

## 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.

Exopharm was recently granted Human Research Ethics Committee approval to commence the PLEXOVAL wound healing study with its Plexaris™ (exosomes from platelets) product. The trial is approved under the Australian Clinical Trials Notification (CTN) scheme.

This first-in-human clinical trial will investigate autologous (from the same person) Plexaris (exosomes from blood platelets) administered once by local injection. The study will track participants over 42 days from dosing. Cohort 1 involves up to 15 participants and Cohort 2 involves up to 5 participants.

The main readouts of the PLEXOVAL study will be safety, wound closure and scarring.

The PLEXOVAL study involves two sites; the Royal Melbourne Hospital and the Australian Red Cross Blood Service.

The principal investigator of the study is Associate Professor Johannes Kern MD, PhD, FEBDV, FACD of the Dermatology Department, Royal Melbourne Hospital. The principal investigator is a practicing dermatologist and dermatopathologist and a Fellow of Australasian College of Dermatologists.

The study is being facilitated by Accelagen, a Melbourne based Contract Research Organisation (CRO).

Dr Ian Dixon, Exopharm's Founder CEO and Managing Director said "Wounds and poor wound healing are medical problems affecting thousands of Australians every year. As we age our ability to heal declines and the prevalence of chronic wounds increases. Exosomes from platelets have

been shown in animal studies to improve wound closure and reduce scarring. This human study is looking at whether our Plexaris product might become a useful improved treatment option.”

“This PLEXOVAL study positions Exopharm as a leader in the cell-free exosome field of regenerative medicine world-wide. Our LEAP Technology allows us to manufacture an exosome product that has the properties a pharmaceutical company would look for. The main purpose of this small study is to demonstrate safety of the product and potentially show signs of efficacy.”

Exopharm is manufacturing the Plexaris product at its Fitzroy manufacturing facility.

### **PLEXOVAL study outline:**

The PLEXOVAL study is a first-in-human prospective open-label, single dose study to evaluate the safety, tolerability and biological activity of platelet-derived extracellular vesicles for the augmentation of wound healing.

The PLEXOVAL study is a Phase 1 study and is primarily assessing the safety of Plexaris. Secondary outcomes will investigate signals of benefits in wound closure, wound strength, wound histology and scar formation.

PLEXOVAL stands for **P**rospective open-**L**abel, single dose proof of concept study to **E**valuate the safety, tolerability and biological activity of Platelet-derived **EX**tracellular Vesicles, on the augmentation of **wO**und healing rate and effect on scar formation following skin punch biopsy in healthy Volunteer **AduL**ts.

Exopharm has contracted the Australian Red Cross Blood Service to collect platelets from the study participants at a regular Donor Centre. The platelets will be tested at the Blood Service's Melbourne Processing centre and transferred to the Exopharm Manufacturing site. Exopharm will process them using the LEAP Technology in a sterile biologics manufacturing facility to produce each patient's individual (autologous) Plexaris product.

Participants will then visit the Royal Melbourne Hospital and have Plexaris administered by injection under oversight by the principal investigator Associate Professor Johannes Kern. Following treatment, participants will be assessed over a 42-day period and study results will be entered into a data management system for later analysis.

A study report will be provided to Exopharm, expected sometime before mid CY '20.

***Further details of the PLEXOVAL study can be found in Appendix A.***

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## **ABOUT EXOPHARM**

Exopharm Limited (“Exopharm” or the “Company”) (ASX:EX1) is a clinical stage Australian regenerative medicine biopharmaceutical company seeking to develop and commercialise exosomes as therapeutic agents – initially a product called Plexaris™ and later a product called Exomeres™.

These products are exosomes that are derived from human platelets in relation to Plexaris, and adult stem cells in relation to Exomeres, and purified using the LEAP Technology and referred to as biologic products.

As its primary focus, Exopharm aims to be a leader in the field of human therapeutics using exosomes as regenerative medicine products for health span related conditions.

The Development Program: The Company’s main objectives for the next 12 months are to complete the following stages of its Development Program:

1. manufacturing - make and supply clinical grade autologous Plexaris product and development of the Exomere manufacturing process;
2. clinical use - initial small-scale human clinical studies of autologous Plexaris in wound healing;
3. supporting research and development activities - conducting research activities to support the ongoing Development Program and the development of related intellectual property; and
4. to also investigate other LEAP Technology Opportunities.

## **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.

## **Appendix A: Details of the PLEXOVAL clinical trial**

<b>Topic</b>	<b>Description</b>
Name, unique identifier of the trial and general description:	<p>PLEXOVAL is a first-in-human (FIH) study primarily looking at the safety of autologous Plexaris as a local injection and also looking at secondary signals of wound closure, wound strength, wound histology and scar formation.</p> <p><b>PLEXOVAL:</b> PLEXOVAL stands for <b>P</b>rospective open-<b>L</b>abel, single dose proof of concept study to <b>E</b>valuate the safety, tolerability and biological activity of Platelet-derived <b>E</b>Xtracellular Vesicles, on the augmentation of <b>w</b>Ound healing rate and effect on scar formation following skin punch biopsy in healthy Volunteer <b>A</b>du<b>L</b>ts.</p> <p>Exopharm is the sponsor of the PLEXOVAL study. The study is expected to involve up to 20 participants – up to 15 in cohort 1 and up to 5 in cohort 2.</p> <p>Autologous Plexaris will be sourced from platelets collected from the participant at an apheresis unit in Melbourne. Platelets from the donor will be processed at Exopharm’s manufacturing facility in Melbourne. Participants will have autologous Plexaris administered by injection under the oversight of the Principal Investigator.</p>
Study Phase/Type:	Phase 1
Primary endpoint(s):	- Safety and absence of adverse reactions
Secondary endpoint(s):	- wound closure; - wound strength; - wound histology; and - scarring.
Blinding status:	Open label
Product status:	<p>Experimental product.</p> <p>Manufacture: The product is to be purified from platelets by Exopharm’s in-house manufacturing team. Exopharm uses a licensed TGA approved sterile facility for manufacture of clinical grade product for this study.</p> <p>The manufacturing system and the product is not cGMP at this stage (and does not need to be).</p>
Treatment method, route, frequency, dose levels:	<p>Cohort 1: Dosage level: Single dose (more details not disclosed) Frequency: administered once Route: intradermal injection Test follow-up duration: 42 days post injection</p> <p>Cohort 2: Dosage level: Single dose (more details not disclosed) Frequency: administered once Route: intradermal injection</p>

	Test follow-up duration: 42 days post injection
Number of trial subjects:	Cohort 1 involves up to 15 participants Cohort 2 involves up to 5 participants.
Description of Control Group:	Each participant will receive two punch biopsies – one on each shoulder. Only one wound site treated with administration of Plexaris, so the other wound site acts as a control.
Subject selection criteria:	Healthy paid volunteers agreed between 18-35
Principal Investigator:	A/Prof Johannes Kern Dermatology Department Royal Melbourne Hospital
Contract Research Organisation:	Accelagen
Trial locations: (number of trial sites/locations and country)	The clinical trial includes two trial sites, being <ul style="list-style-type: none"> <li>- The Royal Melbourne Hospital (RMH); and</li> <li>- The Australian Red Cross Blood Service in Melbourne.</li> </ul>
Trial Partners:	None
Expected duration/timing:	The trial is expected to run through the second half of CY 2019 (subject to successful patient recruitment), with study results expected in the first half CY 2020.
Additional information:	Exopharm is sponsoring the PLEXOVAL study which is being managed by Accelagen, a Contract Research Organisation (CRO) on behalf of Exopharm.
Trial standard: The standard to which the trial will be conducted, e.g. good clinical practice (GCP):	In conformance with the hospital's standards and the requirements of the hospital's HREC.
The expected cost of the trial:	The expected total study cost circa \$1,000,000 (excluding manufacture costs) and ongoing/forecast expenditure will be disclosed in the Appendix 4C.
The source of funding:	Internal cash reserves
Definitions	cGMP: current good manufacturing practice HREC: Human Research Ethics Committee FIH: first-in-human CTN: Australian Clinical Trials Notification