PRESS RELEASE

For immediate release
For medical, trade & investor media only

New data presented at OARSI 2021 Virtual World Congress by AKL Research and Development advances understanding of biological effects of its investigational osteoarthritis drug APPA to protect against joint damage

Findings suggest APPA's mode of action targets multiple pathways involved in osteoarthritis

Stevenage, UK, April 29, 2021 – AKL Research and Development (AKLRD), a pharmaceutical company which develops novel solutions for inflammatory diseases with a high unmet need, today unveils new data at the Osteoarthritis Research Society International (OARSI) Virtual World Congress (April 29 – May 1) indicating its investigational oral osteoarthritis (OA) drug APPA can modulate cellular function, reduce inflammation and inhibit bone resorption associated with joint degradation caused by the disease.

Results from one study, conducted by Nordic Biosciences using ex vivo tissue explants, found that APPA, an NRf2 and NFkB regulator, reduces inflammation-derived tissue turnover in human cartilage explants and inhibits RANKL-mediated osteoclastogenesis and bone resorption by human osteoclasts. These findings indicate that APPA modulates the cellular function of both chondrocytes and osteoclasts, respectively responsible for the maintenance and repair of cartilage and bone, suggesting it may inhibit the mechanism associated with joint degradation in arthritic disease.

Results from a second study, conducted by Instituto de Investigación Biomedica da Coruña, using human articular chondrocytes, showed that APPA significantly reduces the gene expression induced by inflammatory cytokines IL-1β of IL-8, TNF-α and cartilaginous degrading enzymes MMP-13 and MMP-3. In addition, experiments using human cartilage explants stimulated with IL-1β, found that APPA significantly increases levels of proteoglycans in the intermedial layer.

Consultant Rheumatologist Professor Robert Moots, who led APPA's Phase I trial at Liverpool University's Institute of Ageing and Chronic Disease, said: "Osteoarthritis is a cause of much misery and pain worldwide. Despite advances in understanding the pathological processes that underlie this, our best treatments today remain embarrassingly crude – cut out the sore joint or prescribe painkillers. These new data add important new pieces to the jigsaw puzzle that suggests a potentially exciting and effective role for APPA in treating this chronic and debilitating disease."

These latest results build on previously published data in the journal Inflammopharmacology in 2020 showing that in activated neutrophils APPA as an NFkB and Nrf2 gene transcription modulator, provides an anti-inflammatory effect by regulating the cross-talk between these two signalling molecules in the inflammatory process[1]. Similarly, APPA was shown to significantly decrease joint damage scores, improve weight bearing and reduce incapacity in a series of rat meniscal tear models of OA[2].

---

[1] Inflammopharmacology volume 28, pages1223–1235(2020)

[2] Osteoarthritis and Cartilage 20 (2012) S54–S296

*Please note: APPA is an investigational medicine and not yet approved for use.

PRESS RELEASE

For immediate release
For medical, trade & investor media only

Alan Reynolds, Chief Scientific Officer at AKLRD, said: "We are encouraged to see the results from these two studies which provide an important step in understanding the effects of APPA on the tissues involved in the joint. This builds on earlier research looking at neutrophils which showed that APPA may have significant anti-inflammatory potential. Taken together, this growing body of evidence suggests that APPA appears to work across multiple pathways to reduce pain and slow the progression of damage in patients with osteoarthritis, a disease which is a significant burden on those it affects."

Regulatory guidance from the FDA states that any new OA drug targeting disease modification must also demonstrate symptomatic pain relief.[1] APPA, which is currently in a Phase II clinical trial with results expected in July 2021, is a leading oral new chemical entity (NCE) in the biopharma pipeline that targets multiple signalling pathways to deliver both pain relief and disease modification in OA. Other drugs currently in development mostly inhibit single pathways.

Because OA is a disease of the whole joint, any new drug is likely to need to show it has an effect on the multiple signalling pathways involved in bone, cartilage and synovium with the aim of treating pain, improving function and halting disease progression. The disease affects 7% of the global population, more than 500 million people worldwide, and it is the third most rapidly rising condition worldwide, just behind diabetes and dementia[2].

ENDS

For more information, please contact:

Alan Reynolds
CSO, AKL Research & Development
ar@aklrd.com

Alexandra Harrison
The Difference Collective
T: 07525 144230
alexandra.harrison@thedifferencecollective.com

NOTES TO EDITORS:

About APPA

- APPA is oral, patented, fixed-dose combination of two synthetically produced, synergistic, secondary metabolites of plant origin, which exerts its anti-inflammatory effect by modulating the pathways of intracellular signalling molecules, NFkB and Nrf2. Related to innate immune responses, APPA also inhibits the formation of neutrophil extracellular traps (NETs).
- APPA is unique because it directly affects inflammation at its source by re-balancing NFkB and Nrf2. APPA regulates rather than blocks the immune response, allowing the body to maintain host defence mechanisms.

*Please note: APPA is an investigational medicine and not yet approved for use.

PRESS RELEASE

For immediate release
For medical, trade & investor media only

About AKLRD

- The primary focus of AKL Research & Development (AKLRD) is inflammatory diseases, particularly those related to the disruption of the immune system, such as OA.
- It identifies secondary metabolites of plant origin with proven efficacy and safety, which are then synthesised before undergoing standard pharmaceutical clinical development. This innovative approach greatly increases the chances of success, while reducing the likelihood of unexpected side effects.
- AKLRD is based at the Stevenage Bioscience Catalyst, Stevenage, Herts UK. For more information, visit us at: http://aklrd.com

About Osteoarthritis

- Osteoarthritis (OA) is a common, debilitating, degenerative disease of the joints involving the cartilage and its surrounding tissues[1].
- More than half of all people over the age of 65 have OA, and it is the third most rapidly rising condition globally, just behind diabetes and dementia[2].
- There are no drugs approved for preventing or slowing OA disease progression[3].
- Patients typically rely on pain relief, including non-steroidal anti-inflammatory drugs (NSAIDs) and steroids to manage symptoms.

---

[1] FOOD AND DRUG ADMINISTRATION: Osteoarthritis: Structural Endpoints for the Development of Drugs, Devices, and Biological Products for Treatment Guidance for Industry. 2018. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/osteoarthritis-structural-endpoints-development-drugs

[2] Global Burden of Disease Collaborative Network Global Burden of Disease Study 2019 (GBD 2019) results. http://ghdx.healthdata.org/gbd-results-tool

[3] Sokolove J, Lepus CM. Role of inflammation in the pathogenesis of osteoarthritis: latest findings and interpretations. Ther Adv Muscloskelet Dis. 2013 5(2):77-94

*Please note: APPA is an investigational medicine and not yet approved for use.