

# SMALL MOLECULE HDAC6 INHIBITORS

Reference No. B73271

## CHALLENGE

Emerging evidence suggests the utility of histone deacetylase inhibitors (HDACi) in the **treatment of chronic immune and inflammatory disorders** such as **rheumatoid arthritis (RA)**. Several studies have shown the decreasing effect of selective HDAC6 inhibitors on the secretion of pro-inflammatory cytokines in vitro and a significant therapeutic response has been demonstrated in animal inflammatory disease models.

## INNOVATION

Here we present with **Marbostat** new small molecule inhibitors of HDAC6 that, in contrast to the established HDAC6 inhibitor Tubastatin A, are both **more potent and specific**, and most importantly they **highly and selectively inhibit** the enzyme activity of **HDAC6** without destroying the protein.

## COMMERCIAL OPPORTUNITIES

Provision of a viable alternative to first line NSAIDs (non-steroidal anti-inflammatory drugs) in the treatment of RA:

- reduced clinical score in mouse model (weaker signs of: synovial inflammation, paw thickness, cellular invasion/degradation of cartilage and bone erosion in joints)
- more potent/specific than Tubastatin A
- water soluble
- no toxic side effects were observed

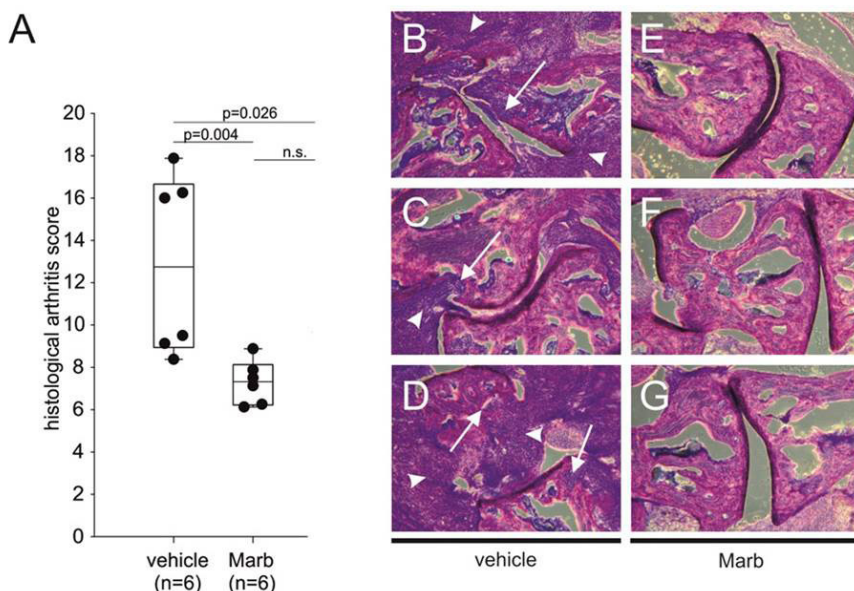


Figure: Representative DMMB staining of affected joints in a collagen induced arthritis (CIA) model.

Dark purple color indicates presence of sulfated glycosaminoglycans in articular cartilage. Vehicle treated animals display signs of synovial inflammation and cellular invasion (arrow heads) and degradation/erosion of cartilage/bone tissue in the joint (arrows). Marbostat 100 (Marb)-treated animals display weaker signs of inflammation, invasion and degradation/erosion.

## DEVELOPMENT STATUS

- currently: enantiomer analysis and oral administration
- to be done (partners):
- analysis of the therapeutic range and toxicity in animal models
- Pharmacology /analysis of substrates for more information on the molecular level



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**IP rights:**  
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