



**TFF TAC Data Presented at 44<sup>th</sup> Annual ISHLT Meeting  
Late Breaking Abstract Oral Presentation  
April 13, 2024**

# Safe Harbor Statement

## **SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

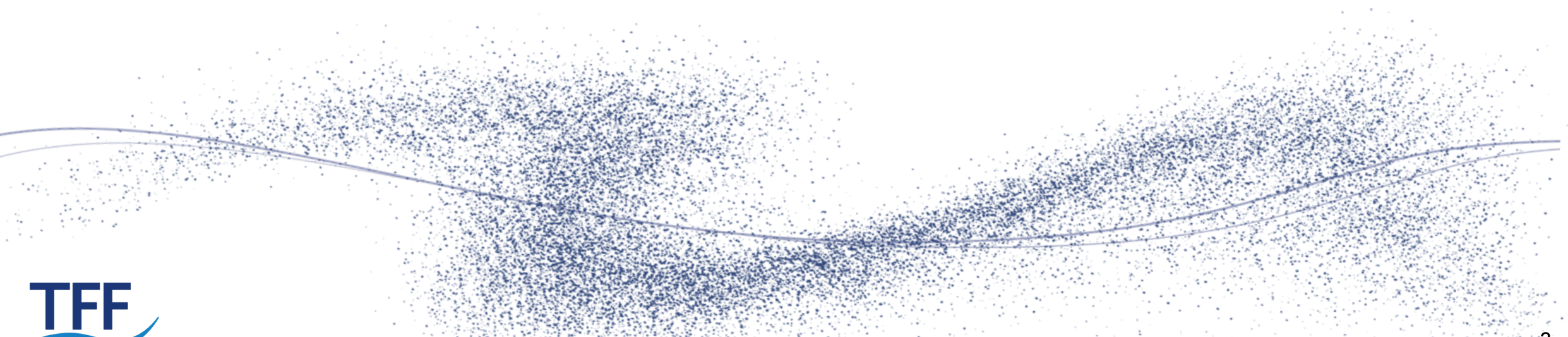
This document contains forward-looking statements concerning TFF Pharmaceuticals, Inc. (“TFF”, “TFF Pharmaceuticals”, the “Company,” “we,” “us,” and “our”). The words “believe,” “may,” “will,” “potentially,” “estimate,” “continue,” “anticipate,” “intend,” “could,” “would,” “project,” “plan,” “expect” and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements. These forward-looking statements include, but are not limited to, statements concerning the following:

- the benefits of our TFF platform;
- advancement of TFF TAC into potentially registration-enabling studies;
- TFF TAC’s substantial market opportunity;
- the expectation that the further data from the ongoing Phase 2 clinical trial for TFF TAC and will be consistent with the data readouts for each product candidate to date

Those forward-looking statements involve known and unknown risks, uncertainties and other factors that could cause actual results to differ materially. Among those factors are: (i) the risk that the further data from the ongoing Phase 2 clinical trials for TFF TAC will not be favorably consistent with the initial data readouts, (ii) the risk that we may not be able to advance to registration-enabling studies for TFF TAC, (iii) success in early phases of pre-clinical and clinicals trials do not ensure later clinical trials will be successful; (iv) no drug product incorporating the TFF platform has received FDA pre-market approval or otherwise been incorporated into a commercial drug product, (v) the Company has no current agreements or understandings with any large pharmaceutical companies for the development of a drug product incorporating the TFF platform, (vi) the risk that the Company may not be able to obtain additional working capital with which to continue the Phase 2 clinical trials and or advance to the initiation of registration-enabling studies, for TFF TAC as and when needed and (vii) those other risks disclosed in the section “Risk Factors” included in the Company’s Annual Report on Form 10-K filed with the SEC on March 28, 2024 and subsequently filed reports. TFF Pharmaceuticals cautions readers not to place undue reliance on any forward-looking statements. TFF Pharmaceuticals does not undertake, and specifically disclaims, any obligation to update or revise such statements to reflect new circumstances or unanticipated events as they occur, except as required by law.

This document contains only basic information concerning TFF. Because it is a summary it does not contain all of the information you should consider before investing. Please refer to our reports and registration statements on file with the SEC for more comprehensive information concerning TFF Pharmaceuticals.

# TFF TAC Clinical Data Update



# Introduction

- Successful lung transplant requires significant systemic immunosuppression, but this comes at the cost of significant systemic toxicity
- Significant renal impairment is one such example (~25% @5yrs post-lung transplant)
- Substituting oral tacrolimus with Tacrolimus Inhalation Powder (TFF TAC) may be able to still prevent lung allograft rejection while enabling lower systemic tacrolimus blood levels and potentially lessening renal toxicity

# Inhalation Device for Lung Deposition



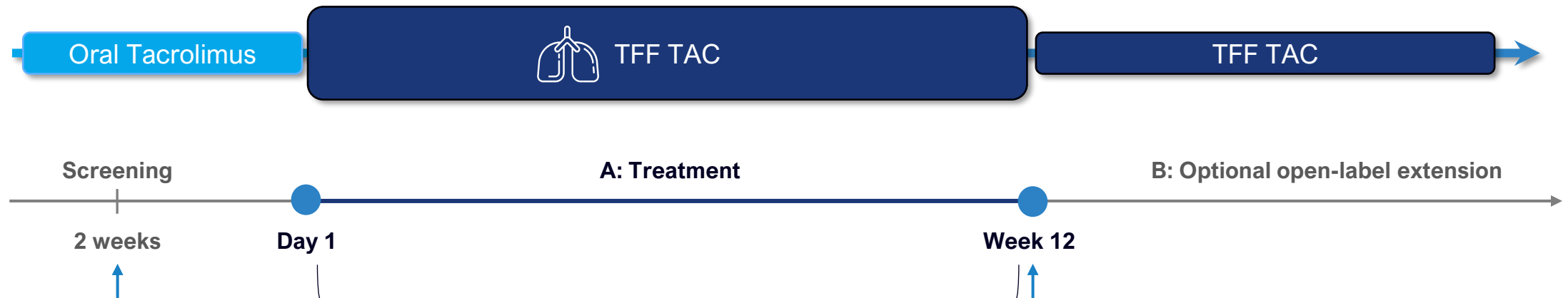
- TFF TAC utilizes Thin Film Freezing particle engineering technology (TFF Pharmaceuticals)
- Dry powder (3.2 $\mu$ m diam) in 1mg & 0.25mg capsules, delivered by a simple handheld inhaler\*
- 1-2 x daily

\*FDA Cleared Plastiape RS00 monodose device



# Phase 2 Study Design in Lung Transplant Patients

- **Design:** Open label study of TFF TAC lung transplant recipients requiring reduced tacrolimus blood levels due to renal toxicity
- **Duration:** Part **A:** 12 weeks; Part **B:** optional safety extension
- **Endpoints:** Safety & tolerability, renal function, acute allograft rejection



- Bronchoscopy & mucosal biopsy MMDx
- Spirometry
- Donor-derived cell-free DNA assay
- Donor Specific Antibody (DSA)
- CT chest

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# Phase 2 Study Inclusion Criteria

- >18 years
- >6 months post bilateral lung transplant
- Triple immunosuppression
- Stable (infection/rejection/reflux)
- >40% predicted FEV1
- Creatinine >124 $\mu$ mol/L or eGFR < 45 mL/min/1.73m<sup>2</sup>\*
- Non-smoker

\*GFR<45mL/min/1.73m<sup>2</sup> is consistent with moderate to severe chronic kidney disease

FEV1: Forced Expiratory Volume in One Second  
eGFR: Estimated Glomerular Filtration Rate

# Baseline Characteristics and Demographics

Patient	Age (years)	Sex	Race	Years since transplant	CLAD	Years with kidney disease	Time on TFF TAC (weeks)	Disposition
Pt 1	73	M	W	9	No	5	49	Chose to proceed to Part B
Pt 2	73	F	W	8	No	6	40	Chose to proceed to Part B
Pt 3	68	M	W	5	No	4	33	Chose to proceed to Part B
Pt 4	67	F	W	3	No	2.5	20	Chose to proceed to Part B
Pt 5	64	M	W	3	No	2.5	12	Still in Part A
Pt 6	52	F	W	23	No	7	9	Still in Part A
Pt 7	41	F	W	0.75	No	N/A	6	Still in Part A
Pt 8	56	M	NH	1.25	No	2	5	Still in Part A

CLAD: Chronic Lung Allograft Dysfunction

W: white ; F: female; M: male; NH: Native Hawaiian

N/A: not available

Data is from TFF-T2-001 pre-database lock; Data cut off date: 3/25/24



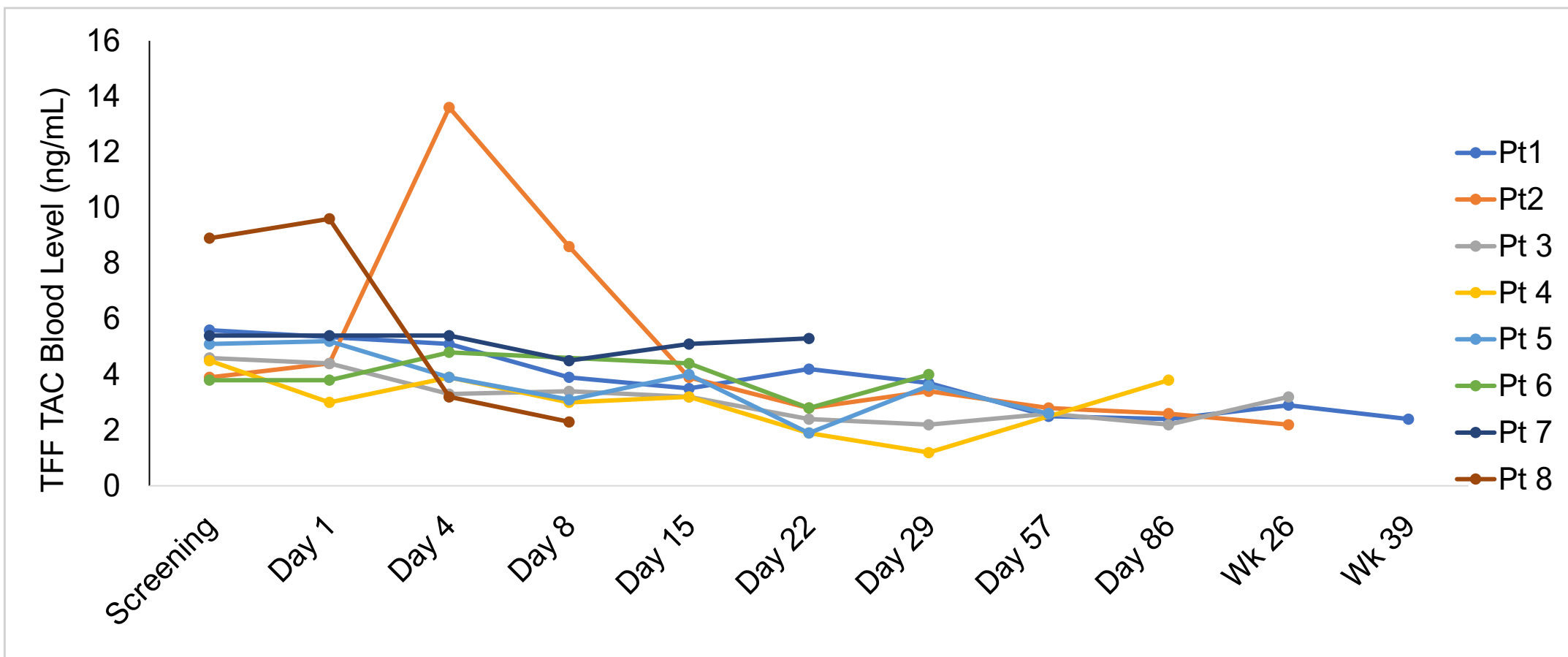
# Data Suggest TFF TAC Prevents Rejection at a Fraction Of Oral Tacrolimus Dose With Reduced Systemic Exposures

Reduction in systemic exposures to 2/3 are expected to decrease toxicities

Patient	Stable* TFF TAC: Oral Tac Dose (mg)	Stable TFF TAC/Oral Tac Dose	Trough TFF TAC: Oral Tac Blood Level (ng/mL)	Trough TFF TAC/Oral Tac Blood Level
Pt 1	0.75 : 5	1/7	2.4 : 5.6	~1/2
Pt 2	0.25 : 1	1/4	2.2 : 3.9	~1/2
Pt 3	0.5 : 5.5	1/11	3.2 : 4.6	~2/3
Pt 4	0.5 : 2	1/4	3.8 : 4.5	~1
Pt 5	0.375 : 3	1/8	2.6 : 5.1	~1/2
Pt 6	0.75 : 3	1/4	4.0 : 3.8	~1
Pt 7	1.5 : 13	1/9	5.3 : 5.4	~1
Pt 8	0.5 : 6	1/12	2.3 : 8.9	~1/4
Average		~1/6 (17%)		~2/3 (66%)

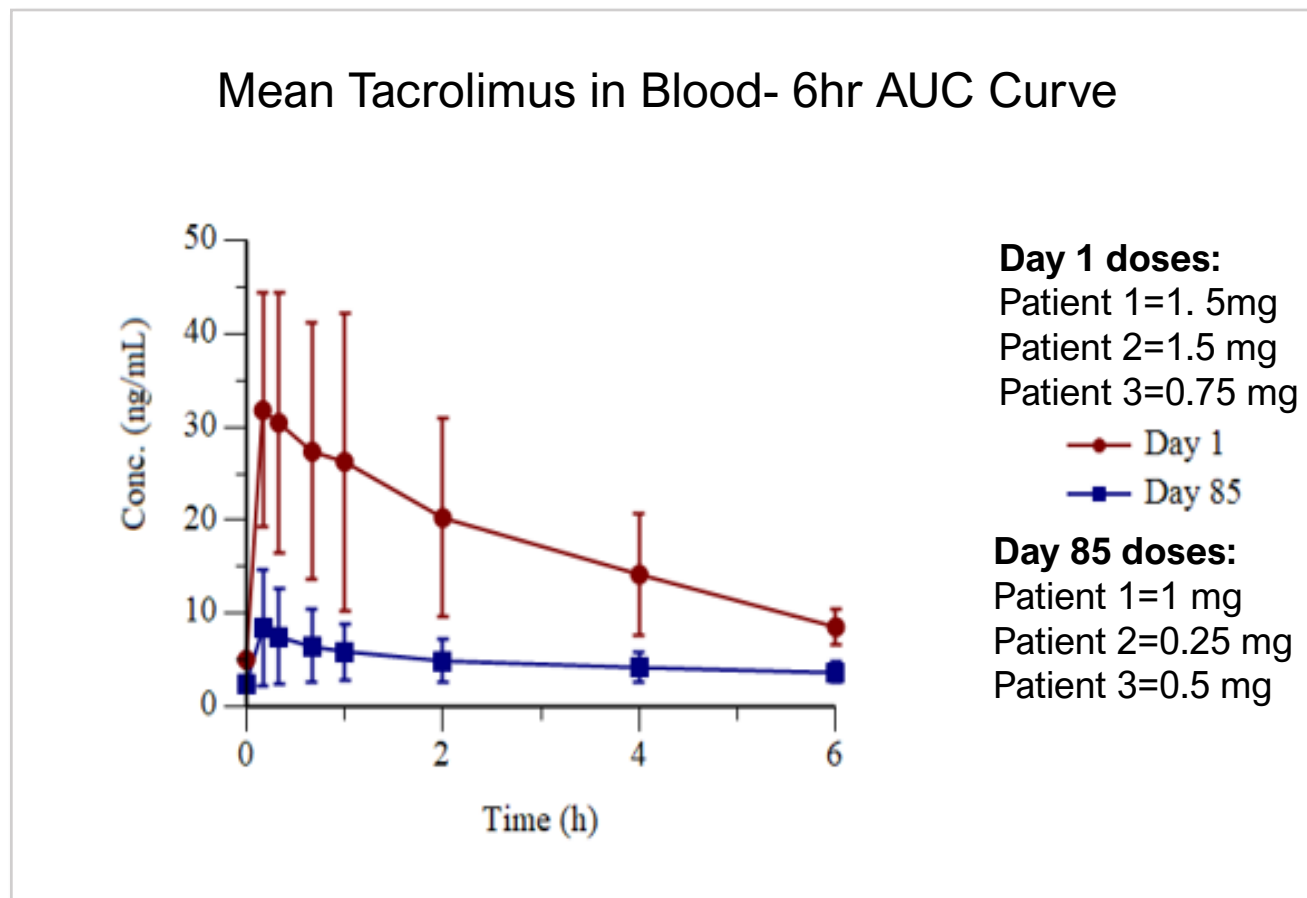
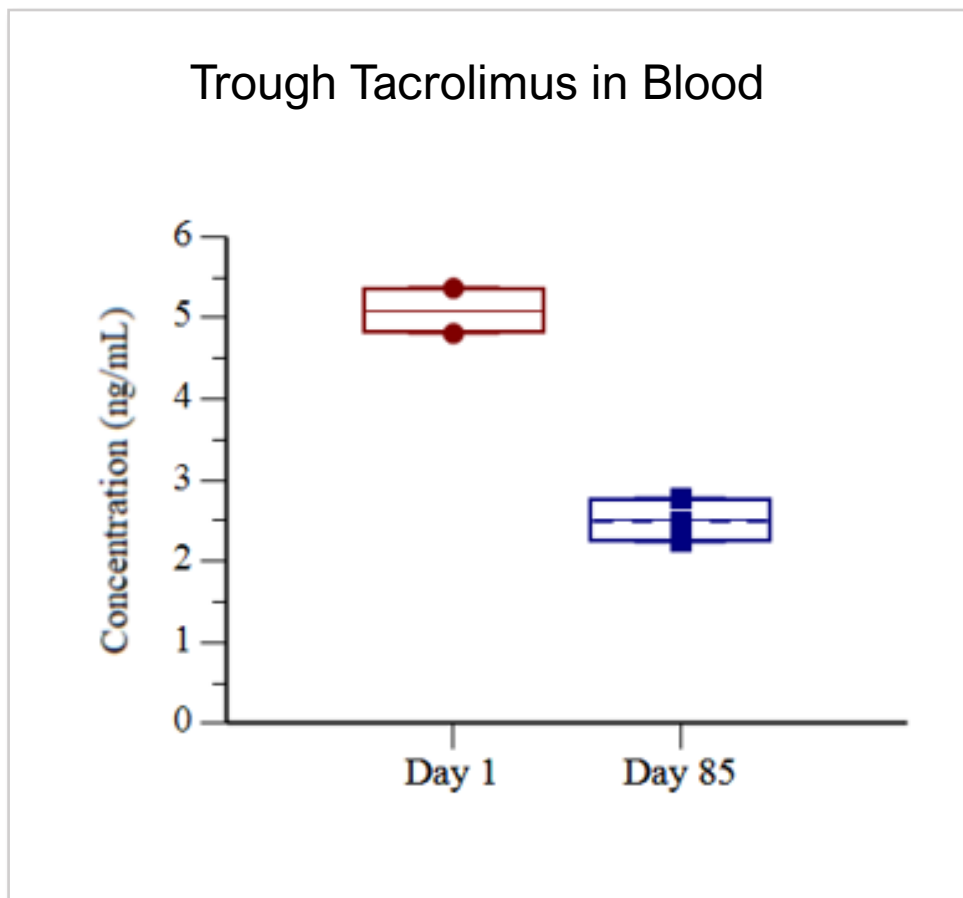
\*Stable dose is defined as no change in dose level or frequency for 3 consecutive weeks

# Blood Trough Levels



TFF TAC dose is reduced over time to protect the kidneys resulting in diminished tacrolimus blood levels; no acute rejection despite decrease in TFF TAC dose and systemic exposures

# Lower Doses of TFF TAC Result in Diminished Systemic Exposures and Less Pharmacokinetic Variability with Chronic Dosing



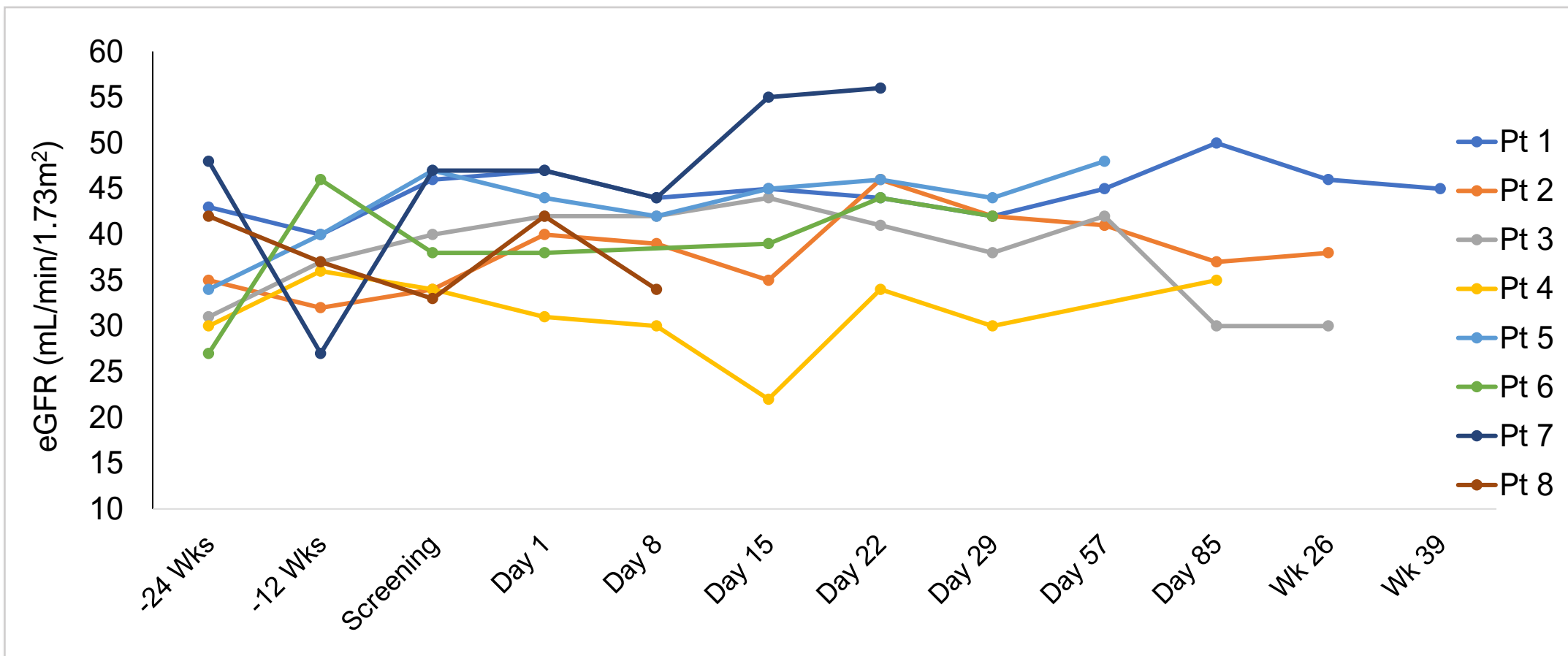
Reduced pharmacokinetic variability is predicted to decrease risk of rejection and toxicities



AUC: Area Under the Concentration-Time

Data is from TFF-T2-001 pre-database lock; Data cut off date: 3/8/24

# Renal Function Maintained

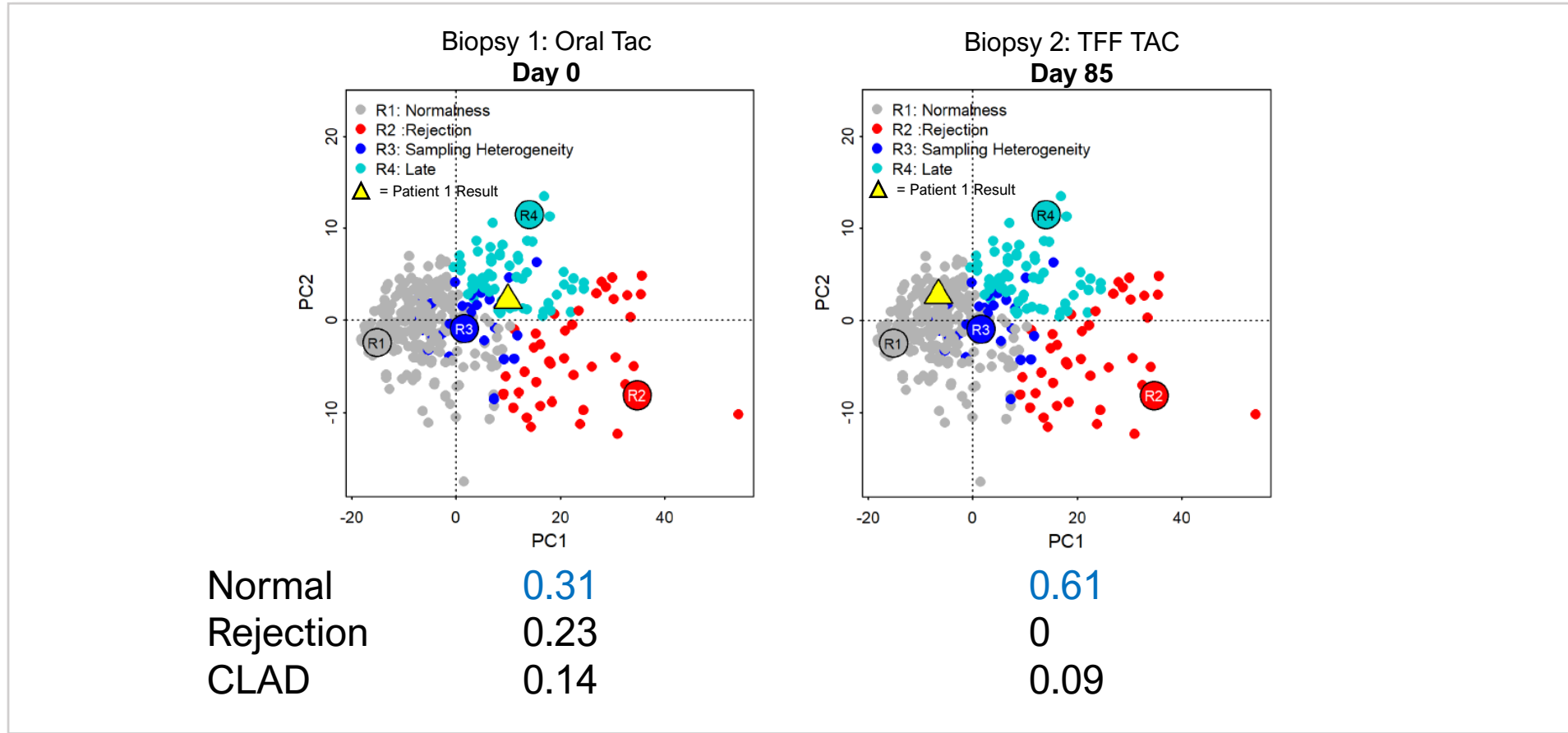


# Normalization of Rejection-Related Gene Expression Following Transition From Oral Tacrolimus to TFF TAC

## Gene Expression Analysis Using MMDx

- No gene expression evidence of rejection in 4/4 patients with available gene expression data on endobronchial biopsies:
  - Rejection-related genes normalized in 3/3 patients with abnormal expression of rejection-related genes at baseline while on oral tacrolimus
  - Rejection-related genes remained normal in one patient with normal expression at baseline

# Patient 1: MMDx Gene Expression Analysis Following Transition from Oral Tacrolimus to TFF TAC



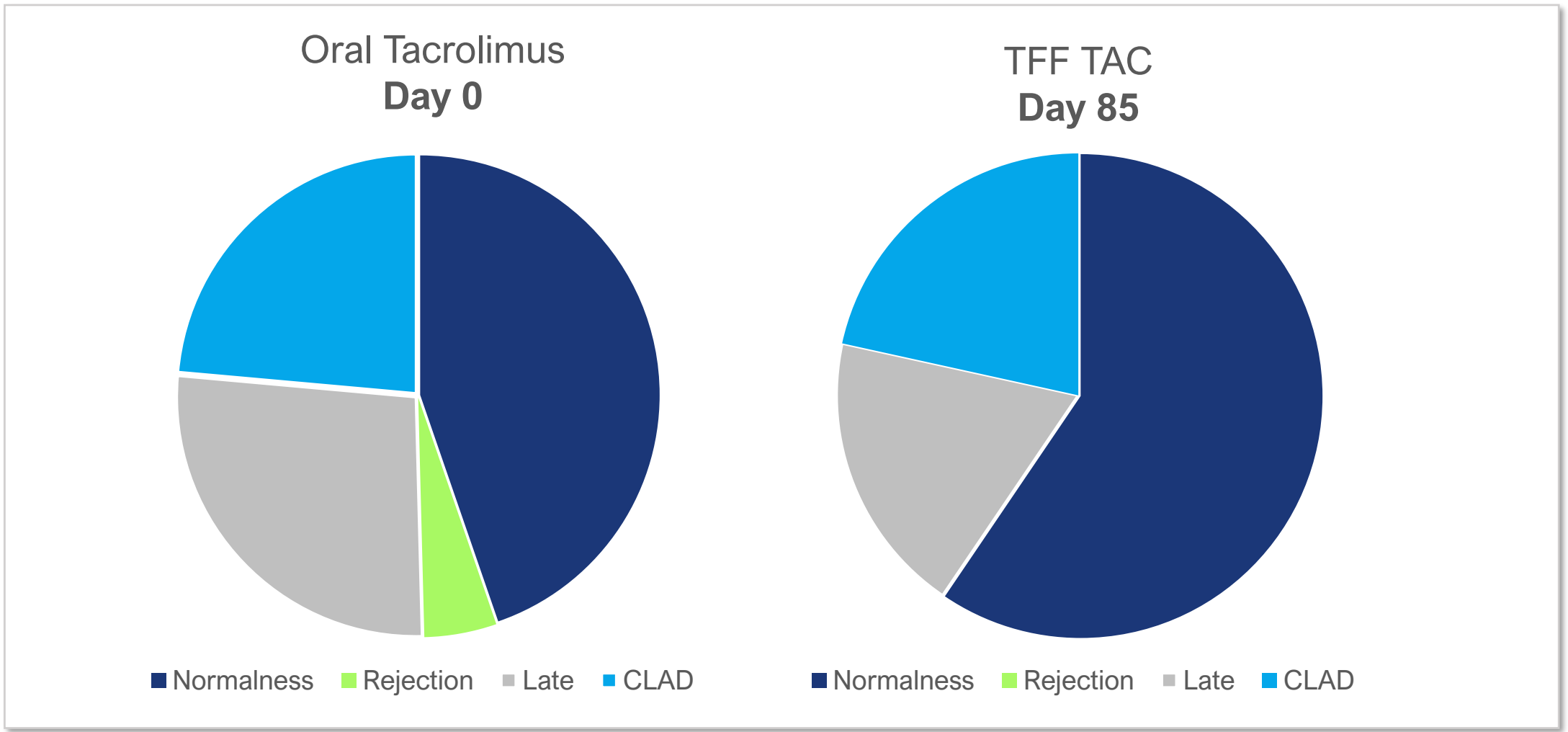
Patient 1's gene expression shifted from a profile consistent with rejection and CLAD to a more normal profile upon transition to TFF TAC



MMDx: Molecular Microscope Diagnostic System



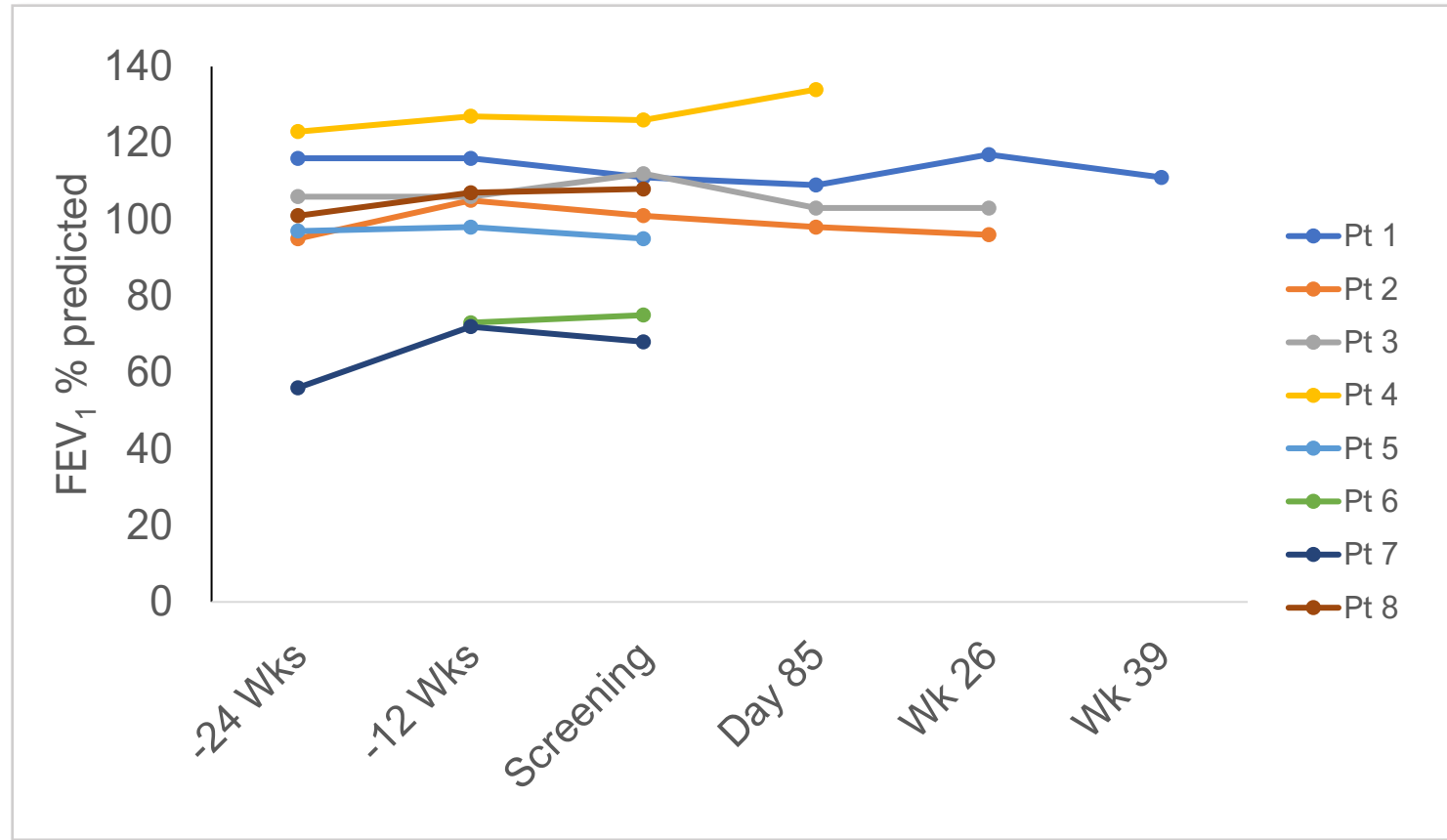
# MMDx Analysis: Increase in Normal Gene Expression



# Number of Abnormally Expressed Genes Decreased on TFF TAC

	Patient 1		Patient 2		Patient 3		Patient 4	
Gene Sets	Day 0	Day 85	Day 0	Day 85	Day 0	Day 85	Day 0	Day 85
Endothelium Related	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Rejection Related	Abnormal	Slightly Abnormal	Abnormal	Slightly Abnormal	Normal	Normal	Slightly Abnormal	Normal
	Abnormal	Normal	Slightly Abnormal	Normal	Normal	Normal	Slightly Abnormal	Normal
	Abnormal	Normal	Slightly Abnormal	Slightly Abnormal	Normal	Normal	Abnormal	Normal
	Abnormal	Normal	Slightly Abnormal	Normal	Normal	Normal	Slightly Abnormal	Normal
	Abnormal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
	Abnormal	Slightly Abnormal	Slightly Abnormal	Slightly Abnormal	Normal	Normal	Slightly Abnormal	Slightly Abnormal
	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Injury Related	Slightly Abnormal	Abnormal	Normal	Slightly Abnormal	Normal	Normal	Normal	Normal
	Slightly Abnormal	Normal	Normal	Normal	Slightly Abnormal	Normal	Normal	Normal
Late Atrophy/Scarring Related	Abnormal	Normal	Normal	Normal	Normal	Normal	Normal	Slightly Abnormal
	Slightly Abnormal	Slightly Abnormal	Normal	Normal	Normal	Normal	Slightly Abnormal	Abnormal
Other	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Normal	Abnormal
<b>Abnormal Count:</b>	<b>11</b>	<b>5</b>	<b>6</b>	<b>5</b>	<b>2</b>	<b>1</b>	<b>6</b>	<b>4</b>

# Lung Function Remained Stable on TFF TAC



# Adverse Events

- Infections
  - COVID x4
    - Complicated x1 with decreased lung FEV<sub>1</sub>
  - Lower Respiratory Tract Infection x1 picornavirus
    - Complicated by pleurisy, coronary angiogram pseudoaneurysm, atrial fibrillation, oral candida
- Headache x2, tremor x1
- Increased creatinine x3
  - Ultimately recovered in 2/3, recovering in 1/3

The adverse event profile of TFF TAC is compatible with that of oral tacrolimus

FEV1: Forced Expiratory Volume in One Second

Data is from TFF-T2-001 pre-database lock; Data cut off date: 3/8/24

# Summary

## Efficacy

- Successful transition of 8/8 from oral tac to TFF TAC
- No evidence of acute rejection
  - No signs and symptoms suggestive of acute rejection
  - No use of pulse corticosteroids for treatment of rejection
  - No spirometry deterioration suggestive of acute rejection
  - No CXR findings suggestive of acute rejection
  - No mucosal biopsy evidence of acute rejection

## Safety

- No mortality
- No TFF TAC discontinuation due to an AE
- Majority of AEs were  $\leq$  Grade 2 severity
- Maintenance of lung function
- Maintenance of renal function

## Tolerability

- Simple to use
- 1-2 times daily
- Stable levels
- 4/4 completing Part A continued on TFF TAC in Part B

# Conclusion

- TFF TAC shows promise as a simple, safe lung transplant immunosuppressant
- Emerging experience, biomarker levels, gene expression & further immunological assessment will prove key in potentially enabling us to evaluate if even lower blood tac levels are possible
- The current study may be initiating changes to tac dosing too late to influence renal deterioration in some transplant recipients
- If current trends continue, then TFF TAC may be indicated earlier post-lung transplant – before systemic damage (e.g. renal impairment) becomes established





THANK YOU