Astex To Present Data From Its FGFR Inhibitor Programme at the American Association for Cancer Research (AACR) 102nd Annual Meeting 2011

Cambridge, UK, 29th March 2011.

Astex Therapeutics, the UK-based biotechnology company developing targeted therapies for oncology, today announced that it is to present new data on Fibroblast Growth Factor Receptor (FGFR) inhibitors from its drug discovery research collaboration with Janssen Pharmaceutica and the Cancer Research UK Drug Discovery Group at the Newcastle Cancer Centre (NCC), Northern Institute for Cancer Research, Newcastle University, UK. The Astex presentation will be made during the AACR 102nd Annual Meeting, April 2-6 2011, at the Orange County Convention Center, Orlando, Florida, USA.

Fibroblast Growth Factor Receptor (FGFR) signalling is a key target in the molecular pathology of cancer. Astex's FGFR inhibitor programme was partnered with Janssen Pharmaceutica in June 2008 in a deal valued at more than $500M to Astex. Astex and Janssen scientists will present data on a fragment screening campaign against the tyrosine kinase domain of FGFR1. The presentation will focus on previously undescribed FGFR1 kinase inhibitors that have been optimised for selectivity versus other protein kinases, for example FLT3, using structure-based design. Astex's collaborative programme with Janssen Pharmaceutica and NCC is currently in preclinical development with selection of a development candidate anticipated in 2011.

-ends-

Contact

Jeremy Carmichael, PhD
Director of Business Development

Tel: +44(0)1223 226200
j.carmichael@astex-therapeutics.com

About Astex Therapeutics

Astex is a UK-based biotechnology company that discovers and develops novel small molecule therapeutics. Using its pioneering fragment-based drug discovery platform Pyramid™, Astex has built a pipeline of five molecularly targeted oncology drugs, of which three are currently being tested in clinical trials and two are in pre-clinical development.

In addition to its proprietary research programmes, Astex's productivity in lead discovery has been endorsed through numerous partnerships with major pharmaceutical companies, including AstraZeneca, Bayer-Schering, Boehringer Ingelheim, GlaxoSmithKline, Novartis and Johnson & Johnson.

For further information on Astex please visit the Company's website at www.astex-therapeutics.com

AACR presentation:

Presentation Title: Fragment based drug discovery of selective inhibitors of Fibroblast Growth Factor Receptor (FGFR)

Abstract Number: 1361
Session Title: Drug Design and Lead Optimization 1
Presentation Time: Mon, Apr 4, 8:00 AM - 12:00 PM
Location: Exhibit Hall A4-C, Poster Section 16
Poster Section: 16
Poster Board Number: 18

Author Block:

Gordon Saxty[1], R. Akkari[2], P. Angibaud[2], J. Arts[2], P. Benderitter[2], V. Berdini[1], P. Bonnet[2], A. Cleasby[1], W. Embrechts[2], E. Freyne[2], R. Gilissen[2], P. King[2], J. Lacrampe[2], Y. Ligny[2], A. Madin[1], S. Mcclue[2], L. Mevellec[2], C. W. Murray[1], H. Newell[3], M. Page[2], A. Papanikos[2], T. Perera[2], O. Querolle[2], D. C. Rees[1], S. J. Rich[1], S. M. Saalau-Bethell[1], E. Sement[2], Y. Simmonet[2], M. Squires[1], V. Tronel[2], G. A. Ward[1], M. Willems[2], Wroblowski B[2], N. T. Thompson[1].

[1]Astex Therapeutics, Cambridge, United Kingdom;
[2]Janssen Oncology R&D, Beerse, Belgium;
[3]Newcastle Cancer Centre, Northern Institute for Cancer Research, Newcastle University, United Kingdom

Abstract Body:

Recent data in a number of tumour types has implicated Fibroblast Growth Factor (FGF) and Fibroblast Growth Factor Receptor (FGFR) signalling as being key to the molecular pathology of cancer.

A fragment screening campaign was conducted against the tyrosine kinase domain of FGFR1 to detect low molecular weight compounds that bound to the hinge region of the kinase. The screening produced several fragment inhibitors (molecular weight <250 Da) in the micromolar range and their binding modes were confirmed by X-ray crystallography. We selected an imidazo[1,2-a]pyridine fragment that was 120 uM versus FGFR3 in the kinase inhibition bioassay. Subsequently, in the fragments-to-leads stage a detailed structural understanding of the binding interactions between the fragment and its protein kinase target, using X-ray crystallography, led to the identification of a 0.003 uM inhibitor of FGFR3 in the kinase bioassay, with significant selectivity versus VEGFR2 and FLT3.

The poster will focus on the description of previously undescribed compounds bearing an imidazo[1,2-a]pyridine core scaffold where selectivity versus other protein kinases, for example FLT3, is obtained using the X-ray crystal structure and structure-based design. In summary we will illustrate how X-ray crystallography and fragment-based drug design (FBDD) can be used to discover compounds with activity in an FGFR driven xenograft model when dosed by the oral route.