Charles Stacey – President & CEO, Cerecin (November 2018)

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Dr Charles Stacey, president and CEO of Brain Health company Cerecin, formerly Accera, discusses the rebrand, new investment, the company's relocation to Asia, and the upcoming rollout of a global Phase III clinical trial for its innovative new Alzheimer's drug.

These are exciting times for the company with a new investment boost of USD 50 million, a rebrand from Accera to Cerecin and an expansion that sees the move of your global headquarters from Colorado to Singapore. Can you begin by outlining the rationale behind this move and the potential impact of these changes?

We have been based in Colorado since the early 2000s, quietly plugging away developing our therapeutic platform primarily for Alzheimer's Disease (AD) but also for other neurological indications. We have taken our technology through a fairly traditional development path – pre-clinical outlook models, Phase I, Phase II and preparing for Phase III.

The company is now approaching a significant phase in its development. On the clinical side, we are preparing for a very large global Phase III study for our AD drug which will require coordinating clinical trial sites across the world. Operationally there was a need to have a base outside of the US.

Our previous clinical trials have shown that our compound has a particular effect on patients who do not possess a particular gene. That genotype is more prevalent in Asian people, so it makes sense that we run a large proportion of our clinical trials there where our medicine will be more effective.

On the manufacturing side, the predominant raw material that goes into our drug compound is derived from palm and coconut oil, which mainly grow in this part of the world, especially in Malaysia and Indonesia. Therefore, in terms of future manufacturing partnerships, it makes a lot of operational sense to be here.

The third piece of the puzzle is around commercialization. In the US, we have a commercial medical food product – Axona – for the dietary management of patients living with mild- to moderate-level AD. This product has been on the market for around eight years and we plan to launch it across Asia. It, therefore, makes sense to be closer to our Asian commercialization partners to be able to support and manage them throughout this rollout.

Within Asia, why did you choose Singapore as a base?

As a small, innovative biotech company, we are looking for three things: good science, good talent and capital. Singapore has all three. It has world-class science and scientific institutions that we can draw from in terms of support as well as building out our pipeline. On the talent side, Singapore is the regional centre for most of the Big Pharma companies and most of the big CROs, meaning that there is a lot of talent here to draw on. The majority of venture capital is in the US and the public funding sources that would understand this degree and specialisation of drug development tend to be in the US. However, there is a fair amount of life sciences venture capital in Singapore as well as government support in terms of grants and other forms of support.

Singapore is English-speaking, very friendly towards international companies and has world-class corporate governance. Another important factor is its proximity to some of our key markets such as China, Korea and Japan, without the complexities of doing business in those countries.

How are you planning to execute your upcoming global Phase III trial and avoid the blowouts at that stage that so many other companies have faced with AD drugs?

As a smaller company, we will obviously be leaning heavily on CROs for this trial. In terms of

preparation, setting up this Singapore base and building up our clinical operations team is key. We are also doing a number of preparatory studies before embarking on the trial.

In terms of why so many companies have failed at the Phase III stage, I feel that the industry has focused too heavily on amyloid as a drug target. Amyloid is for sure a piece of the puzzle but is almost certainly not the only piece. As a community, we are recognizing the need for mechanistic diversity and to examine other targets.

Another contributory factor to previous Phase III failures has been the rush to these trials with programs that have not been adequately de-risked. Because there are so many AD patients and such a need for therapeutics, the market is enormous. Therefore, Big Pharma sees the dollar signs and rushes into these trials.

From a clinical strategy perspective, my team and myself know that we cannot afford to do multiple Phase III trials – we need to do one and get it right. These preliminary studies may take a couple of years to complete but they will allow us to de-risk the eventual Phase III study as much as possible. We are carrying out smaller clinical trials to get our protocol as tight as possible so that when we do launch the Phase III trial itself, we will have a sound operation base, a team to execute on it, and a CRO with a global reach that will best serve our needs.

How have you de-risked your upcoming Phase III trial?

Risk can be thought of in many ways. Clinically, there are a number of standard steps that can be taken to ensure as much risk is taken out as possible. We have taken some of these steps already in terms of formulation and protocol, but we are constantly looking at how we can improve and make our studies more operationally robust. With clinical trials, it is all about variance of data. Therefore, as we move into a very large Phase III, we are looking to ensure our data are as clean as possible, our patient group is as tight as can be, and our clinical trial sites are selected to offer as little variance as possible. Every country you add brings different issues in terms of language variations and endpoints, which ultimately make Phase III studies in AD especially complex.

In Phase II and III trials, the aim is to prove efficacy but also safety. Our program is de-risked in that sense because our active ingredient – although a small molecule drug – is derived from palm or coconut oil, a food source. Many previous drugs have failed at this stage simply due to safety and toxicity concerns, whereas our safety profile is very good.

Another, often overlooked, piece of the puzzle is the commercial risk inherent in many programs which we do not have. Some of the antibodies being developed for AD are hugely expensive programs and the drugs – should they prove successful clinically – will face serious challenges commercially. If a drug potentially costs tens of thousands of dollars, added to infusion and monitoring costs, and aims to serve two million patients in the US alone, the costs will be astronomical. Even if efficacy is proved, to actually get payers to reimburse that drug will be a tall order. Can the company demonstrate adequate efficacy to justify these costs?

We are fortunate in that as we are developing a small molecule drug – while we have not yet specified a potential price – from a commercial perspective, it is de-risked compared to some of the biological therapies being developed.

Tell us about your financing. Even with the new cash injection, the launching of a global Phase III trial entails a high cash burn rate.

As a private company, our financing to date has been through venture capital and equity investment from partners. The majority of that investment has come from Inventages, the venture capital arm of the Nestlé group in the form of equity. Our recent big announcement was that Wilmar has come in alongside Inventages as an equity investor. We take investment for one stage at a time and currently are fully funded until our next inflection point, which is the rollout of our Phase III program. That said we are always looking to speak to interested investment groups.

For the next round of investment, we are looking at the various funding options available: raising money privately from current investors as well as new private investors as well as raising the money publicly. Several companies with Phase III-ready AD assets have raised the money for their studies via the public markets. The third funding option is Big Pharma – either via an outright acquisition or through a sponsorship of the Phase III program for some sort of rights in return. At this stage, it is important for a company like ours to keep all options open!

Given that your current partners are not from the world of Big Pharma, what do they bring aside from capital?

Nestlé, via Inventages, has been an investor for a number of years and has identified healthcare as an important strategic direction, creating a sizeable life sciences group in the form of Nestlé Health Science, the CEO of which comes from the pharma industry. As one of the biggest medical nutrition groups in the world, they have a deep knowledge of that market and capabilities across clinical and product development as well as commercialization which we can draw upon. We are independent of Nestlé, but we benefit from their expertise and have representatives of both Inventages and Nestlé on our board of directors.

Wilmar brings a deep knowledge of agricultural manufacturing and the oleochemical industry. They also have a strong knowledge of the Asian markets and a very deep distribution network across Asia.

For a company like ours, the traditional path is to have partnered with Big Pharma by this stage out of necessity more than anything else – the capital required to reach this stage is significant. However, this is always done with the recognition that the smaller company is limiting its options with regards to eventual acquisition and partnerships. We have been very fortunate that we have been able to get to where we are without this limitation. Now, when we look for clinical or commercial partners, we have the full suite of options open to us and can choose the partner that serves us best rather than being tied to a previous funder.

What is the rationale behind the rebranding from Accera to Cerecin?

The name Accera has served us very well, but this is an exciting new stage for the company, moving to a completely different part of the world, building a new team and engaging with new partners. Therefore, we decided to mark this inflection point with a rebrand. By embarking on this next stage of our program, we are now thinking more broadly. AD has dominated our clinical program for a long time, but we have great science, a great team and great fundamentals that we are now looking to leverage across other assets. We are starting early-stage programs for other

indications within neurology and we are also looking to in-license other assets. Therefore, the company now has a broader commitment to neurotherapeutics and the entire brain health space. The rebranding recognizes and reflects that – Cerecin is a melding of ‘cerebrum’, the Latin word for brain, and ‘medicine’.

Axona is your only product currently on the market. What do you see as its role in AD care?

Axona is a medical food, on the market in the US since 2009, for the dietary management of mild to moderate severity AD and there are a number of patients that take it routinely. Our previous clinical studies have demonstrated efficacy behind the product.

We are often asked whether the medical food is a stepping stone to the drug and whether the two can co-exist. Alzheimer’s is an unusual disease in that there is now recognized to be a very long prodromal phase – the very early form of the disease when memory is deteriorating but a person remains functionally independent. AD patients tend to be diagnosed in their mid-60s or 70s but the prodromal phase, when the pathological changes are happening in the brain, can start two or three decades beforehand in patients at risk of AD in their 30s or 40s.

While the drug product will be approved be for patients with mild to moderate AD who have already been diagnosed by their doctor, for us, there is a broader question: if these processes start in the brain, is there a biological need for some sort of therapeutic product earlier in the disease course? If there is, then what does that product look like? It is entirely possible that this product will not be a drug product at all. That is where we see the potential for a nutritional therapeutic such as a medical food to treat this huge number of patients at risk- thereby providing therapeutic benefit but in a different format and price point to a drug.

To what extent do Cerecin’s therapies represent a reconfiguration in the approach to Alzheimer’s?

Our approach is very different. Cerecin ultimately is looking to tackling the whole spectrum of cognitive decline; preventative care through Axona and the disease state with a de-risked, small molecule drug about to go through Phase III. All this is good news for payers with overstretched budgets looking for novel solutions. We are fortunate that our investigational drug is a small molecule and can be priced accordingly, we hope to be able to have an impact on many AD patients and ultimately curtail some of the phenomenal costs associated with the disease.

What is your main challenge ahead?

The main challenge will be executing our plans and making sure that we are ready to roll out our Phase III trial. We are standing at a critical juncture and I am spending a lot of my time recruiting the right team and laying the foundations for success. We are embracing these challenges. At the end of the day, we have one of the most exciting current assets in AD that is differentiated and de-risked and could bring considerable benefits to millions of patients worldwide.

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