TIZIANA LIFE SCIENCES PLC (NASDAQ:TLSA)

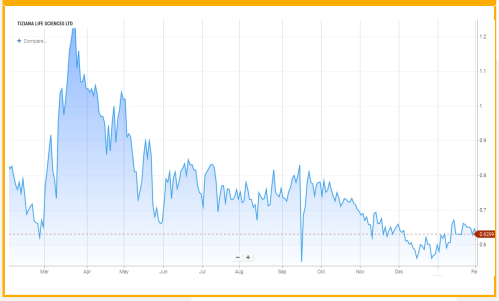
2 February 2023

proactive research

Healthcare

52-WEEK HIGH	**$1.38**
52-WEEK LOW	**$0.53**
PRICE	**$0.61**
MARKET CAP MLN	$62.39

Share Price



Major Shareholders

Shares in issue	102,272,614
Avg Three-month trading volume	316,663
Primary Index	NASDAQ
Next Key Announcement	FY 22 results

Company Information

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2023 clinical outlook

Progress is expected though 2023

Tiziana's lead product is foralumab, a fully human antibody. This is administered to mucosal surfaces in the nose (intranasal) to boost regulatory T-cell (T-reg) responses with the aim of controlling autoimmune disease progression in central nervous system (CNS) indications like multiple sclerosis (MS) and Alzheimer's disease (AD).

The lead indication for intranasal foralumab is non-active secondary progressive multiple sclerosis (SPMS). Non-active SPMS is a late-stage condition where patients continue to deteriorate but do not experience sudden flare-ups of the disease. The first two enrolled patients in the ongoing expanded access study showed encouraging responses. Tiziana has now recruited four more patients who were dosed in January. A further cohort of four is expected to be dosed from Q223 onwards. With planned completion of the necessary preclinical studies in Q123, we anticipate an IND filing by mid-2023 and a Phase 2 trial starting from Q323.

Other projects are an extension of foralumab into AD with a planned IND by early autumn and a trial projected to start by late 2023. An academic grant-funded project researching into foralumab for amyotrophic lateral sclerosis might lead to a further indication.

The milciclib anti-cancer project is paused but an IND for a Phase 2 in non-small cell lung cancer in combination with gemcitabine has been filed. Tiziana believes that a granted IND will maximise the value. Also, the monoclonal TZLS-501 for use in lung disease is being de-prioritised.

Financials

Tiziana Life Sciences interim results to 30 June 2022 showed cash of US$26.5mln, down from US$42.2mln on 31 December 2021. Operational cash use in H122 was US$11.9mln indicating potential year-end cash of around USA$14mln (before any loans).

Tiziana notes that it has cash to run the Phase 2 trial in MS and has no requirement to raise further capital in 2023. Non-dilutive funding (loans and grants) will be used for any AD trial and other developments.

Cash on 30 June was US$26.5mln. H122 operational cash use was US$11.9mln comprising R&D at US$7.5mln, and admin of about US$3.1mln. There were non-cash FX gains of US$3.7mln and share-based gains of US$2.4mln. Working capital outflows were about US$1.3mln. Shares valued at US$808k were purchased for treasury in H1-22. There was a related-party investment of US$2.7mln in March 2022. A loan facility of up to US$2mln was granted to another related party in H222 and might lower December cash.

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.

MS focus continues

Tiziana continues to make progress in MS with nasally delivered foralumab. In MS, Tiziana is targeting intranasal foralumab at non-active secondary progressive disease (SPMS). 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 (ocrelizumab Genentech) an infusion (considered the most effective drug for SMPS) and Mayzent, an oral product. Both have strong side effects.

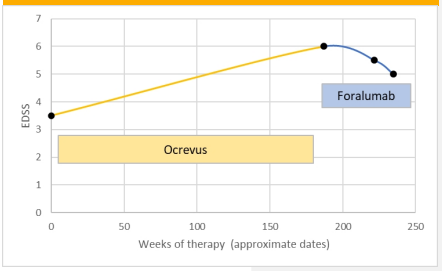
Additional clinical progress

Tiziana has disclosed some selected data on the first two SPMS patients enrolled in the open-label intermediate-size patient population expanded access program. Patients in the expanded access program receive a nasal spray of foralumab (50mcg; three times a week for two weeks, followed by one week off). The dose can be increased to 100mcg on the same schedule if needed.

From January 2022, after three months of treatment with foralumab, the second patient showed a 10-30% improvement measured by imaging and by neurologic examination. This patient also recorded improvements in the timed 25-foot walk test (T25FW), a functional clinical endpoint. By September 2022, the second patient could walk 100 metres before they needed a cane; this shows increased motor neurone control. This second patient had received Ocrevus from 2018 but this was discontinued in 2021 due to disease progression.

A January 2023 update reported that after 11 months of dosing there were additional clinical improvements in the second patient. On the expanded disability status scale (EDSS) the score on enrolment was 6.0; the score on starting Ocrevus in 2018 had been 3.5 – note that lower scores show an improvement in MS, higher scores a deterioration. The EDSS score fell to 5.5 in September and was 5.0 in December (Chart 1). By December, the patient could walk 200 metres without a cane.

Chart 1 - MS Progress



Source: Tiziana data, ProActive Chart

There were further imaging results showing improvement in microglial activation; microglial cells are the brain's immune cells and cause MS so lower activation is encouraging. The results are consistent with previously reported data from the first SPMS patient; the first patient had also failed on Ocrevus.

These data are still effectively a clinical anecdote (two uncontrolled patients) but are suggestive of possible efficacy in SMPS patients who have exhausted all other therapeutic options. Another four patients were enrolled in November in the first of two cohorts with a further four patients planned in H1 2023.

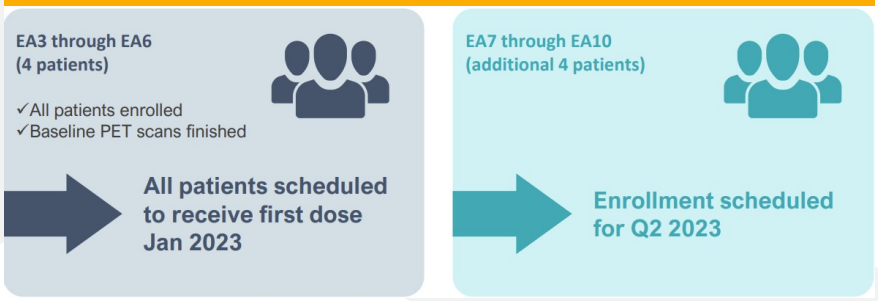
Tiziana expects to file an IND application during 2023. The anticipated Phase 2 will use a mutli-dose nasal delivery device. The required compatibility, stability and characterisation studies needed will be completed, according to Tiziana, in Q123. Preclinical 13-week toxicology data was announced in December 22. Further clinical data may enable Tiziana to partner the drug; partnering would be needed in our view as MS is a complex indication and market.

Pipeline status

Tiziana has focused its development onto foralumab.

The current MS study is uncontrolled but should give valuable data. We assume that each successive four-patient cohort will provide three months of data. The first cohort was enrolled by early November and will be dosed from January, Exhibit 1; the three-month data is therefore due in April. This could enable the second cohort to enrol from May.

Exhibit 1 - MS Expanded Cohort progression



Source: Tiziana

If so, the full dataset on 10 patients (including the initial two) will be available from Q323.

However, Tiziana can file the IND for the Phase 2 once all necessary preclinical work is completed. We anticipate the IND filing by mid-2023 and the Phase 2 start, in line with management expectations, in Q323.

2023 outlook

The new clinical data for 2023 will be from the 10 open-label extension trial in non-progressing SPMS currently underway. Phase 2 studies typically take over a year to run (although we have no disclosure of potential Phase 2 designs), so the earliest partnering point might be H224 onwards. Non-active secondary MS needs less aggressive therapies to retard progression so foralumab could find a clear market niche.

Exhibit 2 shows the optimised strategy to maximise value. This focuses on intranasal foralumab with de-prioritised projects on oral foralumab, the anti-cancer drug milciclib and TZLS-501 (the anti-inflammatory anti-IL-6 receptor antibody). An IND may be filed for milciclib but no trial is currently planned.

Exhibit 2 - Planned optimal use of funds

Focus on intranasal foralumab allows for efficient use of funds and staff

Sufficient cash reserves to perform Phase 2 MS trial
- Plan to use **non-dilutive** funding for Alzheimer's Disease, ALS, and T1D studies
- No anticipated requirement to raise capital in 2023

Deprioritized program development in oral foralumab, milciclib, and our fully human anti IL-6 receptor inhaled antibody

Source: Tiziana

Foralumab in Alzheimer's disease was discussed in our November note. The earliest date for a trial expected by Tiziana is late 2023. Although initial Phase 1 trials can be run on a small scale, Alzheimer's disease requires major partners to progress and fund the extensive and long-duration trials needed. The attrition rate on projects has historically been very high and lecanemab (FDA approved in January 2023) shows a relatively modest response in early stage patients.

Finances and cash needs

In cash terms, Tiziana will need to conserve resources, depending on its H222 expenditure with 30 June cash of US$26.5mln, down from US$42.2mln on 31 December 2021. Operational cash use in H122 was US$11.9mln indicating potential year-end cash of around USA $14mln (before any related-party loans). The need to focus on the lead project is reflected in the optimised strategy, discussed above.

Positively, Tiziana notes, (Exhibit 2) that it has cash reserves to run the Phase 2 trial in MS and has no requirement for further capital in 2023. Non-dilutive funding (like loans and grants) will be used for any AD trial.

In H122, Tiziana spent US$808k on share repurchase of 912,825 shares for treasury. There were 102,272,614 ordinary shares as of 31 January 2023 (website).

Tiziana made an investment of USA$2.7mln in an OTC-listed cancer company, Accustem, controlled by a related party (Mr Cerrone). The IPO price was US$2.0 on 2 March 2022. At the current price of $0.87, the investment would now be valued at about US$1.2mln. Tiziana appears to have been the sole investor in that round. Acustem is a diagnostics business developing a 20-gene test to predict cancer recurrence risk. It is a Tiziana spin-out but now independent.

In August 2022, Tiziana issued a short-term credit facility to Okyo Pharma, a related party, for US$2mln. The loan is available for a period of six months upon first draw-down and carries an interest rate of 16%, with additional default interest of 4% if the loan is not repaid after the six-month period. Up to late December, US$1mln had been drawn.

Tiziana has been given an additional 180-day compliance period, with a new deadline of 12 June 2023, to regain compliance with Nasdaq's minimum bid price rule. This requires the price to be over US$1.00 for ten consecutive trading days.

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