



BIOTECH, ALZHEIMER'S, DRUGS

Allon Treads Into the Great Unknown, Alzheimer's Disease, With New Kind of Drug

Luke Timmerman 4/6/10



It must take real guts, or maybe hubris, to try to do what [Allon Therapeutics](#) is attempting. This Vancouver, BC-based biotech company has designed a drug that is made to work unlike anything else on the market against some of the world's major neurodegenerative diseases, like Alzheimer's.

Scientists don't really know what causes Alzheimer's, and they don't have a consensus on what is going wrong at the molecular level that leads to the heartbreaking loss of cognition and memory that an estimated [4.5 million](#) people in the U.S. suffer from as they grow old. Quite a few biotech companies have failed with once-promising drugs for this disease—San Francisco-based Medivation (NASDAQ: [MDVN](#)), and Salt Lake City-based Myriad Pharmaceuticals (NASDAQ: [MYRX](#)) are a couple that leap to mind.

Yet Allon (UH-lahn) remains in the game, and CEO Gordon McCauley insists that things are still looking up.

“What I find fascinating about the standard of care today is that there is \$6.5 billion of drugs sold to treat Alzheimer's per year, and they all have one common characteristic. They don't do much,” McCauley says. “They have nasty side effects, and provide some relief from symptoms for about six months. There's a real opportunity for a therapeutic with disease-modifying potential.”

Allon (TSX: [NPC](#)) is placing its bet on what is known as the “tau tangle” hypothesis. For years, many researchers and drugmakers have been pursuing the notion that a buildup of amyloid beta plaques in the brain is the primary culprit causing Alzheimer's. Break up the amyloid, or prevent it from building up, and you can treat the disease. That effort hasn't borne fruit yet, McCauley says.

A dueling school of thought, which Allon has thrown its resources behind, says that key structural components of neurons, called tau, get broken up into fragments and form tangles as neurons die over time. That process happens when people don't produce enough of a couple proteins called activity-dependent neuroprotective protein (ADNP) and activity-dependent neurotrophic factor (ADNF). Allon's idea was to create a small peptide fragment, called davenutide, which is meant to restore that neuroprotective function. If it works as designed, the drug ought to prevent tau tangles from building up, and keep people's minds sharp.



Gordon McCauley

The Allon drug has been in some small trials to date, and McCauley characterizes them in a bullish way. The company ran a study that randomly assigned 144 patients with a mild form of cognitive impairment to get a low or high dose of the Allon drug or a placebo. This study didn't look at the main patient population of people with mild-to-moderate Alzheimer's, and it didn't measure one of the main goals that's usually required in an Alzheimer's study by the FDA—what is known as ADAS-cog. Nonetheless, Allon says it is encouraged because the study found a statistically significant improvement in the cognition score it used, that results were better at a higher dose, and that the results appeared to last—at least through the 12-week study duration.

Allon is hoping that study will entice yet another Big Pharma company to boldly step up with a plan to run the rigorous and expensive trials that will be required by the FDA for a new Alzheimer's drug. It also has some evidence from a study of 60 patients with schizophrenia which it says suggests there may be a cognitive benefit from taking davenutide. That trial didn't reach a statistically significant result on the main goal, although it did show such a benefit on a secondary score which measures things like whether a patient can manage their own transportation, banking affairs, and so on, McCauley says.

Last week, Allon released some imaging data which verified that davenutide was having an effect on a biomarker that's thought to be related to brain health—which might explain why schizophrenia patients appeared to be able to better function on davenutide.

Taken together, this is evidence McCauley says ought to provide a strong signal that Allon is onto something in treating neurodegenerative disease by preventing the buildup of tau tangles. And this is an avenue of research that all the major Big Pharma companies are pursuing in the early stages, along with at least one other biotech company, Singapore-based TauRx.

"We have a bunch of data that suggests this data is working on the tau pathology, and we'd argue ours is the most advanced tau therapy in the world," McCauley says.

Sounds great, but with a stock price of 56 cents as of yesterday, the world appears to want to see a little more proof. Allon has about \$11 million in cash, and access to a \$10 million line of credit. The company has about 20 employees, and a cash spending rate of about \$750,000 a month, McCauley said last month at the Life Science Innovation Northwest conference in Seattle. That means Allon has enough cash to be able to reach its next set of clinical trial milestones, he says.

One key catalyst would be whether Allon can secure a partner to help tackle monster markets like Alzheimer's and schizophrenia, which are too big for a small biotech company like Allon to handle on its own. What Allon is banking on for now is a classic rare disease strategy, in which it retains 100 percent ownership of the rights to its drug for a condition called progressive supranuclear palsy, which is a subtype of frontotemporal dementia.

This disease is attractive to Allon for a number of reasons. It's a severe cognitive disorder that's thought to affect a small number of people—about 20,000 in the U.S. There are no effective FDA-approved therapies. The diagnosis provides a clear homogenous patient population upfront, so there shouldn't be any confusion about whether it can enroll patients in a clinical trial with a consistent form of disease. And there are clinically-validated measurements which can say with a high degree of certainty whether the drug is actually helping—rather than a “surrogate” marker which is really an extrapolation that doctors use to try to suggest that a drug might be correlated with the kind of outcome the patient wants.

Given all of those factors, it's possible that Allon could persuade the FDA to go along with a proposal for a single clinical trial that could pave the way for U.S. market clearance. If Allon can prove that, it's possible that the company could be ready to file for FDA approval of davenotide for this disorder as soon as 2012. If—and this is still a very big if—Allon can get to that point, it will be in position to tap a market that's worth an estimated \$300 million a year, McCauley says, and it will have solid evidence that will give potential partners confidence to invest in trials for the really big markets of Alzheimer's and schizophrenia.

“This is the kind of indication that every biotech company dreams of,” McCauley says.

But aren't pharma partners scared off by the colossal failure of dimebon, from Medivation and Pfizer, in a pivotal clinical trial of Alzheimer's disease, even after it produced impressive data from a mid-stage trial? McCauley wouldn't say directly how that flame-out affected his company's partnership prospects, but he noted that it wasn't made to work on tau tangles.

“From our perspective, it has opened people's eyes to different approaches,” McCauley says. “At end of the day, we'll probably discover it's really a combination [of tau tangles, and amyloid plaques]. One causes the other, or it involves a feedback mechanism.”

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