



ASX ANNOUNCEMENT

INVESTOR DECK

05 March 2020

Melbourne, Australia: Regenerative medicine company Exopharm Limited (ASX:EX1) is pleased to provide an updated Investor Deck which is attached to this release.

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

Company and Media Enquiries

For further information about this announcement, please contact:

Dr Ian Dixon, MBA

Founder and Managing Director

P: +61 (0)3 9111 0026

ian.dixon@exopharm.com

Join our mailing list to receive updates:

info@exopharm.com

www.exopharm.com

P: +61 (0)3 9111 0026

Rudi Michelson

Monsoon Communications

Tel: +61 (0)3 9620 3333

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.



Introduction to Exopharm Ltd.

March 2020

IMPORTANT INFORMATION



- **Purpose of presentation:** This presentation (including this document, any related video or oral presentation, any question and answer session and any written or oral material discussed or distributed in relation to this presentation) has been prepared by Exopharm Limited (ACN 163 765 991) (**Exopharm** or **Company**). This presentation is intended for sophisticated or professional investors (as those terms are defined in the *Corporations Act 2001* (Cth)), and their professional investment advisors and has been prepared for the sole purpose of providing general high-level information on Exopharm and its operations.
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Overview

- Exopharm is an Australian clinical stage biotechnology company with a rapidly-developing technology platform for turning exosomes into medicines
- 24 staff (currently) based in Melbourne, Victoria
- Publicly-traded on the ASX (ASX:EX1) (listed Dec 2018)

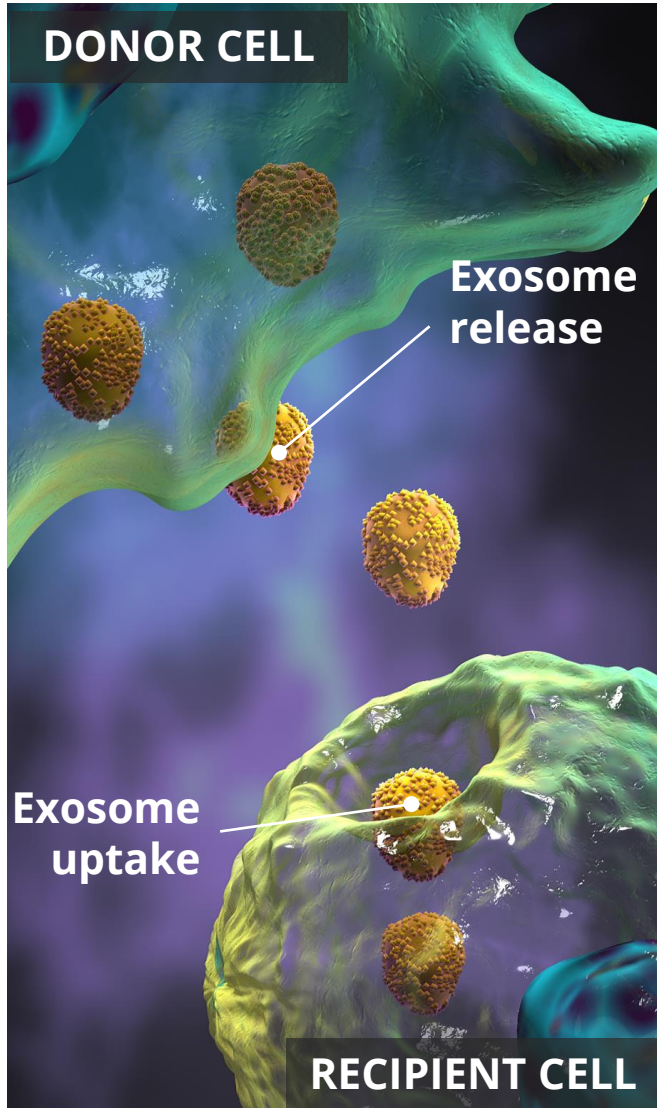
Financials (as of 01/01/2020)

- 95.47 million shares outstanding with a market capitalisation of \$24.8 million
- Cash balance of \$5.88 million
- Quarterly burn rate (per Dec 4C) of \$1.85 million

Priorities

- Leverage our unique access to exosomes to partner with established biopharmaceutical and cell therapy companies
- Advance early products through clinical trials
- Accelerate the development of our exosome generation, manufacturing and characterization technologies
- Add institutional investors/strategic partners to the share register

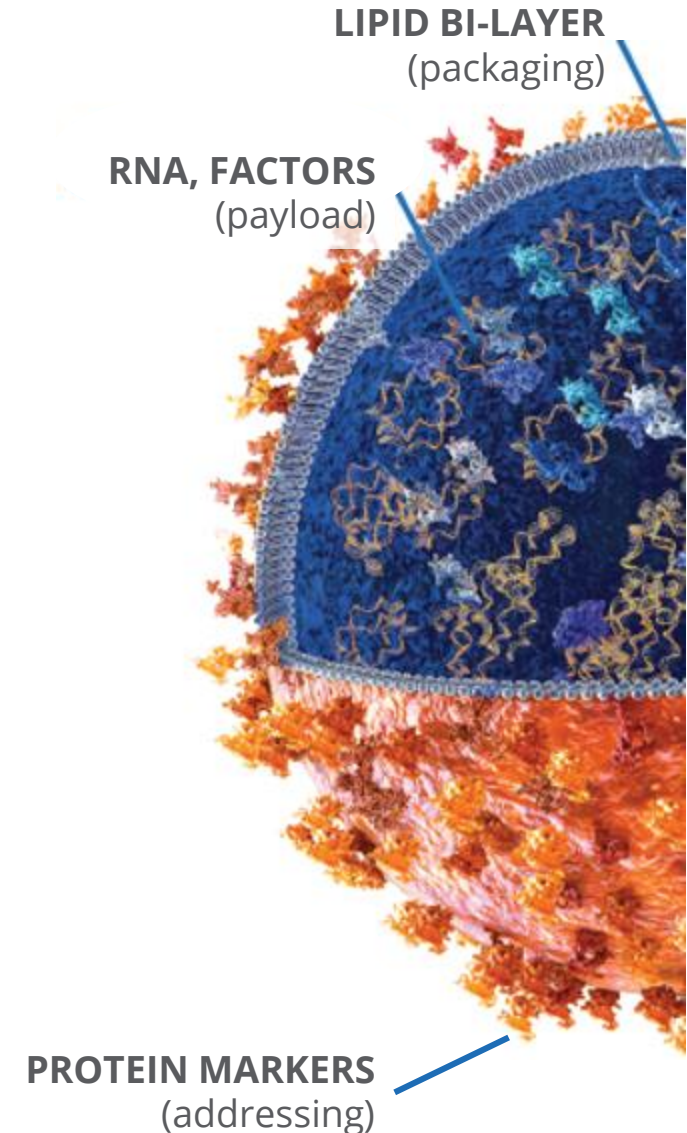
EVs: the Body's Delivery Packets



Extra-cellular Vesicles (or EVs, also referred to as exosomes) are the key intracellular delivery mechanism

EV's consist of three parts:

1. **Address:** External protein markers that provide identifying information about the donor and recipient cells
2. **Package:** Lipid bi-layer that holds the EV in tact
3. **Payload:** The contents of the EV, comprised of RNA fragments (often miRNA), growth factors, and free proteins



EV Therapies May Replace Cell Therapies



EVs from stem cells deliver their payloads to existing cells, reducing inflammation and promoting regeneration and healing by **multiple mechanisms**

Stem cells appear to work by orchestrating and guiding existing cells to heal and grow, rather than by replacing them

“In the cases where cells and their respective exosomes were studied in parallel, exosome treatment has demonstrated a similar or even superior therapeutic capacity to MSC treatment”

doi: 10.3389/fcvm2017.00063 2017

“In comparison to cell-based therapies, this cell-free regenerative strategy offers a lower risk and potentially higher scalability”

doi: 10.3390/cells7080110 2018



news feature

Exosome redux

Adult stem cell companies are pivoting their businesses to commercialize exosomes as therapeutics.

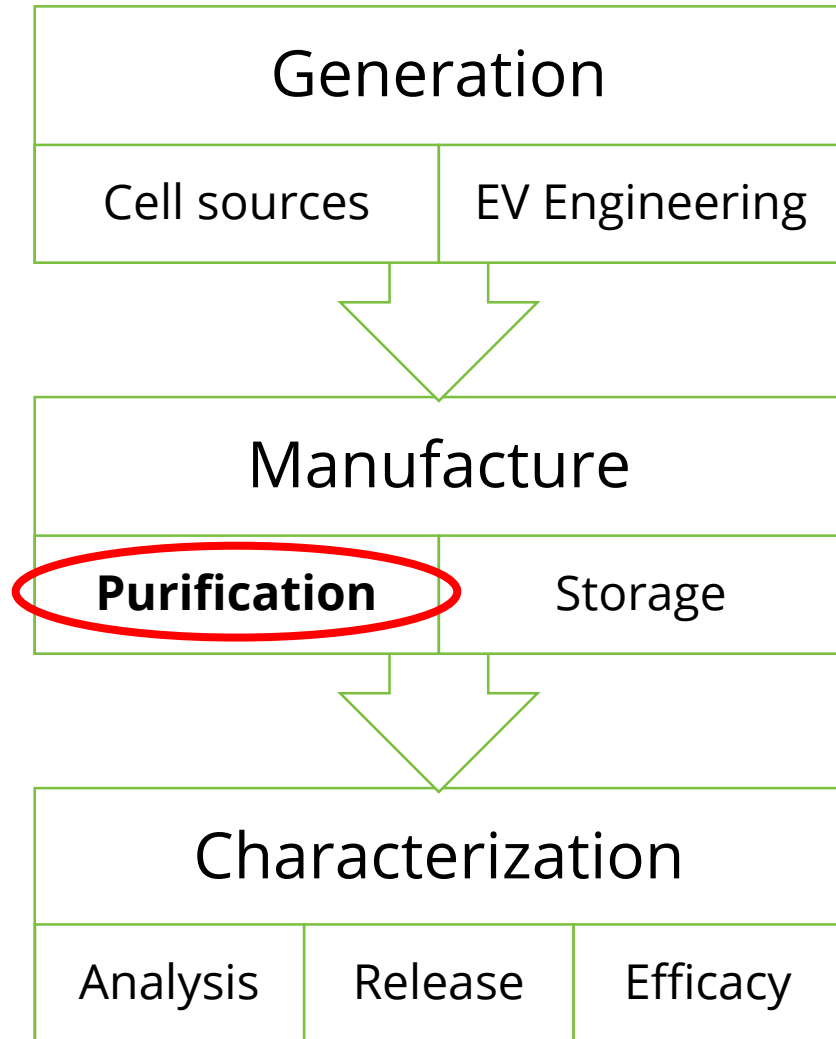
NATURE BIOTECHNOLOGY | VOL 37 | DECEMBER 2019 | 1395-1400 | www.nature.com/naturebiotechnology

EVs are Capturing the Attention of the Therapies Markets – Recent Developments



Established Company	EV Partner	Interaction
Jazz Pharmaceuticals (NASDAQ: JAZZ) US\$8.6 billion	Codiak Biosciences Private US	Access to Codiak's exosome platform for cancer through therapies Undisclosed upfront with milestones exceeding \$1 billion
Roche (SWX: ROG) CHF 271 billion	Puretech Health PLC (LON: PRTC) GBP 860 million	Milk-derived exosome technology US\$36 million upfront with milestones exceeding \$1 billion
Bio-Techne Corp (NASDAQ: TECH) US\$8.3 billion	Exosome Diagnostics, Inc. Acquired	Acquisition of diagnostic technology US\$250 million upfront with additional US\$325 million in milestones

Challenge: The Bottleneck Problem



Trillions of exosomes are naturally produced in the human body, yet the purification of these natural nano-scale particles as a proper drug product is a major challenge.

- “Despite these advances, a major **bottleneck** of MSC (Mesenchymal stem cell) derived EV (MSC-EV) - based applications in clinics **is the inefficient production and purification** of clinical-grade EVs”*
- “Currently, there is **no state-of-the-art technology to isolate EVs**, for either therapeutic application or basic research.”**

References

* Liu *et al* Stem Cells, 2019, doi.org/10.1002/stem.2996

** Lener *et al* Journal of Extracellular Vesicles, 2015, 4: 30087

Ligand-based Exosome Affinity Purification

Exopharm invented and owns all LEAP™ IP, patent applications and associated know-how

The LEAP technology is:

- Gentle and selective;
- Based on inexpensive materials;
- Highly scalable;
- Easily combinable with other manufacturing operations

LEAP Provides Exopharm a Substantial Competitive Advantage by:

1. Providing early access to EVs, allowing Exopharm to build **additional know-how and IP** in the areas of EV generation and characterization
2. Supplying sufficient clinical grade material for **multiple pre-clinical studies**
3. Positioning Exopharm as an ideal **partner for incumbents interested in investing** in EV therapies

Leading into Clinical Trials

Exosome redux

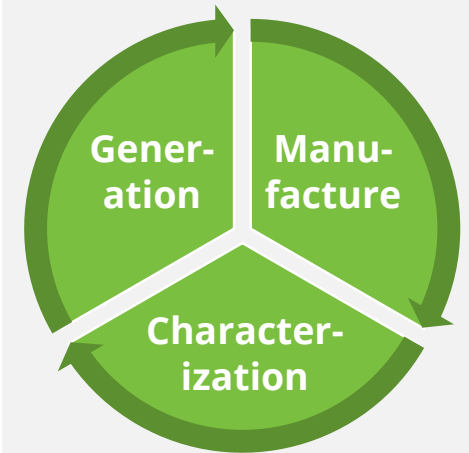
Adult stem cell companies are pivoting their businesses to commercialize exosomes as therapeutics.

news feature

DECEMBER 2019

NATURE BIOTECHNOLOGY | VOL 37 | DECEMBER 2019 | 1395-1400 | www.nature.com/naturebiotechnology

Companies Reviewed: 14	Planning Clinical Trials: 5	Clinical Trials Running: 1
Aegle Therapeutics Alxerion Biotech Anjarium Biosciences Aruna Biomedical Capricor Therapeutics Codiak Biosciences Evox Therapeutics ExoCoBio Exopharm Ltd NeurExo Sciences PureTech Health ReNeuron Tavec Pharma Versatope Therapeutics	Aegle Therapeutics Codiak Biosciences Capricor Therapeutics Evox Therapeutics Exopharm Ltd	Exopharm Ltd (first dosing Jan 2020)



LEAP has set off a virtuous circle of innovation that is accelerating Exopharm toward clinical applications of EVs



Age-related EV Applications

Extracellular vesicles and aging

Paul D. Robbins

Department of Molecular Medicine and the Center on Aging, the Scripps Research Institute, Jupiter, Florida, USA
doi: 10.21037/sci.2017.12.03

“These chronic diseases account for 75% of our healthcare costs, amounting to approximately \$3 trillion in costs last year alone.” “Given the diverse roles of blood-borne EVs in modulating not only the immune response, but also angiogenesis and tissue regeneration, they likely play a key role in modulating the aging process.”



REGENERATIVE MEDICINE

Highly purified human extracellular vesicles produced by stem cells alleviate aging cellular phenotypes of senescent human cells

Johns Hopkins University
School of Medicine, Baltimore,
Maryland;

2019

All major tissue areas ...

Neurons, axons, dental, liver, skin, muscle, blood vessels (vascular disease), heart (cardiac), pancreas, kidney, cartilage (joints), skeleton (bones) and other degenerative conditions

Exosomal regenerative potential in various tissues and organs

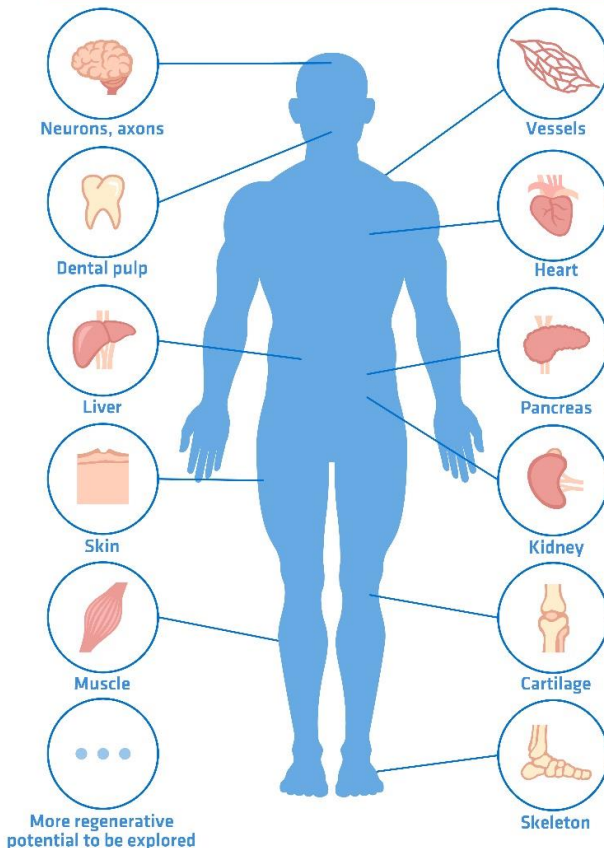
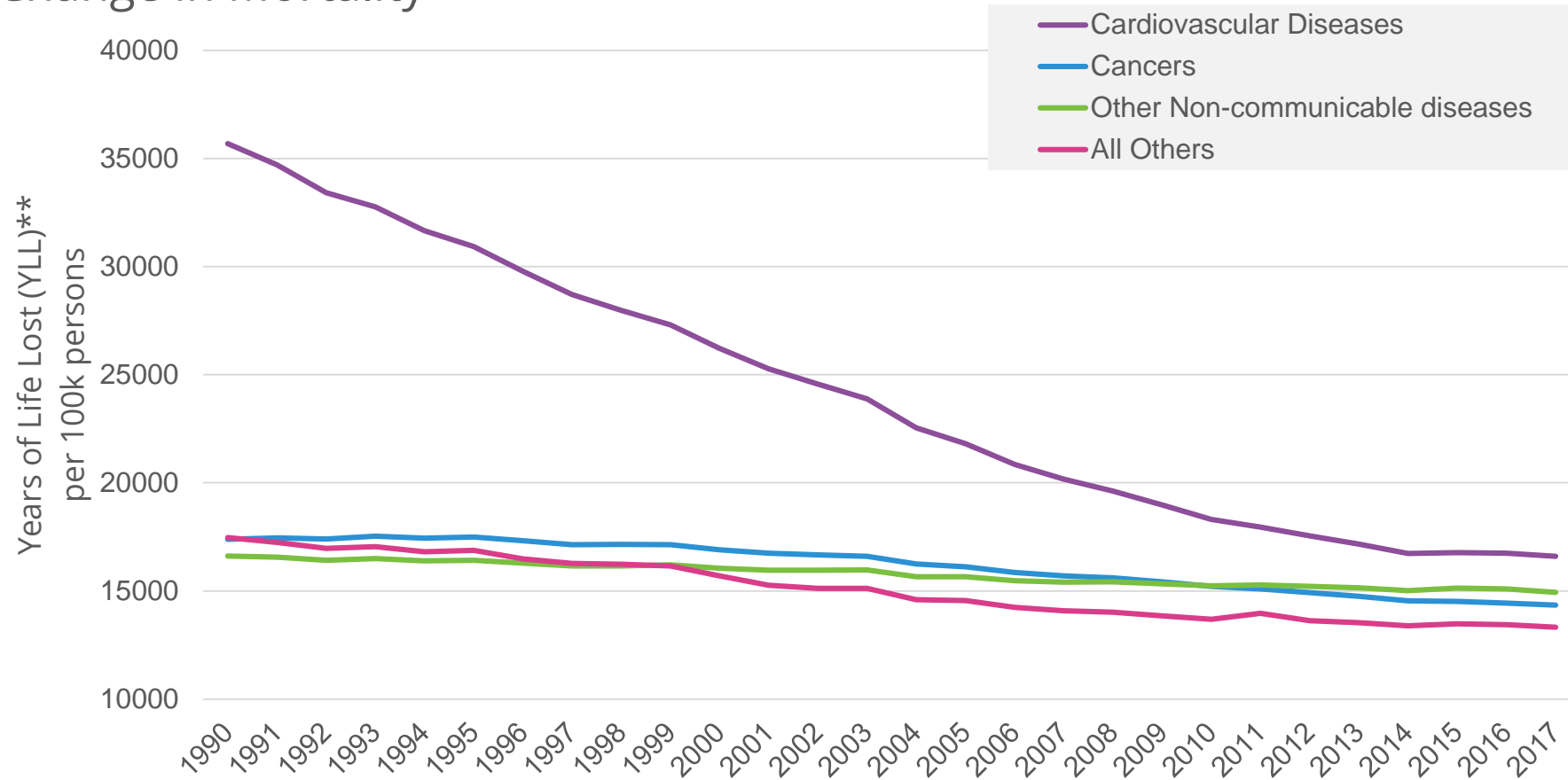


Figure adapted from Jing et al 2018
doi.org/10.1016/j.trsl.2018.01.005

Reducing Mortality: Healthcare's Success

Change in Mortality*



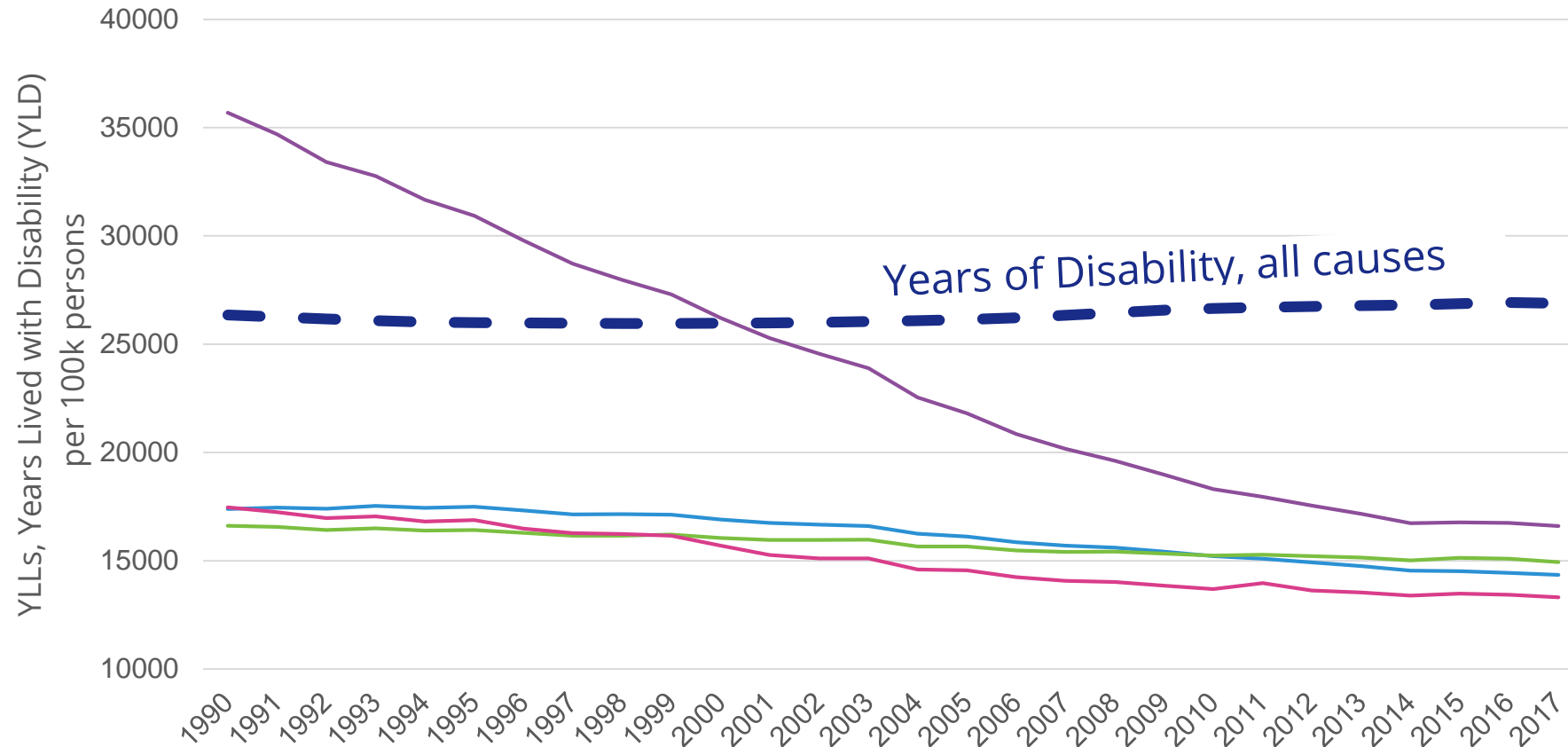
* Figures apply to 70+ year old's from High SDI countries

** YLL (Years of Life Lost) is a WHO-defined measure to calculate the total number of years a disease shortened the lives of a population.

Source: 2019 Institute for Health Metrics Evaluation. Used with permission. All rights reserved.

Reducing Disability: Healthcare's Failure

Changes in Mortality, Disability*



Today, we are far more likely to experience years of disability than lose years to **cardiovascular disease and cancer combined**

Disability is rising

Disability improvement is our greatest unmet need

* For 70+ year old's from High SDI countries

** YLD (Years Lived with Disability) is a WHO-defined measure to calculate the total number of years a disease creates disability weighted by the degree of disablement) in the lives of a population.

Source: 2019 Institute for Health Metrics Evaluation. Used with permission. All rights reserved.

Sources of Disability*: The Hot Spots

	Sources of Disability	YLD
1	Musculoskeletal disorders	5,045
2	Sense organ diseases	3,535
3	Cardiovascular diseases	3,249
4	Neurological disorders	2,326
5	Diabetes and kidney diseases	2,316
6	Unintentional injuries	2,243
7	Chronic respiratory diseases	2,089
8	Mental disorders	1,526
9	Other non-communicable diseases	1,241
10	Skin and subcutaneous diseases	810
	All other	1,539

Hearing	2,562
Low back pain	2,476
Neck pain	996
Osteoarthritis	886
Vision	828
All other	832

* Excluding cancer, for 70+ year old's from High SDI countries

Source: 2019 Institute for Health Metrics Evaluation. Used with permission. All rights reserved.

Sources of Disability: Can EV's Help?

Disability Hot Spot	YLD
Hearing	2,562
Low back pain	2,476
Neck pain	996
Osteoarthritis	886
Vision	828

Lu et al. *Stem Cell Research & Therapy* (2017) 8:108
DOI 10.1186/s13287-017-0563-9

Stem Cell Research & Therapy

RESEARCH

Open Access



Exosomes as potential alternatives to stem cell therapy for intervertebral disc degeneration: in-vitro study on exosomes in interaction of nucleus pulposus cells and bone marrow mesenchymal stem cells

Kang Lu¹, Hai-yin Li¹, Kuang Yang¹, Jun-long Wu¹, Xiao-wei Cai², Yue Zhou¹ and Chang-qing Li^{1*}

Wang et al. *Stem Cell Research & Therapy* (2017) 8:189
DOI 10.1186/s13287-017-0632-0

Stem Cell Research & Therapy

RESEARCH

Open Access



Exosomes from embryonic mesenchymal stem cells alleviate osteoarthritis through balancing synthesis and degradation of cartilage extracellular matrix

Yafei Wang^{1,2†}, Dongsheng Yu^{1,2†}, Zhiming Liu^{1,2}, Fang Zhou^{1,2}, Jun Dai^{1,2}, Bingbing Wu^{1,2}, Jing Zhou^{1,2,3}, Boon Chin Heng⁴, Xiao Hui Zou⁵, Hongwei Ouyang^{1,2,6,7} and Hua Liu^{1,2,8*}

frontiers
in Cellular Neuroscience

ORIGINAL RESEARCH
published: 29 November 2019
doi: 10.3389/fncel.2019.00530

Extracellular Vesicles From Auditory Cells as Nanocarriers for Anti-inflammatory Drugs and Pro-resolving Mediators

Gilda M. Kalinec¹, Lucy Gao², Whitaker Cohn³, Julian P. Whitelegge², Kym F. Faul¹ and Federico Kalinec^{1*}

¹Department of Head and Neck Surgery, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, United States, ²Pasarrow Mass Spectrometry Laboratory, Department of Psychiatry and Biobehavioral Sciences, Jane and Terry Semel Institute for Neuroscience and Human Behavior, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, United States

Journal of Neurotrauma, Vol. 34, No. 24 | Original Articles

Systemic Administration of Exosomes Released from Mesenchymal Stromal Cells Attenuates Apoptosis, Inflammation, and Promotes Angiogenesis after Spinal Cord Injury in Rats

Jiang-Hu Huang, Xiao-Ming Yin, Yang Xu, Chun-Cai Xu, Xi Lin, Fu-Biao Ye, Yong Cao and Fei-Yue Lin

Published Online: 15 Dec 2017 | <https://doi.org/10.1089/neu.2017.5063>

Research Paper

PAIN

PAIN 160 (2019) 210–223

© 2018 International Association for the Study of Pain

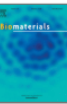
Mesenchymal stem cell exosomes as a cell-free therapy for nerve injury-induced pain in rats

Sheng-Jie Shiu^a, Ruey-Hong Rau^b, Han-Shiang Shiu^c, Yi-Wei Hung^a, Zhi-Xiang Li^d, Kuender D. Yang^{d,e,f}, Jen-Kun Cheng^{a,h,*}



Biomaterials

Volume 156, February 2018, Pages 16–27



MSC exosomes mediate cartilage repair by enhancing proliferation, attenuating apoptosis and modulating immune reactivity

Shipin Zhang^a, Shang Jiunn Chuah^a, Ruenn Chai Lai^b, James Hoi Po Hui^{c,d}, Sai Kiang Lim^{b,e}, Wei Seong Toh^{a,d}

Therapeutic Potential of Mesenchymal Stem Cell-Derived Exosomes in the Treatment of Eye Diseases

C. Randall Harrell, Bojana Simovic Markovic, Crissy Fellabaum, Aleksandar Arsenijevic, Valentin Djonov, Nebojsa Arsenijevic, and Vladislav Volarevic

Substantial evidence from animal studies shows that EV's protect against damage and promote the repair of tissues across the body

PLEXOVAL I Update (autologous Plexaris)



ASX ANNOUNCEMENT & MEDIA RELEASE

PLEXOVAL EXOSOME WOUND HEALING HUMAN STUDY STARTS

- A world-first study using cell free exosome product manufactured using Exopharm's LEAP Technology
- Study sites at the Royal Melbourne Hospital and Australian Red Cross Blood Service
- Results by mid 2020

26 August 2019

Melbourne, Australia: Regenerative medicine company Exopharm Limited (ASX:EX1) announces the start of the PLEXOVAL Phase 1 study, the first human clinical trial using exosomes for wound healing.

This is an important step forward as a clinical stage company and world leader in exosome therapeutics for regenerative medicine.

All regulatory and site approvals have been obtained and sites are currently preparing for the initiation of recruitment and dosing.

20 participant Phase I study to evaluate the safety, tolerability and biological activity of Plexaris™ in a wound healing context

- Cohort 1: 15 participants - 42 day wound healing evaluation
- Cohort 2: 5 participants - 30 day biological activity assessment

Initial dosing began in January

Planning underway for Plexoval II – Phase I study to evaluate Allogeneic Plexaris

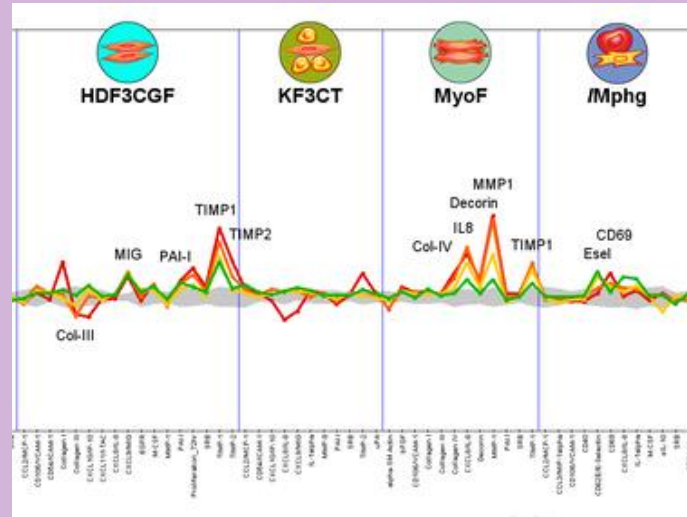


Cevaris Pre-clinical Update

**BioMAP®
(Eurofins)**

**Diversity PLUS
Data Report**

- Cevaris is neither cytotoxic nor antiproliferative
- Changes in cell biomarkers positive for tissue remodelling, inflammation, immunomodulation



**Mobility: Active
studies in animals**

- Joint
- Muscle
- Nerve

**Sensory: Active
studies in animals**

- Eye
- Hearing



Cevaris products are isolated from mesenchymal stromal cells, previously referred to as "Exomere"

ASX ANNOUNCEMENT & MEDIA RELEASE

Independent Plexaris and Cevaris testing shows positive and unique results

HIGHLIGHTS

- Exopharm is a world leader in the manufacture of exosome products
- Exosomes have the potential to replace stem cells as medicines
- BioMAP external testing validates possible safety and mechanism of action
- Positive BioMAP testing provides a basis for further testing and future potential clinical trials

12 February 2020

Melbourne, Australia:

BioMAP testing of Exopharm's exosome platform has validated safety and mechanism of action (MOA) and found that they have different and distinct activities compared to 4,500 other drugs. This confirms this therapeutic approach is a distinct and potentially new class of medicine.

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.

ASX ANNOUNCEMENT & MEDIA RELEASE

Cevaris testing shows positive results in models of erectile dysfunction

HIGHLIGHTS

- Exopharm is a world leader in the manufacture of exosome products. Its two core exosome products are Plexaris and Cevaris
- Exosomes have the potential to treat a range of medical conditions
- Independent testing by PELVIPHARM shows potency of Cevaris in models of erectile dysfunction and provides a basis for further testing and future potential clinical trials in post-operative erectile dysfunction

19 February 2020

Melbourne, Australia:

Independent testing of Exopharm's exosome Cevaris product in ex vivo models of erectile dysfunction (ED) has demonstrated that a Cevaris treatment provided statistically significant improvement in muscle contraction and release.

ASX ANNOUNCEMENT & MEDIA RELEASE

Cevaris testing shows positive results in bladder control model

HIGHLIGHTS

- Positive PELVIPHARM testing provides a basis for further testing and future potential clinical trials in urinary bladder control
- Treatment with Exopharm's Cevaris could improve bladder control by improving contractile performance and strength







20 February 2020

Melbourne, Australia: Independent testing of Exopharm Limited's (ASX:EX1) Cevaris has shown that the exosome product could be a potential treatment for bladder control dysfunction, which affects more than five million Australians.

We believe that

1. EV treatments are an entirely new therapeutic modality that will reshape biomedicine in the years to come
2. EV medicines will help people worldwide overcome disabilities that accumulate later in life
3. Exopharm will be a world leader in the:
 - Development and commercialization of technologies for generating, manufacturing, and characterizing EV's
 - Clinical advancement of EV-based medicines

Development Summary Roadmap

	2019	2020	2021	2022
Testing (in vitro, ex vivo)	Various	<ul style="list-style-type: none"> • ED • Bladder control • Cancer • Autoimmune 	<ul style="list-style-type: none"> • Autosomal conditions (orphan indications) • Transplant rejection 	
Non-clinical (animal testing)	Wound healing 	<ul style="list-style-type: none"> • Erectile Dysfunction (ED) • Bladder control • Ocular (eye)  <ul style="list-style-type: none"> • Aging • OA 		
Phase I	PLEXOVAL study with autologous Plexaris	Allogeneic Plexaris safety study 	Cevaris safety studies <ul style="list-style-type: none"> • Dry Age-related Macular Degeneration (AMD) • ED  	
Phase IIa				<ul style="list-style-type: none"> • Dry AMD • ED 
Phase IIb				

Objective: One wholly-owned high value Phase IIb asset

Partnering is a Near-term Opportunity



Exopharm is a world leader in the exosome field

- Manufacturing: IP-protected, proprietary isolation and characterization
- Clinical leadership: First in human clinical trial for exosome-based medicine

Exopharm's technology and products are multi-functional

- Capitalise on LEAP and other eVICI Technologies
- Multiple partnership deals are possible, because applications and indications are very diverse

There is strong interest in partnering in the exosome field internationally, with high-value deals already being done

Early deals with low pre-deal investment will generate non-dilutive funding for Exopharm's clinical program

One Phase IIb clinical asset

Leverage EV platform to drive one single, high value Phase IIb asset owned completely by EX1 (e.g. Opthea OPT-302)

- Low investment early work in Mobility and Sensory regenerative areas
- Limited number of de-risked Phase IIa human studies that will identify best Phase IIb asset

Partnering: all other products

Leverage EV platform to become cash positive and minimize dilution during clinical development

- Early partnerships in non-core therapeutic areas (cancer, neurology, cardiac, etc) and technologies (diagnostics)
- Mid-stage partnerships to advance other Phase I and IIa assets

Strategy:

- Produce a high-value, wholly owned clinical asset
- Generate early revenue and move to cash flow positive
- Create multiple pathways to value
- Minimise equity dilution

Leadership: Global corporate experience



Ivan Jasenko
Regulatory Affairs



Dr Angus Tester
Clinical Trials



Michael Whitmore
Manufacturing



Dr Patrick James
Analytics



Dr Andrew Coley
Research



Dr Lieven Huang
Business
Development



Our Senior Team



Dr Ian Dixon
Founder
Managing Director

- Over 20 years experience in bringing cell-derived therapies to patients
- Founded Cynata Inc (now ASX:CYP) – a clinical-stage, world-wide leader in iPSC-derived cell therapy technology
- Co-inventor and original investor in Exopharm's LEAP technology

Dr Gregor Lichtfuss
Chief Operating Officer



- Co-inventor of the LEAP technology, a patent-pending advance in exosome isolation
- Leads R&D, manufacturing, and clinical trials
- Previous experience launching biotechnology companies

Dr Chris Baldwin
Chief Commercial Officer



- Twenty years experience in pharma, blood and plasma products, and medical devices
- Leads strategy, partnerships and marketing
- Strategy, sales and marketing experience across Asia Pacific, North America, and Europe

- EX1's early IP for exosome isolation (*LEAP Technology*) is being leveraged to create a broad range of exosome manufacturing know-how and places EX1 at the front of the field worldwide
- EX1's Plexaris exosome product is the first proprietary exosome-based regenerative medicine to reach human clinical trials worldwide
- EX1's team (25 people at present) has the broad manufacturing, analytic, IP, scientific and commercial experience to generate shareholder value
- EX1 is aiming to do multiple partnership deals with biopharmaceutical companies and build revenue and cashflow

Thank you

Exopharm Ltd (ASX-EX1)

Dr Chris Baldwin

Chief Commercial Officer
chris.baldwin@exopharm.com
+61 450 290 280

P: (+61) 3 9111 0026
Level 17, 31 Queen Street,
Melbourne Victoria 3000

www.exopharm.com

Refreshing Medicine, Today