ASX Release

5 June 2024

AROVELLA ACHIEVES IMPORTANT MILESTONE BY COMPLETING PROCESS DEVELOPMENT AND SCALE-UP FOR MANUFACTURE OF ALA-101

Highlights:

- **Critical process finalised for GMP manufacturing of ALA-101, demonstrating a high yield of CAR19-positive iNKT cells with very high purity**
- **Process suitable for large-scale and late-phase clinical development**
- **Process maintains highly cytotoxic iNKT cell phenotype**
- **Progressing to engineering and GMP batches to produce material for phase 1 clinical trials**
- **Arovella's proprietary manufacturing process suitable for all of Arovella's current and future iNKT cell programs**

MELBOURNE, AUSTRALIA 5 June 2024: Arovella Therapeutics Ltd (ASX: ALA), a biotechnology company focused on developing its invariant Natural Killer T (iNKT) cell therapy platform, is pleased to announce that it has achieved a significant milestone by completing process development for its patent protected manufacturing process required for large-scale Good Manufacturing Practice (GMP) manufacturing of its lead product, ALA-101.

The modular, semi-automated process, developed at Cell Therapies Pty Ltd, is suitable for large-scale manufacturing and produces a high yield of Chimeric Antigen Receptor (CAR)-positive iNKT cells with very high purity. A well-controlled and reproducible GMP manufacturing process is essential for regulatory approval for first-in-human clinical trials. Arovella can now proceed with engineering and GMP batches to produce material for phase 1 clinical trials. The manufacturing process uses well-known automated cell therapy equipment, significantly reducing technology transfer risks to new jurisdictions.

The final product characteristics are consistent with the expectations of global regulators such as the US FDA for product quality and safety. The process maintains the beneficial highly cytotoxic CD4-negative population of iNKT cells, as described in Arovella's licensed patents, that have been shown to be more cytotoxic than CD4+ cells in a recent presentation at the American Association for Cancer Research (AACR) Annual Meeting. The expectation is that a balanced product with a mix of these cell phenotypes may lead to superior efficacy.

Achievement of this milestone will facilitate Arovella's pipeline expansion for its CAR-iNKT cell platform. The manufacturing process can be applied to all of Arovella's future CAR-iNKT cell products, significantly reducing the time required to proceed from proof-of-concept data to clinical manufacture for programs with new CARs. Different CARs that recognise different tumour types can be added to iNKT cells through the use of new lentiviral vectors that will be manufactured to GMP standards (for example, Claudin 18.2-targeting CAR-iNKT cells).

Managing Director, Dr Michael Baker, commented, "Process development for our CAR-iNKT manufacturing process has been a primary focus for Arovella over the past year, and it is incredibly exciting to have completed this step. For all cell therapy products, the manufacturing process defines your product. We have been diligent to ensure that our proprietary manufacturing process is robust and delivers high-yield, high-purity products. This enables us to achieve our vision of taking allogeneic CAR-iNKT cells into clinical trials and, ultimately, commercial development. I am proud of the team for achieving this milestone and thankful to Cell Therapies Pty Ltd for their partnership and the experience they have contributed.

We look forward to continuing this momentum as we progress towards our phase 1 clinical trial for ALA-101."

Release authorised by the Managing Director and Chief Executive Officer of Arovella Therapeutics Limited.

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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'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 glycolipid 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. Arovella is also expanding into solid tumour treatment through its CLDN18.2-targeting technology licensed from Sparx Group. Arovella will also incorporate its IL-12-TM technology into its solid tumour programs.

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.

For more information, visit www.arovella.com

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