Tiziana Plans IND for Intranasal Alzheimer's Treatment with Promising CNS History

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Tiziana Life Sciences plans to submit an Investigational New Drug Application for a Phase I trial studying intranasal formulab, a novel treatment option for Alzheimer's Disease, the company **announced** Wednesday.

Intranasal formulab, also known as anti-CD3, is unique among CNS-related treatment options because of the way it is administered and the way it reacts in the body by naturally inducing regulatory T cells. The treatment has already shown promise for patients with other CNS-related inflammatory diseases.

Dr. Howard Weiner, co-director of the Ann Romney Center for Neurologic Diseases at Brigham and Women's Hospital at Harvard Medical School, told *BioSpace* he believes an intranasal mechanism of action is a "very broad approach to treating neurological diseases."

Two patients with secondary progressive multiple sclerosis (SPMS) previously **showed clinical improvement** with the drug as measured by the Expanded Disability Status Scale (EDSS) after being administered the treatment over a six-month period.

With few treatment options available for patients specifically with SPMS, instransal foralumab presents a promising possibility for advancement against this CNS-related inflammatory disease.

"What makes it different than other anti-CD3s that have been out there is the fact that it's fully human and it's delivered locally," said Dr. Matthew Davis, RPh, chief scientific officer and chief medical officer of Tiziana Life Sciences.

He emphasized the treatment is "a very targeted, clean delivery system that allows the effect of the antibody to be seen in the body without needing the antibody itself to be throughout the body."

A Potential Three-in-One Treatment

Though the symptoms of SPMS and Alzheimer's disease (AD) are notably different, Tiziana believes formulab will still show improvement in AD.

The treatment works by dampening microglial activation in the brain, which is a hallmark mechanism of CNS-related diseases. This inflammation in the brain is what drives diseases like AD, ALS and SPMS.

The two SPMS patients treated **showed decreased microglial inflammation**, as did the animal models for MS and AD.

While MS patients don't have problems with cognition in the same way as AD patients, they do face problems with walking and physical function. Weiner believes administering this treatment in humans will reduce cognition issues in AD patients, similarly to how it reduced physical symptoms in SPMS patients and animal models.

Weiner said he believes the success of this treatment may spark other treatments with a similar mechanism of action.

Davis, who works on drug development, said the phrase "kill early, kill often" applies to the way this treatment is being studied. If the targeted microglial activation did not show an effect from the treatment, the trial would not proceed.

As the treatment moves forward in AD, Weiner noted the drug could also treat ALS, another CNS-related disease.

Because the mucosal immune system involves the gut, respiratory and nasal cavities, the body has a natural anatomy to interface with the environment. Intranasal treatment "stimulates the immune system in a natural way," he said.

This delivery method has aided in safety testing.

The company has "seen no safety signals at all in animals" that have been tested and no significant side effects have been recorded in the human trials for MS, Davis said.

Despite the T-regulator cells circulating, there have been no systemic effects recorded, which leads Tiziana to believe "the safety profile should be superior to a non-nasally delivered antibody."

Tiziana plans to file the IND by the third quarter of 2023 and start the Phase I program at the end of 2023. The company previously received an affirmative written response from the FDA for its pre-Investigational New Drug Application.

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