Tiziana Life Sciences Plc (TLSA – $0.73*)
Buy; $3.00 PT; $71.3M Market Cap
Breaking News
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SPMS Patient #1 6-Month Imaging, Biomarker and Functional Data Continues to Impress; Reit. Buy, $3 PT

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Summary and Recommendation

On 3/10, BMO, Tiziana Life Sciences (TLSA) released positive clinical data from their first patient with secondary progressive multiple sclerosis (SPMS) treated for 6 months with intranasally administered foralumab, a fully human anti-CD3 monoclonal antibody. Recall, TLSA previously reported 3-month favorable data suggesting halting of the disease, with no safety liabilities. (link) Here, both 3- and 6-month standardized uptake value ratio (SUVR) data are presented highlighting the overall positive whole-brain effects stemming from foralumab treatment, i.e., -23% and -38%, respectively, when compared to a pseudo reference region that showed minimal change in PET SUV across time point. Moreover, when broken down into regions of the brain, beneficial effects were further identified, i.e., -23% and -38% (cerebral cortex), -20% and -50% (thalamus), -25% and -36% (white matter), and -22% and -38% (cerebellum) (all 3-month and 6-month, respectively), underscoring the sustained treatment effects. Importantly, published PET studies have indicated a notable increase of microglial activation in SPMS patients, with BIIB's Tysabri as the only anti-inflammatory drug to have previously reported any treatment effect, i.e., ~-20% at 1 year but no meaningful EDSS improvement observed until 4-year longitudinal analysis. No such effect on microglial activation at such a short treatment period is reported with S1P1 modulators, to the best of our knowledge. Here, reported PET data indicate that treatment inhibited microglial activation both at 3- and 6-months, and was seen in all parts of the brain tested, which was corroborated via a corresponding decrease in pro-inflammatory cytokines from patient serum, including interferon-gamma (IFN-g), interleukin 18 (IL-18), IL-1β and IL-6, as well as physical benefits including improvements in Timed 25-Foot Walk Test (T25FW), 9-Hole Peg Test (9HPT), and Symbol Digit Modality Test (SDMT), overall reporting the first validation of foralumab therapy as a potential intranasal take home immunotherapy for SPMS.

Of note, this patient had previously experienced worsening disease progression despite cycling through several MS therapies with the patient's gait and limb strength particularly deteriorating over the prior two years before foralumab therapy. Subsequently, TLSA has now received FDA authorization to continue treating this patient for an additional 6 months to determine if 12 months of consistent treatment maintains clinical stabilization and provides sustained clinical benefits. Since MRI activity is less likely detected in non-active SPMS with such a short treatment period, investigators anticipate conducting MRI scans evaluating disease activity and progression at the 10-12 month treatment period. TLSA currently has $40M on the balance sheet, implying (1) cash runway through the end of 2023, and (2) notably an EV of <$30M indicative of over-sold levels amid macro sector headwinds for small-cap biotechs, which recently prompted mgmt. to implement a stock repurchase program for up to $5M of TLSA's common shares at any time.

Key Points

- **Puts foralumab on the map as disease-modifying therapeutic for neurodegenerative diseases; MS only a start, in our view.** We are particularly encouraged by foralumab's novel mechanism of significantly reducing microglial activation incrementally being validated with this dataset, which TLSA will look to replicate in a second SPMS patient now enrolled in the study and mgmt. guiding to generating 3-month PET imaging data in 2Q. (*continued on pg.2*)

Also encouraging on safety, patient-level data being generated is informative of company's ongoing correspondence with FDA for full IND acceptance with TLSA looking to further expand enrollment to ~10 patients in the interim that could result in a robust package for supporting progression into a regular way Ph. II placebo-controlled SPMS study. Mgmt. has similar efforts underway in Europe to expand foralumab exposure selectively amid inbound interest from multiple study investigators. Furthermore, TLSA continues to explore add'l neurodegenerative indications, such as Alzheimer's disease, where microglial activation is increasingly evaluated as a key component of disease pathogenesis and progression.

KOL event scheduled on March 14th at 11 am ET, with Drs. Howard Weiner, Tanuja Chitnis, Lawrence Steinman, and Tarun Singhal to discuss the current treatment landscape in inflammatory neurodegenerative disease, as well as the potential for new, locally acting therapies capable of crossing the blood-brain barrier, which poses a unique challenge for drug delivery to the central nervous system.

Valuation

We base our Buy rating and 12-month price target of $3 per share on a discounted cash flow (DCF) analysis of revenue and cash flow projection through 2030. Our projections of free cash flow to the firm from sales of oral foralumab for moderate to severe Crohn's disease and nasal foralumab for non-active SPMS are adjusted and weighted based on historical regulatory approval rates of similar treatments at similar stages of development. Our DCF analysis applies a WACC-calculated 14.5% discount rate and a 2% terminal growth rate, in line with other clinical-stage biotech companies, yielding an implied enterprise value of $78M. For 2030, the final projected year of our model, we forecast $500M in total risk-adjusted revenue, which assumes a 35% probability of clinical and regulatory success for oral foralumab and 25% for nasal foralumab. Of note, nasal foralumab could potentially pursue approval via orphan drug designation, in our opinion, intended for rare diseases or conditions that affect less than 200,000 individuals in the U.S. Through this regulatory pathway, TLSA will be able to have the agency involved in the early stages regarding the trial design and endpoint selection and likely facilitate expedited approval, given the unmet need. We currently do not ascribe any value in our model to TZLS-501 and milciclib, as we await additional clinical data and subsequent guidance on the regulatory path to market.

Risks

Clinical risks. It is uncertain whether the clinical benefit observed in the clinical studies for foralumab and future registrational trials will be sufficient to support regulatory approval in the U.S., Europe, and other countries. Negative safety and/or efficacy findings in these trials could lead to downward revisions to our price target.

Regulatory risks. The regulatory pathway for all of TLSA's programs in the U.S. is uncertain, and it is unclear whether positive data will be sufficient for a New Drug Application (NDA) submission for each program in the U.S. Additionally, there is no certainty that any of TLSA's drugs will be approved or reimbursed. If the regulatory path for TLSA's candidates is more complex and/or time-consuming than anticipated, there could be a materially negative impact to our estimates and price target, even with success in achieving clinical endpoints.

IP risks. The patent protection related to foralumab and other candidates may expire in the near term and be subject to litigations from competitors. For example, the methods of use patent, pertaining to autoimmune or Inflammatory disease and disorder, for foralumab is expected to expire in 2025.

Commercialization risks. The market potential of TLSA's therapies may not be as significant as projected. In addition, TLSA will need to establish a sales and medical affairs infrastructure in the U.S., Europe, and other geographies for foralumab and other pipeline candidates.

Financing risk. With approximately $66M in cash and cash equivalents, TLSA will likely need to raise additional capital for continued clinical and preclinical candidate development, perhaps via additional equity financing, before reaching profitability, likely resulting in equity share dilution.

Stock price volatility. Share price volatility is common for developmental biopharma firms like Tiziana Life Sciences.

*Closing price of last trading day immediately prior to the date of this publication unless otherwise indicated.

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