repeated measurements method.

Supplemental Table 2: **Summary of secondary endpoints (change from baseline) at week 12[a,b]**

	n	LSM change (90% CI)	Difference vs placebo LSM (90% CI)	P-value[c]
SDAI				
Placebo	18	–14·44 (–19·84, –9·04)	–	–
ABBV-599	52	–28·06 (–31·22, –24·89)	–13·62 (–19·77, –7·46)	0·00033
ELS 60 mg	35	–18·01 (–21·86, –14·15)	–3·57 (–10·09, 2·96)	0·37
ELS 20 mg	29	–17·12 (–21·20, –13·05)	–2·68 (–9·39, 4·02)	0·51
ELS 5 mg	32	–16·73 (–20·65, –12·81)	–2·29 (–8·88, 4·29)	0·57
UPA 15 mg	36	–29·65 (–33·42, –25·88)	–15·21 (–21·71, –8·71)	0·00015
Patient's assessment of pain[d]				
Placebo	18	–23·37 (–33·74, –13·01)	–	–
ABBV-599	54	–32·27 (–38·32, –26·23)	–8·90 (–20·73, 2·93)	0·22
ELS 60 mg	35	–19·52 (–26·97, –12·06)	3·86 (–8·72, 16·43)	0·61
ELS 20 mg	29	–10·46 (–18·38, –2·55)	12·91 (–0·03, 25·86)	0·10
ELS 5 mg	35	–17·84 (–25·13, –10·55)	5·53 (–7·01, 18·07)	0·47
UPA 15 mg	37	–38·34 (–45·57, –31·12)	–14·97 (–27·44, –2·50)	0·049
PGA				
Placebo	18	–19·55 (–30·15, –8·95)	–	–
ABBV-599	54	–30·52 (–36·72, –24·32)	–10·97 (–23·07, 1·13)	0·14
ELS 60 mg	35	–19·47 (–27·13, –11·81)	0·08 (–12·82, 12·98)	0·99
ELS 20 mg	29	–8·45 (–16·58, –0·33)	11·09 (–2·16, 24·35)	0·17
ELS 5 mg	35	–16·40 (–23·89, –8·92)	3·14 (–9·69, 15·98)	0·67
UPA 15 mg	37	–33·53 (–40·94, –26·13)	–13·99 (–26·77, –1·20)	0·072
PhGA				
Placebo	18	–23·19 (–31·69, –14·69)	–	–
ABBV-599	53	–46·98 (–52·00, –41·96)	–23·79 (–33·46, –14·11)	<0·0001
ELS 60 mg	35	–30·15 (–36·28, –24·03)	–6·96 (–17·27, 3·34)	0·27
ELS 20 mg	29	–31·68 (–38·19, –25·18)	–8·49 (–19·10, 2·12)	0·19
ELS 5 mg	33	–24·55 (–30·75, –18·36)	–1·36 (–11·73, 9·00)	0·83
UPA 15 mg	36	–50·89 (–56·87, –44·91)	–27·70 (–37·95, –17·45)	<0·0001
hsCRP, mg/L				
Placebo	18	1·45 (–5·10, 8·00)	–	–
ABBV-599	56	–10·95 (–14·73, –7·18)	–12·40 (–19·89, –4·91)	0·0068
ELS 60 mg	36	–4·58 (–9·26, 0·09)	–6·03 (–14·01, 1·96)	0·21
ELS 20 mg	31	–5·78 (–10·77, –0·78)	–7·23 (–15·42, 0·97)	0·15
ELS 5 mg	34	–0·81 (–5·58, 3·97)	–2·25 (–10·31, 5·80)	0·64
UPA 15 mg	37	–7·44 (–12·03, -2·86)	–8·89 (–16·84, –0·94)	0·066
DAS28 ESR				
Placebo	18	–1·18 (–1·71, –0·64)	–	–
ABBV-599	54	–2·53 (–2·84, –2·22)	–1·35 (–1·97, –0·74)	0·00033
ELS 60 mg	35	–1·41 (–1·80, –1·03)	–0·23 (–0·88, 0·42)	0·56
ELS 20 mg	29	–1·24 (–1·65, –0·83)	–0·06 (–0·73, 0·61)	0·88
ELS 5 mg	35	–1·44 (–1·82, –1·06)	–0·26 (–0·91, 0·39)	0·51
UPA 15 mg	37	–2·88 (–3·25, –2·50)	–1·70 (–2·34, –1·05)	<0·0001
Morning stiffness[e]				
Placebo	18	–1·61 (–2·60, –0·63)	–	–
ABBV-599	54	–3·23 (–3·81, –2·65)	–1·62 (–2·74, –0·49)	0·018
ELS 60 mg	34	–1·27 (–1·99, –0·56)	0·34 (–0·86, 1·54)	0·64
ELS 20 mg	29	–1·30 (–2·06, –0·55)	0·31 (–0·92, 1·54)	0·68
ELS 5 mg	35	–1·66 (–2·36, –0·97)	–0·05 (–1·24, 1·14)	0·94
UPA 15 mg	36	–3·36 (–4·06, –2·67)	–1·75 (–2·95, –0·56)	0·016
Swollen joint count[f]				
Placebo	18	–5·58 (–8·05, –3·11)	–	–
ABBV-599	56	–10·86 (–12·29, –9·44)	–5·28 (–8·09, –2·47)	0·0021
ELS 60 mg	36	–6·68 (–8·44, –4·92)	–1·10 (–4·09, 1·89)	0·54
ELS 20 mg	31	–7·85 (–9·70, –6·01)	–2·27 (–5·33, 0·78)	0·22
ELS 5 mg	35	–8·59 (–10·35, –6·83)	–3·01 (–6·01, –0·01)	0·099
UPA 15 mg	37	–11·14 (–12·86, –9·42)	–5·56 (–8·54, –2·58)	0·0023
Tender joint count[g]				
Placebo	18	–8·47 (–12·81, –4·12)	–	–
ABBV-599	56	–16·33 (–18·84, –13·83)	–7·87 (–12·79, –2·94)	0·0090
ELS 60 mg	36	–9·14 (–12·23, –6·05)	–0·68 (–5·92, 4·57)	0·83
ELS 20 mg	31	–9·33 (–12·55, –6·12)	–0·87 (–6·22, 4·48)	0·79
ELS 5 mg	35	–12·58 (–15·64, –9·52)	–4·11 (–9·36, 1·13)	0·20
UPA 15 mg	37	–17·56 (–20·58, –14·53)	–9·09 (–14·32, –3·86)	0·0045

DAS28 ESR=disease activity score 28 based on erythrocyte sedimentation rate; hsCRP=high-sensitivity C-reactive protein; ELS=elsubrutinib; LSM=least-squares mean; PGA=Patient's Global Assessment (based on a 100-mm horizontal VAS); PhGA=Physician's Global Assessment (based on a 100-mm horizontal VAS); SDAI=Simplified Disease Activity Index; UPA=upadacitinib; VAS=visual analog scale.

[a]Based on patients with non-missing baseline and ≥1 post-baseline value.
[b]Baseline is defined as the last non-missing value prior to the first dose of study drug.
[c]P-values are based on a mixed-effect model repeated measurements method.
[d]Based on a 100-mm horizontal VAS.
[e]Severity based on an 11-point scale.
[f]Based on 66 assessed joints.
[g]Based on 68 assessed joints.

Supplemental Table 3: **Summary of secondary endpoints (response rate analyses) at week 12[a]**

	n	Responders n (%) [90% CI][a]	P-value[b] vs placebo
Boolean remission			
Placebo	19	0 [0, 12]	–
ABBV-599	62	7 (11) [6, 20]	0·0051
ELS 60 mg	41	4 (10) [4, 20]	0·027
ELS 20 mg	39	1 (3) [1, 11]	0·31
ELS 5 mg	41	1 (2) [1, 10]	0·31
UPA 15 mg	40	4 (10) [5, 21]	0·035
DAS28 CRP ≤3.2[c]			
Placebo	19	4 (21) [10, 40]	–
ABBV-599	62	26 (42) [32, 52]	0·061
ELS 60 mg	41	9 (22) [13, 34]	0·92
ELS 20 mg	39	4 (10) [5, 21]	0·35
ELS 5 mg	41	6 (15) [8, 26]	0·57
UPA 15 mg	40	22 (55) [42, 67]	0·0043
CDAI ≤10[c]			
Placebo	19	5 (26) [13, 45]	–
ABBV-599	62	23 (37) [28, 48]	0·36
ELS 60 mg	41	14 (34) [23, 47]	0·51
ELS 20 mg	39	7 (18) [10, 30]	0·53
ELS 5 mg	41	7 (17) [10, 29]	0·44
UPA 15 mg	40	23 (58) [45, 69]	0·010
DAS28 CRP 2.6–3.2[d]			
Placebo	19	2 (11) [4, 27]	–
ABBV-599	62	6 (10) [5, 18]	0·96
ELS 60 mg	41	1 (2) [1, 10]	0·26
ELS 20 mg	39	1 (3) [1, 11]	0·30
ELS 5 mg	41	2 (5) [2, 14]	0·48
UPA 15 mg	40	5 (13) [6, 24]	0·76
CDAI 2.8–10[d]			
Placebo	19	4 (21) [10, 40]	–
ABBV-599	62	14 (23) [15, 32]	0·89
ELS 60 mg	41	11 (27) [17, 39]	0·61
ELS 20 mg	39	5 (13) [6, 24]	0·47
ELS 5 mg	41	7 (17) [10, 29]	0·74
UPA 15 mg	40	17 (43) [31, 55]	0·060

CDAI=clinical disease activity index; DAS28 CRP=disease activity score 28 based on C-reactive protein; MOA=mechanism of action.

[a]90% CIs for response rate is based on the Wilson's score method.
[b]Based on Cochran-Mantel-Haenszel test stratified by number of prior biologic disease modifying antirheumatic drug used (failed 1 or 2 biologics with the same MOA, or failed ≥3 biologics with the same MOA and/or ≥2 biologics with multiple MOA.
[c]Low disease activity.
[d]Low disease activity but not clinical remission.

Supplemental Table 4: **Adverse events of special interest**

	ABBV-599 (n=62)	ELS 60 mg (n=41)	ELS 20 mg (n=39)	ELS 5 mg (n=41)	UPA 15 mg (n=40)	Placebo (n=19)
Any AE of special interest, n (%)	2 (3)[*]	0 (0)	0 (0)	3 (7)	3 (8)	2 (11)
Serious infections	0 (0)	0 (0)	0 (0)	1 (2)[†]	0 (0)	0 (0)
Opportunistic infection excluding tuberculosis and herpes zoster	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Malignancy	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)
Lymphoma	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hepatic disorder[‡]	0 (0)	0 (0)	0 (0)	0 (0)	2 (5)[§]	0 (0)
Gastrointestinal perforations	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Anaemia	0 (0)	0 (0)	0 (0)	1 (2)[¶]	0 (0)	0 (0)
Neutropenia	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)
Lymphopenia	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)
Herpes zoster	1 (2)[ǁ]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Renal dysfunction	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Active tuberculosis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Latent tuberculosis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Any adjudicated MACE[**]	0 (0)	0 (0)	0 (0)	1 (2)[††]	0 (0)	0 (0)
Any adjudicated VTEs[‡‡]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

AE=adverse event; ALT=alanine aminotransferase; AST=aspartate aminotransferase; CV=cardiovascular; ELS=elsubrutinib; MACE=major adverse cardiovascular event; UPA=upadacitinib; VTE=venous thromboembolic event. *Includes one patient (2%) with creatine phosphokinase increased, not shown. [†]Serious pyelonephritis, which was not considered related to study treatment. The outcome is unknown as the patient was lost to follow-up. [‡]Defined as hepatic events and increased hepatic transaminases.

[§]One patient had mild, asymptomatic increase in ALT that resolved without intervention or study drug interruption. The other patient had asymptomatic increases in ALT and AST >3 × the upper limit of normal that required study drug interruption and resolved with concomitant treatment. [¶]Mild, asymptomatic anaemia that was not considered related to study drug by the investigator and was ongoing at the end of study. [ǁ]Non-serious, involving unilateral L3 and L4 dermatomes, and had a reasonable possibility of being related to the study drug by the investigator. [**]Defined as CV death (includes acute myocardial infarction, sudden cardiac death, heart failure, CV procedure–related death, death due to CV haemorrhage, fatal stroke, pulmonary embolism, and other CV causes), non-fatal myocardial infarction, and non-fatal stroke. [††]Cardiac arrest that was not considered related to study treatment by the investigator and resulted in the patient's death. [‡‡]VTEs include deep vein thrombosis and pulmonary embolism.

Supplemental Table 5: **Change in laboratory parameters from baseline to week 12[a]**

Parameter	n	Visit mean		LSM change (95% CI)	Difference vs placebo LSM (95% CI)
		Baseline[b]	Week 12		
Hemoglobin (g/L)					
Placebo	18	131·9	127·4	-4·5 (-8·10, -0·90)	–
ABBV-599	59	131·1	127·9	-3·2 (-5·16, -1·18)	1·3 (-2·79, 5·45)
ELS 60 mg	37	131·1	127·6	-3·5 (-6·03, -1·00)	1.0 (-3·41, 5·38)
ELS 20 mg	33	131·7	128·9	-2·7 (-5·39, -0·07)	1·8 (-2·71, 6·25)
ELS 5 mg	35	130·3	127·6	-2·7 (-5·24, -0·07)	1·8 (-2·59, 6·28)
UPA 15 mg	38	125·3	126·1	0·8 (-1·69, 3·27)	5·3 (0·91, 9·67)
Hematocrit (fraction of 1)					
Placebo	18	0·402	0·394	-0·008 (-0·0197, 0·0031)	–
ABBV-599	59	0·398	0·387	-0·011 (-0·0171, -0·0046)	-0·003 (-0·0155, 0·0105)
ELS 60 mg	37	0·399	0·391	-0·008 (-0·0163, -0·0004)	0 (-0·0139, 0·0138)
ELS 20 mg	33	0·403	0·394	-0·009 (-0·0178, -0·0010)	-0·001 (-0·0152, 0·0131)
ELS 5 mg	35	0·397	0·391	-0·006 (-0·0142, 0·0022)	0·002 (-0·0117, 0·0164)
UPA 15 mg	38	0·387	0·383	-0·004 (-0·0121, 0·0036)	0·004 (-0·0097, 0·0180)
Platelets (10^9/L)					
Placebo	17	318·5	306·5	-12·1 (-38·50, 14·38)	–
ABBV-599	59	305·7	269·8	-35·8 (-50·04, -21·66)	-23·8 (-53·80, 6·22)
ELS 60 mg	37	303·7	272·3	-31·4 (-49·35, -13·51)	-19·4 (-51·31, 12·57)
ELS 20 mg	33	282·3	268·2	-14·1 (-33·10, 4·86)	-2·1 (-34·61, 30·48)
ELS 5 mg	35	317·7	301·9	-15·8 (-34·20, 2·65)	-3·7 (-35·94, 28·51)
UPA 15 mg	38	317·9	299·6	-18·2 (-35·92, -0·55)	-6·2 (-37·99, 25·63)
Leukocytes (10^9/L)					
Placebo	18	9·76	9·57	-0·19 (-1·058, 0·674)	–
ABBV-599	59	8·21	7·45	-0·76 (-1·241, -0·285)	-0·57 (-1·561, 0·418)
ELS 60 mg	37	8·20	7·98	-0·21 (-0·815, 0·394)	-0·02 (-1·075, 1·037)
ELS 20 mg	33	7·79	7·73	-0·06 (-0·700, 0·580)	0·13 (-0·945, 1·208)
ELS 5 mg	35	8·46	8·47	0·01 (-0·608, 0·634)	0·20 (-0·861, 1·270)
UPA 15 mg	38	7·90	6·69	-1·21 (-1·802, -0·610)	-1·01 (-2·066, 0·037)
Neutrophils (10^9/L)					
Placebo	18	7·028	6·948	-0·08 (-0·9122, 0·7522)	–
ABBV-599	59	5·824	4·957	-0·867 (-1·3263, -0·4069)	-0·787 (-1·7373, 0·1641)
ELS 60 mg	37	5·686	5·485	-0·201 (-0·7818, 0·3791)	-0·121 (-1·1360, 0·8933)
ELS 20 mg	33	5·254	5·132	-0·123 (-0·7374, 0·4919)	-0·043 (-1·0773, 0·9919)
ELS 5 mg	35	6·095	6·017	-0·077 (-0·6740, 0·5197)	0·003 (-1·0212, 1·0270)
UPA 15 mg	38	5·241	4·322	-0·919 (-1·4917, -0·3462)	-0·839 (-1·8492, 0·1713)
Lymphocytes (10^9/L)					
Placebo	18	2·048	1·882	-0·167 (-0·4127, 0·0794)	–
ABBV-599	59	1·710	1·875	0·165 (0·0290, 0·3008)	0·332 (0·0505, 0·6127)
ELS 60 mg	37	1·857	1·842	-0·015 (-0·1865, 0·1568)	0·152 (-0·1482, 0·4518)
ELS 20 mg	33	1·887	1·938	0·051 (-0·1305, 0·2330)	0·218 (-0·0880, 0·5238)
ELS 5 mg	35	1·675	1·753	0·078 (-0·0982, 0·2548)	0·245 (-0·0579, 0·5478)
UPA 15 mg	38	2·001	1·825	-0·177 (-0·3459, -0·0072)	-0·01 (-0·3086, 0·2888)
Monocytes (10^9/L)					
Placebo	18	0·461	0·542	0·082 (0·0040, 0·1594)	–
ABBV-599	59	0·451	0·456	0·005 (-0·0382, 0·0477)	-0·077 (-0·1657, 0·0118)
ELS 60 mg	37	0·431	0·442	0·011 (-0·0434, 0·0650)	-0·071 (-0·1656, 0·0239)
ELS 20 mg	33	0·433	0·440	0·007 (-0·0504, 0·0644)	-0·075 (-0·1713, 0·0219)
ELS 5 mg	35	0·432	0·467	0·035 (-0·0206, 0·0909)	-0·047 (-0·1421, 0·0491)
UPA 15 mg	38	0·428	0·376	-0·052 (-0·1051, 0·0019)	-0·133 (-0·2276, -0·0389)
Alanine aminotransferase (U/L)					
Placebo	18	18·1	16·7	-1·4 (-6·15, 3·37)	–
ABBV-599	59	20·1	23·3	3·2 (0·61, 5·87)	4·6 (-0·81, 10·06)
ELS 60 mg	36	20·3	19·1	-1·2 (-4·53, 2·20)	0·2 (-5·61, 6·05)
ELS 20 mg	33	22·2	18·6	-3·6 (-7·12, -0·09)	-2·2 (-8·13, 3·70)
ELS 5 mg	35	19·0	19·2	0·3 (-3·16, 3·67)	1·6 (-4·21, 7·50)
UPA 15 mg	38	18·9	19·7	0·8 (-2·46, 4·09)	2·2 (-3·57, 7·98)
Aspartate aminotransferase (U/L)					
Placebo	18	18·9	18·4	-0·5 (-4·01, 3·01)	–
ABBV-599	59	19·6	24·2	4·6 (2·67, 6·55)	5·1 (1·10, 9·13)
ELS 60 mg	36	22·8	19·6	-3·3 (-5·74, -0·76)	-2·8 (-7·05, 1·55)
ELS 20 mg	33	21·9	19·1	-2·8 (-5·41, -0·22)	-2·3 (-6·69, 2·05)
ELS 5 mg	35	19·8	19·7	-0·1 (-2·58, 2·46)	0·4 (-3·88, 4·77)
UPA 15 mg	38	20·2	23·0	2·8 (0·40, 5·23)	3·3 (-0·95, 7·58)
Alkaline phosphatase (U/L)					
Placebo	18	83·9	79·6	-4·3 (-11·56, 3·01)	–
ABBV-599	59	81·8	70·5	-11·4 (-15·41, -7·37)	-7·1 (-15·44, 1·21)

Supplemental Table 5: **Change in laboratory parameters from baseline to week 12[a]**

Parameter	n	Visit mean		LSM change (95% CI)	Difference vs placebo LSM (95% CI)
		Baseline[b]	Week 12		
ELS 60 mg	36	95·5	91·2	-4·4 (-9·51, 0·79)	-0·1 (-9·01, 8·84)
ELS 20 mg	33	80·1	77·6	-2·5 (-7·84, 2·93)	1·8 (-7·23, 10·88)
ELS 5 mg	35	96·3	92·2	-4·1 (-9·34, 1·11)	0·2 (-8·80, 9·13)
UPA 15 mg	38	90·6	74·4	-16·3 (-21·28, -11·25)	-12·0 (-20·83, -3·14)
Bilirubin (µmol/L)					
Placebo	18	7·0	5·9	-1·2 (-2·52, 0·12)	–
ABBV-599	59	6·3	7·3	1·0 (0·22, 1·68)	2·2 (0·64, 3·66)
ELS 60 mg	36	6·6	6·2	-0·4 (-1·34, 0·52)	0·8 (-0·83, 2·40)
ELS 20 mg	33	6·6	7·0	0·4 (-0·55, 1·40)	1·6 (-0·01, 3·27)
ELS 5 mg	35	7·3	6·9	-0·4 (-1·31, 0·59)	0·8 (-0·79, 2·46)
UPA 15 mg	38	6·3	7·0	0·6 (-0·27, 1·55)	1·8 (0·24, 3·44)
Creatinine (umol/L)					
Placebo	18	75·1	73·7	-1·4 (-5·26, 2·46)	
ABBV-599	59	67·2	71·8	4·7 (2·54, 6·81)	6·1 (1·66, 10·48)
ELS 60 mg	36	68·9	69·1	0·2 (-2·50, 2·96)	1·6 (-3·10, 6·36)
ELS 20 mg	33	68·8	70·0	1·2 (-1·61, 4·10)	2·6 (-2·16, 7·44)
ELS 5 mg	35	67·3	68·6	1·4 (-1·41, 4·13)	2·8 (-2·00, 7·51)
UPA 15 mg	38	67·6	68·9	1·3 (-1·34, 3·97)	2·7 (-1·97, 7·40)
Cholesterol (mmol/L)					
Placebo	18	4·935	4·843	-0·092 (-0·4120, 0·2278)	–
ABBV-599	59	4·645	5·213	0·568 (0·3916, 0·7449)	0·660 (0·2948, 1·0258)
ELS 60 mg	36	4·963	4·930	-0·033 (-0·2594, 0·1930)	0·059 (-0·3329, 0·4507)
ELS 20 mg	33	4·988	5·007	0·02 (-0·2165, 0·2560)	0·112 (-0·2859, 0·5095)
ELS 5 mg	35	4·995	4·968	-0·028 (-0·2570, 0·2019)	0·065 (-0·3291, 0·4582)
UPA 15 mg	38	5·08	5·779	0·699 (0·4789, 0·9192)	0·791 (0·4028, 1·1795)
HDL cholesterol (mmol/L)					
Placebo	18	1·612	1·589	-0·023 (-0·1337, 0·0879)	–
ABBV-599	59	1·428	1·650	0·222 (0·1606, 0·2830)	0·245 (0·1181, 0·3712)
ELS 60 mg	36	1·610	1·602	-0·008 (-0·0863, 0·0704)	0·015 (-0·1208, 0·1506)
ELS 20 mg	33	1·513	1·538	0·025 (-0·0567, 0·1070)	0·048 (-0·0897, 0·1858)
ELS 5 mg	35	1·507	1·586	0·079 (-0·0001, 0·1588)	0·102 (-0·0341, 0·2386)
UPA 15 mg	38	1·486	1·715	0·228 (0·1522, 0·3047)	0·251 (0·1168, 0·3858)
LDL cholesterol (mmol/L)					
Placebo	18	2·595	2·593	-0·002 (-0·2623, 0·2580)	–
ABBV-599	59	2·562	2·888	0·325 (0·1818, 0·4691)	0·328 (0·0305, 0·6248)
ELS 60 mg	36	2·724	2·695	-0·028 (-0·2121, 0·1558)	-0·026 (-0·3446, 0·2926)
ELS 20 mg	33	2·739	2·758	0·019 (-0·1729, 0·2113)	0·021 (-0·3020, 0·3447)
ELS 5 mg	35	2·755	2·743	-0·013 (-0·1994, 0·1737)	-0·011 (-0·3308, 0·3094)
UPA 15 mg	38	2·906	3·405	0·499 (0·3199, 0·6780)	0·501 (0·1853, 0·8168)
Triglycerides (mmol/L)					
Placebo	18	1·593	1·451	-0·142 (-0·3834, 0·1003)	–
ABBV-599	59	1·427	1·477	0·05 (-0·0836, 0·1835)	0·192 (-0·0848, 0·4678)
ELS 60 mg	36	1·375	1·384	0·01 (-0·1615, 0·1805)	0·151 (-0·1451, 0·4473)
ELS 20 mg	33	1·609	1·555	-0·054 (-0·2321, 0·1251)	0·088 (-0·2126, 0·3887)
ELS 5 mg	35	1·599	1·398	-0·201 (-0·3743, -0·0275)	-0·059 (-0·3569, 0·2382)
UPA 15 mg	38	1·499	1·443	-0·057 (-0·2232, 0·1097)	0·085 (-0·2087, 0·3784)

ELS=elsubrutinib; LSM=least-squares mean; UPA=upadacitinib

[a]Based on patients with non-missing baseline and ≥1 post-baseline value·

[b]Baseline is defined as the last non-missing value prior to the first dose of study drug·

Supplemental Table 6: **Change from baseline to week 12 in DAS28 (CRP) based on historical placebo and upadacitinib data**

	Within-group change from baseline			Difference *vs* placebo or UPA (posterior)			
Treatment (Data source)	**N**	**Mean**	**SE**	**Mean (90% credible interval)**	**SE**	**P (posterior treatment difference < 0)**	**Bayesian success (>0·95)**
Fixed borrowing 20 historical placebo patients							
Placebo (in trial)	18	–1·12	0·31				
Placebo (historical)	20	–0·80	0·34				
Placebo (posterior)		–0·97	0·23				
ELS 60 mg (in trial)	35	–1·52	0·23	–0·55 (–1·07 to –0·02)	0·32	0·96	Y
ELS 20 mg (in trial)	29	–1·32	0·24	–0·35 (–0·89 to 0·20)	0·33	0·85	N
ELS 5 mg (in trial)	34	–1·33	0·22	–0·36 (–0·89 to 0·16)	0·32	0·87	N
Fixed borrowing 40 historical UPA patients							
UPA (in trial)	37	–2·87	0·22				
UPA (historical)	40	–2·32	0·25				
UPA (posterior)		–2·63	0·16				
ABBV-599 (60 mg/15 mg) (in trial)	54	–2·56	0·18	0·07 (–0·33 to 0·47)	0·25	0·39	N

The mean within group for data source in trial is the least squares mean from ABBV-599 and UPA estimated by mixed-effect repeated-measurements model including stratification factor·

CRP=C-reactive protein; DAS28=disease activity score; ELS=elsubrutinib, UPA=upadacitinib·

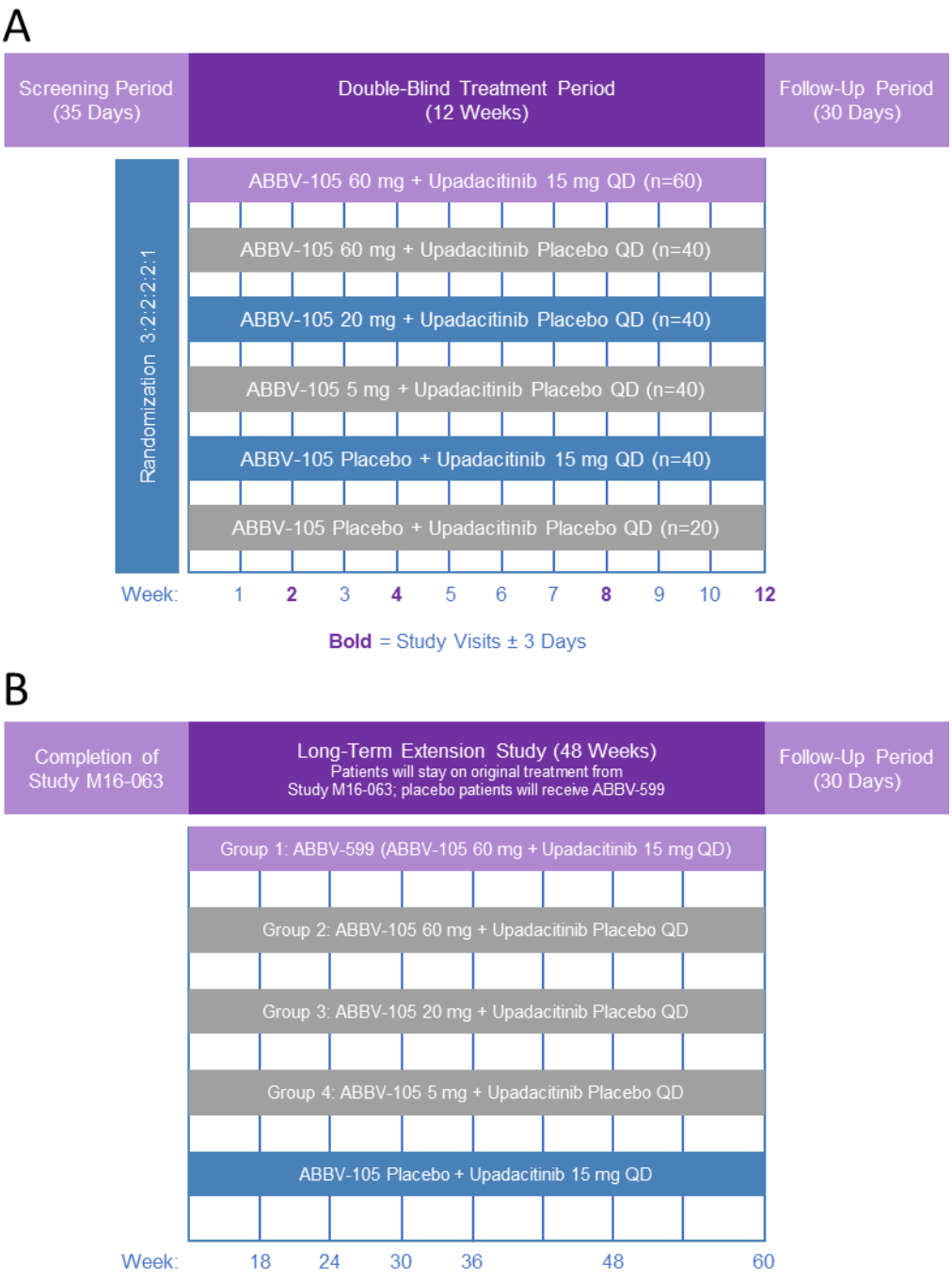
Supplemental Table 7: **Safety summary for the long-term extension**

	ABBV-599 (n=28)	ELS 60 mg (n=16)	ELS 20 mg (n=12)	ELS 5 mg (n=12)	UPA 15 mg (n=20)	Placebo to ABBV-599 (n=9)
Any TEAE, n (%)	11 (39)	10 (63)	3 (25)	5 (42)	7 (35)	3 (33)
AE with reasonable possibility of being drug related*	5 (18)	5 (31)	0 (0)	2 (17)	2 (10)	1 (11)
Severe AE	1 (4)	0 (0)	0 (0)	1 (8)	1 (5)	0 (0)
Serious AE	1 (4)[†]	0 (0)	0 (0)	0 (0)	1 (5)[‡]	0 (0)
AE leading to study drug discontinuation	1 (4)	2 (13)	0 (0)	0 (0)	0 (0)	0 (0)
Deaths	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
AEs of special interest, n (%)						
Malignancy	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)
Hepatic disorder[§]	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Anaemia	0 (0)	0 (0)	0 (0)	2 (17)	0 (0)	0 (0)
CPK elevation	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

AE=adverse event; CPK=creatine phosphokinase; ELS=elsubrutinib; TEAE=treatment-emergent adverse events; UPA=upadacitinib·

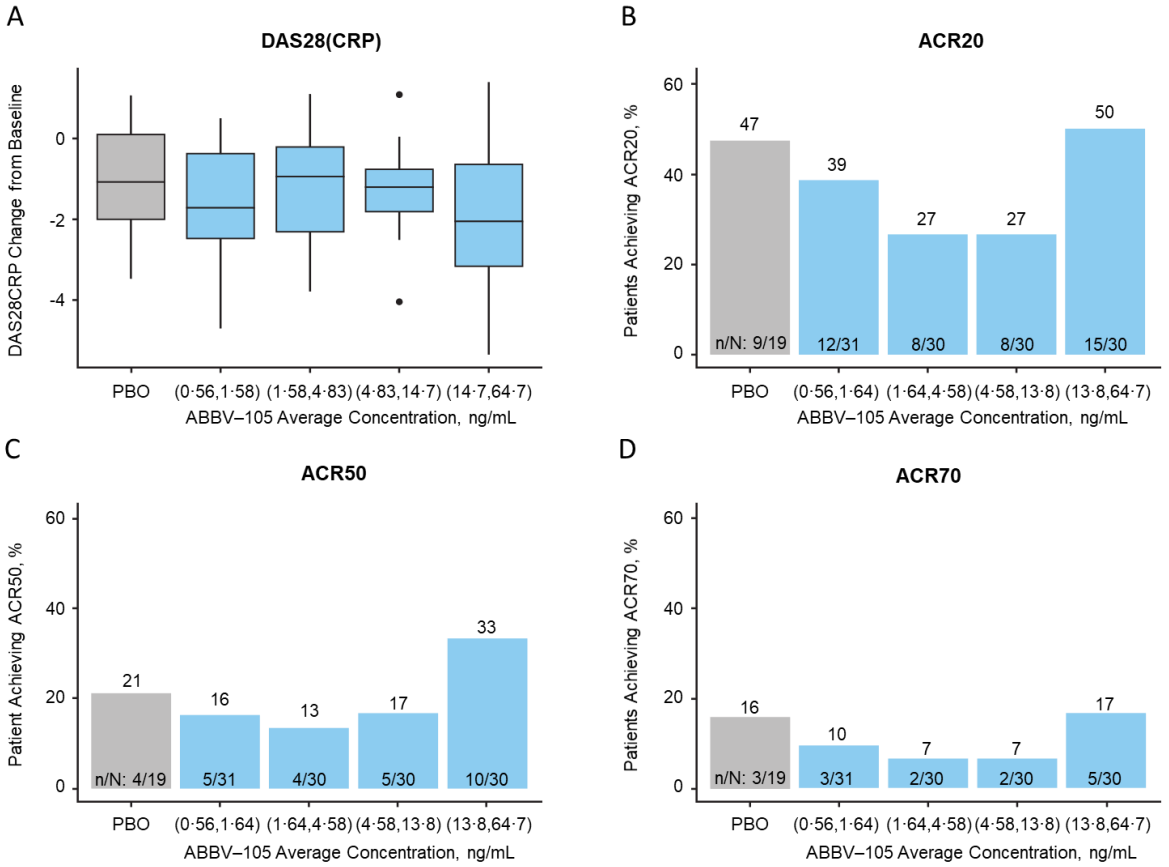
*As assessed by investigator· [†]Pulmonary adenocarcinoma that was considered possibly related to study drug (the duration of study drug treatment prior to the diagnosis was approximately 10 months)· The patient was withdrawn from the study per the protocol· [‡]Periprosthetic fracture that was unrelated to study drug· The patient was hospitalised and study treatment was interrupted· [§]Defined as hepatic events and increased hepatic transaminases·

Supplemental Figure 1: **Study design** (A) Double-blind phase; (B) long-term extension·



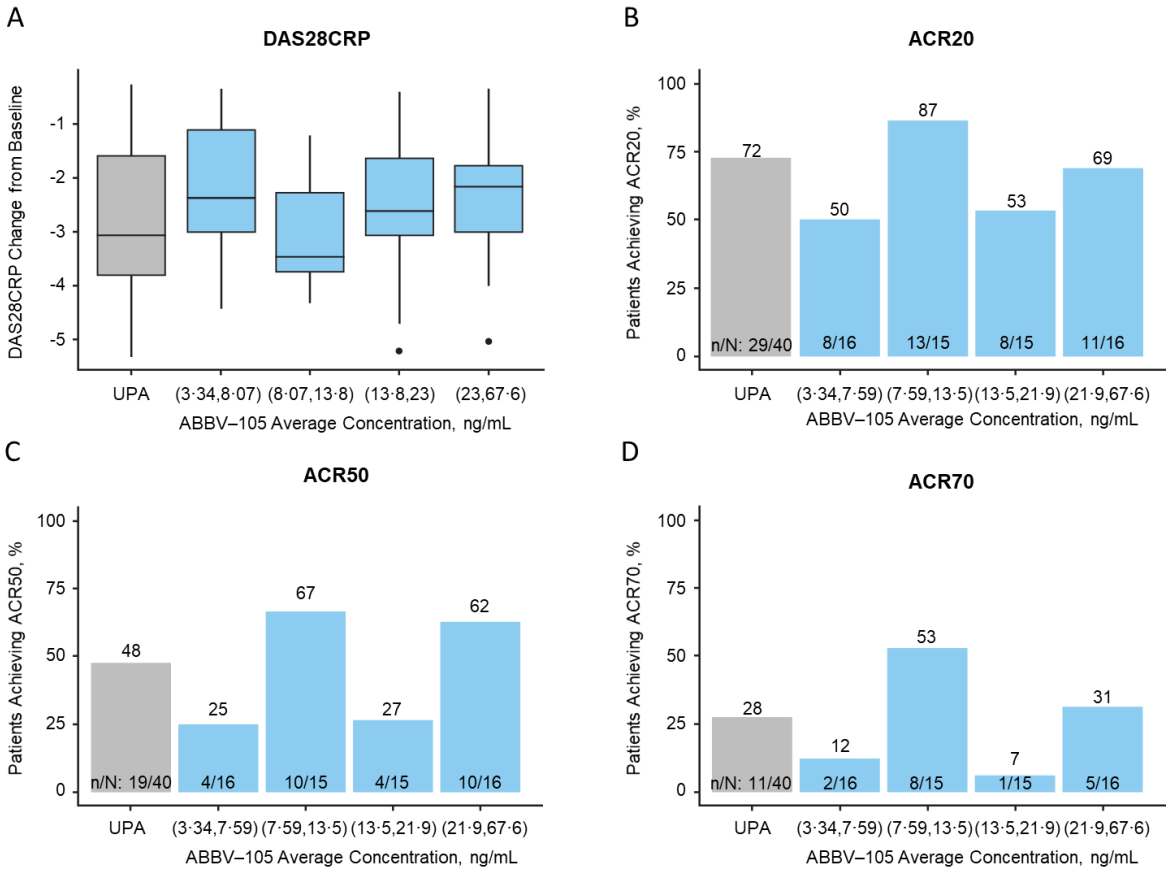
ABBV-105=elsubrutinib; QD=once daily·

Supplemental Figure 2: **Efficacy endpoints by mean plasma concentration of elsubrutinib for patients treated with elsubrutinib** (A) DAS28 (CRP); (B) ACR20; (C) ACR50; (D) ACR70.



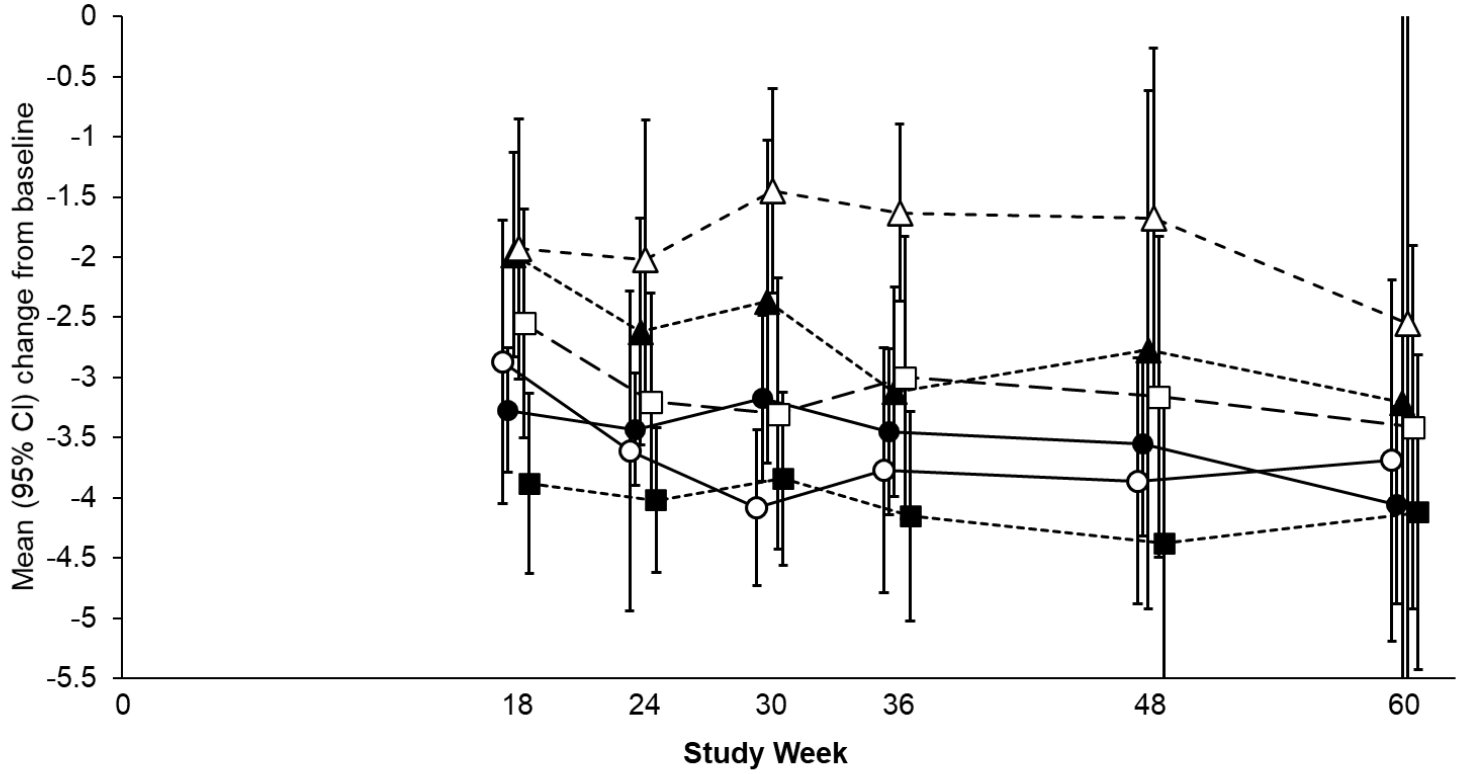
ABBV-105=elsubrutinib; ACR20/50/70=American College of Rheumatology 20%, 50%, and 70% response criteria; DAS28 (CRP)=disease activity score (28 joints) using C-reactive protein; PBO=placebo

Supplemental Figure 3: ***Efficacy endpoints by mean plasma concentration of elsubrutinib for patients treated with ABBV-599*** *(A) DAS28 (CRP); (B) ACR20; (C) ACR50; (D) ACR70·*



ABBV-105=elsubrutinib; ACR20/50/70=American College of Rheumatology 20%, 50%, and 70% response criteria; DAS28 (CRP)=disease activity score (28 joints) using C-reactive protein; UPA, upadacitinib.

Supplemental Figure 4: **Mean (95% CI) change from baseline in DAS28 (CRP) over time during the long-term extension·**



Treatment group (n)							
Placebo to ABBV-599	9	8	7	8	6	6	4
ABBV-599 to ABBV-599	27	22	26	22	23	17	9
Elsubrutinib 60 mg	16	15	13	13	8	6	2
Elsubrutinib 20 mg	10	7	7	5	3	3	2
Elsubrutinib 5 mg	12	10	10	10	10	8	5
Upadacitinib 15 mg	20	18	17	16	12	8	5

Site Country	Site Location Name	Principal Investigator
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Canada	Manitoba Clinic	McCarthy, Timothy, Dr.
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Hungary	Revita Reumatologiai Rendelo	Cseuz, Regina, Dr.
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Spain	Hospital Universitario A Coru?a - CHUAC	Blanco, Francisco, Dr.
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Spain	Duplicate_Hospital Santa Creu i Sant Pau	Corominas Macias, Hector
Spain	Hospital Universitario Virgen de las Nieves	Caliz, Rafael
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United Kingdom	The Newcastle Upon Tyne Hospitals NHS Foundation Trust	Isaacs, John, Prof.
United Kingdom	Warrington and Halton Teaching Hosp NHS Foundation Trust	Salih, Abdelrazig, Dr.
United Kingdom	Whipps Cross Univ Hospital	Tahir, Hasan, Dr.
United States	SW Rheumatology Res LLC	Singhal, Atul, Dr.
United States	Clinical Investigation Specialists - Skokie	Hozman, Robert, Dr.
United States	DM Clinical Research	Ali, Shaikh Arif, Dr.
United States	Clinical Research West FL	Janer, Edgard, Dr.
United States	Tekton Research, Inc	Pickrell, Paul, Dr.
United States	Rheumatology and Pulmonary cli	Saikali, Wassim, Dr.
United States	Clinical Res of West FL, Inc	Levin, Robert, Dr.
United States	Nashville Arthritis and Rheumatology	Collins, Robert, Dr.
United States	Accurate Clinical Research	Waller, Philip
United States	Arthritis Associates	Weiss, David, Dr.
United States	HMD Research LLC	Heuer, Marvin, Dr.
United States	Omega Research Maitland, LLC	Ayesu, Kwabena, Dr.
United States	Inland Rheum Clin Trials Inc	Lee, Eric, Dr.
United States	New Horizons Clinical Research	Pordy, Michael, Dr.
United States	Lakes Research, LLC	Fernandez, Benidecto, Dr.
United States	DJL Clinical Research, PLLC	Herron Box, Emily, Dr.
United States	Physician Research Collaboration (PRC)	Churchill, Melvin, Dr.
United States	West Texas Clinical Research	Vasandani, Jitendra, Dr.
United States	Accurate Clinical Management	DeJesus, Alex, Dr.
United States	Kendall South Medical Center, Inc	Arce Nunez, Esperanza, Dr.
United States	Sun Research Institute	Dukes, Carl, Dr.
United States	Rheumatology Center of San Diego	Rivera, Tania, Dr.
United States	Health Research of Oklahoma	Codding, Christine, Dr.
United States	Metroplex Clinical Research	Fleischmann, Roy, Dr.
United States	Arthritis Northwest, PLLC	Butler, Jeffrey, Dr.

United States	Millennium Research	Kohen, Michael, Dr.
United States	Tidewater Physicians Medical Center	Mizelle, Kristi, Dr.
United States	Rheumatic Disease Clinical Research Center	Pegram, Samuel, Dr.
United States	Rheumatology Clinic of Houston	Rehman, Qaiser, Dr.
United States	STAT Research, Inc	Wolfe, Sanford, Dr.
United States	Arth and Osteo Clin Brazo Valley	Pocurull, Ricardo, Dr.
United States	Advanced Clinical Care	Birbara, Charles, Dr.
United States	AZ Arthritis and Rheum Researc	Kreutz, Daniel, Dr.
United States	The Arthritis & Diabetes Clinic, Inc	Mallepalli, Jyothi, Dr.
United States	ForCare Clinical Research	Ramani, Priya
United States	June DO, PC	June, Joshua, Dr.
United States	North Mississippi Med Clinics	King, Charles, Dr.
United States	Clayton Medical Associates dba Saint Louis Rheumatology	Ronholm, Chad, Dr.
United States	Institute of Arthritis Researc	Scoville, Craig, Dr.
United States	Cape Fear Arthritis Care	Snow, David, Dr.
United States	AZ Arthritis & Rheum Research	Swarup, Areena, Dr.
United States	Integral Rheumatology & Immunology Specialists	Valenzuela, Guillermo, Dr.
United States	Aurora Rheumatology and Immunotherapy Center	Wells, Alvin, Dr.
United States	Arthritis & Osteoporosis Clinic	Fung, H.S. Eugene, Dr.
United States	St Anthony Comprehensive Research Institute	Gonzalez-Paoli, Julio, Dr.
United States	Great Lakes Clinical Trials	Jain, Manish, Dr.
United States	Marietta Memorial Hospital	Krant, Jonathan, Dr.
United States	Florida Medical Clinic	Rodriguez, Ernesto, Dr.
United States	West Tennessee Research Inst	Aelion, Jacob, Dr.
United States	BayCare Medical Group	Burnette, Michael, Dr.
United States	Trinity Universal Res Assoc	Joseph, John, Dr.
United States	DHMC	Rigby, William
United States	Amarillo Ctr for Clin Research	Saadeh, Constantine, Dr.
United States	SunValley Arthritis Center, Lt	Schechtman, Joy, Dr.
United States	International Medical Research - Ormond	Tsai, Yong, Dr.
United States	Arthritis Center, Inc	Zagar, Karen, Dr.
United States	Medallion Clinical Research Institute, LLC	Alper, Jeffrey, Dr.
United States	Purushotham, Akther & Roshan K	Kotha, Roshan, Dr.
United States	Arthritis and Osteo Assoc	Snyder, Arthur, Dr.
United States	Mansfield Health Center	Vasudevan, Sreekala, Dr.
United States	Beals Instititute	Beals, Carol, Dr.
United States	EmergeOrtho, P A	Belhorn, Linda, Dr.
United States	Riverside Clinical Research	Chang, Margaret, Dr.
United States	Deerbrook Medical Associates	Fenton, Ira

United States	Rheum Assoc of Central FL	Freeman, Pamela, Dr.
United States	University of Washington	Han, Kwanghoon, Dr.
United States	Sierra Rheumatology	Haselwood, Douglas, Dr.
United States	Western Washington Arthritis C	Jimenez, Richard, Dr.
United States	Bay Area Arthritis and Osteo	Joshi, Vipul, Dr.
United States	NY Arthritis Clinic	Katz, Victoria
United States	Ocean Rheumatology	Kumar, Ramesh, Dr.
United States	UC Davis Medical Center - Inte	Lane, Nancy
United States	PRN of Kansas	Malik, Basit
United States	Center for Arthritis and Osteo	Mehta, Daksha
United States	Valerius Medical Group	Neal, Nathaniel
United States	Rheumatology Consultants of Delaware	Pando, Jose
United States	St Joseph Heritage Healthcare	Pang, Shirley, Dr.
United States	Iraj Sabahi Research, Inc	Sabahi, Iraj
United States	Univ of Michigan Hospitals	Schiopu, Elena
United States	Rheum Assoc of North Alabama	Shergy, William, Dr.
United States	Medvin Clinical Research	Su, Tien-I, Dr.
United States	Clinical Research Ctr Reading	Walker, Nancy, Dr.
United States	Trinity Universal Research Association	Zahabi-Unwala, Fehmida, Dr.