Enabling Breakthrough Immunotherapies via Novel Routes of Drug Delivery

NASDAQ: TLSA

tiziana LIFE SCIENCES

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Investment Highlights

Innovative, clinically-validated, drug delivery platform enabling improved delivery routes for immunotherapies.
Recent clinical data support the MOA

Global IP protection of antibody formulation technology until 2040, can be applied across different molecules.
Strong IP protection for lead assets Milciclib and Foralumab

Partnership with Precision Biosciences for lymphodepletion ahead of CAR-T procedures.
Collaboration ongoing

Targeting the global $150+ billion market for antibody treatments[1].
Clinical data validate MOA for nasal administration

Experienced scientific advisory board and management team that has brought four drugs to market.
Demonstrated Bench to market experience

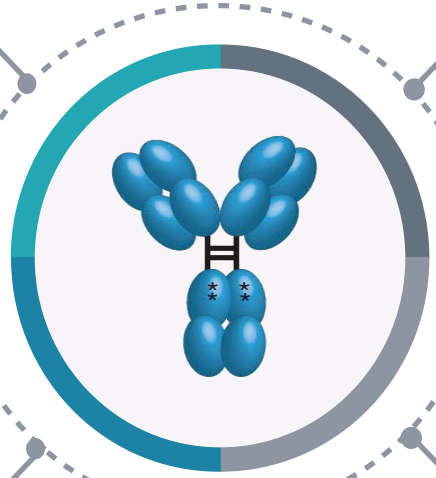
Source: [1] Lu et al. Journal of Biomedical Science (2020) 27:1

The Antibody Market is Enormous and Offers Significant Opportunities for Reformulation

Global Market was Valued at $150 Billion in 2019 and is Expected to Grow to $300 Billion by 2025[1]

Traditional administration is systemic, costly and burdensome to patients

Drug level in blood is high during the first few hours after dosing



Systemic treatment requires higher doses causing toxicity

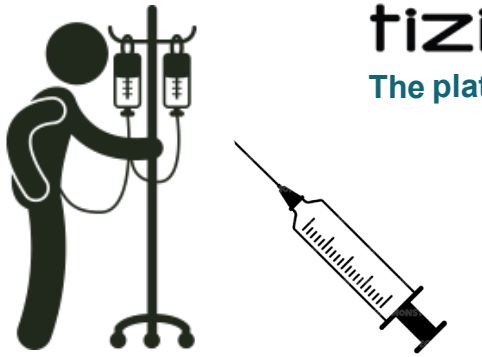
Compliance may be compromised due to the inconvenience of injecting subcutaneously or outpatient intravenous dosing visits

Source: [1] Lu et al. Journal of Biomedical Science (2020) 27:1

A Revolutionary Platform

Antibody Administration: Switching From IV and SC To Oral, Nasal And Inhaled Routes

Today's Options for Antibody Administration are Subcutaneous or Intravenous (IV)



tiziana

The platform enables…

Foralumab
Oral administration
For Crohn's Disease
IBD

Foralumab
Nasal administration
Multiple Sclerosis
Neurodegenerative diseases

TZLS- 501 Anti- IL6R
Direct delivery to lungs with a portable inhaler for pulmonary diseases

Benefits of non-systemic dosing

- Improved patient compliance
- Local activity instead of systemic distribution; may minimize side effects
- Anticipated lower cost of goods and lower price of administration

Our Pipeline

Five Clinical Studies completed. All with positive data

	Subject	PC	IND	Phase 1/IAP	Phase 2	Phase 3
FORALUMAB *Fully human anti-CD3 mAb*	Intranasal	Progressive Multiple Sclerosis (expanded program)			Ongoing IAP, 6 months data showed positive clinical response	
	Oral	Crohn's Disease			2Q 2022 Phase 1b	
	Subcutaneous	Type 1 Diabetes			2Q-2022 IND Submission	
ANTI IL-6 RECEPTOR *Fully human mAb*	Inhalation	Pulmonary Fibrosis			3Q-2022 IND Submission	
MILCICLIB *Pan-CDK inhibitor*	Oral	Milciclib + Gemcitabine in NSCLC Kras+ mutants			2Q-2022 IND Submission	

Near-Term Milestones

1Q 2022

FORALUMAB

T1 Diabetes (Sub-cutaneous)

Submission of IND and initiation of Phase 1a trial in healthy volunteers

Crohn's disease (oral)

Amended Protocol for evaluation of potential 'take-home' oral capsules in mild to moderate Crohn's Disease patients has been submitted.

Multiple sclerosis (intranasal)

Readout of 6-month clinical data in secondary progressive multiple sclerosis (SPMS) in the first patient under the individual patient access (IPA) program.

2Q 2022

FORALUMAB

Multiple sclerosis (intranasal)

Readout of 6-month clinical data in secondary progressive multiple sclerosis (SPMS) reported: Positive clinical responses. Second patient 3-months data anticipated May 2022.

Crohn's disease (oral)

Initiation of trial with 'take-home' oral capsules in mild to moderate Crohn's Disease patients. May 2022

MILCICLIB

KRAS+ NSCLC (oral)

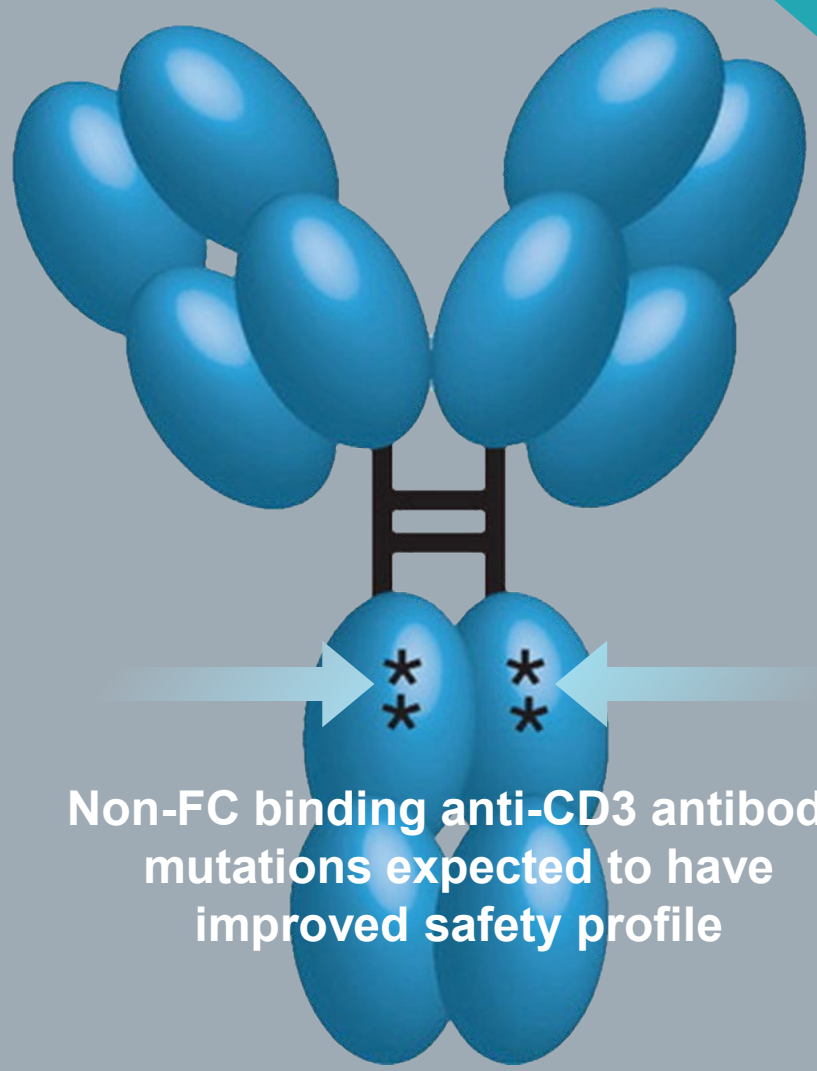
Filing of IND and Initiation of Phase 2 trial in KRAS+ NSCLC patients with combination of milciclib + gemcitabine

TLSA is Attractively Positioned Amongst Companies Developing Similar Pipeline Assets

CapIQ ID or Ticker	Company	Ticker	Market Cap (M, USD)	Therapeutic Focus
TLSA	**Tiziana Life Sciences PLC**	**TLSA**	**$ 78.9**	**Immunology, Oncology and Virology**
DTIL	Precision BioSciences, Inc.	DTIL	$ 260.08	Oncology (CAR-T)
NKTX	Nkarta, Inc.	NKTX	$ 308.74	Oncology (CAR-NK)
PRVB	Provention Bio, Inc.	PRVB	$ 413.20	Immunology (Type 1 Diabetes)
TGTX	TG Therapeutics, Inc.	TGTX	$ 1,296.41	Immunology
IMVT	Immunovant, Inc.	IMVT	$ 662.29	Immunology
ABSCF	AB Sciences S.A	ABSCF	$ 508.40	Neurodegenerative
MNOV	MediciNova, Inc	MNOV	$ 118.19	Neurodegenerative
ALT	Altimmune, Inc.	ALT	$ 359.97	Intranasal Vaccine

Lead Asset:
Foralumab

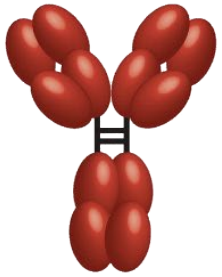
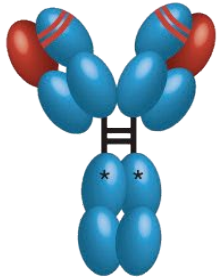
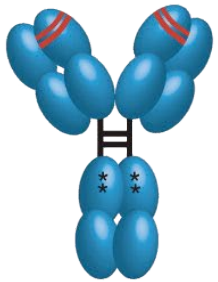
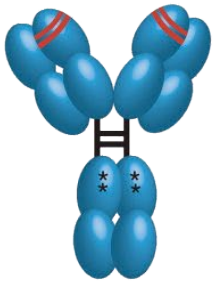
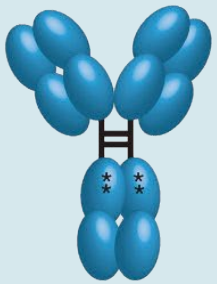
The only **fully human** anti-CD3 monoclonal antibody in clinical studies



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

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

CD3-specific Monoclonal Antibodies in Clinical Development

OKT3	ChAglyCD3	(Ala-Ala) hOKT3γ1	Nuvion	**Foralumab**
Muromonab*	Otelixizumab	Teplizumab	Visilizumab	
				
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

Rodent Origin

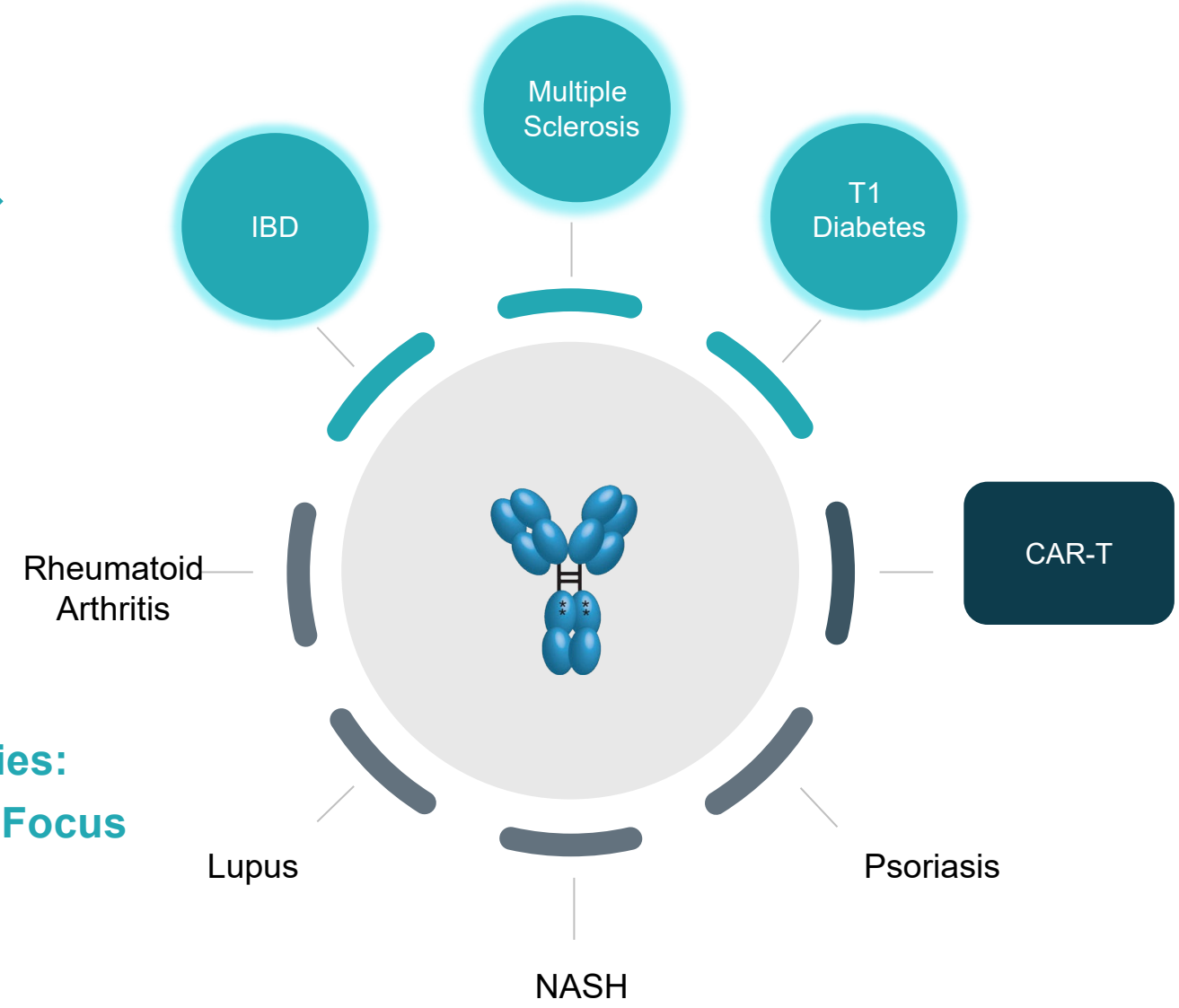
Human Origin * Point Mutation

First Ever Patent Granted for Oral Immunotherapy

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

CD3-specific Monoclonal Antibodies in Clinical Development

Broad Market Opportunities: Our Current Therapeutic Focus



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

Precision Biosciences (Nasdaq: DTIL) Licensing Collaboration Validates Our Technology

First foralumab Program to be Tested Will be in Combination with an Anti-CD19 CAR-T

- Exclusive agreement allowing Precision to explore Tiziana's fully human anti-CD3 monoclonal antibody (mAb), foralumab, as an agent to induce tolerance of allogeneic CAR-T cells to potentially improve the clinical outcome of Precision's CAR-T cell therapy programs
- Foralumab to be used as a potential mild pre-conditioning and lymphodepleting agent to replace or reduce doses of cyclophosphamide/fludarabine (Cy/Flu)

Upfront payments

- Multiple payments commensurate with meeting specified successful milestones
- Royalties
- Additional royalty options for subsequently developed CAR-T products
- Precision to be responsible for the development, commercialization and costs for use of foralumab

Intranasal Foralumab for Treatment of Neurodegenerative Diseases (Multiple Sclerosis)

Local activity with improved safety and lowered dosing

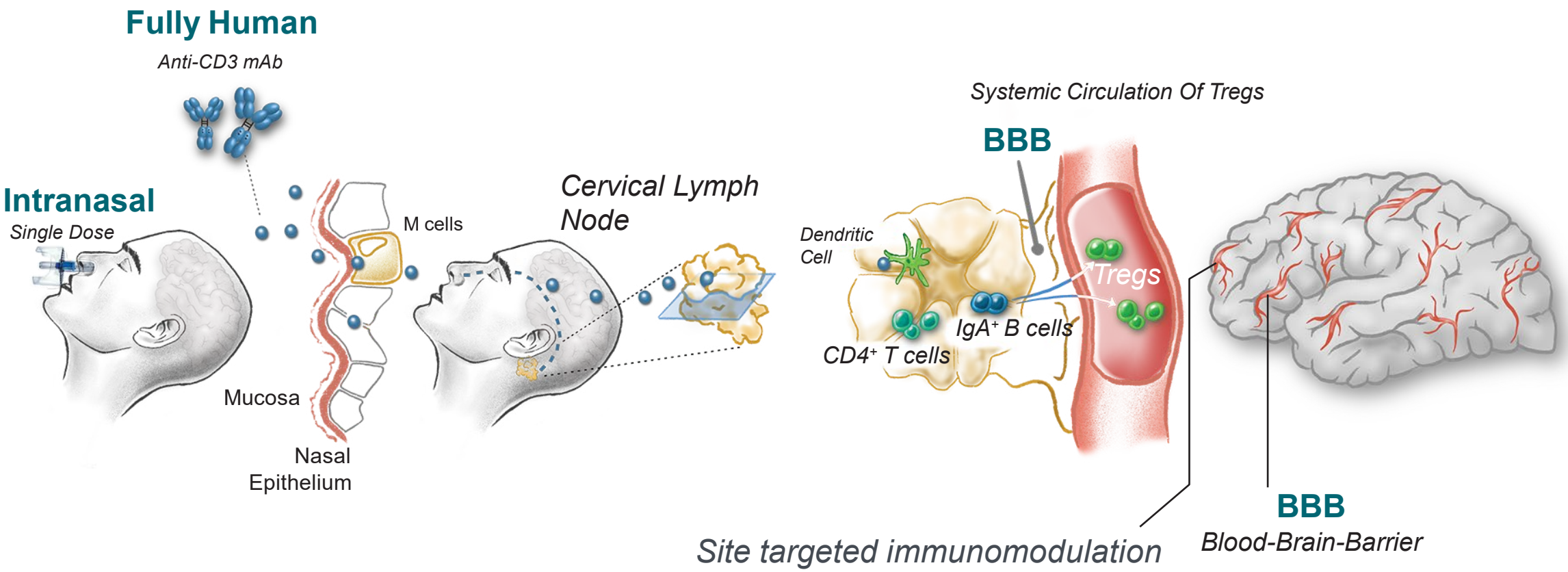
Fully Human

Anti-CD3 mAb

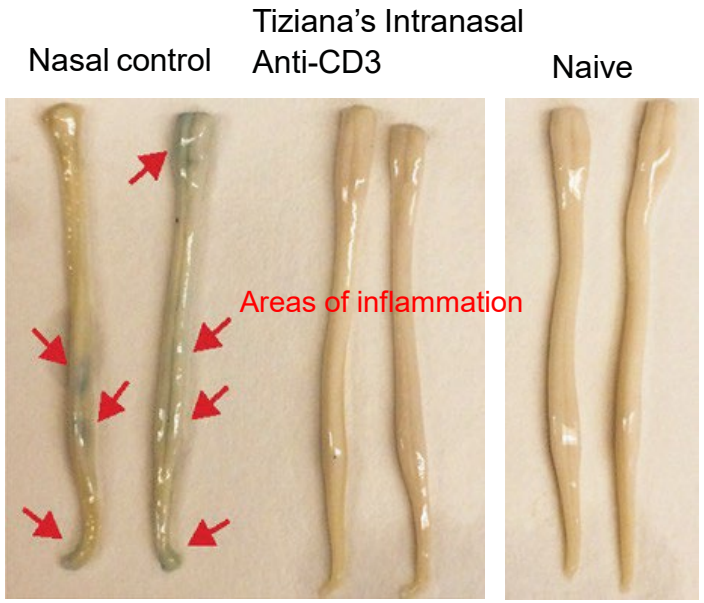
Intranasal

Intranasally-Administered Foralumab for Neurodegenerative Diseases

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

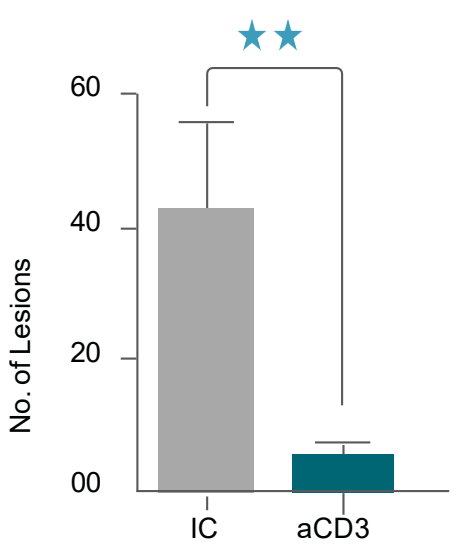


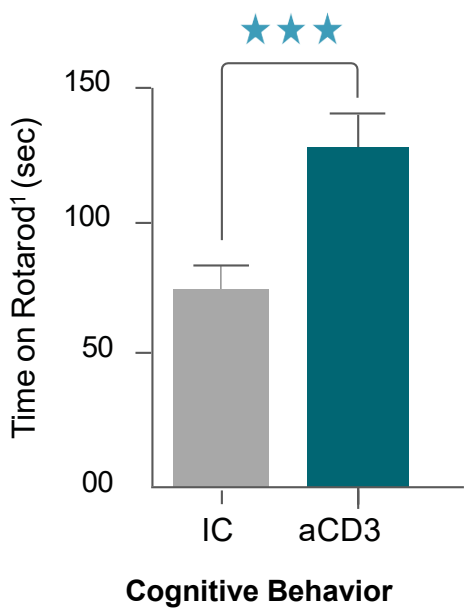
Intranasally-Administered Foralumab Mechanism of Action
(Validated in Animal Studies)



Progressive EAE [2] = Model for MS (spinal cords)

Effective in suppressing symptoms of multiple sclerosis (MS) in animal studies





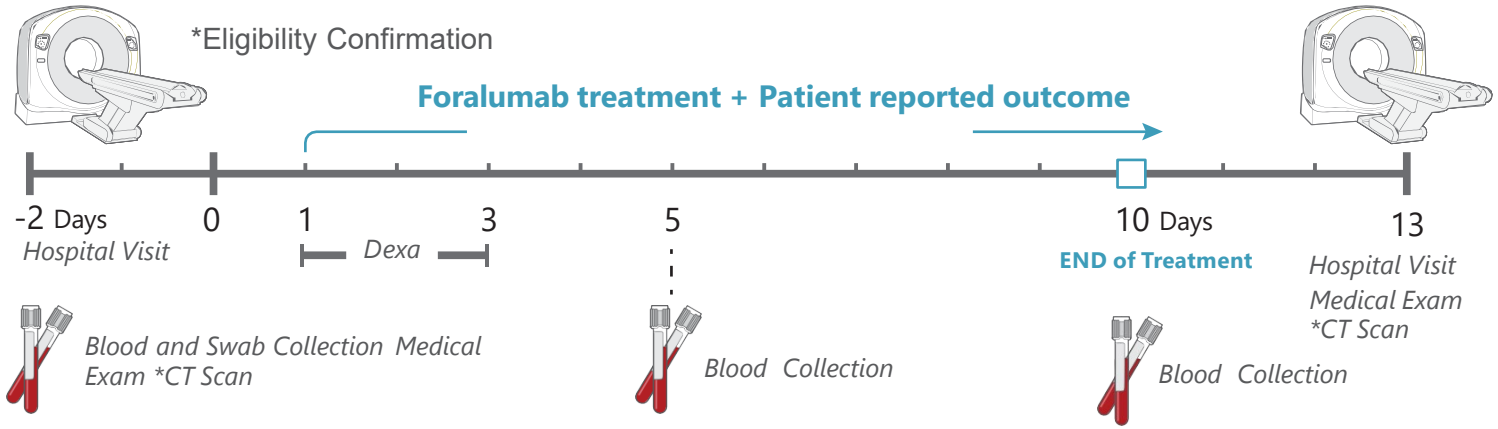
[1] Rotarod = forced motor activity performance test

[2]EAE = experimental autoimmune encephalitis

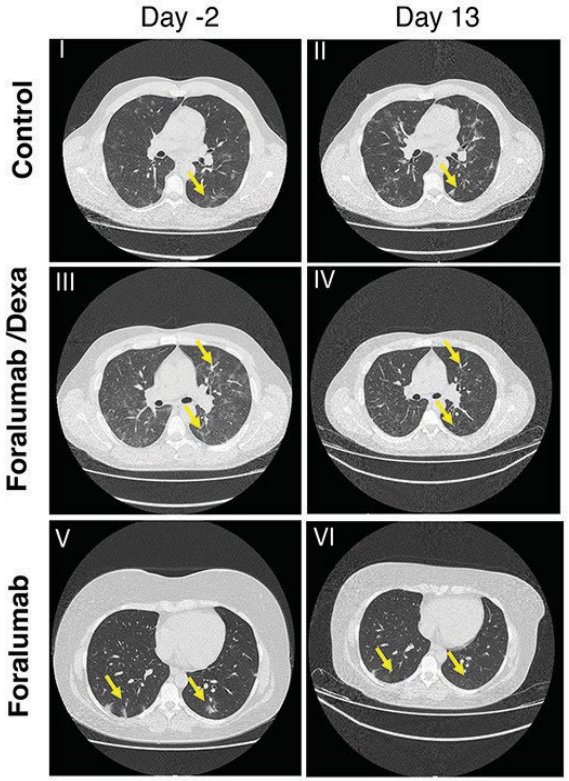
Work completed by Prof. Howard Weiner. Mayo, Lior, et al. "IL-10-dependent Tr1 cells attenuate astrocyte activation and ameliorate chronic central nervous system inflammation." Brain 139.7 (2016): 1939-1957.

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

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



CT Scan of Patients' Lungs



Results: Biomarkers measured via cytokines and C-reactive proteins

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

Phase 1 Clinical Trial in Healthy Volunteers with Intranasally-Administered Foralumab Showed No Apparent Symptoms of Adverse Events

Immuno-biomarkers

Downregulation: Cytotoxic CD8 cells , IFN-gamma

Upregulation: IL-10, T regulatory cells (Tregs)

Tregs are capable of crossing blood-brain barrier to elicit site targeted immunomodulation

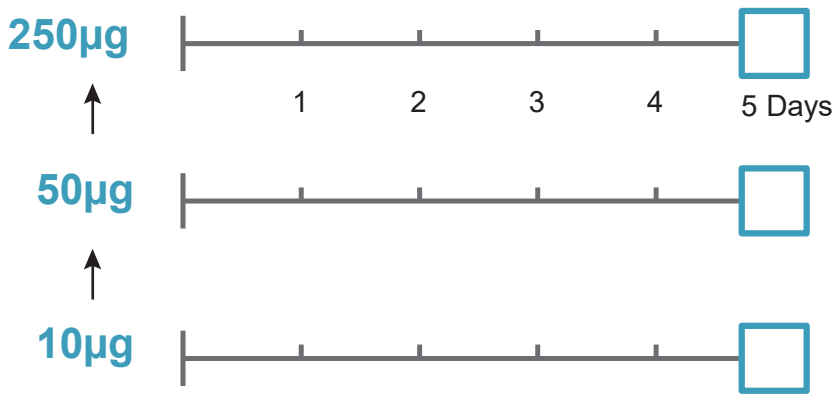
Healthy Subjects

6 active and 3 placebo patients in each dose level
Treated for 5 consecutive days using a hand-held spray device

Dose-ranging

Double-blinded

Placebo-controlled



- **No Systemic Absorption (targeted effect)**
- **Positive outcome from Immuno-biomarker analysis**
- **Well-tolerated & no local irritation**

Intranasally Administered Foralumab in SPMS Patient: 6-Month Treatment Data

First patient was dosed with intranasal foralumab M-W-F for two weeks with a subsequent 1-week washout period for 6-month period. Data consistent with 3-month period.

Positive Results: The regimen was well-tolerated with associated beneficial clinical and biomarker changes.

Clinical Results

PET imaging data

- Indicated continued inhibition of microglial cell activation
- The reduction in microglial activation was seen in all parts of brain
- Suppression of microglial activation further increased after six months of treatment

Clinical Test Evaluation

- Improvement in Timed 25-Foot Walk Test (T25FW)
- 9-Hole Peg Test (9HPT)
- Symbol Digit Modality Test (SDMT)

Biologic Response

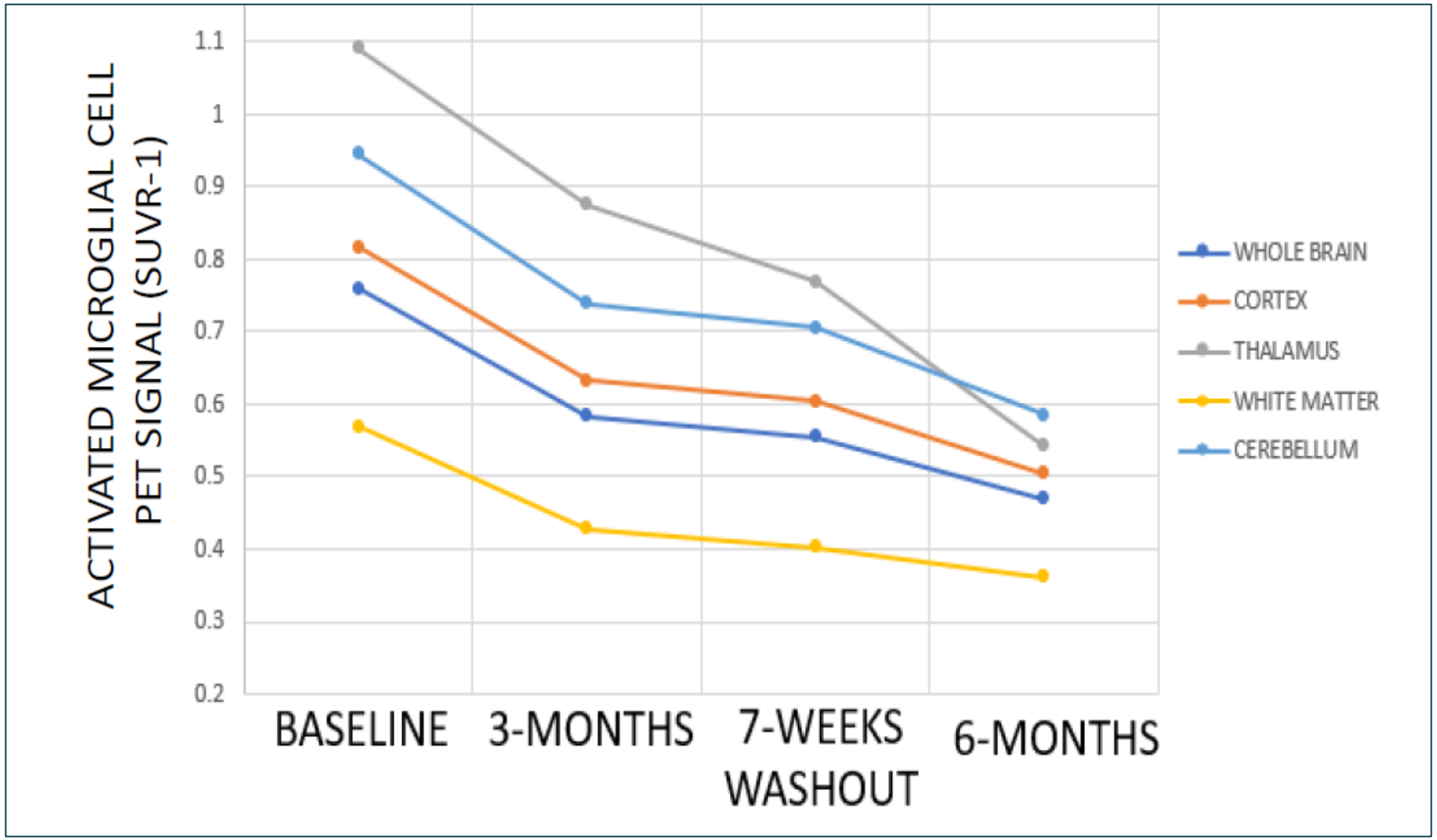
Biomarker changes

Downregulated serum levels of pro-inflammatory cytokines*, including:

- Interferon-gamma (IFN-g)
- Interleukin (IL)-18
- IL-1b
- IL-6

*These biomarkers are known to be associated with multiple sclerosis pathogenesis and progression

Graph Depicting Microglial Activation PET signal in Different Regions of the Brain at Various Time Points



Intranasally Administered Foralumab in SPMS Patient: 6-Month Treatment Data

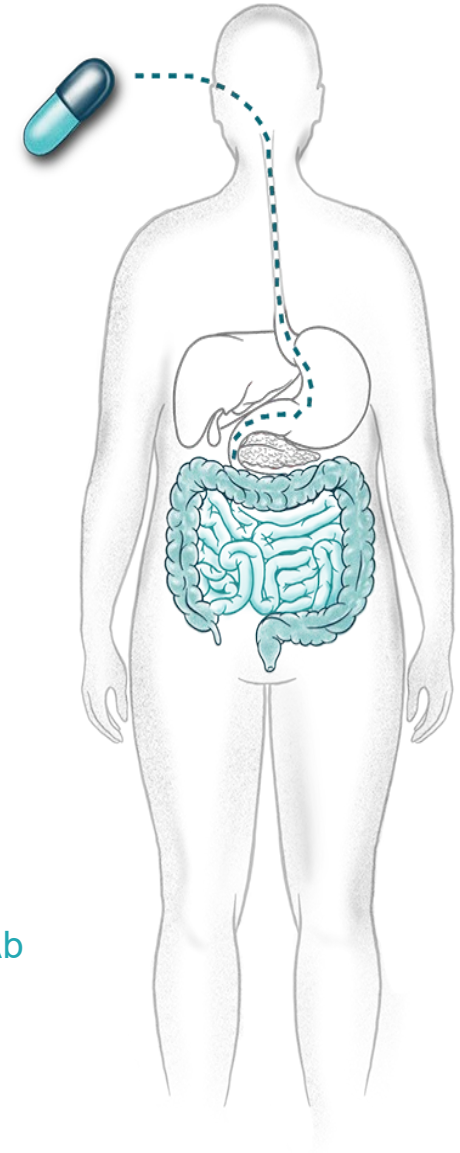
Percent Reduction* in Microglial PET Signal After Starting Intranasal Foralumab as Compared to Baseline, in Whole Brain and Selected Brain Regions

	WHOLE BRAIN	CEREBRAL CORTEX	THALAMUS	WHITE MATTER	CEREBELLUM
3 months	-23%	-23%	-20%	-25%	-22%
6 months	-38%	-38%	-50%	-36%	-38%

*Percent reduction is based on changes from baseline in SUVR-1, a surrogate index for PET binding potential. SUVR=Standardized Uptake Value Ratio, calculated with reference to a pseudo reference region in cerebral white matter that showed minimal change in PET SUV, across time points.

Published PET studies have shown an increase in activated microglial cells in patients with secondary progressive MS (SPMS), and an increase associated with higher scores on the Expanded Disability Status Scale (EDSS), a widely-used scale to measure disability.

Oral Foralumab for Inflammatory Bowel Diseases (Crohn’s Disease)

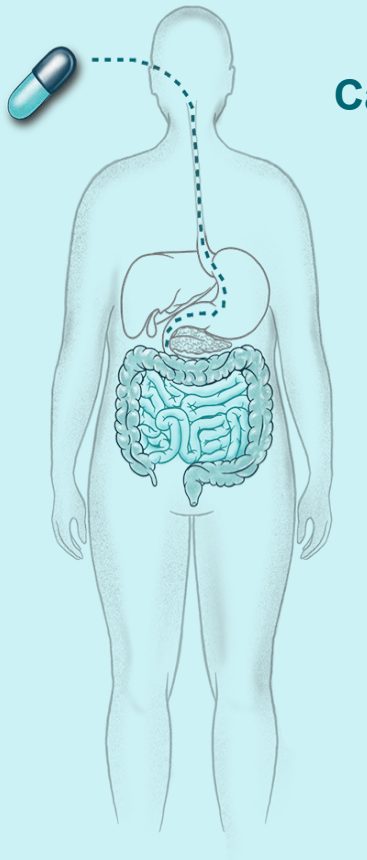


Oral capsules

Foralumab, a fully human anti-CD3 mAb

Orally-Administered Foralumab in Phase 1a Trial in Healthy Volunteers

Phase 1b Trial in Crohn's Disease Patients to Begin Q2 '22



Capsule taken orally

Clinical results

Single ascending dose, double-blind, placebo-controlled study in healthy subjects

Foralumab administered at 1.25, 2.5 and 5.0 mg/dose in enteric-coated capsules

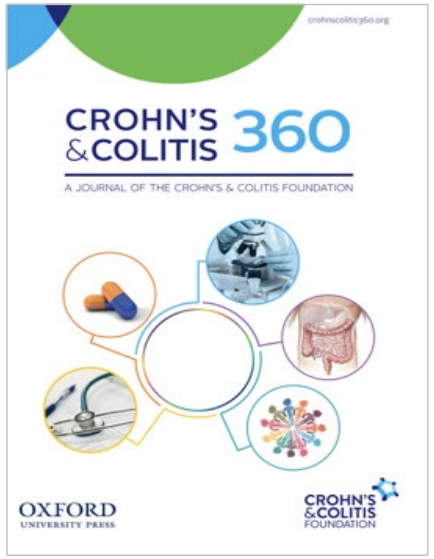
Well-tolerated at all doses tested and no drug-related safety issues observed

No systemic absorption of orally administered foralumab

Validated Proof of Concept for Oral Administration of OKT3, an Anti-CD3 mAb, in Ulcerative Colitis

Key Findings

- OKT3 was approved for renal transplantation patients but is now off the market due to toxicity concerns
- Prof. Snapper, et al., of Harvard Medical School conducted an exploratory study with oral OKT3 treatmen in patients with ulcerative colitis, an inflammatory bowel disease



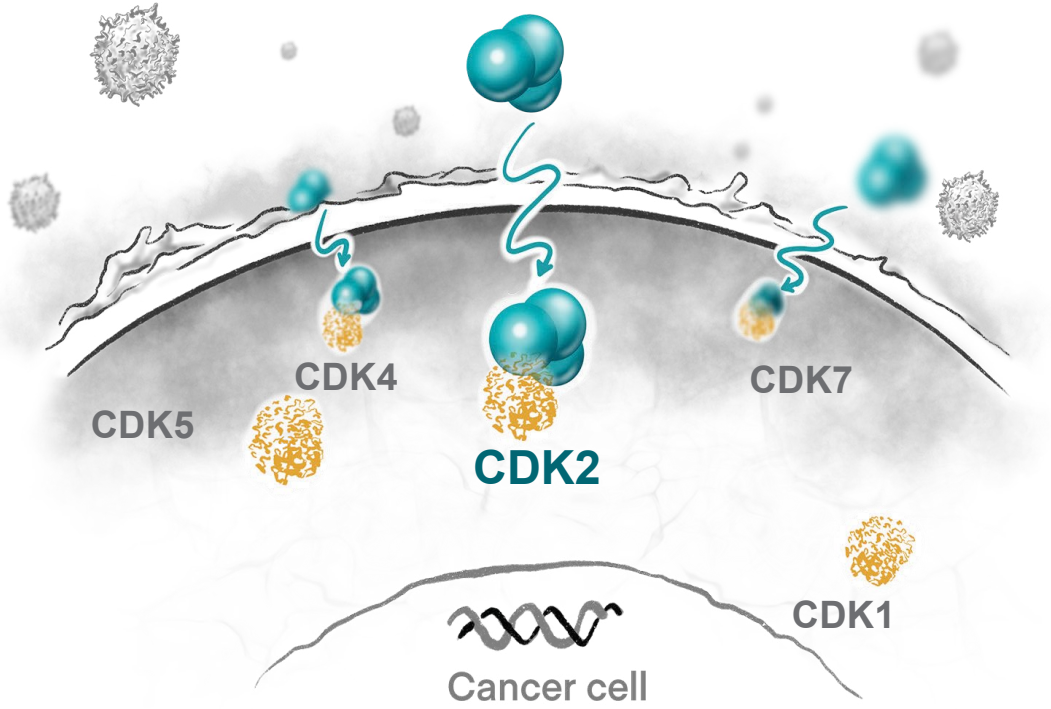
- Biologic response of increased proliferation and anti-inflammatory gene expression profile in peripheral blood mononuclear cells
- 3 of 6 patients had a clinical response including one patient in clinical remission
- Treatment was well-tolerated with no serious treatment-related adverse events
- Patients with moderate-to-severe ulcerative colitis received oral OKT3, a fully-murine anti-CD3 mAb once daily for 30 days

* Boden, E. K., Canavan, J. B., Moran, C. J., McCann, K., Dunn, W. A., Farraye, F. A., Ananthakrishnan, A. N., Yajnik, V., Gandhi, R., Nguyen, D. D., Bhan, Aantibodies. K., Weiner, H. L., Korzenik, J. R., Snapper, S. B. Immunologic alterations associated with oral delivery of anti-CD3 (OKT3) monoclonal in patients with moderate-to-severe ulcerative colitis. Crohn's & Colitis 360 (2019). 183: 240-246.

Oral Milciclib for NSCLC

Broad-spectrum inhibitory activities of milciclib on CDKs are favorable

Milciclib



Specifically downregulates miR-221/miR-222 pair and c-myc.

Phase 1 Study of Milciclib + Gemcitabine in Refractory Solid Tumors

Trial Design

16 Patients with refractory solid tumors

Treated with oral milciclib at three dose levels **(45, 60, and 80 mg/m^2/day)**

With a fixed dose of IV gemcitabine **(1000 mg/m^2/day)**

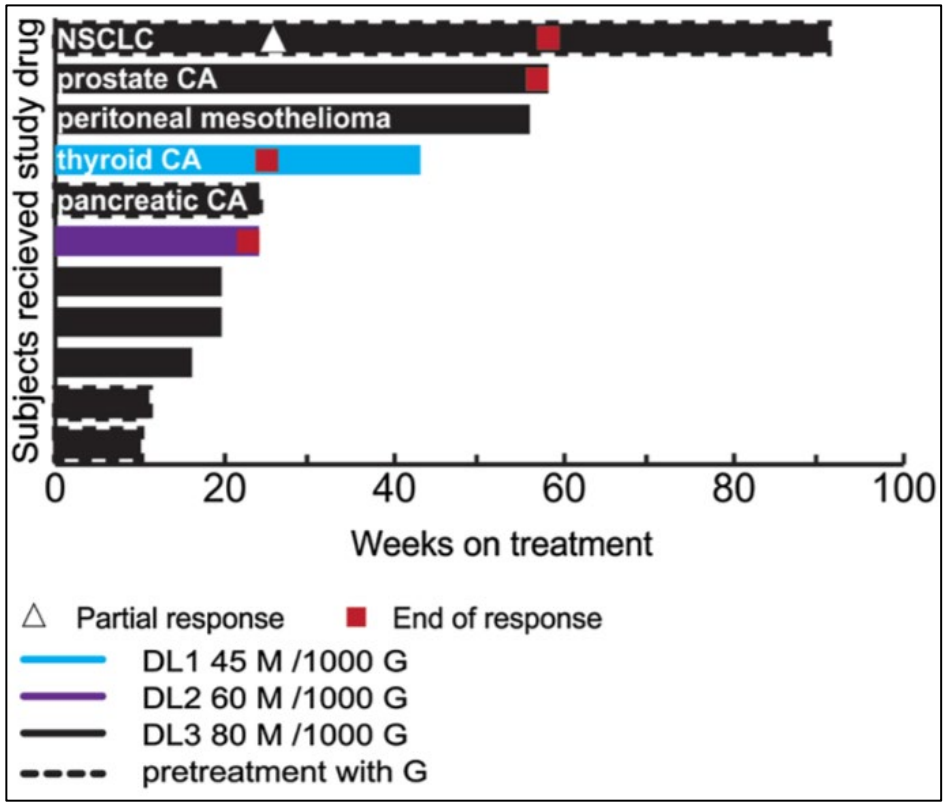
Results

Milciclib was well-tolerated with manageable side effects

Overall response rate was 36%

Clinical activity was observed in patients with variety of solid cancers who were non-responders to all existing chemotherapy

Recommended Phase 2 dose (RPD) found to be 80mg/m^2/day



Swimmer plot showing treatment duration. Tumor type was indicated for patients having a prolonged stable disease or a partial response.

M = milciclib
G = gemcitabine

Cancer Chemotherapy and Pharmacology, June 2017, 79(6), 1257-1265

Milciclib: Successful Validation in Phase 2 trial in Sorafenib-Resistant HCC supports further testing in NSCLC with KRAS mutations

HCC is a complex and heterogenous cancer associated with multiple etiological factors that make treatment challenging and may benefit from a broad-spectrum approach

Primary endpoint: Safety

✓ **Well-tolerated**

Treatment was well-tolerated and adverse events were manageable with no drug related deaths in the trial

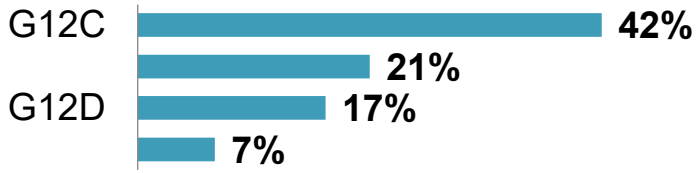
Secondary endpoints:

- **TTP 5.9 months**
  - Median Time-to-Progression
- **SD 61%**
  - Patients with stable disease
- **CBR 64%**
  - Patients showed clinical benefit response

NSCLC is a complex and heterogenous cancer with multiple genetic mutations

K-RAS and EGFR mutations predominate in NSCLC

KRAS Mutations: **30% of NSCLC**



KRAS mutations correlated with:

- Higher exonic mutation rate
- Smoking genomic signature
- STK11 mutation
- P53 mutation

10 to 100-fold higher mutation rate than EGFR-mutated or KRAS wild-type tumors

TTP = time to disease progression

SD = stabilization of disease

CBR = clinical benefit ratio

Sholl, Lynette M., et al. "Multi-institutional oncogenic driver mutation analysis in lung adenocarcinoma: the lung cancer mutation consortium experience." *Journal of thoracic oncology* 10.5 (2015): 768-777.

Executive Management Team

Deep Drug Development Expertise with Proven Track Record; Independently Bringing Four Drugs to Market

Kunwar Shailubhai

PhD, MBA CEO & CSO

Executive Director Co-founder, EVP & CSO of Synergy Pharmaceuticals, NASDAQ: SGYP Inventor of antibody oral formulation technology. Pioneer of GC-C agonist technology

Inventor of approved drug TRULANCE®.
Dolcantide successfully completed Phase 2 trial

Prior experience at Callisto Pharmaceuticals (NASDAQ: CLSP) and Monsanto

Gabriele Cerrone

MBA Executive Chairman

Founder and chairman of two biotech companies with market cap over $2B

Inhibitex sale for $2.5B

Prior experience at Synergy, Trovagene, Gensignia, Rasna, Contravir, and Siga Technologies

Co-founded NASDAQ: HEPH, CLSP, RASP, CRDF

John Brancaccio

Non-Executive Director

Over 35 years financial experience in pharma/biotech/medical devices with over 15 years experience with multiple public companies

Management and SEC reporting

Private and public fundraising experience

Willy Simon

Non-Executive Director

Career as an executive in the banking and corporate finance sector and director of publicly listed companies

Kredietbank N.V., Citibank, Generale Bank NL, CEO of Fortis Investment Management

Chairman of Bank Oyens & van Eeghen, Partner at Redi & Partners

Scientific Advisory Committee

World renowned scientists with proven track records in drug discovery and development

Howard Weiner, MD

CHAIRMAN

Professor of Neurology at Harvard Medical School.

Director and Founder of the Partners MS Center and Co-Director of the Ann Romney Center for Neurologic Diseases

Pioneered investigation of the mucosal immune system for the treatment of autoimmune and other diseases

Kevan Herold, MD

MEMBER

Professor of Immunobiology and Medicine and Deputy Director, Yale Center for Clinical Investigation

Director of the Yale Diabetes Center and Director of the TrialNet Center at Yale

Expert in autoimmune diseases and anti-CD3 monoclonal antibody therapies

Arun Sanyal, MD

MEMBER

Charles Caravati Distinguished Professor and Chair, Division of Gastroenterology, Hepatology and Nutrition at Virginia Commonwealth University School of Medicine

Leader in the field of liver diseases

Napoleone Ferrara , MD

MEMBER

Inventor of Avastin® ($6.67Bn/yr)*; 2010 Lasker Award

Senior Deputy Director Basic Sciences, Moores Cancer Center, UC San Diego

Distinguished Prof of Pathology, School of Medicine, UC San Diego

Tanuja Chitnis, MD

MEMBER

Professor of Neurology at Harvard Medical School.

Senior Scientist at the Ann Romney Center for Neurologic Diseases at Brigham and Women's Hospital (BWH)

Board-certified neurologist specializing in multiple sclerosis (MS) related neuro-immunological disorders and leads several research studies and clinical trials in these areas

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