Update report prepared for Siobhan's Superstar Legacy in conjunction with Dr Sally George

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Here, at The Institute of Cancer Research, we are passionate about transforming treatment for children with cancer – by applying our growing knowledge about the biology of the disease. We want to find ways to cure those children who don't respond to current treatments – or who initially respond, only to later relapse. And we have a strong focus on finding treatments for certain rarer types of children's cancer where there are currently no effective treatments at all. We are working for these advances while always keeping in mind that survivors from children's cancer should have a long life ahead of them, and so treatments should be as kind as possible, and free of long-term side effects.

The key to achieving our vision is world-class science – to understand why children's cancers develop, and why some respond to treatment while others do not. Cancers in young people are fundamentally different from those in adults. Scientists are working hard to untangle their complex biology, ecosystems and evolution and turn this knowledge into sophisticated new tests and treatments. We are uncovering the molecular switches that turn on cancer in children, and the complex changes that can allow it to resist treatment. We are learning to predict which children are likely to relapse after treatment, and to find ways of treating them with new targeted drugs, immunotherapies and combinations that offer the best possible chance of cure.

Driving forward vital research into neuroblastoma targets

The Developmental Oncology Group, led by Dr Sally George, was established in March 2023. The laboratory is primarily focused on research into the common poor outcome childhood cancer neuroblastoma. We now have three post-doctoral fellows in post, all working on individual projects which are focused on how different factors (including altered *telomere maintenance and specific genetic alterations) affect the ability of neuroblastoma cells to differentiate, and to respond to novel and targeted therapeutics.

* Telomeres are repetitive DNA sequences located at the ends of chromosomes that play a crucial role in maintaining the stability and integrity of the genome. They protect the genetic material from deterioration and prevent chromosomes from sticking together.

The funding provided by Siobhan's Superstar Legacy – for which we are extremely grateful - has been ringfenced to employ a Scientific Officer to support the research being carried out in the Developmental Oncology Group. After external advertisement, and a competitive application process, we appointed Matthew Shipley as a Scientific Officer who started at the ICR on 6th November 2023. Matthew has a B.Sc. in Neuroscience from Edinburgh University and a Masters' Degree in Cancer Research and Precision Oncology from The University of Glasgow. Matthew has very quickly integrated into the team. His role includes general essential tasks in cell line culture and maintenance, cryopreservation of tumour samples derived from pre-clinical models, maintaining levels of

laboratory consumables and ensuring the smooth running of projects and processes in the lab. He has also independently performing a number of experiments, most notably he is working together with a post-doctoral fellow in our lab on a project to understand whether neuroblastoma with ATRX mutations shown preferential sensitivity to inhibition of USP7 – a protein found in various cancers and which high proliferation of generally indicates a poor prognosis. Here, he has performed genetic knockdown experiments, assessed protein expression by western blot and performed cell viability assays.

Overall, Matthew's appointment has already significantly improved the effective running of the lab and enabled us to move faster with the conducting of experiments. In addition, we are hoping to support Matthew's educational development with his long-term plan being to obtain a 4-year PhD fellowship which would enable him to build on this experience and drive an independent research project in the field of neuroblastoma research.

Thank you once again to everyone at Siobhan's Superstar Legacy for your incredible support and interest in our work here at the ICR, we are extremely grateful.

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