

# Enabling Breakthrough Immunotherapies via Novel Routes of Drug Delivery



NASDAQ: TLSA

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### **Investment Highlights**





Innovative, clinicallyvalidated, 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







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



## **A Revolutionary Platform**

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



# 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 of Novel Immunotherapies and Oncology**

Four Clinical Studies With Positive data completed 2019-2020

	Subject	PC	IND	Phase 1/IAP	Phase 2	Phase 3
<b>FORALUMAB</b> Fully human anti-CD3 mAb	Intranasal	Progressive Multiple \$	Sclerosis (expanded proc	gram)	Ongoing IAP trial	
	Intranasal	COVID-19			First ever validation of meaning the second se	chanism of action through
	Oral	Enteric Coated Oral C	Capsules for Crohn's Dise	ease	Completed (Submitted Pl	hase 1b amended protocol)
	Subcutaneous	Type 1 Diabetes			1Q-2022 IND Submission	
<b>MILCICLIB</b> Pan-CDK inhibitor	Oral	Milciclib + Gemcitabin	e in Refractory Solid Tumo	ors	Completed: Strong clinic	cal response in NSCLC
	Oral	KRAS+ NSCLC (Milcic	clib + Gemcitabine)		1Q-2022 IND Submission (new indi	cation)
	Oral	HCC monotherapy in S	Sorafenib Resistant Patier	nts		Asset only/Partnership consideration for Asia- Pacific territory



# Lead Program

# 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

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

**CD3-specific Monoclonal Antibodies in Clinical Development** 



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

#### Announced September 2, 2021

- 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 preconditioning 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 Acts via Site Targeted Immunomodulation

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



- 1. Phase 1 trial in healthy volunteers
- 2. Exploratory trial in Covid-19
- 3. Ongoing clinical study in secondary progressive multiple sclerosis (SPM)



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

First Validation that Intranasally Administered Foralumab is Well-tolerated and the Treatment Provides Clinical Benefits via Immunomodulation



#### **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

#### **CT Scan of Patients' Lungs**





## Ongoing Multiple Sclerosis Trial with Intranasally Administered Foralumab under the Individual Access Program

- Chronic dosing for at least 6 months is necessary for achieving meaningful clinical responses in Secondary Progressive Multiple Sclerosis (SPMS). FDA allowed 6 months of dosing under an Individual expanded access program (IAP).
- Clinical data from the first patient, after completing 3 out of 6 months, suggested that the treatment was well tolerated with a favorable clinical response. Patient is continuing with the treatment and clinical data after 6 months of dosing will be available Q2 2022
- FDA has allowed enrollment of second patient in trial under this program at the Brigham and Women's Hospital (BWH), Harvard University, Boston, MA
- Investigators at BWH will be monitoring detailed safety, neurological, and Positron Emission Tomography (PET) to evaluate microglial activation in both patients. Modification of immunological and neurodegenerative markers will also be included as part of the standard investigation to be conducted by BWH.



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

Local mode of action with improved safety and lowered dosing levels, and enhanced convenience



### Oral capsules

Foralumab, a fully human anti-CD3 mAb



## **Clinical Development of Orally-Administered Foralumab for Crohn's Disease**

Phase 1b Trial in Crohn's Disease Patients to Begin Q1 '22



#### **Phase 1a Clinical results**

- 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

#### Phase 1b Clinical study

An amended IND has been submitted for Phase 1b study with orally administered foralumab in patients with Crohn's Disease

**Primary endpoint**: safety and tolerability

Secondary endpoints: PK and PD effects



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