

A Time for Optimism

Presented by **Preston W. Campbell, III, M.D.**
President and CEO, Cystic Fibrosis Foundation

**Cystic fibrosis is a
devastating disease,
so is there really any
reason to be optimistic?**

**In 1955, children were
not expected to live long
enough to go to school**

Today

- More than half of CF individuals are adults
- Median survival is now 47 years
- Significant research advances have occurred
- Ten CF therapies are FDA approved
- Three CF therapies target the basic defect (CFTR)
and more are on the way

**Great story — buy why
should this make me
optimistic about the future?**

Reason #1:

There is no community like CF

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- It is a worldwide uniquely collaborative and committed community
 - Patients and families
 - Care teams and scientists
 - Industry
- Laser focused on finding a cure
- Never underestimate them!

Reason #2

CF care continues to improve

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- Multidisciplinary care guided by “best practice”
- Registry data allows quality improvement
- Technology has the potential to radically improve care by informing decisions

Reason #3

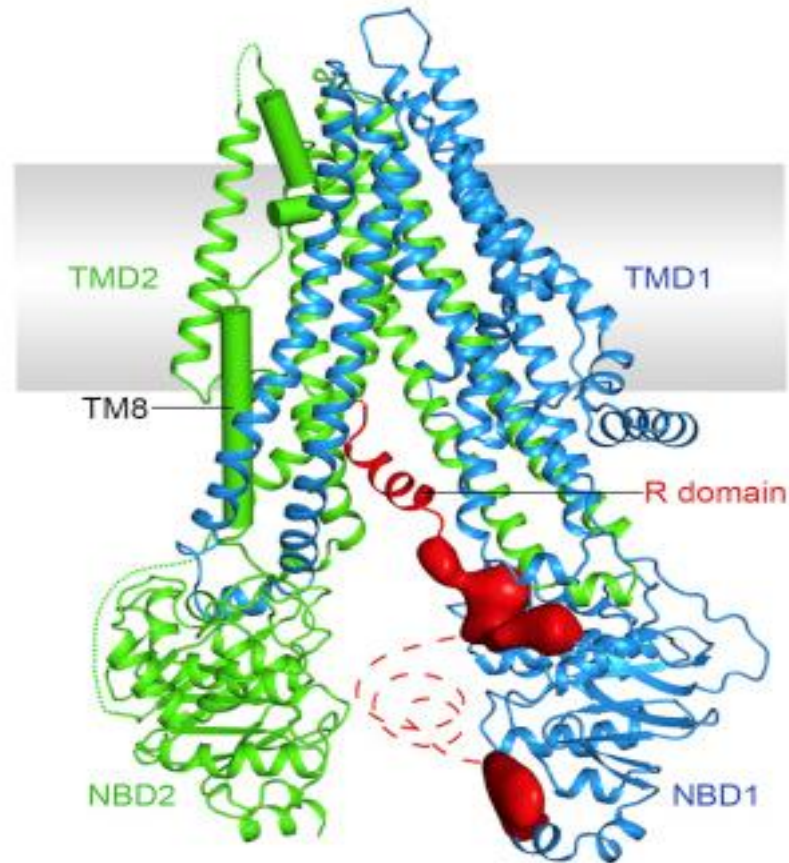
Scientific advances continue

Scientific advances continue

ARTICLE

Molecular Structure of the Human CFTR Ion Channel

Fangyu Liu⁶, Zhe Zhang⁶, László Csanády, David C. Gadsby, Jue Chen⁷  



Liu et al, Cell, 2017

Reason #4:

Drug development is accelerating.
There are more new potential therapies
being evaluated than ever before.

Foundation-supported research programs

| Therapeutic Area | Active Companies 2016 | Funded programs | Target/Strategy |
|-------------------------------|-----------------------|-----------------|---|
| Anti-Infective | 43 | 7 | MDR Pseudomonas, MRSA, NTM, Burkholderia, Fungi |
| Inflammation | 17 | 4 | LTA4H, CR ₂ , AA/DHA, HNE |
| CFTR modulation | 13 | 6 | Potentiators, correctors, amplifiers |
| CFTR nonsense and Restoration | 13 | 6 | Small molecule screening, mRNA, |
| Mucociliary clearance | 15 | 5 | Mucolytics, ASL |
| Gene editing | 8 | 3 | CRISPR, ZnF |
| Gene delivery | 6 | 2 | viral (AAV), non-viral (LNPs) |
| Nutrition | <u>3</u> | <u>2</u> | Lipase, In-line cartridge |
| Total | 118 | 35 | |

We met with 140 companies in 2017 and will oversee over 50 CF trials in 2018

Reason #5

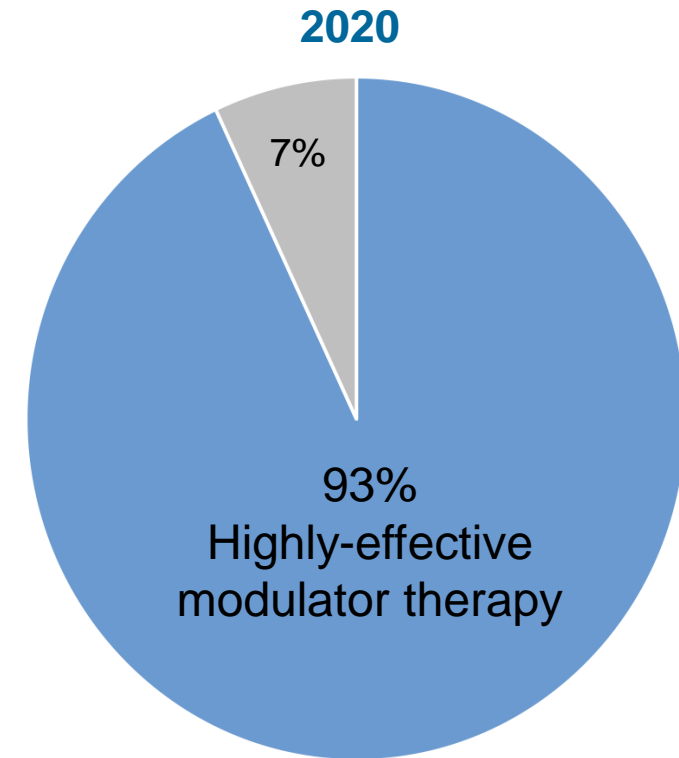
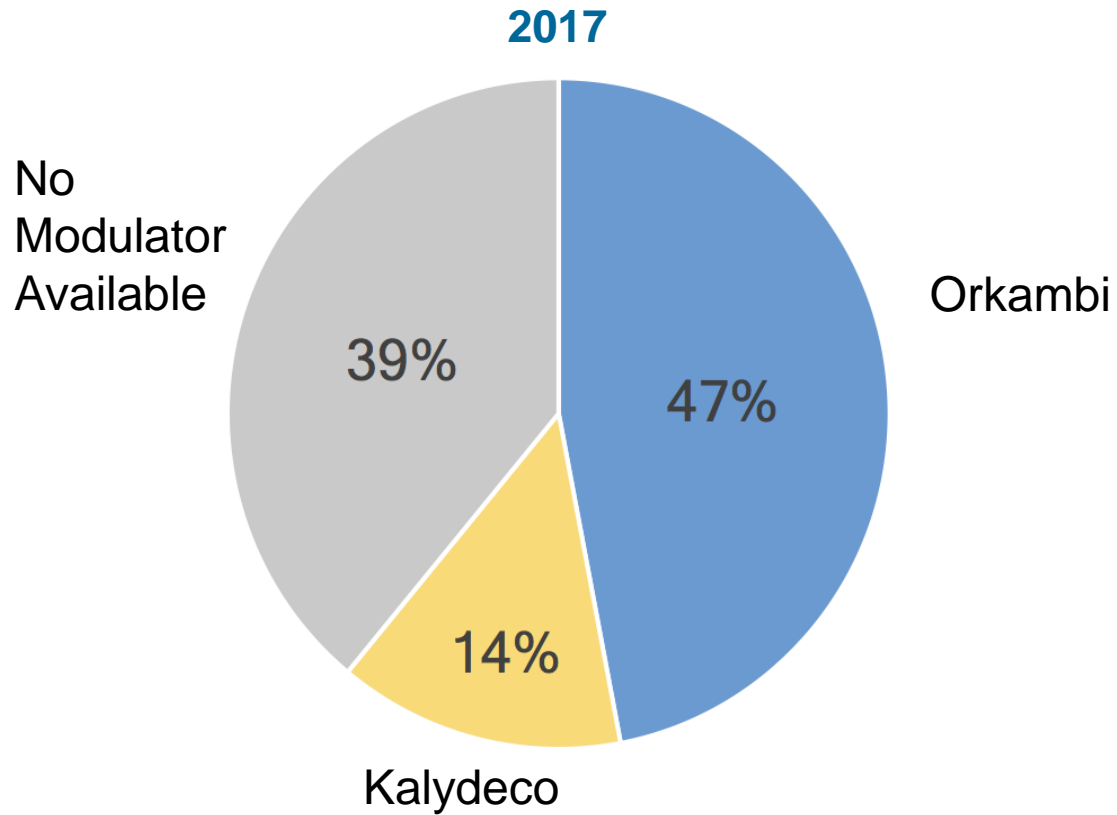
CFTR Modulator development is
very exciting

FDA approvals

- Kalydeco – 2012
- Orkambi – 2015
- Symdeko – 2018
- Vertex next generation expected in 2020

- Other CFTR modulator programs are very promising and advancing rapidly

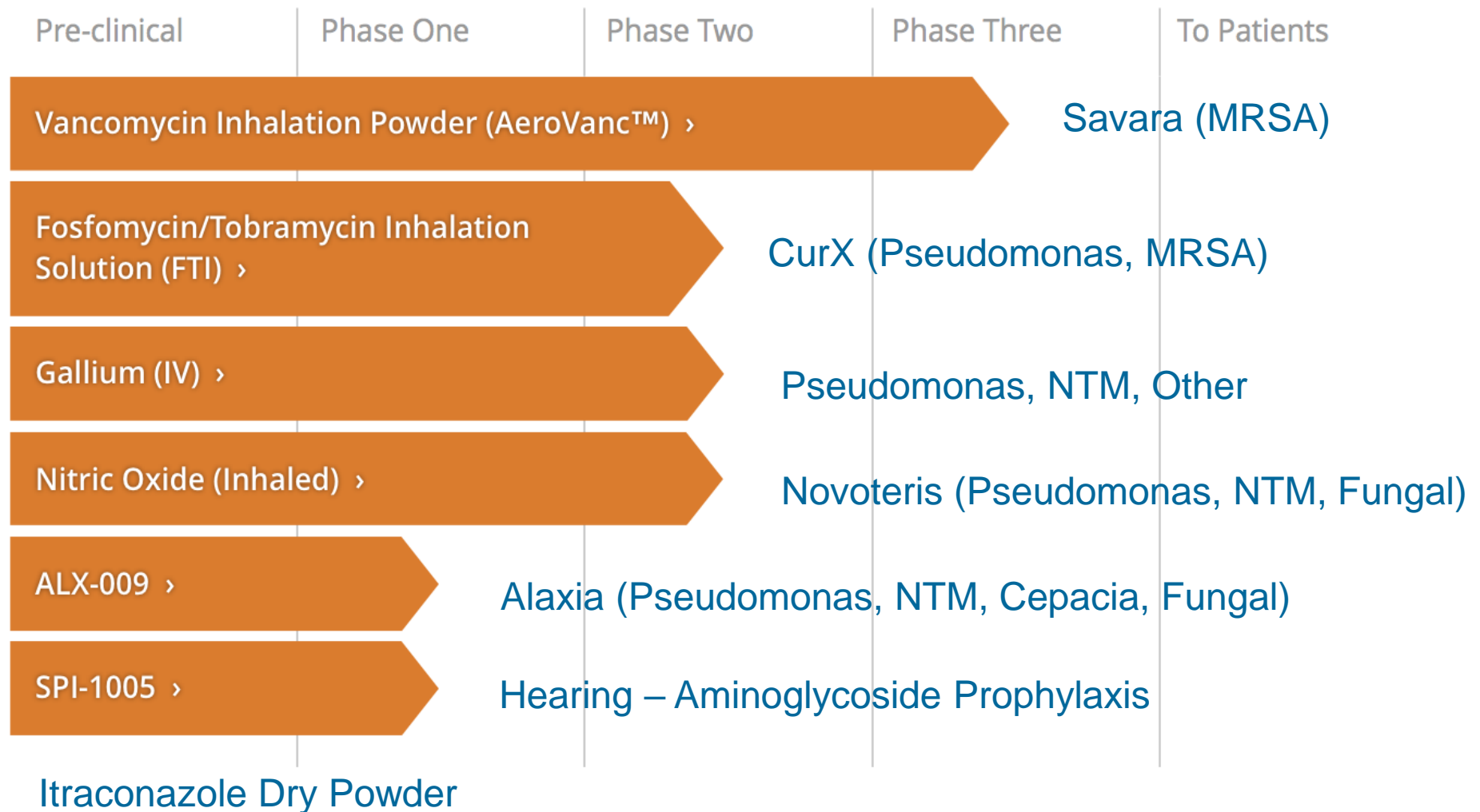
Progress in CFTR modulators



Reason #6

The therapeutic pipeline holds more promising therapies which treat the complications of CF than ever before

Anti-infectives



IV Gallium

Safety and effectiveness of IV gallium nitrate in CF adults

- Gallium is a metal that is similar to iron, which is needed by bacteria to grow
- Gallium is active against most CF pathogens
- An initial Phase 2 IV gallium trial reduced multidrug resistant *Pseudomonas* infection and improved FEV₁
- A larger follow-up Phase 2 IV gallium trial is enrolling now:
 - 52 of 120 participants are enrolled

NTM trial starting

Inhaled nitric oxide

Phase 2 Study of Inhaled Nitric Oxide (Novoteris NO-CF-02E)

- Nitric oxide is used by the body in its defense against bacterial infection
- Nitric oxide gas has been shown to be a potent killer of almost all types of bacteria
- Trial beginning enrollment this month at four sites
- Nitric oxide gas inhaled nasally four times a day for 10 days
- Measure lung function and bacterial counts

NTM trial started

Motif Bio (Iclaprim)

Iclaprim: IV Iclaprim 80 mg q12h

- Have completed and had positive results in two phase 3 trials for skin and soft tissue infections
- Pulmonary availability
- Phase 3 Pneumonia study about to start
- Potential highly active against **MRSA**, ***B. Cepacia***
- CF Foundation supporting testing currently against **Achromobacter**, **Stenotrophomonas**

Anti-inflammatory clinical trials

Corbus JBT-101

Novel Mechanism: Cannabinoid type 2 receptor (CB2) agonist (Phase 2b: N=415)

(Reduces pro-inflammatory mediators. Induces anti-inflammatory cytokines)

Celaxsys CTX-4430

Oral inhibitor of Leukotriene A4 Hydrolase (LTA4H) (Phase 2b:N=195)

(Reduces elevated LTB4, neutrophil infiltration, and neutrophil elastase)

Laurent LAU-7B

Oral Corrector of AA/DHA imbalance (Phase 2: N= 120)

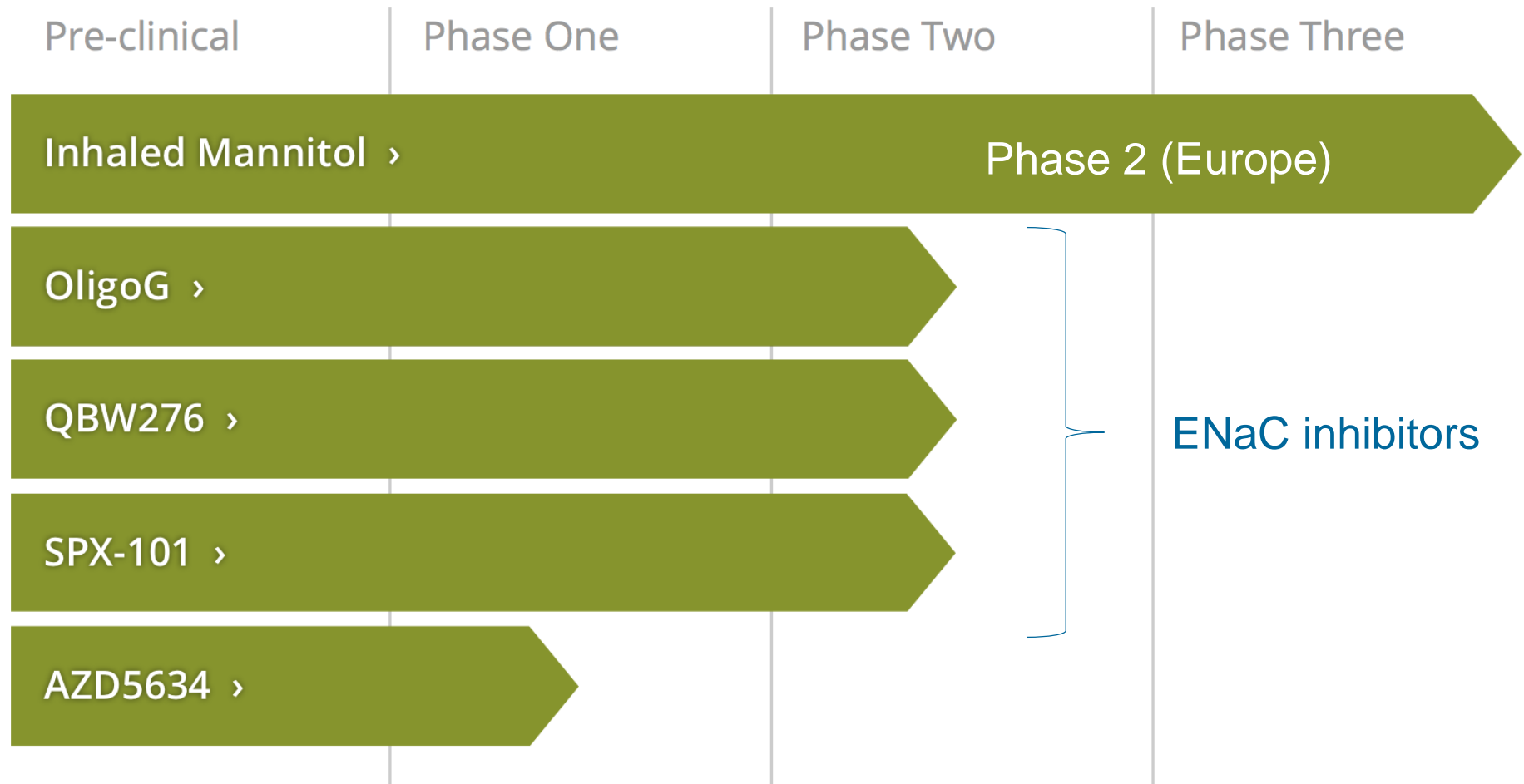
(Previously studied and found safe in other diseases; reduces inflammatory fatty acid imbalance characteristic of CF)

Polyphor POL-6014

Inhaled potent inhibitor of Human Neutrophil Elastase (phase 2, Europe)

(Phase 2A to determine safety and POC)

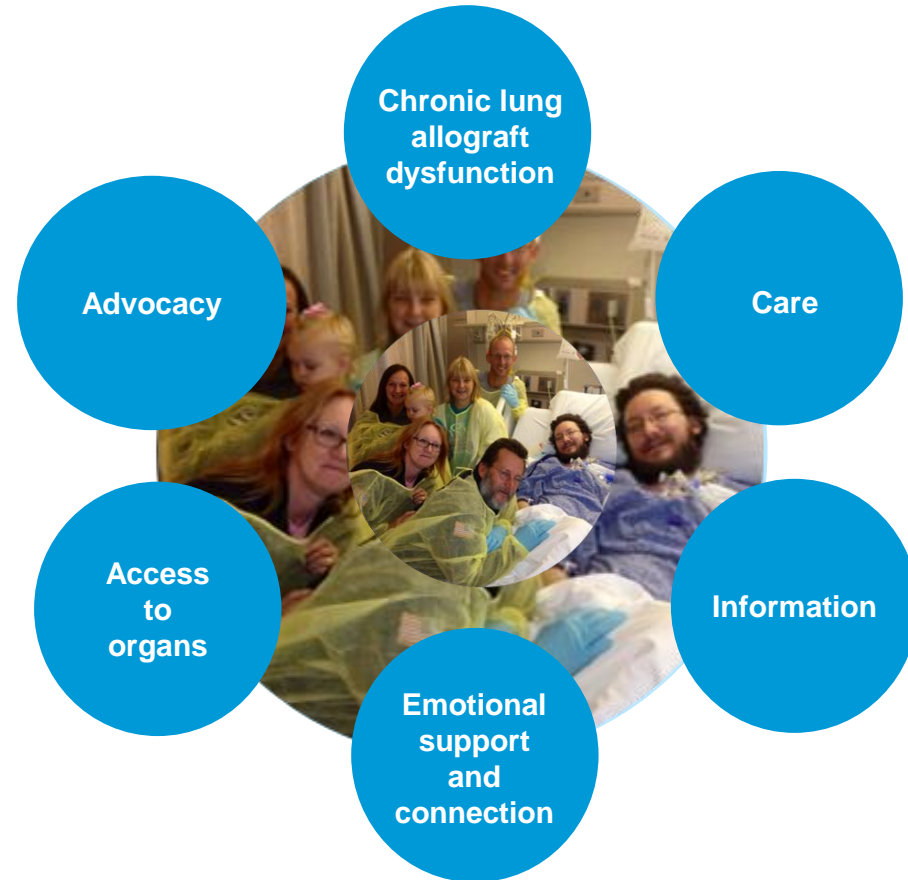
Mucociliary clearance



Reason #7

The Foundation is focused on lung transplant

The CF Foundation takes on lung transplant



Reason #8

Gene editing advances now
allow us to focus on a cure

Thank you.