

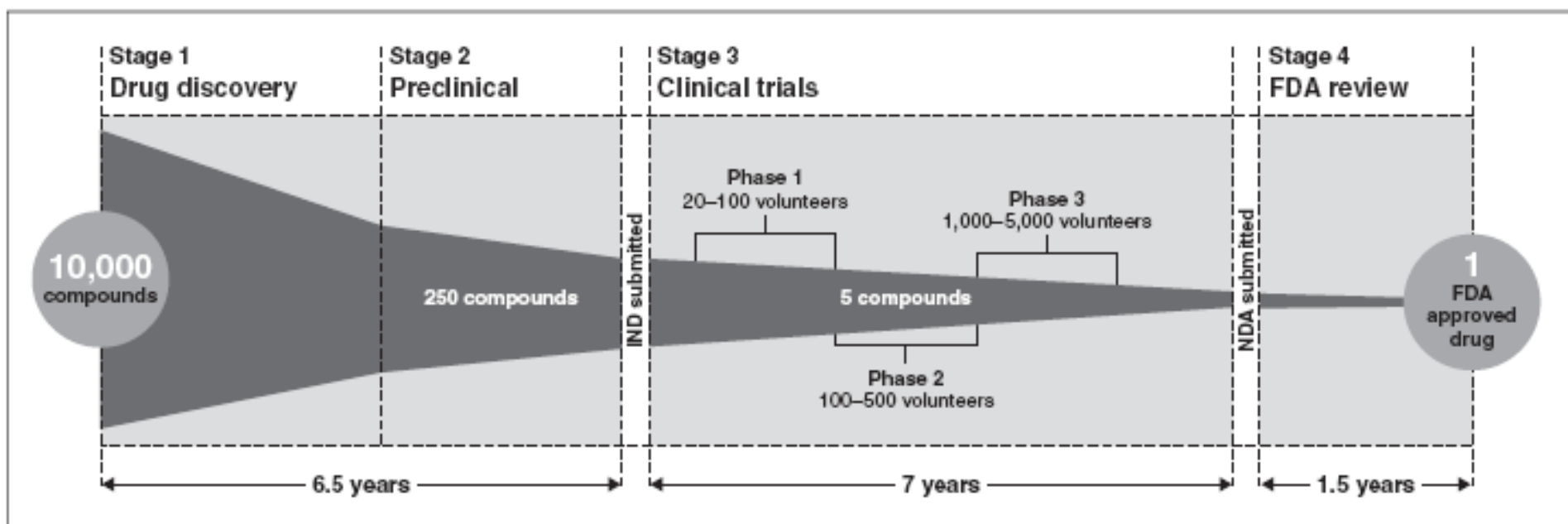
Vertex Pharmaceuticals and
the Cystic Fibrosis Foundation:
A case study of Venture Philanthropy in Biotech

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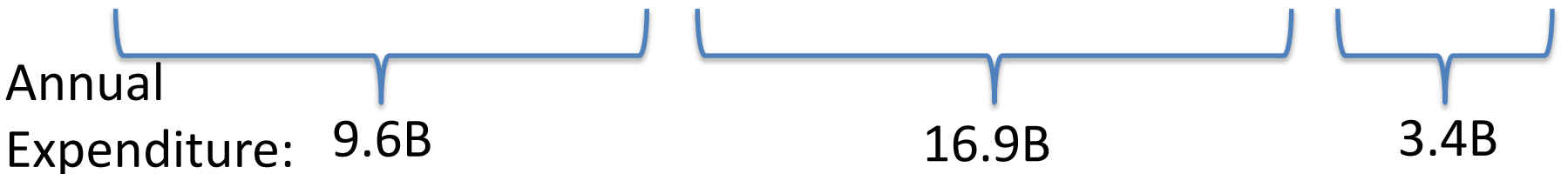
Harvard Biotech Journal Club

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The drug development timeline



Source: Pharmaceutical Research and Manufacturers of America.



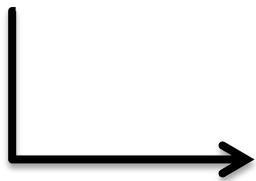
Source: HBS Case no.9-808-005

Funding sources for Biotech

- Venture capitalists
- Large pharmaceutical companies
- Angel investors
- IPO

The GAP: How about rare diseases?

Venture Philanthropy

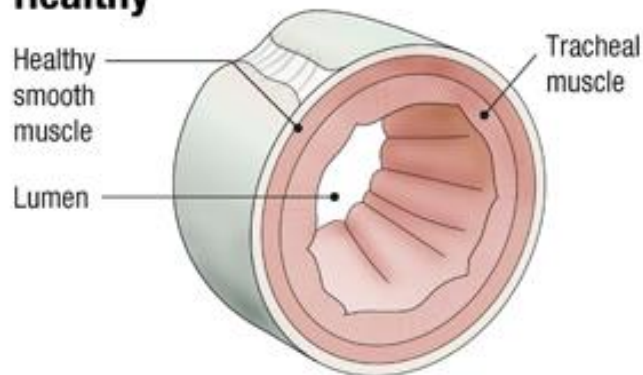


e.g. The Cystic Fibrosis Foundation

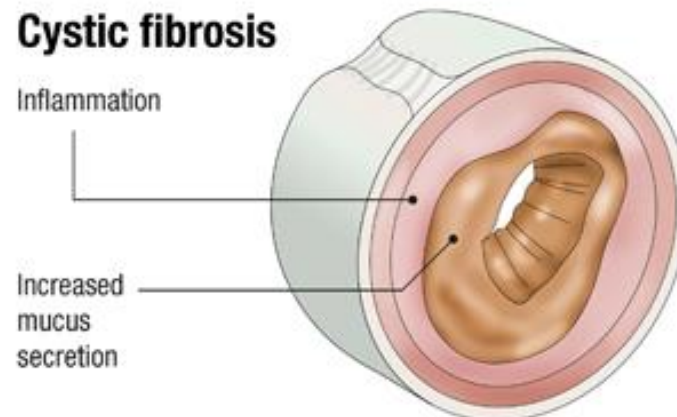
Cystic Fibrosis - symptoms

- Production of thick and sticky mucus and digestive fluids
- Blockade of airways and pancreatic duct
- Coughing, wheezing, inflammation, scar tissues (fibrosis) in the lungs, digestive problems

Healthy

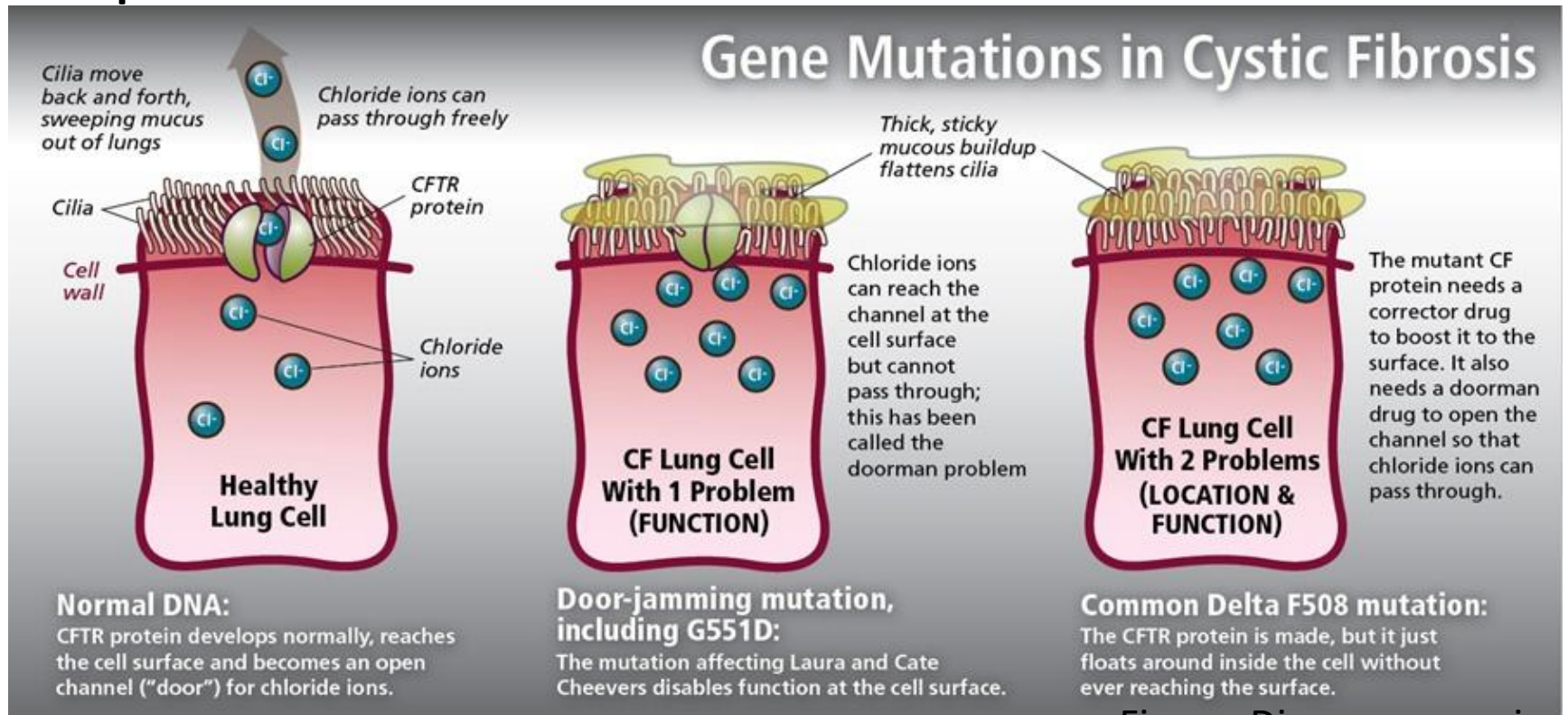


Cystic fibrosis



Cystic Fibrosis – Genetics & Pathophysiology

- Genetic disease – autosomal recessive
- Gene: *CFTR*, identified in 1989
- Incidence: 1 in 3,500 births; 30,000 CF patients in the US



Cystic Fibrosis – Diagnosis & treatment

Diagnosis – Genetic test, Sweat test

Treatment

- Antibiotics: e.g. azithromycin (oral), tobramycin (inhale)
- Mucolytic agents: acetylcysteine
- Bronchodilators
- Chest physical therapy

Manage symptoms and reduce complications,
doesn't treat underlying cause

The Cystic Fibrosis Foundation

- Founded in 1955 by a group of parents whose kids have CF
- Raised \$75M/year
- Invested over \$595M in academic research since late 1980s
- Funding led to discovery of the *CFTR* gene in 1989

CFF Therapeutics Development Program



Robert J. Beall, President & CEO of CFF:
“Our pipeline for CFTR modulators was dry,
and our financial supporters were getting anxious.”

1998: Established the therapeutics development program
to fund CF drug development in for-profit biotech companies

Discussion:

- Is it an easy decision for Dr. Beall to begin funding for profit ventures?
- What are some obstacles/risks he might face during this process?

Stakeholders:

Donors

Academic researchers

Biotech companies

CFF volunteers/employees

Largest Cystic Fibrosis Foundation grants by 2001

Company	Grants (\$ million)	Goal
Aurora Biosciences	\$46.9	Drugs to target deficient protein
Altus Biologics	25.0	Drug to replace missing digestive enzyme
Structural GenomiX	13.2	Identify the 3-D structure of key protein
Chiron	1.7	Drugs to target bacteria in lungs
Copernicus Gene System	0.5	Gene therapy

Source: "Drug Money," *Forbes*, April 2001, http://findarticles.com/p/articles/mi_kmfor/is_200104/ai_n15380079, accessed August 17, 2007.

Aurora Biosciences



- Founded by UCSD scientists Roger Tsien, Charles Zuker and Michael Geoffrey in 1995
- Develop high-throughput screening methods for drug discovery
- IPO in 1997
- Received \$46.9M funding from CFF in 2000
- Acquired by Vertex Pharmaceuticals in 2001

Vertex Pharmaceuticals



- Founded by Joshua Boger and Kevin Kinsella in 1989 in Boston
- IPO in 1991
- Strong pipeline in 2001: 12 drug candidates, 7 in phase II trials
- One approved drug: Amprenavir, HIV protease inhibitor (discovered by Vertex, licensed to Glaxo Wellcome)

THERAPEUTIC AREA	PRODUCT/TARGET	RESEARCH	PRECLINICAL	PHASE I	PHASE II	PHASE III	NDA/MRA	MARKET	MECHANISM OF ACTION	PARTNERS	VERTEX COMMERCIAL RIGHTS
HIV	Agenerase™	█	█	█	█	█	█	█	HIV protease inhibitor	Glaxo Wellcome Kissei	Co-promote (US/Europe) Supply (Japan)
	VX-175	█	█	█	█				HIV protease inhibitor	Glaxo Wellcome	Co-promote (US/Europe)
HEPATITIS C	VX-497	█	█	█	█				IMPDH inhibitor		Worldwide rights
	HCV protease inhibitor	█							HCV protease inhibitor	Eli Lilly	Co-promote (US); Supply (Worldwide)
	HCV helicase inhibitor	█							HCV helicase inhibitor		Worldwide rights
CANCER	Incel™	█	█	█	█				MDR reversal agent		Worldwide rights
	VX-853	█	█	█	█				MDR reversal agent		Worldwide rights
AUTOIMMUNE	VX-148	█	█						IMPDH inhibitor		Worldwide rights
INFLAMMATION	VX-740	█	█	█	█				ICE (caspase 1) inhibitor	Aventis	Co-promote (US/Europe)
	VX-745	█	█	█	█				p38 MAP kinase inhibitor	Kissei	Worldwide rights (ex-Asia); Supply (Asia)
NEUROLOGICAL	Timcodar	█	█	█	█				Neurophilin compound	Schering AG (option)	Profit sharing (US); Supply (Asia)
	Caspases	█							Caspase inhibitor	Taisho	Worldwide rights (ex-Asia); Supply (Asia)
	Kinases*	█							Kinase inhibitors	Novartis	Co-promote (US/Europe)

*Collaboration with Novartis includes kinases involved in neurological disease, cancer, inflammatory disease, and many other disease areas.

Discussion

After the acquisition of Aurora, should Vertex continue the partnership with the CFF?

Points to consider:

- Allocation of company's resources: CF vs other pipeline drugs
- Reactions from investors?
- Alignment of objectives: For-profit public company vs Non-profit foundation
- What are the advantages of philanthropic funding?

Kalydeco (ivacaftor)

- FDA approval in 2012
- First drug to treat the underlying cause of CF
- A CFTR potentiator → improves Cl^- transport
- Target patients with G551D mutation
- 4% of CF patients, ~1,200 in the US

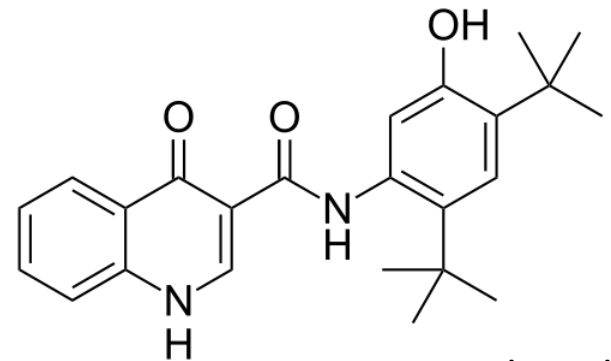


Figure: Wikipedia

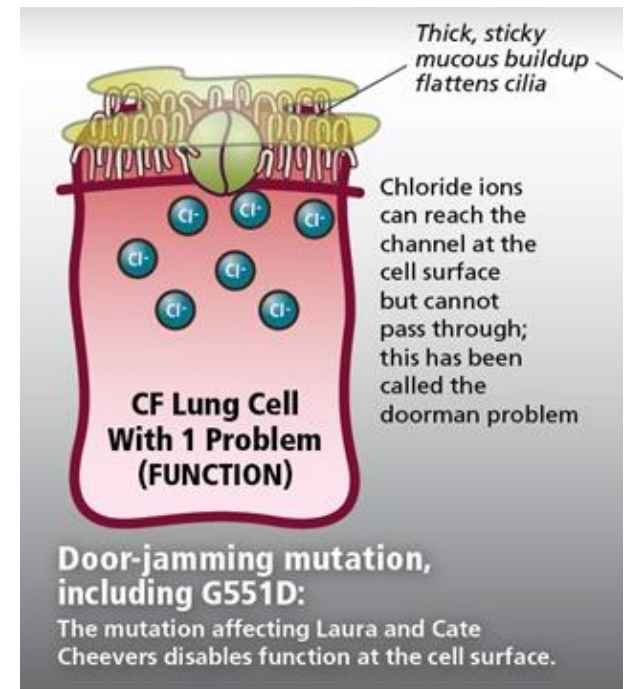


Figure: Discovermagazine.com

What's the price tag?

Is it more or less expensive than Sovaldi?

Sovaldi:

Treat Hepatitis C (~3M patients in the US)

\$1,000/day for 12 weeks (i.e. \$84,000)

Kalydeco:

Treat CF with G551D mutations (~1,200 patients in the US)

Life-long treatment

Kalydeco's price

- \$311,000/year (i.e. \$852/day)
- 54% of Vertex's revenue in 2014
- The CFF provided \$150M for the development of Kalydeco in return for royalty rights
- Sold the royalty rights for \$3.3B in 2014
- What do you think is the public opinion about this?

Orkambi (Ivacaftor + Lumacaftor)

- Target CF patients with the more common F508del mutation
- Lumacaftor: Chaperone → increase # of CFTR proteins on the cell surface
- FDA approval in 2015
- Price: \$259,000/year

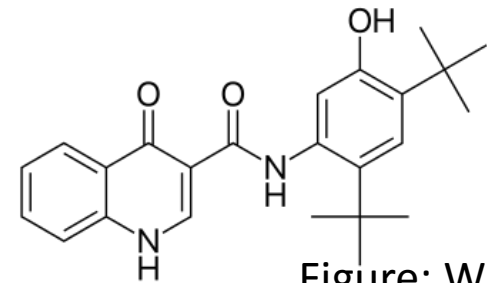
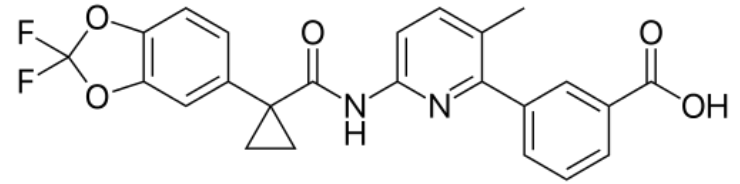


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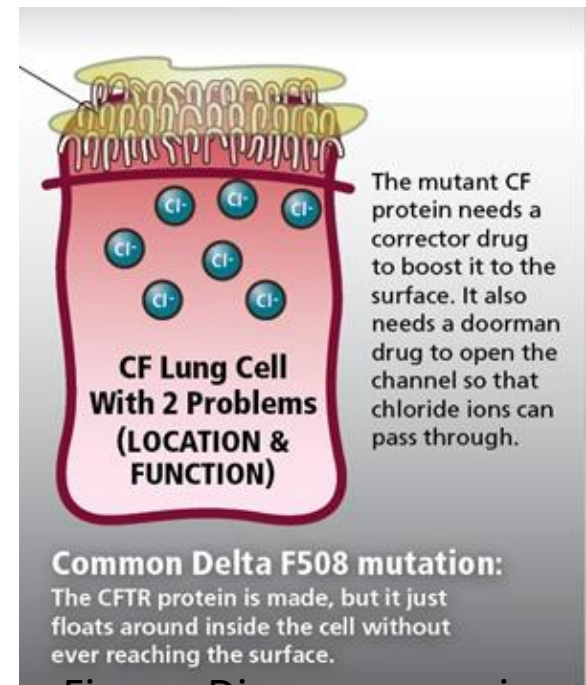


Figure: Discovermagazine.com

Other Venture Philanthropies

Charity (Focus)	Main Forms of Investment	Selected Firms Spun Out or (Co)-Seeded
Cystic Fibrosis Foundation	Royalties; milestone-based grants	
Project A.L.S.		
Alzheimer's Drug Discovery Foundation (Alzheimer's disease and cognitive aging)	Convertible notes; milestone-based grants	Allon Therapeutics; Zapaq
Juvenile Diabetes Research Foundation	Milestone-driven grants; equity; royalties	
Leukemia & Lymphoma Society (blood cancers)	Grants	
Michael J. Fox Foundation (Parkinson's)	Grants; royalties	
Stanley Medical Research Institute (schizophrenia & bipolar disorder)	Grants; equity; royalties	

Other Venture Philanthropies

Blanchette Rockefeller Neurosciences Institute (Alzheimer's & neurological disorders)	Equity	Neuroscience Research Venture, Inc.
ABC ² (brain cancer)	Grants	
ALS Therapy Development Foundation (Lou Gehrig's disease)	Grants; equity	Alsgen
Multiple Myeloma Research Foundation	Grants	
Melanoma Therapeutics Foundation	Equity; royalties	Accelerate Cancer Therapeutics (ACT Biotech)
Christopher Reeve Foundation		
Families of Spinal Muscular Atrophy	Grants	
Goldhirsch Foundation		

Source: Adapted from "Venture Philanthropy: The New Venture Capital?" *Start-Up Magazine*, March 2007.