Understanding the Effects of Healthcare Disparities on OA Symptomatology, Disease Progression, and Treatment Response

Request for Proposal

Purpose and Intent

Flexion Therapeutics, Inc. issues this RFP for research studies evaluating osteoarthritis (OA) symptomatology, disease progression, and treatment response with triamcinolone acetonide extended release (TA-ER) in patients with knee OA, who have historically been under-represented in musculoskeletal research.

Target Audience

Healthcare professionals involved in the care of patients with knee osteoarthritis.

Timeline

The RFP application will remain open through 2021.

Background

Healthcare disparities in race/ethnicity, socio-economic status (SES), and access to care have been extensively documented in orthopedics.[1] Despite this, awareness regarding many of these disparities in musculoskeletal care is low among orthopedic health care providers.[2] In recent years, there has been an increased emphasis on evaluating the effects of these disparities on patient health, quality of care, access to care, and outcomes within orthopedics.[1,3-6] Further contributing to these disparities is the lack of diverse populations in research cohorts, which experts call a missed scientific opportunity to fully understand the factors that lead to poor health and disease.[7] With the advent of new multidisciplinary studies capable of evaluating the

complex associations between genes, socioeconomics, and environmental exposures, it is imperative that biomedical research be inclusive.[4,7] Awareness, education, and inclusion of healthcare disparities in research will advance efforts toward achieving health equality.[8]

TA-ER is an extended-release formulation of triamcinolone acetonide that has been studied in multiple phase 2 and phase 3 studies. However, TA-ER has been primarily studied in Whites, with 80.7% Whites in the Phase 3 study.[9] In addition, similar to other osteoarthritis studies, trials with TA-ER have not collected or evaluated demographic data relating to other social determinants of health (e.g., SES, history of access to care.)[10]

Scope of Work

The successful applicant will prepare a research proposal that explores and further characterizes underrepresented populations in orthopedics and their responsiveness to TA-ER. The study proposal should focus on patients (≥ 40 yoa) with primary knee osteoarthritis. Study proposals could consider:

- racial disparities in diseases explained within the framework of the social determinants of health [8,11]
- phenotypic race distinguished from genetic ancestry [8]
- structural barriers to health that overlap with race, including socioeconomic status, discrimination, insurance status, access to OA treatments, transportation, environmental exposures, criminal history, documentation status, English proficiency, and neighborhood violence[11]
- Data in expanded populations where demographics are self-reported and data collection is non-binary.

Study proposals should clearly define the osteoarthritis patient population to be included (i.e. radiographic Kellgren-Lawrence grade of osteoarthritis, history of synovitis and/or effusion, etc.) and should evaluate symptomatology, disease progression, and/or treatment responses. Study evaluations may include any of the following:

- Assessments of pain, stiffness, and physical function
- patient reported outcomes
- Measures of disease progression
- Additional biomarkers distinguishing OA phenotypes
- Safety assessments.

Flexion's IIR review committee will consider funding awards inclusive of indirect costs for the conduct of the study based on a budget within fair market value.

Your concept proposal will be considered by Flexion's cross-functional research committee that meets routinely to review IIR proposals. Flexion may make suggestions to improve the scientific merit of the proposal and enhance consistency with Flexion's support approval criteria. The principal investigator will have full and final discretion and responsibility for all aspects of the study design, implementation, data analysis, and data dissemination, including compliance with all laws and regulations applicable to research sponsors. The terms under which Flexion will provide support must be contained in a written agreement. Flexion provides no guarantees that research committee will provide support for your proposal.

TA-ER is marketed under the tradename ZILRETTA. Please see full Prescribing Information at **ZILRETTALabel.com**

The information within this RFP is not intended to promote any use of the product that is inconsistent with its approved labeling, nor does this RFP provide comprehensive information regarding TA-ER.

References

1. Pandya NK, Wustrack R, Metz L, Ward D. Current concepts in Orthopaedic care Disparities. *J Am Acad Orthop Surg.* 2018: 26:823-832.
2. Adelani MA, O'Connor MI. Perspectives of Orthopedic Surgeons on Racial/Ethnic Disparities in Care. *J Racial Ethn Health Disparities.* 2017 Aug;4(4):758-762. doi: 10.1007/s40615-016-0279-z. Epub 2016 Aug 29. PMID: 27571957.
3. Jordan JM. An Ongoing Assessment of Osteoarthritis in African Americans and Caucasians in North Carolina: The Johnston County Osteoarthritis Project. *Transactions of the American Clinical and Climatological Association.* 2015;126:77-86.
4. Pierson E, et al. An algorithmic approach to reducing unexplained pain disparities in underserved populations. *Nature Medicine.* 2021;27:136-140.
5. Ezomo OT, et al. Where DoWe Stand Today on Racial and Ethnic Health Disparities? An Analysis of Primary Total Hip Arthroplasty From a 2011-2017 National Database. *Arthroplasty Today.* 2020;6:872-876.
6. Cusano A, et al. Where Do We Stand Today on Racial and Ethnic Health Inequities? Analysis of Primary Total Knee Arthroplasty from a 2011–2017 National Database. *Journal of Racial and Ethnic Health Disparities (2020).*
7. Konkel L. Racial and Ethnic Disparities in Research Studies: The Challenge of Creating More Diverse Cohorts. *Environ Health Perspect.* 2015;123(12):A297-A302. doi:10.1289/ehp.123-A297.
8. Reyes AM, Katz JM. Racial/Ethnic and Socioeconomic Disparities in Osteoarthritis Management. *Rheum Dis Clin N Am.* 2021;47:21–40.
9. Cerdeña JP, Plaisime MV, Tsai J. From race-based to race-conscious medicine: how anti-racist uprisings call us to act. *Lancet* 2020. Oct 10;396(10257):1125-1128. doi: 10.1016/S0140-6736(20)32076-6. PMID: 33038972.
10. Conaghan PG, et al. Effects of a Single Intra-Articular Injection of a Microsphere Formulation of Triamcinolone Acetonide on Knee Osteoarthritis Pain: A Double-Blinded, Randomized, Placebo-Controlled, Multinational Study. *J Bone Joint Surg Am*. 2018 Apr 18;100(8):666-677.
11. Braveman P. Health disparities and health equity: concepts and measurement. *Annu Rev Public Health*. 2006;27:167–94.