ASX ANNOUNCEMENT

Exopharm Shareholder Update

- PLEXOVAL II safety study, first-in-human, off-the-shelf Plexaris™ dosing is complete
- Exosome TX conference demonstrating LEAP™ technology and its economic benefits has led to multiple partnership leads
- Fortrexo CoV is progressing rapidly

22 December 2020, Melbourne, Australia: Exopharm Limited (ASX:EX1) is a clinical stage Australian company using exosomes (extracellular vesicles (EVs)) from cells to generate a new class of cell-free medicines. Exopharm is a leader in the manufacture and experimental clinical use of EV medicines.

Building tangible value

Exopharm is based on a big idea – that exosomes or extracellular vesicles (EVs for short) are in the process of becoming the *next big thing* in medicine.

Cashed-up pharmaceutical companies also see the value of EV medicines even before products have been fully defined, much less tested. Lilly (previously Eli Lilly), Takeda, Sarepta Therapeutics and Jazz Pharma have each done preclinical EV deals with upfront cash payments of around A$80m each since January 2019. The deals are spread between just two specialist EV companies: Codiak Biosciences Inc. (formed in 2015) and unlisted EVOX Therapeutics Ltd (formed in 2016).

Exopharm (ASX: EX1) is one of only two listed pure-play EV medicine companies worldwide, the other being Codiak (NASDAQ: CDAK), which has a market capitalisation of around A$400m.

Exopharm's initial focus was regenerative medicine using naïve EVs (NEVs) from stem cells purified with its LEAP manufacturing technology, while Codiak and EVOX have been the leaders in the design of engineered EV (EEVs) field until recently.

All that changed earlier in 2020 when Exopharm announced it had in-licensed two important EEV technologies from US researchers: LOAD and EVPS. With LOAD and EVPS, Exopharm has closed the gap with Codiak and EVOX in the EEV field.

The LOAD technology gives Exopharm a proprietary EEV product applicable to many uses, which facilitates multiple potential deals. The EVPS technology allows Exopharm to target its EEVs to selected cell types and organs (eg. brain). Together, LEAP, LOAD and EVPS enable Exopharm to make many versions of EEV products and potentially enter into multiple partnership transactions just as Codiak and EVOX have already done.

EEVs are an emerging form of precision medicine with huge promise and application in key areas such as neurological, cardiac and cancer. You can think about EEVs as stealth drones that are directed to certain cell types and carrying a powerful cargo. As natural EVs are designed by nature for exactly this role, EEVs avoid the limitations of other delivery vehicles such as liposomes, which the body ultimately detects and rejects, thereby eliminating their ability to deliver cargo.

One example of the Exopharm EEV products is Fortrexo CoV, presently preparing for testing as a way to halt SARS-COV2 infections at their outset.

Using our technologies to make many different products, our aim is to deliver a robust and ongoing revenue stream from multiple deals across manufacturing technologies. While our emphasis has swung to EEVs, we continue progressing our proprietary Plexaris and Cevaris NEV products not only for their own sake, but as building blocks in the regulatory landscape for the more sophisticated and powerful EEVs.

Milestones met

Earlier in 2020 we identified six major milestones from our three program areas (Technology, Naïve EVs and Engineered EVs) for 2020.

In spite of the challenges from COVID-19, five major milestones have been fully achieved, with the sixth on track for achievement in January ‘21.

2021 promises to be a year of further transformation, as Exopharm looks to build visibility and credibility with industry partners and investors.

Table 1. List of major milestones for 2020 across focus areas.

Area	Milestone	Status
Technology	Additional IP	**Achieved**: Filing of Exoria patent
	Demonstrate economics of LEAP purification	**Achieved**: Presentation at Exosome TX outlined world-beating COGS for EV production
Naïve EVs	Plexoval II	**Achieved**: All patients dosed with final follow-ups in January
	Non-clinical results	**Achieved**: Biodistribution study in mice and tubule formation in endothelial cell assays
Engineered EVs	Fortrexo COV POC Results	**Incomplete**: Integration of EVPS and LOAD components delayed due to third-party issues; expecting completion in January
	CNS Design	**Achieved**: "Cognevo" work plan commenced including the addition of key CNS EV researchers to Advisory Panel

<u>Fortrexo CoV</u>

Our innovation team has invented a special version of EEVs, using LOAD and EVPS, called *Fortrexo CoV*. Prototype Fortexo CoV is being made at our Melbourne laboratory and will undergo initial testing in early 2021. If it performs as we expect, the next stages of development will be animal studies and then potentially a clinical trial. A patent application for antiviral versions of Fortrexo has been lodged and it can be reconfigured to address other viruses such as influenza, other coronaviruses and hepatitis.

Our aim is to commence partnering Fortrexo CoV after animal data is in hand. Other versions of antiviral Fortrexo could be partnered separately.

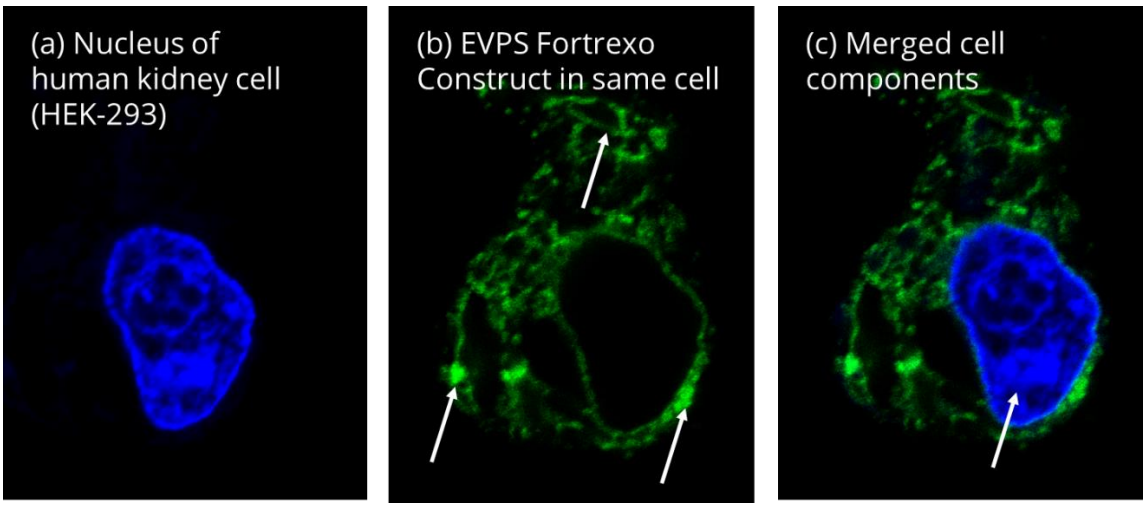

Figure 2. A human kidney cell transfected with the Fortrexo EVPS construct to place with SARS-CoV2 spike protein into surface of EVS. In (a), the nucleus of the cell is identified with a blue fluorescing dye. In (b), the EVPS constructs fluoresce green, identifying the location of the SARS-COV2 spike protein. The highly localized and structured presence in (b) shows that the construct is being incorporated into cellular membranes, the precursor to the cell producing EVs with the spike protein. In (c) the overlapping images confirm the absence of the EVPS construct within the nucleus, further evidence that the construct is localized as expected.

Exoria™

Exoria was invented by our team to solve another problem plaguing the EV field: how to tag, count and track invisible EVs. Exoria started as an in-house analytics tool but is likely to be sold to the EV industry, starting in CY 2021. A patent application for Exoria will be lodged in the next few days.

NEVs for regenerative medicine: harnessing nature

Exopharm started out with a focus on naïve (or natural) EVs (NEVs) from adult stem cells. NEVs from adult stem cells have the potential to deliver the benefits of stem cell therapies without the problems of the stem cells themselves.

Over the past year we have added to our in-house stem cell capabilities and have two NEV programs – Plexaris (NEVs from donated blood platelets) and Cevaris (NEVs from adult stem cells).

Allogeneic (unmatched, off-the-shelf) Plexaris is now in our second clinical trial called Plexoval II. This trial has been fully dosed with 11 participants, with final follow-ups expected in January and a final report in the month following. A Cevaris study is being planned for late CY ’21 / early CY ’22 – potentially in osteoarthritis.

The commercial aim is to take one NEV product through to the completion of a Phase IIb study and then partner it. All other NEV products will be available for partnering before that.

The surprising but powerful regenerative capacity of NEVs is being described in hundreds of publications, as researchers seek to explain how EVs from stem cells work – and why they are better than using the stem cells as a medicine. The science is pointing towards NEVs having a rich and broad regenerative effect via multiple concurrent biological pathways – effectively reprograming cells to reduce inflammation, become more stem cell-like and have a 'younger' phenotype.

EEVs for precision medicine: hope for the hopeless

EEVs are of extreme interest to the pharmaceutical industry as they offer a better way of delivering drugs to selected cells/tissues, providing new treatments to diseases now considered untreatable.

Many of the most promising drugs for untreatable diseases have 'delivery' problems. They are effective in laboratory experiments, but they cannot reach diseased tissues in sufficient quantities in human trials. Sadly, their promise lies unfulfilled. This phenomenon is so common, the pharmaceutical industry even has a term for them: "stranded assets." Investment in stranded assets must be halted unless some solution for the delivery problem can be found. Exopharm's EEVs (using LOAD and/or EVPS) are a promising solution for these delivery problems, especially for the difficult central nervous system (CNS) applications. Our CNS focused EEV project, known as Cognevo, is designed to show potential partners with stranded assets exactly how EEVs could unlock the value in these promising medicines. Exopharm is in discussions with potential partners about using EEVs to deliver stranded assets.

Working towards multiple revenue streams

The strategy and business model of Exopharm is clear, if a little complicated. We are pushing towards generating licensing and deals revenue on multiple fronts and leveraging multiple products and technologies in this fast-emerging field of EV medicine.

We really have *three* interrelated parts of our business:

- The *EEV* part of our business is working alongside Codiak and EVOX to satisfy the needs of well-funded pharmaceutical and biotechnology companies that want to harness EEVs as *precision medicines*. Our aim is to get our fair share of future transactions in the EEV field.
- The *NEV* part of our business is in the *regenerative medicine* field, so we are working alongside the stem cell companies to treat conditions that affect health span, mobility, sensory acuity and the like. In this area we rely upon the advantages of EVs over stem cells as the medicine.

- The *IP* part of our business is about building deals-based revenue and financial value out of key EV-related technologies – in-licensing, in-house developments and know-how and out-licensing. Non-exclusive out-licensing of our LEAP manufacturing technology is a part of this.

Expert people and commercialisation focus

Biotechnology is also about people and ambition.

Over the past three years, Exopharm has built a team of over 40 full-time people here in Melbourne. The Exopharm team covers all of the key areas needed for success in biotechnology – manufacturing, adult stem cell processing, EV design, testing, clinical trials management, analytics, commercialisation and partnering, IP management, project management, investor relations and more. Our people have worked for companies such as CSL, Amgen, McKinsey and Company, Goldman Sachs, Polynovo, Opthea, Cynata and more.

Our commercial and business development team consists of four people full-time. We have also engaged partnering experts to assist us work towards our first deals. In preparation for these partnerships, Exopharm is establishing Exopharm GmbH in January 2021 as a wholly-owned subsidiary based in Basel, Switzerland. Two of our BD team will be based there to bring us closer to key potential collaborators.

Conclusion and perspective

EVs are emerging as a hot new area in biopharmaceuticals and some big deals are being done with very early-stage assets/products. Some commentators have likened it to a gold rush.

The medical needs that EEVs (as precision medicines) and NEVs (as regenerative medicines) can address are important and potentially financially valuable.

Exopharm is a commercially focused clinical-stage company with a clear (but multi-faceted) plan to build multiple robust deal and licensing revenue streams over the short-term and into the future. We now have the products, technology and team to be a worthy participant in this emerging field.

Our aim is to grow and build a real biotechnology company based upon important technologies and rigorous science. Our LEAP manufacturing technology gives Exopharm a strong position as the EV field matures and wants to manufacture real EV products at scale.

As our efforts convert into important milestones, we should expect to see the value of Exopharm better match the valuations ascribed to companies such as Codiak and EVOX.

Milestones for CY 2021 will include a first out-licensing deal, conclusion of the Plexoval II study, OA animal study results, Fortrexo CoV animal study results, preparation for the Cevaris first-in-human study and the commercial release of Exoria. Building tangible financial value is the objective.

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

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ABOUT EXOPHARM

Exopharm Limited (ASX:EX1) is a clinical-stage Australian exosome medicine company developing naïve exosome products for regenerative medicine and engineered exosomes for new precision medicines.

Exosomes (or EVs) are small particles naturally produced by cells, which deliver therapeutic 'cargoes' to other cells to reduce inflammation and promote regeneration. EVs are plentiful in our youth but decline with age. Recent research points to naïve EV medicines as a way to extend the number of healthy, functional years. EVs secreted by stem cells could be used in place of stem-cell therapy with equal or greater benefit without the problems associate with stem-cell therapies.

Engineered EVs (EEVs) are an important emerging technology for the delivery of precision medicines. By altering proteins on the surface of EVs and adding custom cargoes such as RNA and small molecules, EEVs hold promise in a variety of untreatable diseases.

While trillions of EVs are produced by stem cells, the development of EVs as medicines has been hampered by the challenge of purifying EVs. Exopharm owns a purification technology called Ligand-based Exosome Affinity Purification (LEAP). LEAP technology and associated manufacturing know-how places Exopharm as a global leader in this emerging field. Exopharm

is a clinical stage company with pending and current trials for wound healing, hearing loss and osteoporosis.

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.