



ASX ANNOUNCEMENT

Media Release: Erectile Dysfunction a Potential Target for Exopharm's Exosomes

14 February 2020

Melbourne, Australia:

Please find overleaf a copy of a media release regarding 'Erectile Dysfunction a Potential Target for Exopharm's Exosomes' which was released today.

By the Board - this announcement has been authorised for release by the board.

Media Release

Erectile Dysfunction a Potential Target for Exopharm's Exosomes

An Australian-developed regenerative therapy is exploring the possibility of a treatment for Erectile dysfunction (ED) through stimulating the regenerative and healing capacities of the body. Exopharm Limited (ASX: EX1) has been testing its exosomes – natural cellular particles secreted by stem cells, and purified through Exopharm's proprietary technology – to test their ability to reverse post-operative tissue damage, and thus, to restore erectile function.

ED is a common but highly problematic condition among men aged in their 50s and older; and is a condition that often brings psychological and emotional damage to compound the physical.

ED first burst out from behind the wall of shamed whisper in 1998, when Pfizer's drug Viagra (sildenafil) won US Food and Drug Administration (FDA) approval – and entered the popular consciousness in a manner rare for a drug. Viagra grew into one of the world's best-selling medications, with global sales of more than US\$2 billion (\$2.1 billion) at their peak in 2012. Along the way, it – and similar drugs – lifted the lid on the strong demand for treatments for the condition.

"Animal studies show that exosomes have great potential for reversing a variety of conditions that affect the human "health span," which is defined as the number of healthy, functional years that a person lives," says Dr Ian Dixon, founder and CEO of Exopharm.

"ED, with all of its connotations of loss of – or impact on – men's sexual function, is a perfect example of a 'health span' condition. While ED may be considered to be non-medical, ED is linked to higher suicide rates, reduced life expectancy and clinical depression,^{2,3,4}" he adds. Other examples of health span-related conditions include dry age-related macular degeneration (AMD) and osteoarthritis.

ED is common among middle-aged and older men, and increases in prevalence with age. The condition affects approximately 50% of men at 50 years old, 60% of men at 60 and 70% of men at 70.¹ But ED can also be the result of prostatectomy (partial or complete removal of the prostate gland) and rectal surgery – both of which are usually linked to cancer.

While Viagra and a variety of competitor drugs address ED, Dixon says they are usually ineffective on damaged tissue.

"Sildenafil and other phosphodiesterase type 5 inhibitor (PDE5-i) drugs are effective where there is generally healthy physiological structure of penile tissue, and where the nitric oxide signalling pathway that triggers erection remains intact.⁵"

"Damage or degeneration to one or more of the system of nerves, blood vessels and muscle cells required for erection can render PDE5-i drugs ineffective. For example, damage to the cavernous nerve during pelvic surgery (that is, for prostate or colorectal cancer) are common causes of ED, affecting up to 85% of men following radical prostatectomy. PDE5-i drugs typically have little effect in these cases.⁶"

But regenerative medicine based on stem cells has shown great potential for reversing hard-to-treat ED in animal models, Dr Dixon says. "Preliminary work has shown that, in animal models, stem cells can promote the regeneration of muscle and nerve cells in and around the penis, initiating recovery of erectile function. However, researchers have found that a major limitation of stem-cell injections for ED is that blood flow rapidly washes the cells away from the site of damage, limiting their therapeutic effects.⁵"

To address this problem, Exopharm has developed therapeutic exosome products as an alternative to stem-cell therapies. "As with essentially all stem-cell therapies, the main way in which stem cells act on the body is by releasing tiny regenerative packets of lipids, proteins and genetic material in the form of ribonucleic acid (RNA), called exosomes."

Exosomes are produced by virtually all cell types in the body, and are an essential component of cell-to-cell signalling. "Exosomes released by regenerative cells, such as stem cells, can have a powerful rejuvenating effect on the cells that take them up. They are also considered to be an inherently safer and less expensive therapy compared to injections of live cells.⁷ Increasingly, ED researchers are turning to exosomes as the most promising next generation treatment for ED, and we see our planned clinical trial as a major step in fostering this line of thinking."

How it works: Hitting a Nerve

Achieving erection is a multi-step process involving several tissue types. In a healthy male, erection is initiated by the cavernous nerve, which activates the nitric oxide (NO) signalling pathway. NO release by the cavernous nerve and by endothelium cells in the penis causes corporal smooth muscle relaxation, which increases blood penile flow leading to erection.²

Damage to the cavernous nerve – a common side effect of prostate or colorectal surgery – has downstream effects on penis physiology. The lack of nerve signalling leads to the deterioration and decline of corporal smooth muscle cells, which PDE5-i treatment fails to prevent. Smooth muscle cell death via apoptosis, and chronic inflammation can set in, leading to the gradual conversion of remaining smooth muscle cells into fibroblasts.⁸

Exosomes derived from stem cells have shown the potential to reverse this damage and rescue erectile function.^{8,9} Exosomes can protect smooth muscle cells from apoptosis, and prevent fibrosis, while the corporeal nerve regenerates following surgery, avoiding ED, researchers showed.

Researchers have recently demonstrated that exosomes can also promote repair to damaged nerves. Exosomes derived from stem cells can reduce inflammation, scarring and apoptotic cell death of nerve cells, promoting nerve regeneration and recovery following trauma.^{10,11}

Age-related ED and exosomes

Exosomes can also be a regenerative tonic to treat non-surgical causes of ED. Although the condition is increasingly prevalent with age, several age-related diseases are associated with high levels of ED. For example, the incidence of ED in men with diabetes is two- to three-fold higher than the general population.⁵ Key factors contributing to ED include the impaired blood circulation and nerve damage associated with diabetes.

Injections with exosomes can ameliorate diabetes-related ED, animal research has recently shown.¹² Exosomes promote penile neural regeneration, smooth muscle regeneration and reduced collagen deposits, enhancing erectile function, the study showed. Proangiogenic RNAs in the exosomes, promoting new blood vessel formation, is the potential mechanism behind the effect, the researchers conclude.

Conclusion

Exosomes hold much promise in the treatment of age-related disease: treating the underlying causes that leave humans susceptible to conditions from cancer to Alzheimer's disease.^{7,13}

Exosomes can reactivate the natural regenerative processes that rapidly repair damage when we are young, but which become less effective with age.^{14,15} A growing list of animal studies has already shown exosomes can directly initiate tissue regeneration to restore erectile function in models of ED, but so far no human trials with exosomes have commenced.

Exopharm, a leader in the exosome medicine field, will soon report on studies that may support a clinical trial to treat post-operative ED with exosomes.

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ABOUT EXOPHARM

Exopharm Limited (ASX:EX1) is a clinical-stage Australian regenerative medicine company developing therapeutic exosome products as alternatives to stem-cell therapies.

Exosomes are small particles naturally produced by cells, which deliver therapeutic 'cargoes' to other cells to reduce inflammation and promote regeneration. Exosomes are plentiful in our youth but decline with age. Recent research points to exosomes as a way to extend the number of healthy, functional years (extending health span).

Exosomes secreted by stem cells could be used instead of stem-cell therapy with equal or greater benefit – and without the problems of stem-cell therapies. They could be used to deliver targeted 'novel' drugs and have potential as diagnostics.

While trillions of exosomes are produced by stem cells, the real challenge is to 'purify' them as drug products. Exopharm owns a purification technology called Ligand-based Exosome Affinity Purification (LEAP). LEAP technology and associated know-how places Exopharm at the forefront of this emerging field worldwide. Exopharm is at clinical stage with pending and current trials for wound healing, dry aged-related macular degeneration and osteoporosis.

Exopharm was founded in 2013 by Dr Ian Dixon, co-founder of the ASX-listed stem-cell therapy developer Cynata Therapeutics. He was also a director of Cell Therapies, which produced adult stem cells for ASX-listed stem cell company Mesoblast. Exopharm listed on the ASX in December 2018.

FORWARD LOOKING STATEMENTS

This announcement contains forward-looking statements which incorporate an element of uncertainty or risk, such as 'intends', 'may', 'could', 'believes', 'estimates', 'targets', 'aims', 'plans' or 'expects'. These statements are based on an evaluation of current corporate estimates, economic and operating conditions, as well as assumptions regarding future events. These events are, as at the date of this announcement, expected to take place, but there cannot be any guarantee that such events will occur as anticipated or at all given that many of the events are outside of Exopharm's control or subject to the success of the Development Program. Furthermore, the Company is subject to several risks as disclosed in the Prospectus dated 6 November 2018.

INHERENT RISKS OF INVESTMENT IN BIOTECHNOLOGY COMPANIES

There are a number of inherent risks associated with the development of biopharmaceutical products to a marketable stage. The lengthy clinical trial process is designed to assess the safety and efficacy of a drug prior to commercialisation and a significant proportion of drugs fail one or both of these criteria. Other risks include uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Companies such as Exopharm are dependent on the success of their research and development projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Therefore, investment in companies specialising in drug development must be regarded as highly speculative. Exopharm strongly recommends that professional investment advice be sought prior to such investments.