ASX Release

27 June 2023

iNKT CYTOKINE TECHNOLOGY ENHANCES iNKT CELL PERSISTENCE AND ANTI-TUMOUR ACITIVTY – CLARIFYING INFORMATION

MELBOURNE, AUSTRALIA 27 June 2023: Arovella Therapeutics Ltd (ASX: ALA), a biotechnology company focused on developing its invariant Natural Killer T (iNKT) cell therapy platform, here provides additional clarifying information pertaining to its announcement on 26 June 2023 regarding the positive data obtained for its cytokine technology under Option. In particular, further information is provided regarding the experimental results.

In a study of 16 mice in a solid tumour xenograft model, mice were treated with either CAR-iNKT cells (n=4) or CAR-iNKT cells that were engineered to express a cytokine (n = 8) and monitored for survival over ~61 days. A negative control group of untreated animals was also included (n=4). Treatment of the mice with CAR-iNKT cells that were engineered to express a cytokine extended the lifespan of mice relative to CAR-iNKT cells that did not express the cytokine. In the negative control group (untreated), all mice died within 26 days. Treatment with CAR-iNKT cells increased animal survival, with all 4 animals surviving for at least 30 days. However, all CAR-iNKT treated mice died within 49 days. In contrast, mice treated with CAR-iNKT cells containing a cytokine all lived to at least 40 days and 75% of the animals survived until the end of the study at 61 days. The improvement in survival for cells containing the cytokine was statistically significant ($p<0.05$).

The number of iNKT cells circulating in peripheral blood of the mice was also assessed four weeks after treatment. The number of circulating iNKT cells after four weeks of treatment was approximately 10-fold higher for iNKT cells that contained the cytokine than for CAR-iNKT cells that did not contain the cytokine, indicating that the presence of the cytokine enhanced the number and persistence of iNKT cells *in vivo*. The increase in cell number observed in the CAR-iNKT cells producing the cytokine was statistically significant ($p<0.01$).

Mouse models provide an effective way to assess the activity of "living therapies", such as CAR-iNKT cells. The models permit the transplant of human tumour cell lines as xenografts, that can then be established in mice. Once the tumour cells have engrafted, the therapy can be administered to assess its ability to control or eliminate the tumour cells. Murine species are the most frequently used model species to assess adoptive cell therapies such as CAR-iNKT. Advantages of using mouse models include the speed of testing, direct evaluation of the therapy and that a broad range of tumour cell lines can be tested. Limitations of mouse models include the lack of spontaneous tumours, and that xenogeneic graft versus host disease prevents longitudinal studies[1].

The Option agreement with UNC Lineberger was executed in December 2022 and announced to ASX on 20 December 2022. The Option is an Exclusive Option with a 15-month term and the Option payment of US$15k

[1] Duncan *et al.*, 2022 Applying a Clinical Lens to Animal Models of CAR-T Cell Therapies.

was payable on receipt of positive experimental data, which has now been received.

Arovella and UNC Lineberger are currently in discussions about the terms of a formal, definitive licence agreement relating to the cytokine technology. Entry to any such licence agreement will be subject to Arovella completing due diligence to its satisfaction, and the parties completing negotiations on commercial terms. Whilst the parties expect to execute a licence agreement before the expiry of the Option term in March 2024, these discussions and negotiations are ongoing, and there is no certainty that these discussions will lead to a formal licence agreement being signed. At this preliminary stage, the Company is not able to provide further information on the terms, or forecast the financial impact, of the licence agreement. Arovella will provide further updates to the market in line with its disclosure obligations.

This announcement has been approved for release by Arovella's Board of Directors.

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NOTES TO EDITORS:

About Arovella Therapeutics Ltd

Arovella Therapeutics Ltd (ASX: ALA) is a biotechnology company focused on developing its invariant natural killer T (iNKT) cell therapy platform from Imperial College London to treat blood cancers and solid tumours. Arovella is also expanding its DKK1-peptide targeting technology licenced from MD Anderson and used in conjunction with its iNKT cell therapy platform. Arovella's lead product is ALA-101. ALA-101 consists of CAR19-iNKT cells that have been modified to produce a Chimeric Antigen Receptor (CAR) that targets CD19. CD19 is an antigen found on the surface of numerous cancer types. iNKT cells also contain an invariant T cell receptor (iTCR) that targets α-GalCer bound CD1d, another antigen found on the surface of several cancer types. ALA-101 is being developed as an allogeneic cell therapy, which means it can be given from a healthy donor to a patient.

Glossary: iNKT cell – invariant Natural Killer T cells; **CAR** – Chimeric Antigen Receptor that can be introduced into immune cells to target cancer cells; **TCR** – T cell receptors are a group of proteins found on immune cells that recognise fragments of antigens as peptides bound to MHC complexes; **B-cell lymphoma** – A type of cancer that forms in B cells (a type of immune system cell); **CD1d** – Cluster of differentiation 1, which is expressed on some immune cells and cancer cells; **aGalCer** – alpha-galactosylceramide is a specific ligand for human and mouse natural killer T cells. It is a synthetic glycolipid.

The Company is also commercialising ZolpiMist™ to treat short-term insomnia.

For more information, visit www.arovella.com

This announcement contains certain statements which may constitute forward-looking statements or information ("forward-looking statements"), including statements regarding negotiations with third parties and regulatory approvals. These forward-looking statements are based on certain key expectations and assumptions, including assumptions regarding the actions of third parties and financial terms. These factors

and assumptions are based upon currently available information, and the forward-looking statements herein speak only of the date hereof. Although the expectations and assumptions reflected in the forward-looking statements are reasonable in the view of the Company's directors and management, reliance should not be placed on such statements as there is no assurance that they will prove correct. This is because forward-looking statements are subject to known and unknown risks, uncertainties and other factors that could influence actual results or events and cause actual results or events to differ materially from those stated, anticipated or implied in the forward-looking statements. These risks include but are not limited to: uncertainties and other factors that are beyond the control of the Company; global economic conditions; the risk associated with foreign currencies; and risk associated with securities market volatility. The Company assumes no obligation to update any forward-looking statements or to update the reasons why actual results could differ from those reflected in the forward-looking statements, except as required by Australian securities laws and ASX Listing Rules.