SUPPLEMENTARY MATERIAL

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| Korea   | Seoul National University Hospital                | Jin Kyun Park |
| Korea   | Pusan National University Hospital                | Seung-Geun Lee|
| Korea   | Seoul National University Bundang Hospital        | Yun Jong Lee  |
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| Taiwan  | Chang Gung Medical Foundation, Kaohsiung Chang Gung Memorial Hospital | Tien Tsai Cheng|
| Taiwan  | Kaohsiung Medical University Chung-Ho Memorial Hospital | Wen Chan Tsai|
| Taiwan  | China Medical University Hospital                 | Chung Ming Huang|
| Taiwan  | Taichung Veterans General Hospital                | Hsin Hua Chen |
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| Taiwan  | National Taiwan University Hospital               | Cheng Han Wu  |
| Taiwan  | Tri-Service General Hospital                      | Hsiang Cheng Chen|
| Site Number | Site Name                               | Name of institutional review board/independent ethics committee                                      |
|------------|-----------------------------------------|---------------------------------------------------------------------------------------------------|
| 01         | Juntendo University Hospital            | Juntendo University Hospital Institutional Review Board                                            |
| 02         | St. Luke's International Hospital       | St. Luke's International Hospital Institutional Review Board                                       |
| 03         | Katayama Seikeigeka Rheumatism Clinic  | Toyooka Central Hospital Institutional Review Board                                                 |
| 04         | Tokyo Women's Medical University Hospital| Tokyo Women's Medical University Institutional Review Board                                         |
| 05         | Tokyo Women's Medical University Yachiyo Medical Center | Tokyo Women's Medical University Institutional Review Board                                    |
| 06         | Fujita Health University Hospital       | Fujita Health University Hospital Institutional Review Board                                       |
| 07         | Tenri Hospital                          | Tenri Hospital Institutional Review Board                                                        |
| 08         | Osaka University Hospital               | Institutional Review Board of Osaka University Hospital                                           |
| 09         | Osaka City University Hospital          | Osaka City University Hospital Institutional Review Board                                          |
| 10         | Osaka City General Hospital             | Local Incorporated Administrative Agency Osaka City Hospital Organization Osaka City General Hospital Institutional Review Board |
| 11         | National Hospital Organization Osaka Minami Medical Center | National Hospital Organization Osaka Minami Medical Center Institutional Review Board         |
| 12         | Yukioka Hospital                        | Tokai Memorial Hospital Institutional Review Board                                                |
| 13         | Hyogo College of Medicine               | Hyogo College of Medicine Institutional Review Board                                               |
| 14         | Okayama Saiseikai General Hospital Outpatient Center | Okayama Saiseikai General Hospital Institutional Review Board                                   |
| 15         | Kagawa University Hospital              | Kagawa University Hospital Institutional Review Board                                              |
| 16         | Kyushu University Hospital              | Kyushu University Hospital Institutional Review Board                                              |
|   | Hospital Name                          | Institutional Review Board Name                                      |
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|17 | Fukuoka University Hospital           | Fukuoka University Hospital Institutional Review Board              |
|18 | Okinawa Prefectural Chubu Hospital    | Okinawa Prefectural Chubu Hospital Institutional Review Board       |
|20 | Sasebo Chuo Hospital                  | Sasebo Chuo Hospital Institutional Review Board                     |
|21 | Tomishiro Central Hospital            | Tomishiro Central Hospital Institutional Review Board               |
|22 | Hokkaido University Hospital          | Hokkaido University Hospital Institutional Review Board             |
|23 | Toho University Ohashi Medical Center | Toho University Medical Center Institutional Review Board           |
|25 | Kochi Medical School Hospital         | Kochi Medical School Hospital Institutional Review Board            |
|28 | Toho University Omori Medical Center  | Toho University Medical Center Institutional Review Board           |
|29 | Chihaya Hospital                      | Haradoi Hospital Institutional Review Board                        |
|50 | Kyung Hee University Hospital         | Kyung Hee University Hospital Institutional Review Board            |
|51 | Inha University Hospital              | Inha University Hospital Institutional Review Board                  |
|52 | Chonnam National University Hospital  | Chonnam National University Hospital Institutional Review Board     |
|53 | Ajou University Hospital              | Ajou University Hospital Institutional Review Board                 |
|54 | Chungnam National University Hospital | Chungnam National University Hospital Institutional Review Board     |
|55 | Hanyang University Seoul Hospital     | Hanyang University Seoul Hospital Institutional Review Board         |
|56 | Daegu Catholic University Medical Center | Daegu Catholic University Medical Center Institutional Review Board |
|57 | The catholic university of Korea Seoul St. Mary’s Hospital | The Catholic University of Korea Seoul St. Mary’s Hospital Institutional Review Board |
|58 | Seoul National University Hospital    | Seoul National University Hospital Institutional Review Board       |
| 59 | Pusan National University Hospital | Pusan National University Hospital Institutional Review Board |
| 60 | Seoul National University Bundang Hospital | Seoul National University Bundang Hospital Institutional Review Board |
| 61 | Konkuk University Medical Center | Konkuk University Medical Center Institutional Review Board |
| 70 | Chung Shan Medical University Hospital | The Institution Review Board Chung Shan Medical University Hospital |
| 71 | Chang Gung Medical Foundation, Kaohsiung Chang Gung Memorial Hospital | Chang Gung Medical Foundation Institutional Review Board |
| 72 | Kaohsiung Medical University Chung-Ho Memorial Hospital | Kaohsiung Medical University Chung-Ho Memorial Hospital Institutional Review Board |
| 73 | China Medical University Hospital | China Medical University & Hospital Research Ethics Committee |
| 74 | Taichung Veterans General Hospital | Institutional Review Board I & II of Taichung Veterans General Hospital |
| 75 | National Cheng Kung University Hospital | Institutional Review Board, National Cheng Kung University Hospital |
| 76 | Chang Gung Medical Foundation, LinKou Chang Gung Memorial Hospital | Chang Gung Medical Foundation Institutional Review Board |
| 77 | Cathay General Hospital | Institutional Review Board of the Cathay General Hospital |
| 78 | Kaohsiung Veterans General Hospital | Kaohsiung Veterans General Hospital Institutional Review Board |
| 79 | National Taiwan University Hospital | Research Ethics Committee, National Taiwan University Hospital |
| 80 | Tri-Service General Hospital | Institutional Review Board, Tri-Service General Hospital |
**Table S1. Patient inclusion and exclusion criteria**

| Inclusion criteria                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |  
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|  
| 1) Personally submitted written voluntary informed consent to participate in the study (if a minor at the time of consent, written informed consent had to be obtained from his or her legally acceptable representative as well)                                                                                                                                                    |  
| 2) Aged ≥18 years at the time of consent (the cut-off age depended on the local law)                                                                                                                                                                                                                                                                                                                                                                                                  |  
| 3) Patient with age at onset <45 years and continuous chronic back pain for ≥3 months fulfills the ASAS classification criteria of axSpA (with the exception of Crohn’s disease)                                                                                                                                                                                                                               |  
| AS patients: Patient had radiographic evidence of sacroiliitis grade ≥2 bilaterally or grade 3 to 4 unilaterally (image obtained within 6 months prior to the time of consent may be used; centrally read) and at least one of the SpA features specified in the ASAS classification criteria of axSpA (with the exception of Crohn’s disease)                                                                                                      |  
| OR                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  
| nr-axSpA patients: Patient did not have radiographic evidence of sacroiliitis grade ≥2 bilaterally or grade 3 to 4 unilaterally (image obtained within 6 months prior to the time of consent may be used; centrally read)                                                                                                                                                                                                                           |  
| AND                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |  
| Patient met either of the following criteria:                                                                                                                                                                                                                                                                                                                                                                                                                                    |  
| • Presence of inflammatory lesions of sacroiliac joint on MRI of SPARCC level ≥2 (centrally read) and at least one of the SpA features specified in the ASAS classification criteria of axSpA (with the exception of Crohn’s disease)                                                                                                                                                                                                                     |  
| • Positive test for HLA-B27* and the presence of at least 2 of the SpA features specified in the ASAS classification criteria of axSpA (with the exception of Crohn’s disease), one of which had to be elevated CRP† (>ULN)                                                                                                                                                                                                                      |  
| 4) Patient had BASDAI score ≥4 at screening and enrollment                                                                                                                                                                                                                                                                                                                                                                                                                        |  

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5) Patient had spinal pain score (BASDAI question #2) ≥4 at screening and enrollment

6) Patient had had adequate therapy with oral NSAIDs for back pain for at least 3 months with inadequate treatment response before enrollment (however, patients with contraindication or intolerance to oral NSAIDs might be enrolled even if the patient did not meet the above criterion).

7) For patients receiving non-biologic DMARDs (methotrexate or sulfasalazine): the patient had received treatment for ≥3 months prior to initiation of study drug, with a stable dose for ≥4 weeks prior to initiation of study drug.

8) For patient receiving oral corticosteroids: the patient had received treatment for ≥4 weeks prior to initiation of study drug.

9) No findings in chest X-ray (or chest CT scan) suggestive of active tuberculosis, meeting any of the following criteria at screening:
   - Negative QuantiFERON or T-spot test
   - “Borderline” or “invalid” result of QuantiFERON or T-spot test, and negative result in re-testing
   - “Borderline” result in re-testing QuantiFERON or T-spot test, and taking anti-tuberculosis agents (isoniazid, as a general rule) on a regular basis since at least 3 weeks before the start of study drug administration
   - Positive result in QuantiFERON or T-spot test (including retest) or “invalid” result in re-testing QuantiFERON or T-spot test, but no findings in chest CT scan suggestive of active tuberculosis, and taking anti-tuberculosis agents (isoniazid, as a general rule) on a regular basis since at least 3 weeks before the start of study drug administration.

### Exclusion criteria

1) Complete ankylosis (fusion) of the spine

2) Active ongoing inflammatory diseases other than axSpA that might confound the evaluation of brodalumab therapy, including reactive arthritis, spondyloarthritis associated with inflammatory bowel disease, SAPHO syndrome (pustulotic arthro-osteitis), fibromyalgia, ankylosing spinal hyperostosis, osteitis condensans illi, spondylosis deformans, or osteoarthritis sacroiliac joint disease

3) Planned surgical intervention between enrollment and week 16

4) Active infection or history of infections as follows:
   - Any active infection for which systemic anti-infectives were used within 4 weeks prior to the first study drug administration
• A serious infection, defined as requiring hospitalization or intravenous anti-infectives within 8 weeks prior to the first study drug administration
• Recurrent or chronic infections or other active infection that, in the opinion of the investigators, might cause this study to be detrimental to the patient

5) Any systemic disease (e.g., renal failure, heart failure, hypertension, liver disease, diabetes, anemia) considered by the investigators to be clinically significant and uncontrolled

6) Known history of HIV infection

7) Positive result in any item of the infection tests (HBs antigen, HBs antibody, HBc antibody, HCV antibody, HIV antigen/antibody, or HTLV-1 antibody) with the exception of the following cases:
   • Negative HBs antigen and positive HBc antibody and/or HBs antibody and with a HBV-DNA level below the detection sensitivity (such patients were required to undergo the HBV-DNA assay at 4-week intervals). However, HBV-DNA measurement was not required for patients who were positive for antibodies produced after hepatitis B vaccination and who were not affected with hepatitis B at screening.

8) History of myocardial infarction, unstable angina pectoris, or stroke within the past 12 months prior to the first study drug administration

9) Any active malignancy, including evidence of cutaneous basal or squamous cell carcinoma or melanoma

10) History of malignancy within 5 years prior to enrollment except treated and considered cured cutaneous basal or squamous cell carcinoma, in situ cervical cancer, or in situ breast ductal carcinoma

11) Any concurrent medical condition or electrocardiogram abnormality that, in the opinion of the investigators, could cause this study to be detrimental to the patient

12) History of Crohn’s disease

13) Any of the following laboratory abnormalities at screening:
   • Aspartate aminotransferase or alanine aminotransferase >2 × upper limit of normal
   • Serum direct bilirubin ≥1.5 mg/dL (25.7 μmol/L)
   • White blood cell count <3000/μL
- Neutrophil count <2000/μL

14) Any other laboratory abnormality that, in the opinion of the investigators, would prevent the patient from completing the study or would interfere with the interpretation of the study results

15) Use of DMARDs other than a stable dose of methotrexate or sulfasalazine, or history of having received live vaccine(s) within 4 weeks of the first dose of the study drug

16) Use of any narcotic analgesics (excluding tramadol) or medical marijuana within 1 week prior to enrollment

17) Prior history of >1 anti-TNF therapy

18) Patient had used commercially available or investigational biologic therapies as follows:
   - Anti-TNF therapy: Within 4 weeks prior to study drug initiation for etanercept, within 8 weeks for infliximab, and within 10 weeks for other anti-TNF agents (e.g., adalimumab, golimumab, certolizumab-pegol)
   - Anti-IL-17 biologics (e.g., brodalumab, secukinumab, ixekizumab)
   - Anti-IL-12/IL-23 biologic therapy (e.g., ustekinumab, briakinumab) within 6 months prior to study drug initiation.

19) History of treatment with any intra-articular/intramuscular corticosteroids or systemic corticosteroids (other than oral corticosteroids) within 4 weeks before the start of study drug administration

20) History of participation in a clinical study with a drug other than brodalumab or with an unapproved medical device within 4 months before study drug administration in this study

21) Planned participation in another clinical study during this study

22) Known sensitivity to any of the products or components to be administered during dosing

23) Patient was not likely to complete all protocol-required study visits or procedures and/or to comply with all required study procedures to the best of the patient’s and investigator’s knowledge

24) History or evidence of suicidal ideation (severity of 4 or 5) or any suicidal behavior based on an assessment with the C-SSRS at enrollment

25) History or evidence of a psychiatric disorder, alcohol abuse, and/or substance abuse
26) Severe depression based on a total score of ≥15 on the PHQ-8 at enrollment (Note: patients with a total score of 10 to 14 on the PHQ-8 should be referred to a mental healthcare professional)

27) History or evidence of any other clinically significant disorder, condition, or disease (with the exception of those outlined above) that, in the opinion of the investigators, would pose a risk to patient safety or interfere with the study evaluation, procedures, or completion

28) Pregnant or lactating women or women who were willing to have a child within 8 weeks after the last dose of the study drug

29) Women of child-bearing potential (except for permanently sterilized, postmenopausal [defined as amenorrhea ≥12 consecutive months without an alternative medical cause], or anatomically not of childbearing potential) with a positive pregnancy test (assessed by a serum pregnancy test during screening and a urine pregnancy test at enrollment)

30) Women of child-bearing potential who did not agree to use effective contraception from the day of providing consent through 8 weeks after the last dose of the study drug. Fertile men who did not agree to use effective contraception through 8 weeks from the day of the first dose to after the last dose of the study drug. Effective contraception was defined as using any two of the following methods: condom, oral contraceptives, intrauterine contraceptive device, and diaphragm, or practice true abstinence from sexual intercourse. The investigators thoroughly explained the risks in pregnancy and the effective contraceptive methods to the patients

31) Anyone otherwise considered unsuitable for the study by the investigators

*Previous positive test result or positive result at screening
†Limited to the elevation of CRP (centrally measured) that was attributed to axSpA

AS, ankylosing spondylitis. ASAS, Assessment of SpondyloArthritis International Society; axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CRP, C-reactive protein; C-SSRS, Columbia-Suicide Severity Rating Scale; CT, computed tomography; DMARD, disease-modifying antirheumatic drug; DNA, deoxyribonucleic acid; HBc, hepatitis B core; HBs, hepatitis B surface; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HLA, human leukocyte antigen; HTLV-1, human T-lymphotropic virus type 1; IL, interleukin; nr-axSpA, nonradiographic axial spondyloarthritis; NSAID, nonsteroidal anti-inflammatory drugs; MRI, magnetic resonance imaging; PHQ-8, Patient Health Questionnaire-8; SAPHO, synovitis, acne, pustulosis, hyperostosis, osteitis; SpA, spondyloarthritis; SPARCC, SpA Research Consortium of Canada level; TNF, tumor necrosis factor; ULN, upper limit of normal
Table S2. Protocol amendments in inclusion criteria for axSpA

| Before Amendment                          | After Amendment                                                  | Remarks                                                                 |
|------------------------------------------|------------------------------------------------------------------|-------------------------------------------------------------------------|
| **Version 2.0**                          |                                                                  |                                                                         |
| Patient fulfills the ASAS classification criteria for axSpA (with the exception of the Crohn’s disease criterion) for >3 months |                                                                  |                                                                         |
| AS: Patient has radiographic evidence of sacroiliitis grade ≥2 bilaterally or grade 3 to 4 unilaterally (image must have been obtained ≤6 months from the time of screening; centrally read) |                                                                  |                                                                         |
| OR                                       |                                                                  |                                                                         |
| nr-axSpA: Patient does not have radiographic evidence of sacroiliitis grade ≥2 bilaterally or grade 3 to 4 unilaterally (image must have been obtained ≤6 months from the time of screening; centrally read) |                                                                  |                                                                         |
| **Version 3.0**                          |                                                                  |                                                                         |
| Version 3.0                              |                                                                  |                                                                         |
| Patient with age at onset <45 years and continuous chronic back pain for ≥3 months fulfills the ASAS classification criteria for axSpA (with the exception of the Crohn’s disease criterion) |                                                                  | Description of patients has been revised according to the ASAS classification criteria |
| AS: Patient has radiographic evidence of sacroiliitis grade ≥2 bilaterally or grade 3 to 4 unilaterally (image obtained within 6 months prior to the time of consent may be used; centrally read) |                                                                  | Timing of assessments was revised to clearly define the starting point for imaging |
| OR                                       |                                                                  |                                                                         |
| nr-axSpA: Patient does not have radiographic evidence of sacroiliitis grade ≥2 bilaterally or grade 3 to 4 unilaterally (image obtained within 6 months prior to the time of consent may be used; centrally read) |                                                                  |                                                                         |
| **Version 3.0**                          |                                                                  |                                                                         |
| Version 4.0                              |                                                                  |                                                                         |
| Patient with age at onset <45 years and continuous chronic back pain for ≥3 months fulfills the ASAS classification criteria for axSpA (with the exception of the Crohn’s disease criterion) |                                                                  | Patients who are positive for HLA-B27 and have at least two SpA features will also be enrolled in the study, according to the ASAS classification criteria |
| AS patients: Patient has radiographic evidence |                                                                  |                                                                         |
| **Version 4.0**                          |                                                                  |                                                                         |
| Version 4.0                              |                                                                  |                                                                         |
| Patient with age at onset <45 years and continuous chronic back pain for ≥3 months fulfills the ASAS classification criteria for axSpA (with the exception of the Crohn’s disease criterion) |                                                                  | One of the two SpA features must be elevated |
| AS patients: Patient has radiographic evidence |                                                                  | CRP, because the 2016 update of the ASAS- |

CRP, because the 2016 update of the ASAS-
of sacroiliitis grade ≥2 bilaterally or grade 3 to 4 unilaterally (image obtained within 6 months prior to the time of consent may be used; centrally read)

OR

nr-axSpA patients: Patient does not have radiographic evidence of sacroiliitis grade ≥2 bilaterally or grade 3 to 4 unilaterally (image obtained within 6 months prior to the time of consent may be used; centrally read)

AND

Presence of inflammatory lesions of the sacroiliac joint on MRI of SPARCC level ≥2 (centrally read)

of sacroiliitis grade ≥2 bilaterally or grade 3 to 4 unilaterally (image obtained within 6 months prior to the time of consent may be used; centrally read) and at least one of the SpA features specified in the ASAS classification criteria for axSpA (with the exception of Crohn’s disease criterion)

OR

nr-axSpA patients: Patient does not have radiographic evidence of sacroiliitis grade ≥2 bilaterally or grade 3 to 4 unilaterally (image obtained within 6 months prior to the time of consent may be used; centrally read)

AND

Patient meets either of the following criteria:

• Presence of inflammatory lesions of the sacroiliac joint on MRI of SPARCC level ≥2 (centrally read) and at least one of the SpA features specified in the ASAS classification criteria for axSpA (with the exception of Crohn’s disease criterion)

• Positive test for HLA-B27* and the presence of at least two of the SpA features specified in the ASAS classification criteria for axSpA (with the exception of Crohn’s disease criterion), one of which must be elevated CRP† (>ULN)

EULAR management recommendations specify elevated CRP and MRI findings as diagnostic criteria for patients with axSpA who are eligible for treatment with biologics
*Previous positive test result or positive result at screening.
†Limited to the elevation of centrally measured CRP that is attributable to axSpA.
AS, ankylosing spondyloarthritis; ASAS, Assessment of SpondyloArthritis International Society; axSpA, axial spondyloarthritis; CRP, C-reactive protein; EULAR, European League Against Rheumatism; HLA, human leukocyte antigen; nr-axSpA, nonradiographic axial spondyloarthritis; MRI, magnetic resonance imaging; SpA, spondyloarthritis; SPARCC, Spondyloarthritis Research Consortium of Canada; ULN, upper limit of normal.
Table S3. List of EOI categories

| EOI Label                                      | Identified Risks/Potential Risks for Brodalumab | Search Strategy                                      |
|-----------------------------------------------|-------------------------------------------------|-----------------------------------------------------|
| Neutrophil count decreased                    | Identified risks                                | Sponsor-defined EOI                                 |
| Serious infections                            | Identified risks                                | Infections and infestations (SOC) and serious AEs    |
| Serious hypersensitivity                      | Identified risks                                | Hypersensitivity (SMQs) and serious AE               |
| Malignancy                                    | Potential risks                                 | Malignancies (SMQs)                                 |
| Inflammatory bowel disease                    | Potential risks                                 | Sponsor-defined EOI, gastrointestinal ulceration (SMQ), and ischemic colitis (SMQs) |
| Suicide/self-injury–related events            | Potential risks                                 | Suicide/self-injury (SMQs)                           |

AE, adverse event; EOI, event of interest; MedDRA, Medical Dictionary for Regulatory Activities; SMQ, standardized MedDRA queries; SOC, system organ class.
### Table S4. Search list for PT for sponsor-defined EOI

| Neutrophil Count Decreased | Inflammatory Bowel Disease |
|----------------------------|----------------------------|
| Autoimmune neutropenia     | Colonic abscess            |
| Band neutrophil count decreased | Crohn’s disease         |
| Band neutrophil percentage decreased | Enteritis               |
| Benign ethnic neutropenia  | Inflammatory bowel disease|
| CSF granulocyte count abnormal | Large intestinal ulcer perforation |
| CSF neutrophil count decreased | Metastatic cutaneous Crohn’s disease |
| CSF polymorphonuclear cell count decreased | Small intestinal ulcer perforation |
| CSF white blood cell count decreased |                      |
| Cyclic neutropenia         |                            |
| Differential white blood cell count abnormal |                     |
| Enteritis leukopenic        |                            |
| Febrile neutropenia        |                            |
| Granulocyte count decreased |                            |
| Granulocytopenia            |                            |
| Granulocytopenia neonatal   |                            |
| Idiopathic neutropenia     |                            |
| Leukopenia                  |                            |
| Leukopenia neonatal         |                            |
| Neutropenia                 |                            |
| Neutropenia neonatal        |                            |
| Neutropenic colitis         |                            |
| Neutropenic infection       |                            |
| Neutropenic sepsis          |                            |
| Neutrophil count abnormal   |   |
|----------------------------|---|
| Neutrophil count decreased  |   |
| Neutrophil percentage abnormal |   |
| Neutrophil percentage decreased |   |
| Radiation leukopenia        |   |
| White blood cell analysis abnormal |   |
| White blood cell count abnormal |   |
| White blood cell count decreased |   |

CSF, cerebrospinal fluid; EOI, event of interest; PT, preferred term.
Table S5. ASAS response in the overall population and subgroups

| Population/Timepoint | Brodalumab 210 mg n/N (%); 95% CI | Placebo n/N (%); 95% CI |
|----------------------|-----------------------------------|-------------------------|
| **ASAS 40 response** |                                   |                         |
| **Overall population** | N=80                             | N=79                    |
| Week 2               | 13/80 (16.3) (8.9, 26.2)         | 2/78 (2.6) (0.3, 9.0)   |
| Week 4               | 21/79 (26.6) (17.3, 37.7)       | 9/74 (12.2) (5.7, 21.8) |
| Week 8               | 31/78 (39.7) (28.8, 51.5)       | 16/74 (21.6) (12.9, 32.7) |
| Week 12              | 26/75 (34.7) (24.0, 46.5)       | 19/71 (26.8) (16.9, 38.6) |
| Week 16              | 35/77 (45.5) (34.1, 57.2)       | 19/69 (27.5) (17.5, 39.6) |
| Week 16 (NRI)        | 35/80 (43.8) (32.7, 55.3)       | 19/79 (24.1) (15.1, 35.0) |
| **Ankylosing spondylitis** | N=63                             | N=62                    |
| Week 2               | 8/63 (12.7) (5.6, 23.5)         | 1/61 (1.6) (0.0, 8.8)   |
| Week 4               | 15/62 (24.2) (14.2, 36.7)       | 5/59 (8.5) (2.8, 18.7)  |
| Week 8               | 23/61 (37.7) (25.6, 51.0)       | 12/59 (20.3) (11.0, 32.8) |
| Week        | Nonradiographic axSpA | HLA-B27 positive |
|-------------|-----------------------|------------------|
|             | N=17                  | N=68             |
| Week 2      | 5/17 (29.4) (10.3, 56.0) | 10/68 (14.7) (7.3, 25.4) |
| Week 4      | 6/17 (35.3) (14.2, 61.7) | 18/68 (26.5) (16.5, 38.6) |
| Week 8      | 8/17 (47.1) (23.0, 72.2) | 27/68 (39.7) |
| Week 12     | 6/16 (37.5) (15.2, 64.6) | 10/68 (14.7) |
| Week 16     | 6/17 (35.3) (14.2, 61.7) | 14/61 (23.0) |
| Week 16 (NRI) | 6/17 (35.3) (14.2, 61.7) | 18/68 (26.5) |
|             | 29/60 (48.3) (35.2, 61.6) | 15/56 (26.8) (22.1, 47.4) |
| Week 16 (NRI) | 29/63 (46.0) (33.4, 59.1) | 16/62 (25.8) (15.5, 38.5) |
|                         | (28.0, 52.3) | (13.2, 35.5) |
|-------------------------|--------------|--------------|
| Week 12                 | 23/66 (34.8) | 15/59 (25.4) |
|                         | (23.5, 47.6) | (15.0, 38.4) |
| Week 16                 | 31/68 (45.6) | 16/59 (27.1) |
|                         | (33.5, 58.1) | (16.4, 40.3) |
| Week 16 (NRI)           | 31/68 (45.6) | 16/65 (24.6) |
|                         | (33.5, 58.1) | (14.8, 36.9) |
| HLA-B27 negative        | N=12         | N=14         |
| Week 2                  | 3/12 (25.0)  | 0/14 (0.0)   |
|                         | (5.5, 57.2)  | (0.0, 23.2)  |
| Week 4                  | 3/11 (27.3)  | 2/13 (15.4)  |
|                         | (6.0, 61.0)  | (1.9, 45.4)  |
| Week 8                  | 4/10 (40.0)  | 2/13 (15.4)  |
|                         | (12.2, 73.8) | (1.9, 45.4)  |
| Week 12                 | 3/9 (33.3)   | 4/12 (33.3)  |
|                         | (7.5, 70.1)  | (9.9, 65.1)  |
| Week 16                 | 4/9 (44.4)   | 3/10 (30.0)  |
|                         | (13.7, 78.8) | (6.7, 65.2)  |
| Week 16 (NRI)           | 4/12 (33.3)  | 3/14 (21.4)  |
|                         | (9.9, 65.1)  | (4.7, 50.8)  |
| CRP ≥ULN                | N=50         | N=53         |
| Week 2                  | 11/50 (22.0) | 1/53 (1.9)   |
|                         | (11.5, 36.0) | (0.0, 10.1)  |
| Week 4                  | 16/49 (32.7) | 7/49 (14.3)  |
|                         | (19.9, 47.5) | (5.9, 27.2)  |
| Week   | Count/Total (Percentage) | Lower 95% CI | Upper 95% CI |
|--------|--------------------------|--------------|--------------|
| Week 8 | 24/49 (49.0) (34.4, 63.7) |              |              |
|        | 12/49 (24.5) (13.3, 38.9) |              |              |
| Week 12| 19/47 (40.4) (26.4, 55.7) |              |              |
|        | 14/47 (29.8) (17.3, 44.9) |              |              |
| Week 16| 26/49 (53.1) (38.3, 67.5) |              |              |
|        | 15/47 (31.9) (19.1, 47.1) |              |              |
| Week 16 (NRI) | 26/50 (52.0) (37.4, 66.3) |              |              |
|        | 15/53 (28.3) (16.8, 42.3) |              |              |
| CRP <ULN | N=30                      | N=26         |
| Week 2 | 2/30 (6.7) (0.8, 22.1)    | 1/25 (4.0) (0.1, 20.4) |
| Week 4 | 5/30 (16.7) (5.6, 34.7)   | 2/25 (8.0) (1.0, 26.0) |
| Week 8 | 7/29 (24.1) (10.3, 43.5)  | 4/25 (16.0) (4.5, 36.1) |
| Week 12| 7/28 (25.0) (10.7, 44.9)  | 5/24 (20.8) (7.1, 42.2) |
| Week 16| 9/28 (32.1) (15.9, 52.4)  | 4/22 (18.2) (5.2, 40.3) |
| Week 16 (NRI) | 9/30 (30.0) (14.7, 49.4) | 4/26 (15.4) (4.4, 34.9) |

**ASAS 20 response**

| Overall population | N=80 | N=79 |
|--------------------|------|------|
| Week 2             | 34/80 (42.5) (31.5, 54.1) | 13/78 (16.7) (9.2, 26.8) |
| Week     | Count | Percentage | Confidence Interval |
|----------|-------|------------|---------------------|
| Week 4   | 42/79 | 53.2%      | (41.6, 64.5)        |
| Week 8   | 50/78 | 64.1%      | (52.4, 74.7)        |
| Week 12  | 53/75 | 70.7%      | (59.0, 80.6)        |
| Week 16  | 54/77 | 70.1%      | (58.6, 80.0)        |
| Week 16 (NRI) | 54/80 | 67.5% | (56.1, 77.6)        |

ASAS, Assessment of SpondyloArthritis International Society; axSpA, axial spondyloarthritis; CI, confidence interval; CRP, C-reactive protein; HLA, human leukocyte antigen; NRI, nonresponder imputation; ULN, upper limit of normal.
Table S6. ASAS 40 response by MRI status of sacroiliac joints in nr-axSpA subpopulation

| Timepoint   | MRI positive                  | MRI negative                  |
|-------------|-------------------------------|-------------------------------|
|             | MRI positive                  | MRI negative                  |
|             | n/N (%) (95% CI)             | n/N (%) (95% CI)             |
|             | Brodalumab 210 mg N=14       | Brodalumab 210 mg N=3         | Placebo N=2 |
| Week 2      | 4/14 (28.6) (8.4, 58.1)      | 1/3 (33.3) (0.8, 90.6)       | 0/2 (0.0) (0.0, 84.2) |
| Week 4      | 5/14 (35.7) (12.8, 64.9)     | 4/12 (33.3) (9.9, 65.1)      | 1/3 (33.3) (0.8, 90.6) | 0/2 (0.0) (0.0, 84.2) |
| Week 8      | 6/14 (42.9) (17.7, 71.1)     | 4/12 (33.3) (9.9, 65.1)      | 2/3 (66.7) (9.4, 99.2) | 0/2 (0.0) (0.0, 84.2) |
| Week 12     | 5/13 (38.5) (13.9, 68.4)     | 4/12 (33.3) (9.9, 65.1)      | 1/3 (33.3) (0.8, 90.6) | 0/2 (0.0) (0.0, 84.2) |
| Week 16     | 5/14 (35.7) (12.8, 64.9)     | 3/12 (25.0) (5.5, 57.2)      | 1/3 (33.3) (0.8, 90.6) | 0/2 (0.0) (0.0, 84.2) |
| Week 16 (NRI) | 5/14 (35.7) (12.8, 64.9) | 3/14 (21.4) (4.7, 50.8)      | 1/3 (33.3) (0.8, 90.6) | 0/2 (0.0) (0.0, 84.2) |

CI, confidence interval; MRI, magnetic resonance imaging; NRI, nonresponder imputation
Table S7. Change from baseline in other measures at week 16 (full analysis set)

| Patient-Reported Outcome            | Brodalumab 210 mg N=80 | Placebo N=79 |
|-------------------------------------|-------------------------|--------------|
| BASFI*                              | −1.1 (1.8)              | −0.7 (2.2)   |
| BASDAI†                            | −2.9 (2.1)              | −2.4 (1.9)   |
| BASMI‡                             | −0.3 (1.2)              | −0.1 (1.2)   |
| ASQoL†                             | −3.7 (4.2)              | −4.0 (3.9)   |
| SF-36v2¶                           | 9.9 (13.8)              | 10.6 (15.8)  |
| Enthesitis count†                   | −1.2 (2.5)              | −1.1 (2.9)   |
| Swollen joint count**               | −0.9 (1.9)              | −0.7 (4.5)   |
| Average PGA of spinal pain         | −2.99 (2.32)            | −2.30 (2.56) |
| Total PGA of spinal pain†‡‡         | −2.9 (2.3)              | −2.3 (2.5)   |
| Nocturnal PGA of spinal pain        | −3.1 (2.5)              | −2.3 (2.8)   |
| PGA of axSpA‡‡‡                     | −2.8 (2.4)              | −2.2 (2.5)   |

All data are mean (SD).

ASQoL, Ankylosing Spondylitis Quality of Life Questionnaire; axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; PGA, Patient Global Assessment; SD, standard deviation; SF-36v2, Short Form-36 Health Survey, version 2.

*BASFI is composed of ten items and uses an 11-point numerical rating scale labeled from “0=easy” to “10=impossible.”

†BASDAI is composed of six items and uses an 11-point numerical rating scale labeled from “0=none” to “10=very severe” for the first five items and “0=0 hours” to “10=2 or more hours” for the sixth item.

‡BASMI is composed of five indices that are scored based on observed values, and the total score (0-10) is used to assess spinal and hip joint mobility and leg position.

ASQoL comprises 18 items and uses a dichotomous response scale (yes=1 or no=0) for each of the items, where “yes” indicates that axSpA has an adverse effect on
the quality of life. The ASQoL total score ranges from 0 to 18, with higher scores indicating worse quality of life.

The SF-36v2 contains 36 items and yields assessments of eight domains of health-related quality of life and is calculated based on the validation testing of a three-component model (Physical Component Summary, Mental Component Summary, and Role/Social Component Summary) of SF-36 scores.

The enthesis count was defined as the number of “presence” assessed on 13 entheses using the Maastricht Ankylosing Spondylitis Enthesitis Score.

Swollen joint count was defined as the number of “positive” assessed on 44 swollen joints.

PGA of spinal pain is a two-item questionnaire and uses an 11-point numerical rating scale labeled from “0=no pain” to “10=most severe pain.”

PGA of axSpA is a single-item global measure of disease activity and uses an 11-point numerical rating scale labeled from “0=not active” to “10=very active.”

The full analysis set consisted of all randomized patients associated with the assigned treatment excluding those who received no study drug or had no post-dosing efficacy data available.