# SUPPLEMENTAL MATERIALS

## Supplemental Methods

### *Calculation of the number and proportion of patients under projection*

To project the number and proportion of randomised patients who will achieve remission by week 48, we performed the following calculations:

Group 1

1. Number of patients in remission at week 16: the observed remission rate at week 16 is 65% (39/[39 + 21]). For the 80 patients (89 randomised – 9 dropout) who have reached or will reach week 16, it is expected that 52 patients (80 × 65%) will have remission and 28 will not.
2. Number of patients in remission at week 32: the observed remission rate at week 32 is 40% (6/[6 + 9]). The observed dropout rate between week 16 and week 32 is 9.5% (2/21). Of the 28 patients proceeding to week 32, we expect 3 dropouts, and 25 patients will have the week 32 assessment. For the 25 patients who have reached or are going into week 32, it is expected that 10 patients (25 × 40%) will have remission and 15 will not.
3. Number of patients in remission at week 48: the observed remission rate at week 48 is 0% (0/[0 + 2]). The observed dropout rate between week 32 and week 48 is 44.4% (4/9). Of the 16 patients proceeding to week 48, we expect 7 dropouts, and 9 patients will have the week 48 assessment. It is expected that all 9 patients reaching the week 48 assessment will be non-remission patients (i.e., the total number of patients in remission at week 48 is 0).
4. Based on the above calculations, of the 89 randomised patients for Group 1, 62 (52 + 10 + 0) patients will achieve remission by week 48. The remission rate is 70% (62/89).

Group 2

1. Number of patients in remission at week 16: the observed remission rate at week 16 is 37.6% (35/[35 + 58]). For the 123 patients (130 randomised – 7 dropout) who have reached or will reach week 16, it is expected that 46 patients will have remission and 77 will not.
2. Number of patients in remission at week 32: the observed remission rate at week 32 is 26.7% (8/[8 + 22]). The observed dropout rate between week 16 and week 32 is 20.7% (12/58). Of the 77 patients proceeding to week 32, we expect 16 (77 × 20.7%) dropouts, and 61 patients will have the week 32 assessment. It is expected that 16 patients (61 × 26.7%) will have remission and 45 will not.
3. Number of patients in remission at week 48: the observed remission rate at week 48 is 38.5% (5/[5 + 8]). The observed dropout rate between week 32 and week 48 is 13.6% (3/22). Of the 45 patients proceeding to week 48, we expect 6 dropouts, and 39 patients

will have the week 48 assessment. It is expected that 15 patients (61 × 26.7%) will have remission and 24 will not.

4. Based on the above calculations, of the 130 randomised patients for Group 2, 77 (46 + 16 + 15) patients will achieve remission by week 48. The remission rate is 59% (77/130).

Group 3

1. Number of patients in remission at week 16: the observed remission rate at week 16 is 38.4% (56/[56 + 90]). For the 200 patients (213 randomised – 13 dropout) who have reached or will reach week 16, it is expected that 77 patients will have remission and 123 will not.
2. Number of patients in remission at week 32: the observed remission rate at week 32 is 16.1% (10/[10 + 52]). The observed dropout rate between week 16 and week 32 is 11.1% (10/90). Of the 123 patients proceeding to week 32, we expect 14 (123 × 11.1%) dropouts, and 109 patients will have the week 32 assessment. Then it is expected that 18 patients (109 × 16.1%) will have remission and 91 will not.
3. Number of patients in remission at week 48: the observed remission rate at week 48 is 20.8% (5/[5 + 19]). The observed dropout rate between week 32 and week 48 is 23.1% (12/52). Of the 91 patients proceeding to week 48, we expect 21 dropouts, and 70 patients will have the week 48 assessment. It is expected that 15 patients (70 × 20.8%) will have remission and 55 will not.
4. Based on the above calculations, of the 213 randomised patients for Group 3, 110 (77 + 18 + 15) patients will achieve remission by week 48. The remission rate is 52% (110/213).

## Supplemental Table 1. Time and events schedule†

| **Visit** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9/EOS** |
|---|---|---|---|---|---|---|---|---|---|
| **Week** | **Screening** | **R** | **8** | **16** | **32** | **48** | **64** | **80** | **96** |
| **Study Day** | **-28 to -1** | **1** | **57** | **113** | **225** | **337** | **449** | **561** | **673** |
| **Recommended Visit Window (days)** | | **0** | **±7** | **+21** | **+21** | **+21** | **±14** | **±14** | **±14** |
| Informed consent | X | | | | | | | | |
| Assess inclusion/exclusion | X | | | | | | | | |
| Confirm inclusion/exclusion | | X | | | | | | | |
| Demographics | X | | | | | | | | |
| Medical/surgical/medication history | X | X | | | | | | | |
| Complete physical examination | X | | | | | | | | |
| Partial physical examination (symptom-driven) | | X | X | X | X | X | X | X | X |
| Vital signs | X | X | X | X | X | X | X | X | X |
| Haematology (including CRP levels) | X | X | X | X | X | X | X | X | X |
| Serum chemistry | X | X | | X | X | X | X | X | X |
| SOC TB (QuantiFERON), hepatitis B and C Tests (unless negative result within 12 months) | X | | | | | | | | |
| Stool sample for *C. difficile* and stool culture | X | | | | | | | | |
| Urinalysis | X | X | | X | X | X | X | X | X |
| Serum pregnancy test | X | | | | | | | | |
| Urine pregnancy test | | X | X | X | X | X | X | X | X |
| Partial Mayo Clinic Score | | | X | | | | X | X | |
| Flexible sigmoidoscopy with biopsy | X | | | X | X | X | | | X |
| Central assessment of endoscopy and histology | X | | | X | X | X | | | X |
| Mayo Clinic Score | X | | | X | X | X | | | X |
| SIQ-UC with PGI-S/PGI-C (if appropriate language version available) | | X | | X | X | X | X | X | X |
| CGI-S, CGI-C (if SIQ-UC being completed) | | X | | X | X | X | X | X | X |
| IBDQ | | X | | X | X | X | X | X | X |
| WPAI-UC | | X | | X | X | X | X | X | X |
| IWRS randomisation (target assignment) | | X | | | | | | | |
| Determine algorithm based on existing UC therapy | | X | | | | | | | |
| Study drug dosing (if applicable) | | X | | | | | | | |
| Algorithm compliance | | | | X | X | X | X | X | X |
| Remission target assessment | | | | X | (X) | (X) | | | X |
| Corticosteroid taper (if applicable) | | (X) | (X) | (X) | (X) | | | | |
| Faecal calprotectin | | X | X | X | X | X | | | X |
| Urine, stool, colonic mucosa, and serum samples for biomarkers and drug concentrations‡ | X | | | X | X | X | X | X | X |
| Dispense stool diary | X | X | X | X | X | X | X | X | |
| Review stool diary | | X | X | X | X | X | X | X | X |
| Concomitant medications | | X | X | X | X | X | X | X | X |
| Adverse event assessment | X | X | X | X | X | X | X | X | X |
| Schedule return visit | X | X | X | X | X | X | X | X | |

| Visit | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9/EOS |
|---|---|---|---|---|---|---|---|---|---|
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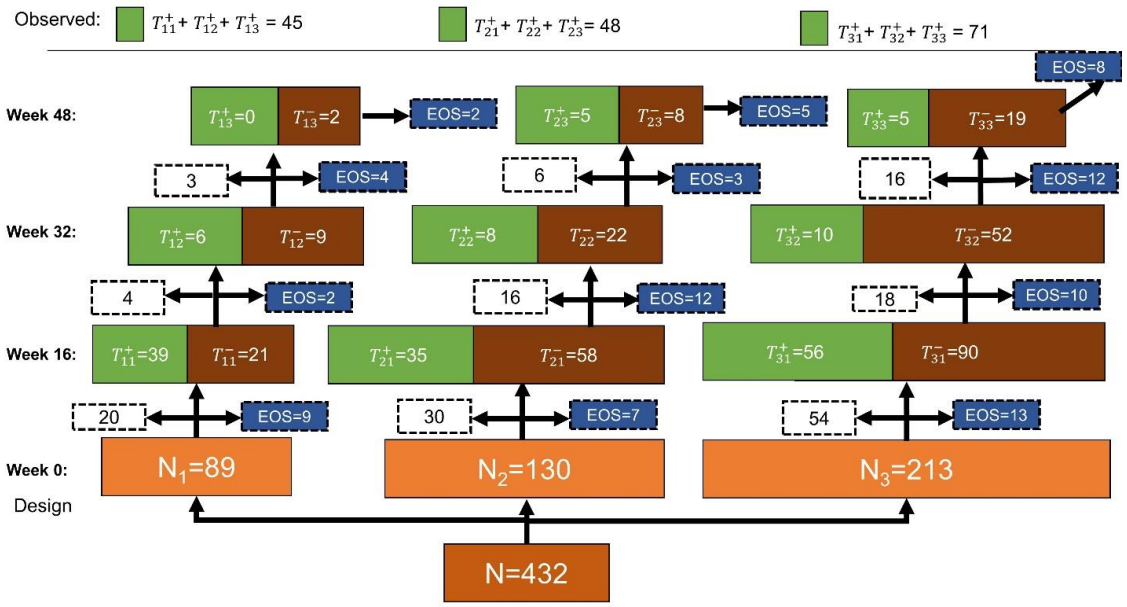
| **Study Day** | **-28 to -1** | **1** | **57** | **113** | **225** | **337** | **449** | **561** | **673** |
| **Recommended Visit Window (days)** | | **0** | **±7** | **+21** | **+21** | **+21** | **±14** | **±14** | **±14** |

Abbreviations: CGI-C, Clinical Global Impressions - Change; CGI-S, Clinical Global Impressions - Severity; C. difficile, Clostridioides difficile; CRP, C-reactive protein; EOS, end of study; IBDQ, Inflammatory Bowel Disease Questionnaire; IWRS, interactive web response system; PGI-C, Patient Global Impressions - Change; PGI-S, Patient Global Impressions - Severity; R, randomisation; SIQ-UC, Symptoms and Impacts Questionnaire for Ulcerative Colitis; SOC, standard of care; TB, tuberculosis; WPAI UC, Work Productivity and Activity Impairment – Ulcerative Colitis.

† Patient confidentiality will be maintained. Information collected will comply with the requirements for the protection of privacy of individually identifiable health information and will be made publicly available only to the extent permitted by the applicable laws and regulations. Study records will identify the patient by initials, where permitted, and the assigned patient identification number.

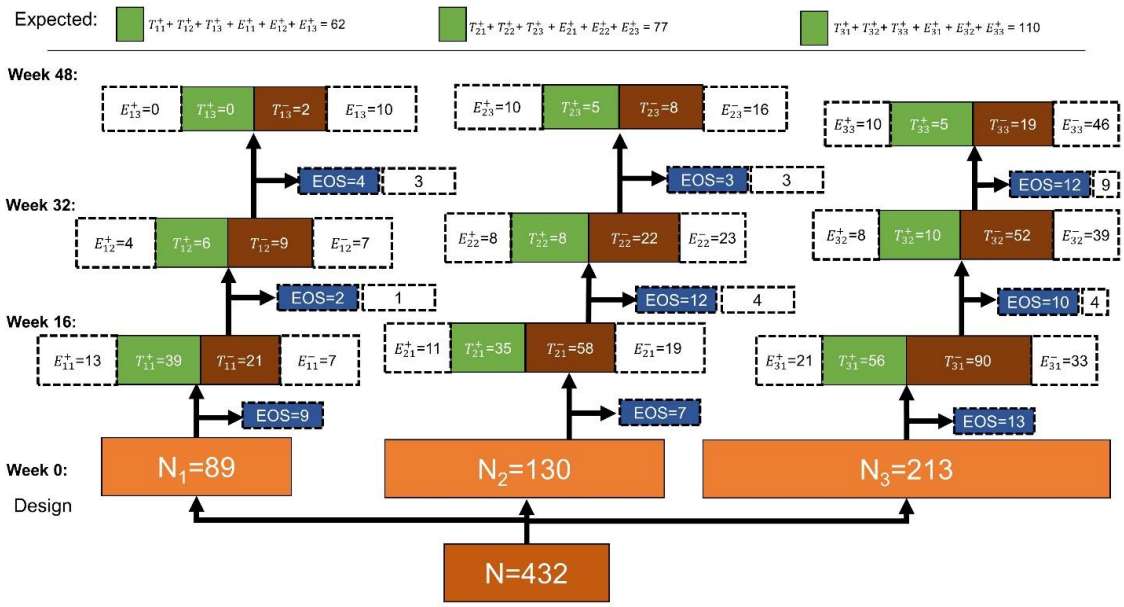
‡ Patients will be asked to provide optional consent to store and use data for the purpose of performing future exploratory research. Upon consent, samples collected will be deidentified and stored in a central laboratory, a secure location, for up to 25 years after study completion. Sample collection, storage, and use of samples and data for future research will comply with the local guidance and/or applicable international guidance.

**Supplemental Figure 1. Patient flow as of 1 March 2023**




Green box: number of patients who achieved treatment target at the visit time point; brown box: number of patients who did not achieve treatment target at the visit time point; dashed white box: patients who were still on their way to the nearest visit time point; blue box: patients who dropped out of the study to the nearest visit time.

**Supplemental Figure 2. Patient flow with remission rate projection**




Green box: number of patients who achieved treatment target at the visit time point; brown box: number of patients who did not achieve treatment target at the visit time point; dashed white box: patients who would be classified as achieving or not achieving targeted remission based on the estimated remission rate; blue box: patients who dropped out of the study to the nearest visit time.