

## ASX RELEASE

### **Benitec Biopharma and Medistem Technologies Successfully Combined in Preclinical Stem Cell Therapy for Rheumatoid Arthritis**

**Sydney, February 7, 2012**

Sydney, Australia February 7, 2012 Benitec Biopharma (ASX: BLT) and Medistem (Pinksheets: MEDS) announced today the successful treatment of rheumatoid arthritis in preclinical models using Benitec Biopharma's patented gene silencing technology applied to stem cell-derived immune system cells called dendritic cells. The studies, which were led by Dr. Wei-Ping Min of the University of Western Ontario, were published in *the Journal of Translational Medicine* on the 31<sup>st</sup> January 2012<sup>1</sup>. Benitec Biopharma's CEO Dr Peter French and Medistem's scientist Dr Rosalia De Nochea Champion were co-authors on the paper

"In 2003, Dr Wei-Ping Min's group, together with Medistem's CEO Dr Thomas Ichim, were the first to apply the technology of RNA Interference to the immune system, by silencing the autoimmune disease-associated gene IL-12p35<sup>2</sup>," said Dr. Peter French. "In the current paper, Dr. Min expanded these studies to a disease-relevant model, and using stem cell-derived dendritic cells was capable of developing promising preclinical data relevant to rheumatoid arthritis."

By specifically "silencing" various genes, Benitec Biopharma's ddRNAi technology is capable of modulating stem cells outside of the body, in order to endow them with new desired therapeutic activities. The first clinical study which combined stem cell therapy with Benitec Biopharma's ddRNAi technology was in a trial of AIDS-related lymphoma patients, the results of which were published in 2010 and showed the safety and feasibility of the approach<sup>3</sup>.

In the current paper, ddRNAi was used to generate dendritic cells that acted as a "tolerogenic vaccine", which specifically blocked the pathological immune response in rheumatoid arthritis, without blocking healthy immune responses. It is contemplated that by blocking pathological immunity, ddRNAi-modified stem cell-based therapies, such as those being developed by Medistem, could provide novel treatment and curative approaches to tissue that has been damaged. In the case of rheumatoid arthritis the tissue would be cartilage and synovium.

"Medistem is the first company to take a stem cell from discovery to clinical trials in the short span of four years" said Dr. Weiping Min. "This is a unique example of merging basic research, as performed in my laboratory with the translational expertise of Dr. Ichim's company."

Medistem has previously published work in the area of rheumatoid arthritis, however the company's main efforts are currently focused on heart failure, for which it has started the RECOVER-ERC 60 patient double blind, dose escalating, placebo controlled trial using its Endometrial Regenerative Cell (ERC) universal donor stem cell. The company also has a critical limb ischemia trial recently approved by the FDA.

"In our opinion the Benitec Biopharma technology platform is the only means of inducing the stable expression of gene silencing in a stem cell," said Dr Ichim, CEO of Medistem. "Given that Benitec Biopharma has pioneered ddRNAi for human therapy, and has been involved in applying it to stem cell manipulation, we are eager to continue our collaborations and finding means of leveraging the unique properties of the ERCs with the transformational technology of ddRNAi to develop novel cell therapies for a range of chronic life-threatening human diseases."

"Benitec Biopharma and Medistem are in discussions as to how to advance this work both in rheumatoid arthritis and in a range of other disease states that would lend themselves to such a novel combination therapy," Dr French added.



### **About Medistem**

About Medistem Inc. Medistem Inc. is a biotechnology company developing technologies related to adult stem cell extraction, manipulation, and use for treating inflammatory and degenerative diseases. The company's lead product, the endometrial regenerative cell (ERC), is a "universal donor" stem cell being developed for critical limb ischemia and heart failure. A publication describing the support for use of ERC for this condition may be found at <http://www.translational-medicine.com/content/pdf/1479-5876-6-45.pdf>.

Cautionary Statement: This release does not constitute an offer to sell or a solicitation of an offer to buy any of our securities. This press release may contain certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. Future events and actual results could differ materially from those set forth in, contemplated by, or underlying the forward-looking information. Factors which may cause actual results to differ from our forward-looking statements are discussed in our Form 10-K for the year ended December 31, 2007 as filed with the Securities and Exchange Commission.

### **Medistem Contact:**

Thomas Ichim  
Chief Executive Officer  
Medistem Inc.  
9255 Towne Centre Drive  
Suite 450  
San Diego  
CA 92122  
858 349 3617  
858 642 0027  
[www.medisteminc.com](http://www.medisteminc.com)  
twitter: @thomasichim

### **About Benitec Biopharma**

Benitec Biopharma Ltd is developing novel treatments for chronic and life-threatening conditions based on targeted gene-silencing activity using a transformational technology: DNA-directed RNA interference (ddRNAi) - sometimes called expressed RNAi. The technology's potential to address unmet medical needs and to cure disease results from its demonstrated ability to permanently silence genes which cause the condition. Importantly, this technology's target gene and related gene pathways will rarely have presented as a therapeutic avenue for research for the traditional small molecule agents, currently accounting for the majority of today's pharmaceutical products.

Benitec now either owns or exclusively licenses from CSIRO more than 40 granted or allowed patents in the field of RNA interference for human therapeutic applications. Patents have been granted in key territories such as the USA, the UK, Japan, Europe, Canada and Australia. In addition, Benitec has almost 50 patent applications pending for which it is the owner or exclusive licensee from CSIRO, and has further intellectual property under development as a result of its pipeline program.



Founded in 1997 and trading publicly since 2001, Benitec Biopharma is listed on the Australian Securities Exchange (ASX) under the symbol "BLT". Benitec aims to deliver a range of novel ddRNAi-based therapeutics to the clinic in partnership with the pharmaceutical industry. In addition to its focused R&D strategy in infectious diseases, cancer and chronic cancer-associated pain, Benitec Biopharma is pursuing programs with licensees.

**Benitec Biopharma Contact:**

Dr Peter French  
Chief Executive Officer  
Tel: +61 (0)412 457 595  
pfrench@benitec.com  
www.benitec.com

**References**

1. Li, R *et al.* Gene silencing of IL-12 in dendritic cells inhibits autoimmune arthritis. *Journal of Translational Medicine* 2012, 10:19 doi:10.1186/1479-5876-10-19.
2. Hill JA *et al.* Immune modulation by silencing IL-12 production in dendritic cells using small interfering RNA. *The Journal of Immunology*, 2003, 171: 691-696.
3. DiGiusto DL *et al.* RNA-based gene therapy for HIV with lentiviral vector–modified CD34+ cells in patients undergoing transplantation for AIDS-Related Lymphoma. *Science Translational Medicine*, 2(36): 36ra43.