Tiziana Life Sciences Plc (TLSA – $0.84*)
Buy; $3.00 PT; $94.1M Market Cap
Company Update
Wednesday, June 7, 2023

Secondary Progressive MS Patient-Level Data Continues to Improve; De-risks Upcoming Ph. IIa; Reit. Buy, $3 PT

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Summary and Recommendation

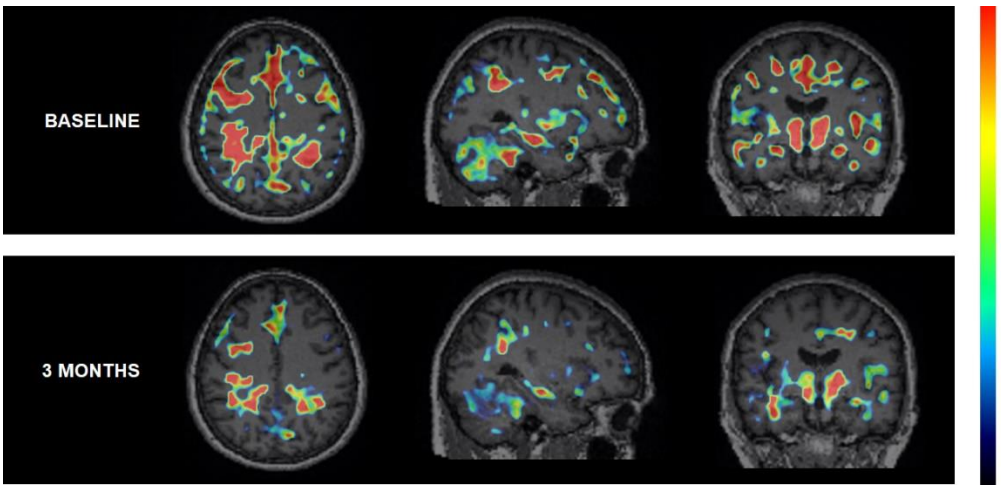
We return to our Buy-rated Tiziana Life Sciences (TLSA, $3 PT) thesis following company's impressive data release accompanied by webinar featuring leading KOL Howard L. Weiner, M.D., Chairman of TLSA's Scientific Advisory Board and Co-Director of the Ann Romney Center for Neurologic Diseases at Brigham and Women's Hospital; noting that a total of five out of six emergency access (EA) patients with non-active secondary-progressive multiple sclerosis (na-SPMS) have now demonstrated a reduction in microglia activation as demonstrated by Positron Emission Tomography (PET) following 3-months of treatment with nasal foralumab (Exhibit 1). Importantly, all six patients had clinically regressed on ocrelizumab treatment, highlighting the potential efficacy of foralumab in this setting. These data confirm and build on the previously reported first two positive EA patient data that had both already demonstrated favorable treatment improvements. Recall EA1 previously demonstrated whole-brain foralumab treatment effects at 3- and 6-months of treatment, including standardized uptake value ratio (SUVR) data of -23% and -38%, respectively, when compared to a pseudo reference region that showed minimal change in PET SUV across time points (Exhibit 2). Additional data from EA2 continued the trend, as well as being able to walk 100 meters without a cane following eight months of treatment and improving to 200 meters by 11 months. EDSS scores also were noteworthy, previously worsening from 3.5 in 2018 to 6.0 in 2021 despite ocrelizumab therapy, but demonstrating improvements from 6.0 to 5.5 following eight months of treatment and further to 5.0 following 11 months of treatment, demonstrating a full point of improvement, something not typically seen in MS patients. All EA patients had previously failed ocrelizumab treatment, and MS patients, in general, do not see a reduction in microglial activity, thus suggesting these data particularly stand out, in our opinion. Full data from EA1-EA6, potentially also including EA7-10, including patient level (1) disability scores, i.e., EDSS, 25ft walk, and fatigue score; (2) biomarker data, i.e., CSF readouts on NFL, etc., interleukins, and cytokines; and (3) QoL scores are expected at ECTRIMS on 10/11-13. When coupled with our recent MS prescriber survey involving familiarity with anti-CD3 therapeutic approach, we continue to view foralumab as an important novel therapeutic within the MS clinical development landscape (link).

Key Points

- **Moving past emergency access, TLSA on track for imminent Ph. IIa initiation.** TLSA recently submitted their MS IND on 6/2, advancing their emergency access to full IND by submitting 3-month tox data, patient-level adverse events, and Ph. IIa protocol to the FDA. TLSA anticipates receiving FDA feedback/comments within ~30-days; however, since TLSA has already been operating under an EA IND, TLSA won't necessarily receive a may proceed letter and could initiate Ph. IIa study if no FDA response is received within the 30-day waiting period. TLSA plans to initiate a 3-month Ph. IIa placebo-controlled trial in 54 na-SPMS patients, evaluating the safety and efficacy of 50 mg and 100 mg intranasal foralumab vs placebo. The Ph. IIa trial will incorporate the 3-month PET scan as the primary endpoint, the same already demonstrating positive efficacy in EA1-EA6, which we view as de-risking to the outcome from the study onset (Exhibit 2). Additional efficacy evaluations include

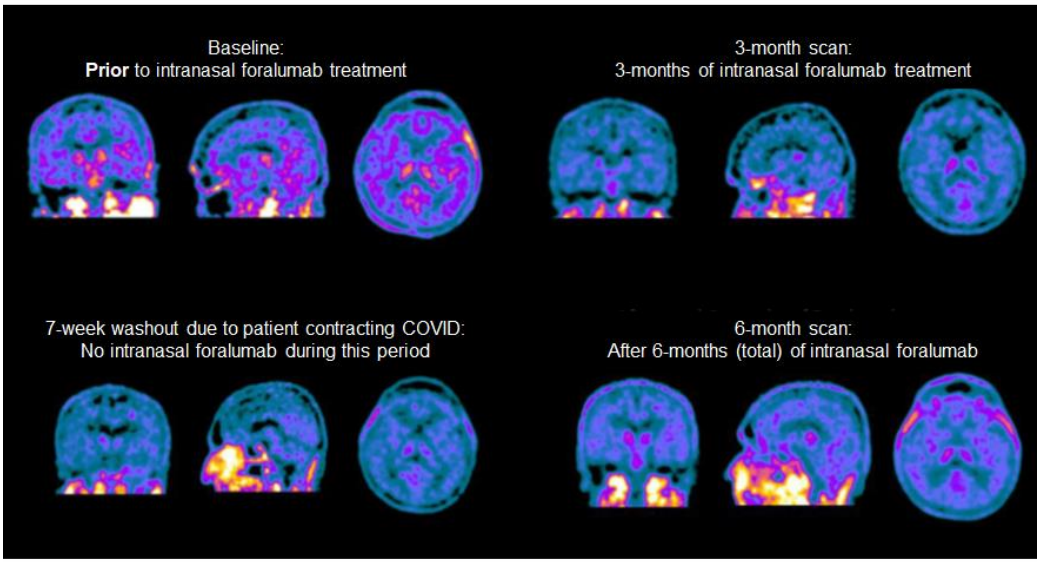
PET and MRI scans, biomarkers (NFL, GFAP), and clinical evaluations (EDSS, T25FW, 9HPT-D, MSWS-12, and MFIS). Apart from MS, activated microglia are also believed to play a role in the pathogenesis of multiple neuroinflammatory diseases, including MS, Alzheimer's disease (AD), and amyotrophic lateral sclerosis (ALS), where microglia are key effectors of demyelination, the protective sheath covering of nerve fibers. Separately, TLSA also has plans to file an IND for Alzheimer's Disease (AD) in June.

Exhibit 1. Representative EA3-6 Patient PET Image Highlighting Marked Reduction in Microglia Activation



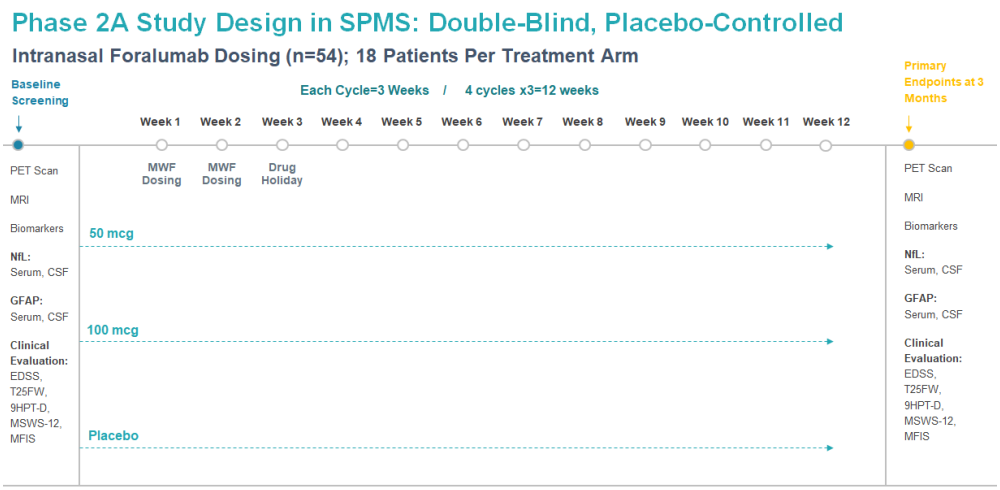
Source: TLSA company filings, and Singhal T et al. Nasal foralumab attenuates microglial activation in nonactive-SPMS patients. Manuscript in preparation.

Exhibit 2. Marked Reduction in Microglia Activation Following Foralumab Treatment



Source: TLSA company filings.

Exhibit 3. 3-Month Placebo Controlled Phase IIa Study Design



Source: TLSA company filings

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 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 $63M. For 2030, the final projected year of our model, we forecast $173M in total risk-adjusted revenue, which assumes a 25% probability of clinical and regulatory success for nasal foralumab.

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 $18M 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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