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In India, Small Research Firms Aim Big

India is not known for developing drugs, let alone cancer drugs, but a few small and niche firms are trying exactly that, reports **Hari Pulakkat**

R&d WARRIORS: Team members of Aurigene Discovery, led by CSN Murthy, CEO (extreme right); and Monideepa Roy, associate director of Invictus, a startup focused on cancer drugs

Photo: AMRENDRA JHA

This February, the Bangalore-based drug discovery services company Aurigene Discovery Technologies signed an agreement with Pierre Fabre, a French pharmaceutical company. It was to develop into clinical trials a new molecule, called AUNP-12, supposed to be effective against several types of cancers. Although seemingly a minor announcement, it was loaded with implications. It was the first anti-cancer molecule that Aurigene has licensed. It was also the first molecule from India in an emerging class of cancer drugs, supposed to change the face of cancer therapy in the next decade.

Aurigene, a 100% subsidiary of Dr Reddy's Laboratories, was set up in 2001 to provide drug discovery services to other pharma companies, while Dr Reddy's continued its own drug discovery and development. This model initially hit roadblocks, but business improved later on. In 2009, Dr Reddy's transferred all its discovery-related assets to Aurigene and opted out of this risky activity. Aurigene now continues offering drug discovery services to external customers while doing its own drug discovery programmes.

In the last five years, Aurigene has spent Rs 200 crore on internal cancer drug discovery programmes. Now it spends Rs 50-60 crore every year on cancer drug discovery, and has seven molecules a year or two away from hitting clinical trials. They are in a hot new area: immunotherapy. This emerging area, which has seen the launch of the first few products recently, is expected to change the direction of cancer treatment. Although ridden with failures, drug discovery is still active in many Indian companies, but it is not often that a drug candidate out of India is licensed in an emerging area. Says CSN Murthy, CEO of Aurigene: "It was a significant event for us because it was a validation of our differentiated assets."

Although several global Big Pharma and biotech start-ups have immunotherapy molecules, Aurigene has a completely different class of them: peptides and peptidomimetics (molecules that mimic peptides). Aurigene is the only company in the world developing peptides against immune checkpoints, natural mechanisms that cancers hijack to evade the immune system. No one knows what kind of molecules, and in what combination, will be effective in cancer immunotherapy. But Aurigene's pipeline and the recent deal have brought it to the notice of the international drug discovery community.

Although drug discovery in India is two decades old, it has not yet set the industry on fire, and the global pharma market is still looking forward to a drug discovered in the country. But cancer drug discovery is not absent in India. Piramal Group, for example, has four molecules in clinical trials but none in areas that are completely novel. Now, a few smaller Indian companies are looking to wet their feet in unchartered waters. It is fraught with risks, but the rewards of success are extremely high.

New Templates

Consider Invictus Oncology, a Delhi-based company. It grew out of a Harvard research project, which developed a method to get a drug directly into cancer cells. The method is known as supramolecular chemistry, which consists of building molecular systems out of smaller components. It is like building a structure with Lego blocks, each individual block being a separate drug. A large drug complex can evade the healthy tissues, which have small pores, and go directly to the cancer cells. It is a powerful method in principle. No company in the market is using this method yet; not many are even exploring this method for cancer drugs.

Invictus was set up in 2011 with a total funding of $4 million from investment firms Navam Capital and Aarin Capital. It was then the first cancer-focussed drug discovery company in India. Instead of just using old molecules in a new way, it is also developing new molecules to be used with the new method. If the method works well, it would need an additional $20 million to take the drug to phase-II clinical trials, after which it needs to look for a partner. "It is a very audacious goal," says Ranjan Pai, CEO of Manipal Education and Medical Group, and an investor in Aarin Capital. "But if this is successful, people will realise that it can be done out of India."

The method of Invictus can be used with many existing drugs as well. Cisplatin, a powerful but toxic platinum-based drug that is now out of patent, can be made less toxic by supramolecular chemistry. Cisplatin goes through the kidney pores and thus harms this organ, while a fabricated Cisplatin-based larger molecule cannot go to any tissue but the cancer. Invictus is designing its own platinum drugs as well that are less toxic than Cisplatin. Says Shiladitya Sengupta, assistant professor at Harvard Medical School and Invictus co-founder: "We are developing a technology platform rather than a few drugs." The first of its drugs could be a year-and-a-half from clinical trials.

While we wait for Invictus to file an investigational new drug (IND) application, another Delhi-based firm is also readying an anti-cancer molecule. Curadev, set up in 2010 to do drug discovery, does services like Aurigene for its bread and butter while also working on its own programmes.

According to Arjun Surya, chief scientific officer of Curadev, the company has a few molecules under development, including for cancer immunotherapy, for which it has filed patent applications. The area of immunotherapy is so hot that Curadev had already got enquiries for acquiring this asset, but the company is pressing on to develop it on its own. With all these programmes now accelerating, no one should be surprised if an Indian anti-cancer molecule hits the market in a decade.

Indian Anti-Cancer R&D: a Timeline

Till 1990s
Cancer biology research in government labs, no attempt to make drugs

Early-1990s to 2000
Large pharma companies Dr Reddy's and Ranbaxy set up drug discovery units, focus on developing simple molecules and 'me-too' drugs. No significant cancer drug programmes, but the foundations are laid for future programmes

2000 to 2010
Indian drug discovery programmes struggle. Clinical trials start in India as a business, creating a skill-base for drug development. Biocon forms strategic partnership on cancer drug development with Cuban firm CIMAB

2000 to 2014
Some start-ups and small companies find promising anti-cancer candidates, raising the hope that an Indian molecule will move into clinical trials within the next four years