Tiziana Life Sciences Plc (TLSA – $0.71*)
Buy; $3.00 PT; $70.2M Market Cap
Breaking News
Wednesday, September 21, 2022

SPMS Patient #2 6-Month Clinical Improvements Encouraging; Pipeline Expansion Intriguing Amid Continued Insider Buying. Reit. Buy.

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Summary and Recommendation

On 9/20, BMO, Tiziana Life Sciences (TLSA—Buy, $3 PT) reported updated results from ongoing intranasal foralumab study in secondary progressive multiple sclerosis (SPMS) of the second treated Expanded Access patient (EA2) following six months of foralumab treatment totaling 10.5 treatment cycles, highlighted by the continued clinical improvements, including (1) the ability of the patient to walk 100 meters without a cane or need to rest, compared to only three months ago in which a cane was required; and (2) a corresponding clinically meaningful improvement in the Expanded Disability Status Scale (EDSS) of 0.5, including a stable pyramidal score, one of eight functional systems (FS) scores that did not worsen over time. Notably, this patient had previously been reported to demonstrate a roughly 10-30% reduction in PET imaging signal, suggesting an inhibition of microglial activation across all brain regions, i.e., cortex, thalamus, white matter, and cerebellum, as well as clinical improvements in a neurological exam and in the timed 25-foot walk test.

An additional 6-month follow-up PET imaging scan is expected in 4Q22, which would confirm reduced microglial activation, as well as provide support from the first patient treated. Recall, in the first patient tested following 6-months of treatment PET data indicate that treatment inhibited microglial activation at 6-months, as well as at 3-months, in all parts of the brain tested. Importantly, the data corresponded to a decrease in pro-inflammatory cytokines from the patient's serum, including interferon-gamma (IFN-g), interleukin 18 (IL-18), IL-1β, and IL-6. Further, standardized uptake value ratio (SUVR) data highlighted the overall positive whole-brain effects stemming from foralumab treatment, i.e., -38% when compared to a pseudo reference region that showed minimal change in PET SUV across time point, but which was also further exemplified when broken down into regions of the brain; -38% (cerebral cortex),-50% (thalamus), -36% (white matter), and -38% (cerebellum). Together, these data all led to improvements in Timed 25-Foot Walk Test (T25FW), 9-Hole Peg Test (9HPT), and Symbol Digit Modality Test (SDMT), which is continued to see here.

Key Points

Now with two patients reporting at least 6-months data, TLSA has plans to enroll an additional four patients in 4Q22, which follows the receipt of a "Study May Proceed" letter from the FDA permitting the ongoing Expanded Access IND program for intranasal foralumab to enroll up to eight additional secondary progressive multiple sclerosis (SPMS) patients. Recall, when initiated, the FDA required the first enrolled patient to demonstrate a clean safety profile following three months of treatment, then allowing treatment to continue to six months, at which point, a second patient was also allowed to enroll since foralumab is a fully humanized anti-CD3 antibody that cannot crossreact with CD3 from other species and thus, has had limited scope of preclinical toxicology studies to evaluate longer-term chronic dosing exposure.

Continued recent insider buying reaffirms strength to pipeline execution, despite ongoing CEO transition, and is further supported by foralumab-focused indication expansion efforts, i.e., (1) a presentation at AAIC'22 (11/29-12/2), "Treatment of Alzheimer's disease by modulation

of microglial neuroinflammation by nasal anti-CD3 mAb", demonstrated the restored activity of microglia and cognitive improvements in an animal model of Alzheimer's disease following intranasal administration, and (2) recent awarding of a Lawrence & Isabel Barnett Drug Development Program grant to the Ann Romney Center for Neurologic Diseases at the Brigham and Women's Hospital to explore intranasal foralumab in an animal model of amyotrophic lateral sclerosis (ALS).

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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