BIOCENTURY
3:01 AM GMT, MAY 6, 2017

FINDING GEMS IN INDIA

BY EMILY CUKIER-MEISNER, SENIOR WRITER

For **Agios Pharmaceuticals Inc.**, the decision to license molecules from Indian CRO **Aurigene Discovery Technologies Ltd.** was a special case intended to save time getting a new project off the ground, rather than part of a strategy of hunting for compounds in India or anywhere else.

For Aurigene, though, the deal is one step among many in an ongoing transition into a biotech with commercial ambitions.

On April 27, the partners announced that Aurigene had granted Agios exclusive rights to develop and commercialize a portfolio of small molecules that hit an undisclosed cancer metabolism target. The deal included a $3 million upfront payment and up to $17 million in milestones per program, plus low single-digit royalties for Aurigene, a subsidiary of **Dr. Reddy's Laboratories Ltd.**

Agios CSO Scott Biller said the deal grew out of an unrelated discovery collaboration between the partners that began in 2011. Biller, who had worked with Aurigene when he was head of chemistry at **Novartis AG**, recommended that Agios use Aurigene for that project.

"Because of the quality of the work it saved us a few of the steps in the chemistry that was done."

Scott Biller, Agios

He said Aurigene stood out among Indian CROs because it takes a Western biotech-like approach to drug discovery, employing cross-functional scientific teams that run the gamut of drug discovery capabilities, rather than specializing in individual tasks.

"Aurigene brings something unique to the table where they can very capably run an entire program. I think that's a special niche they fill," he said.

Biller said the initial project put the companies' scientists in regular contact. Through those connections, the companies realized that Aurigene had a series of molecules that hit a target Agios had identified as relating to a metabolite important in certain cancer types.

Aurigene had been studying the molecules for oncology and inflammation. In 2012, the partners began a collaboration to study them in cancer metabolism.

Agios used the molecules to build an understanding of the target biology in cancer and metabolism, and the target's role in specific tumor types. The biotech decided to in-license the molecules once it felt confident it had found valuable uses for them.

Though the target is undisclosed, Biller said it affects a different part of the metabolome than Agios' other cancer metabolism compounds with a "very orthogonal" mechanism. Agios' cancer metabolism portfolio includes molecules that target isocitrate dehydrogenase (IDH) enzymes and **methylthioadenosine phosphorylase (MTAP)**.

Biller said while Agios could have created compounds against the target itself, using Aurigene's existing molecules saved a "couple of years" of development time.

"This is a slight difference from what we've typically done, but because of the quality of the work it saved us a few of the steps in the chemistry that was done," he said.

Biller said Agios is open to similar types of deals but is not searching a specific region of the globe to find them. Instead, the company is scouring the literature and attending major conferences to look for ways its expertise in cancer metabolism, metabolic immuno-oncology and rare genetic metabolic diseases could complement the ideas or programs of another party.

BUILDING A BIOTECH

For Aurigene, the deal is one of several, with more to come.

"Aurigene pioneered a business model that was self-sustaining by building partnerships with leading pharma companies and biotechs in the US and Europe," Aurigene's CEO, CSN Murthy, said in an email to BioCentury.

He said those partnerships turned into relationships with five or six companies that have lasted at least seven years. A few of these collaborations have yielded clinical candidates.

Curis Inc. has in-licensed at least three products developed with Aurigene under a January 2015 collaboration, license and option agreement for immuno-oncology and precision oncology compounds. The most advanced compound is **CA-170**, an oral small molecule antagonist of **PD-L1**, **PD-L2** and **V-region immunoglobulin-containing suppressor of T cell activation (VISTA)**. It is in Phase I testing to treat solid tumors and lymphomas.

Aurigene and **Orion Corp.** began a research collaboration in 2007 and have announced at least three epigenetic oncology programs. The most advanced is **ODM-207**, a BET bromodomain inhibitor in Phase I testing to treat cancer.

Other partners include **Johnson & Johnson**'s Janssen Pharmaceutica N.V. subsidiary, **Debiopharm Group**, **Endo International plc** and **Laboratoires Pierre Fabre S.A.**

Murthy said in 2010 Aurigene had generated enough revenues from its partnerships to start building its own pipeline in oncology and inflammation. The oncology programs include small molecule checkpoint inhibitors and modulators of epigenetic targets. In inflammation it is focused on the Th17 pathway.

He said Aurigene's goal is to create first- or best-in-class products by choosing targets with strong biologic rationale that have proved difficult to drug. Aurigene has multiple approaches it can use to tackle them, including using peptides and peptidomimetics, small molecule non-covalent and covalent inhibitors and fragment-based screening.

The company employs roughly 270 chemists and 200 biologists whose specialties include medicinal chemistry, peptide chemistry, process chemistry and biochemistry, cell and molecular biology, structural biology, ADME/PK, pharmacology, toxicology and pharmaceutical development.

The company now hopes to bring programs through clinical proof of concept before seeking a partnership or co-development agreement.

Murthy said until now, Aurigene has kept rights in India and sometimes in Southeast Asian countries in its deals. Going forward the company may consider keeping rights in additional territories, including the U.S. or EU.

Aurigene plans to file INDs for two wholly owned programs in 1Q18: a **RAR-related orphan receptor C** (**RORC**; RORgamma) inverse agonist being studied to treat inflammatory disorders, and a selective covalent inhibitor of **cyclin dependent kinase 7 (CDK7)** being evaluated for cancer.

COMPANIES AND INSTITUTIONS MENTIONED

Agios Pharmaceuticals Inc. (NASDAQ:AGIO), Cambridge, Mass.
Curis Inc. (NASDAQ:CRIS), Lexington, Mass.
Debiopharm Group, Lausanne, Switzerland
Dr. Reddy's Laboratories Ltd. (NYSE:RDY), Hyderabad, India
Endo International plc (NASDAQ:ENDP), Dublin, Ireland
Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.
Laboratoires Pierre Fabre S.A., Castres, France
Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland
Orion Corp. (HSE:ORNAV; HSE:ORNBV), Espoo, Finland

REFERENCES

Ward, M. **"Metabolic drive."** *BioCentury* (2010)