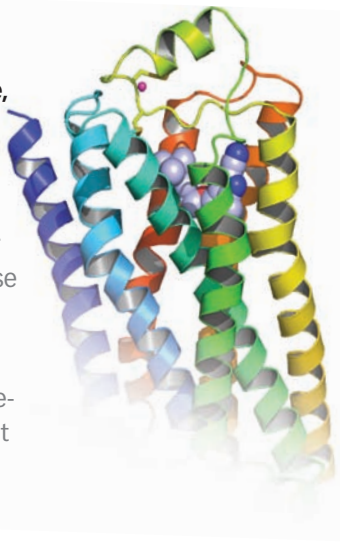
HEPTARES therapeutics

Heptares.com November 2011

Company background

Heptares is a pioneer in the discovery of new medicines targeting G-protein-coupled receptors (GPCRs). Leveraging its deep GPCR expertise and a revolutionary discovery engine, Heptares has built a powerful and fully-integrated drug discovery platform enabling it to generate a pipeline of first-in-class and best-in-class GPCR-targeted medicines, focused on CNS and metabolic indications.



GPCRs represent the single most important family of drug targets in the human body. Yet, due to their inherent instability when removed from cell membranes, little or no structural information about these valuable targets has been available to drive structure-based drug discovery programmes.

The Heptares StaR® (Stabilised Receptor) technology enables the first-ever thermo-stabilisation of GPCRs. This breakthrough allows Heptares scientists to resolve GPCR structures and deploy structure-based drug discovery techniques, such as Biophysical Mapping™, X-ray crystallography and fragment screening, to identify potent and selective drug candidates to previously undruggable targets.

Heptares has raised more than $40 million from leading life science venture investors and signed drug discovery collaborations with AstraZeneca, Shire, Takeda and Novartis.

Business Development

Heptares is leveraging its transformational StaR® platform to generate a broad and deep pipeline of first-in-class and best-in-class GPCR-targeted medicines. The Company is focused on advancing novel drug candidates, both NCEs and antibodies, in the areas of CNS and metabolic disease.

The scope of the opportunity using the Heptares approach extends well beyond its growing pipeline. Large and untapped regions of the GPCR target universe, previously regarded as undruggable, are now tractable for rational drug discovery using the Heptares approach.

The Company has established four major collaborations with pharmaceutical companies seeking access to this broader GPCR target landscape:

- Four-year collaboration with AstraZeneca (2011) focused on developing small molecule and antibody candidates targeting specific GPCRs linked to CNS/pain, CV/metabolic and inflammatory disorders.
- Exclusive option agreement with Shire (2011) for novel small molecule adenosine A_{2A} antagonist with best-in-class potential for the treatment of CNS diseases.
- Approximately $100 million drug discovery collaboration with Takeda was begun in 2011 focused on a GPCR linked to CNS disorders.
- $200 million option deal with the Novartis Option Fund (2009), focused on single GPCR target of strategic interest to Novartis. Novartis and Heptares jointly announced the successful first-ever stabilization of this previously intractable GPCR using the Heptares technology.

Expertise

Heptares was founded in 2007 to advance breakthrough GPCR discovery technologies originating from the MRC Laboratory of Molecular Biology (Cambridge, UK). These technologies are based on the pioneering work of the founding scientists Richard Henderson and Chris Tate, and of a wider group of MRC scientists, including Gebhard Schertler (MRC LMB), and Ed Hulme (National Institute of Medical Research, London, UK).

Heptares retains exclusive consultancies and active collaboration with LMB and has rights to all IP generated from LMB relating to the application of the technology to GPCRs and other transmembrane proteins.

The Company is led by a management team that combines world-class GPCR research and drug discovery expertise with proven biotechnology leadership experience. This team is further supported by leading venture capital investors and an expert scientific advisory board.

Management

Dr Malcolm Weir
Chief Executive Officer and Founder

Dr Fiona Marshall
Chief Scientific Officer and Founder

Dan Grau
President

Dr Barry Kenny
Chief Business Officer

Dr Miles Congreve
Head of Chemistry

Board of Directors

John Berriman
Chairman

Dr Richard Henderson
MRC Laboratory of Molecular Biology (LMB)

Dr Martin Murphy
MVM Life Science Partners

Dr Michael Steinmetz
Clarus Ventures

Dr Anja Koenig
Novartis Option Fund

Funding History

2009

$30 million raised in a Series A private round from Clarus Ventures, Novartis Option Fund and MVM

2007-2008

Seed funding from MVM

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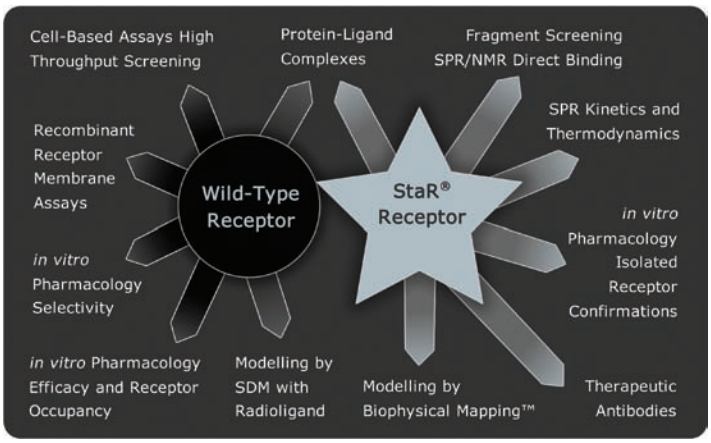
StaR® Technology

A StaR® is a stabilised GPCR containing a small number of point mutations that greatly improve its thermostability. StaR® technology is transferrable across GPCR families and allows the selection of stable, functionally relevant, purified conformations of targeted GPCRs that retain their drug-binding characteristics.

StaR® technology for the first time allows powerful, precision discovery methods to be applied to GPCRs.



StaRs®: an Enabling Technology for GPCR Drug Discovery

Pipeline

Heptares is deploying its StaR® technology, alone and in collaboration with partners, to discover new medicines enabled by proprietary GPCR structural biology:

THERAPEUTIC AREA	GPCR	INDICATION(S)	PROFILE
CNS			
	M1	Alzheimer's / Schizophrenia	First M1 subtype selective agonist. Marketed acetylcholinesterase inhibitors activate multiple muscarinic receptors indirectly and non-selectively, causing side-effects and limiting efficacy.
	Orexin	Chronic insomnia, anxiety and addiction	Novel dual orexin receptor antagonist with superior selectivity, safety and pharmacokinetic profile.
	mGluR2	Schizophrenia	Novel mGluR2 receptor positive allosteric modulator with potential best-in-class pharmacokinetic, safety, and selectivity profile. mGluR2 modulators offer a new mechanism of action with clinical efficacy in treating both positive and negative symptoms of schizophrenia.
	mGluR5	Anxiety	Novel mGluR5 receptor negative allosteric modulator with potential best-in-class pharmacokinetic, safety, and selectivity profile. mGluR5 modulators offer a new mechanism of action clinically validated in anxiety and related psychiatric disorders.
Metabolic			
	GLP-1	Type 2 Diabetes	First oral once-daily GLP-1 agonist. GLP-1 is a breakthrough mechanism for controlling glycaemia and reducing weight in type 2 diabetics. Current GLP-1 mimetics are injectables only.
Oncology			
	CXCR-4	Cancer / HIV	First oral once-daily CXCR-4 antagonist. CXCR-4 is a highly promising new target for treating cancer and other diseases. Alternative approaches are limited by their injectable routes of administration.

PARTNER	GPCR	ALLIANCE SCOPE
AstraZeneca		
	Undisclosed	Four-year collaboration (2011) focused on developing small molecule and antibody candidates targeting specific GPCRs linked to CNS/pain, CV/metabolic and inflammatory disorders
Shire		
	A_{2A}	Exclusive option agreement (signed in 2011) for novel small molecule adenosine A_{2A} antagonist with best-in-class potential for the treatment of CNS diseases.
Takeda Pharmaceutical Company		
	Undisclosed	In 2011, Heptares and Takeda signed an approximately $100M deal focused on a specific GPCR target linked to CNS disease
Novartis Option Fund		
	Undisclosed	In 2009, Heptares and the Novartis Option Fund signed a $200M, single-target alliance