Cancer matchmaker

By Lev Osherovich, Senior Writer

As pharma increasingly look to offload early stage R&D expenses, **Cancer Research Technology Ltd.**, the commercial arm of biomedical charity **Cancer Research UK**, has seen more uptake of its partnered consortium model for commercializing the discoveries of its stable of academic researchers. This year, Cancer Research Technology has expanded its anchor collaboration with **AstraZeneca plc** by brokering two more deals between the pharma and academic teams.

CRT brings together researchers across the U.K. with similar interests and organizes them into teams to work on specific discovery projects, said CSO Clive Stanway. CRT's academic consortia focus on mechanisms in cancer that are potentially targetable but require additional tool building and proof-of-concept work before entering pharma pipelines.

Each consortium consists of academic researchers at four to six laboratories across the U.K. "We pick leaders and work with them to create plans and select other team members. There's a joint management team, and CRT has rights to the IP that comes out," said Stanway.

"We aim to have four or five consortia going at any given time," added CEO Keith Blundy. "Some of these projects might be about validating a target, some might be about medicinal chemistry."

Discovery work is done primarily at team member institutions. CRT provides administrative support and technical services such as medicinal chemistry on an as-needed basis. CRT is putting about \$1 million into each consortium to cover at least 2 years of work.

According to Blundy, CRT wants to be a one-stop shop for pharma and biotech seeking expertise and services in the cancer space. In exchange for upfront cash, a company receives the right of first refusal to new IP emerging from a given consortium.

In effect, the consortia serve as outsourced R&D units for pharma. This arrangement "aligns well with current pharma strategy to externalize research activity but retain access to early research, keeping an eye on a mix of projects in a variety of areas," said Blundy.

AstraZeneca is the first pharma to come on board. In 2010, AstraZeneca and CRT launched a jointly funded, three-year discovery-stage collaboration in cancer metabolism. Work on that project is underway at CRT's Discovery Laboratories facilities in London and Cambridge and at AstraZeneca's facility in Cheshire.

This year, the company signed deals with two CRT-managed academic research consortia focused on tumor cell senescence and lipid metabolism.

Essence of senescence

The first of AstraZeneca's 2011 CRT deals was with **Senectus**

Therapeutics Ltd., an academic consortium that spun out into a company. Senectus is seeking ways to trigger senescence or nonapoptotic growth arrest in tumor cells.

Senectus had its origins as a CRT-managed collaboration between researchers at the **University of Glasgow**, the **University of London**, **Cold Spring Harbor Laboratory** and research tool developer **Horizon Discovery Ltd.** In 2009, Senectus was incorporated. The company has since raised £1.2 million (\$2 million) from CRT.

"Cell senescence is a normal process that's a barrier to cancer development. It limits the growth of normal cells," said consortium leader W. Nicol Keith, a professor of molecular oncology at University of Glasgow. "Senescent cells don't die, but they don't divide. Cancer cells have latent senescent signaling, but it's either not at a high enough level or it's not engaging the final steps. We want to force cancer cells to reengage the senescence program."

Senectus is screening for markers of senescence in tumor cells, potentially targetable pathways and, with AstraZeneca's help, small molecules that hit undisclosed targets involved in senescence.

Keith said it is difficult to clearly define which cells in a tumor are undergoing senescence, thus making it hard to screen for agents that induce the process. The partnership with AstraZeneca provided access to the pharma's compound library, which Keith said allowed Senectus to validate its proposed screening strategy using newly identified markers.

"There was initially a barrier to convincing pharma that senescence was interesting, so we needed to generate the evidence," said Keith. After gaining access to AstraZeneca's small molecule library, "we showed them that we could get something sensible using their own reagents and they came on board."

Accelerated metabolism

In September, AstraZeneca and CRT assembled an academic research consortium focused on abnormal lipid metabolism in tumor cells.

That team is headed by Eyal Gottlieb, professor of molecular cell biology at **The Beatson Institute for Cancer Research**, and includes researchers at the **University of Oxford**, the **Babraham Institute**, **Imperial College London** and Cancer Research UK's **London Research Institute**.

"Rapidly growing cancer cells need to build a lot of lipids for cell membranes and organelles," said Gottlieb. The consortium aims to identify the specific lipids that are aberrantly produced in tumor cells and to find targets involved in their biosynthesis.

CRT and AstraZeneca each invested £300,000 (\$476,500) to fund discovery-stage work for 2 years, with AstraZeneca retaining right of first refusal to new discoveries.

A third CRT-managed consortium launched in January and is unpartnered. It is focused on cancer stem cells and received £500,000 (\$794,000) from CRT. That team is led by Fiona Watt, professor of molecular genetics and deputy director of Cancer Research UK's **Cambridge Research Institute**.

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COMPANIES AND INSTITUTIONS MENTIONED

AstraZeneca plc (LSE:AZN; NYSE:AZN), London, U.K.
Babraham Institute, Cambridge, U.K.
The Beatson Institute for Cancer Research, Glasgow, U.K.
Cambridge Research Institute, Cambridge, U.K.
Cancer Research Technology Ltd., London, U.K.
Cancer Research UK, London, U.K.
Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.

Horizon Discovery Ltd., Cambridge, U.K.
Imperial College London, London, U.K.
London Research Institute, London, U.K.
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