Abcam Licenses Novel Ceefourin Inhibitors of Multidrug Resistance Protein 4 from Children’s Cancer Institute

Compounds allow further exploration of MRP4 function and have potential in cancer therapeutic development

Sydney, Australia and Cambridge, UK, 22nd September, 2014: Children’s Cancer Institute and Abcam plc, a global leader in the supply of innovative protein research tools and services, announced today that they have entered into an exclusive licence, supply and distribution agreement for multidrug resistance protein 4 (MRP4/ABCC4) inhibitors, Ceefourin™ 1 and Ceefourin™ 2, for research purposes.

The first known selective inhibitors of MRP4, Ceefourin 1 and Ceefourin 2, are potent, chemically distinct compounds and represent important tools for investigating essential cellular processes such as multidrug resistance. The compounds will enable the further exploration of MRP4 function and have potential in development of therapeutic drugs to treat cancer. The novel MRP4 inhibitors were discovered and characterised by Children’s Cancer Institute.

MRP4 is a protein that belongs to the ATP-Binding Cassette (ABC) transporter superfamily of membrane pumps that export molecules from the cell. MRP4 effectively effluxes elements that are potentially toxic to the cell, protecting it from deleterious chemical build-ups and from xenobiotics, such as environmental toxins. Previous research on MRP4 and other ABC transporter family members has shown that these proteins are often ‘hijacked’ by cancer cells, which produce them at high levels to pump out chemotherapy drugs, effectively protecting the cancer cells from treatment.

Up to this point, researchers have not had access to effective MRP4 inhibitors without substantial confounding off-target effects. Highly specific research reagents are crucial to accurately defining how these proteins work. Furthermore, used together, these compounds provide a complementary toolset for the research community, with the potential for enabling studies in the field to be more effective and insightful, and deliver results faster.

Professor Murray Norris, Lead researcher and Children’s Cancer Institute Deputy Director, said: “We are delighted to be able to make these research reagents available to the scientific community worldwide through our partnership with Abcam. These compounds will enable researchers to obtain new insights into MRP4 function and to modulate extracellular drug
transport."

Matthew Roe, Head of Reagents, Abcam said: "We are very pleased to partner with Children’s Cancer Institute, and to manage distribution of these reagents to the research community, helping to increase the impact of their findings and help scientists discover more."

The Ceefourin MRP4 inhibitors now available from Abcam include:

**Ceefourin™ 1 (ab145144)**

Selective MRP4 inhibitor. A benzothiazol compound which potently and selectively inhibits MRP4-mediated substrate efflux. For example, Ceefourin 1 inhibits MRP4-mediated D-luciferin transport (IC₅₀ = 1.5µM) as measured indirectly using a bioluminescence assay in HEK293-MRP4 cells with stable luciferase expression. Ceefourin 1 exhibits no detectable inhibition of other ABC transporters such as Pgp, ABCG2 and MRP1, MRP2, MRP3 and MRP5, and is non-toxic in normal fibroblast and cancer cell lines tested up to 50µM. Ceefourin 1 displays metabolic (half-life >30 min) and acid stability (half-life >24hrs at 37°C, pH 2) in a mouse liver microsomal assay and acid-stability assay, respectively.

**Ceefourin™ 2 (ab145145)**

Selective MRP4 inhibitor. A pyrazolopyrimidine compound which potently inhibits MRP4-mediated substrate efflux. For example, Ceefourin 2 inhibits MRP4-mediated D-luciferin transport (IC₅₀ = 7.0µM) as measured indirectly using a bioluminescence assay in HEK293-MRP4 cells with stable luciferase expression. Ceefourin 2 exhibits no detectable inhibition of other ABC transporters, such as Pgp, ABCG2 and MRP1, MRP2, MRP3 and MRP5. Ceefourin 2 displayed limited toxicity in two of eleven cancer cell lines tested up to 50µM, and exhibited no toxicity in two normal fibroblast lines tested to the same concentration. Ceefourin 2 shows metabolic stability (half-life >30 min) in a mouse liver microsomal assay and limited acid-stability (half-life < 2 hr at 37°C, pH 2).

Ceefourin™ is a trademark of Children’s Cancer Institute. Ceefourin 1 and Ceefourin 2 are claimed under Australian provisional patent application 2014902472.

The licence agreement was facilitated by Bio-Link Australia, a life sciences commercialisation company.
Notes for Editors


Media enquiries:
For Children’s Cancer Institute
Catherine Arnott
Media & Communications Advisor
Tel: +61 02 9385 8879
Email: carnott@ccia.org.au

For Abcam
Zyme Communications
Katie Odgaard
Tel: +44 (0)7787 502 947
Email: katie.odgaard@zymecomunications.com

About Children’s Cancer Institute
Children’s Cancer Institute is the only independent medical research institute in Australia dedicated 100% to childhood cancer research, existing solely to cure childhood cancer and improve the quality of life for survivors. We focus on translational research, working closely with clinicians to ensure our discoveries are progressed into clinical trials and actual treatments for kids with cancer as quickly as possible. Children's Cancer Institute first opened its research laboratories in 1984 and has since grown to employ more than 195 staff and students, establishing a national and international reputation for scientific excellence. For more information, visit www.childrenscancerinstitute.org.au.

About Abcam
Abcam plc is a global leader in the supply of life science research tools, with a wide range of products and expert technical support, enabling scientists to analyse living cells at the molecular level and improving the understanding of health and disease.

Abcam is committed to providing scientists with an extensive choice of reagents and tools, with the most comprehensive, honest and up-to-date datasheets and customer reviews, fast delivery and helpful customer service & technical support. The Company’s catalogue evolves with scientific research trends and is growing each year to provide customers with products to meet their research needs. The range now includes primary and secondary antibodies, proteins, peptides, lysates, biochemicals, immunoassays and other kits. Abcam also supports its customers by hosting a range of global scientific events, forums and webinars, providing opportunities for scientists to get together and present their work.
Headquartered in Cambridge, UK, Abcam has eight global subsidiary offices enabling local services, multi-language support and next-day delivery to over 100 countries. The Company was founded in 1998, and now employs over 740 FTEs. Abcam was admitted to AIM in 2005 (AIM: ABC). To find out more, please visit www.abcam.com

About Bio-Link
Bio-Link Australia Pty. Ltd. is a life sciences commercialisation company which facilitates partnerships in the biopharma, medical device and diagnostic industries. Bio-Link has offices in Sydney and Melbourne, Australia, and clients including leading Australian and international biotechnology and medical device companies and medical research institutions. For more information, visit www.bio-link.com