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WELCOME

Advancing Care, One Breath at a Time

Seabreeze STAT Trials Investigator Meeting

San Diego, CA | Friday, September 12, 2025

Investigator Meeting Agenda | San Diego, CA

Seabreeze STAT Trials - ***Advancing Care, One Breath at a Time***

Time (PT)	Session Title	Speaker(s)
08:30–08:40	**Welcome to Seabreeze STAT Trials:** Why This Program Matters	Dr. Barry Quart (Connect)
08:40–08:55	**Meet the Minds Behind the Mission (Introductions & Team Overview)** 🎉 *Trivia Showdown - Compete for prizes while mastering the protocols*	Dr. Raul Collazo, Master of Ceremonies (Connect)
08:55–09:10	**Tech Check:** iPad Setup & Interactive Tools Demo	Turner Papke (Array)
09:10–09:45	🎉 **Rademikibart Revealed:** The Science Driving the Trials + Live Q&A	Dr. Cristian Rodriguez (Connect)
09:45–10:00	🎉 **Safety Snapshot & Reporting**	Kimberly Manhard (Connect)
10:00–10:20	-- *Break & Take a Breather*	—
10:20–11:20	🎉 **Protocol Power Hour:** Asthma & COPD Essentials + Live Q&A	Dr. Marisa “MJ” Jones, Guy Boccia (Connect)
11:20–12:00	**Breath by Breath:** Spirometry & FeNO in Action	Dr. Erin Lennox (ZEPHYRx)
12:00–01:30	-- **Lunch & Learning Stations** • Spirometry Demo • Study Start-Up Station	All
01:30-01:40	**Diving into Labs:** Navigating Blood and the Lab Workflow	Guy Boccia (Connect)
01:40–01:50	🎉 **Behind the Scenes:** How Safety Committees Keep Trials on Course	Radha Adivikolanu (Connect)
01:50–02:50	**Recruitment That Works:** • Top Tips from an Expert • Table Talk / Voicing Innovative Recruitment	 Dr. Sanjay Ramakrishnan (ABRA Lead Investigator) All
02:50–03:10	**Tech at the Core:** Randomization Meets Data	Guy Boccia (Connect)
03:10–03:25	-- *Break & Moment to Breathe*	—
03:25–04:10	🎉 **Study Expectations & Monitoring with Meaning:** Oversight to Drive Quality	Aubree Malan (ProPharma Group)
04:10–04:30	**Closing Notes and Winning Moments (Trivia Champions!)**	All

🎉 **Trivia Tip:** Watch for this symbol on the agenda - fastest correct responders have a shot at *prizes*.

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Break – Return at **10:20 am PT**

🫁 Take a Breather

– Join us in the foyer for light snacks and a moment to recharge.

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Protocol Power Hour

Protocols Overview

Seabreeze STAT ASTHMA

Seabreeze STAT COPD

Marisa "MJ" Jones, PharmD
Clinical Trials Associate Manager

Protocol Amendment Summary

Asthma

- **1.1** (20Mar2025)
  - Initial version
- **2.0** (03Jul2025)
  - Limits radiation exposure per UK requirement
  - Minor SoA changes to reduce redundancies
- **3.0** (24Jul2025)
  - Allows historical FeNO for inclusion (if stable)

COPD

- **1.1** (20Mar2025)
  - Initial version
- **1.2** (09Jun2025)
  - Limits radiation exposure per UK requirement
- **2.0** (25Jul2025)
  - Allows historical FeNO for inclusion (if stable)
  - Minor SoA changes to reduce redundancies

SoA = schedule of assessments
FeNO = fractional exhaled nitric oxide test; measure of inflammation in the lungs

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Protocol Overview

CBP-201-206

Seabreeze STAT ASTHMA

CBP-201-207

Seabreeze STAT COPD

- **Phase 2, randomized, double-blind, parallel-group, placebo-controlled trials to evaluate the efficacy and safety of rademikibart as add-on treatment for acute exacerbation**
- **Number of Sites:** Approx. 50 sites per study
- **Countries:** US, Argentina, Australia, UK, Serbia, Georgia
- **Number of participants**: 160 randomized per study
- **Duration:** 8-34 weeks, dependent on enrollment channel

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Population and Endpoints

Population		
Seabreeze STAT ASTHMA	Adolescents and adults (12-75)	• ≥1 exacerbation in prior 12 months • Current acute exacerbation requiring an urgent healthcare visit • Eosinophilic phenotype
Seabreeze STAT COPD	Adults (40-80)	

Primary Endpoint	Secondary Endpoints	Key Exploratory Endpoints
Treatment Failure (28 days after randomization): includes death (any cause), (re)admission to hospital, urgent visit to outpatient/ED provider for symptom worsening, or necessity to intensify pharmacologic treatment.	Rate of exacerbations Time to new exacerbation Absolute change in post-bronchodilator FEV_1 Mean change in respiratory symptoms Safety	Time to ready for discharge in hospitalized patients Disease specific-PROs

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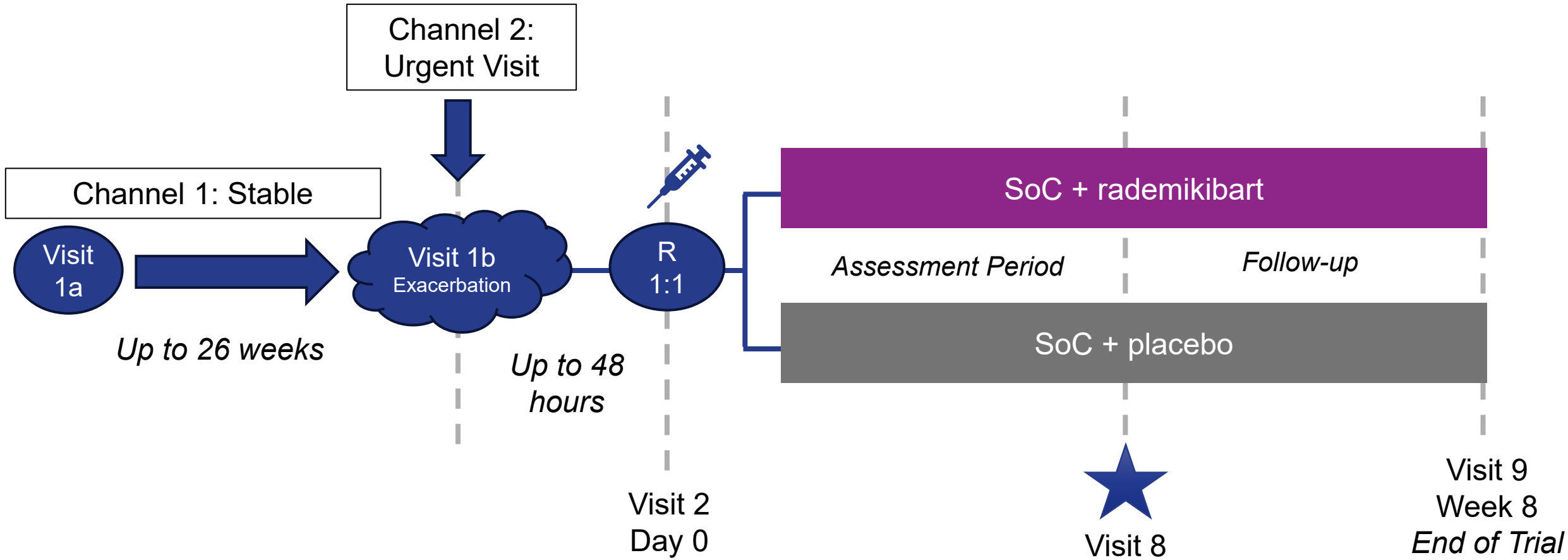
Schema for Seabreeze STAT Trials



SoC = standard of care

Question

What is the primary endpoint of the studies?

A. Absolute change from baseline in post-bronchodilator FEV_1.
B. Treatment failure rate within 28 days after randomization.
C. Incidence of adverse events.
D. Treatment failure within 56 days after randomization.

Channel 1

For Channel 1 only, current or historical EOS ≥ 250 cells/µL and/or FeNO ≥ 25 ppb

A person whose asthma or COPD is currently stable is screened at the study site (V1a)

He/she consents and is determined to be eligible.

The site calls the participant every 4 weeks while waiting for a potential exacerbation

If the participant does not have a qualifying exacerbation within the 26-week Screening Period, they will be considered a screen failure

The participant has an exacerbation and calls the site.

The site instructs the participant to go to an ER, urgent care center, or the study site

The participant is re-screened to ensure the current exacerbation meets study criteria (V1b)

EOS ≥ 300 cells/µL is required at V1b

The participant's eligibility is reconfirmed. They are randomized and dosed. (V2/D0)

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Channel 2

A person who is experiencing an exacerbation goes to the ER or urgent care center

He/she is consented, screened and is determined to be eligible (V1b)

EOS ≥ 300 cells/μL is required at V1b

The participant is randomized and dosed (V2/D0)

Question

- What is the duration of the clinical trials for participants?
  A. 35 weeks
  B. Up to 34 weeks
  C. 8 weeks
  D. Both B and C

Trial Comparison

Asthma

- Stratification:
  - by age (≥18 vs <18 years old)
  - by baseline smoking status (current smokers vs former smokers or non-smokers)
- PROs
  - ACQ-5
  - Modified Borg Dyspnea Scale
- Assessments:
  - PEF will be assessed daily

COPD

- Stratification:
  - by severity of the COPD exacerbation (requiring hospitalization or not)
  - by baseline smoking status (current or former)
- PROs
  - EXACT-PRO
  - Dyspnea NRS
  - CAT
  - SGRQ
- Assessments:
  - PARC and fibrinogen will be assessed
  - Venous blood gas will be assessed (if hospitalized)

Question

- How will participants be stratified for the studies?
  - A. Age
  - B. Age and smoking status
  - C. Hospitalization and smoking status
  - D. Eosinophil count and smoking status
  - E. Gender
  - **F. Both B and C**
  - G. Both C and D

Key Inclusion Criteria – Both Studies

- Diagnosis of asthma or COPD for ≥12 months
- 1 exacerbation requiring the use of systemic corticosteroids within 12 months
- Channel 1 only (stable condition):
  - Historical **EOS ≥250** cells/µL and/or FeNO ≥25 ppb within 12 months prior to Screening Visit 1a
  - Current or historic evidence of spirometry confirming variable airflow limitation (asthma) or airflow obstruction (COPD)
- Both Channels:
  - Acute exacerbation requiring an urgent healthcare visit
  - **EOS ≥300** cells/µL at the time of exacerbation (V1b)

Inclusion Criteria Comparison

Asthma

- Age
  - ≥12 to ≤75 years
- Weight
  - ≥40 kg
- Chest X-ray or CT Scan
  - At V1a or V1b or within 12 months of screening
- Smoking
  - Current or former smokers are excluded if
    - <30 years old: Smoked for ≥5 pack-years.
    - ≥30 years old: Smoked for ≥10 pack-years
- Stable maintenance medication for 30 days
- FEV_1
  - Inc. #13: FEV_1 ≥30% predicted prior to receiving IP on Day 0.

COPD

- Age
  - 40 to 80 years
- Weight
  - ≥45 kg and BMI 16-35 kg/m2
- Chest X-ray or CT Scan
  - At V1b only
- Smoking
  - Inc. criteria #7: Current or former smoker with a history of smoking of ≥10 pack-years

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Question

- How many exacerbations is a participant required to have in the past year to be eligible?
  - A. 0
  - **B. 1**
  - C. 2
  - D. 3
  - E. 3.5

Key Exclusion Criteria – Both Studies

- Hypersensitivity to or recent use of **biologic therapy** (within 16 weeks or 5 half-lives of randomization)
- Immunosuppressive medications or history of **immunosuppression**
- Unstable **heart disease**, cardiac arrhythmias, heart failure, uncontrolled hypertension, clinically significant abnormalities in ECG
- Clinically significant **pulmonary disease** other than asthma or COPD
- **Fever** recorded as >38°C and/or a suspected **pulmonary infection**
- ALT or AST ≥2.5 × ULN and/or bilirubin ≥1.5 × ULN
- Live, attenuated vaccines (4 weeks prior to randomization or planned during study)

Exclusion Criteria Comparison

Asthma

- Previous intubation for exacerbation
- Exacerbation etiology: anaphylaxis or aspirin-induced
- Exposure to fumes
- Bronchial thermoplasty within 12 months

COPD

- TIA or stroke within 6 months
- Lung surgery/resection
- Long Term Oxygen Therapy (LTOT) > 15 hrs/day
- Macrolide therapy
  - Exc. #17: long-term macrolide therapy, unless on stable therapy for >12 months
- SoC for index exacerbation
  - Exc. #20: Current COPD exacerbation for which SoC was started >48 hours prior to Screening Visit 1b.

Schedule of Assessments Comparison

Asthma

Procedures	Screening		Randomization/ Baseline	Post-IP Treatment Assessment						Follow-up
VISIT	V1a[a]	V1b[a,b]	V2[c]	V3[d]	V4[d]	V5	V6	V7[e]	V8	V9
DAY	Up to 26 Weeks to D-1	Up to 48 hrs to D0	0	1	2	3	7 ±2 days	14 ±2 days	28 ±3 days	56 ±3 days
WEEK							1	2	4	8
Written informed consent/assent and HIPAA	X	X[a]								
Demographics	X	X[a]								
Previous medical and surgical history[f]	X	X[a]								
Chest X-ray or CT[g]		X								
Verify eligibility criteria	X	X	X							
Smoking status review	X	X					X		X	X
Prior & concomitant medications	X	X	X	X	X	X	X	X	X	X
e-diary registration & training			X[h]							
Review e-diary						X	X		X	X

COPD

Procedures	Screening		Randomization/ Baseline	IP Treatment Assessment						Follow-up
VISIT	V1a[a]	V1b[a,b]	V2[c]	V3[d]	V4[d]	V5	V6	V7[e]	V8	V9
DAY	Up to 26 weeks to D-1	Up to 48 hrs to D0	0	1	2	3	7 ±2 days	14 ±2 days	28 ±3 days	56 ±3 days
WEEK							1	2	4	8
Written informed consent and HIPAA	X	X[a]								
Demographics	X	X[a]								
Previous medical and surgical history[f]	X	X[a]								
Chest X-ray or CT		X								
Verify eligibility criteria	X	X								
Smoking status review	X	X					X		X	X
Prior & concomitant medications	X	X	X	X	X	X	X	X	X	X
e-diary registration & training			X[g]							
Review e-diary						X	X		X	X

Schedule of Assessments Comparison (continued)

Asthma

Procedures	Screening		Randomization/ Baseline	Post-IP Treatment Assessment						Follow-up
VISIT	V1a[a]	V1b[a,b]	V2[c]	V3[d]	V4[d]	V5	V6	V7[e]	V8	V9
DAY	Up to 26 Weeks to D-1	Up to 48 hrs to D0	0	1	2	3	7 ±2 days	14 ±2 days	28 ±3 days	56 ±3 days
WEEK							1	2	4	8
Trial Treatment/Rescue Medication										
Randomization and assignment of trial product kit number			X							
IP administration			X							
Review rescue medication use			X	X	X	X	X		X	X
Safety										
Complete physical examination[i]	X	X								X
Symptom-directed physical examination[i]			X	X	X	X	X		X	
Assess injection site(s)[j]			X	X	X	X	X		X	
Body weight, height[k]	X	X							X	X
Vital signs, oxygen saturation[l]	X	X	X	X	X	X	X		X	X
ECG (12-lead)[m]	X	X					X			X

COPD

Procedures	Screening		Randomization/ Baseline	IP Treatment Assessment						Follow-up
VISIT	V1a[a]	V1b[a,b]	V2[c]	V3[d]	V4[d]	V5	V6	V7[e]	V8	V9
DAY	Up to 26 weeks to D-1	Up to 48 hrs to D0	0	1	2	3	7 ±2 days	14 ±2 days	28 ±3 days	56 ±3 days
WEEK							1	2	4	8
Interventional Treatment /Rescue Medication										
Randomization and assignment of trial product kit number			X							
IP administration			X							
Review rescue medication use			X	X	X	X	X		X	X
Safety										
Complete physical examination[h]	X	X								X
Symptom-directed physical examination[h]			X	X	X	X	X		X	
Assess injection site(s)[l]			X	X	X	X	X		X	
Body weight, height[j]	X	X							X	X
Vital signs, oxygen saturation[k]	X	X	X	X	X	X	X		X	X
ECG (12 lead)[l]	X	X					X			X

Schedule of Assessments Comparison (continued)

Asthma

Procedures	Screening		Randomization/ Baseline	Post-IP Treatment Assessment						Follow-up
VISIT	V1a[a]	V1b[a,b]	V2[c]	V3[d]	V4[d]	V5	V6	V7[e]	V8	V9
DAY	Up to 26 Weeks to D-1	Up to 48 hrs to D0	0	1	2	3	7 ±2 days	14 ±2 days	28 ±3 days	56 ±3 days
WEEK							1	2	4	8
Hematology, clinical chemistry, urinalysis[n]	X	X[o]	X[o]				X		X	X
Pregnancy (β-hCG blood) test[p]	X	X								
Urine pregnancy test[q]			X						X	X
AE reporting, including SAEs and AESIs	X	X	X	X	X	X	X	X	X	X
PK/Immunogenicity/Pharmacodynamics/Immunogenicity										
Plasma PK samples for rademikibart concentration[r]			X			X	X		X	X
Blood sample for biomarker analysis			X				X		X	X
FeNO	X	X	X			X	X		X	X
ADAs and nAbs[r]			X						X	X

COPD

Procedures	Screening		Randomization/ Baseline	IP Treatment Assessment						Follow-up
VISIT	V1a[a]	V1b[a,b]	V2[c]	V3[d]	V4[d]	V5	V6	V7[e]	V8	V9
DAY	Up to 26 weeks to D-1	Up to 48 hrs to D0	0	1	2	3	7 ±2 days	14 ±2 days	28 ±3 days	56 ±3 days
WEEK							1	2	4	8
Hematology, clinical chemistry, urinalysis[m]	X	X[n]	X[n]				X		X	X
Pregnancy (β-hCG blood) test[o]	X	X								
Urine pregnancy test[p]			X						X	X
AE reporting, including SAEs and AESIs	X	X	X	X	X	X	X	X	X	X
Pharmacokinetics/Immunogenicity/Pharmacodynamic										
Plasma PK samples for rademikibart concentration[q]			X			X	X		X	X
Blood sample for biomarker analysis			X				X		X	X
FeNO	X	X	X			X	X		X	X
ADAs and nAbs[q]			X						X	X

Schedule of Assessments Comparison (continued)

Asthma

Procedures	Screening		Randomization/ Baseline	Post-IP Treatment Assessment						Follow-up
VISIT	V1a[a]	V1b[a,b]	V2[c]	V3[d]	V4[d]	V5	V6	V7[e]	V8	V9
DAY	Up to 26 Weeks to D-1	Up to 48 hrs to D0	0	1	2	3	7 ±2 days	14 ±2 days	28 ±3 days	56 ±3 days
WEEK							1	2	4	8
Efficacy										
Assessment (by Investigator) of asthma exacerbations			X	X	X	X	X	X	X	X
Spirometry or peak flow		X								
Spirometry (pre-BD)[s]	X					X	X		X	X
Spirometry (post-BD)[t]	X		X	X[u]	X[u]	X	X		X	X
Home peak flow monitoring[v]			←	—	—	—	—	—	→	
ACQ-5[w]			X				X	X	X	X
Modified Borg Dyspnea Scale		X	X			X	X		X	X
Health care resource utilization			X						X	X
Time to Ready-for-Discharge			←	—	—	—	—	—	→	

COPD

Procedures	Screening		Randomization/ Baseline	IP Treatment Assessment						Follow-up
VISIT	V1a[a]	V1b[a,b]	V2[c]	V3[d]	V4[d]	V5	V6	V7[e]	V8	V9
DAY	Up to 26 weeks to D-1	Up to 48 hrs to D0	0	1	2	3	7 ±2 days	14 ±2 days	28 ±3 days	56 ±3 days
WEEK							1	2	4	8
Efficacy										
Assessment (by Investigator) of COPD exacerbation			X	X	X	X	X	X	X	X
Venous blood gas analysis[r]			X	X	X	X				
Spirometry (pre-BD)[s]	X						X		X	X
Spirometry (post-BD)[t]	X	X	X	X[u]	X[u]	X	X		X	X
EXACT-PRO[v]			Daily (e-diary) from V2 to Week 8							
Dyspnea NRS			Daily (e-diary) from Screening V1b to Week 8							
CAT[w]			X				X	X	X	X
SGRQ[x]			X						X	X
Health care resource utilization			X						X	X
Time to Ready-for-Discharge			—	—	—	—	—	—	→	

Patient Reported Outcomes (PROs)

Asthma

- In-Clinic
  - ACQ-5
  - Modified Borg Dyspnea
  - HCRU
- At home
  - PEF AM / PM
  - Symptom diary AM / PM

COPD

- In-Clinic
  - SGRQ
  - CAT
  - HCRU
- At home
  - Symptom diary AM / PM
    - Dyspnea NRS
  - Exact PRO - PM

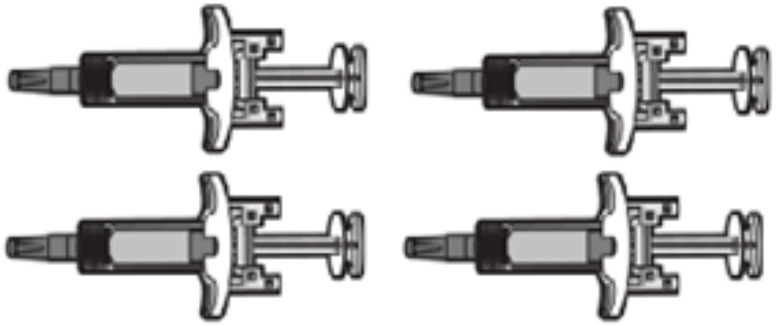
Investigational Product (IP): Rademikibart and Matching Placebo

Prefilled Syringes:

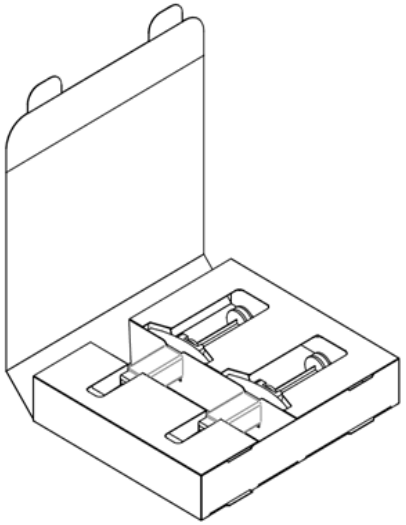
- Rademikibart 600 mg dose (4mL), administered as 4 SC injections of 1 mL each.
- Matching placebo (4mL), administered as 4 SC injections of 1 mL each.

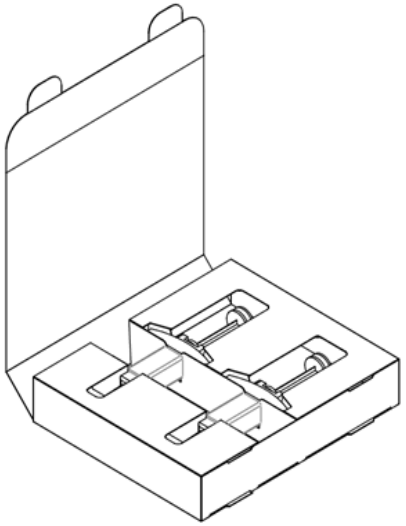
Investigational product (rademikibart 600 mg SC or placebo SC) will be administered on Day 0 only.

Rademikibart drug product and matching placebo solution are to be stored between 2°C to 8°C.



Packaging and Labeling





IP will be provided as follows:

- **Rademikibart** solution for injection is packaged as 2 single-dose 1 mL pre-filled syringes packaged in a cardboard carton with a supportive custom insert.
- **Placebo** solution for injection is packaged as 2 single-dose 1 mL pre-filled syringes packaged in a cardboard carton with a supportive custom insert.

Each carton of IP will include a label containing the following:

- Subject ID (write in field)
- Protocol number
- Sponsor name and address
- IP information
- Storage conditions
- Lot number
- Medication number: Called "Drug Unit ID" in IRT; assigned by the IRT system.

Question

- How should the IP be stored?
  A. Controlled room temperature
  B. -70º C, Frozen
  C. 2-8º C, Refrigerated
  D. -20º C, Frozen

Preparation and Administration

Preparation:

Lay the IP Syringes on a flat surface and let them naturally warm to room temperature for approximately 30 minutes in order to minimize discomfort to the participant during administration.

REFER TO PHARMACY MANUAL for detailed preparation instructions.

Dosing: 4 subcutaneous (SC) injections on Day Zero only.

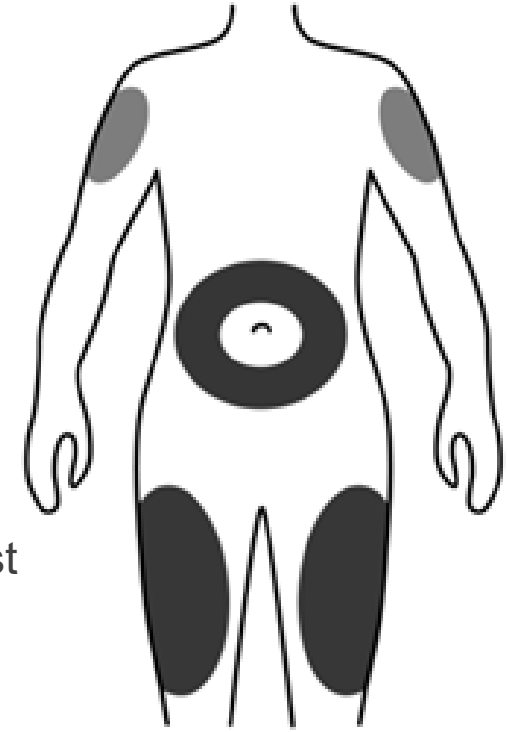
Locations: Upper Arm, Anterior Thigh, Abdomen

Distance between SC Injections: It is recommended to choose a different anatomical site to inject from each IP Syringe. At a minimum, each injection site should be separated by at least 3 cm.

The skin to be pinched to isolate the SC tissue from the muscle.

Insert the needle at a 45-degree angle and slowly inject (recommend at least a 5 second duration)

DO NOT MASSAGE site after injection.



Administration of Investigator and Assessment

Participants will be monitored and assessed for up to 2 hours following the administration of IP.

During this time, and prior to discharge from the site, the site staff will observe for the following injection site reactions:

- Pain
- Erythema/redness
- Itching/scratching/pruritus
- Warmth to touch

Additionally, when the participant returns for Day 7 Visit, the site staff should inquire about any sign/symptoms of an injection site reaction that occurred after discharge from the prior site visit.

- Reference-Protocol Appendix D: Injection Site Reaction Assessment Tool

Question

- How many subcutaneous injections will participants receive?
  - **A. 4**
  - B. 2
  - C. 1
  - D. 5

- Are dose modifications permitted?
  - A. Yes
  - **B. No**
  - C. With medical monitor approval

Emergency Unblinding

Blinding is maintained by assigning medication numbers (kit numbers) to each package-with this number on both the box and the Study Drug.

Kit numbers are assigned according to a pre-defined randomization schedule which is maintained within the IRT system.

The IRT will provide access to unblinded participant treatment in the case of a **medical emergency**, via a code break module. Whenever possible, the Investigator should contact the Sponsor prior to unblinding.

In the case of any intentional or accidental unblinding, the Sponsor or designee must be notified immediately. Whenever a treatment sequence is prematurely unblinded, the reason, date, and time of the unblinding, and the individual who broke the blind must be documented.

Questions??

Seabreeze STAT Asthma / COPD Investigator Meeting

Erin Lennox, PhD
VP Clinical Research, ZEPHRYx

Technology Overview

SCREENING & IN-CLINIC TESTING

NiOX Panel app

- In-clinic FeNO

ZEPHYRx Kiosk app

- In-clinic Spirometry
- In-clinic eCOA
  - **COPD**
    - CAT
    - SGRQ
    - EXACT
  - **Asthma**
    - ACQ-5
    - Modified Borg Dyspnea Scale

HOME TESTING

Participant's own phone with the Breathe Easy App installed

Asthma

- Twice daily ediary
- Twice daily peak flow (PEF)

COPD

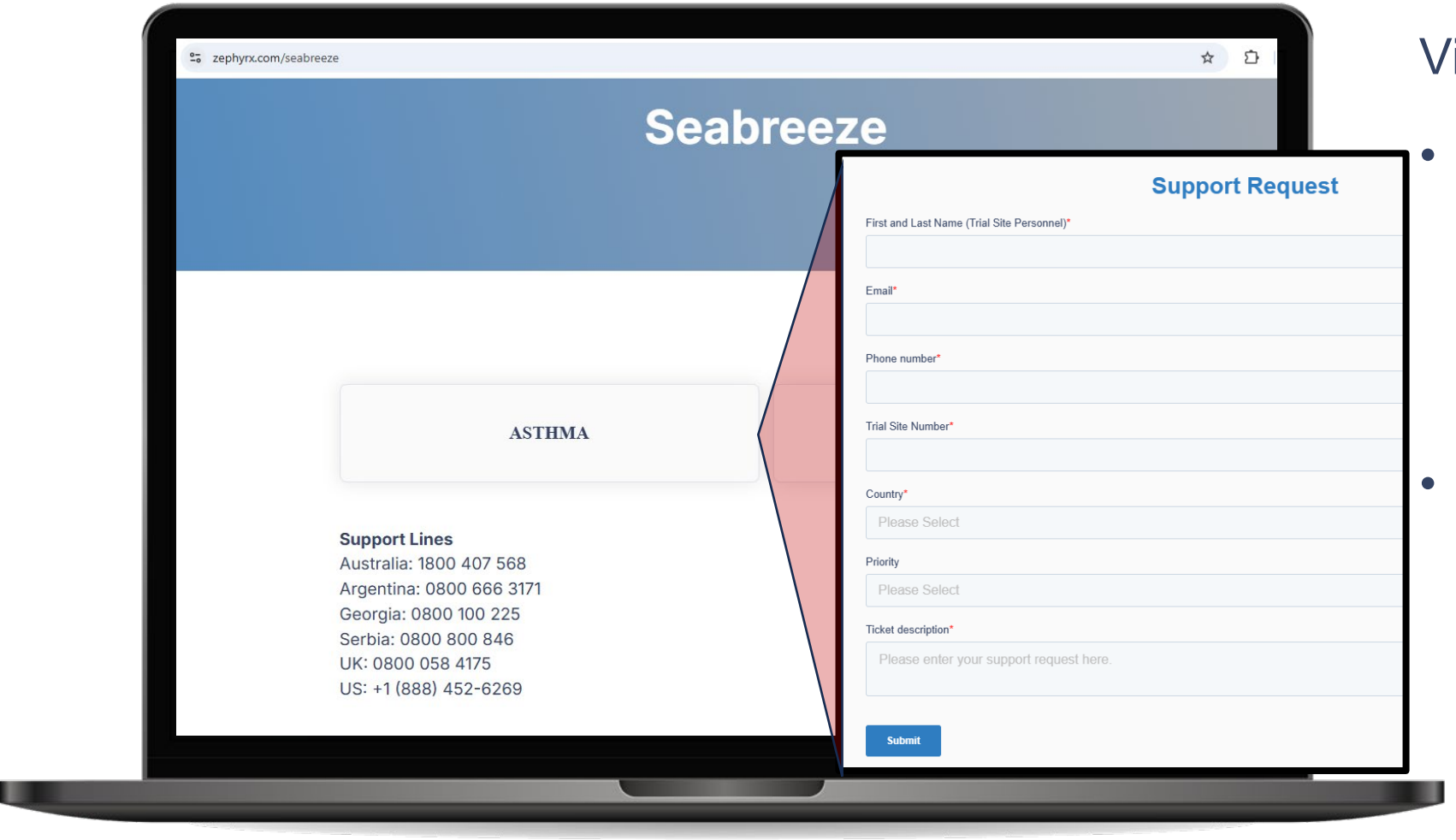
- Twice daily ediary
- Daily EXACT-Pro symptom diary

Study Equipment Overview

What you will receive in your kit:

Endpoint	Item	Quantity
In-Clinic Spirometry & eCOAs	Spirobank Smart II (with charger)	1
	Samsung Galaxy A9+ Tablet with the ZEPHYRx Kiosk App	1
	Disposable Turbine/Filter Combo	50
	Nose Clips	50
In Clinic FeNO	NiOX FeNO Device	1
	FeNO Filters (TK-100)	100
	Windows Surface Tablet with the NiOX Panel App	1
Home PEF and ediary (Asthma Study Only)	Spirobank Smart (with noseclips and batteries)	4

Study Support



Visit zephyrx.com/seabreeze for

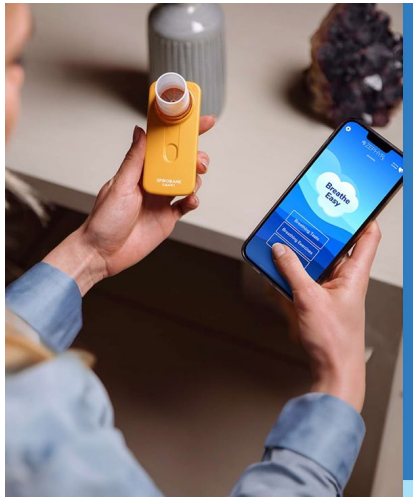
- Country Specific Toll-Free Phone Lines for urgent support
  - 24/7 phone support
- Or Select your Study and Submit a support request

Replacing Devices

- ✓ If sites require replacement of any devices, or consumable replenishment they submit a support request at zephyrx.com/seabreeze
- ✓ and select either Asthma/COPD study.
- ✓ Estimated delivery time is 7-35 days based on country requirements.
- ✓ Upon confirmation of receipt, ZEPHYRx can set up a support call with the site to integrate the new device(s) into the platform and ensure seamless transfer of data and usage.

Site Training Materials (sent via email)

Site Training Platform User Guides



ZEPHYRx

Platform User Guide

Seabreeze STAT Asthma
V3.0
August, 2025

Seabreeze

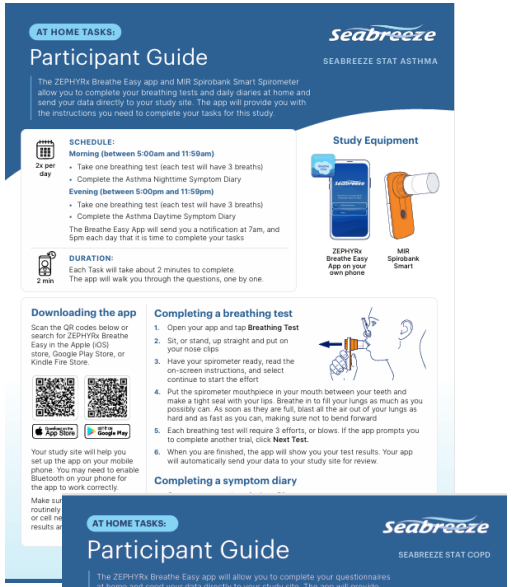
ZEPHYRx

Platform User Guide

Seabreeze STAT COPD
V3.0
August, 2025

Seabreeze

Participant User Guides



AT HOME TASKS:

Participant Guide

Seabreeze

SEABREEZE STAT ASTHMA

The ZEPHYRx Breathe Easy app and MIR Spirobank Smart Spirometer allow you to complete your breathing tests and daily diaries at home and send your data directly to your study site. The app will provide you with the instructions you need to complete your tasks for this study.

SCHEDULE:
Morning (between 5:00am and 11:59am)
- Take one breathing test (each test will have 3 breaths)
- Complete the Asthma Nighttime Symptom Diary

Evening (between 5:00pm and 11:59pm)
- Take one breathing test (each test will have 3 breaths)
- Complete the Asthma Daytime Symptom Diary

The Breathe Easy App will send you a notification at 7am, and 5pm each day that it is time to complete your tasks

DURATION:
Each Task will take about 2 minutes to complete.
The app will walk you through the questions, one by one.

Study Equipment

ZEPHYRx Breathe Easy App on your own phone

MIR Spirobank Smart

Downloading the app

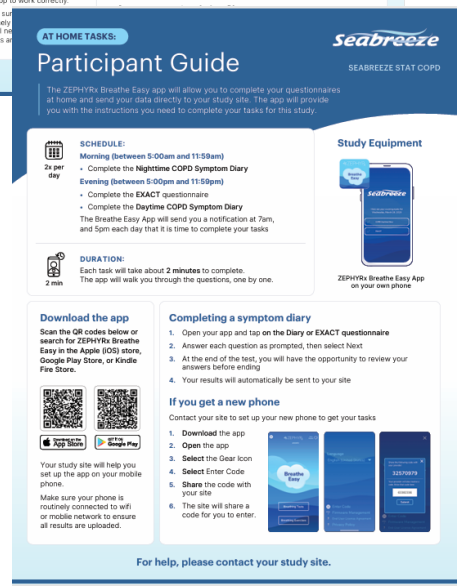
Scan the QR codes below or search for ZEPHYRx Breathe Easy in the Apple (iOS) store, Google Play Store, or Kindle Fire Store.

Your study site will help you set up the app on your mobile phone. You may need to enable Bluetooth on your phone for the app to work correctly.

Completing a breathing test

1. Open your app and tap **Breathing Test**
2. Sit, or stand, up straight and put on your nose clips
3. Have your spirometer ready, read the on-screen instructions, and select continue to start the effort
4. Put the spirometer mouthpiece in your mouth between your teeth and make a tight seal with your lips. Breathe in to fill your lungs as much as you possibly can. As soon as they are full, blast all the air out of your lungs as hard and as fast as you can, making sure not to bend forward
5. Each breathing test will require 3 efforts, or blows. If the app prompts you to complete another trial, click **Next Test**.
6. When you are finished, the app will show you your test results. Your app will automatically send your data to your study site for review.

Completing a symptom diary



AT HOME TASKS:

Participant Guide

Seabreeze

SEABREEZE STAT COPD

The ZEPHYRx Breathe Easy app will allow you to complete your questionnaires at home and send your data directly to your study site. The app will provide you with the instructions you need to complete your tasks for this study.

SCHEDULE:
Morning (between 5:00am and 11:59am)
- Complete the **Nighttime COPD Symptom Diary**

Evening (between 5:00pm and 11:59pm)
- Complete the **EXACT** questionnaire
- Complete the **Daytime COPD Symptom Diary**

The Breathe Easy App will send you a notification at 7am, and 5pm each day that it is time to complete your tasks

DURATION:
Each task will take about **2 minutes** to complete.
The app will walk you through the questions, one by one.

Study Equipment

ZEPHYRx Breathe Easy App on your own phone

Download the app

Scan the QR codes below or search for ZEPHYRx Breathe Easy in the Apple (iOS) store, Google Play Store, or Kindle Fire Store.

Your study site will help you set up the app on your mobile phone.

Make sure your phone is routinely connected to wifi or mobile network to ensure all results are uploaded.

Completing a symptom diary

1. Open your app and tap **on the Diary or EXACT questionnaire**
2. Answer each question as prompted, then select Next
3. At the end of the test, you will have the opportunity to review your answers before ending
4. Your results will automatically be sent to your site

If you get a new phone

Contact your site to set up your new phone to get your tasks

1. **Download** the app
2. **Open** the app
3. **Select** the Gear Icon
4. **Select** Enter Code
5. **Share** the code with your site
6. The site will share a code for you to enter.

For help, please contact your study site.

ATS/ERS 2019 Overview

ZEPHYRx

ATS/ERS 2019 Overview

In 2005 the American Thoracic Society (ATS) and the European Respiratory Society (ERS) jointly adopted technical standards for conducting spirometry. These standards aimed to provide guidance for conducting proper spirometry testing in order to improve accuracy and interpretation of results, and provide a better patient experience. In 2019 these standards were updated to take full advantage of current technical capabilities. ZEPHYRx uses the updated ATS/ERS 2019 Standards of Spirometry (referred to in this document as ATS 2019) to evaluate each PFT effort and series performed with ZEPHYRx Breath Easy, and ZEPHYRx Kiosk apps. This document summarizes some of the key components from ATS 2019 to help site coordinators understand why their study participants' PFT results are being displayed and scored the way they are. For a full overview, you can read the entire ATS 2019 document at https://www.atsjournals.org/doi/full/10.1164/rccm.201908-1590ST[1]

How does ATS 2019 differ from ATS 2005?

If you are already familiar with the ATS 2005 standards, you may recognize that there are a few main differences in the 2019 standards. The key components that are implemented by ZEPHYRx are:

1. *The use of Series level Grades for FEV1 and FVC.* We will provide a letter grade of A, B, C, D, E, F, or U both FEV1 and FVC for each series that is based on the quality of the efforts that were part of that series.
2. *Separate Acceptability values for FEV1 and FVC.* In the 2015 standards, each effort was either marked as Acceptable or Unacceptable. In the 2019 standards, this is broken down into two separate scores: FEV1 acceptability, and FVC acceptability. The FEV1 acceptability is based on the quality of the first second of the maneuver, whereas the FVC acceptability is about the quality of the whole maneuver, with a focus on the End of Forced Expiration (or EOFE), which is the end of the big exhale. The 2019 standards also introduce the concept of "usability" which means that while not acceptable, an effort may be the best a patient can do, and can still be useful.
3. *New Criteria for the End of the Forced Expiration (EOFE).* Previously referred to as End of Test (EOT) criteria, the new EOFE criteria focus on participant either reaching an expiratory plateau (low flow over the final second of the exhalation), reaching 15 seconds of forced exhalation (instead of 6 seconds in the 2005 standards), or achieving a repeatable FVC value.
4. *The importance of the final inspiratory loop.* ATS 2019 requires the patient to perform a big inhalation at the end of their forced expiration, closing the flow volume loop

1 Hour Training Session with ZEPHYRx

A Calendly link will be sent with the training materials to sign up for your training session

- We ask that site staff try to sign up for a single group session if multiple staff members require training.
- We ask that site staff attend training on a device that has a working camera and microphone, so we can communicate effectively

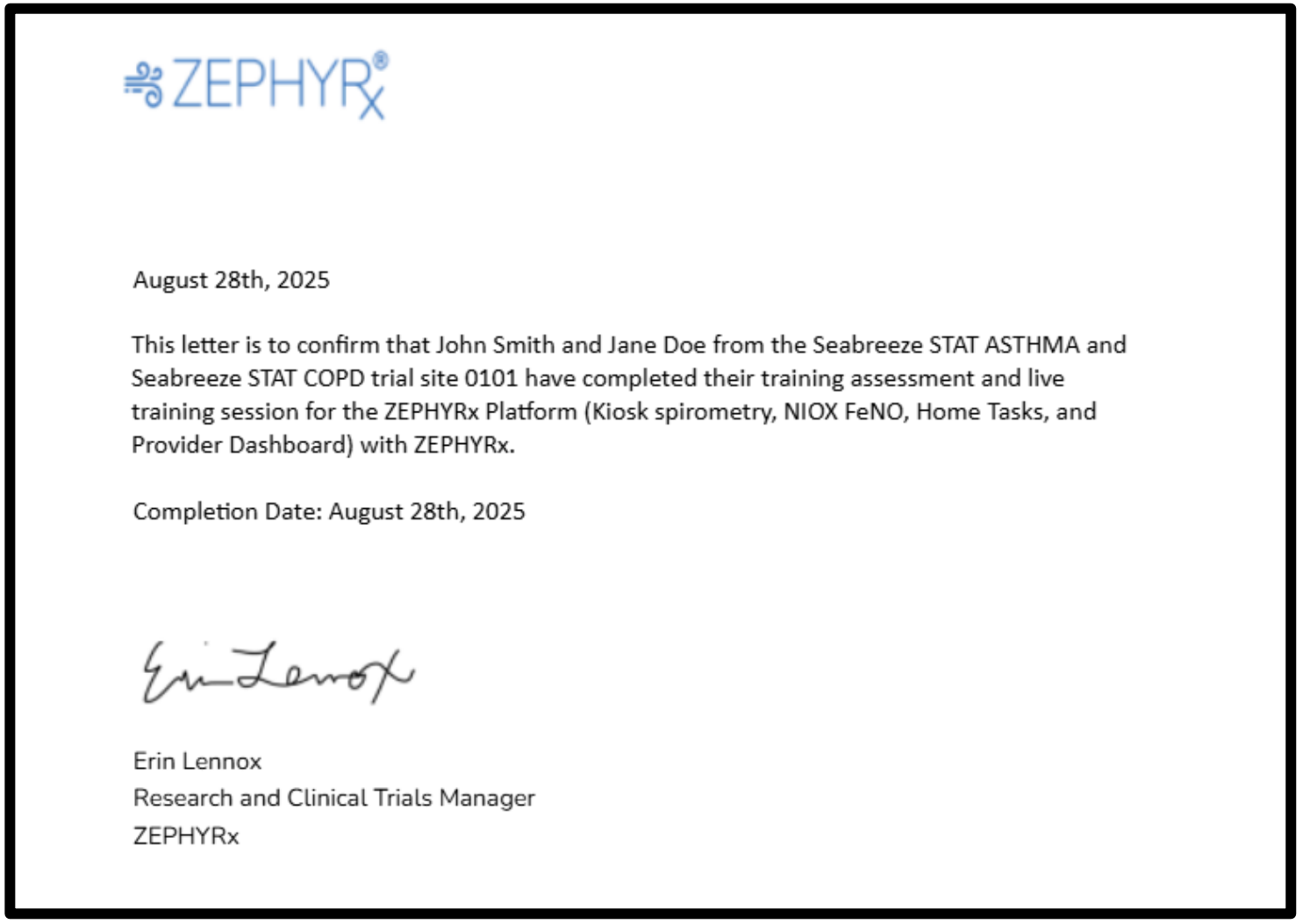
Training Session Topics:

1. Setup Kiosk and FeNO systems
2. Confirm Bluetooth, WIFI connection and cell service and troubleshoot issues
3. Walkthrough the ZEPHYRx Provider Dashboard.
4. FAQ about the ZEPHYRx Platform.
5. Overview the Spirometry and FeNO Maneuvers
6. Conduct a Test Spirometry and Test FeNO Session

*Access to the ZEPHYRx Dashboard is sent once the site staff sign up for training via Calendly or at the start of the live training session to ensure only trained staff are receiving access and invitation links don't expire.

**For unresponsive sites, ZEPHYRx will reach out to CRA teams for assistance.

Training Certification



ZEPHYRx®

August 28th, 2025

This letter is to confirm that John Smith and Jane Doe from the Seabreeze STAT ASTHMA and Seabreeze STAT COPD trial site 0101 have completed their training assessment and live training session for the ZEPHYRx Platform (Kiosk spirometry, NIOX FeNO, Home Tasks, and Provider Dashboard) with ZEPHYRx.

Completion Date: August 28th, 2025

Erin Lennox
Research and Clinical Trials Manager
ZEPHYRx

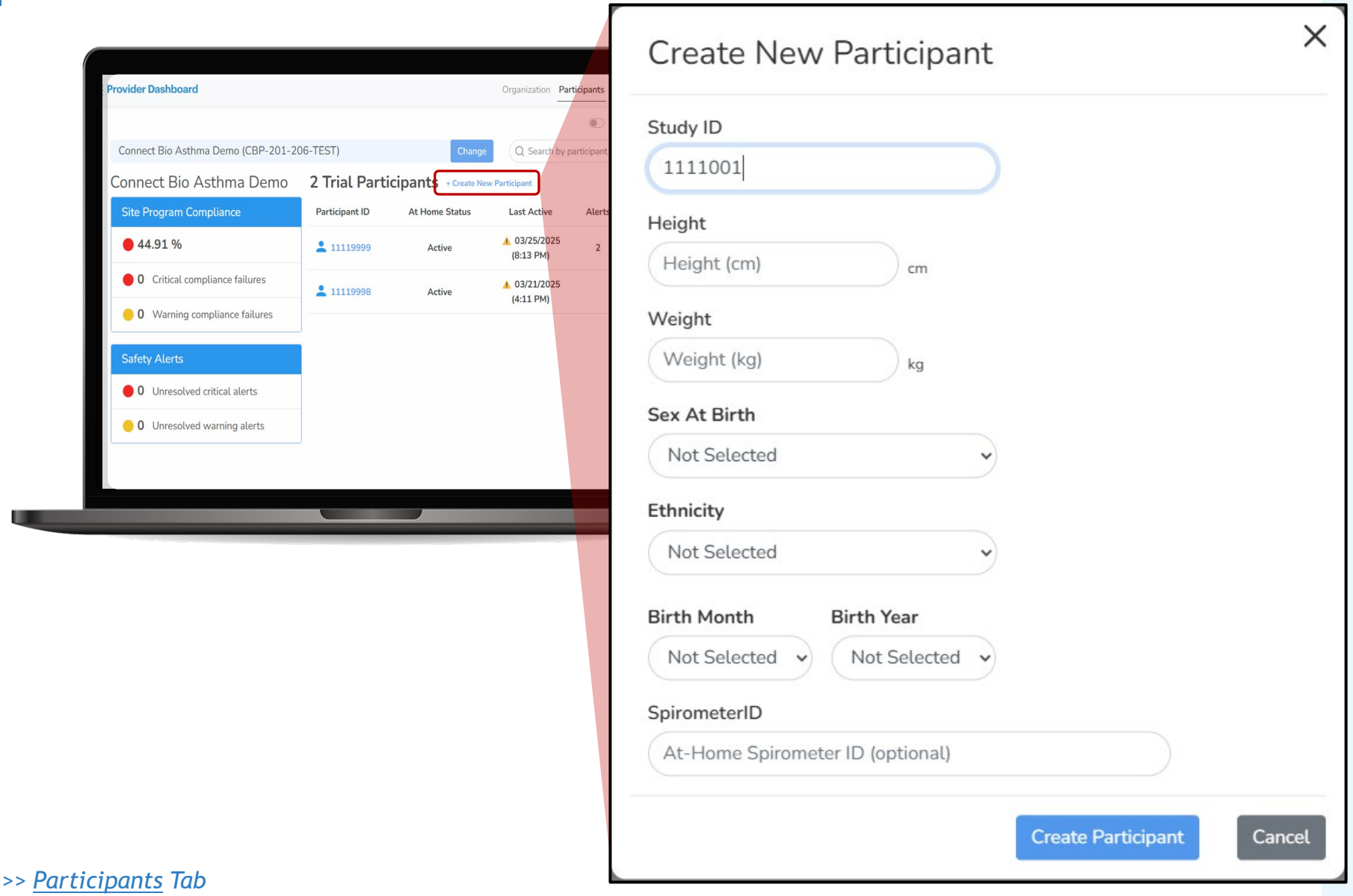
Upon successful completion of the Live Training Session

Sites will receive a Spirometry Training Certificate

*CRA teams will be copied into emails containing training certificate for record keeping.

Provider Dashboard

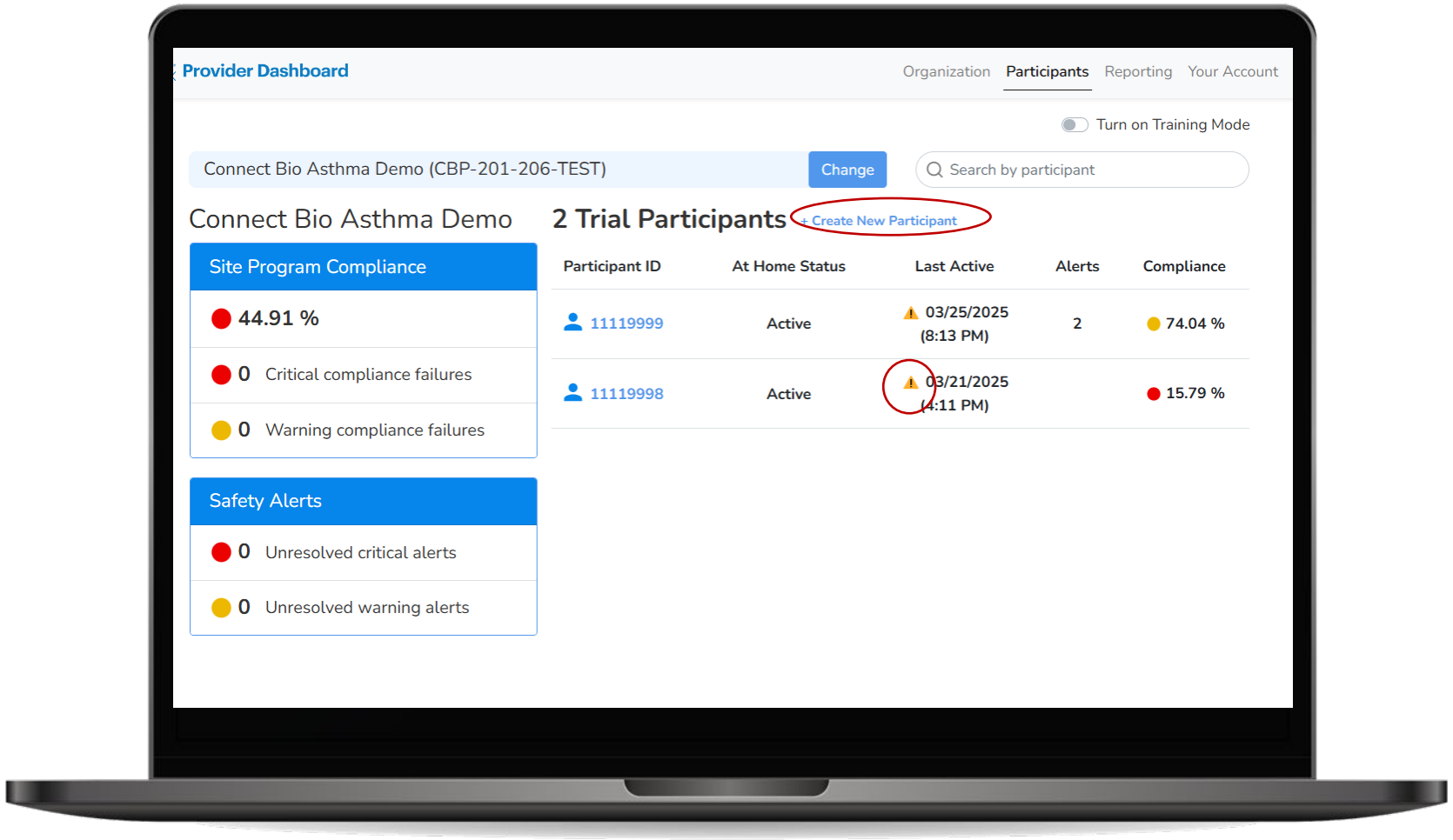
Create A New Participant



- ✓ Study ID: 4-digit site ID, 3-digit subject ID (e.g. 1111001)
- ✓ Enter all demographics
- ✓ Enter Home Spirometer ID (Asthma only)

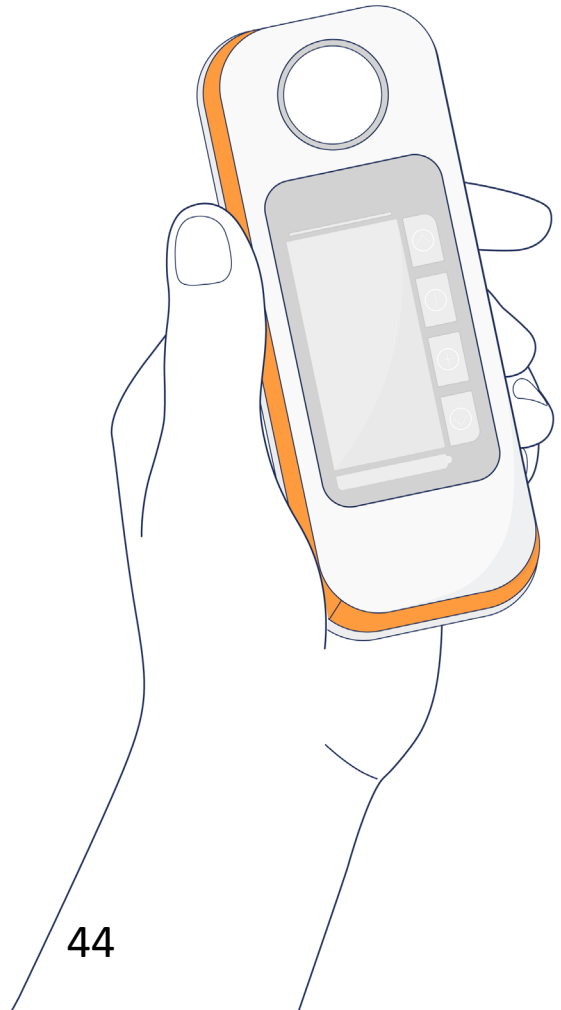
>> *Participants Tab*

Site Dashboard Overview



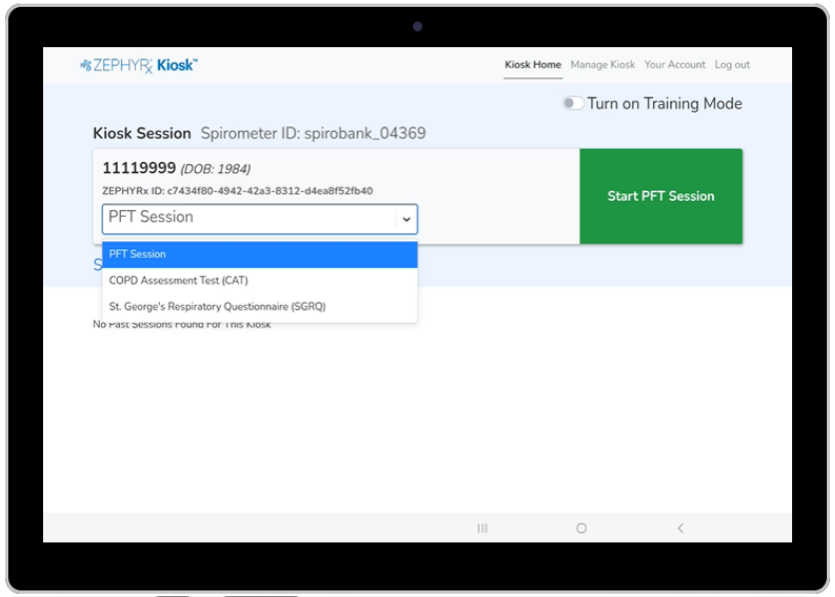
- ✓ Select **Participants** tab
- ✓ View site-level **compliance and safety alerts**
- ✓ **Create New Participants**
- ✓ View Participant Offline Alerts

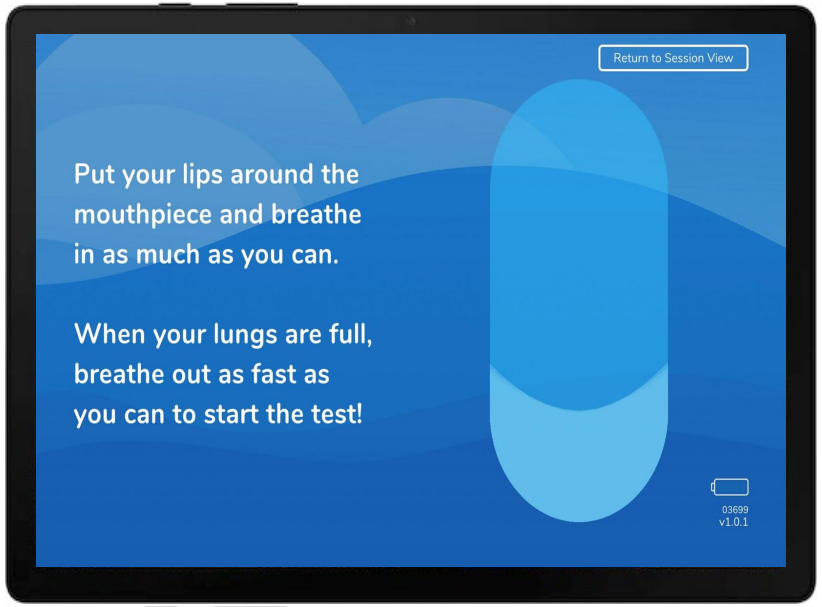
>> *Participants Tab*

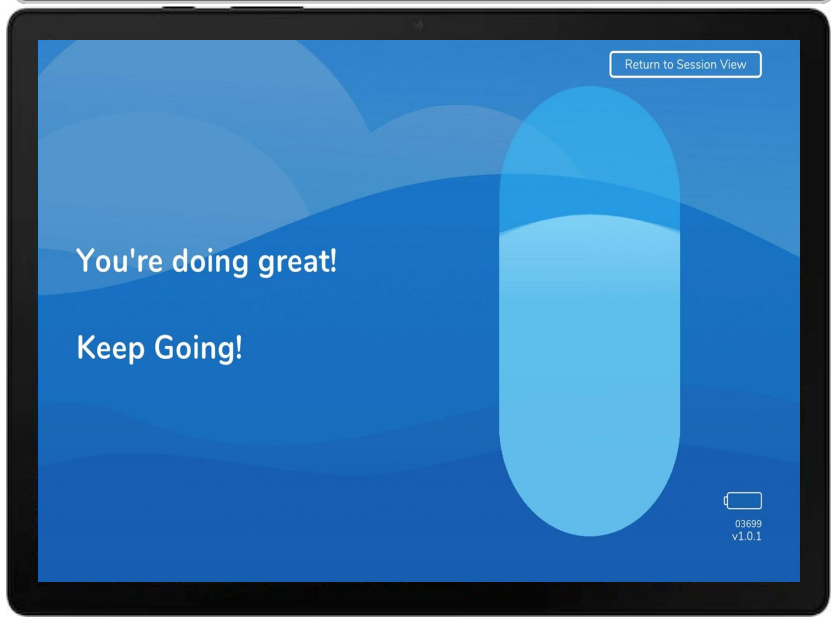


In-Clinic Kiosk Spirometry

Kiosk Spirometry



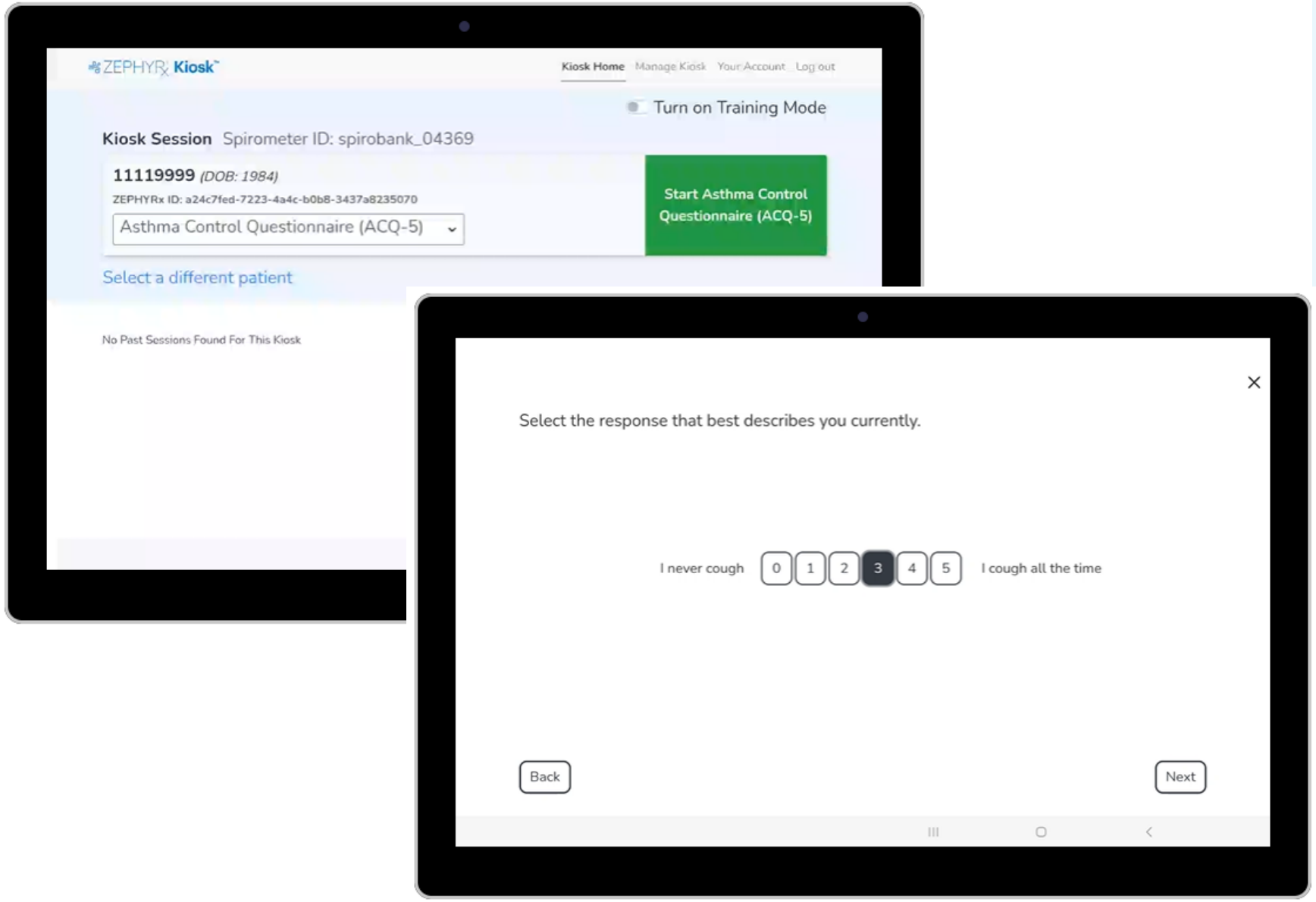




- **Select PFT**
- **Coach participant** using on-screen instructions
- **Conduct 3 – 8 efforts**, aiming for 3 acceptable efforts
- View Results

In-Clinic Kiosk eCOAs

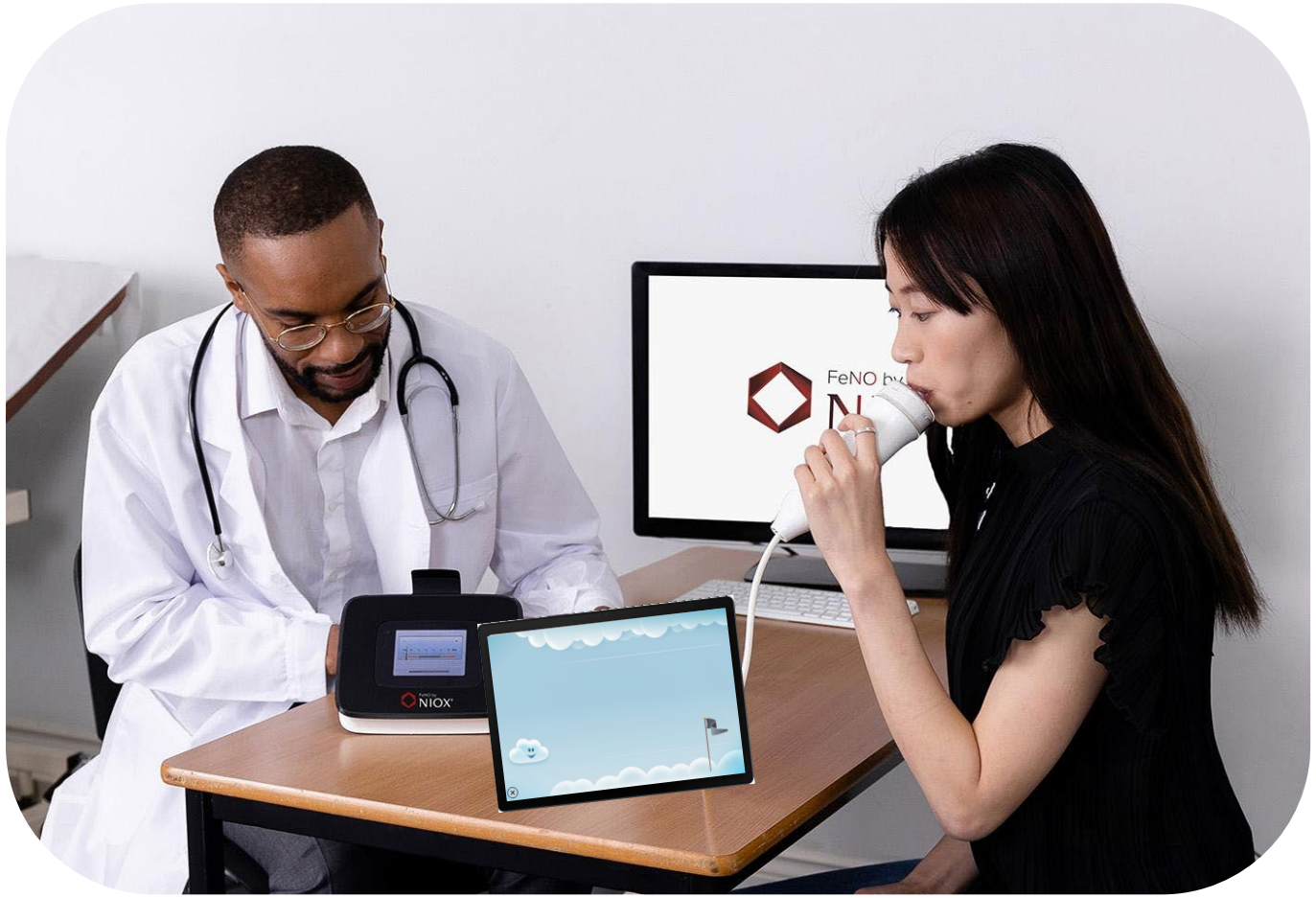
Kiosk eCOAs



- Select your Participant or Create a new participant
- Select the desired eCOA
- Confirm the Participant Demographics
- Select Language
- Participant Completes the Assessment

In-Clinic FeNO

FeNO Maneuver

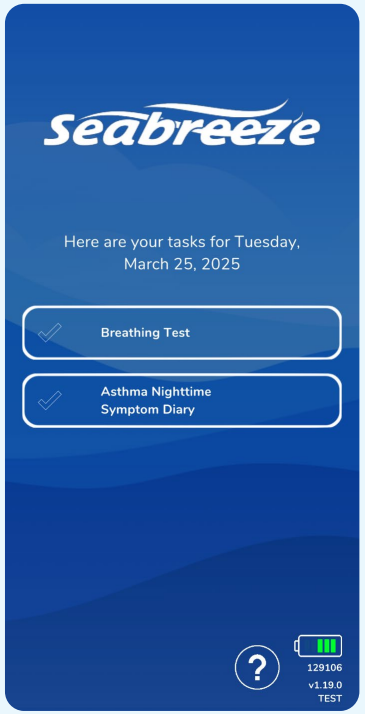


On The Windows Surface Tablet

- ✓ Install the filter
- ✓ Open the NiOX Panel App
- ✓ Select the Particapnt ID
- ✓ Coach the Participant through the maneuver
- ✓ View results in the Provider Dashboard

Home Tasks: Asthma

Home Equipment

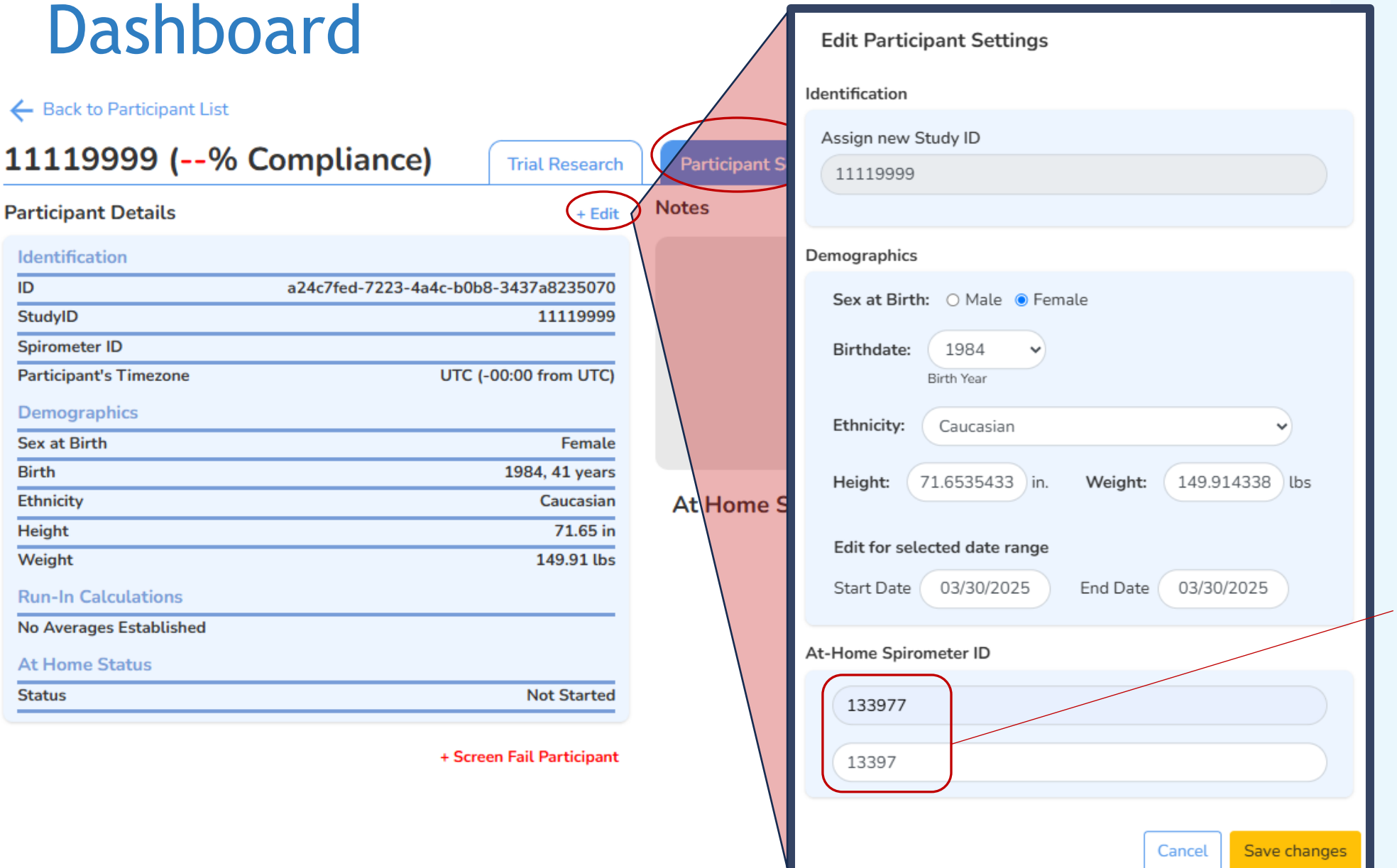


Participant's mobile phone with the Breathe Easy App Installed

MIR Spirobank Smart

Note: Contact your CRA if you have a channel 1 patient that does not have a phone or tablet to request an ediary device.

Pair Home Spirometer in the Provider Dashboard



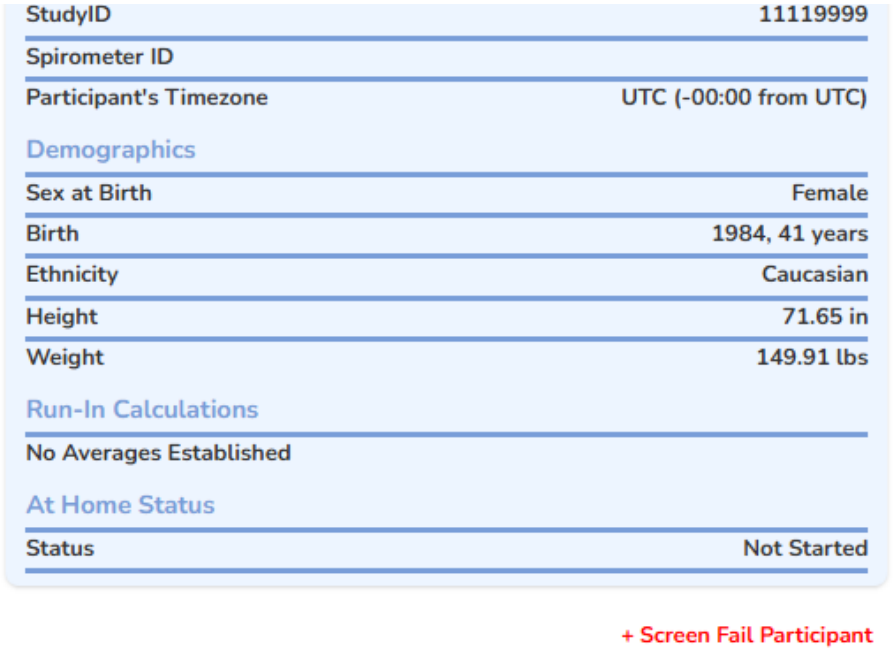
Prior to distributing the spirometer to the participant:

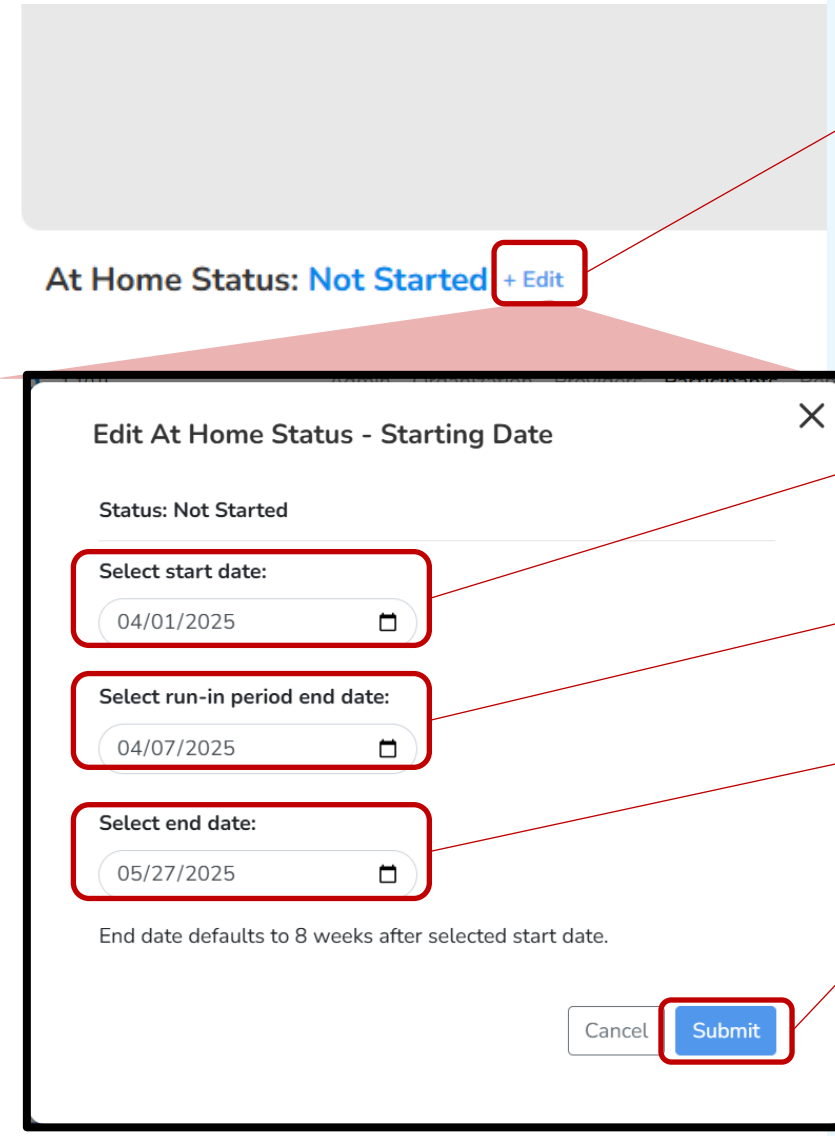
- ✓ Go to the **Participant Settings** Tab
- ✓ Select **"Edit"**

- ✓ Enter the 6 Digit spirometer ID:

e.g. A23-Z133977

Set At-Home Task Start Date





⚠ Participants will not see ediary tasks on their phone if the start date is not set.

- ✓ From the **Participant Settings** tab, select **Edit** next to the at home status
- ✓ select **Start Date:**
  - ✓ **Start date** should be set at V1b as current date
  - ✓ **Run-in period end date** should be set 1 week post start date
  - ✓ **End date** will default to 8 weeks after start date, but can be updated as needed
- ✓ Select **Submit**

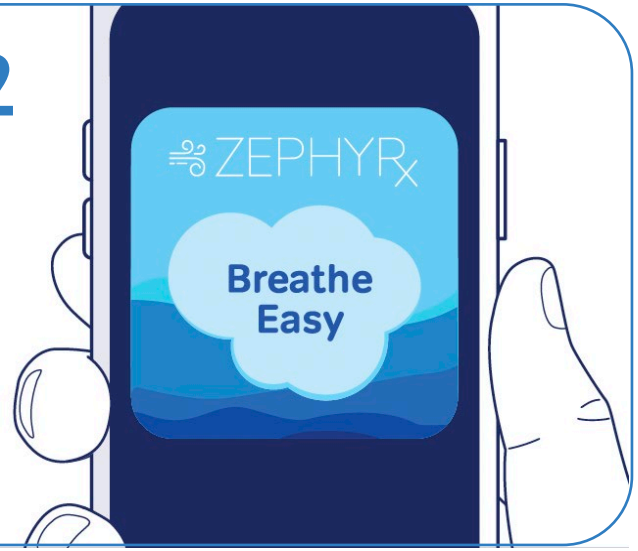
Connect Spirometer to Breathe Easy App

1

for iPhone

for Android

2

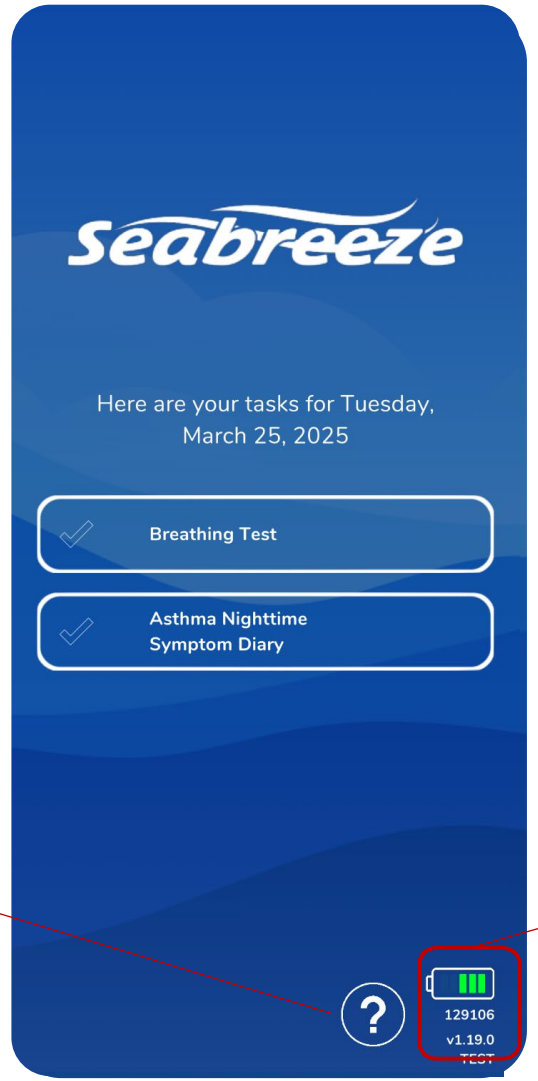


3

1. **Download the Breathe Easy App** to the participant's phone
2. Open **Breathe Easy** app
3. The **spirometer's ID** number will pop up on-screen, select the ID to connect device

Note: This step should not be done until the Spirometer has been paired to the participant's account through the dashboard

Participant App Overview



- ✓ troubleshooting tips
- ✓ set language

- ✓ spirometer battery life
- ✓ spirometer ID
- ✓ app version

Once the run-in start date is reached, the participant will start receiving their tasks

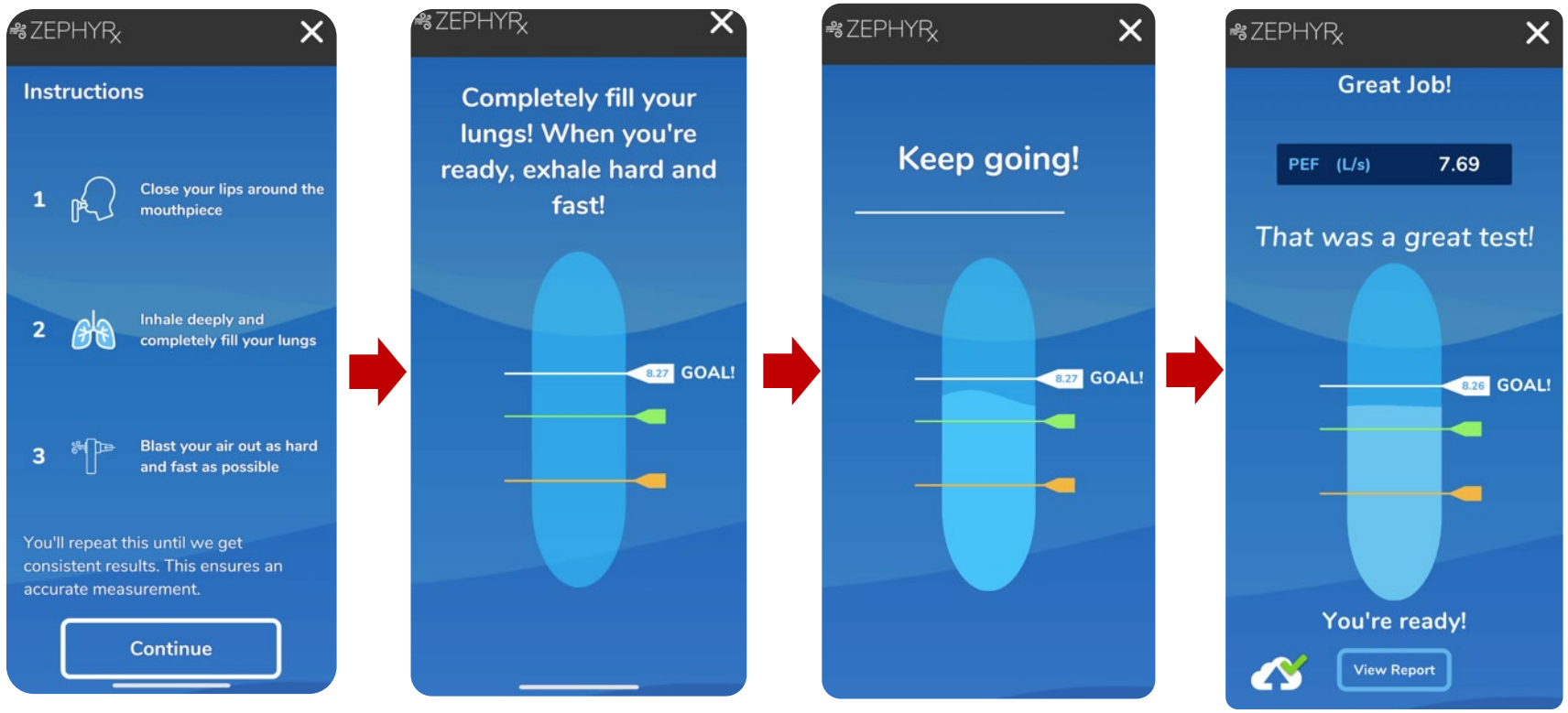
- ✓ **Results are transmitted in real-time** to the dashboard
- ✓ **Tasks can not be completed** outside of the window

Morning PEF Test Task Window
5:00am – 11:59am

Evening PEF Test Task Window
5:00pm – 11:59pm

Reminder notifications will be sent at 7:00am and 5:00pm

Peak Flow Tasks



- ✓ Participants complete breathing tests with **results sent in real-time** to the Provider Dashboard
  - ✓ Each PEF test consists of **3 efforts**, or maneuvers
- ✓ **Step-by-step instructions** and sound queues walk participants through their breathing test

Home Tasks: COPD

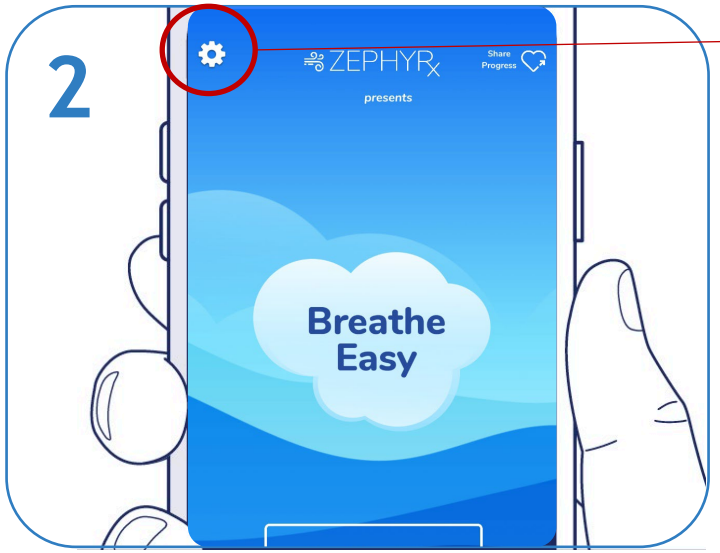
Help Participant Download the Breathe Easy App

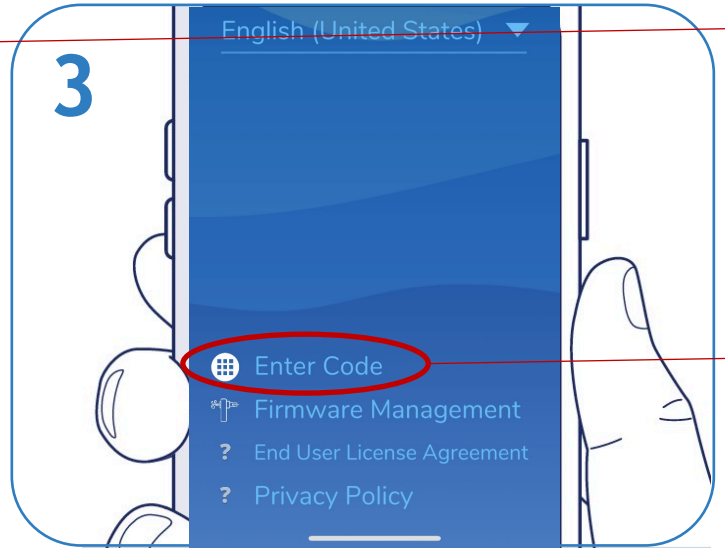
Note: Contact your CRA if you have a channel 1 patient that does not have a phone or tablet to request an ediary device.

1

for iPhone

for Android

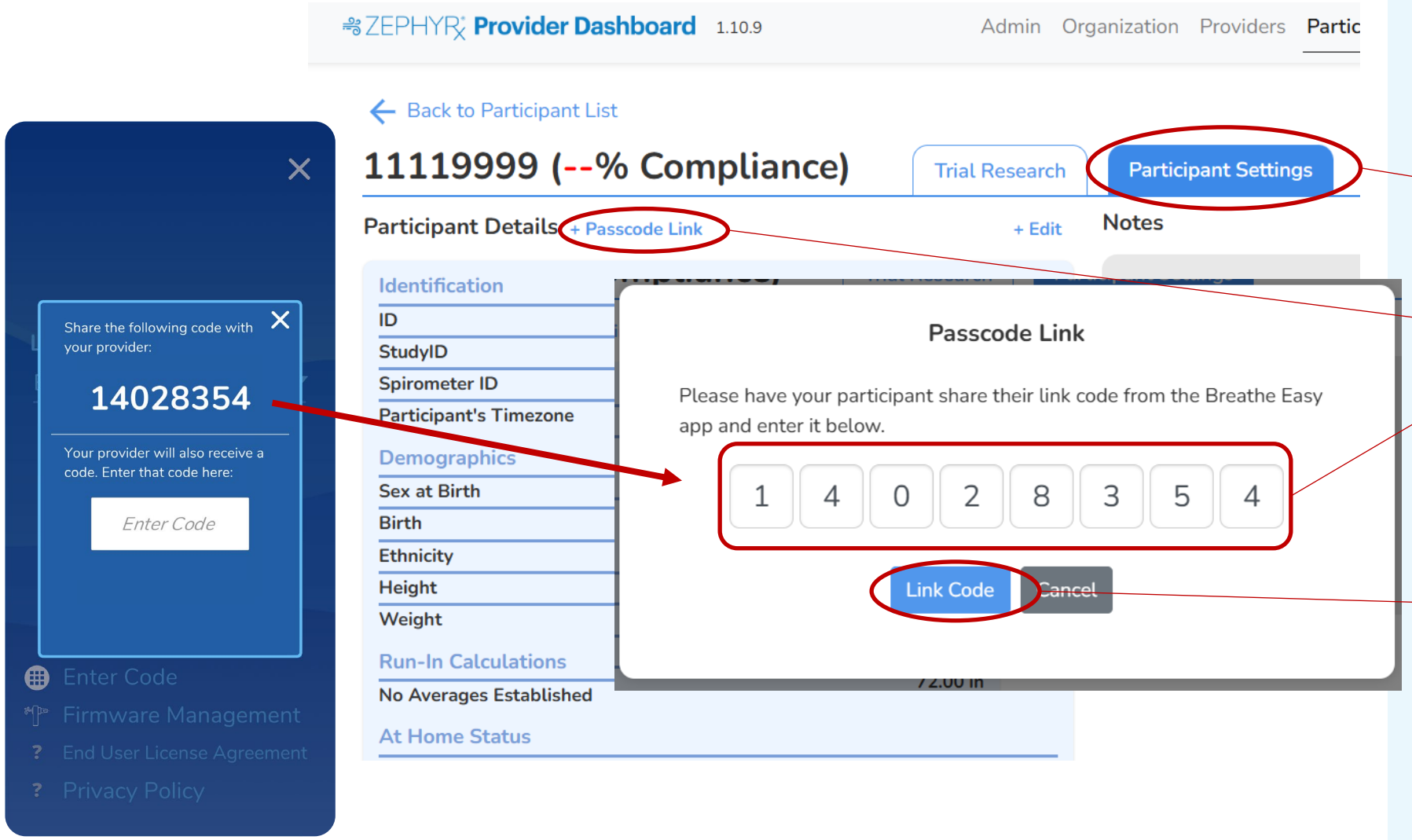




To Pair the Participant's phone to the ZEPHYRx Dashboard:

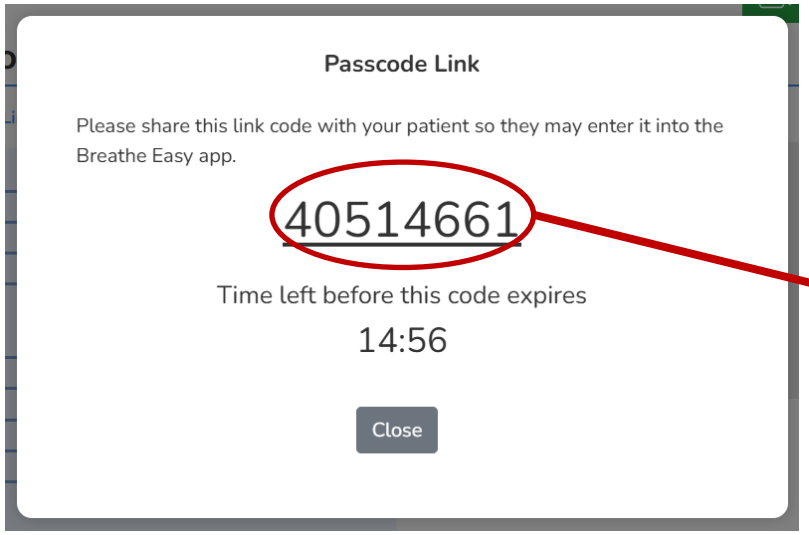
1. **Download the Breathe Easy App** to the participant's phone
2. Launch the app and select the **Settings** icon in the top right corner
3. Select "**Enter Code**"

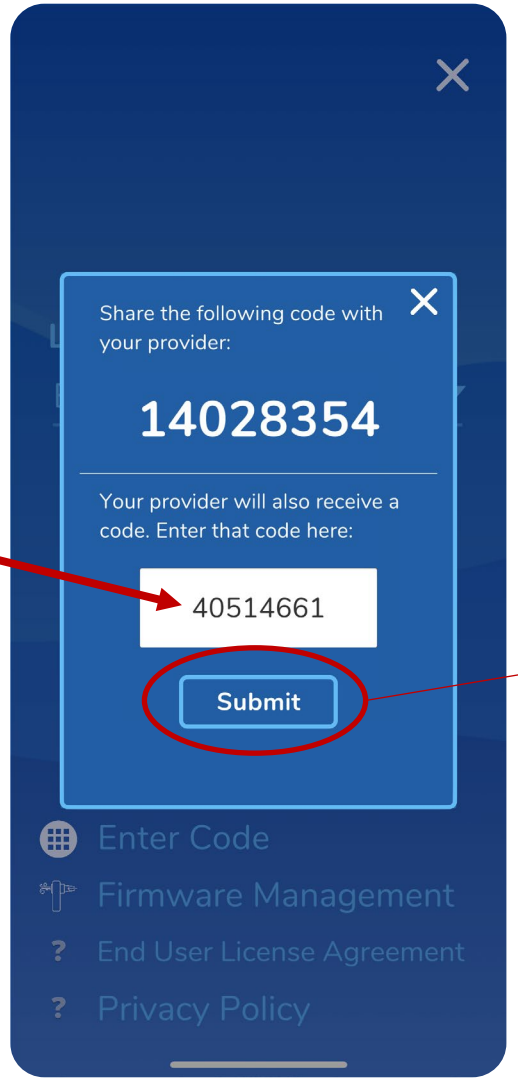
Pair the Participant's Phone to the Dashboard

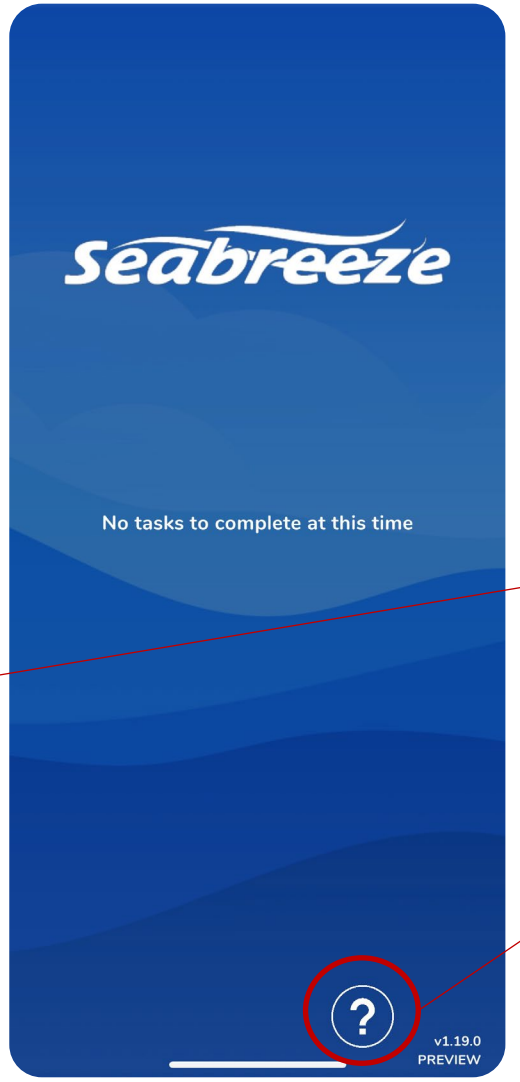


1. Find the participant in the dashboard
2. Select **Participant Settings** tab
3. Select **+Passcode Link**
4. **Enter the number** on the participant's phone into the dashboard
5. Select **Link Code**

Help Participant Download the Breathe Easy App



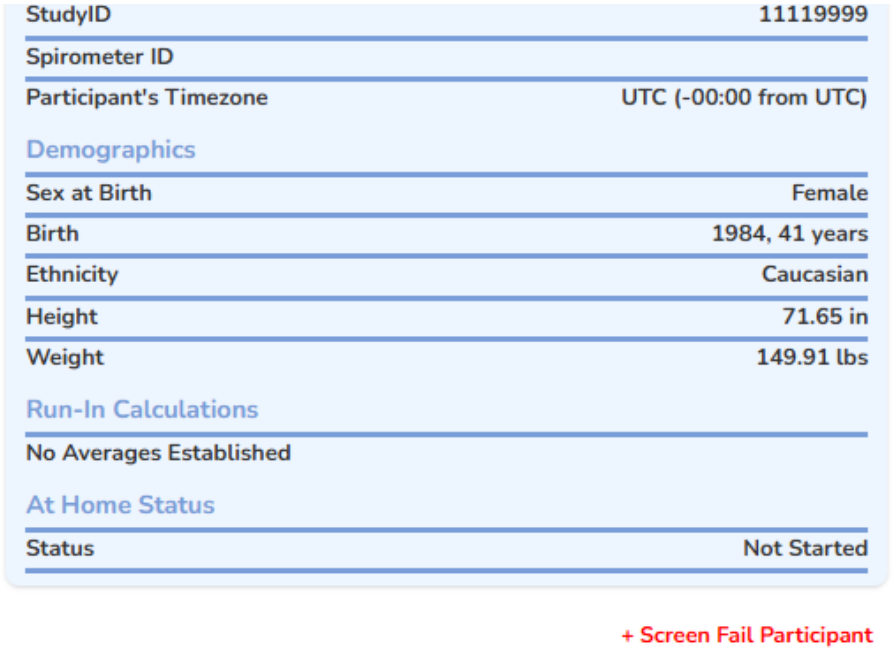


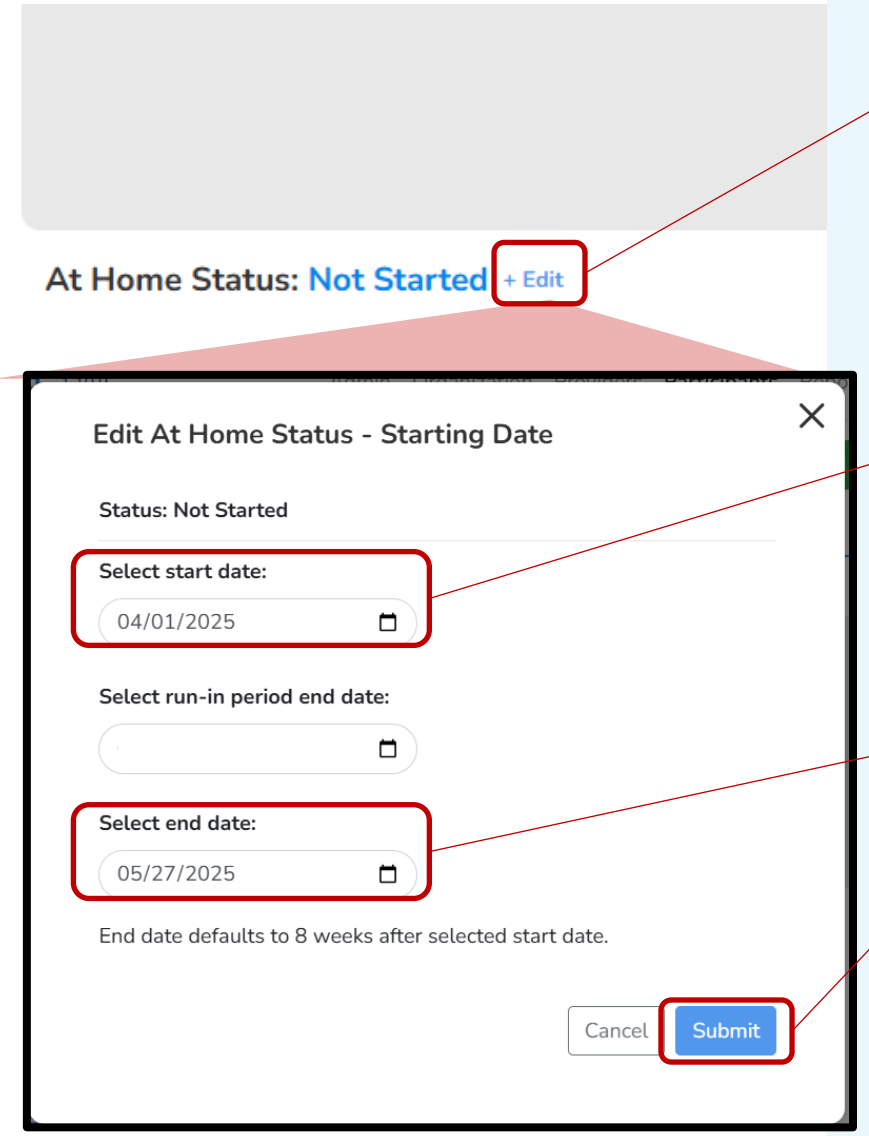


1. Once the participant's code is entered into the dashboard, **a second code will be generated** in the dashboard
2. **Enter** that into the participant's Phone
3. Select **Submit**
4. Once submitted, you will see the **app study home screen**
5. Select the **? Icon** to set participant language

Note: If the participant gets a new phone, or deletes their app, you will need to repeat this pairing process

Set At-Home Task Start Date



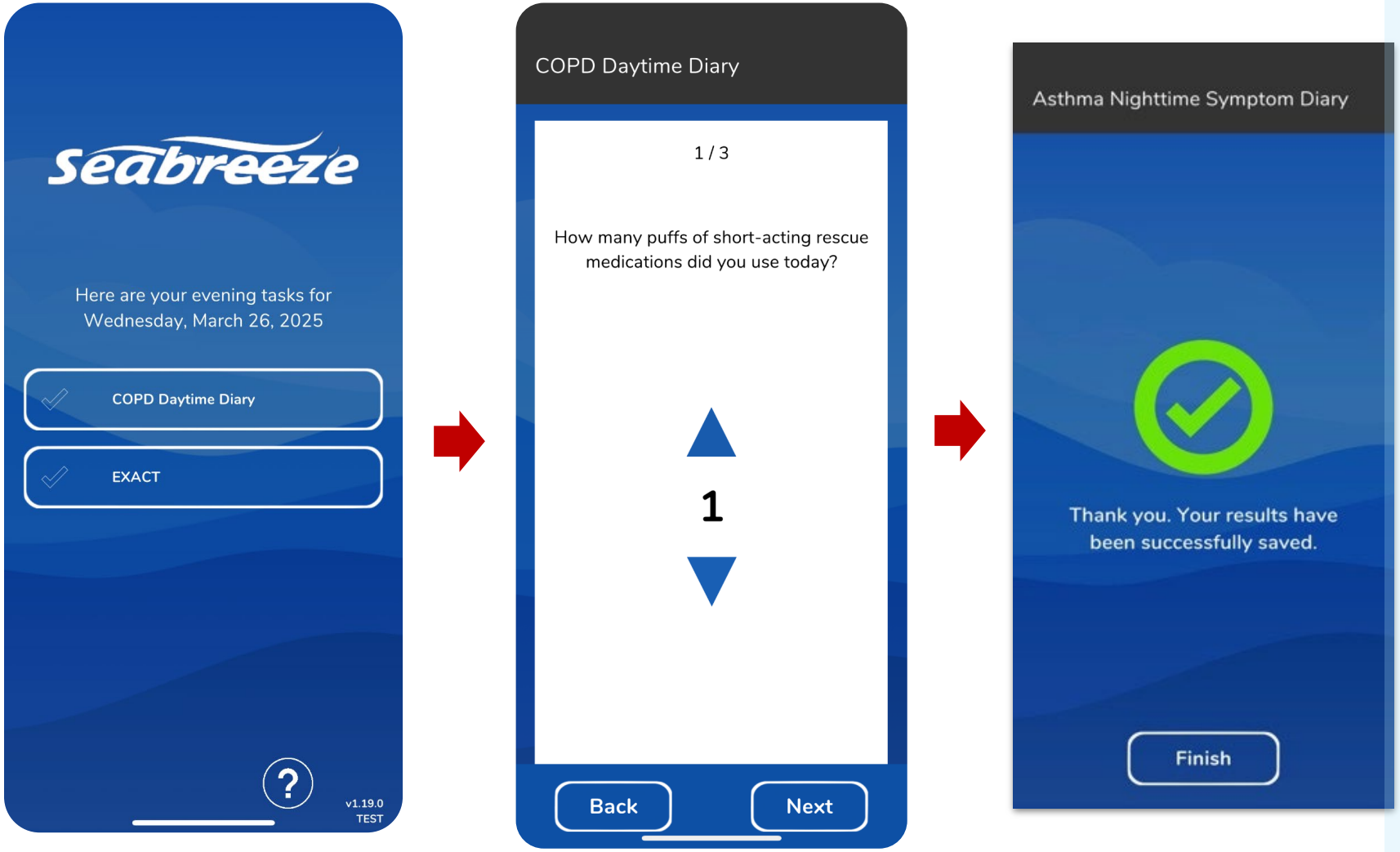


- ✓ From the **Participant Settings** tab, select **Edit** next to the at home status
- ✓ select **Start Date:**
  - ✓ **Start date** should be set at V1b as current date
  - ✓ **Run-in period end date** should be set as date of V2
  - ✓ **End date** will default to 8 weeks after start date, but can be updated as needed
- ✓ Select **Submit**

⚠ Participants will not see ediary tasks on their phone if the start date is not set.

Participants will not see the EXACT evening task until a run-in end date is set, OR a V2 label is applied either to a kiosk spirometry session or eCOA

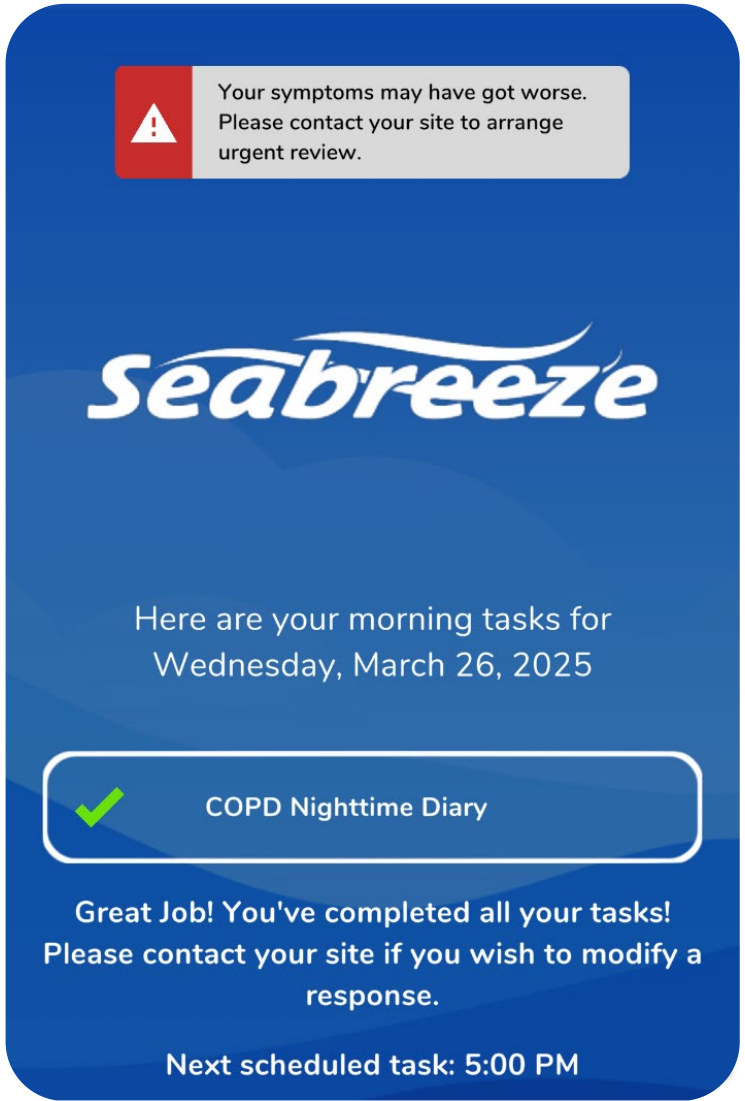
ePRO: EXACT and Symptom Diaries



- ✓ Participant completes The **Daytime symptom diary** (SABA/nebulizer question plus dyspnea NRS), plus **EXACT-PRO** every Evening
- ✓ Participant completes the **Nighttime symptom diary** (SABA questions plus dyspnea NRS) every morning
- ✓ Results sent in real-time to the Provider Dashboard

For more information about home tasks, view the at home user guide

Safety Alerts & Reminder Notifications



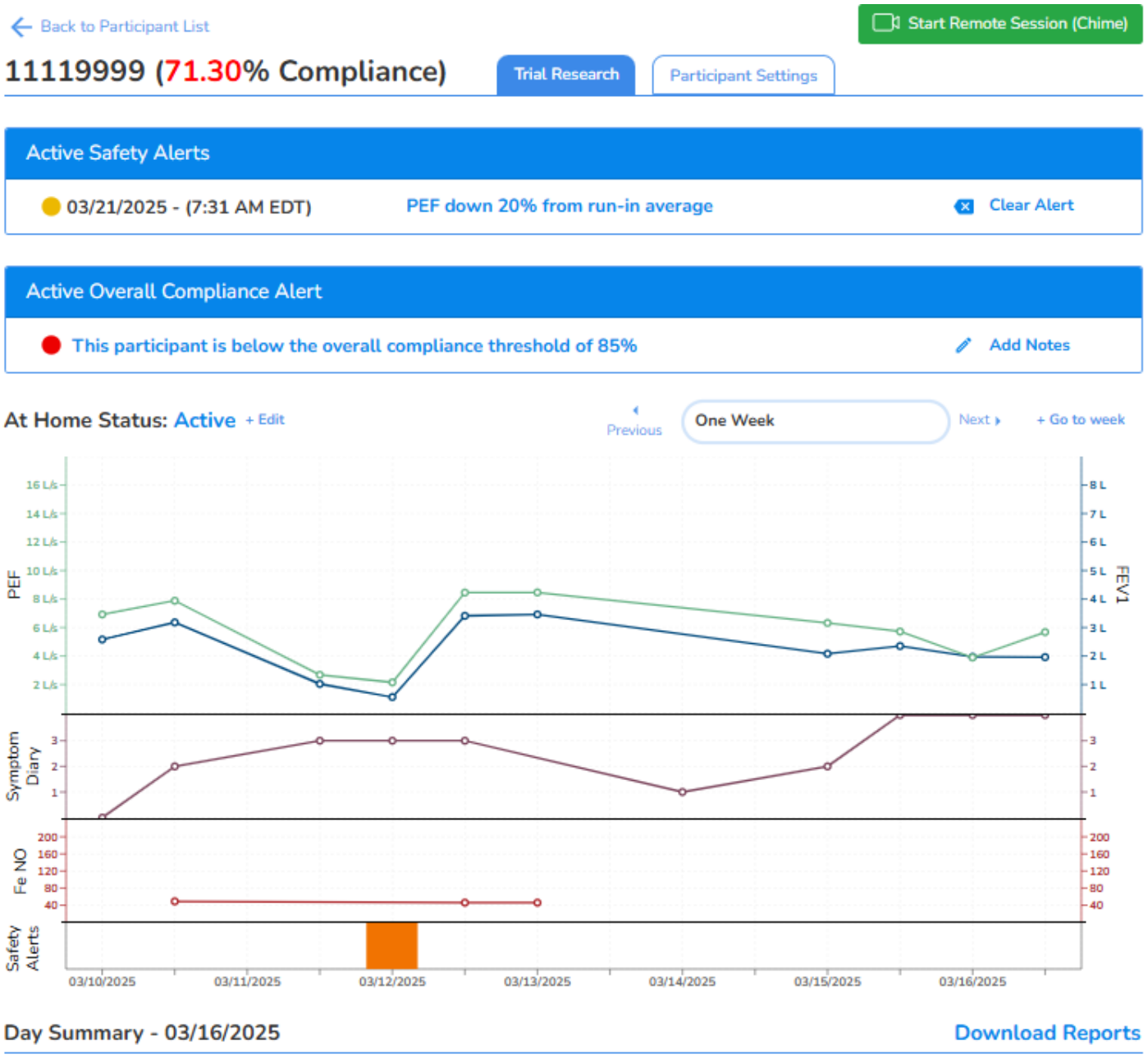
- ✓ Site and participants **receive alerts** for
  - ✓ At least 6 reliever inhalations of SABA in a 24-hour period on 2 of 3 successive days
  - ✓ Nebulizer use (any number of treatments) on 2 of 3 successive days

  Asthma Only:

  - ✓ Fall in PEF value of 20% or more, when compared to their baseline (first week of study) value for 2 of 3 successive days
  - ✓ Highest possible Asthma Symptom Scores reported on 2 of 3 successive days

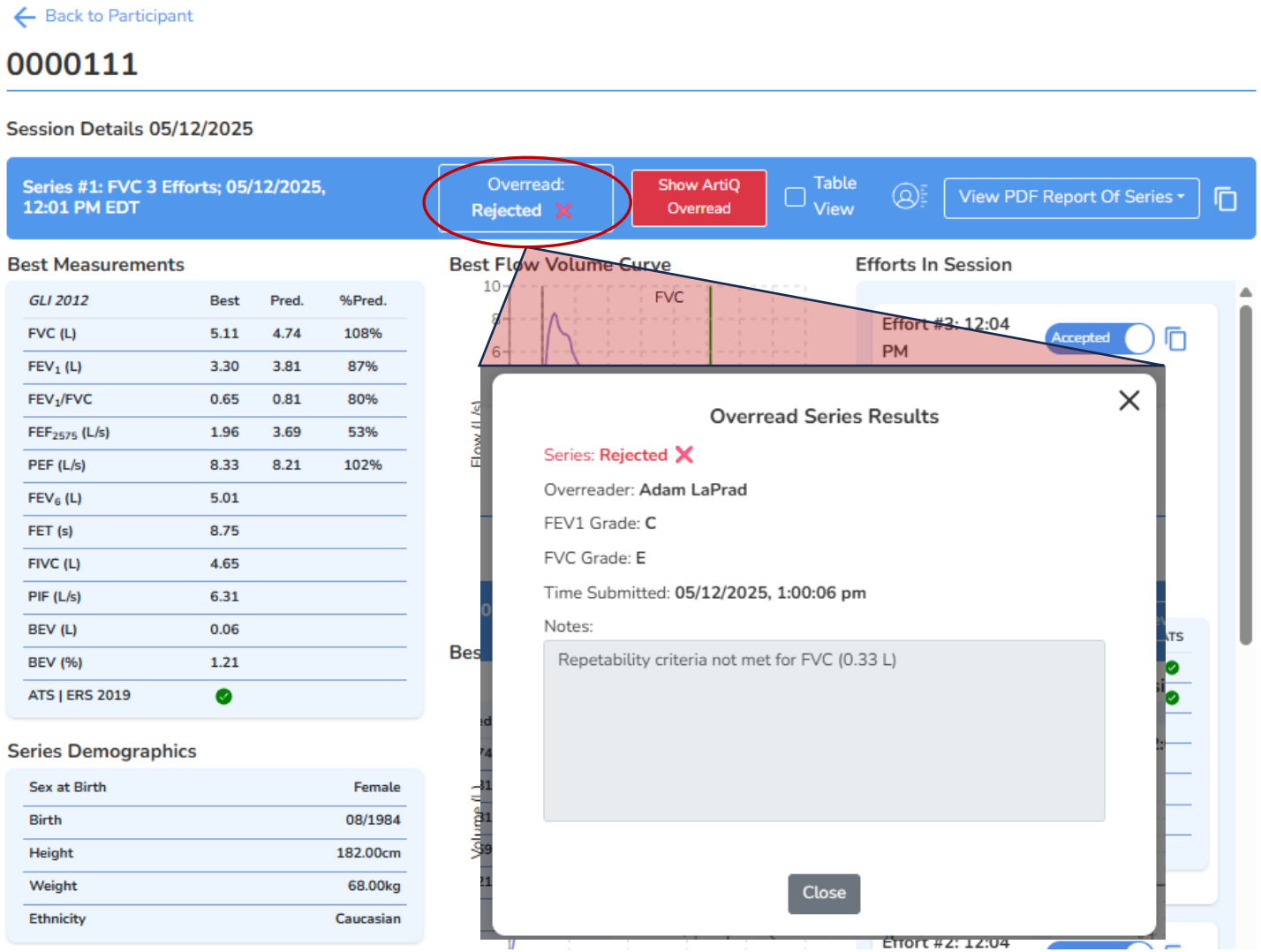
Viewing Participant Results & Alerts on the Provider Dashboard

Participant Dashboard Overview



- ✓ Monitor Home Task Compliance
- ✓ Manage safety alerts
- ✓ View daily task activity
- ✓ View all assessment results
- ✓ Print Reports
- ✓ View Overreading Results

Human Overreading

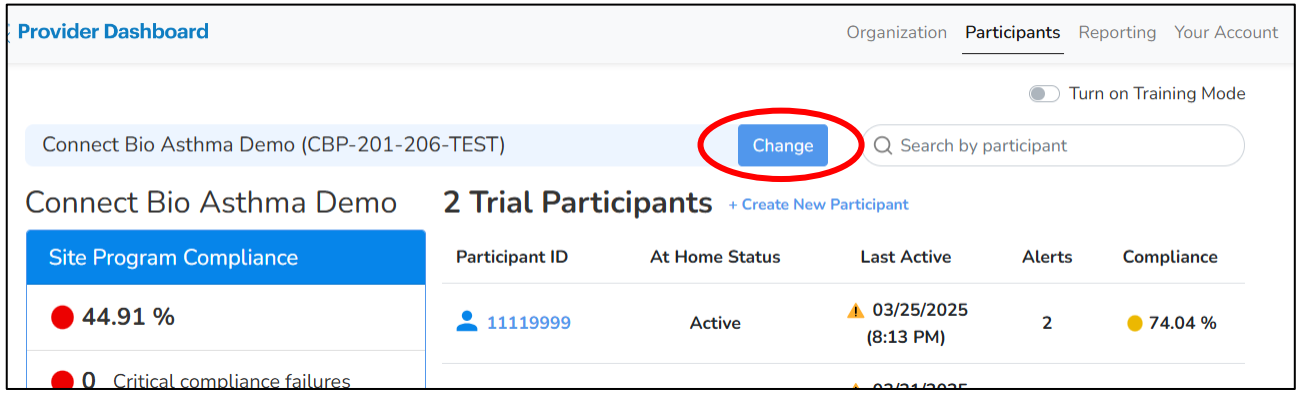


- Within 24 hours of the test, spirometry results will be overread by a human overreader
- You will receive an email notification that your series has been overread
- Click on the link in the email to go to the series
- Click on the Overread box to view the overreader's assigned grade and notes
- If the overreader rejects the series, you should bring the participant back to the clinic to repeat the assessment

>> Home

Support Notes for Sites in Both Studies

- If your site is part of both the Seabreeze Asthma and Seabreeze COPD studies, ensure the correct equipment and correct dashboard is being used for each study.
  - The tablets, and spirometers are not interchangeable – each study has a designated set of equipment – stickered with the study name
  - The FeNO Machine is the only piece of equipment that will have one unit used by both the COPD and Asthma studies (though with the study specified tablets)
  - Be sure you are viewing the correct dashboard before creating participants, or editing participant data. You can use the “Change” button to toggle between your dashboard sites



Lunch and Learning – Return at **01:30 pm PT**

Let's Lunch in the Atrium!

- Fuel up, mingle, and enjoy the break.

 ZEPHYRx Spirometry Demo Station

- Hands-on experience with the device — come see it in action!

 Study Start-Up Station

- Get prepped and ready — all the essentials in one spot!

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