Tiziana Life Sciences Plc (TLSA – $1.96*)
Buy; $8.00 PT; $160.6M Market Cap
Company Update
Friday, September 10, 2021

Frosting on the Cake with Foralumab's Foray Into Lymphodepletion Via DTIL Strategic Partnership; Reit. Buy, $8 PT

Mayank Mamtani
646-885-5463
mmamtani@brileyfin.com

Yuan Zhi, Ph.D.
703-312-1776
yzhi@brileyfin.com

Summary and Recommendation

Earlier in the month, Precision BioSciences (DTIL) announced an exclusive license agreement to gain access to Tiziana's anti-CD3 antibody, foralumab, for evaluation as a lymphodepletion agent with DTIL's industry-leading allogeneic CAR T portfolio. Recall, foralumab is a fully humanized anti-CD3 antibody, currently in clinical development for intranasal delivery in COVID and multiple sclerosis (MS), as well as oral delivery for Crohn's Disease (CD). The breadth of formulation and indication coverage, within foralumab's extensive patent portfolio, allows for this niche application being carved out that only applies exclusively to allogeneic CAR T modality; leaving TLSA with freedom to operate in striking additional strategic arrangements with additional cell therapy modalities, also in need of innovating lymphodepleting strategies. Before infusion of engineered T cells, patients are given a conditioning regimen (chemotherapy-based) to clear lymphoma cells, a procedure called lymphodepletion, to "make room" for the new cells, specifically to decrease immunogenicity and increase persistence of infused CAR T cells. Post conditioning, the engineered T cells, sourced from the patient/donor, are infused into the patient, where these cells essentially rebuild the patient's immune system. However, the conventional chemo-based conditioning regimen is associated with risk, including short-term and long-term toxicities, where some patients fail to tolerate the conditioning regimen, thereby rendering the CAR T therapy less efficacious. Anti-CD3 antibody has been used to modulate and eliminate CD3+ T cells.

Recall, DTIL used its genome editing platform to deplete CD3 in CAR T cells, producing allogeneic CAR T candidates that are >99.9% CD3-negative. Adding anti-CD3 antibody could theoretically selectively modulate and eliminate CD3+ T cells from the host, while leaving infused CD3- T cells intact. Therefore, foralumab will be used in the conditioning step to reduce the dose of chemo, as well as in maintenance aiming to extend the survival of allogeneic T cells. TLSA has filed a patent application covering the use of foralumab in CAR T cell therapy, pending US patent office decision. As an analog, Allogene has deployed an anti-CD52 antibody to increase the anti-lymphoma effect and CAR T-cell persistence of their allogeneic T cells. Broadly, immune modulating drug class for hematological cell therapy applications have recently attracted big pharma M&A interest, notably Sanofi's recent acquisition of Kadmon for $1.9B to add FDA-approved ROCK-2–targeting transplant medicine. While the deal terms between TLSA and DTIL on foralumab aren't disclosed, we view this transaction to be accretive to our core thesis centered around foralumab's application in progressive MS and CD. While TLSA executes on key IND-enabling studies for intranasal formalumab, we highlight the expanded access program remains on track testing six-month treatment of foralumab in a progressive MS patient with a robust safety profile already observed with three cycles of treatment. Mgmt. commented the biomarker and MRI data from this patient to be released by the year-end. In the meantime, the Ph. II trial of progressive MS is expected to be initiated in 1Q22, while Ph. Ib/IIa trial for CD remains on track to be initiated in 4Q21. Reiterate Buy and $8 PT.

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 13.5% discount rate and a 2% terminal growth rate, in line with other clinical-stage biotech companies, yielding an implied enterprise value of $365M. 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 $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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