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The Transition Year

Picking the lead candidates for Transition Therapeutics will be a decisive move for Tony Cruz, PhD

Transition Therapeutics Inc. isn't a company that sits back and lets things happen. This Toronto-based biopharmaceutical firm is all about action.

The company currently has three lead molecules, discovery programs for five validated targets and four products in clinical development for indications such as diabetes, Alzheimer's disease and hepatitis C. Over the coming year, Transition not only plans to move its candidates forward, but will also be looking to partner some of its products, and eventually branch out on the U.S. stock exchange.

And next 12 months will not only be busy, but also decisive for Transition. But Tony Cruz, PhD, Transition's founder and CEO, doesn't mind this busy juggling act.

"We know that it is a tough business," Cruz says. "And only one or two things that we have are going to work."

In an effort to protect its interests, the company has put its eggs into many baskets, trying to spread the risk around, while at the same time, increasing its chances of success.

"Based on the data that we're getting, we're going to put the emphasis on two of the leading technologies out of those (four or five). And that's where the company is going to put most of its money," he says. "What you have, I hope, is reduced the risk significantly with the little burn that you've had by having multiple programs, but I feel like now we have a much better chance of making it."

Broadening the Pipeline

Transition didn't always have such a broad pipeline. The company started in 1998 focusing on a cell's transition from a normal to a diseased state—work based on Cruz's research. *Biotechnology Focus* covered the company in those preliminary years in our April 2001 issue.

Early on, however, the company realized a shift needed to be made.

"We started the company in that area, and I think the data was very, very supportive, and still is," Cruz says. "The only problem is that in a new technology like that, it would take a long time to develop and to establish, and therefore Transition just did not have the kind of funds that are necessary to carry a platform of that nature."

The company changed directions, acquiring the Islet Neogenesis Therapy (I.N.T.™) from Waratah Pharmaceuticals Inc., which merged with Transition. I.N.T. has the ability to stimulate the regeneration of islets that are lost in both Type I and II diabetics.

Two candidates came out of I.N.T.: GLP1-I.N.T., which is currently in preclinical development for Type I and II diabetes; and E1-I.N.T., which is partnered with Novo Nordisk (Bagsvaerd, Denmark) and is in two exploratory Phase II clinical trials for both Type I and II diabetic patients.

Transition and Novo recently reworked the deal, which the two companies originally signed in August 2004. At the time, the arrangement saw Novo agreeing to develop the broad I.N.T. program.

Partnering with Novo was a strategic move that made good business sense, Cruz says. "Novo Nordisk is a very well-established company in diabetes . . . and they have a history in the diabetes program," he says.

Novo also had a GLP1 program (liraglutide) that had demonstrated good data in Phase II trials. The idea was that Novo would develop liraglutide and gastrin, and Transition would develop E1-I.N.T., which Novo would have access to.

The new arrangement has Transition essentially taking back the GLP1-I.N.T. program, as the current deal sees the company regaining exclusive ownership and rights to all I.N.T. programs, except for E1-I.N.T., which Novo is currently developing.

This amended deal sees Transition receiving \$1 million US this year from Novo, with future developmental milestone payments potentially totaling \$46 million US plus commercial milestones and royalties on sales of E1-I.N.T. products.

Earlier this year, Transition moved into a new area when it gained AZD-103—a disease-modifying agent that reduces the accumulation of amyloid beta in the brain, which in turn reduces disease progression and improve symptoms in Alzheimer's animal models — from its acquisition of Ellipsis Neurotherapeutics Inc.

Transition recently announced positive results from a Phase I clinical trial for AZD-103 in which pharmacokinetics, safety and tolerability of a single ascending dose were evaluated. The company received clearance from the U.S. Food and Drug Administration to commence a Phase I evaluating higher doses of AZD-103.

Heavy Hitters

Cruz says that when it comes to this strong product pipeline, Transition has benefited from some good choices.

"I think what we've done in this company is really acquired technologies that look like they have a lot of potential," he says.

But Transition isn't all about in-licensing existing products. The company also puts a focus on drug discovery.

"We also though there was a real opportunity with a drug-discovery platform that was able to now allow the company to decide what are the top five or 10 or 20 key targets in the world, and at the same time, be able to make a decision that we would like to develop a molecule for those targets . . . to then have a lead molecule that's targeted," he says.

The company acquired Optimol™, a technology that identifies and optimizes lead compounds in about six months, from Protana Inc. in 2005.

By identifying targets in six months rather than the traditional two to three years, Cruz says Optimol puts Transition in an advantageous position.

"We think, based on this technology, we can do it much faster, and therefore we would be in a competitive position with other companies that may be working in that same area," he says.

Optimol not only allows Transition to identify the targets faster, but to take advantage of a fast-paced industry, and move into new areas.

"When we see these very high-value targets that are licensed for fairly significant sums of upfront payments and milestones, we now can ask this group to look at developing lead molecules to similar targets," Cruz says. "I think that puts us in a position to be competitive in those areas.

"At the end of the day, the industry, to a large extent, is a 'me too' industry. If one's successful with one technology, everybody goes into that technology."

Seeing it Through

Cruz himself is adept at knowing a success when he sees it. On top of his academic research, Cruz was one of the co-founders of Angiotech Pharmaceuticals Inc. (Vancouver, BC) as well as the Canadian Arthritis Network—one of the Networks of Centres of Excellence.

Though in the past he admits his habit has been to start an endeavour and move on once it has reached a certain level of success, Cruz says Transition is one project he'd like to follow through on.

"This one here, I really would like to see a company in Canada, particularly in Ontario, that would be successful," he says.

"There's still a lot of work to be done in Transition to ensure that it not only leads to one successful product, but that it also has the pipeline as it moves forward that will continue to have more than one successful product."

Though he has his hands full right now, the plan is to have Transition become more focused in the next year.

"This really is a transition year for Transition," Cruz says. "We're picking the horses that we're going to bet on to move forward . . . so it really is a defining moment."