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Zacks Small-Cap Research (NOTE)

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Tiziana Life Sciences PLC (TLSA: NASDAQ)

TLSA: First Phase II SPMS Patient Dosed

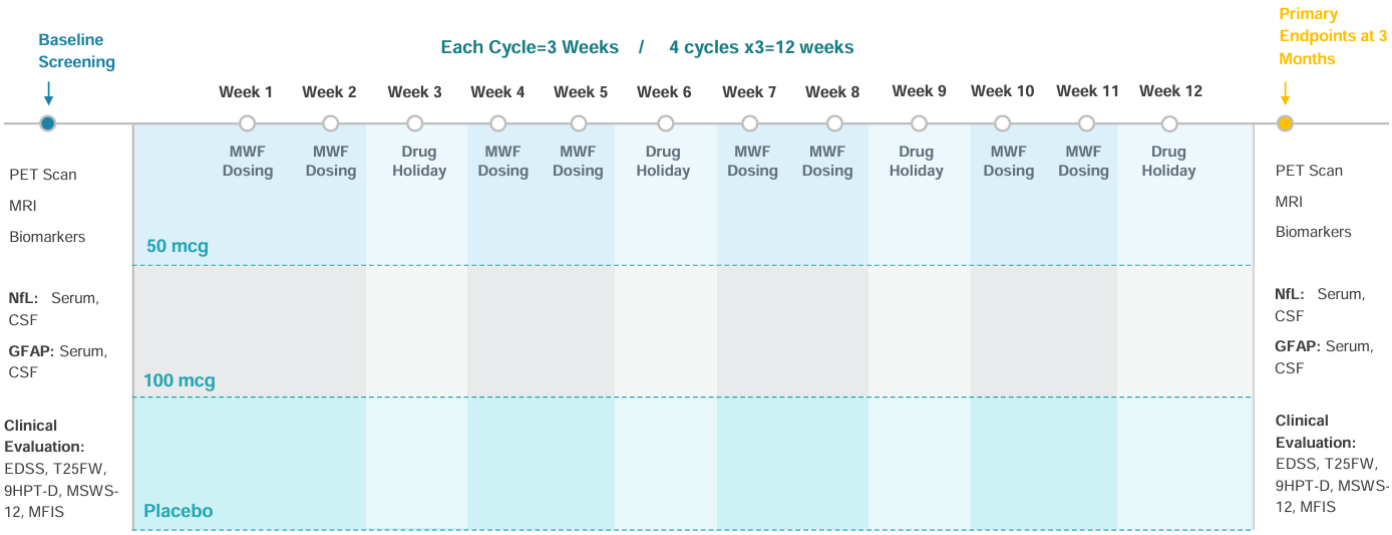
Research Note

Tiziana Life Sciences PLC (NASDAQ: TLSA) has achieved a significant milestone dosing its first patient in its Phase IIa study comparing two doses of intranasal foralumab and placebo in patients with non-active secondary-progressive multiple sclerosis (na-SPMS). The company also recently dosed four new patients in its expanded access (EA) multiple sclerosis program, reported improvements in fatigue and broadened its intellectual property protection related to combination therapy for foralumab and GLP-1 receptor agonists. Management is also engaging with stakeholders at conferences, presenting at BIO Europe and Biotech Showcase in San Francisco.

Phase IIa (na-SPMS)

Tiziana announced on September 26th that it had initiated its Phase IIa clinical trial evaluating intranasal foralumab for na-SPMS. The company held an investigators' meeting and began work to add six to ten new trial sites in addition to the original site at Brigham and Women's Hospital to recruit patients. The primary endpoint for the trial will be the change in microglial activation based on Positron Emission Tomography (PET) scans. Clinical evaluations will include the Expanded Disability Status Scale (EDSS), Quality of Life (QoL) assessments and the Modified Fatigue Impact Scale (MFIS) which assesses parameters that are essential to everyday life. Biomarkers will be monitored and assessed for predictive relevance. 54 patients will be divided equally among the three arms of 50 mcg and 100 mcg of nasal foralumab compared with placebo.

Exhibit I – Phase IIa SPMS Clinical Trial Design[1]



[1] Source: Corporate presentation, October, 2023.

On December 19th, Tiziana announced that it had dosed the first patient in the Phase IIa trial. As of the date of the press release, six sites had been recruited for the trial. Tiziana anticipates adding new locations over the next months and, if all goes as expected, the complement of sites could support full enrollment by mid-year. If this were achieved, topline could be available before year end.

The FDA will allow for at-home administration of nasal foralumab, which will dramatically improve the burden of the trial on enrollees. The Aptar Unit Dose Device will be used to administer foralumab intranasally. The mist created by the device contains the drug substance which is absorbed through the nasal membranes allowing rapid drug delivery to the brain.

Close consultation with the FDA are expected after the Phase IIa to determine the path forward. As we look ahead, either a Phase IIb or a pivotal trial may be required. Pivotal studies demand a longer observation period of a year or two and could include endpoints such as EDSS, 25-foot walk test and pyramidal scores. Although it has not been used to obtain approval, fatigue could be an endpoint as well, given the burden of this symptom for multiple sclerosis patients and the improvement that has been observed in those taking foralumab. Expedited treatment is also a possibility if safety and efficacy are supportive. No therapies are approved for na-SPMS and it is a serious disease, characteristics that could enable the use of Fast Track and Breakthrough Therapy designations for this indication.

Expanded Access (na-SPMS)

In October, Tiziana announced impressive results for its expanded access (EA) cohort of six patients who were receiving intranasal foralumab to treat na-SPMS. The six-month results span multiple parameters and demonstrated a positive result in five of the six subjects. Parallel work on these subjects showed an improvement in microglial activation as measured in PET scans. Trial participants had been nasally administered the anti-CD3 monoclonal antibody foralumab over a six-month period. The first update identified a qualitative reduction in microglial activation while the second identified overall improvements in the enrolled patients' measures for multiple sclerosis (MS).

Success with the first six patients prompted the enrollment of four additional subjects, which was announced in a November press release. These patients, as with the others before them, will be treated at the Brigham and Women's Hospital, bringing the total to 10 individuals enrolled in the EA program. The program has helped Tiziana refine dosing, drug use, and take into account patient feedback to improve the design of future studies.

A recent FDA guidance document entitled Demonstrating Substantial Evidence of Effectiveness With One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence was published in September 2023. It suggests that data generated in EA programs can be considered as part of confirmatory evidence when evaluating a product for approval. As written in section III.G. "if the patient outcome information collected under expanded access use of the drug is of sufficient quantity and quality to be highly persuasive, the information may be considered for use as confirmatory evidence." Allowing this data will help support the case for a safe and effective drug.

Additional good news about the EA program was shared in a January 8th press release updating stakeholders on patients' progress. At the three month mark, six of eight enrolled subjects have shown an improvement in fatigue scores measured by the Modified Fatigue Impact Scale (MFIS). This finding was substantiated with a PET scan showing a reduction in microglial activation in the same six patients. Two additional subjects will have completed three months of treatment and will be available for evaluation by the end of January 2024. The correlation between PET-validated reduction in microglial activation and improvement in fatigue suggests that these metrics may serve as effective biomarkers of success.

New Patent Application

Tiziana filed for a new patent application for combination therapy of foralumab with GLP-1 receptor agonists. The patent application describes the potential for foralumab to provide additional risk reduction for heart attack, stroke, and peripheral vascular disease. A combination of foralumab and a GLP-1 receptor agonist administered to patients may contribute importantly to further risk reduction in this at-risk patient population. The company's press release cited Novo Nordisk's SELECT trial which demonstrated a 20% reduction in major adverse cardiovascular events (MACE) such as heart attack, stroke, and peripheral vascular disease, with semaglutide. Tiziana's scientific advisor, Dr. Harold Weiner notes that obesity and type 2 diabetes are associated with inflammation in the liver, adipose and vascular tissue which can detract from cardiovascular health.

At Home Dosing

One of the primary difficulties of administering monoclonal antibodies is that they are usually infused, which requires a trip to the hospital or clinic. The requirement to go on site also means that patients with severe mobility problems are burdened with travel into densely populated areas multiple times per week to receive their therapy. Limited mobility is a common hardship for severe MS patients.

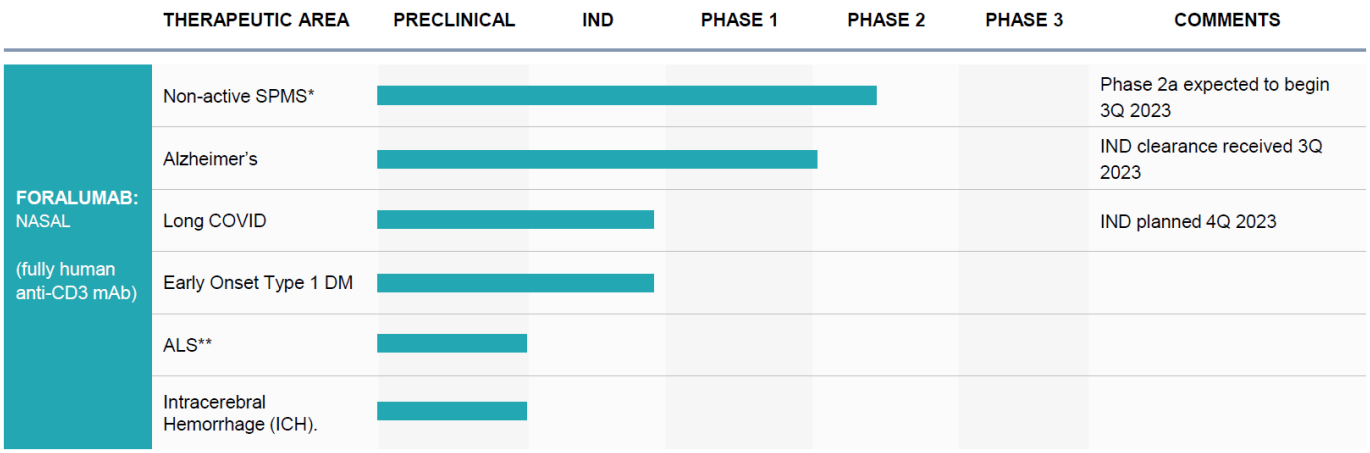
Tiziana overcame the first hurdle related to infusion and was able to develop a nasally administered formulation of foralumab; however, for the EA clinical trial, it remained necessary for the drug to be administered by a clinic-based provider due to the lack of safety data. The protocol for the na-SPMS trial required that the drug be administered three times per week at the MS clinic at Mass Brigham, which placed a large burden on patients and caregivers.

In an October 18th press release, Tiziana announced that the FDA will allow a protocol change to allow for at-home dosing now that nasal foralumab is better understood. Some initial training is required; however, the shift to at-home treatment is a significant improvement in accessibility and convenience. Previously, those in the EA program were required to visit the hospital three times per week. Under the new protocol, they will only be required to visit the clinic one time every three weeks. At-home administration will also be used for the upcoming Phase IIa study which is expected to start in November. The device used to administer nasal foralumab is the Aptar Unit Dose Device, which is well understood and has been in broad use for some time.

Milestones

- Filing of IND for foralumab in AD – 3Q:23
- AD IND clearance – August 2023
- Launch of Phase IIa trial in na-SPMS – September 2023
- Attendance at Biotech Showcase – January 2024
- Interim readout for EA na-SPMS trial – January 2024
- Full enrollment of Phase IIa trial in na-SPMS – mid-year 2024
- Results from initial AD clinical study – 2H:24

Exhibit II – Tiziana Development Pipeline[2]



Summary

Tiziana has continued to advance its na-SPMS programs, enrolling its first patient in the Phase IIa and reporting improved fatigue and reduced microglial activation in many of the EA patients. 2024 should continue to be busy for the MS programs with two more EA patients ready for their three-month evaluations at the end of January, the addition of more sites for the Phase IIa trial, and, if all goes to plan, topline results from the Phase IIa before year end. Company executives are also sharing the news with stakeholders at investor events and scientific conferences including Biotech Showcase, which is being held this week in San Francisco.

[2] Source: Corporate presentation, October, 2023.

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