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**BONE MEDICAL ANNOUNCES SUCCESSFUL PRE CLINICAL TRIAL RESULTS  
for Oral Therapeutics to Treat Rheumatoid Arthritis**

Biopharmaceutical development company Bone Medical Limited (**ASX: BNE**) is delighted to announce the successful completion of an initial study with the Institute of Bone and Joint Research (IBJR) to advance the Company's rheumatoid arthritis product BN006.

Bone Medical's product BN006 is being developed to regulate tumour necrosis factor (TNF) levels, the primary contributing factor in rheumatoid arthritis. The current global market for injected anti-TNF products is approximately US\$3.3 billion per annum, with sales expected to grow beyond US\$5 billion by 2005.

The IBJR study successfully demonstrated that the lead candidate from Bone Medical's library of TNF regulators can reduce levels of TNF in an animal model of its release. A fact sheet on the study is attached.

Bone Medical's Chief Operating Officer John Fitzgerald said that this was a major outcome for the Company as it is a tremendous leap in product development to move from being effective on cell lines arrayed in a dish to being effective in a living animal with its numerous inter-related biological systems.

"This study used a substance called LPS to promote inflammation and TNF release in the test animals. When pre-treated with BN006 the amount of TNF released was significantly reduced without being completely eliminated, which is important to avoid side effects, and the weight loss normally seen with elevated TNF levels was also reduced" said Mr Fitzgerald. "Whilst the results from this initial study are preliminary, they are most encouraging and very exciting for the Company."

"With rising concerns over side effects of products to treat rheumatoid arthritis, and the recent withdrawal of a leading arthritis product which sold US\$1.5 billion per annum and treated tens of millions of patients worldwide, we believe BN006 is well placed to eventually help fill the increasing treatment void."

"These results will allow the Company to push ahead with further pre-clinical testing of this variant of BN006 and to investigate the potential of other members of the BN006 library of peptides," he said.

"This is another significant milestone achieved for Bone Medical and further demonstrates our ability to deliver milestones as promised."

In summary, BN006 may have significant competitive advantages:

- Unlike antibody based products which are delivered either as injections or infusions, BN006 has the potential to be taken as a tablet
- It does not completely eliminate TNF from the system, a substance essential to the body's normal immune responses; thus it is envisaged patients may not suffer from the same side effects as currently available products
- Current TNF antibody treatments are expensive and complex to manufacture, whereas BN006 variants have already been pilot manufactured using a relatively simple synthetic process.

- ENDS -

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### **About Bone Medical Limited**

Bone Medical Limited is an international biopharmaceutical development company positioned to exploit the growing market in the treatment of bone disease particularly in osteoporosis and arthritis. Bone has a portfolio of biopharmaceutical development projects for the treatment of bone disease including,

#### Osteoporosis

- oral calcitonin BN002
- oral parathyroid hormone BN003
- combination therapy

#### Arthritis

- TNF regulators BN006
- bone cell regulators BN005/BN008
- joint protection & collagen tolerance BN007

### **About the Institute of Bone and Joint Research (IBJR)**

Bone entered into an agreement with the Institute of Bone and Joint Research (IBJR) at Sydney's Royal North Shore Hospital to test the efficacy and safety characteristics of BN006 in animals.

The IBJR was established in 1999 to provide an Institute devoted to advancing the understanding of the disorders and diseases of the musculoskeletal system, their diagnosis and treatments. The Institute is lead by Professor Philip Sambrook, the Florence & Cope Professor of Rheumatology at the University of Sydney and a member of several international Scientific Editorial Boards. Professor Sambrook has also served on the Asia Pacific League of Associations for Rheumatology (APLAR), is Vice President of the Asia Pacific Osteoporosis Foundation and a member of the Osteoporosis Australia Board.



## **Impact of a BN006 Variant on LPS-induced TNF-alpha Release in Rats.**

### **AIMS**

Determine the potential of a single dose of a variant of BN006 to modulate intraperitoneal LPS-induced elevation of serum tumour necrosis factor- $\alpha$  (TNF) over a 24 hour time period in rats.

### **STUDY DESIGN & METHODS**

- Adult female rats given a single intraperitoneal injection of either vehicle or compound.
- Animals received a second intraperitoneal injection 30 minutes later of either saline or LPS.
- N = 6 animals per group.

### **RESULTS**

- BN006 variant significantly reduced LPS-induced weight loss ( $p < 0.05$ ).
- The BN006 variant markedly reduced plasma TNF compared to LPS alone ( $p < 0.05$ ).
- LPS-treated rats showed a higher number of intraperitoneal leukocytes compared to the BN006 variant. However due to the large variation in cell influx the difference between the groups was not statistically significant.
- No histomorphological evidence of toxic effects of the BN006 variant was noted.

### **CONCLUSIONS**

The experiment shows that the BN006 variant can significantly reduce some of the deleterious effects of peritoneal LPS injection. The suppression of TNF by this compound at the 1.5 hour time point was not followed by a later rebound or release from suppression.

### **NEXT STEPS**

The next development stages include further investigating the current peptide in a suitable animal model of arthritis and commencing mechanism of action studies.