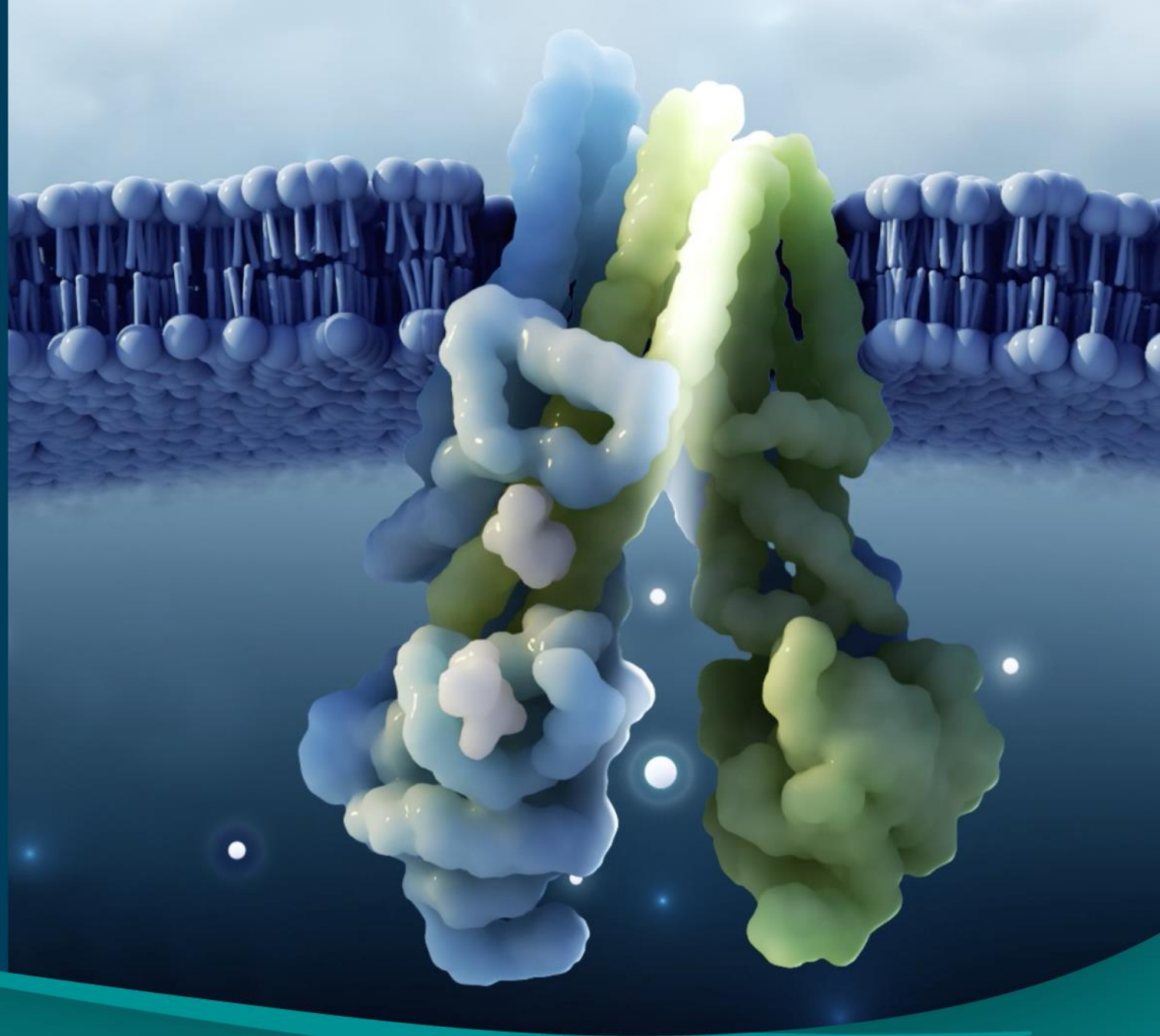


Sionna Therapeutics

*Stifel Healthcare
Conference
November 15, 2022*

sionna[™]



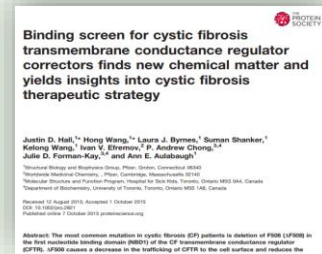
Sionna's differentiated approach focused on NBD1 has a clear path to POC with the potential to deliver best-in-class efficacy

HIGH UNMET NEED IN LARGE MARKET



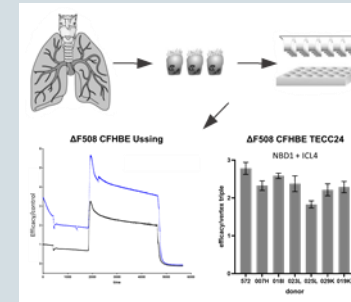
Despite current treatments, unmet need is high in the \$9B market

NBD1, THE HOLY GRAIL FOR CFTR



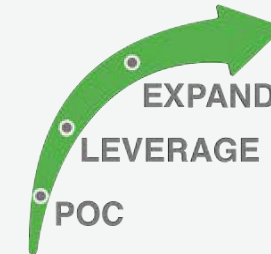
NBD1 is the key to deliver full CFTR function and has been considered 'undruggable'

PREDICTIVE ASSAYS/BIOMARKERS



CFHBE assay and sweat chloride biomarker consistently predict clinical efficacy driving near-term value inflection

FRANCHISE DRIVES STRATEGIC OPTIONALITY



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



Charlotte McKee, MD
Chief Medical Officer



John Macor, PhD
Chief Scientific Officer



Elena Ridloff
Chief Financial Officer



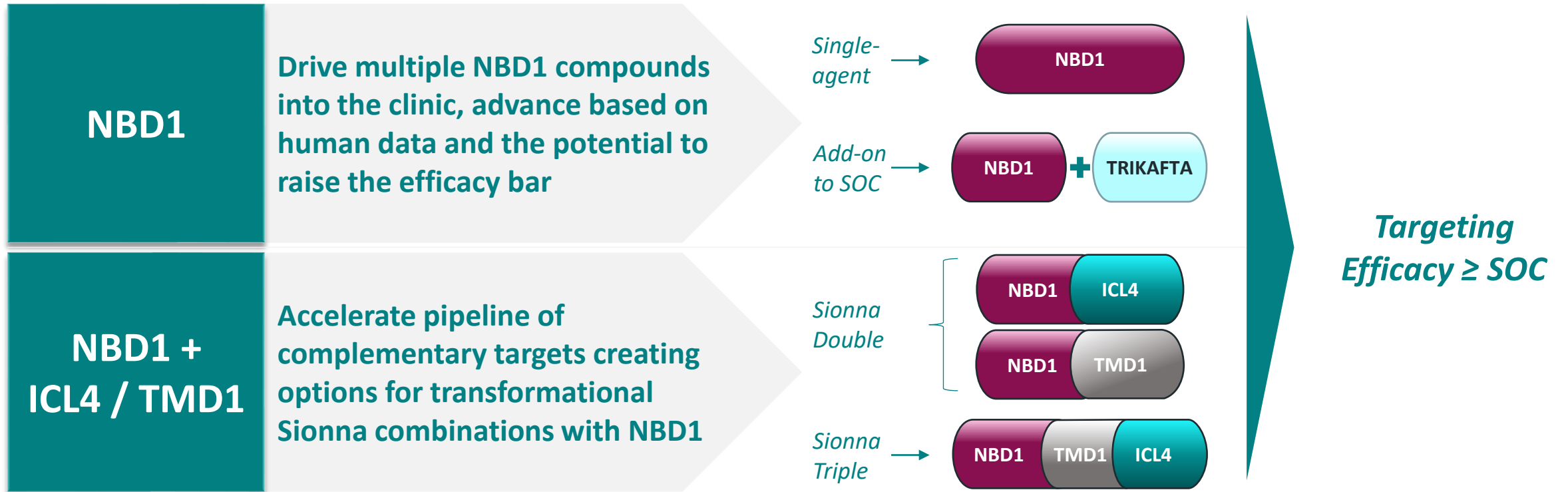
Greg Hurlbut, PhD
Co-Founder
SVP, Discovery Research



Mark Munson, PhD
Co-Founder
VP, Medicinal Chemistry



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



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

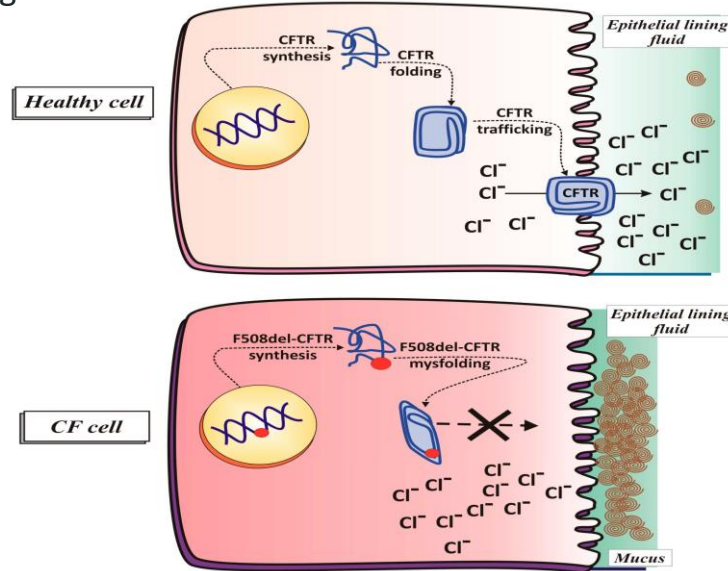
The breadth and depth of our franchise drives strategic optionality

MECHANISM / PROGRAM	DISCOVERY	PRE-CLINICAL	IND-ENABLING	PHASE 1	Upcoming Milestones
NBD1 SION-638					IND submission 1H23
NBD1 Additional Candidates					DC nominations within 6-18 months
ICL4 SION-109					IND submission 1H23
ICL4 Additional Candidates					
TMD1 Candidates					DC nomination within 12-18 months

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

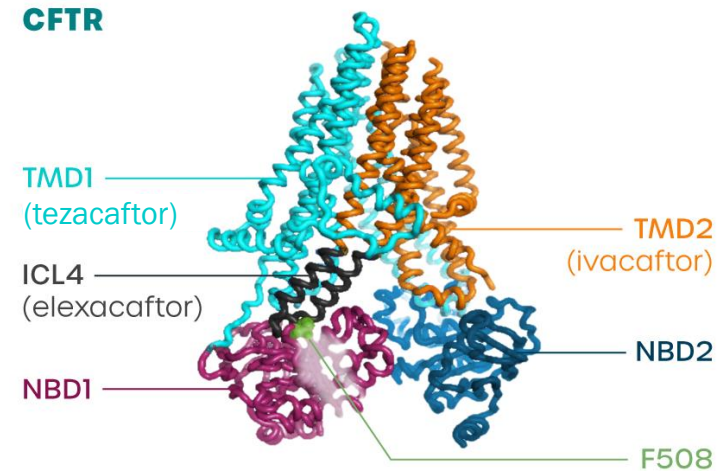


The Importance of NBD1

- F508 is present within CFTR's NBD1 domain
- $\Delta F508$ causes NBD1 to unfold at body temperature and weakens NBD1's interface with other regions; these defects cripple CFTR folding, trafficking and function
- **None of the existing correctors or potentiators address both $\Delta F508$ -CFTR's assembly and its NBD1 instability defects**

NBD1 is the key to full CFTR correction

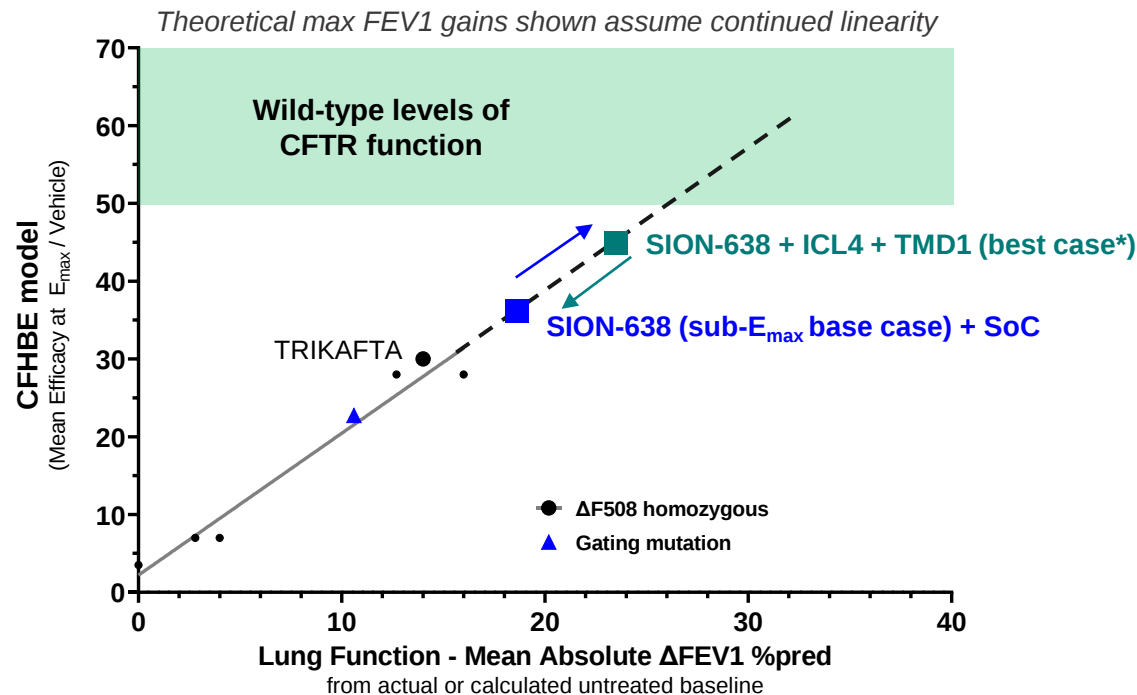
CFTR



*The CFHBE assay is the validated
in-vitro model that has consistently
predicted clinical outcomes*

SION-638 is the first-in-class, clinical stage NBD1 compound and the foundation of a combination product delivering higher efficacy

SION-638 CFHBE assay data



*Sionna triple at E_{max}

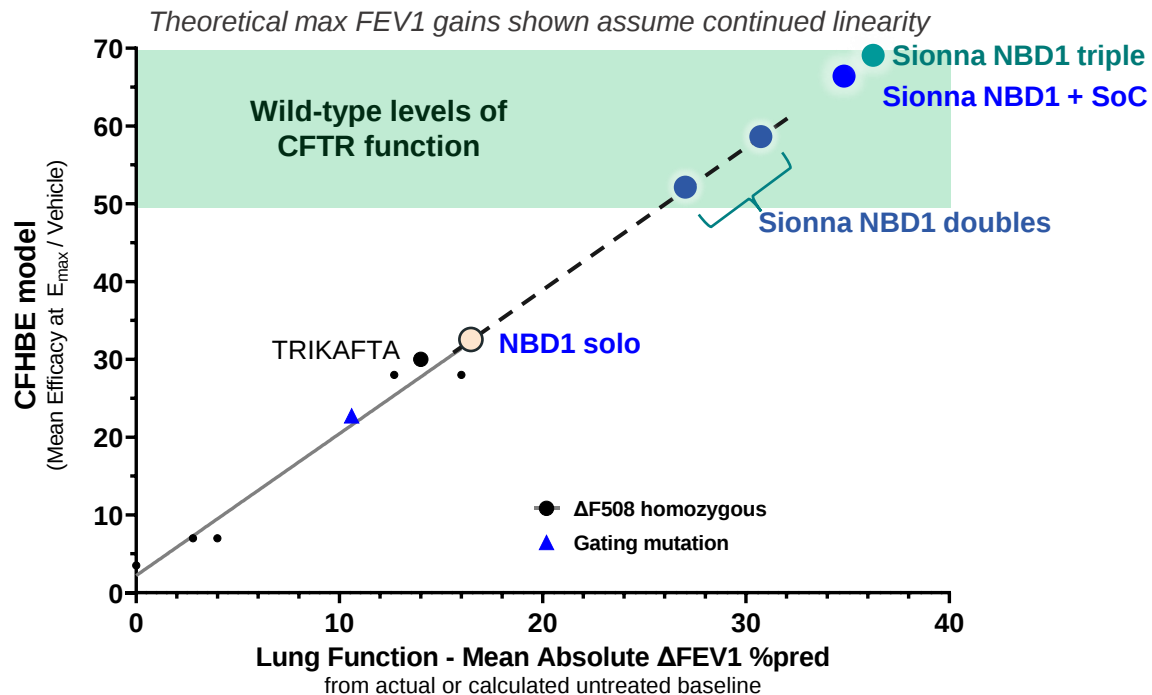
Multiple options to raise the efficacy bar

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

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

Portfolio of additional NBD1 candidates enabling multiple paths to normalize CFTR function

Potential of NBD1 additional candidates at $E_{\max}$



Plotted efficacy of a representative lead NBD1 compound

Multiple options to raise the efficacy bar

In the clinically predictive CFHBE assay Sionna candidates 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

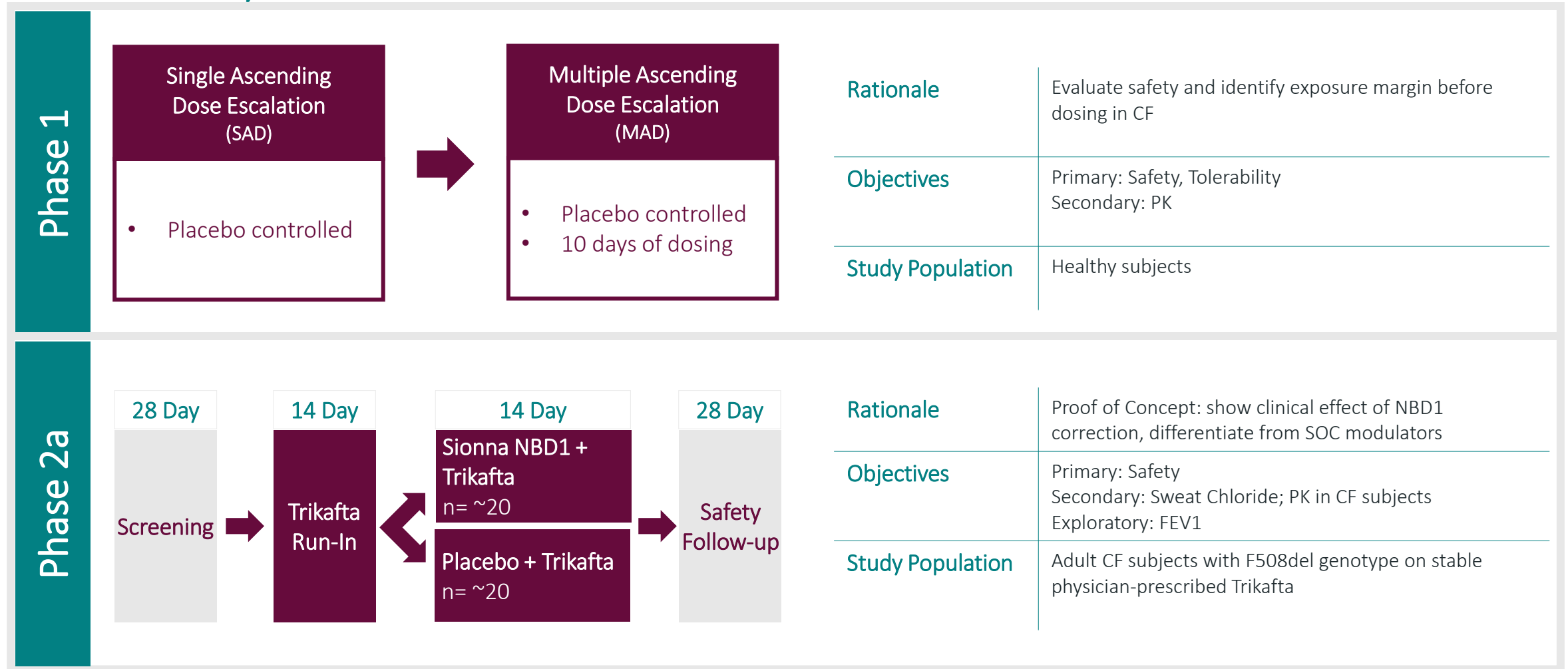
*The portfolio and clinical strategy
deliver several near-term value
inflections*

NBD1 Series 1 SION-638 is on-track for 1H23 IND submission

Drive **NBD1 Series 1**, SION-638, into the clinic as an add-on to SOC and/or the foundation of a Sionna proprietary combo

- **A robust preclinical data package supports advancement**
- **Completed IND-enabling studies support development**
 - GLP tox studies in rat and dog completed
 - High dose NOAEL in both species, no findings considered adverse
 - 14-day coverage supports clinical development through Phase 2a
 - hERG, dog CV telemetry, rat CNS and respiratory studies
 - GLP Ames, in vitro and in vivo micronucleus
- **API manufacturing completed to support early clinical development**

Clinical strategy for SION-638 is a healthy volunteer Ph1 study followed by a Ph2a POC as an add-on to Trikafta



IND submission planned for SION-109 (ICL4 directed compound) in 1H23, advancing path to Sionna proprietary combination

Invest in a **franchise of MOAs** to deliver Sionna combination therapies to raise the efficacy bar

- **A robust preclinical data package supports advancement**
 - Promising potency and drug-like profile
 - Highly tractable predicted clinical dose
 - Clean exploratory 14-day rat and dog tox with margins that support targeted exposure
 - API manufacturing completed to support early clinical development
- **IND-enabling studies in progress to support a potential IND in 1H23**
 - Most studies now in reporting phase, all on-track
- **Profiling underway of ICL4 back-ups with differentiated properties**

\$111M Series B financing completed 1H22 provides capital to advance through multiple value creating milestones

- ~\$150M raised since company founding in 2019
- Over-subscribed \$111M Series B financing
- Financing provides capital into 1H2024 to advance SION-638 and SION-109 through Phase 1 and advance additional NBD1 candidates to DC

RACAPITAL

 **ATLAS** VENTURE

 **TPG**



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

ADVANCE



SION-638 TO THE CLINIC

Submit IND for SION-638 in 1H23

ACCELERATE



ADDITIONAL NBD1 CANDIDATES

Drive additional DCs within next 6-18 months

PROGRESS



THE PIPELINE

Submit IND for SION-109 (ICL4 candidate) in 1H23

BUILD



COMPANY & CAPABILITIES

Execute the strategy, grow the company and build capabilities

The background of the slide is a microscopic image of tissue, likely showing glandular structures. A horizontal band of lighter, more translucent tissue runs across the middle of the image. The text "Thank you" is centered within this lighter band.

Thank you