Foralumab Gains Expanded Access for SPMS and Advances to Phase II in COVID

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NASDAQ:TLSA | LSE:TILS

Tiziana Life Sciences (NASDAQ: TLSA) (LSE: TILS) disseminated two press releases today updating investors on progress in its Foralumab programs that will address COVID-19 and secondary progressive multiple sclerosis (SPMS). The company is developing Foralumab in multiple indications that benefit from the biologic's calming of the immune system. The drug is a fully human anti-CD3 monoclonal antibody (mAb) that binds to the CD3 receptor on T-cells, thereby modulating the immune response.

In a morning press release, Tiziana disclosed that the FDA cleared an application to use nasally administered Foralumab to treat a subject with SPMS via the Individual Patient Expanded Access Program. This route of delivery is a more direct pathway[1] to the central nervous system (CNS) where the demyelinating of nerve cells in Multiple Sclerosis (MS) occurs. Although this work is not intended to support the ultimate approval of Foralumab for use in SPMS, it will inform stakeholders about the potential benefits of the drug and treat a patient with a serious or life-threatening condition who lacks other alternatives. The Expanded Access program is not intended to provide information about the safety or effectiveness of Foralumab, but will bring the product to the attention of regulatory authorities and investors.

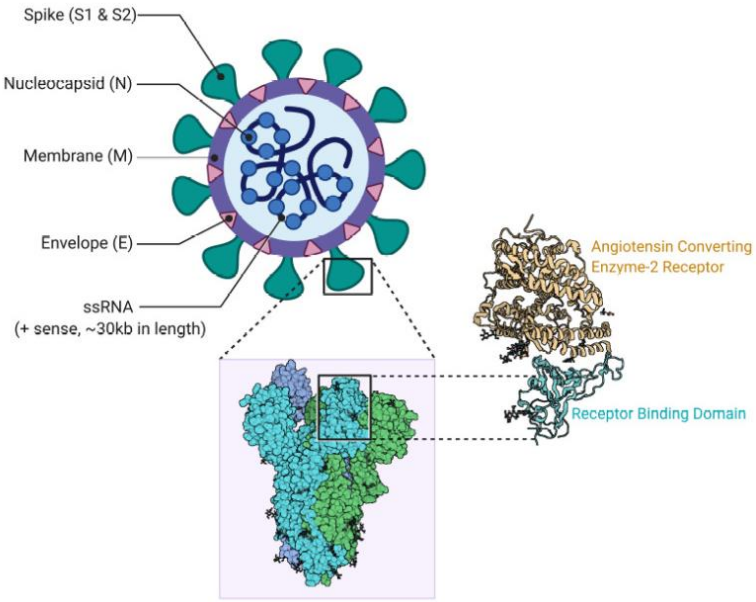
This dispensation will be the first granted to a nasally administered antibody for SPMS. The treatment will take place at the Brigham and Women's Hospital at Harvard University and is expected to begin in 2Q:21 and last for six months. Data collection will include routine safety, neurological, imaging and positron emission tomography (PET) studies to evaluate microglial imaging.

[1] Ladel, S. *et al*. Allogenic Fc Domain-Facilitated Uptake of IgG in Nasal *Lamina Propria*: Friend or Foe for Intranasal CNS Delivery? Pharmaceutics. 2018 Sep; 10(3): 107.

The Expanded Access follows the completion of a Phase I safety trial in Foralumab that performed a multiple ascending dose, once per day dosing with nasally administered drug. No drug-related safety issues were reported up to 250 mg. There are few effective treatments for SPMS and available therapy only works in a minority of the population, highlighting a substantial unmet need. One of the stakeholders in the trial and a neurologist who specializes in MS, Dr. Tanuja Chitnis, believes that "Nasal Foralumab could revolutionize treatment for [SPMS]."

Foralumab has been used in other indications and recently reported data from a clinical study in Brazil in patients with mild to moderate COVID-19 symptoms which we outline here. The data from the Phase I showed a reduction in lung inflammation and in pro-inflammatory biomarkers including IL-6 and C-Reactive Protein (CRP). This treatment for COVID-19 symptoms is variant-agnostic and modulates the immune system's response to the virus rather addressing the virus itself. This feature may allow Foralumab to serve as a valuable tool against a variety of respiratory diseases and their mutations as it reduces the damage caused by the patient's own immune system.

SARS-CoV-2 Structure[2]



Following the success of the Phase I trial in COVID-19 announced last month, Tiziana reported its plans today to launch a Phase II study in moderate to severe hospitalized COVID-19 patients. The effort will examine the benefits of nasally administered Foralumab in these individuals along with standard of care treatment. If successful, this effort will demonstrate the safety and efficacy of a potent immunomodulator used against this respiratory illness.

Foralumab's mechanism of action tempers an overreaction by the immune system and abnormal host response by removing T cells and increasing T regulatory cells (Tregs), whose abnormal frequency and function are implicated in most autoimmune diseases. Its method of administration is equally important, as nasal delivery allows the monoclonal antibody to reach the lung mucosa and act on the

[2] Cascella, M. *et al.* Features, Evaluation, and Treatment of Coronavirus (COVID-19). 2021, StatPearls Publishing LLC.

tissue involved with this respiratory virus. Tiziana expects that the administration of the drug will delay progression of the disease and provide immediate relief to this patient group.

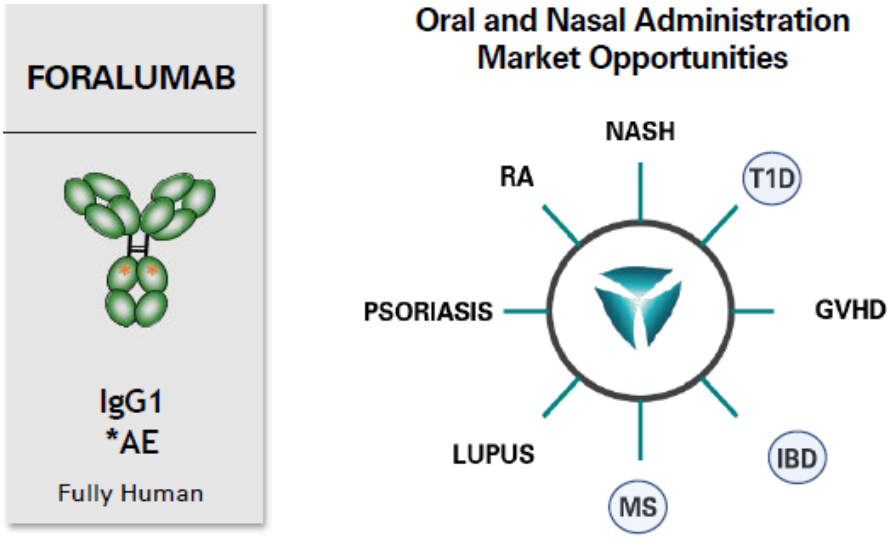
Foralumab

Foralumab is a fully human anti-CD3 mAb that has been in-licensed from Novimmune SA. The fully-human IgG1 antibody has been reconstituted into a lyophilized powder that can be manufactured into a pill or solution form. The drug has been investigated in Phase I and Phase II trials by Novimmune and in Phase I trials by Tiziana for Multiple Sclerosis, Crohn's Disease and most recently COVID-19 using an intranasal administration approach.

Most mAbs are administered via intravenous (IV) infusion; however, there are disadvantages to this approach such as the need for hospital visits, fluid overload, infusion complications (extravasations or air emboli, local infections, hematoma) and allergic reactions including anaphylaxis. Tiziana has overcome this limitation by manufacturing lyophilized and stabilized free flowing powder that can be used in oral and stabilized solution forms. In the COVID-19 study, the stabilized solution form of Foralumab was used for direct delivery via nostrils, which provides for rapid delivery to the nasal mucosa, airway and lungs, precisely the area where it may reduce inflammation by direct application.

Nasal administration allows the biologic to more easily transit the nasal passages to the lungs where it can impact localized inflammation. Anti-CD3 epsilon (ε) chain binding suppresses the immune system by reducing the number of effector T cells and inducing the development of adaptive T regulatory cells, which can suppress immune response. This feature was hypothesized to be particularly valuable in COVID patients who in the worst cases have an overactive immune response and suffer from severe respiratory distress.

Foralumab, Fully Human Anti-CD3[3]



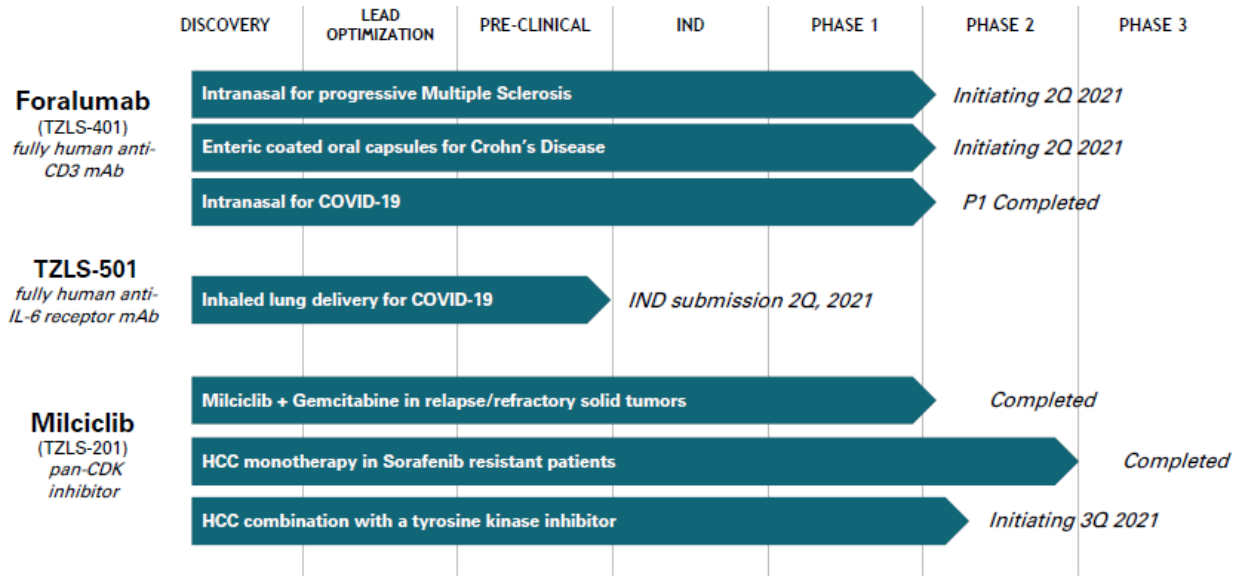
Tiziana Life Sciences

Tiziana Life Sciences is a UK and US headquartered biotechnology company developing therapies for a portfolio of indications including Multiple Sclerosis, Crohn's Disease, COVID-19 and various cancers.

[3] Source: Tiziana Life Sciences January 2021 Corporate Presentation

Two Phase II trials investigating Foralumab are expected to be launched in the second quarter of this year in Multiple Sclerosis and Crohn's Disease. Another Phase II trial for hepatocellular carcinoma (HCC) is targeting launch by the third quarter of 2021 with the investigational drug Milciclib.

Tiziana Pipeline[4]



Summary

Following the successful outcome from the Phase I trial in COVID-19 patients in February, Tiziana has now updated investors with two new material announcements for Foralumab. The biologic was granted Individual Patient Expanded Access in an SPMS patient who was poorly served by existing therapies. The drug will also participate in a Phase II study examining a COVID-19 population with moderate to severe symptoms. If successful, these efforts will demonstrate Foralumab's ability to modulate the immune system via intranasal delivery and address the symptoms and underlying disease.

[4] Source: Tiziana Life Sciences January 2021 Corporate Presentation