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Interview – Accera next up in Alzheimer's disease

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Lilly's solanezumab might have blown up and erased $11bn in market capitalisation this week, but the potential reward from delivering a disease-modifying drug in Alzheimer's disease is too attractive for many companies to ignore.

Colorado-based Accera could have the next major data point in the space: readout of an early phase III trial of a treatment designed to feed impaired brain cells rather than limiting the damage from amyloid plaque, as most of the big pharma projects seek to do. "As of yesterday morning there were nine companies in phase III, and now there are eight in phase III, and only a handful of these are doing this with non-amyloid antibodies," chief executive Charles Stacey tells *EP Vantage* in the wake of the solanezumab readout.

Feed a cold, starve a fever

Accera's hypothesis follows a different track in Alzheimer's science than the amyloid hypothesis, as pursued by Lilly, Roche and others who believe that the characteristic amyloid-beta brain lesions are the primary driver of the disease. Accera's project AC 1204 is a bid to address another marker, impaired glucose metabolism, by supplying energy-starved neurons a different source of fuel.

That fuel is ketone bodies, and AC 1204 contains the active ingredient caprylic triglyceride, which can be metabolised into these molecules to replace glucose metabolism in brain cells.

Accera had tried this path when under a previous chief executive it launched caprylic triglyceride as a medical food called Axona. However, after an US FDA warning letter – the agency said it violated the definition of a medical food because Axona did not manage unique nutritional needs of Alzheimer's patients – the group shifted its focus to getting approval under an NDA. In clinical trials AC 1204 remains a powder formulation that is mixed with liquid or soft foods.

The clinical programme has focused on patients who test negative for the apolipoprotein E gene because of a signal seen in phase II trials. While this targeting could mean that AC 1204 will not be right for all patients, this is still a significant population – ranging from 36% in northern Europe to 50% in the US and 68% in Asia.

Buying six months

The group's first phase III trial, Nourish AD, completed enrolment in May and full results are expected next year. If successful, the data will provide support for designing a pivotal trial that Accera hopes to initiate later in 2017.

Nourish AD has enrolled 420 mild to moderately impaired patients already on Alzheimer's medications randomised to take AC 1204 or placebo for six months, determining changes in cognition using the Adas-Cog measure and a global impression of change rating.

A phase IIb trial found that patients taking AC 1204 had seen a decline on Adas-Cog 3.4 points less than that of patients taking placebo, and the hope is that this first phase III will detect at least a two-point difference to be clinically meaningful. "We think that should be easily achievable," Mr Stacey says.

What would a two-point difference mean for patients? "For a mild to moderate patient you expect them to decline in Adas-Cog score somewhere between four to five points in the course of a year. Essentially what two points means is you are reversing six months of decline."

If successful, AC 1204 would have an advantage over antibodies like Biogen's aducanumab and Roche's crenezumab and gantenerumab, which are being studied to block amyloid beta accumulation in the brain – namely, a lower cost of goods that could translate into a lower price. "We're going to be a small molecule, and we'll price like a small molecule," he says.

However, if it can show a six-month delay in disease progression a value-based pricing argument could be employed because institutional care might be delayed.

"We know that dementia is the most expensive disease indication in the US. We know that it costs the

healthcare system $250bn a year," he says. "By far the majority of that is long-term care. If you decrease that by 10%, 20%, 30%, that has a meaningful effect on the overall costs."

Accera has been backed for years by Nestlé's venture capital arm, Inventages, and also Nestlé's health sciences division, which has provided most of the funds to get AC-1204 to phase III. That would make the food-products giant an obvious buyer in the case of positive data, although Mr Stacey says, "They're an investor. They have no benefits over any other investor. At the same time, clearly, there is an interest."

A buyout would be one possibility should Nourish AD return positive results, with licensing or seeking an IPO among other options the group will be able to consider, Mr Stacey says.

But, for those options to emerge, AC 1204 will have to show something that few other projects have been able to – a meaningful effect on Alzheimer's disease.

Study	**Trial ID**
Nourish AD	NCT01741194

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