

EXPAND & DELIVER



Sigmoid CEO Dr Ivan Coulter

*How does a small drug delivery company overcome the catch-22 of having no research facilities? Sigmoid Pharma's strategy is to link with basic research groups in universities, writes **Claire O'Connell.***

Picture this: you have just started a small company with ambitious plans to tackle big issues in drug delivery. By developing new formulations, you could better control when and how therapeutic drugs get to their sites of action in the body, making some compounds more effective at lower doses, and possibly even reviving abandoned drugs that had been shelved during testing because of delivery issues.

But where does a small start-up get the resources to research and test out their innovations? One route is to link in with university groups, which can in turn benefit from industry exposure and moving their discoveries towards the market.

It's the type of partnership that has worked well for Sigmoid Pharma, explains CEO and co-founder Dr Ivan Coulter. "Sigmoid was a virtual company from the outset, and very early, we recognised the importance of collaboration, with the universities initially and then companies," he says.

DRUG TO TARGET Set up in 2003, the company develops new delivery platforms for drugs to better control their complex journey through the body. It's a journey that first captivated Coulter during his PhD in pharmacology at University

College Dublin and later working with nanotech company N'Tera.

"No matter what the drug is or how powerful it is, it doesn't matter, if it doesn't reach its target, it's not going to be much good," he explains.

Coulter sees three main problems around getting drugs to where they need to go. The harsh and variable environment of the digestive system means many drugs are destroyed en route. The therapeutic compounds may fail to breach the gut wall and get into the blood stream. Then if the drug molecules are clumped together, they won't be able to access their target receptors effectively.

He realised that technologies were being developed to help overcome the individual issues, but he decided to combine the solutions together in a single formulation.

"It's an idea I stole from the electronic sector," says Coulter. "Almost any device you pick up is a composite of different technologies that are bundled or integrated, and new uses are then made of those bundled technologies. So we set about trying to replicate that concept in drug delivery, to bundle technologies that address solubility, permeability and stability simultaneously into one more powerful and flexible technology."

The approach has spawned two delivery platforms: LEDDS and SmPill, formulations that harness signals – like acidity – from the bodily environment to control when the drug is released.

WINNING FORMULA A key part in developing the technologies has been the interaction with university-based researchers, says Coulter.

One of the first came about in 2005 when Sigmoid teamed up with Cormac Taylor, an associate professor at UCD's school of medicine and medical science, whose lab looks at hypoxia and inflammation in the gut.

"He had a lot of systems that we thought could teach us about what we are doing," says Coulter.

The collaboration, which was initially aided by a Science Foundation Ireland grant, has now culminated in a clinical trial involving patients with ulcerative colitis. Using Sigmoid's SmPill, an existing drug is being targeted to the colon as a potential novel treatment. The multi-centre phase II trial is due to finish in 2010, according to Coulter.

"The drug has been around a long time and has been used for other conditions," he says. "So it's tremendously exciting, and it exemplifies the translation of research."

That translation is a key motivator for Prof Taylor: "I trained as a research scientist and I love doing that, but I also see the importance of turning academic discoveries into useful products that are going to be economically and, more importantly for me, clinically useful agents," he says. "I don't have the skillset to take the discoveries to the marketplace, but Ivan can take the baton there."

Taylor also sees the merit in linking up with an Irish company. "If you really think it out, a big pharma coming in is great, but it's likely going to buy up some IP, it's not really going to induce a relocation," he says. One the other hand, he reasons that interacting with the small Irish companies that have been around for a while and are providing jobs here could lead to a more sustainable relationship.

The partnership is ongoing and Taylor sees his lab's role as an important one for Sigmoid's continuing innovation. "It's very powerful for a small company like Sigmoid to have a research arm. We can provide them with the pipeline research agents that may be the next generation of drugs," he says, noting that the area of inflammatory bowel disease offers plenty of scope for improved treatments. "It's a common ailment with quite severe pathology, and the therapeutic options for Crohn's disease or ulcerative colitis are not very impressive."

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CRACKING A TOUGH NUT Another area for the taking is oral vaccines, says Coulter. The harshness of conventional drug formulation and then the rollercoaster of the digestive system spell disaster for many delicate vaccines, but Sigmoid's approach to formulation is building up a track record in getting around those issues, he explains.

For its vaccine work, Sigmoid collaborates with Dr Ed Lavelle, who heads the adjuvant research group at Trinity College Dublin. Coulter and Lavelle had a rapid meeting of minds over the partnership, and their work is now showing that they can target oral vaccines to the gut and raise an impressive immune response.

"A lot of big companies dropped oral vaccination a long time ago; they thought it was too big to crack. So oral vaccine delivery is not for the faint hearted, and I am thrilled with the fact that we have succeeded after three years," says Lavelle.

"It shows that our research has got genuine application to make human vaccines, and it potentially gives us a system that will let us make oral vaccination that's much more relevant, and that other people haven't got, because we know the drugs have gone into the gut and not somewhere else."

As well as the Irish-based collaborations, Sigmoid is working with partners in the US, India and across Europe and targeting other areas such as graft-versus-host disease. "We want to work with people who can not only facilitate but contribute to the understanding," says Coulter. "And I've been lucky: with very few exceptions the people we have been working with are tremendous project managers and very open minded, and they push me as hard as I push them, so it's a real partnership."

Now based at the Invent centre at Dublin City University, Sigmoid has its own feasibility, formulation and manufacturing labs and employs 18 people, and Coulter forecasts a good year for 2010. "I see it as a year of consolidation and results and we will hit some important milestones," he says, stressing that simplicity can be the key to unlocking the potential of therapeutic drugs.

"As the molecular understanding of diseases has improved dramatically, it's leading to the development of much more powerful but more complex molecules that are more specific and powerful in treating these diseases," he says. "But where there is complexity, one always needs a simple solution, so that's why we develop them." 