Charles Stacey â?? President & CEO, Cerecin

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Charles Stacey, President and CEO of Cerecin, discusses the companyâ??s strategic direction and partnerships as it advances its Alzheimerâ??s treatment into Phase 3 trials. He highlights the importance of collaboration with global contract research organizations and large vendors during the clinical development phase. Stacey also shares insights into Cerecinâ??s approach to commercialization, emphasizing the companyâ??s commitment to delivering the treatment to patients and physicians effectively.

When we last spoke four years ago during the COVIDâ??19 pandemic, you had paused the Phase III trial of tricaprilin in Alzheimerâ??s and were optimistic about restarting afterwards. Could you walk through the key developments since then?

Since our last conversation four years ago, the Alzheimerâ??s landscape has transformed significantly and so has our work at Cerecin. First and foremost, several new therapies have gained approval. For physicians and patients, these approvals are vital: after roughly two decades without a single approved Alzheimerâ??s treatment, having options restores hope and underscores the importance of our mission.

From an industry standpoint, these approvals signal that regulators are willing to collaborate closely with companies to find solutions. They also reflect our improved understanding of Alzheimerâ??s biology and the measurement tools now available to define and track meaningful clinical endpoints.

Finally, these successes have reignited investor interest. Both large pharma and venture investors recognize that progress and even modest commercial returns are essential to sustaining a healthy ecosystem. When backers see clear potential for impact and return, they are more inclined to support pioneering approaches like ours.

In short, the approval of new drugs has injected fresh optimism into the field. It validates our efforts, reassures our investors, and motivates us to advance tricaprilin toward patients in 2025 and beyond.

Cerecinâ??s lead molecule is being evaluated across multiple indications Alzheimerâ??s, infantile spasms, migraines, and more. Could you provide an update on its current clinical progress?

When we last spoke during the COVID-19 pandemic, we had planned to initiate our Phase 3 trial. Recognizing the challenges of enrolling vulnerable elderly patients during a global health crisis, we made the prudent decision to pause the trial and focus on our earlier-stage programs. Since then, we have resumed our efforts and last year, we initiated our Phase 3 trial, called ALTER-AD. Recruitment is set to begin this year, involving nearly 100 clinical trial sites worldwide, with a focus on the United States, Canada, and Asia, including Korea, Singapore, and Australia.â??

Our drug specifically targets a genetic subgroup of Alzheimerâ??s patients, thenon-carriers of the APOE4 allele. This subgroup is disproportionately represented in Asia, comprising up to 65â??70% of the Alzheimerâ??s population there, compared to about 45 percent in Western populations. This demographic distribution not only facilitates recruitment but also indicates a potentially larger market in these regions. Additionally, many APOE4 carriers are often enrolled in other studies, so focusing on non-carriers allows us to address an unmet need and streamline our operational efforts.

Recruitment is scheduled to begin at the end of this year. We anticipate approximately 12 months for setup and preparation, followed by an 18 to 20-month recruitment period. After that, there will be a six-month treatment phase. Overall, the study is expected to span about three and a half years, which is fairly standard for neuroscience trials.â??

We are hopeful that there will be significant interest in the study. It involves a novel mechanism, targeting the metabolic deficit that is known to underpin Alzheimerâ??s, and is a first-in-class drug. As previously mentioned, the burden on patients is minimized as much as possible. We are encouraged by the enthusiasm we have seen in similar programs.

How is your team positioned to ensure Cerecin is ready to execute such a large multiâ??country trial across numerous sites?

We are fully aware of the operational, financial, and regulatory complexities involved in conducting a multi-country trial across numerous sites. However, I can confidently say that we are well-prepared to execute this large-scale study.

Over the past 12 months, we have dedicated significant time to planning and setting up the trial. This preparation ensures that once we begin enrollment, we can proceed efficiently. We have identified key geographies and completed the necessary regulatory work to facilitate the distribution of our investigational material to those sites.

Collaboration with our investigators has been a priority. We have worked closely with them to ensure a unified and consistent approach to assessing the study. Their enthusiasm mirrors our own, which is crucial for the success of the trial. We believe there is good reason for this excitement.

This study is our lead program and holds critical importance for us. Concurrently, we recognize a broader trend of increasing interest in neurology and the metabolic space. Positioned at the intersection of these fields, we are, to our knowledge, the only company focused specifically on neurometabolism. This unique position has allowed us to bring in new assets, some of which may have immediate potential.

Patient recruitment in Alzheimerâ??s is particularly challenging. However, with new diagnostic tools thereâ??s significant potential to improve patient identification and trial outcomes. How do you see diagnostic advancements influencing clinical trial strategy in the coming years?

The advancements in diagnostic tools are truly transformative for Alzheimerâ??s clinical trials, impacting both patient engagement and trial design.

On one level, we now have a range of tools from consumer-facing cognitive assessment apps to sophisticated imaging techniques like new forms of PET scans. These tools are crucial for early detection and increasing awareness about cognitive health. In the past, many individuals hesitated to seek a diagnosis, feeling that there were no effective interventions available. However, with the emergence of new treatments, ongoing clinical trials, and lifestyle interventions that can significantly alter risk profiles, both patients and physicians are more proactive. These tools not only facilitate early diagnosis but also encourage participation in clinical trials and sustained engagement throughout the study.

From an operational standpoint, the ability to accurately identify and select appropriate participants has significantly improved. Utilizing accessible, cost-effective, and reliable diagnostic tools ensures that we are enrolling the right individuals, which enhances the quality and efficiency of our trials. This precision in participant selection leads to better-designed studies that are quicker to execute and yield higher-quality data.

Previously, the distribution of trial sites was often constrained by the availability of specific imaging or diagnostic resources. For instance, conducting studies in certain regions was challenging due to limited access to amyloid PET imaging. Now, with the broader availability of this and new technologies, we can expand our trials globally. Take South Korea, for example; despite its population of around 50 million, it boasts one of the highest per capita uses of amyloid PET imaging worldwide. Physicians there are highly advanced and quick to adopt new technologies, and the cost of PET imaging is approximately one-third of that in the United States. This accessibility not only facilitates easier recruitment but also enhances the overall quality and efficiency of studies.

In summary, these diagnostic advancements are reshaping our approach to Alzheimerâ??s clinical trials, allowing for more precise participant selection, improved trial design, and the ability to conduct high-quality studies on a global scale.

What potential do you see for digital tools such as AI and decentralized trial models in reducing patient burden and improve trial accessibility?

This is a significant factor in our approach. In neuroscience trials, it is essential to maintain rigorous standards, incorporating various interventions such as imaging, diagnostics, and cognitive assessments across multiple time points. However, we must balance this rigor with the realities faced by our patient population. Many of our participants are elderly and may experience confusion or discomfort when taken out of familiar environments for extended periods. Therefore, our challenge is to design studies that are both scientifically robust and considerate of patient and physician burden.â??

Fortunately, the design of our drug and the data we have gathered allow us to conduct studies with relatively low patient burden. Our study treatment period spans six months, which is shorter compared to some of the recent studies for anti-amyloid therapies requiring 18 to 24 months. We also have fewer imaging requirements. Our therapy is a liquid emulsion taken orally twice daily, contrasting with treatments that necessitate bi-weekly infusions. While we do perform imaging to monitor for side effects like ARIA, our overall safety monitoring is less intensive.â??

This approach has implications beyond clinical trials. Even with the approval of new drugs, patients often face significant burdens related to administration and monitoring. Our therapyâ??s oral administration at home, combined with an expected favorable side effect profile and minimal safety monitoring, is a compelling proposition. Physicians we consult are enthusiastic about these aspects, as they align with the needs of patients and the practicalities of treatment.

Multiple Alzheimerâ??s therapies have shown only moderate efficacy and now face pricing and approval challenges. Do you view the current market as broadly bullish, or is the reality more nuanced?

You are correct to point out that while recent developments in Alzheimerâ??s therapies are encouraging, the efficacy demonstrated has been modest. The approved drugs target specific patient populations in the early stages of the disease and offer only limited efficacy. They also come with challenges, including high costs, intravenous administration, and notable side effects.â??

Despite these limitations, I view these advancements as a positive shift in the field. Historically, we have seen similar patterns in other therapeutic areas, such as HIV/AIDS and oncology, where initial treatments had limited effectiveness and significant issues. However, these early steps paved the way for more effective therapies over time. I believe we are witnessing a similar evolution in Alzheimerâ??s research.â??

These developments have renewed interest and investment in the field, encouraging companies to pursue further research and development. As we continue to improve our understanding of the disease and refine our approaches to treatment, I am optimistic that we will see more effective therapies emerge.

In our last conversation, you noted that the field has been too focused on amyloidâ??targeting therapies. How does Cerecin explore a more diverse set of targets and mechanisms?

Over the past couple of decades, the field of Alzheimerâ??s research has experienced numerous setbacks, particularly with therapies targeting amyloid. These challenges have underscored the importance of not concentrating solely on a single target, especially in a disease as complex and heterogeneous as Alzheimerâ??s.â??

We now understand more clearly that Alzheimerâ??s is a multifactorial disease. It is not just about amyloid. Tau protein, inflammation, and metabolism all play significant roles in disease progression. Focusing only on one of these elements has limited our ability to make meaningful progress. Fortunately, about five to ten years ago, we began to see a shift in thinking. There was a call for greater mechanistic diversity, and we saw more support both from government and private investors for early-stage development of therapies based on different mechanisms.

At Cerecin, our focus is on addressing the metabolic aspects of neurological diseases. Our lead compound, tricaprilin, is designed to increase brain metabolism by providing an alternative energy substrate, ketone bodies. These ketones are utilized by neuronal mitochondria, converting them into acetyl-CoA, which then enters the citric acid cycle to generate ATP. In Alzheimerâ??s disease, one of the earliest detectable changes is a decline in glucose metabolism in specific brain regions, such as the parietal and temporal lobes and the posterior cingulate. This hypometabolism can be observed even in individuals in their 30s who are at risk for Alzheimerâ??s.

Tricaprilin is efficiently metabolized in the liver into ketone bodies, which serve as an efficient energy source for neurons, potentially compensating for the deficits caused by impaired glucose metabolism. This approach aims to support neuronal function and address one of the diseaseâ??s underlying mechanisms

We have observed a growing recognition among clinicians of the need for multifaceted treatment strategies. Much like in oncology, where combination therapies are standard, there is an understanding that Alzheimerâ??s may require multiple therapeutic targets. Some patients may benefit more from amyloid-targeted treatments, while others may respond better to metabolic interventions. Our goal is to contribute to this diversified therapeutic landscape, providing options that address the various facets of Alzheimerâ??s disease.

With the muchâ??anticipated readouts for GLPâ??1 diabetes and obesity therapies due later this year, how do you expect these results to influence the treatment landscape?

It is an exciting time in this field. Over the past five years, there has been growing enthusiasm around GLP-1 therapies. These drugs modulate and optimize metabolism, showing effects across various chronic diseases, particularly those related to metabolic dysfunction. It is encouraging to see companies like Novo Nordisk conducting studies in Alzheimerâ??s disease. For us, this approach aligns with our focus, as we have been working on metabolic interventions in neurology for 20 years. When larger companies enter this space, it brings more attention to the field, and we welcome comparisons, even though we have been dedicated to this area for decades.â??

With regulators criticized for approving amyloid therapies on preliminary data despite limited efficacy, what reforms would you like to see from regulatory agencies to strengthen the approval process?

I believe the key is staying closely aligned with regulators throughout the entire process. Regulators want to see that companies are thoughtful in their approach and that there is a clear rationale behind every decision. They are experts in their field and are very cautious, always prioritizing patient safety and well-being.

It is important for us to stay in close communication with regulators, ensuring they are aware of our actions and that what we are doing is relevant to both them and to patients and physicians.

You are correct that regulators have faced significant scrutiny in recent years, particularly with regard to drugs that were approved early despite limited evidence of efficacy. I understand why this has led to criticism. However, it is an incredibly challenging space. There is immense pressure to make progress, but that needs to be balanced with ensuring safety and efficacy.

The honest answer is that this situation represents a step toward improving the approval process. It is a learning experience that will help us refine our approach and ultimately develop better drugs with alternative targets, advancing the field while keeping patient care at the forefront.

Partnering is essential for biotechs from CROs and service providers to commercialization partners. What key partnerships does Cerecin have today, and which new collaborators do you expect to bring on board over the next four years?

At Cerecin, we are still a relatively small company, but we have a broad geographical reach. Partnerships are crucial for us, especially as we move into Phase 3 of our Alzheimerâ??s disease study. For this, we work with global contract research organizations (CROs) and large vendors who bring the necessary reach and experience for Phase 3 trials. Their expertise is vital, particularly for a challenging condition like Alzheimerâ??s, where experience in conducting these types of studies is key.

In terms of commercialization, we made the strategic and financial decision to take our Alzheimerâ??s program all the way through Phase 3 to approval. By doing this, we maintain the flexibility and optionality to determine the best way to make our treatment available to patients and physicians â?? be that with ourselves, with a partner or a mix. Ultimately, we recognize that Alzheimerâ??s is a widespread global disease, and large pharmaceutical companies, with their established sales forces and networks, are well positioned to lead in terms of patient access.

We maintain ongoing relationships with most of the major pharma companies and are encouraged by the growing interest in metabolic approaches in neurology and Alzheimerâ??s disease. Many companies that had previously stepped back from the area are now increasing their involvement, and we expect this trend to continue over the next few years. We stay in regular contact with these companies, and they are aware that we are entering Phase 3. Some have already shared their thoughts on our trial design, and we keep the lines of communication open.

Once we have data from our trials, we hope to continue these discussions with potential partners to explore opportunities for collaboration, either globally or in specific regions. Ultimately, our goal is to get our treatment to patients as quickly as possible.

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