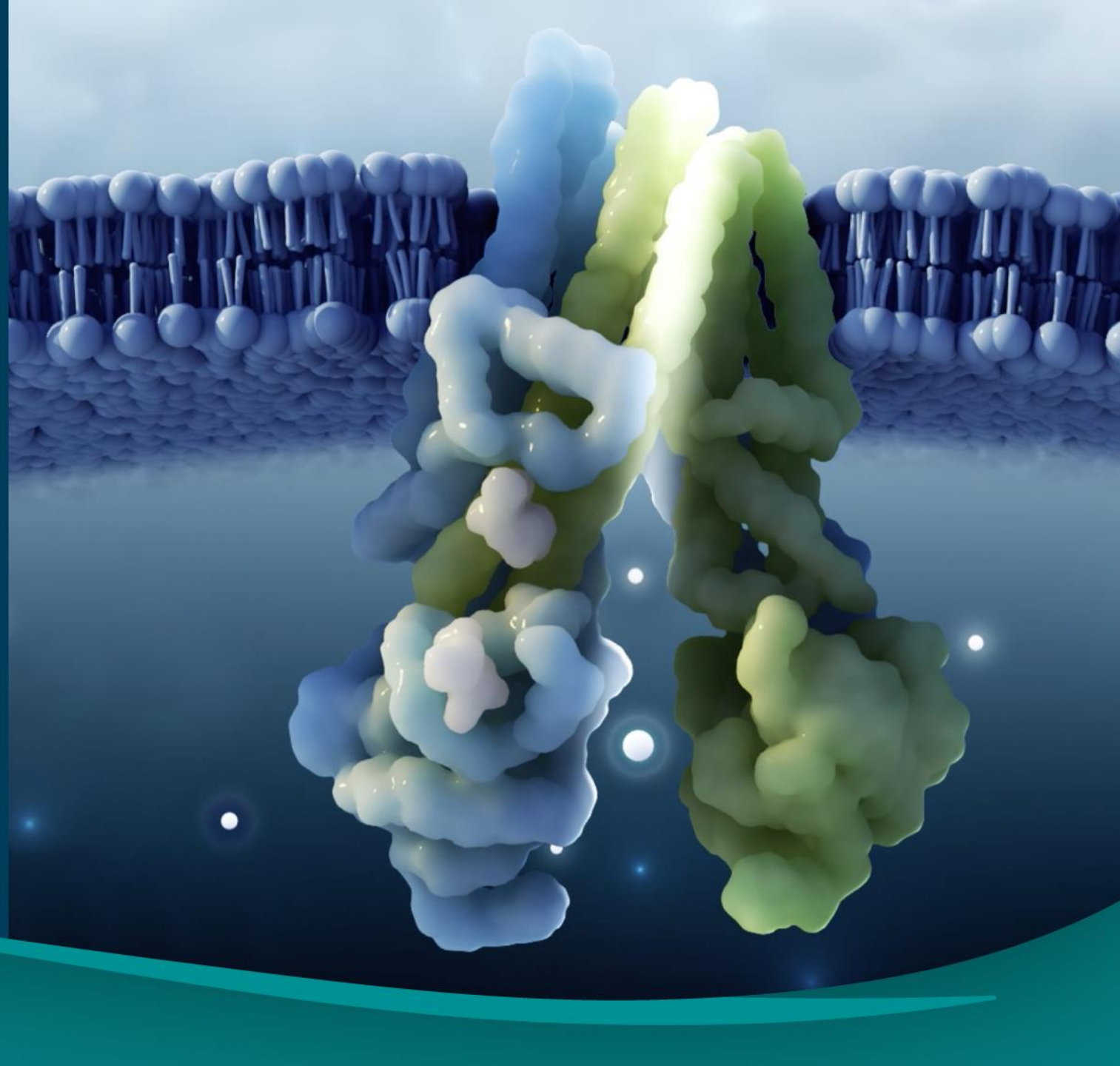
Mike Cloonan, President & CEO

41st Annual J.P. Morgan Healthcare Conference

January 2023



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What if we could deliver full CFTR correction and the optimal clinical benefit for people with Cystic Fibrosis?
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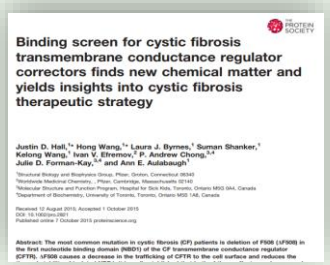
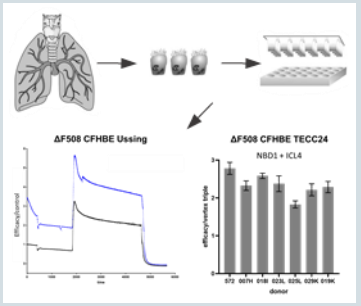
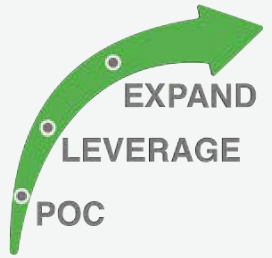
Sionna's differentiated approach focused on NBD1 has a clear path to POC with the potential to deliver best-in-class efficacy

HIGH UNMET NEED IN LARGE MARKET	NBD1, THE HOLY GRAIL FOR CFTR	PREDICTIVE ASSAYS/BIOMARKERS	FRANCHISE DRIVES STRATEGIC OPTIONALITY
			
Despite current treatments, unmet need is high in the $9B market	**NBD1 is the key to deliver full CFTR function and has been considered 'undruggable'**	**CFHBE assay and sweat chloride biomarker consistently predict clinical efficacy driving near-term value inflection**	**A deep pipeline of NBD1 compounds and complementary modulators can significantly raise the efficacy bar**

Led by proven management capable of disrupting the CF market

Mike Cloonan
Chief Executive Officer

Sage Therapeutics™ · Biogen · BAIN & COMPANY

Charlotte McKee, MD
Chief Medical Officer

VERTEX · Infinity PHARMACEUTICALS · TOLERX Immune resolve. · Wyeth · Brigham and Women's Hospital Founding Member, Mass General Brigham

John Macor, PhD
Chief Scientific Officer

sanofi · Pfizer · Bristol Myers Squibb™

Elena Ridloff
Chief Financial Officer

ACADIA · ALEXION

Vanya Sagar
Chief People Officer

Affinivax · sigilon therapeutics · Biogen

Greg Hurlbut, PhD
Co-Founder
SVP, Discovery Research

sanofi genzyme

Mark Munson, PhD
Co-Founder
VP, Medicinal Chemistry

sanofi · AMGEN · ARRAY

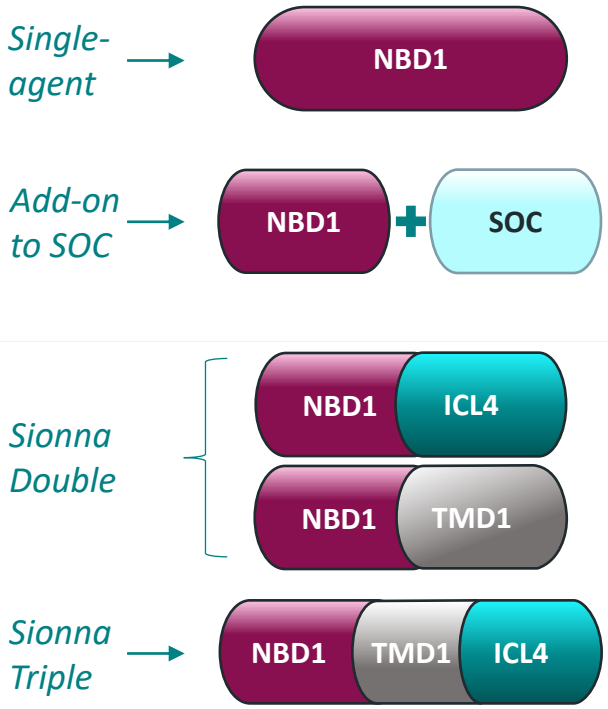
Sionna's strategy is to build a CF franchise across MOAs, anchored by novel NBD1, delivering higher efficacy than SOC

NBD1

Drive multiple NBD1 compounds into the clinic, advance based on human data and the potential to raise the efficacy bar

NBD1 + ICL4 / TMD1

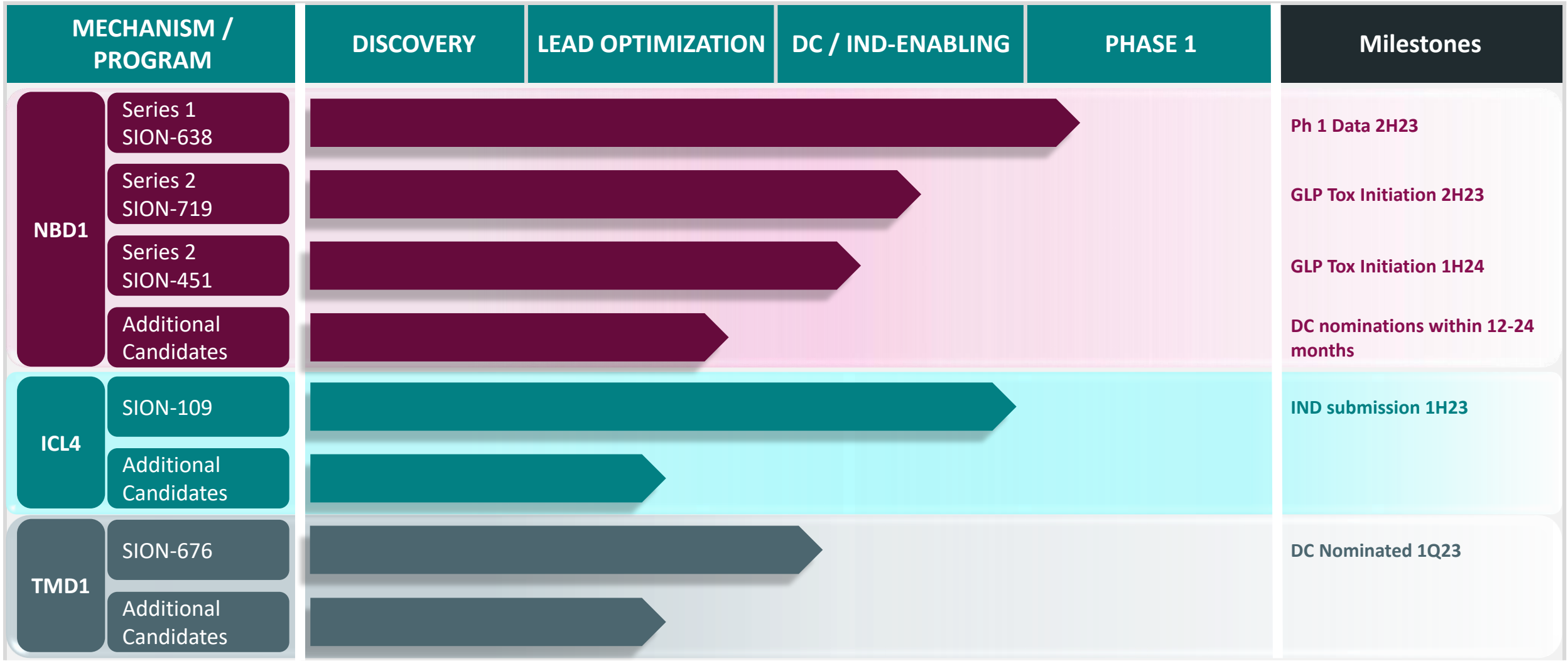
Accelerate pipeline of complementary targets creating options for transformational Sionna combinations with NBD1



Targeting Efficacy ≥ SOC

Vision: Deliver transformational option to fully normalize CFTR function, become the SOC

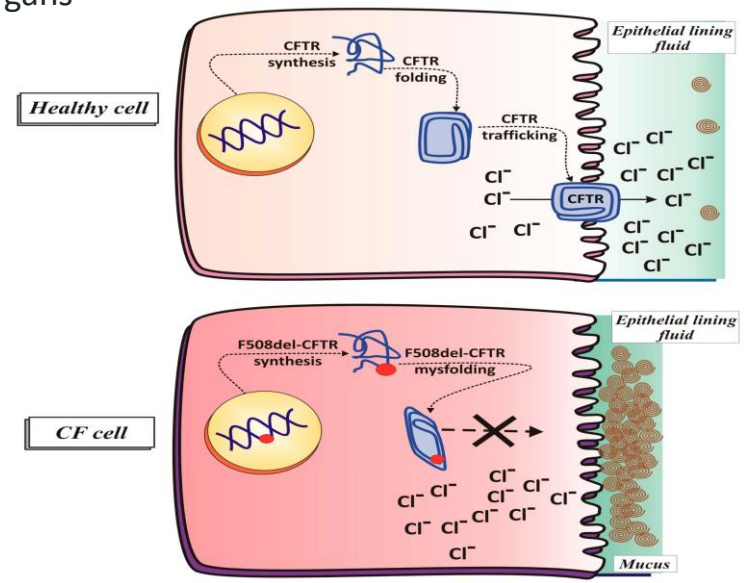
Sionna is advancing a robust pipeline with multiple near-term milestones



CFTR is a fully validated target, and unlocking NBD1 could deliver optimal clinical benefit

The Biology of CF

- Driven by mutation of the CF transmembrane conductance regulator (CFTR)
- CFTR is an epithelial chloride channel essential to the production of thin, freely flowing mucus in the airways, digestive system, and other organs



The Importance of NBD1

- F508 is present within CFTR's NBD1 domain
- ΔF508 causes NBD1 to unfold at body temperature and weakens NBD1's interface with other regions; these defects cripple CFTR folding, trafficking and function
- **<u>None</u> of the existing correctors or potentiators address both ΔF508-CFTR's assembly and its NBD1 instability defects**
- ~90% of patients with CF have a ΔF508 mutation

NBD1 is the key to full CFTR correction

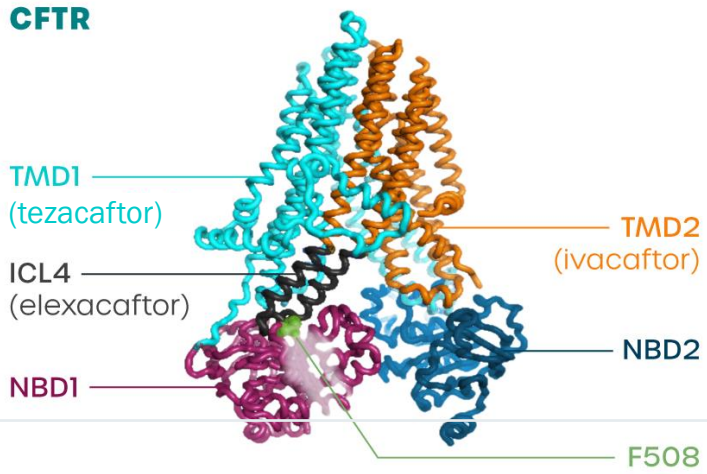
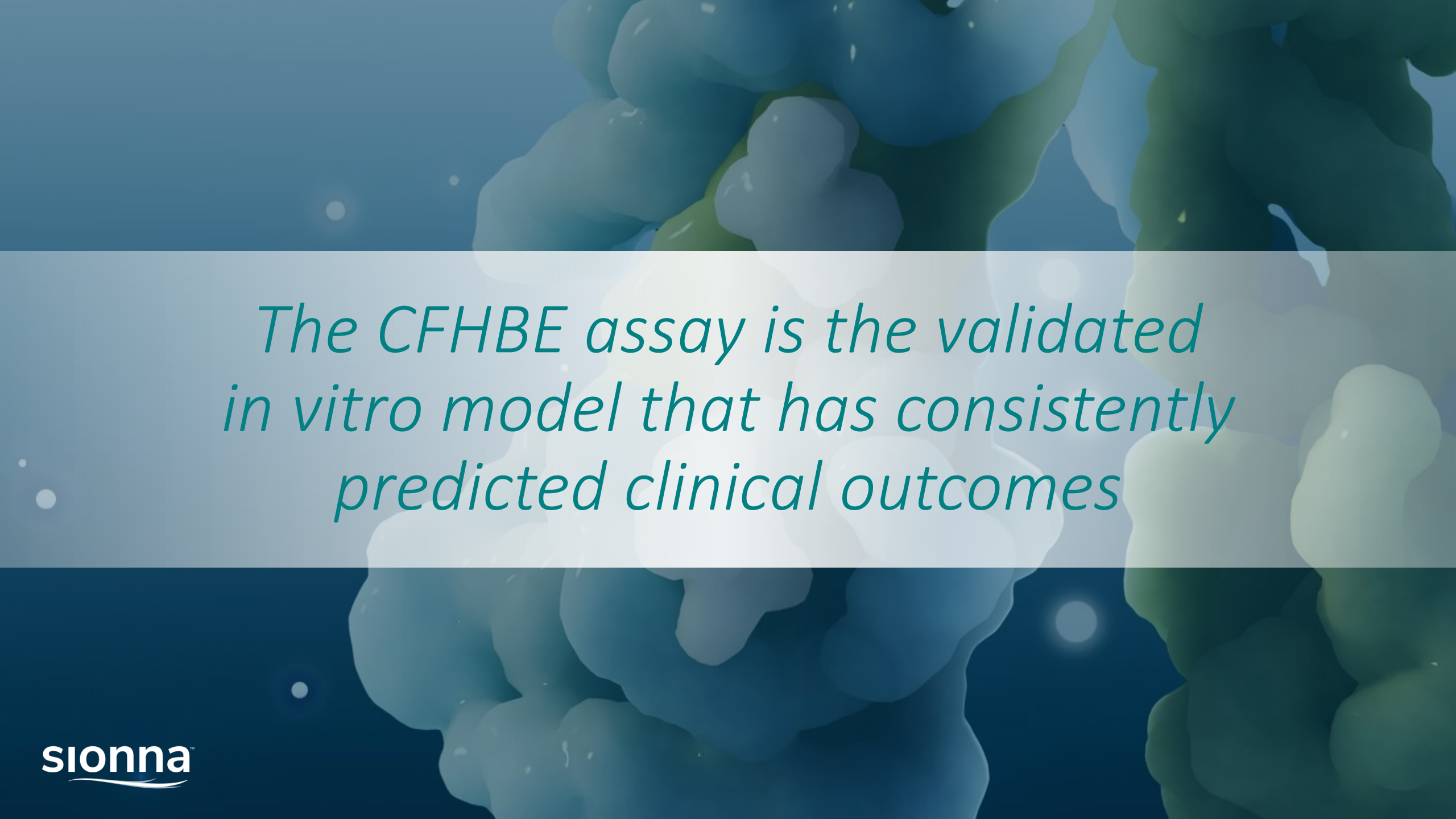


Image Source: J. Clin. Med. 2019, "An Intriguing Involvement of Mitochondria in Cystic Fibrosis"


The CFHBE assay is the validated in vitro model that has consistently predicted clinical outcomes
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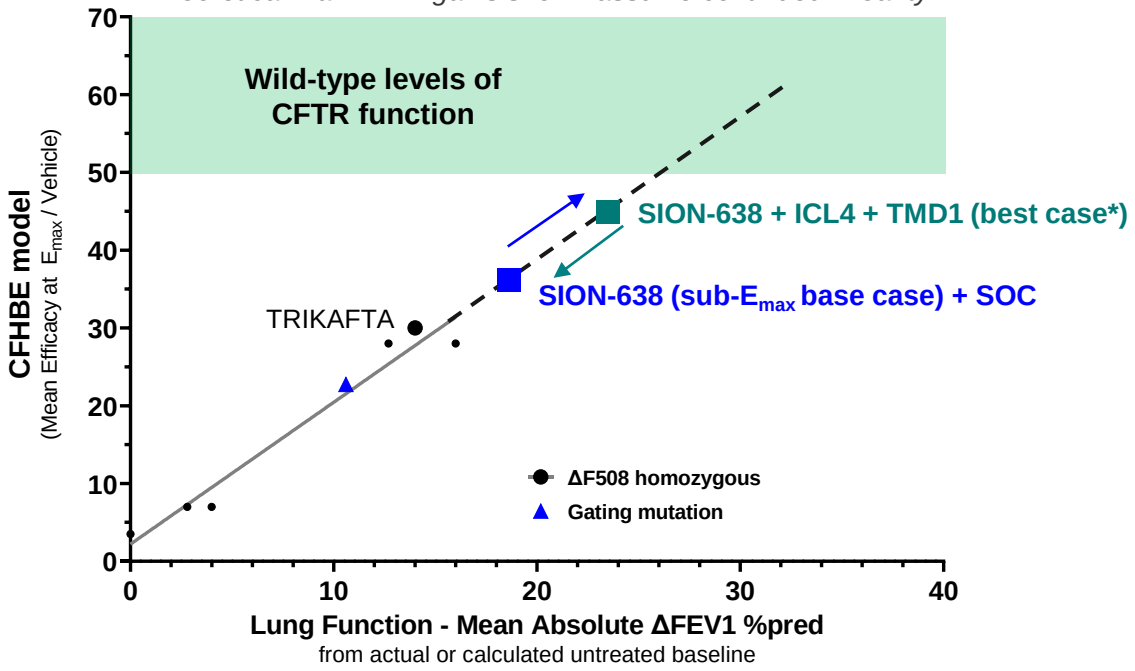
SION-638: First-in-class, clinical stage NBD1 modulator with the potential to deliver higher efficacy

SION-638 CFHBE assay data

Theoretical max FEV1 gains shown assume continued linearity



**Sionna triple at E_{max}*

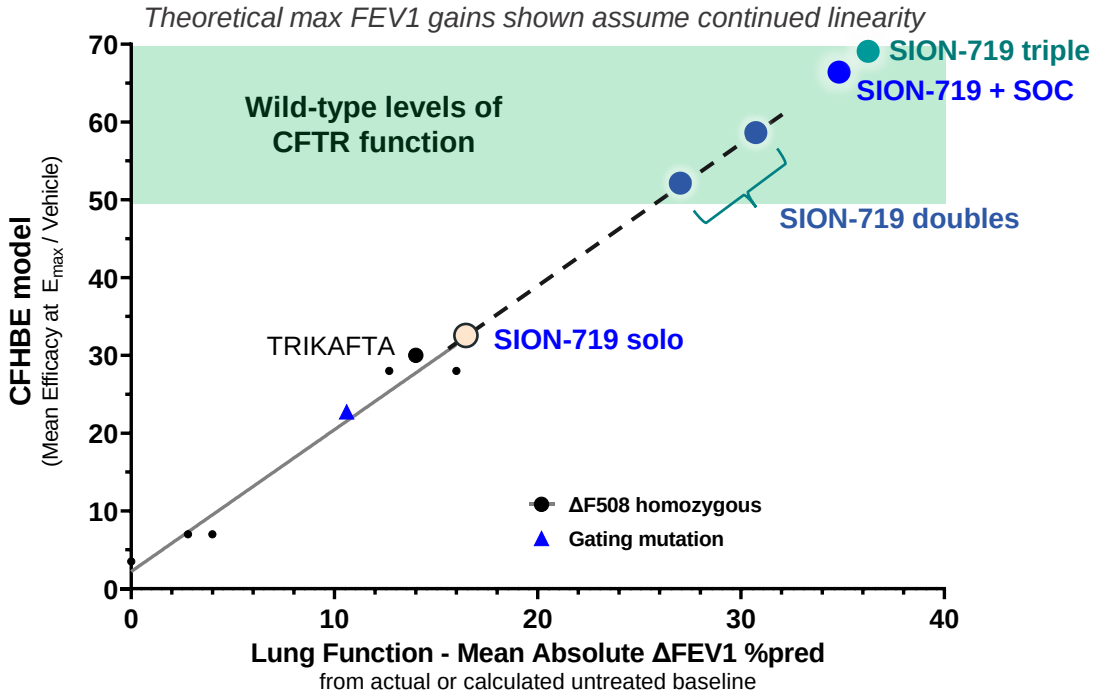
Multiple options to raise the efficacy bar

In the clinically predictive CFHBE assay, SION-638 shows:

- Improved efficacy as add-on to Trikafta vs. Trikafta
- Greater efficacy vs. Trikafta in a Sionna triple combination
- Potential to approach wild-type levels of CFTR function with higher SION-638 exposures

SION-719: Series 2 NBD1 development candidate demonstrates potential to normalize CFTR function

Potential of SION-719 at E_{max}



Multiple options to raise the efficacy bar

In the clinically predictive CFHBE assay Sionna DCs have demonstrated the potential for:

- Single-agent efficacy equivalent to Trikafta
- Wild-type levels of CFTR function in a Sionna combination
- Wild-type levels of CFTR function as add-on to Trikafta
- DC SION-451 has demonstrated similar results in CFHBE assay


The portfolio and clinical strategy deliver several near-term value inflections
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SION-638 Phase 1 study ongoing with data expected 2H23

Phase 1

Single Ascending Dose Escalation (SAD)

- Placebo controlled

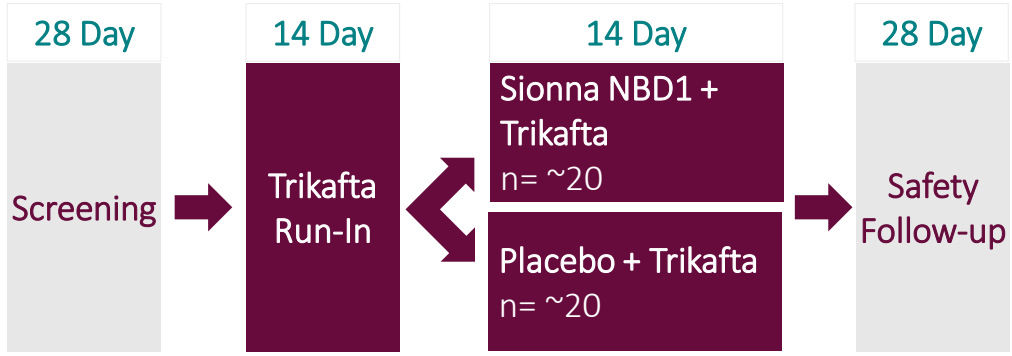
Multiple Ascending Dose Escalation (MAD)

- Placebo controlled
- 10 days of dosing

Rationale	Evaluate safety and identify exposure margin before dosing in CF
Objectives	Primary: Safety, Tolerability Secondary: PK
Study Population	Healthy subjects

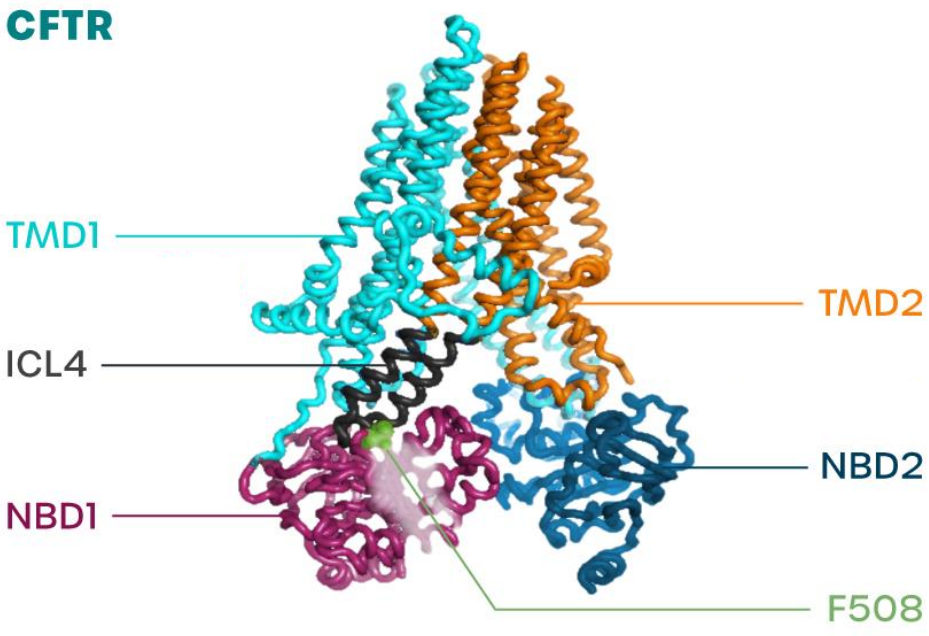
NBD1 Proof-of-Concept study will be a Phase 2a add-on to Trikafta

Phase 2a



Rationale	Proof of Concept: show clinical effect of NBD1 correction, differentiate from SOC modulators
Objectives	Primary: Safety Secondary: Sweat Chloride; PK in CF subjects Exploratory: FEV1
Study Population	Adult CF subjects with ΔF508 genotype on stable dose of physician-prescribed Trikafta

Advancing paths to Sionna proprietary combinations with SION-109 (ICL4 directed) and SION-676 (TMD1 directed)



Robust preclinical data packages support advancement of SION-109 and SION-676

- Attractive potencies and drug-like properties
- Clean exploratory 14-day rat and dog tox with robust margins
- ‘676 significantly more potent than other TMD1 correctors

SION-109 IND-enabling studies complete and support a potential IND in 1H23

SION-109 API and DP manufacturing complete to support Phase 1

Combo Development Strategy: **Advance Sionna proprietary double combination with potential for full CFTR correction**

Sionna is well positioned to advance its pipeline

Over-subscribed $111M Series B financing closed 1H22

~$150M raised since company founding in 2019

Cash runway into 1H24 advancing SION-638 and SION-109 through Phase 1, and 3 additional DCs

RACAPITAL

ATLAS VENTURE

TPG

OrbiMed Healthcare Fund Management

CYSTIC FIBROSIS FOUNDATION

Advancing game changing therapies, building significant near-term value, and driving to raise the efficacy bar in CF

DELIVER **ROBUST NBD1 PORTFOLIO**	**SION-638 Phase 1 enrolling; data 2H23** **SION-719 scale-up ongoing for GLP tox studies 2H23** **SION-451 scale-up ongoing for GLP tox studies 1H24**
ADVANCE **COMPLEMENTARY TARGETS**	**Submit IND for SION-109 (ICL4 candidate) in 1H23** **SION-676 (TMD1 candidate) DC nominated in 1H23**
BUILD **COMPANY CAPABILITIES**	**Execute the strategy, grow the company and build capabilities to become a leader in CF**

Thank you

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