**SUPPLEMENTARY MATERIAL 1. Hypothetical study entry criteria (MODIFIED FROM THE CONCERTO STUDY [NCT01185301])**

***Inclusion Criteria***

* Male and female subjects; age 18 years to 80 years
* Subject has a diagnosis of Rheumatoid Arthritis (RA) as defined by either the 1987-revised American College of Rheumatology (ACR) classification criteria or the new ACR / European League Against Rheumatism (EULAR) diagnostic criteria for RA 2010 and has a disease duration of less than 1 year from diagnosis by a licensed health care provider
* Subject must meet the following criteria:
  + 1. Disease Activity Score of C-reactive Protein (DAS28[CRP]) ≥ 3.2 (at Baseline visit)
    2. At least 6 swollen joints out of 66 assessed (at the Screening and Baseline visits)
    3. At least 8 tender joints out of 68 assessed (at the Screening and Baseline visits)
    4. C-reactive protein (CRP) ≥ 1.5 mg/dL (at the Screening visit only), or erythrocyte sedimentation rate (ESR) ≥ 28 mm/1h (at the Screening and Baseline visits)
    5. Fulfill ³ 1 of the following three criteria: Rheumatoid Factor (RF) positive, have at least 1 bony erosion, anti-cyclic citrullinated peptide (anti-CCP) antibody positive
* Subject is judged to be in good health as determined by the Principal Investigator based upon the results of medical history, laboratory profile, physical examination, chest x-ray (CXR), and a 12-lead electrocardiogram (ECG) performed during screening

***Exclusion Criteria***

* Subject has history of pre-existing insomnia, obstructive sleep apnea, or restless leg syndrome
* Subject has previous exposure to any systemic biologic therapy including adalimumab
* Subject has been previously treated with greater than 1 disease modifying antirheumatic drugs (DMARDs) or with methotrexate (MTX)
* Subject has undergone joint surgery within the preceding two months (at joints to be assessed within the study)
* Subject has chronic arthritis diagnosed before age 17 years
* History of invasive infection (e.g., listeriosis and histoplasmosis), chronic or active Hepatitis C infection, human immunodeficiency virus (HIV) infection, immunodeficiency syndrome, chronic recurring infections or active tuberculosis (TB)
* Hepatitis B virus: hepatitis B surface antigen (HBs Ag) positive (+) or detected sensitivity on the hepatitis B virus DNA (HBV DNA) polymerase chain reaction (PCR) qualitative test
* Infection(s) requiring treatment with intravenous (IV) anti-infectives within 30 days prior to the Baseline Visit or oral anti-infectives within 14 days prior to the Baseline visit
* Female subject who is pregnant or breast-feeding or considering becoming pregnant

**SUPPLEMENTARY MATERIAL 2. Hypothetical study Description of Parameters**

| **Parameter Category** | **Parameter Name** |
| --- | --- |
| Actigraphy Sleep Measures | Sleep Onset Latency |
| Snooze Time |
| Sleep Duration |
| Efficiency |
| Fragmentation |
| Percent Sleep |
| Wake Time |
| Percent Wake |
| Number Wake Bouts |
| Avg Wake Bouts |
| Frequency of wake bouts |
| Activity Count/Wake Min |
| Sleep Time |
| WASO |
| Number Sleep Bouts |
| Avg Sleep Bouts |
| PRO sleep measures | PSQI |
| PRO measures of RA | DLQI |
| HAQ-DI |
| HADS |
| Biological measures of RA Disease Activity | TNF alpha (Serum, Synovial, or Intracellular) |
| DAS28 |
| ACR70 |
| Reference Standard Sleep Measure | PSG |
| Clinical and Demographic Information | Age |
| Sex |
| BMI |

**SUPPLEMENTARY MATERIAL 3. HYPOTHETICAL STUDY ACTIVITIES SCHEDULE**

| **Activity** | **Baseline  (Week -1)** | **Treatment Week 1** | **Treatment Week 12** |
| --- | --- | --- | --- |
| RA disease activity | √ | √ | √ |
| Biological measures of RA | √ | √ | √ |
| PRO measures of RA | √ | √ | √ |
| Actigraphy Sleep Measures | Continuous | √ | √ |
| PSG (sub-study only) | √ | √ | √ |
| PRO measures of sleep | √ | √ | √ |
| Clinical and Demographic Information | √ | √ | √ |

PRO = patient-reported outcome; PSG = polysomnography; RA = rheumatoid arthritis.

**SUPPLEMENTARY MATERIAL 4. LEXICON**

| **Terminology** | **Definition** | **Source** |
| --- | --- | --- |
| Clinical Endpoint | A precisely defined variable is intended to reflect an [outcome](https://www.ncbi.nlm.nih.gov/books/NBK338448/def-item/outcome/) of interest that is statistically analyzed to address a particular research question.  A precise definition of an endpoint typically specifies the type of assessments made, the timing of those assessments, the [assessment](https://www.ncbi.nlm.nih.gov/books/NBK338448/def-item/assessment/) tools used, and possibly other details, as applicable, such as how multiple assessments within an individual are to be combined. | FDA - BEST |
| Biomarker | A defined characteristic that is measured to provide insight into a normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions. Molecular, histologic, radiographic, or physiologic characteristics are types of biomarkers. A biomarker is not an assessment of how a patient feels, functions, or survives. | FDA - BEST |
| Digital Biomarker\* | An objective and quantifiable physiological signal(s) measured by digital technologies. These “digital signals” can be developed as an indicator of disease activity or treatment response. | TransCelerate |
| An objective, quantifiable measure of physiology and/or behavior used as an indicator of biological, pathological process or response to an exposure or an intervention that is derived from a digital measure. The clinical meaning is established by a reliable relationship to an existing, validated endpoint. | EMA Q&A |
| Digital Biomarkers are defined as requirements or specifications that are measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions that can only be measured by a validated DHTT. | PhRMA |
| Clinical Outcome Assessment (COA) | Assessment of a clinical outcome can be made through report by a clinician, a patient, a non-clinician observer or through a performance-based assessment. There are four types of COAs.  Clinician-reported outcome  Observer-reported outcome  Patient-reported outcome (PRO)  Performance outcome (PerfO)  Passive monitoring outcome  Other (wearable sensors) | FDA - [BEST](https://www.fda.gov/downloads/drugs/developmentapprovalprocess/drugdevelopmenttoolsqualificationprogram/ucm510443.pdf)  Resource Glossary |
| Novel Digital Endpoints (NDE)  There is currently no consensus from industry or Health Authorities regarding these definitions. | A precisely defined variable or clinical outcome assessment (COA) that is intended to reflect an [outcome](https://www.ncbi.nlm.nih.gov/books/NBK338448/def-item/outcome/) of interest that is collected and measured through connected digital health technologies (DHT) or biometric monitoring technologies (BioMeTs) in the clinical trial setting. | TransCelerate |
| Digital endpoints are defined as a precisely defined variable intended to reflect an outcome of interest that is statistically analyzable to address a particular research question derived from data captured with a DHTT. | PhRMA |
| Digital Health Technologies (DHT) | DHTTs are defined as electronic technology tools intended for use in clinical investigations (inclusive of clinical trial and post-market settings) or clinical practice. They may, for example, capture data, actively or passively (e.g., measure data and interpret data), educate digitally, or serve as reminders. | PhRMA |
| Biometric Monitoring Technologies (BioMeTs) | Biometric monitoring technologies (BioMeTs) are defined as connected digital medicine tools, processing data captured by mobile sensors using algorithms to generate measures of behavioral and/or physiological function. | (Goldsack, 2020) |

BioMeTs = biometric monitoring technologies; COA = clinical outcome assessment; DHT = digital health technology; DHTT = DHT tool; EMA Q&A = European Medicines Agency Question and Answer; FDA – BEST = United Stated Food and Drug Administration Biomarkers, Endpoints, and other Tools; NDE = novel digital endpoint; PerfO = performance outcome; PhRMA = Pharmaceutical Research and Manufacturers of America; PRO = patient-reported outcome.