

Astex Therapeutics: Fragment-based drug discovery and development

Leadership

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 John Aston MA ACA, *Chief Financial Officer*
 Martin Buckland DPhil MBA, *Chief Business Officer*
 Neil Jones BSc FCA, *Financial Controller*
 Lyn Leaper PhD, *VP Intellectual Property*
 John Lyons PhD, *VP Translational Research*
 Chis Murray PhD, *VP Comp Chem & Informatics*
 David Rees PhD, *VP Medicinal Chemistry*
 Trish Sweeney PhD, *Director of Clinical Operations*
 Neil Thompson PhD, *VP Biology*
 Jeff Yon PhD, *VP Structural Biology*
 Murray Yule MB PhD MRCP, *Dir Clin Development*

Board of Directors

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 Peter Ringrose PhD, *BBSRC, ex BMS/Pfizer*
 Jon Saxe BScHE JD LL.M., *ex-President PDL*
 Patrick Van Beneden MSc, *GIMV*

Company History

Astex was established in 1999 and has raised more than £70M in equity capital and venture debt. The company is located on the Cambridge Science Park, Cambridge, UK.

Investors

Abingworth Management
 Advent International
 Alta Partners
 Apax
 Bayer Schering
 GIMV
 HypoVereinsbank
 Johnson & Johnson Development Corporation
 Novartis
 Oxford Bioscience Partners
 University of Cambridge

The Company

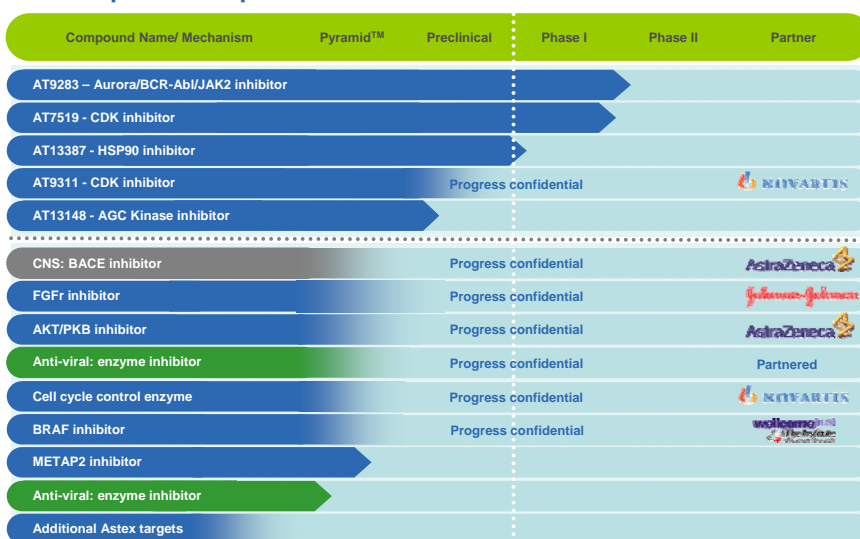
Astex Therapeutics is using an innovative fragment-based drug discovery platform, Pyramid™, to identify and develop new medicines, primarily for the treatment of cancer and anti-infective diseases. The company has established a clinical stage pipeline of novel drug candidates and has significant partnerships with leading pharmaceutical companies including Jansen Pharmaceutica, Novartis and AstraZeneca. All of the products being developed have been discovered at Astex through the use of the company's proprietary technologies. Based on current output, the company expects Pyramid™ to continue to deliver at least one IND candidate per year into the Astex portfolio.

Product Pipeline

AT9283 is a multi-targeted inhibitor of aurora kinases A and B, JAK2 and BCR-Abl kinase. AT9283 is currently being tested in a Phase I/IIa clinical trial in patients with haematological malignancies and in Phase I studies in patients with solid tumours.

AT7519 is a potent cell cycle inhibitor that targets key cyclin dependent kinases

Development Pipeline



resulting in tumour shrinkage. Phase I studies in patients with solid tumours are underway and additional Phase II studies are planned for 2008.

AT13387 is a novel, non-geldanamycin, small molecule inhibitor of Hsp90 that received IND approval in January 2008. Phase I studies in patients with refractory solid tumours are underway.

AT9311 is a differentiated cytostatic cell cycle inhibitor completing formal preclinical development with an IND/CTA expected during 2008.

AT13148 is a novel small molecule inhibitor of AGC Kinases, Akt/PKB and ROCKII. AT13148 is currently in preclinical development with an IND/CTA anticipated during 2009.

Astex also has a deep pipeline of earlier proprietary discovery and development programmes against other novel oncology targets. In addition, Astex has established an exploratory programme directed at antiviral targets.

Strategic Alliances: Drug Discovery & Development

In addition to driving the growth of Astex's in-house oncology pipeline, Pyramid™ underpins the company's drug discovery and development collaborations with major pharmaceutical companies. Fees, funding and milestone payments under these collaborations potentially exceed \$1.6 bn, excluding royalties.

In June 2008, Astex established an alliance with Jansen Pharmaceutica to develop and commercialise compounds arising from its novel FGFR inhibitor programme and two further cancer drug targets.

Astex has also established a cell-cycle inhibitor partnership with Novartis which includes a license to AT9311 and an option to AT7519. In addition, the parties established a new drug discovery alliance focussed on the identification of novel inhibitors of other cell-cycle control enzymes.

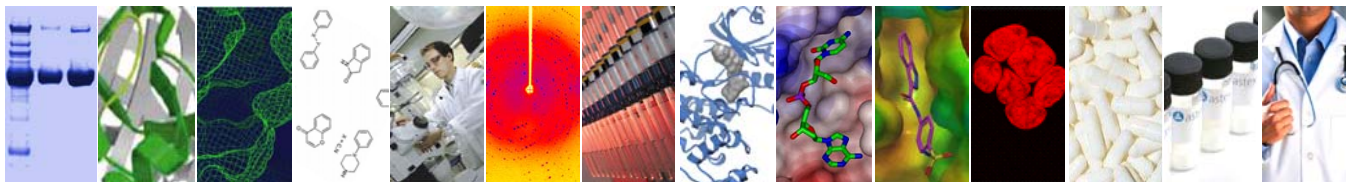


Astex also has a partnership with AstraZeneca focused on identifying and developing novel inhibitors of protein kinase B (PKB/Akt).

The company's ability to address targets that are regarded by the pharmaceutical industry as 'intractable' has led to separate drug discovery collaborations with major pharmaceutical companies including AstraZeneca (BACE inhibitor), Boehringer Ingelheim, Bayer Schering Pharma (formerly Schering AG) and Jansen Pharmaceutica.



These collaborations have validated Astex's Pyramid™ platform and have delivered valuable early drug leads to our corporate partners.



Pyramid™: A new approach to integrated drug discovery & development

Pyramid™ is an integrated, fragment-based approach that rapidly delivers tailored high-quality small molecule drug leads with enhanced therapeutic potential. Pyramid™ defines a process by which a range of high throughput biophysical and computational techniques are used to experimentally characterize the interactions of very low molecular weight synthetic ligands with their target proteins. The productivity of Pyramid™ has allowed the company to generate a robust pipeline of novel “best in class” drug candidates which the company is advancing independently and through valuable strategic partnerships with industry leaders such as Novartis and AstraZeneca.

The Pyramid™ Approach

Traditional high-throughput screening has not delivered on its promise of more new drugs entering clinical trials. This is in part due to the increasing complexity and size of the compounds screened. This problem can be addressed by fragment-based drug discovery which uses very small, low molecular weight drug fragments which have the potential to keep the overall compound complexity and molecular weight low.

Traditional bioassays used in high-throughput screening are unable to detect drug fragments because of their weak binding to the protein target but it is possible to detect such weak binding using X-ray crystallography and other biophysical techniques. Following recent technology developments, including Astex's development of its proprietary software, Autosolve®, to speed the processing of X-ray data, the company can now employ its high throughput X-ray crystallography capability, HTX®, for the rapid detection of fragment binding.

Astex has used Pyramid™ to generate multiple novel lead series against its in-house targets and those of its collaborators, and selected compounds from these programmes are now being progressed in or towards clinical trials.

Cytochrome P450 structural biology

Astex has achieved two major scientific breakthroughs in solving the first human cytochrome P450 (CYP450) structures - 2C9 and 3A4 - key members of this important family of drug metabolising enzymes. Astex's proprietary CYP450 structural information enables the company and its collaborators to generate lead compounds with optimal DMPK properties and to reduce attrition rates in drug development. In 2003 Astex's scientists published the

crystal structure of human CYP450 2C9 in the leading science journal *Nature* and the human CYP450 3A4 structure in *Science* in 2004.

Cytochrome P450 Programme

Astex's pioneering work on solving human cytochrome P450 structures was supported via research agreements with a number of pharmaceutical company partners.



Astex has recently established a programme to offer non-exclusive licenses to its cytochrome P450 patent estate. To date, Astex has announced license agreements with Pfizer Inc. and GSK.

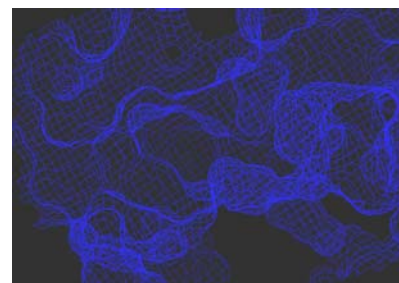


Scientific Advisors

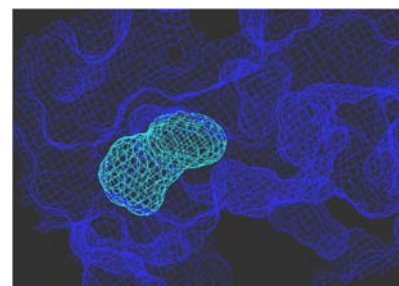
Prof Sir Tom Blundell FRS, *Uni. Cambridge*
 Prof Chris Abell PhD, *Uni. Cambridge*
 Simon Campbell CBE FRS, *ex-Pfizer, ex-Pres RSC*
 Barry Furr OBE MA (Cantab) PhD, *ex AstraZeneca*
 Prof Steve Ley FRS, *Uni. Cambridge*
 Dr. Herbie Newell PhD, *NICR Newcastle*
 Ian Skidmore MA (Oxon) PhD, *ex-GlaxoWellcome*
 Prof Robert Stroud PhD, *UCSF*
 Prof Ashok Venkitaraman MD, *Uni. Cambridge*

Clinical Consultants

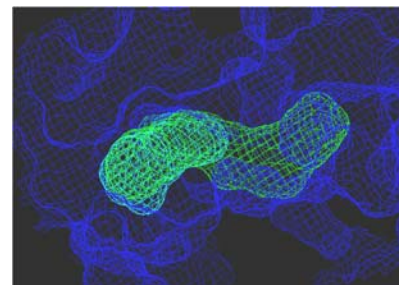
Prof Hilary Calvert MB Bchir MSc MD FRCP
 FMedSci, *NICR, Newcastle*
 Prof Stan Kaye BSc MD FRCP FRCR FRSE
 FMedSci, *Royal Marsden Hospital*
 Prof Ian Judson MA MB BChir MD FRCP, *Royal Marsden Hospital*
 Prof Hagop Kantarjian MD PhD *MD Anderson Cancer Center*
 Dr. Daruka Mahadevan MD PhD, *Uni. Arizona*
 Prof Bruce Ponder MB PhD FRS FRCP FMedSci
Uni. Cambridge
 Prof Lesley Seymour MD FCP(SA) FRCCP,
Queens University, Canada
 Dr. Daniel D. Von Hoff MD FACP, *Uni. Arizona*



Active site unoccupied



Weak fragment bound (mM)



Potent lead bound (nM)

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Contact Details

Astex Therapeutics Limited
 436 Cambridge Science Park
 Milton Road,
 Cambridge CB4 0QA,
 United Kingdom

Tel: +44 (0)1223 226200

Fax: +44 (0)1223 226201

Email: info@astex-therapeutics.com