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NACFC

October 2016

Safe Harbor Statement

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, information pertaining to KALYDECO® and ORKAMBI® and the ongoing discovery, development and commercialization of Vertex's product candidates, including VX-661, VX-371, VX-440, VX-152 and VX-659. While the Company believes that these forward-looking statements are accurate, these statements are subject to risks and uncertainties that could cause actual outcomes to differ materially from the Company's current expectations. These risks and uncertainties include, among others, risks related to commercialization of and reimbursement for KALYDECO and ORKAMBI, the risk that data from the Company's development programs may not support registration or further development of its compounds due to safety, efficacy or other reasons, and the risks and uncertainties listed in the Company's October 25, 2016 press release and under Risk Factors in the Company's 10-K and other filings with the SEC.

Agenda

Jeff Leiden, M.D., Ph.D., President & CEO
- *CF Strategy*

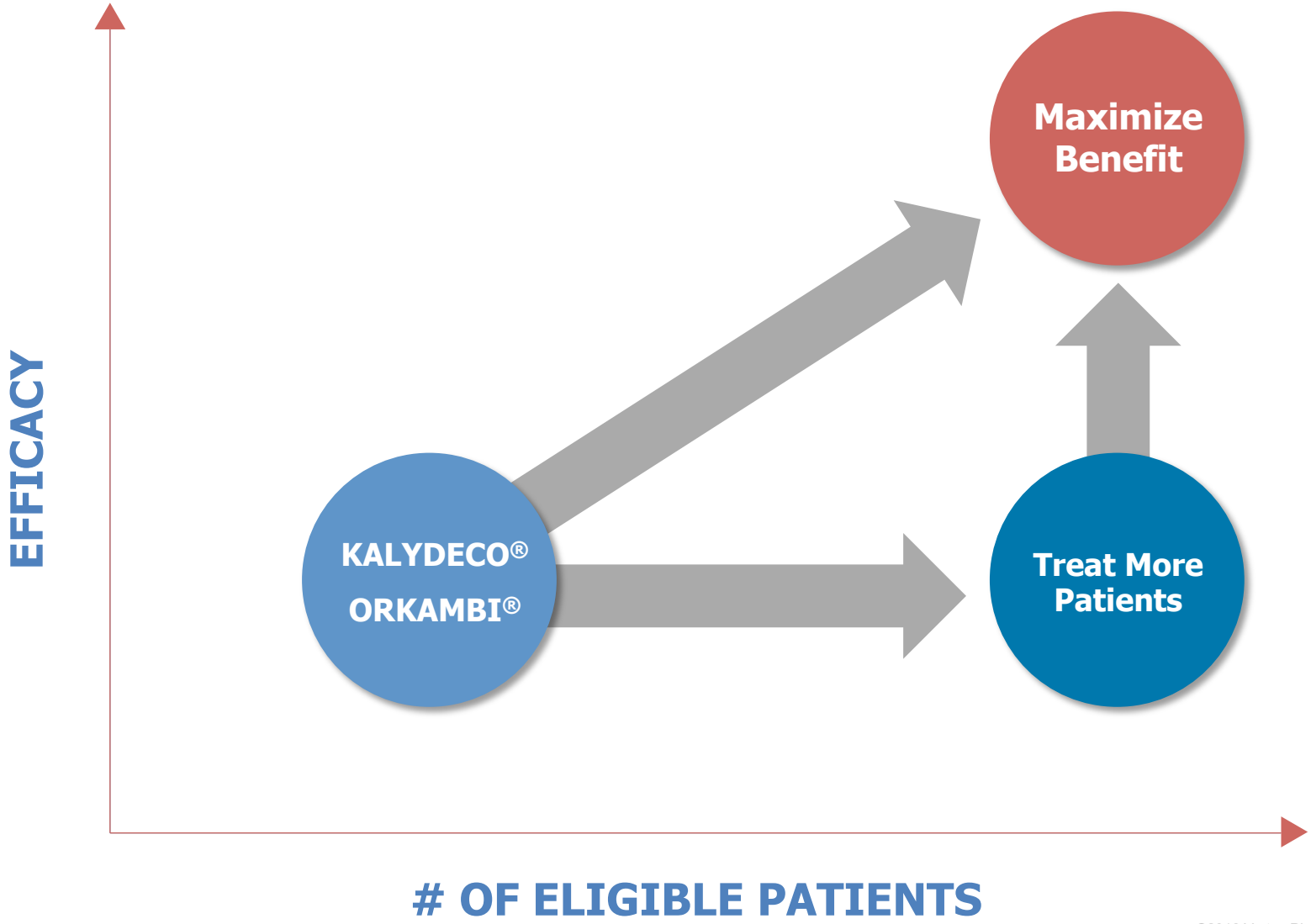
Stuart Arbuckle, EVP & Chief Commercial Officer
- *Treating More People with Approved Medicines*

Jeff Chodakewitz, M.D., EVP & Chief Medical Officer
- *Development Updates*

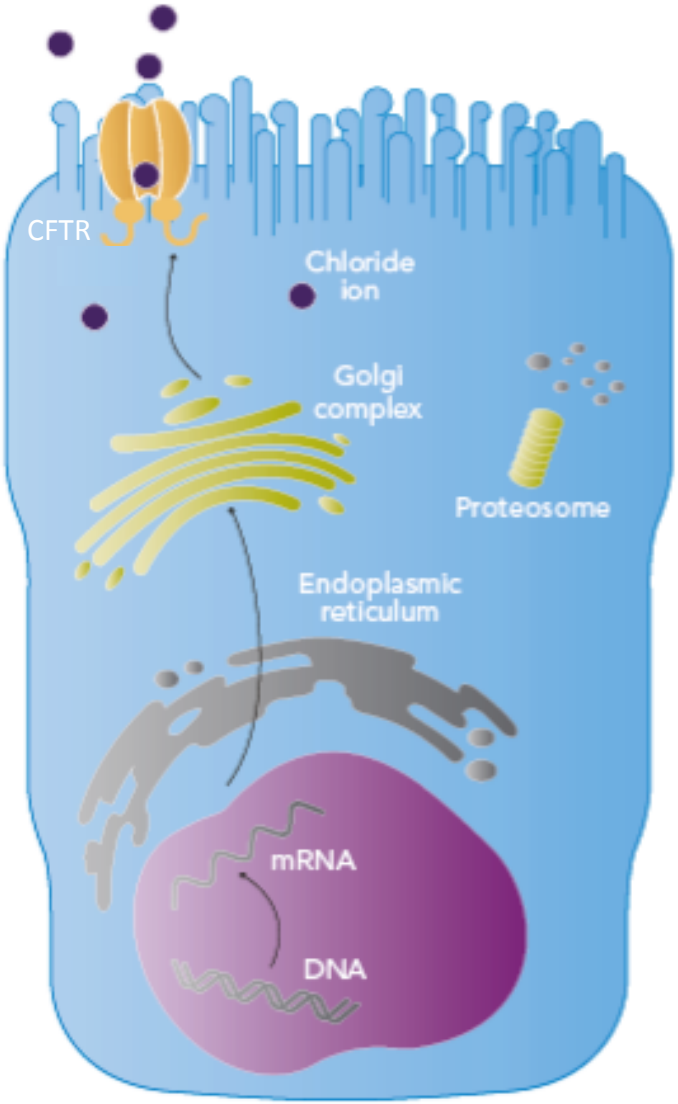
David Altshuler, M.D., Ph.D., EVP & Chief Scientific Officer
- *Seeking Optimal Regimens for All Patients*

Q&A

Goal: Develop Medicines that Maximize Benefit for All CF Patients Starting Early in Life



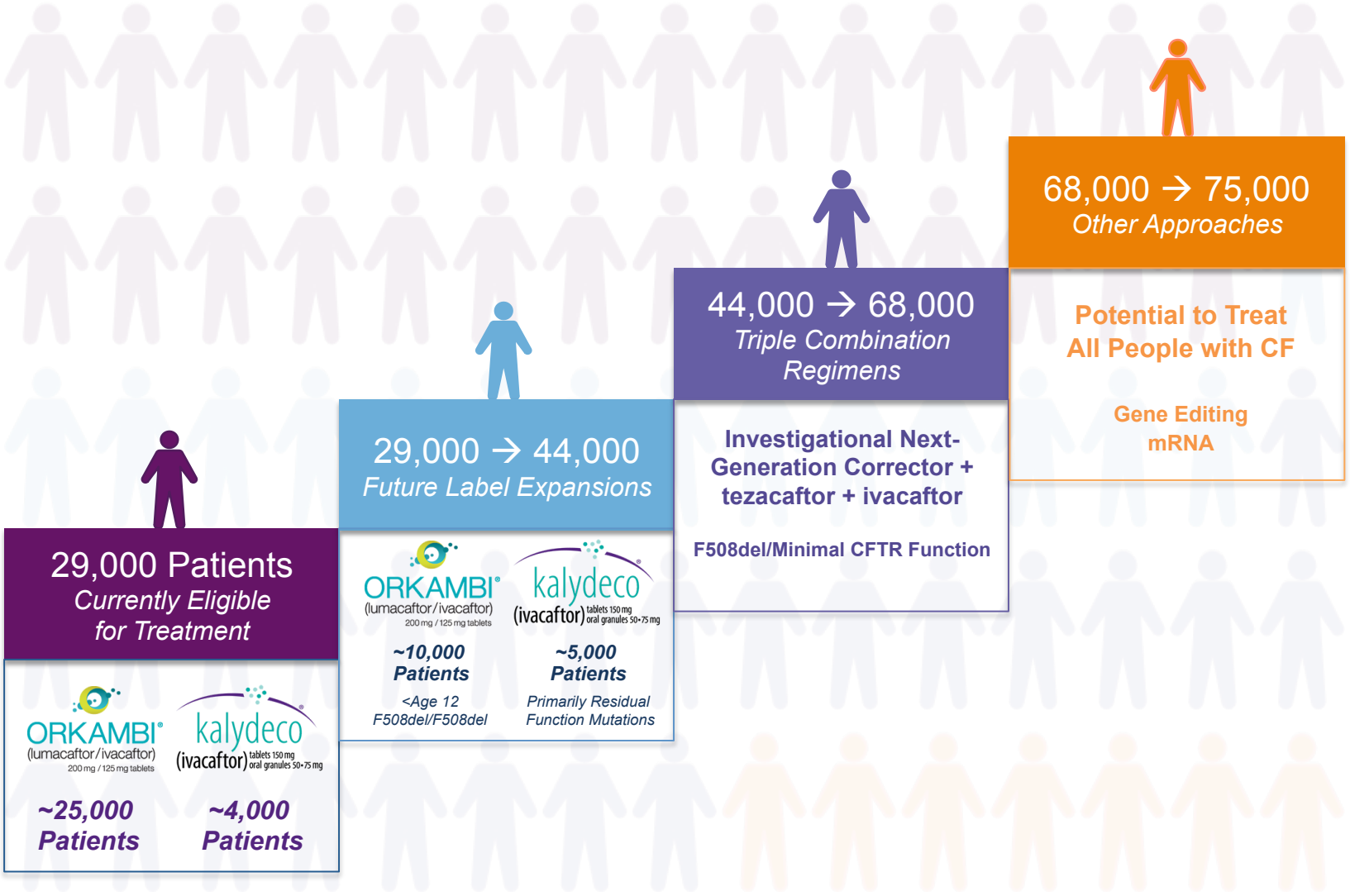
Biological Understanding of CF Provides Path to Develop Medicines for All Patients



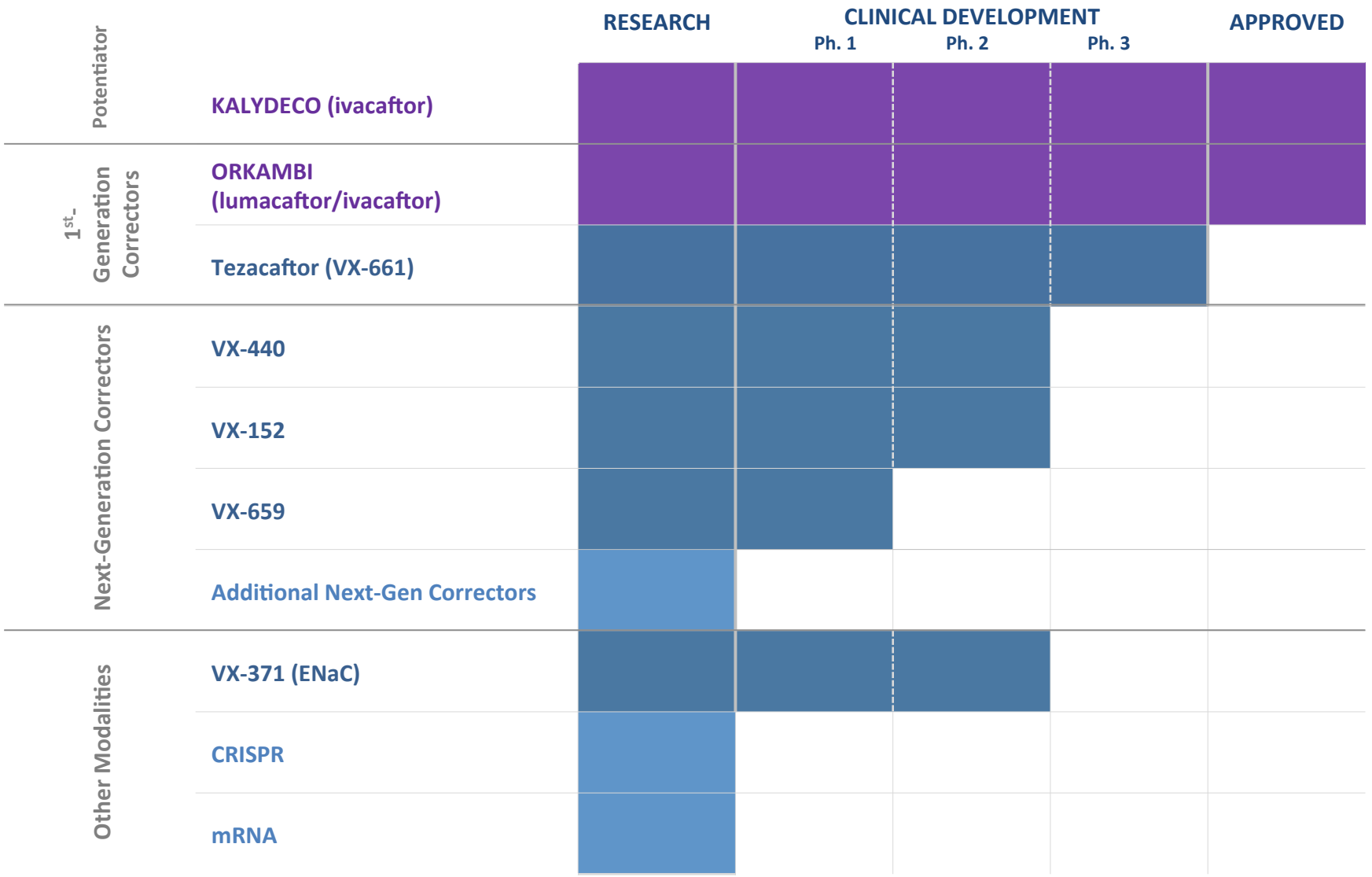
Biological Problem	Therapeutic Approach
Defective CFTR Function	Potentiator: kalydeco (ivacaftor) tablets 150 mg, oral granules 50•75 mg
Defective CFTR Protein Trafficking and Folding	Correctors: ORKAMBI® (lumacaftor/ivacaftor) 200 mg / 125 mg tablets; tezacaftor (VX-661); VX-440; VX-152; VX-659
Defective Protein Synthesis	Genetic Approaches: Gene Editing (CRISPR); mRNA (Moderna); Gene Therapy

Adapted from Lukacs GL, et al. *N Engl J Med*. 2003;349:1401-04.

Path to Treating All Patients



Vertex CF Pipeline



Tezacaftor being evaluated in combination with ivacaftor; VX-440 & VX-152 being evaluated in combination with tezacaftor and ivacaftor

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29,000 Patients Currently Eligible for KALYDECO or ORKAMBI

ORKAMBI®
(lumacaftor/ivacaftor)
200 mg / 125 mg tablets

- First approved in 2015 for patients ages 12+ who have two copies of the F508del mutation
- ~25,000 currently eligible for treatment

kalydeco®
(ivacaftor) tablets 150 mg
oral granules 50•75 mg

- First approved in 2012 for patients ages 6+ who have at least one copy of the G551D mutation
- ~4,000 currently eligible for treatment

~9,000 of the 29,000 eligible patients are currently being treated with KALYDECO or ORKAMBI

Growth for ORKAMBI

Increasing the Number of Eligible Patients Treated

~25,000 Patients Eligible for Treatment with ORKAMBI in U.S., Europe, Australia and Canada

U.S.

Initiated

~6,400 Patients Ages 12+

Not Initiated

~2,100 Ages 12+

~2,400 Ages 6-11
(approved 9/28/16)

Europe, Canada & Australia

Initiated

~900 France

~500 Germany

Not Initiated

~10,500 Europe

~1,500 Canada

~1,000 Australia

Growth for ORKAMBI

Obtaining Global Reimbursement Approvals

EU Reimbursement Status in Key Countries	Clinical Assessment	Economic Assessment	Price Negotiation
England ~2,700 eligible patients	✓ "The committee therefore acknowledged that lumacaftor–ivacaftor was a valuable new therapy for managing cystic fibrosis. It agreed that lumacaftor–ivacaftor has wider benefits to society for people with cystic fibrosis and carers of people with cystic fibrosis..."[1]	✓	Ongoing
Germany ~2,500 eligible patients *~500 Initiated ORKAMBI*	✓ "Considerable Additional Benefit"[2]	✓	Ongoing
France ~1,500 eligible patients *~900 Initiated ORKAMBI*	✓ Medical benefit (SMR): "Important" ✓ Improvement of Medical Benefit (ASMR): "IV"[3]	✓	Ongoing
Italy ~700 eligible patients	✓ Complete	✓	Ongoing
Ireland ~500 eligible patients	✓ Complete	✓	Ongoing

[1] https://www.nice.org.uk/guidance/ta398/chapter/4-Committee-discussion [2] https://www.g-ba.de/downloads/39-261-2603/2016-06-02_AM-RL-XII_Lumacaftor-Ivacaftor_D-204_BAnz.pdf [3] http://www.has-sante.fr/portail/upload/docs/evamed/CT-14927_ORKAMBI_PIC_INS_Avis3_CT14927.pdf

Increasing the Number of Eligible Patients
ORKAMBI and KALYDECO

ORKAMBI® (lumacaftor/ivacaftor) 200 mg / 125 mg tablets

Potential to treat ~10,000 additional children <12 years of age

- Phase 3 efficacy and safety study ongoing to support potential MAA approval in ages 6-11; data expected by year-end
- Phase 3 study in children ages 2-5 ongoing

kalydeco (ivacaftor) tablets 150 mg oral granules 50•75 mg

Potential to treat ~5,000 additional people with residual function mutations and also children <2 years of age

- Approved to treat children ages 2-5 in the U.S. and Europe with gating mutations
- Phase 3 study in infants ages 0-2 ongoing
- Continue to pursue FDA approval for certain residual function mutations

Label expansions could increase eligible patients from

29,000 to 44,000

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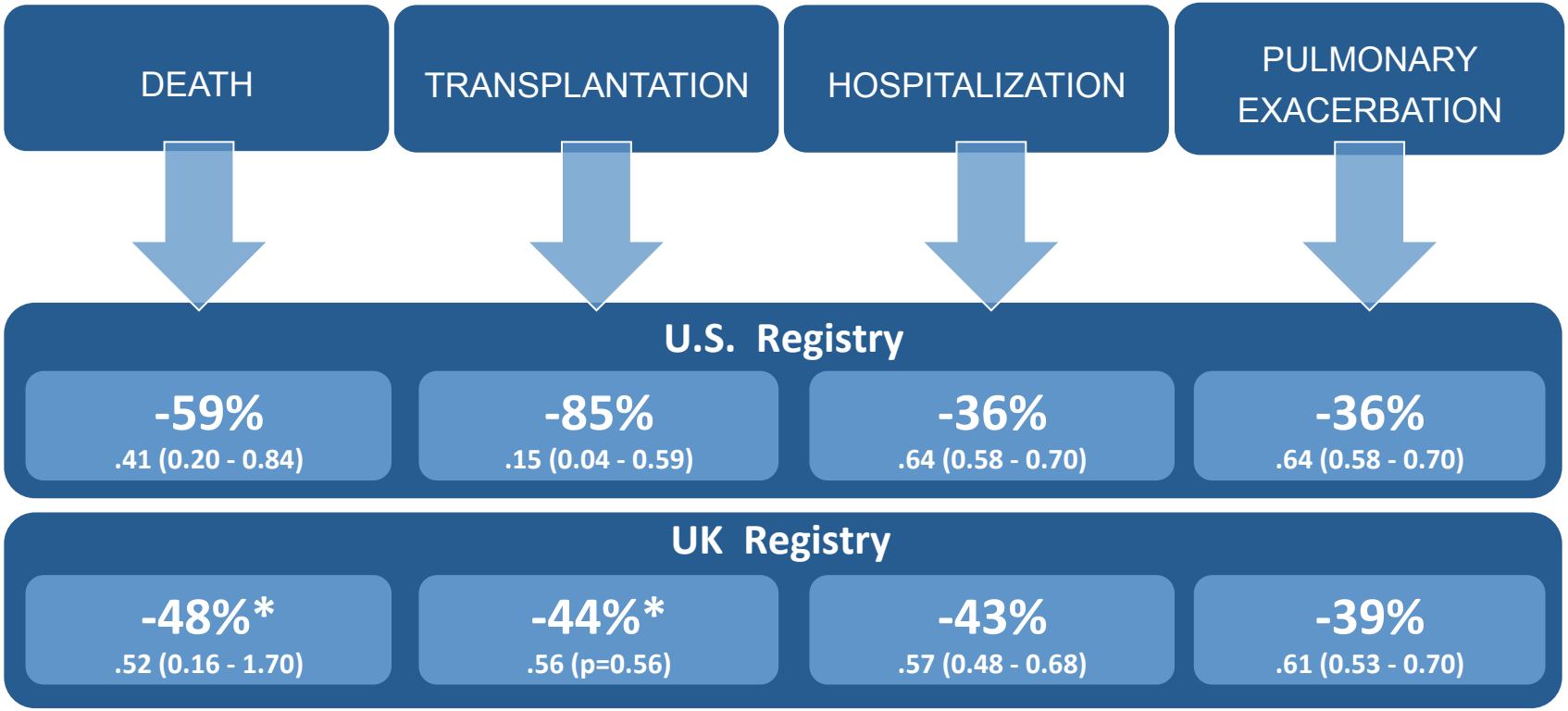
Data Presentations at NACFC Underscore Breadth of Vertex's CF Pipeline

Long-Term Data for ORKAMBI and KALYDECO	ORKAMBI: Long-term Data and Rate of Lung Function Decline Analysis
	KALYDECO: Long-term Data from U.S. and UK Patient Registries
	KALYDECO: Long-term Data from the KIWI Trial (Children Ages 2-5)
Tezacaftor (VX-661)	VX-661: Nonclinical Profile
Path to Treat All Patients	Next-Generation Correctors: In Vitro Efficacy of Multiple Next-Generation Correctors
	ORKAMBI: Data from Open-Label Phase 3 Safety Study in Children Ages 6-11
	Precision Medicine: Bringing New Medicines to All People with CF
	ENaC Inhibition: Potentially Complementary Approach to ORKAMBI

Long-Term Real-World Data for KALYDECO

Interim data from long-term observational safety study using U.S. and UK CF Registries Presented at NACFC



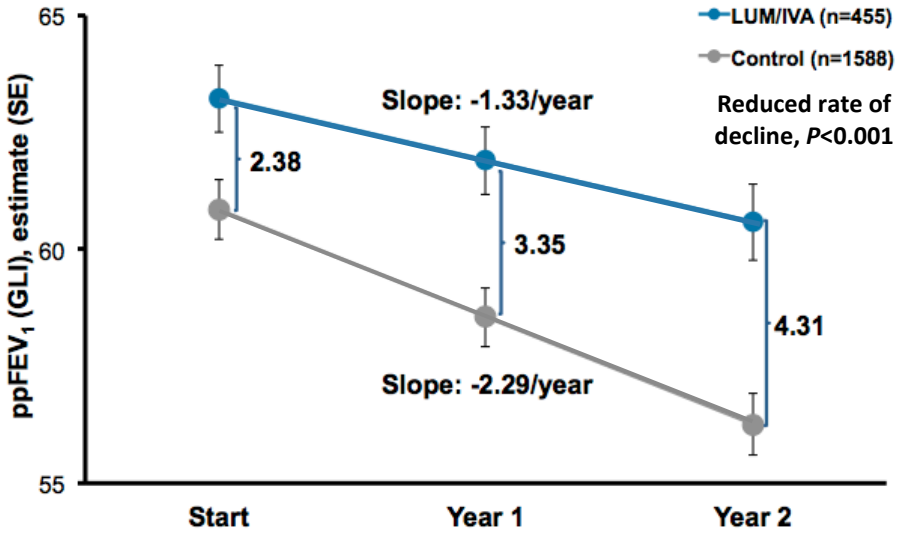
Provided as Percent Reduction with corresponding Risk Ratio (95% CI); *Not Statistically Significant
Average KALYDECO exposure: 2.0 years in U.S. registry and 1.3 years in UK registry;
Potential for confounding cannot be excluded but was partially addressed through matching and stratification

Bessonova et al. Presented at 30th Annual North American Cystic Fibrosis Conference

Slowing the Rate of Lung Function Decline

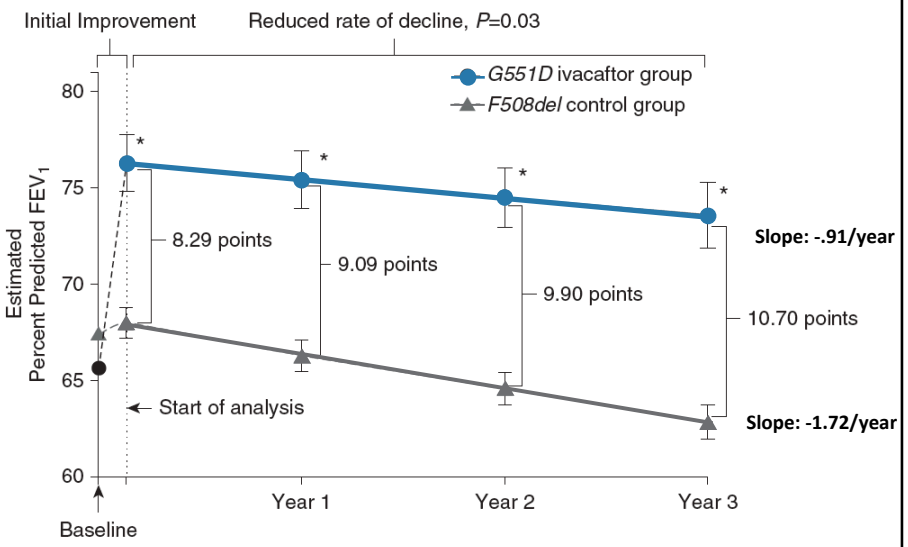
Data from PROGRESS and PERSIST vs. Matched Controls from CFF Registry

ORKAMBI® (lumacaftor/ivacaftor) 200 mg / 125 mg tablets



42% Decrease in Rate of Decline

kalydeco® (ivacaftor) tablets 150 mg oral granules 50•75 mg



47% Decrease in Rate of Decline

For ORKAMBI, estimates of average annual rates of decline were based on comparisons of data for PROGRESS patients with registry data for patients that were propensity-score matched to PROGRESS patients based on known predictors of lung function decline.

For KALYDECO, a similar analysis was conducted comparing data for patients from PERSIST with registry data for F508del matched controls.

Konstan MW, et al. Presented at the 30th North American Cystic Fibrosis Conference, Orlando, Florida, October 27-29, 2016. Poster 180;
Sawicki GS, et al. *Am J Respir Crit Care Med*. 2015;192:836-42. *Am J Respir Crit Care Med*. 2016;193:1317-20 [Erratum].

Tezacaftor (VX-661) + Ivacaftor

Phase 3 Program Generates Safety and Efficacy Data in 1,000+ Patients

Key Role in Development of Triple Combination with Next-Generation Corrector

GENOTYPE	DURATION (n)	DEVELOPMENT STATUS
F508del / F508del	24 Weeks (n=500)	Data Expected 1H17
Residual Function / F508del	Two 8-Week Crossover Treatment Periods (n=200)	Data Expected 1H17
Gating / F508del	8 Weeks (n=200)	Enrollment Completion in Early 2017
Minimal Function / F508del	12 Weeks (n=150) *Study stopped based on futility analysis*	Contributes to Safety Database for VX-661

VX-440 Phase 2 Study Design

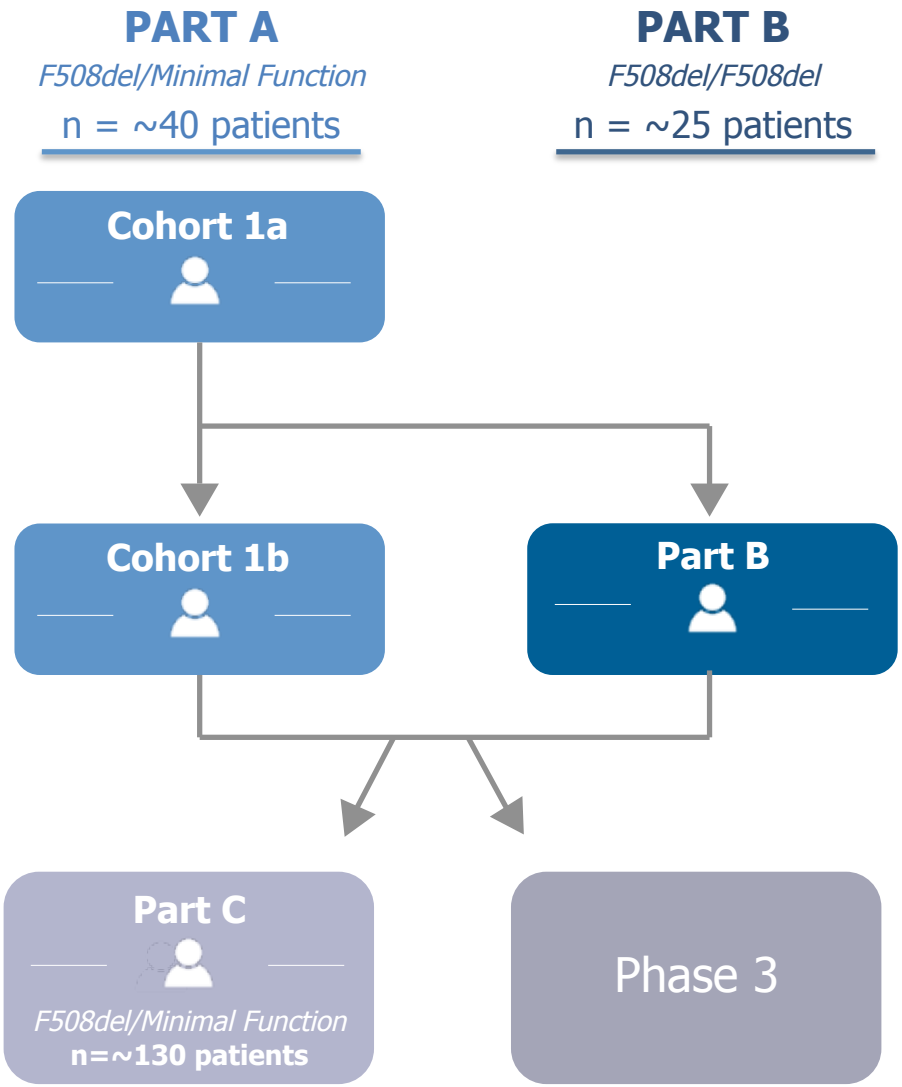
Regimen
4 Weeks of Triple Combination or Placebo (Parts A & B):
- ***VX-440/tezacaftor/ivacaftor***
- ***Part B includes 4-week lead-in and washout periods of only tezacaftor/ivacaftor***

Patient Genotypes:
F508del/Minimal Function (Part A)
F508del/F508del (Part B)

Endpoints:
- **Primary: Safety, Tolerability and Abs. Change in $ppFEV_1$**
- **Secondary: Rel. Change in $ppFEV_1$, Sweat Cl-, CFQ-R Resp. Score, others**

Data Expectation:
2H 2017 (Parts A & B)

Phase 2 Study of VX-152 + tezacaftor + ivacaftor also planned to begin in 2016



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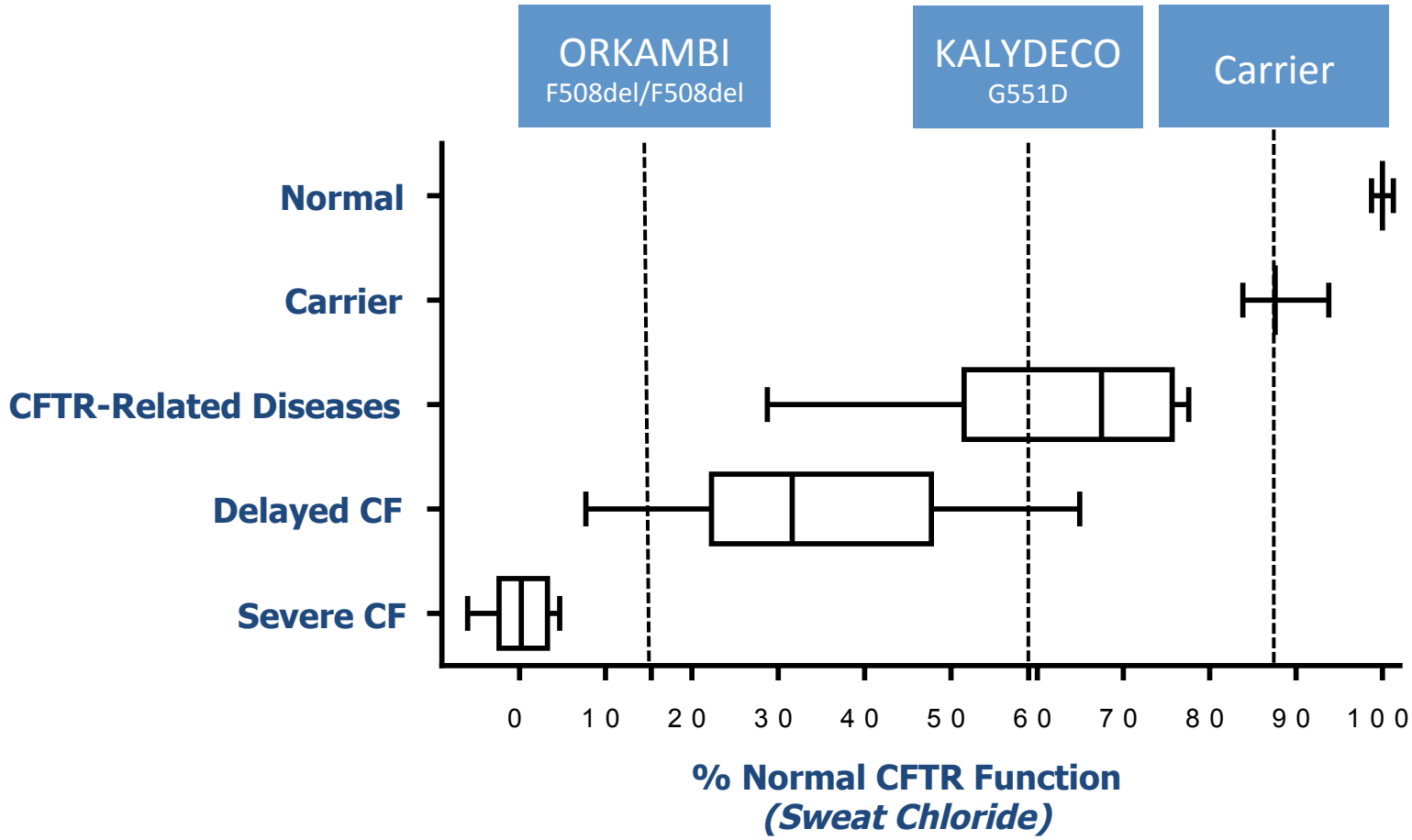
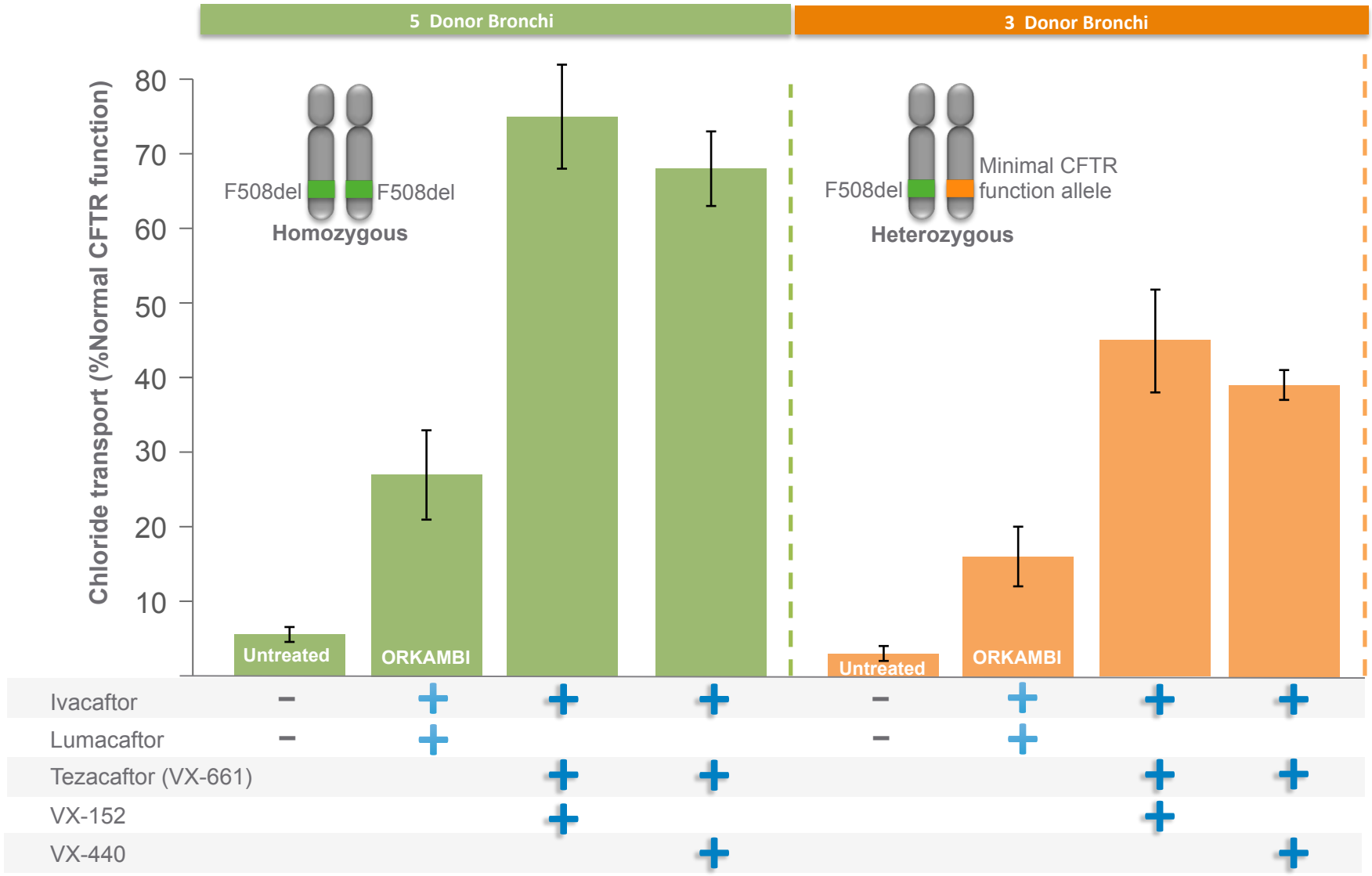
Goal: Carrier-like Benefits for All Patients Early in Life



Riordan JR, et al. *Science.* 1989;245:1066-73; Accurso FJ, et al. *J Cyst Fibros.* 2014;13:139-47;
Boyle MP, et al. *Lancet Respir Med.* 2014;2:527-38; Ramsey BW, et al. *N Engl J Med.* 2011;365:1663-72.

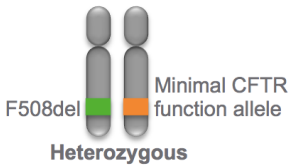
In Vitro Data for VX-440 and VX-152

Presented at NACFC 2015

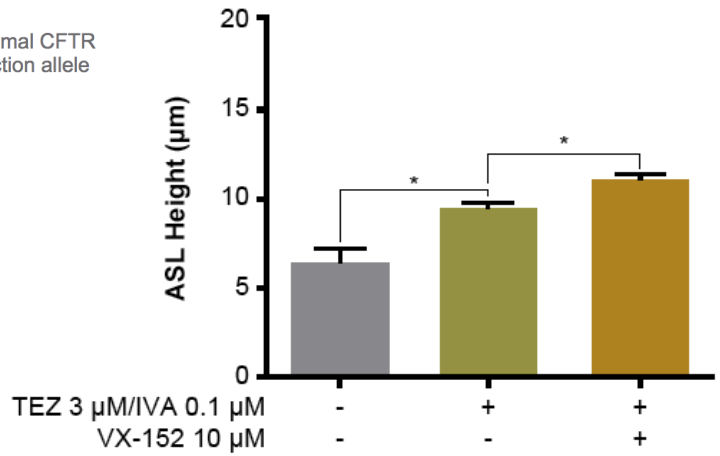


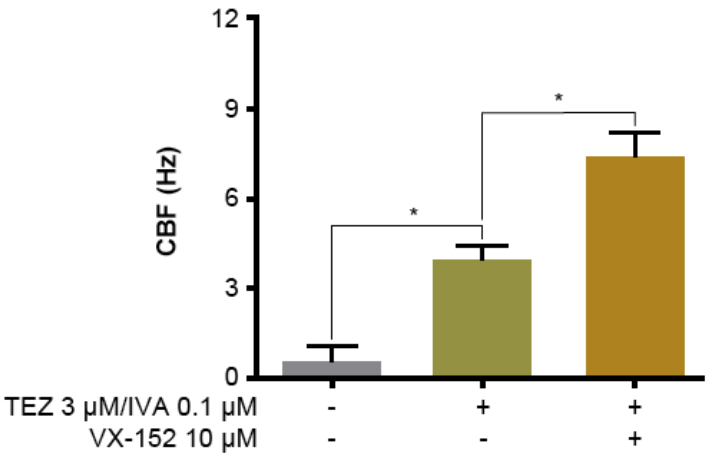
Ussing chamber studies using bronchial epithelial cells expressing the genotypes indicated; Top of bar charts represent EC 90 concentrations; Presented at NACFC investor event 2015

Similar Activity Across Multiple Measurements In Vitro
F508del/Minimal Function



F508del/MF-HBE



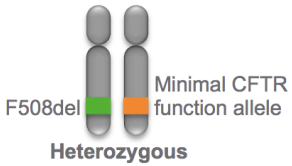


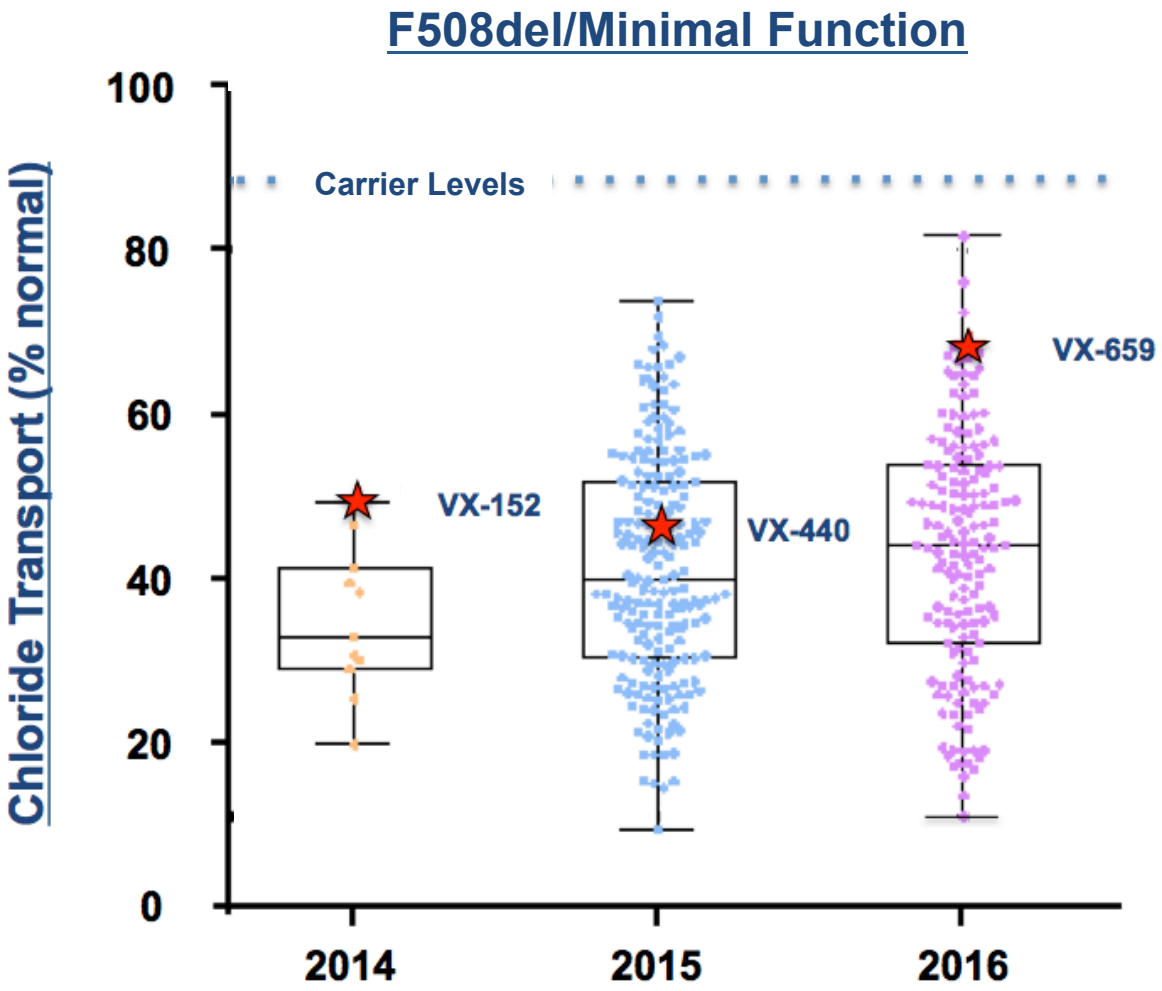
Vehicle | **tezacaftor + ivacaftor** | **tezacaftor + ivacaftor + VX-152**

F508del/G542X-HBE

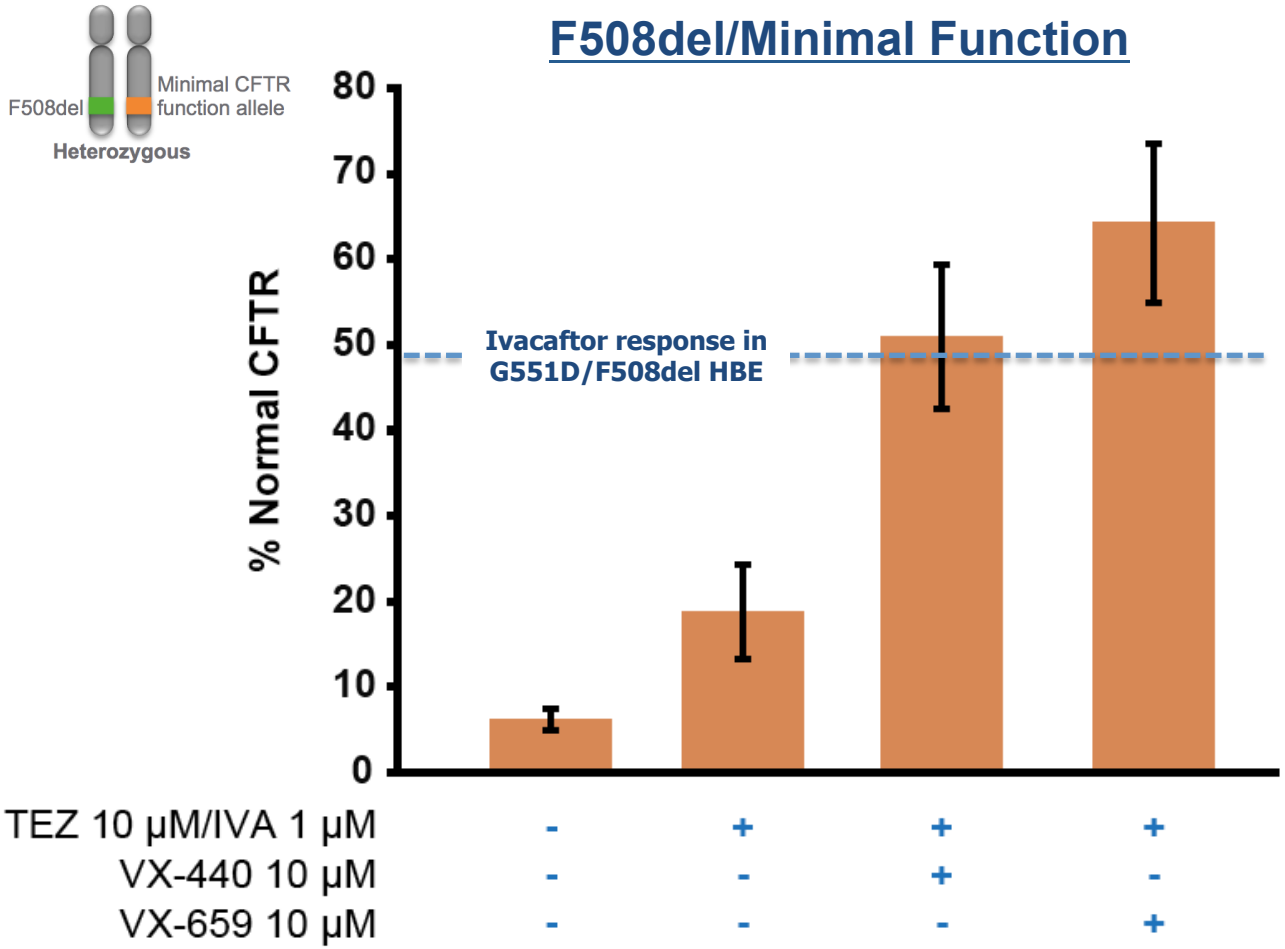
Grootenhuis PDJ, et al. Presented at the 30th North American Cystic Fibrosis Conference, Orlando, Florida, October 27-29, 2016. Poster 188.
Van Goor F, et al. Presented at the 30th North American Cystic Fibrosis Conference, Orlando, Florida, October 27-29, 2016. Symposium S14.4.

Progress in Corrector Chemistry





VX-659 Preclinical Profile



Preclinical Profile

- Higher maximal efficacy vs. VX-440 & VX-152 triple combinations
- Greater potency

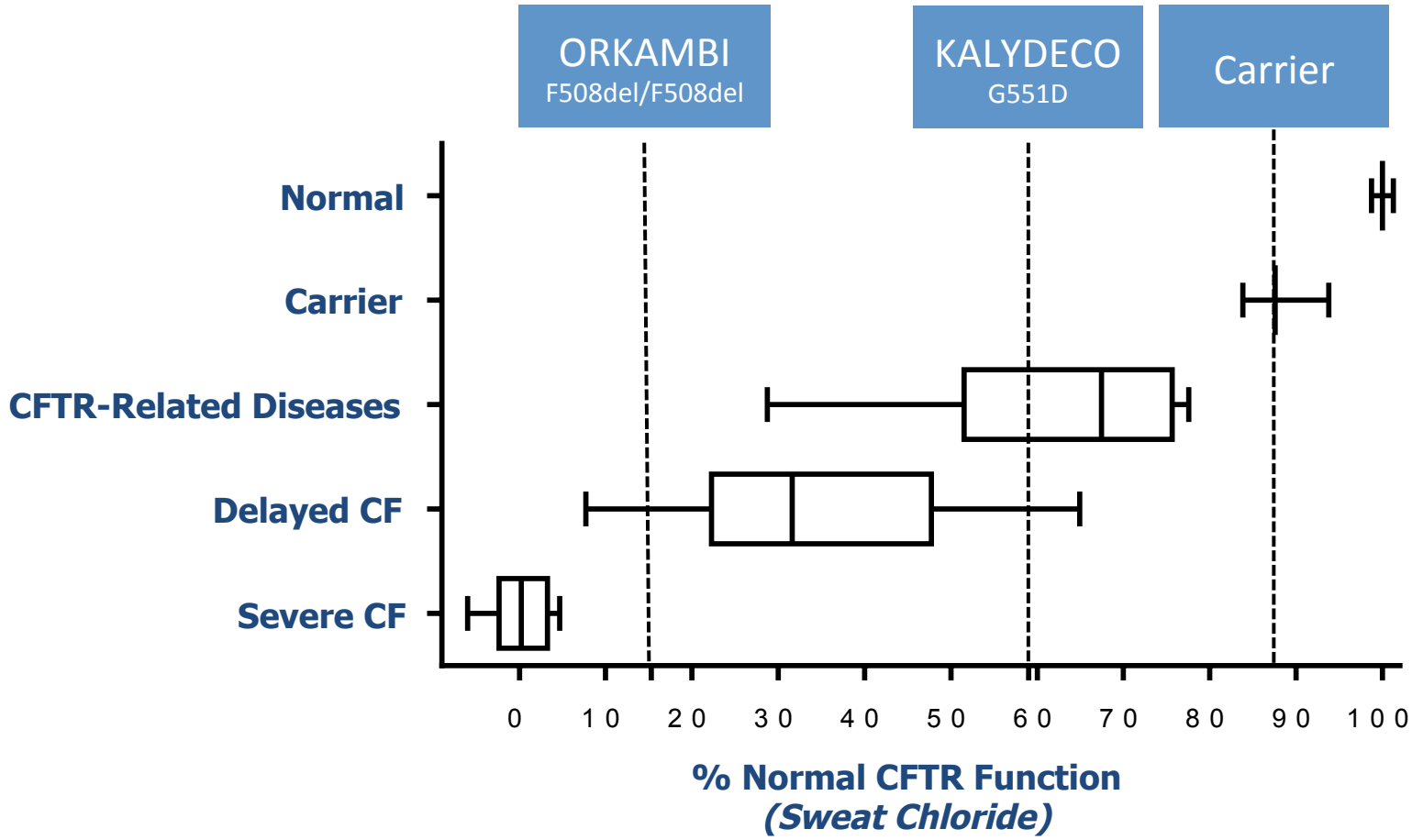
Development Path

- Phase 1 start by end of 2016
- Phase 2 in second half of 2017, pending data

N = 4 donors (2 G542X; 1 3905InsT; 1 E585X); 96-well Ussing + 20% serum; Top of bar charts represent EC 90 concentrations

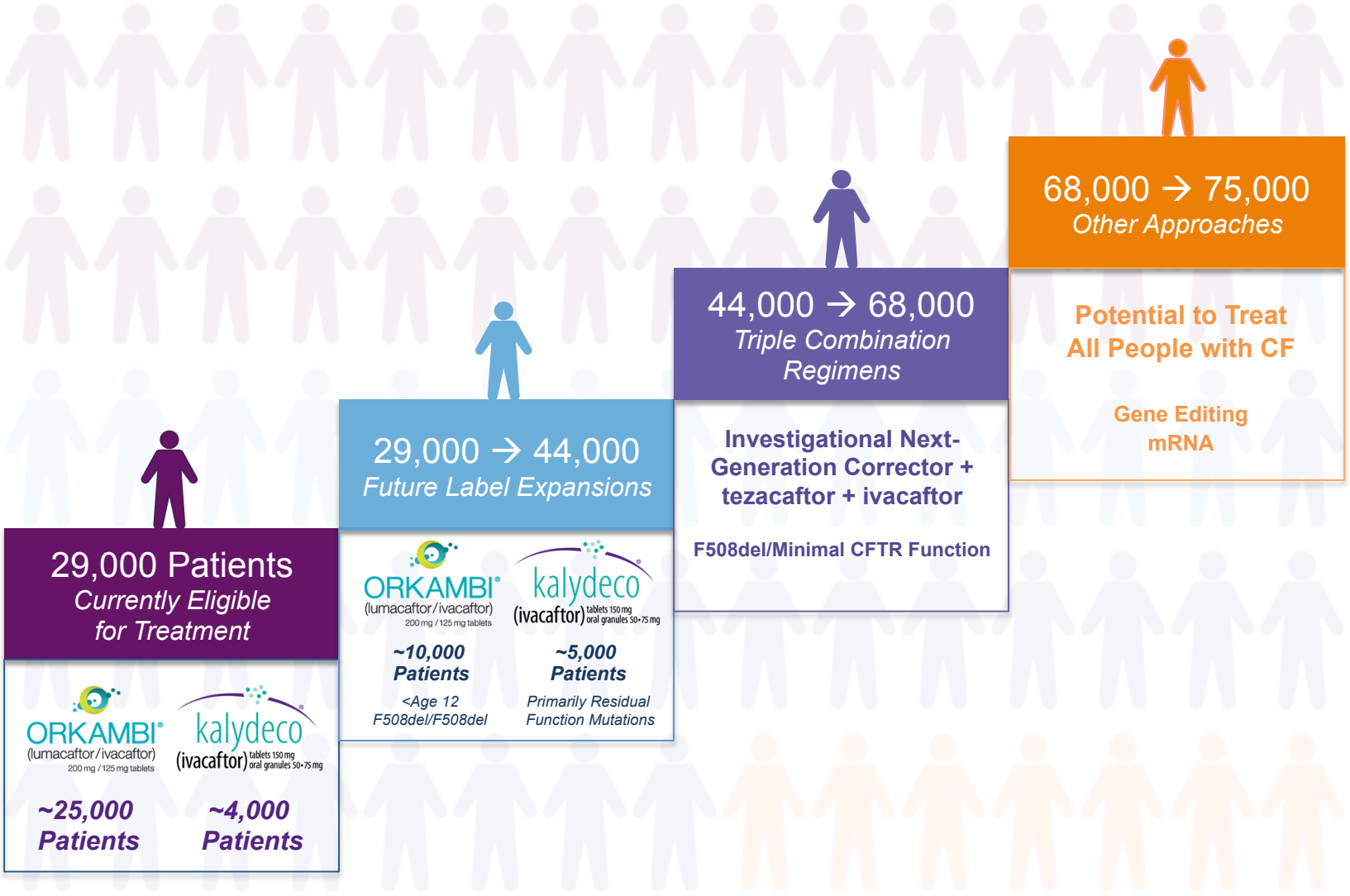
Van Goor F, et al. Presented at the 30th North American Cystic Fibrosis Conference, Orlando, Florida, October 27-29, 2016. Symposium S14.4.

Goal: Carrier-like Benefits for All Patients Early in Life



Adapted from: Riorden JR, et al. *Science*. 1989;245:1066-73. Accurso FJ, et al. *J Cyst Fibros*. 2014;13:139-47.

Path to Treating All Patients



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Questions and Answers