# Impact of TA-ER Treatment of Knee OA in the Background of Rheumatologic Diseases With High Disease Burden

*Request for Proposal*

## Purpose and Intent

Flexion Therapeutics, Inc. issues this request for a prospective clinical research study evaluating the use of triamcinolone acetonide extended-release (TA-ER) for use in patients who suffer from knee osteoarthritis/OA and a concomitant rheumatic disease involving joint inflammation.

## Target Audience

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

## Timeline

The RFP application will remain open through 2021.

## Background

General arthritis has a high prevalence around the world with the most common forms being osteoarthritis 10%, rheumatoid arthritis (RA) 1%, and psoriatic arthritis (PsA) 0.25% and other inflammatory arthritis.[1] In an analysis performed by Charlton et al., among the psoriatic arthritis patients evaluated, over 22.1% also had OA.[2] OA is a cause of severe pain which can be limiting for other functional endpoints.[3] The percentage of psoriatic patients with OA was higher than the in psoriasis alone and the general population. Patients who suffer from compound arthritis (more than one arthritis diagnosis) tend to fail meeting aerobic and muscle strengthening guidelines. This compounds the risk and increases patients' overall morbidity

and mortality. Reports show that when OA and RA are compared using similar subjective questionnaires Multidimensional Health Assessment Questionnaire (MDHAQ) , Routine Assessment of Patient Index Data (RAPID3) as opposed to individualized scales such as WOMAC, the burden of OA is similar to that of RA.[4] These data extend observations that the self-reported disease burden of patients with generalized OA who are seen in rheumatology routine care is greater than that of patients with RA due to patient vs physician reported measures and lack of disease modifying treatments.[5,6] All arthritis forms share common features in the disease process from monocyte infiltration, inflammation, synovial swelling, pannus formation and stiffness in the joints and articular cartilage death.[1] Across all forms of arthritis, NSAIDs and corticosteroids have been used in the treatment of these conditions.

To-date, TA-ER has not been studied for use in patients with knee OA and concomitant rheumatologic conditions.

## Scope of Work

The study proposal should focus on adults with knee OA and concomitant RA, PsA, or another inflammatory arthritis involving the joint(s). Flexion will entertain studies looking to assess the benefit of TA-ER in these patient groups or the added benefit of TA-ER by comparing to a matched OA only group. The study proposal should include assessment of:

- Pain, stiffness and physical function
- Baseline joint inflammation based on clinical markers or imaging
- Patient reported outcomes such as the (MDHAQ) or (RAPID3)
- Disease specific subscales (e.g. Disease Activity Score 28 (DAS28), Clinical Disease Activity Index (CDAI), Psoriatic Arthritis Disease Activity Score (PASDAS)
- Additional biomarkers distinguishing OA phenotypes

To be eligible for consideration, the requestor must be an independent third party. Flexion will not accept proposals that look to analyze the use of TA-ER for isolated extra-articular conditions such as enthesitis or tendonitis unless it/they are in conjunction with a knee OA diagnosis. Patients with underlying rheumatologic conditions must also have been:

- Stable on their background csDMARD rheumatic disease medications[7]
- On concomitant medications consistent with the standard of care.
- Not received any form of vaccination within the past 2 weeks

The Flexion 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


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2. Charlton R, Green A, Shaddick G, Snowball J, Nightingale A, Tillett W, Smith C, McHugh N; PROMPT study group. Risk of osteoarthritis in an incident cohort of people with psoriatic arthritis: a population-based cohort study. *J Rheumatol*. 2020 Nov 15:jrheum.200564. doi: 10.3899/jrheum.200564. Epub ahead of print. PMID: 33191285.
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4. Chua JR, Jamal S, Riad M, Castrejon I, Malfait AM, Block JA, Pincus T. Disease Burden in Osteoarthritis Is Similar to That of Rheumatoid Arthritis at Initial Rheumatology Visit and Significantly Greater Six Months Later. *Arthritis Rheumatol.* 2019 Aug;71(8):1276-1284. doi: 10.1002/art.40869. Epub 2019 Jul 3. PMID: 30891933.
5. Castrejon I, Shakoor N, Chua JR, Block JA. Discordance of global assessment by patients and physicians is higher in osteoarthritis than in rheumatoid arthritis: a cross-sectional study from routine care. *Rheumatol Int.* 2018 Nov;38(11):2137-2145. doi: 10.1007/s00296-018-4166-2. Epub 2018 Oct 6. PMID: 30293155.
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7. Hua C, Buttgereit F, Combe B. Glucocorticoids in rheumatoid arthritis: current status and future studies. RMD Open 2020;6:e000536. doi:10.1136/ rmdopen-2017-000536