The Cystic Fibrosis Foundation receives a royalty on sales of ivacaftor as a result of its financial support of research that led to its development. The following remarks are based on medical evidence and not formulated with any intent to affect sales of ivacaftor because of the foundation’s royalty interest.
Mission of the CF Foundation

To assure the development of the means to cure and control cystic fibrosis and to improve the quality of life for those with the disease
Cystic Fibrosis Foundation: Enabling Success

CF Median Survival (years)

Year


THERAPEUTIC DEVELOPMENT
BASIC RESEARCH
REGISTRY/EPIEMIOLOGY
CARE CENTERS/GUIDELINES
DIAGNOSIS/MANAGEMENT
“The Foundation imposed an urgency and focus that a biotech or pharmaceutical company functioning alone could not muster.”
Age of Diagnosis and Management
Patient Registry
Annual Data Report to the Center Directors
2012

CYSTIC FIBROSIS FOUNDATION
ADDING TOMORROWS
PORT CF: Patient Registry

Web-based system
- Encounter based
- Clinical care management
- Patient education
### Genotype Data

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Number of Patients*</th>
<th>Percent of Patients*</th>
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<tr>
<td>F508del</td>
<td>23,053</td>
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<tr>
<td>G542X</td>
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<td>0.5</td>
</tr>
</tbody>
</table>

*Includes patients with one or two copies of the mutation.
Age of Research
Cystic Fibrosis
Cloning and Genetics
A Working Hypothesis
CFTR Activity: Salt and Water Balance In the Airways

Non-CF Cell

CF Cell
Age of Translation
Drug Development for Cystic Fibrosis

**Statement of Problem:** How do you convince the biopharmaceutical industry to develop drugs for a disease with a population of less than 30,000 patients in the United States, and 70,000 worldwide?

**Solution:** Therapeutics Development Program, initiated in 1998 to provide financial and resource support to pharmaceutical partners to encourage development of new drugs for cystic fibrosis.
National Resource Centers:
- Microbiology
- CFTR measurement
- Imaging
- Infant lung function
- Inflammatory markers
- Cytology

CF Therapeutics Development Centers (75)
- TDN National Resource Centers (6)
- TDN Coordinating Center
Therapeutics Development Program

DISCOVERY
Basic Research
- CFTR Corrector Consortium
- CFTR Structural Consortium
- Mucociliary Clearance Consortium
High-throughput Screening
- Genzyme
- Pfizer
- Proteostasis
- Vertex

Development
IND
Preclinical Safety Testing
TDN
Clinical Dosage and Efficacy
NDA
FDA APPROVAL

Distribution
Available to CF Patients

Bring Existing Drugs for CF Indication

Our Biotech Collaborators
Eli Lilly
Genzyme
GlaxoSmithKline
Insmed
Novartis
Pfizer
Proteostasis
Yasoo
PTC
Pulmatrix
Rempex
Vertex
High-throughput Screening

>10,000 Primary Assays/day
Vertex Screening for CFTR Modulators

Screen Chemical Compounds (hundreds of thousands)
Identify Hits (hundreds)
Validate Hits (~ten)
Select and Optimize Leads (~3)
Nominate Development Candidates in each category (potentiator & corrector)

File IND
Clinical Trials
File NDA

Potentiator Clinical Trials
- Phase 1 in 2006
- Phase 2 in 2007
- Phase 3 in 2009
Registration in 2012

Corrector Candidate
Combined 770/809
2014
2012 - FDA Approves Ivacaftor
Ivacaftor Phase 3 Results of CF Therapies

Relative Change in FEV₁ % Predicted from Baseline (with 95% CI)

- **Ivacaftor**
- **Inhaled Tobramycin**
- **Dornase Alfa**
- **Azithromycin**

Time (weeks)

0 4 8 12 16 20 24 28 32 36 40 44 48
The CF Foundation and Kalydeco in the News

Associated Press
“Vertex drug is breakthrough for handful of CF patients, offers hope to many more”

The New York Times
“FDA approves new cystic fibrosis drug”

npr
“Cystic fibrosis drug wins approval”

CBS Evening News
“Game changer” CF drug receives FDA approval

The Boston Globe
“Vertex gets early OK for new drug”

Reuters
“FDA approves Vertex cystic fibrosis drug”

nature
“U.S. approves Vertex cystic fibrosis drug Kalydeco”

CNBC
“FDA approves Vertex’s cystic fibrosis drug”

FDA Voice
“How science and strategic collaboration led to a new, ‘personalized’ cystic fibrosis treatment for some patients”

Bloomberg
“Vertex receives U.S. FDA approval for Kalydeco to treat cystic fibrosis”
CFF-Supported Research in the News

Combination Trial Headlines from June 24, 2014

**The Wall Street Journal.**
Vertex's Cystic-Fibrosis Treatment Shows Promise

**The New York Times.**
Vertex’s 2-Drug Cystic Fibrosis Pill Shows Promise

**Reuters.**
Vertex cystic fibrosis combo succeeds in key late-stage trials

**Forbes.**
In A Victory For Gene Research, Vertex Drug Combo Clears Lungs Clogged By Cystic Fibrosis

**Bloomberg.**
Vertex Surges After Drug Pair Helps in Cystic Fibrosis

**The Street.**
Vertex Pharma Cystic Fibrosis Combo Therapy Hits Key Endpoints in Two Pivotal Trials

**CNBC.**
Vertex cystic fibrosis combo meets study goals

**Boston Business Journal.**
For patients as well as investors, Vertex drug news is ‘hope delivered’

**Cystic Fibrosis News Today.**
Vertex Kalydeco/Lumacaftor Drug Combo Proves Effective Treating A Broader CF Patient Demographic

**The Boston Globe.**
Vertex’s cystic fibrosis drugs have promising trial
Ongoing Efforts to Identify the Next Generation ΔF508 CFTR Correctors

and more to follow
What have we learned?
• Manage expectations of your volunteers: Venture Philanthropy is not for the faint of heart. There will be disappointments. Diversify (hedge) your portfolio of opportunities.
• Structure your alliance like a business deal with clear-cut milestones and deliverables. This is not an open ended grant. Set out with clear objectives and reasonable timetable in place.
• Establish a Scientific Advisory Committee and schedule regular meetings and updates. In addition, you should establish a Steering Committee made up of representatives from your organization and the alliance partner.
• Do not be afraid of royalties! If your alliance partner is successful with an FDA approval, you should participate in their success. Royalties can provide for revenue to expand your pipeline to even better molecules. Paybacks can be multiples or royalty percentages.
• Make sure that there are interruption clauses in the contract. You need to be able to march in case the company changes control, changes management or focus, or bankruptcy.
• Do not be too onerous in recovering your investment...make recapture of investments or royalties based on FDA approval and not before (i.e., Phase 2 completion, etc.)
• Demanding to be at the pricing table is a deal killer. Recognizing there is no rationale in the pricing process, it may not be in your best interest to be at the table. You can emphasize the importance of assuring the development of programs that will give all patients access, i.e., co-pay program, uninsured programs, etc.
• Do not be afraid of big Pharma. Unlike small biotech companies they have the resources to take your asset through clinical development. In most cases this will involve a “pass off” between the research/discovery component of the company to the clinical development component. If pass off does not occur, interruption clause needs to “kick in” in a timely fashion.
There are resources you can bring to the table that can be just as important as money: natural history of disease (patient registry), identification of patients, clinical trials networks, cell lines, reimbursement and expertise.
• Find a good lawyer experienced in Venture Philanthropy. Do not be fooled--the issues involved here are not a typical corporate deal. There are not many deals you can truly walk away from if the subject is important to you and your patients.
New Mission Statement (2013)
The mission of the Cystic Fibrosis Foundation is to cure cystic fibrosis and to provide all people with the disease the opportunity to lead full, productive lives by funding research and drug development, promoting individualized treatment, and ensuring access to high-quality, specialized care.

Previous Mission Statement (1955)
The mission of the Cystic Fibrosis Foundation is to assure the development of the means to cure and control CF and to improve the quality of life for those with the disease.
Thank you!