Ascent Scientific licenses novel clathrin inhibitors from Freie Universitaet Berlin, University of Newcastle and Children's Medical Research Institute

Bristol, UK, Berlin, Germany, Sydney and Newcastle, Australia, 7th October, 2011

Ascent Scientific, together with Freie Universitaet Berlin, The University of Newcastle and Children's Medical Research Institute today announced that they have entered into an exclusive licence, supply and distribution agreement for the clathrin inhibitors Pitstop 1™ and Pitstop 2™ for research. These novel compounds are the first rationally designed inhibitors of clathrin, and represent important tools for investigating essential cellular processes such as endocytosis. The agreement was facilitated by Bio-Link Australia, a life sciences commercialisation company.

Clathrin, a protein found in coated pits is responsible for clathrin-mediated endocytosis (CME) and is essential for the formation of clathrin-coated vesicles. CME is crucial to many physiological processes including the internalisation of growth factors, receptors, ion channels, adhesion proteins and synaptic vesicle proteins and, notably, is hijacked during the entry of pathogens such as HIV-1.

The novel clathrin inhibitors: Pitstop 1™ and Pitstop 2™, developed by the laboratories of Professor Volker Haucke (Freie Universität Berlin, Germany), Professor Adam McCluskey (University of Newcastle) and Professor Phil Robinson (Children's Medical Research Institute) are exciting new tools for researchers, allowing the further exploration of clathrin function and may also provide potential applications as virus and pathogen entry inhibitors and cell signalling modulators.

Professor Haucke said *"The scientific community has long been awaiting the development of potent and reliable inhibitors of clathrin function, in particular endocytosis. We are excited and happy to now be able to make these available to the scientific community worldwide through Ascent Scientific. These compounds should enable researchers to obtain new insights into clathrin function and to modulate cell signaling as well as neurotransmission. These are exciting times!"*

Professor Adam McCluskey commented, *"Compounds like the Pitstop™ inhibitors become particularly exciting when placed in the hands of the biology community. Their distribution by Ascent Scientific is a major advance and will allow significant new insights into the role of clathrin in diseases."*

Professor Phil Robinson said *"It will be particularly valuable to cell biologists to now be able to choose their own timing of clathrin inhibition to suit their particular research, rather than wait 2-3 three days for a knock-down. We now expect that the ability to combine clathrin and dynamin inhibition will open up new research avenues."*

Steve Roome PhD, General Manager for Ascent Scientific, explained *"These incredibly exciting clathrin inhibitors represent new and powerful tools which equip researchers with the ability to inhibit clathrin function and modulate endocytosis. This should allow further investigation of the function of clathrin whilst providing the potential to explore pathogen entry such as that manipulated by HIV."*

Reference:

von Kleist et al (2011) Role of the clathrin terminal domain in regulating coated pit dynamics revealed by small molecule inhibition. *Cell*,146(3):471-84.

The clathrin inhibitors (and their respective inactive control compounds) now available from Ascent Scientific include:

Pitstop 1™

Novel, selective clathrin inhibitor. Competitively inhibits clathrin terminal domain (TD) to selectively inhibit clathrin mediated endocytosis (IC_{50} ~18 μM for inhibition of amphiphysin association of clathrin TD). Pitstop 1™ exhibits limited cell membrane penetration, however it is active in cells after microinjection.

Pitstop 1™ - negative control

Pitstop 1™ negative control compound is of the same chemical class and has a highly related structure to Pitstop 1™. This compound has a IC50 of amphiphysin binding to the clathrin TD >100μM and has been demonstrated not to block receptor mediated endocytosis up to at least a concentration of 300 μM.

Pitstop 2™

Novel, selective clathrin inhibitor. Competitively inhibits clathrin terminal domain to selectively inhibit clathrin mediated endocytosis (IC_{50} = 12 μM for inhibition of amphiphysin association of Clathrin TD). Pitstop 2™ is cell membrane permeable and interferes with CME entry of HIV and synaptic vesicle recycling.

Pitstop 2™ - negative control

Pitstop 2™ negative control compound is of the same chemical class and has a highly related structure to Pitstop 2™. This compound has a half maximal inhibitory concentration (IC50) of amphiphysin binding to the clathrin terminal domain >100μM and has been demonstrated not to block receptor mediated endocytosis up to at least a concentration of 100 μM.

About Freie Universität Berlin

Freie Universität Berlin is a leading research institution. A full university offering more than 150 degree programs across a wide range of subjects, it is one of nine universities successful in all three funding lines in the German government's Excellence Initiative. Its future development strategy focuses on international cooperation, research development, and support for junior researchers. Freie Universität has seven liaison offices abroad that provide a platform for international networking. www.fu-berlin.de

About The University of Newcastle

Established in 1965, the University of Newcastle in regional NSW (according to the Lonely Planet's guide, the 9th must visit city on the planet) is the most research intensive university outside of an Australian capital city. Ranked ninth among Australia's universities for research, Newcastle's reputation is for innovation, excellence and research with impact. www.newcastle.edu.au

About the Children's Medical Research Institute

Established in 1958 by Sir Lorimer Dods' goals to advance and enhance health care for the benefit of the community. Today, CMRI is committed to excellence in biomedical science, engaging in fundamental research into the causes, prevention, early diagnosis and relief or cure of disease in children. CMRI scientists aim to understand the basic inner workings of our cells and to find better ways to prevent and treat diseases which rob children of their chance at a long and healthy life. Many diseases that affect children, such as cancer and epilepsy, have the same origins in adults. www.cmri.org.au

About Bio-Link Australia

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

About Ascent Scientific, an Abcam company

Ascent Scientific's mission is to progress research by providing biochemicals of high purity and exceptional quality to researchers around the world. Ascent Scientific products have been cited in numerous peer-reviewed publications. The high purity range includes agonists, antagonists, ion channel modulators, enzyme inhibitors and signalling tools for research in areas such as glutamate, GABA, ion channels, cannabinoids, opioids, 5-HT and more. www.acentscientific.com

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