Tiziana Life Sciences Announces New Quantitative PET Imaging Data on Foralumab at the Annual Meeting of the American Academy of Neurology

- *Oral presentation of study shows intranasal foralumab attenuates microglial activation and disease progression in multiple sclerosis (MS) patients with PIRA as measured by changes in PET scans* -

NEW YORK, April 18, 2024 – Tiziana Life Sciences, Ltd. (Nasdaq: TLSA) ("Tiziana" or the "Company"), a biotechnology company developing breakthrough immunomodulation therapies via novel routes of drug delivery, today announces a platform presentation titled, "Treatment of PIRA with Nasal Foralumab Dampens Microglial Activation and Stabilizes Clinical Progression in Non-Active Secondary Progressive MS" at the Annual Meeting of the American Academy of Neurology in Denver, Colorado. The presentation includes new, encouraging quantitative imaging data from foralumab's intermediate-size patient population Expanded Access Program. In the presentation, foralumab, a fully human anti-CD3 monoclonal-antibody showed the attenuation of microglial activation in patients with non-active secondary progressive multiple sclerosis (na-SPMS) based on positron emission tomography (PET) imaging and disease stabilization in na-SPMS patients with disease progression independent of relapse (PIRA).

Gabriele Cerrone, Chairman, acting CEO and founder of Tiziana Life Sciences, commented, "Tiziana is taking a leadership role in focusing on this subset of progressive MS where there are no effective treatments. One of the mechanisms thought to contribute to na-SPMS with PIRA is the activation of microglial cells, for which there have historically been no good biomarkers in humans. However, [F18]PBR06-PET is a novel imaging technique using a ligand with a long half-life, and therefore serves as a viable proof-of-concept to show the binding and dampening of active microglia. We are now able to quantify these immunologic changes via PET scan in na-SPMS patients. The mechanism of action seen thus far with foralumab is significant since a major unmet need in MS is developing therapy for na-SPMS with PIRA and being able to dampen associated neuro inflammation."

The oral presentation, delivered by Tarun Singhal, M.B.B.S., M.D., Director of the PET Imaging Program in Neurologic Diseases at Brigham and Women's Hospital, a founding member of Mass General Brigham Healthcare System, and Associate Professor of Neurology at Harvard Medical School, assesses the effect of intranasal foralumab on microglial activation in na-SPMS patients with PIRA as measured by positron emission tomography (PET) imaging via [F-18]PBR06-PET, a novel, long-half-life ligand used in PET scanning. The study is designed to be open-label and part of the Expanded-Access Program evaluating foralumab in na-SPMS patients that is currently underway.

Five of six patients (83%, 95% confidence interval 44%-97%) showed a qualitative reduction on [F-18]PBR06-PET in multiple brain regions after both 3 and 6 months of nasal foralumab treatment, which implies that there is *in vivo* evidence for reduced microglial activation and neuroinflammation following treatment with nasal foralumab. White matter z-scores (a measure of abnormally increased neuroinflammation) were reduced by 26-36% in the foralumab-treated group at 3 and 6 months, which was >4-5-times higher compared to 6% variability in the test-retest group. Clinically, foralumab-treated patients demonstrated a stable EDSS and improvement in the Modified Fatigue Impact Scale (MFIS). Reduction in fatigue as measured by the MFIS is clinically relevant to the lives of na-SPMS patients and will be a key monitoring parameter moving forward.

Nasal foralumab attenuated microglial activation in na-SPMS patients with PIRA at 3 and 6 months, as evaluated by [F-18]PBR06-PET and was associated with clinical symptom stability. Based on these positive results, a double-blind, placebo-controlled, dose-ranging study of nasal-foralumab in na-SPMS with [F-18]PBR06-PET as a primary endpoint with measures of EDSS and MFIS is underway. This trial (NCT06292923) is important because if the potential to slow disease progression is demonstrated this would align with early treatment intervention.

About Foralumab

Activated T cells play an important role in the inflammatory process. Foralumab, the only fully human anti-CD3 monoclonal antibody (mAb), binds to the T cell receptor and dampens inflammation by modulating T cell function, thereby suppressing effector features in multiple immune cell subsets. This effect has been demonstrated in patients with COVID and with multiple sclerosis, as well as in healthy normal subjects. The non-active SPMS intranasal foralumab Phase 2 trial began screening patients in November of 2023. Immunomodulation by nasal anti-CD3 mAb represents a novel avenue for treatment of neuroinflammatory and neurodegenerative human diseases.[1],[2]

About Tiziana Life Sciences

Tiziana Life Sciences is a clinical-stage biopharmaceutical company developing breakthrough therapies using transformational drug delivery technologies to enable alternative routes of immunotherapy. Tiziana's innovative nasal approach has the potential to provide an improvement in efficacy as well as safety and tolerability compared to intravenous (IV) delivery. Tiziana's lead candidate, intranasal foralumab, which is the only fully human anti-CD3 mAb, has demonstrated a favorable safety profile and clinical response in patients in studies to date. Tiziana's technology for alternative routes of immunotherapy has been patented with several applications pending and is expected to allow for broad pipeline applications.

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[1] https://www.pnas.org/doi/10.1073/pnas.2220272120

[2] https://www.pnas.org/doi/10.1073/pnas.2309221120