**Tiziana Life Sciences Plc (TLSA – $2.65*)**
**Buy; $8.00 PT; $257.9M Market Cap**
Company Update
Tuesday, March 30, 2021

# Timely Ph. II C-19 and MS Updates To Further Showcase the Breadth of Intranasal Foralumab Potential; Reiterate Buy, $8 PT

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## Summary and Recommendation

On 3/30, BMO, Tiziana Life Sciences (TLSA) announced additional clinical development plans for the nasally administered proprietary fully human anti-CD3 mAb, Foralumab, in a Ph. II clinical study in patients with moderate to severe C-19. The clinical update comes on the heels of a recently completed trial in mild to moderate C-19 disease, in which nasal Foralumab demonstrated (1) reduction in systemic inflammation as evidenced on both markers of inflammation, e.g., IL-6 and C-reactive protein; (2) improvement of pulmonary inflammation as measured by CT scans; and (3) notable recovery in disease specific symptoms, e.g., smell and taste of treated patients; indicative of the potential of Foralumab elicit to a potent, ameliorating response to the hyperactivated immune system via the epithelial lining of the nose, respiratory tract, and gut. Further, the drug was well-tolerated, i.e., no grade 3 or 4 severe adverse events (SAEs) in any of the cohorts, supporting advancement into the Ph. II study in relatively more encumbered moderate to severe patients. TLSA plans to conduct the study in Brazil in hospitalized C-19 patients, evaluating the addition of Foralumab to background standard of care therapy.

Importantly, since Foralumab drives anti-inflammatory activity through modulation of the immune system and stimulation of regulatory T cells (Tregs) rather than targeting specific C-19 disease pathogenesis, TLSA believes their in-house mAb may have therapeutic applications in newly identified variants, including from the UK, South Africa, and Brazil. In our view, this update is quite timely, as the company also disclosed clearance of an Individual Patient Expanded Access IND for a Progressive Multiple Sclerosis study in which an SPMS patient will receive a nasally administered antibody for the first time in 2Q21. Additional corporate updates included filing of a 20-F to establish Accustem, commercial manufacturer of multi-gene prognostic breast cancer assay, StemPrintER, as a separate entity from TLSA and finalize a distribution of shares in Accustem to TLSA shareholders via the ADS program. Despite a recent pullback in shares, i.e., -18% MTD vs. -15% XBI, we continue to like the risk-reward set up headed into later-stage clinical trials, which we believe will further showcase the breadth of Foralumab's therapeutic potential across multiple inflammatory diseases.

## Key Points

- **Ph. II C-19 severe disease trial builds on key learnings; and notably informs progression on MS program**. Recall, TLSA recently reported results from a 39-patient study (link), in which Foralumab was evaluated with and without dexamethasone. Foralumab treated patients demonstrated compelling improvements in lung CT scans both as a monotherapy, i.e., 75% and 80% in cohorts 2 and 3 relative to 43% control, and in combination with dexa, which also drove reductions in IL-6 from 69% to 41% and CRP from 85% to 55%. In the upcoming Ph. II study in moderate to severe patients, Foralumab may also be evaluated in emerging variant strains which have the ability to reinfect patients with prior C-19 disease as well as those vaccinated against wild-type C-19, leveraging its unique virus-agnostic mechanism to dampen the overactive immune response in response to pulmonary inflammation through Treg stimulation.

While we remain encouraged about the potential of Foralumab to drive clinically meaningful benefits on both anti-inflammatory markers and patient reported outcomes on improvements in symptomatology, we also note that the study may serve to further de-risk ongoing efforts in a relatively larger market opportunity in progressive MS. For the identified SPMS patient, under an individual Patient Expanded Access program, the treatment is expected to continue for six months, with evaluation to occur on standard neurological assessments as well as microglial imaging on PET to assay modification of immunological and neurodegenerative markers. Recall, the company recently completed a Ph. I multiple ascending dose study in which no drug-related safety issues were reported at doses up to 250mg, in line with observations from the prior proof-of-concept C-19 studies in which treatment of 100mg nasal Foralumab for 10 consecutive days was well-tolerated with no severe adverse events. In parallel, TLSA anticipates clearance of the full IND to commence initiation of Ph. II MS study in the next few weeks.

## Valuation

We base our Buy rating and 12-month price target of $8 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% discount rate and a 2% terminal growth rate, in line with other clinical-stage biotech companies, yielding an implied enterprise value of $383M. For 2030, the final projected year of our model, we forecast $770M 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 $61M 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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|---|---|---|
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