tiziana LIFE SCIENCES

Intranasal Anti-CD3 mAb Therapy to Enable Breakthroughs in Inflammatory Disease

Disclaimer and Forward-Looking Statement

The content of this presentation has been prepared for the purpose of providing general information about, and an overview of, the Company and its business. It is not intended to be a complete review of all matters concerning the Company and nor has it been independently verified. Whilst the presentation has been prepared in good faith and the Company has taken all reasonable care to ensure the information and facts contained in this presentation are accurate and up-to-date, it does not make any representation or warranty, express or implied, as to the accuracy or completeness of any information included in this presentation. Neither the Company nor any of its directors, officers, employees or agents shall be liable for any loss arising directly or indirectly from the use of or reliance upon this presentation or in relation to the adequacy, accuracy, completeness or reasonableness of the information it contains. All and any such liability is expressly excluded to the fullest extent permitted by law. The information in this presentation is subject to updating, completion, revision, further verification and amendment without notice.

This presentation does not constitute or form part of any offer for sale or solicitation of any offer to buy or subscribe for any securities including ordinary shares in the Company nor does it constitute an invitation or inducement to engage in investment activity in relation to any securities, including the ordinary shares of the Company. It does not purport to contain information that shall form the basis of or be relied upon in making such investment decisions. If you require any advice, please consult with a professional financial adviser. All investments are subject to risk. The value of securities may go down as well as up. Past performance cannot be relied on as a guide for future performance.

This presentation may contain certain forward-looking statements concerning the financial condition, results of operations and businesses of the Company. All statements other than statements of historical fact are, or may be deemed to be, forward-looking statements. Forward-looking statements are statements of future expectations that are based on management's current expectations and assumptions and involve known and unknown risks and uncertainties that could cause actual results, performance or events to differ materially from those expressed or implied in these statements. All forward-looking statements contained in this presentation are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. You should not place undue reliance on forward-looking statements. Each forward-looking statement speaks only as of the date of this presentation. The Company does not undertake any obligation to publicly update or revise any forward-looking statement as a result of new information, future events or other information. In light of these risks, results could differ materially from those stated, implied or inferred from the forward-looking statements contained in this presentation.

Investment Highlights

Innovative, clinically-validated, drug delivery platform based on novel MoA achieved with intranasal mode of delivery

Global IP protection of antibody formulation technology until 2040, can be applied across different molecules
Strong IP protection for foralumab

Provention Bio partnership with Sanofi and its subsequent $2.9B acquisition validates the anti-CD3 platform's broad applicability

Targeting the global $150+ billion market for antibody treatments.[1]
Clinical data and publication in *PNAS*[2] validate MOA for intranasal administration

Experienced scientific advisory board and management team that has brought multiple drugs to market

tiziana LIFE SCIENCES

Source: 1 Lu et al. Journal of Biomedical Science (2020) 27:1
[2] PNAS=Proceedings of the National Academy of Sciences journal; https://www.pnas.org/doi/10.1073/pnas.2220272120

Lead Asset is Intranasal Foralumab

Multiple administration routes of a proven systemic anti-inflammatory, patent protected until 2040

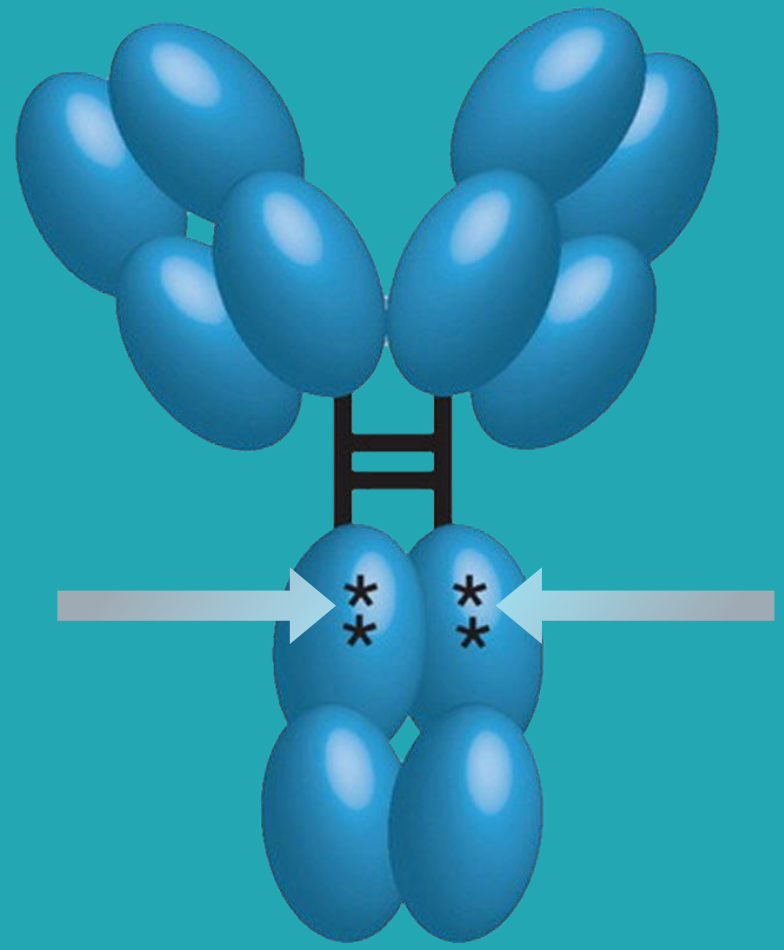
	THERAPEUTIC AREA	PRECLINICAL	IND	PHASE 1	PHASE 2	PHASE 3	COMMENTS
FORALUMAB: NASAL (fully human anti-CD3 mAb)	Non-active SPMS*						Phase 2 expected to begin 3Q 2023
	Alzheimer's						IND planned 2Q 2023
	Long COVID						IND planned 4Q 2023
	Early Onset Type 1 DM						
	ALS**						
	Intracerebral Hemorrhage (ICH)".						
FORALUMAB: SUBCUTANEOUS	Diabetes						Deprioritized
FORALUMAB: ORAL	Crohn's Disease						Deprioritized
MILCICLIB	NSCLC						Deprioritized
IL-6	Inflammatory Diseases						Deprioritized

* Non-Active Secondary Progressive Multiple Sclerosis (expanded program; n=6) ** Grant from Amyotrophic Lateral Sclerosis Association for development

tiziana LIFE SCIENCES

Lead Asset:
Intranasal Foralumab

The only **fully human** anti-CD3 monoclonal antibody in clinical studies

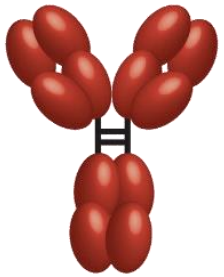
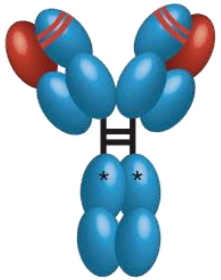
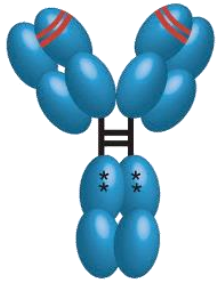
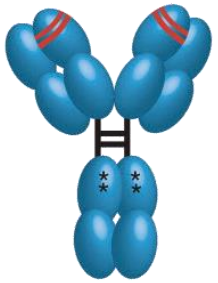
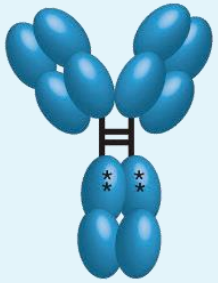


Non-FC binding anti-CD3 antibody mutations expected to have improved safety profile

tiziana
LIFE SCIENCES

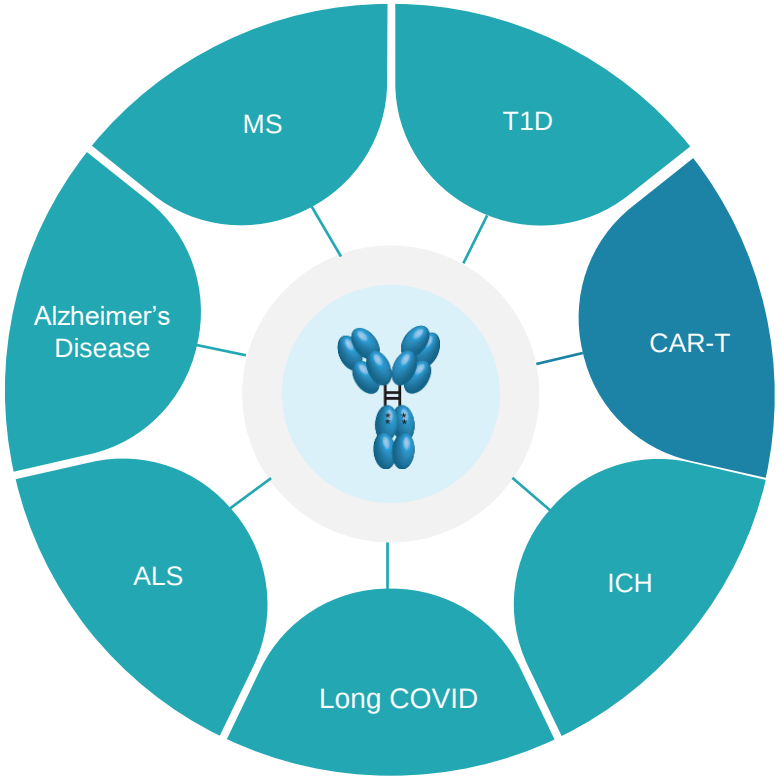
Foralumab is the Only Fully Human Anti-CD3 mAb in Clinical Trials

Approved and Investigational CD3-specific Monoclonal Antibodies

OKT3 **Muromonab†**	**ChAglyCD3** **Otelixizumab**	Aala-Ala) **hOKT3y1** **Teplizumab††**	**Nuvion** **Visilizumab**	**Foralumab**
				
IgG2a	IgG1 N297 / A	IgG2 L234 / A, L235A	IgG2 L234/A, V237/A	IgG1 L234/A, V335E
Fully Murine	Chimeric & Humanized	Humanized	Humanized	Fully Human

† Approved by the FDA for solid organ transplantation immuno-suppression
†† Acquired by Sanofi for $2.9B

Rodent Origin
Human Origin
*Point Mutation



tiziana LIFE SCIENCES

Adapted from: Kuhn, Chantal, and Howard L. Weiner. "Therapeutic anti-CD3 monoclonal antibodies: from bench to bedside." Immunotherapy 8.8 (2016): 889-906.

Proceedings of the National Academy of Sciences Publication Validates Foralumab's MoA

01 Illustrates that the immunological basis of the mechanism of action for intranasal foralumab is based on increasing production of naïve-like T cells and Tregs, while simultaneously decreasing the production of effector T cells

02 Further, highlights how intranasal foralumab has similar immune gene expression effects in COVID patients, Multiple Sclerosis patients and in heathy volunteers

03 Concludes that immunomodulation by nasal anti-CD3 mAb represents a novel avenue for treatment of inflammatory human diseases

04 Having an intranasal fully human monoclonal antibody that positively modulates the immune system allows Tiziana to explore multiple inflammatory disease indications in addition to multiple sclerosis (MS)

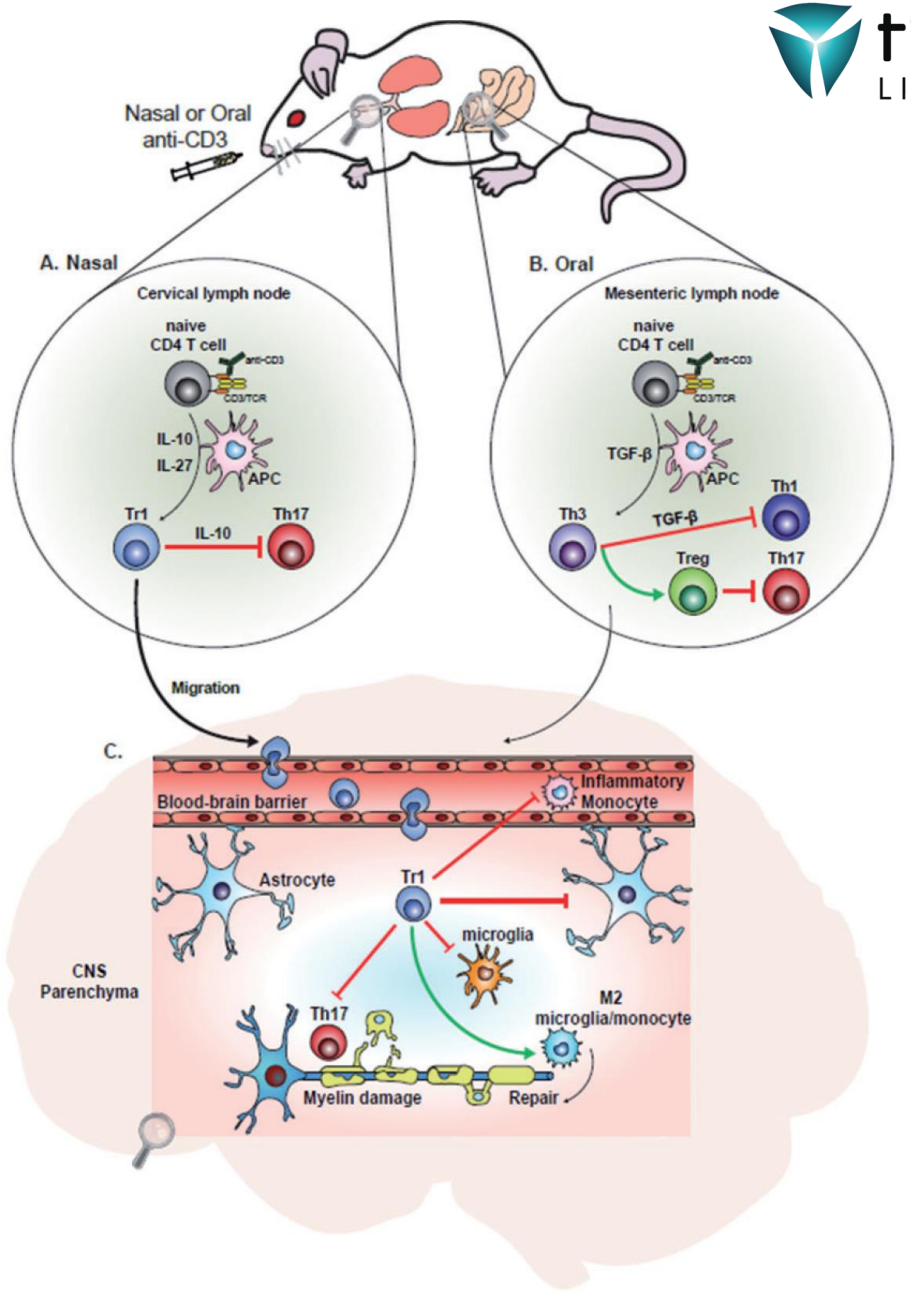
05 Findings are consistent with other research done at the Ann Romney Center; validates rationale for Tiziana's upcoming IND filing to investigate intranasal foralumab in Alzheimer's Disease

06 Dr. Tanuja Chitnis, M.D., Professor of Neurology at Brigham and Women's Hospital, a founding member of Mass General Brigham healthcare system: "…the unique immunomodulatory signature of intranasal foralumab makes it a promising therapeutic candidate for several rare Orphan pediatric neuroinflammatory diseases, which currently remain untreated."

tiziana LIFE SCIENCES

Nasal administration of anti-CD3 mAb (Foralumab) downregulates NKG7 and increases TGFB1 and GIMAP7 expression in T cells in subjects with COVID-19 (Moreira, T.G., et al.)
A copy of the article can be found at pnas.org.

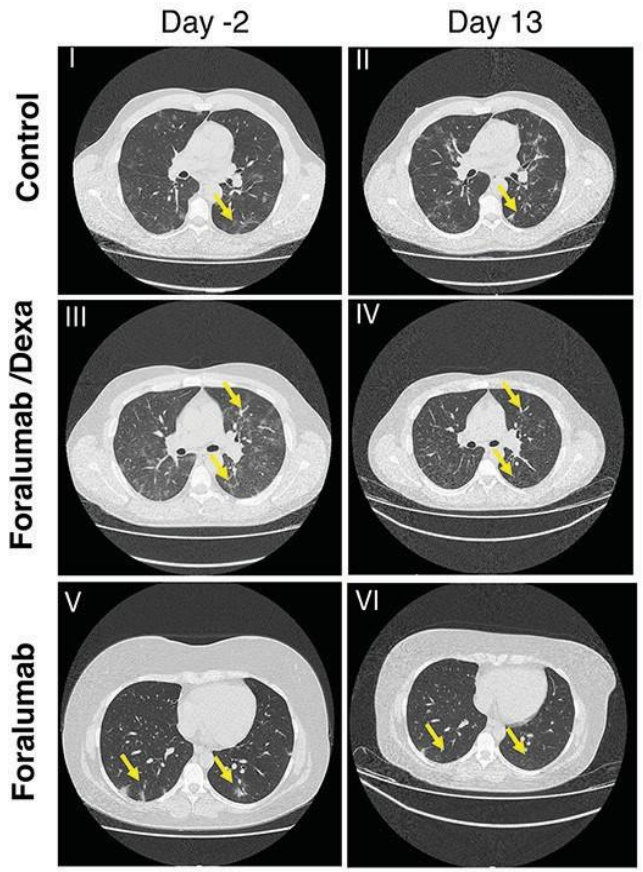
The binding of foralumab to the T-cell receptor complex, through either the nasal or oral route, results in suppression of effector T-cells involved in various inflammatory and autoimmune diseases along with a reduction in inflammatory cytokines and increase in Tregs anti-inflammatory cytokines.



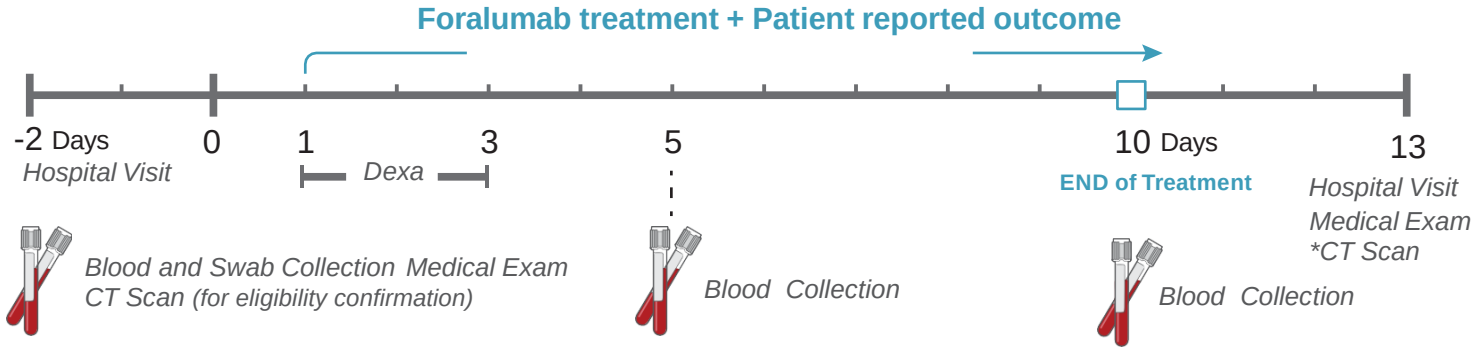
BRAIN 2016: 139; 1866-1878

Foralumab: Clinical Proof of Concept for Intranasal Delivery First Demonstrated in Mild-to-Moderate COVID-19

CT Scan of Patients' Lungs



The First Validation That Intranasally Administered Foralumab is Well-tolerated and the Treatment Provides Clinical Benefits



Results: Biomarkers measured via cytokines and C-reactive proteins

Cohort	Lung CT Scan	Cytokine IL-6	C-Reactive Protein
Evaluable patients	% Improvement	% Reduction	% Reduction
Control, n=14	43	37	40
Foralumab + Dexa, n=12	75	41	55
Foralumab, n=10	**80**	**69**	**85**

Long COVID IND planned Q4 2023

tiziana LIFE SCIENCES

Fully Human
Anti-CD3 mAb

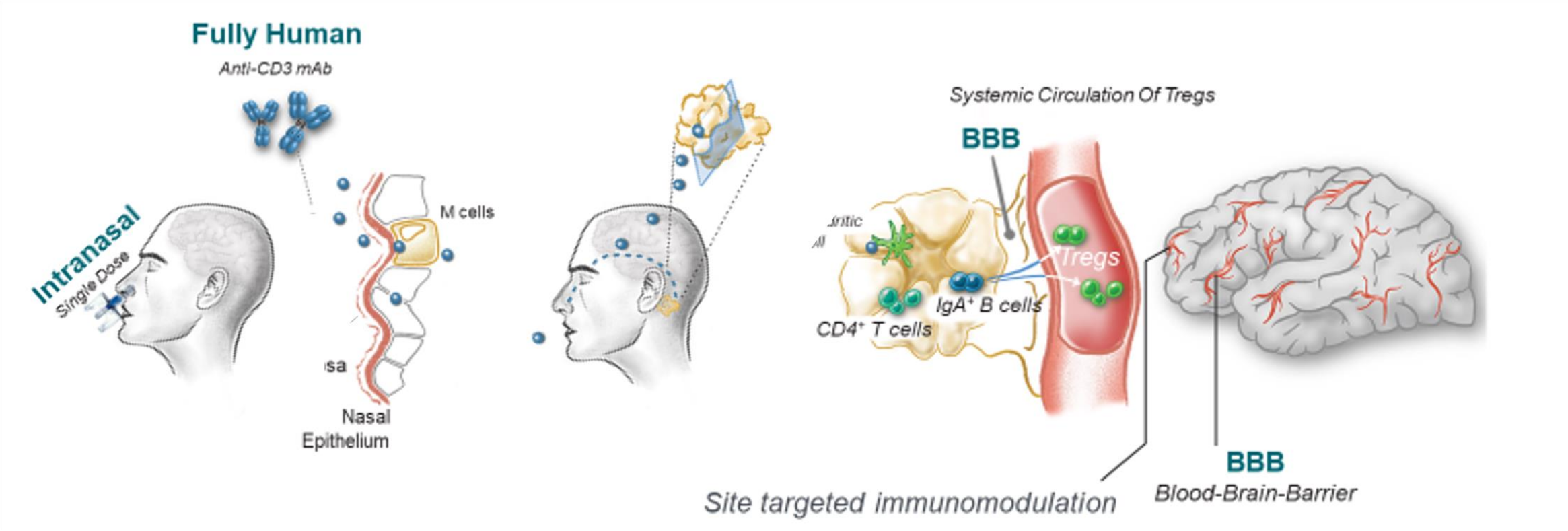
Intranasal

Intranasal Foralumab for Treatment of Neuroinflammatory Diseases (Multiple Sclerosis)

Local application with systemic effect, improved safety and lowered dosing

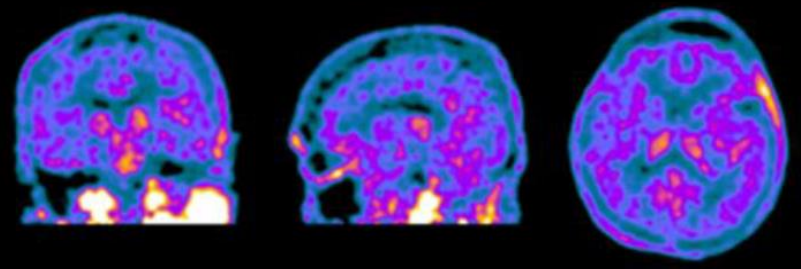
Intranasally-Administered Foralumab for Neuroinflammatory Diseases

An Innovative Approach to Penetrate the Blood Brain Barrier (BBB)

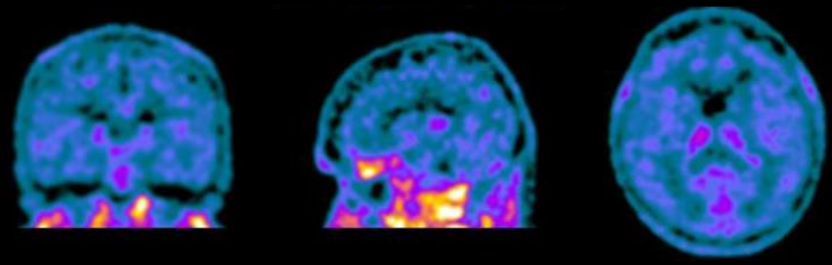


Assessment of Inhibition of Microglial Activation by PET Imaging Following Treatment with Nasally Administered Foralumab in SPMS Patient

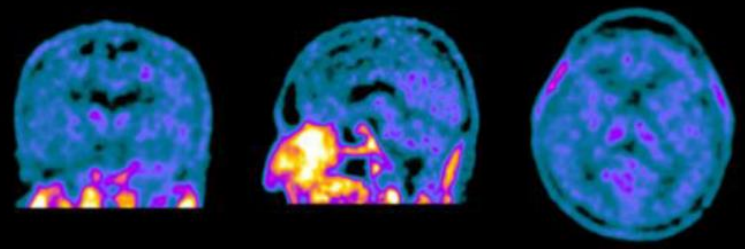
Baseline:
Prior to intranasal foralumab treatment



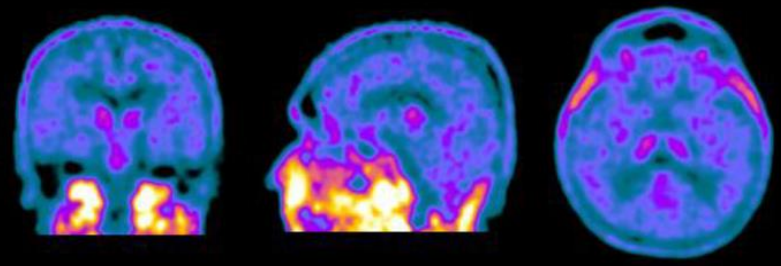
3-month scan:
3-months of intranasal foralumab treatment



7-week washout due to patient contracting COVID:
No intranasal foralumab during this period



6-month scan:
After 6-months (total) of intranasal foralumab



Clinical Update on Patient EA2

2018 – 2021

Patient's non-active SPMS disability progressed

EDSS worsened from 3.5 to 6.0 despite ocrelizumab* therapy

Ocrelizumab was discontinued in 2021

At this time, EA2 required a cane to walk 100 meters.

*$5.6B 2022 WAC

2022

Enrolled in the intranasal foralumab Expanded Access Program (EAP) in January 2022

EA2 able to walk 100 meters without a cane in September 2022

EDSS score improved from 6.0 to 5.5

EA2 able to walk 200 meters without a cane in December 2022

EDSS score improved from 5.5 to 5.0

Pyramidal score continued to remain stable

2023

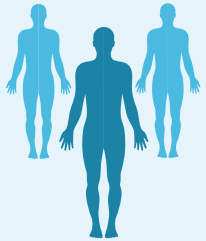
Patient returned to work part-time

Patient continues treatment though our EA Program

Expanded Access (EA) Non-Active MS Program Expanded to 6 Total Non-Active SPMS Patients with the Aim of Enrolling a Total of 10

Patient Progress

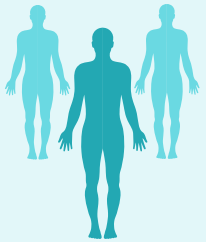
EA3 THROUGH EA6
(4 patients)



- All patients enrolled
- Baseline PET scans finished
- 3-month PET scans and physical assessment pending

All patients receive 3-month dose March 2023

EA7 THROUGH EA10
(additional 4 patients)



Enrollment scheduled for Q2 2023

Phase 2 Planning and Implementation

TYPE C FDA meeting minutes received March 2023 with positive feedback

Design

- Placebo-controlled
- Multi-center
- Dose-ranging
- Established outcome measures

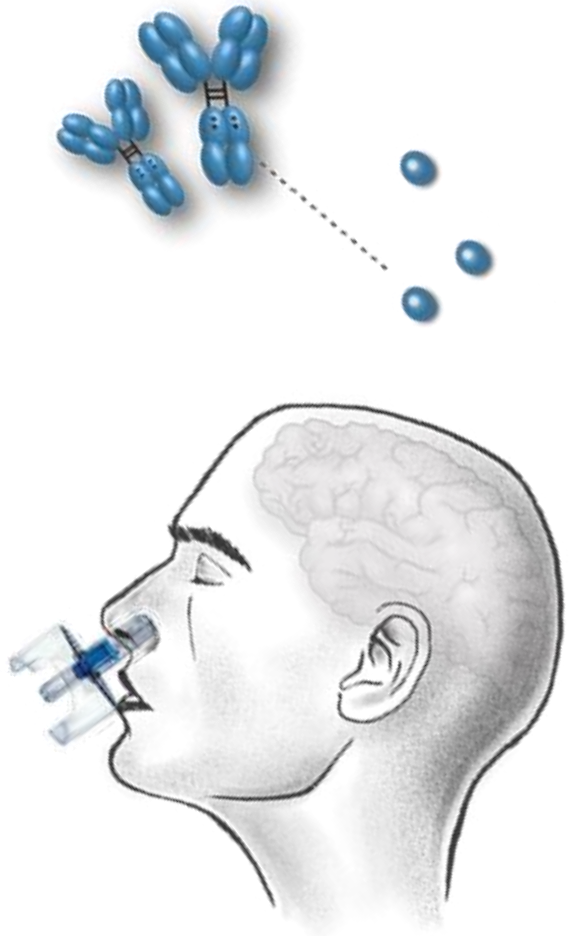
Endpoints

- ☐ PET Scan
- ☐ Expanded Disability Status Scale (EDSS)
- ☐ Improvement in Timed 25-Foot Walk Test (T25FW)

First investigator meeting expected to start Q3 2023

Other Potential CNS-related Indications (Alzheimer's, ALS, Long COVID and Intracerebral Hemorrhage)

Intranasal anti-CD3 provides a unique approach for treating progressive neurologic diseases by modulating microglial cells. The intranasal route of immunotherapy has minimal toxicity and induces regulatory T cells locally, that then migrate to the brain to dampen brain inflammation.



Alzheimer’s Disease Plan is Underway

01

Received (August 2022) an affirmative written response from the FDA on a Pre-Investigational New Drug Application (PIND)

02

Submit an Investigational New Drug Application (IND) in Q2 2023 to conduct a Phase 2 study of intranasal foralumab in Alzheimer's disease patients

03

3-Week toxicology studies completed. 6-month toxicology studies ongoing

Start Phase 2 program in 2H of 2023

Intranasal Foralumab in Amyotrophic Lateral Sclerosis (ALS)

ALS patients have limited therapeutic options and a high unmet need

- In September 2022, a Lawrence & Isabel Barnett Drug Development Program Grant was awarded to the Ann Romney Center for Neurologic Diseases at Brigham and Women's Hospital by the ALS Association.
- This prestigious research grant supports the study of an intranasal anti-CD3 monoclonal antibody (mAb) in an animal model of Amyotrophic Lateral Sclerosis (ALS).
- The grant will allow further study the role of intranasal anti-CD3 mAb in dampening the microglial activation which amplifies ALS disease progression.

> **"We have now seen the potential of intranasal foralumab to dampen microglial activation in three major neuroinflammatory-related diseases, which creates significant optionality for exploring its benefits in some of the most important and burdensome medical conditions of our time."**
>
> **– Dr. Howard Weiner**

In Summary…

An exciting and innovative platform focused in areas of high unmet need, with significant momentum ahead

- Novel, fully human anti-CD3 intranasal mAb for potential treatment of multiple inflammatory diseases
- Mechanism of Action validated in prestigious *Proceedings of National Academy of Sciences* (PNAS)
- Formulation IP Protected until 2040

Q2 2023

IND filing planned in Alzheimer's Disease

2Q 2023

3-month data on four, non-active SPMS patients

3Q 2023

First investigator meeting for Phase 2 in non-active SPMS to begin

US Headquarters (Pennsylvania)

Tiziana Life Science Ltd.
601 New Britain Road
Building 100, Suite 102
Doylestown PA 18901

UK Headquarters (London)

Tiziana Life Sciences plc
14-15 Conduit Street
London
W1D 2XJ

Investors:
+44 7769 88 4020
pspencer@tizianalifesciences.com