TIZIANA LIFE SCIENCES PLC (NASDAQ:TLSA)

3 November 2022

proactive research

Healthcare

52-WEEK HIGH	**$3.29**
52-WEEK LOW	**$0.53**
PRICE	**$1.19**
MARKET CAP MLN	$121.17

Share Price

Major Shareholders

Shares in issue	194,612,289
Avg Three-month trading volume	316,663
Primary Index	NASDAQ

Company Information

Address: Tiziana Life Sciences,
9th Floor 107 Cheapside, London,
United Kingdom, EC2V 6DN
Website: www.tizianalifesciences.com

Analyst Details

John Savin PhD
JSavin@proactiveinvestors.com

Robin Davison
robin@proactiveinvestors.com

Extending into Alzheimers

Progress in MS and moving into Azheimer's

Tiziana Life Sciences has announced that it plans to take foralumab, its fully human anti-CD3 monoclonal, into a clinical study in Alzheimer's disease. The Company obtained good initial results from an animal model. Further preclinical work will be needed before an Investigational New Drug Application can be filed with the US Food & Drug Administration (FDA). This is expected by Q3 2023. Dosing will be intranasal and a Phase 1 could start in H2 2023; as yet, no trial design is available. In mid-2022, lecanemab, an anti-Alzheimer's drug from Eisai and Biogen was reported as slowing disease progression by 27% in early-stage patients although no data has yet been released. Aduhelm, BioGen, was approved in the US in 2021 (after a tortuous process) but sales have been disappointing. As trials in Alzheimer's disease are extremely expensive and prolonged, we envisage that Tiziana will seek to partner the project at the optimal time.

In MS, Tiziana is targetting intranasal foralumab at non-active secondary progressive disease. This is a late-stage condition where patients continue to deteriorate but do not experience sudden flare-ups of the disease. There are two drugs to treat active secondary progressive disease (where flares still occur): Ocrevus an infusion, and Mayzent, an oral product. Both suppress the immune system and have strong side effects. Foralumab should have fewer side effects and be better tolerated.

Tiziana has now extended the current expanded access study by recruiting four more patients as of 2 November; two previous patients are already using the therapy. As result of the favourable safety profile, the FDA in April allowed the study to be expanded by eight patients and potentially test a higher dose of 100mcg (versus 50mcg) if patients appear to benefit. Tiziana withdrew the previously planned Phase 1 study (NCT05029609) in primary and secondary progressive MS for commercial reasons in March.

A trial in Crohn's Disease (NCT05028946) of oral foralumab has been cancelled for commercial reasons. However, a Phase 1b over 28 days in 8 patients is being planned. The foralumab trial in COVID-19 (NCT04983446) has also been withdrawn as the project is not now commercial. There is a grant-funded foralumab research project into Amyotrophic Lateral Sclerosis; this is being run at the Brigham and Women's Hospital. There is no update on the clinical development of milciclib, a chemotherapeutic.

Sharper development focus

Tiziana is starting to focus its development. The current MS study is uncontrolled but should give valuable data. Non-active secondary MS needs less aggressive therapies to retard progression so foralumab could find a clear market niche. Alzheimer's disease trials are some way off, from H2 2023, and would proably need a major partner for development beyond Phase 1. Given the complexity of the disease and lack of clear biological understanding, it is a speculative but nonetheless interesting project. We also note that Dr. Kunwar Shailubhai, who was CEO and CSO, left Tiziana on August 1, 2022.

Gabriele Cerrone, interim CEO and executive chair. He has a track record of corporate financing having listed nine companies, seven on NASDAQ and two in London. He is the former chair of Trovagene, Gensignia, Rasna, Contravir and Okyo. He is also the co-founder and director of two NASDAQ-listed companies that brought drugs from the discovery through to US Food & Drug Administration approval: Synergy Pharmaceuticals and Siga Technologies.

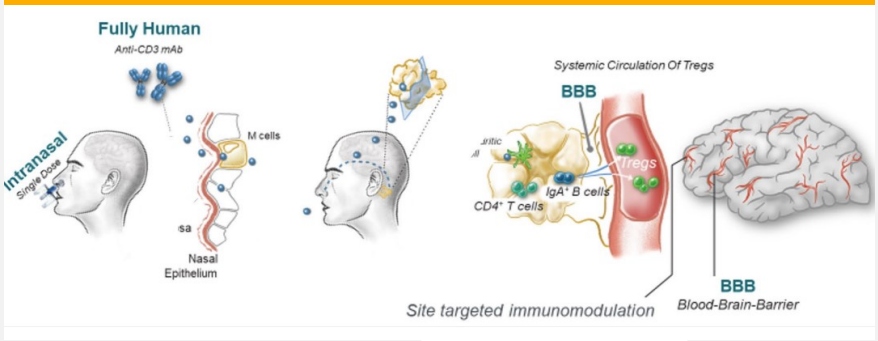
Matthew Davis, Chief Medical Officer and Acting Chief Scientific Officer. Previously, he was He was Chief Scientific Officer and Chief Medical Officer at Endo Pharmaceuticals. Prior to that, Dr. Davis was Chief Medical Officer for Lupin Inc. and URL Pharma, Inc. where he led three NDA approvals. He also was on the executive team that sold URL Pharma to Takeda.

Alzheimers data

A study by Dr Weiner "*Treatment of Alzheimer's disease by modulation of microglial neuro-inflammation by nasal anti-CD3 mAb*" was presented at a recent conference. The idea is to promote homeostatic microglial cells while decreasing degenerative microglial cells: microglial cells are the resident brain immune system and important for brain health.

In the mouse model of Alzheimer's used, cognition improvements were assessed using the Y-maze and Morris water maze tests. Biological improvements were also observed based on restoration of genetic phenotypes as measured by the presence of homeostatic microglia genes detected by Nanostring, a very sensitive direct gene detection technology. It was found that intranasal anti-CD3 induced the migration of regulatory T cells (Tregs) to the brain which then interacted with microglia, Exhibit 1 shows this in humans.

Exhibit 1 - Inranasal foralumab generates brain Tregs



Source: Tiziana

MS progress contunues

Tiziana continues to make progress in MS with nasally delivered foralumab, Exhibit 1. In June, it was reported that positive imaging and functional results were seen in the second patient with secondary progressive multiple sclerosis (SPMS) enrolled in Tiziana's Intermediate-Size Patient Population Expanded Access Program. The data points were measured after three months of treatment and are consistent with the results seen in the first patient. Another four patients have now been recruited in the first of two cohorts.

The second patient is a male in his 40s who was diagnosed with SPMS in 2014. After three months of treatment with foralumab (50mcg; three times a week for two weeks, followed by one week off), the patient showed a 10-30%i improvement measured by imaging and by neurologic examination which is comparable to the imaging changes seen in the first patient at three months. The second patient also recorded improvements in the Timed 25-Foot Walk test (T25FW), a functional clinical endpoint.

The results are consistent with the previously reported data from the first SPMS patient. This patient, a 61-year-old male with SPMS for over 20 years, had previously seen his condition progressively worsen despite more than three years of treatment with ocrelizumab (Ocrevus, Roche), which is considered the most effective drug for SMPS. The patient showed an improvement in the T25FWk from ~40s to ~20-30s after three months.

These consistent data are still effectively a clinical anecdote but are suggestive of possible efficacy in SMPS patients who have exhausted all other therapeutic options. Further results should come next year. The next stage, after the current Intermediate-Size Patient Population Expanded Access Program, could be an open-label Phase 2 study in 10-20 patients. This data may allow Tiziana to partner the drug; partnering would be needed to gain approval.

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London
+44 207 989 0813
The Business Centre
6 Wool House
74 Back Church Lane
London E1 1AF

New York
+1 347 449 0879
767 Third Avenue
Floor 17
New York
NY 10017

Vancouver
+1 604-688-8158
Suite 965
1055 West Georgia Street
Vancouver, B.C. Canada
V6E 3P3

Sydney
+61 (0) 2 9280 0700
Suite 102
55 Mountain Street
Ultimo, NSW 2007