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Heptares raises $21m as cognition candidate approaches clinic

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Heptares' latest funding round demonstrates that private companies do not need to rely on traditional venture funds to raise substantial amounts of money. A $21m Series B round announced today was co-led by the Stanley Family Foundation, a US non-profit group that supports research on schizophrenia and bipolar disorder.

The foundation was attracted by the British company's work on M1 muscarinic receptor agonists; Heptares has a molecule due to enter clinic later this year in cognitive impairment that it believes will overcome the off-target side effects that have stymied other candidates in this class. However, the money can be spent on other projects as well, chief executive Malcolm Weir tells *EP Vantage*, and the extra cash will allow a much broader programme of clinical work to commence.

Fast forward

Mr Weir says Heptares was not actively looking to raise another tranche of money; its needs were being met by the $30m Series A raised in 2009 plus revenues from the six development partnerships it has struck in the past couple of years with the likes of AstraZeneca and Takeda (*EP Vantage Interview - Heptares keeps up deal pace with Astra discovery pact, May 31, 2011*). The terms on the table, however, were considered too favourable to ignore.

"The financing was a result of general networking activities that we do all the time. There was a meeting of minds with the Stanley Family Foundation and current investors. We decided to take the money in and be able to do more with our pipeline. It enables us to deliver on a fuller business plan, and do some things we couldn't do otherwise," he says.

The round was co-led by the foundation, which in a rare step also took a stake in Heptares. Existing investors Clarus Ventures and Takeda Ventures also participated, and the company now has finance in place to take it to early 2017 under current plans.

As well as the cash, The Stanley Family Foundation also brings a wealth of networks and connections in the psychiatry field. Over the past 20 years, through its support of the Stanley Medical Research Institute, the foundation has provided more than $400m in research funding for various groups working on the causes and treatment of schizophrenia and bipolar disorder.

It is directing most of its cash towards psychiatric research at the Broad Institute of the Massachusetts Institute of Technology and Harvard University, which is working towards developing a comprehensive view of the molecular underpinnings of severe mental illness and attempting to elucidate any viable targets for new treatments.

Vote of confidence

Attracting a key player in neuroscience research represents a vote of confidence in Heptares' clinical plans, particularly as previous work with M1 muscarinic agonists in psychiatric disorders has failed to generate leads. Poorly selective agents discovered in the past also hit M4 and M3 receptors, causing tolerability issues in the gut that limited dose and capped efficacy.

"Preclinically we have seen a much improved profile and *in vitro* seen no impact on M4 or M3; [our molecule] is very clean. It gives us a great shot at getting an agent that can be dosed more appropriately," Mr Weir says.

The candidate was designed using Heptares' StaR technology, a structure-based drug-design platform that allows the company to create molecules that can very specifically target previously challenging G protein-coupled receptors.

Muscarinic agonism has long been a focus of research in neuroscience, and the biological importance of M1 receptors in cognition is well understood. They are present in relevant areas of the brain, while animal studies have demonstrated a correlation between their knockout and cognitive decline. Studies of previous M1 agonists have also shown promise, clinically validating the approach, despite their dose-limiting toxicities.

Heptares is already working with advisers on plans for phase I , looking for “smart ways” to show a therapeutic benefit, such as biomarker studies. Given that muscarinic agonism is well validated, Mr Weir believes that strong results from a well-designed phase I programme would be enough to start demonstrating the value in the molecule. The company now has the funds to take it into phase II, but will decide the path forward once data start emerging.

“There is a strong hypothesis for M1 agonism and if we have a selective enough molecule, it should work for cognition in Alzheimer’s and schizophrenia,” Mr Weir says. “It is less well known that schizophrenics also suffer a cognitive decline. Current drugs do nothing for that and in fact make it worse. So a treatment for cognition in schizophrenia is a high unmet need. If we find an agent to treat that directly, it will be a huge advance."

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