

Repositioning Existing Drugs for Rare Diseases

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Rare Disease: A key focus for Pfizer



- Scientific opportunity
- Future therapeutic strategy
- Unmet need



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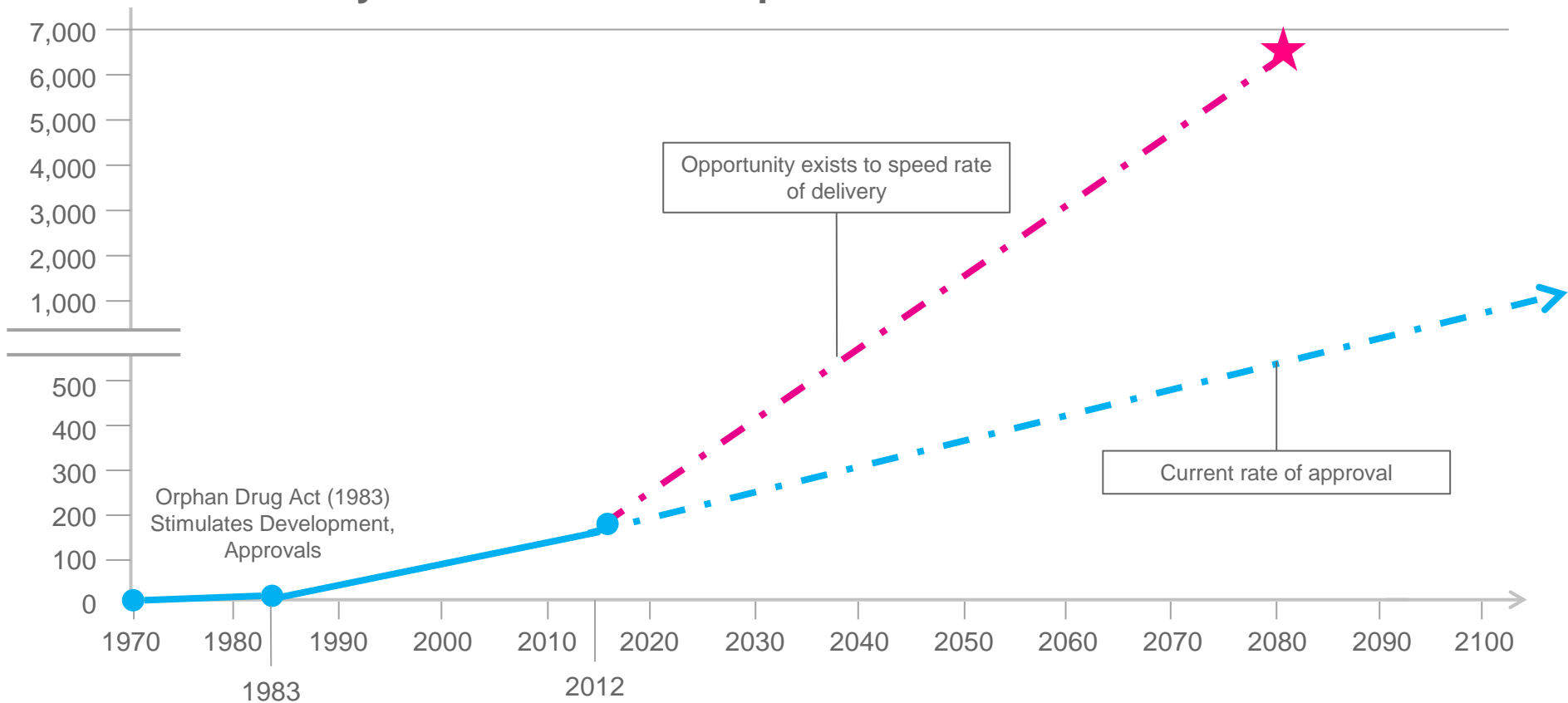
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Delivery of new therapies for rare diseases must be expedited



At the current rate of approval, it will take more than 500 years to deliver therapies for all rare diseases

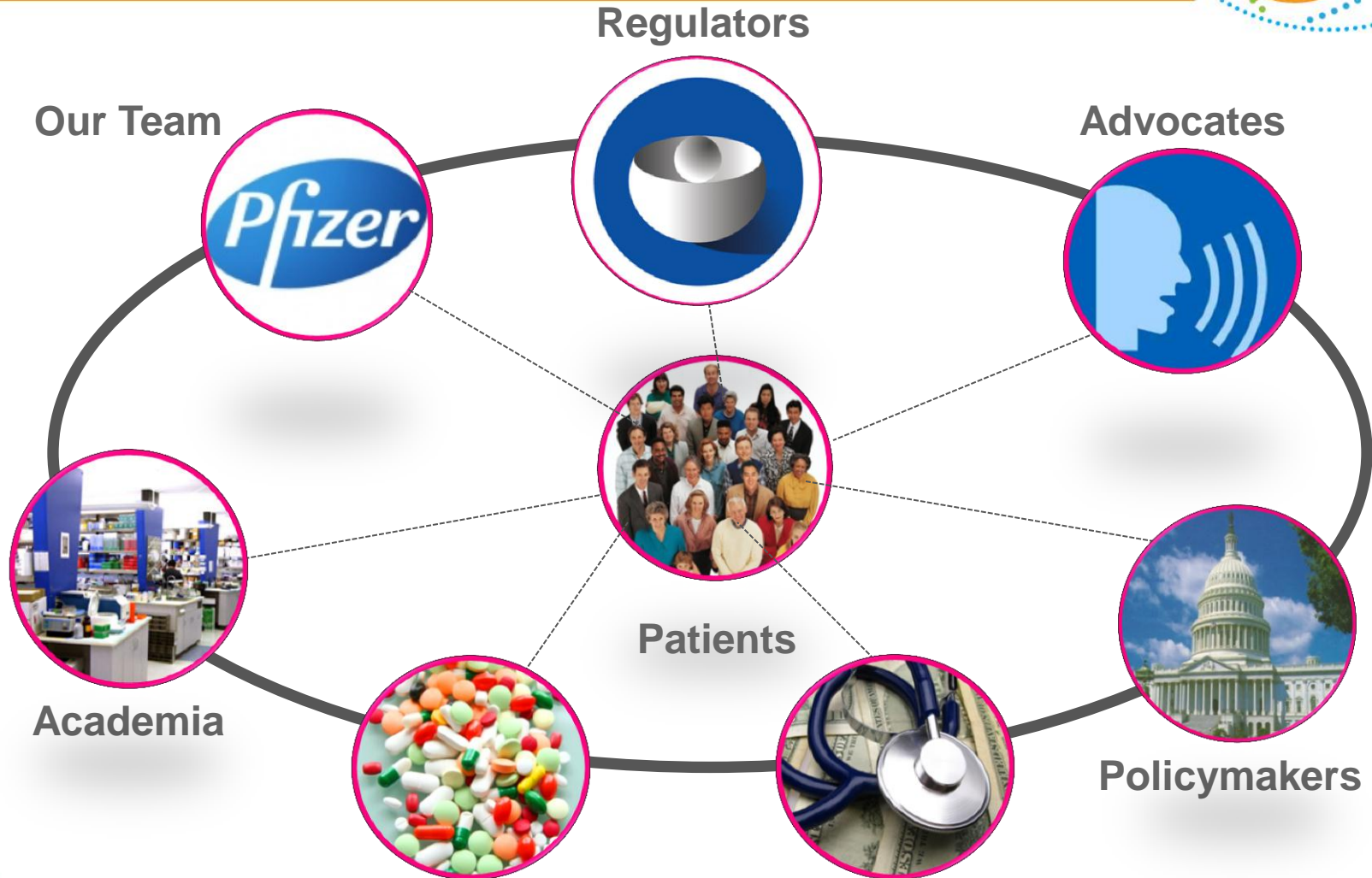


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We must work together if we are to deliver new medicines for rare diseases



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Industry

Payers

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Drug repurposing can deliver therapeutic opportunities



Pfizer Medicines with Indications in Non-Oncologic Rare Diseases

Atnativ[®]

Benefix[®]

Cerebyx[®]

Cordarone[®]

Elelyso[®]

Genotropin[®]

Mycobutin[®]

Refacto[®]

Revatio[®]

Somavert[®]

Vyndaqel[®]

Zinecard[®]

Pfizer Medicines with Indications in Rare Cancers

Aromasin[®]

Bosulif[®]

Ellence[®]

Idamycin[®]

Inlyta[®]

Methotrexate[®]

Neumega[®]

Novantrone[®]

Torisel[®]

Xalkori[®]

“Follow-on” Orphan indication

Oncology

Hematology

Other

Pulmonology

Neuroscience



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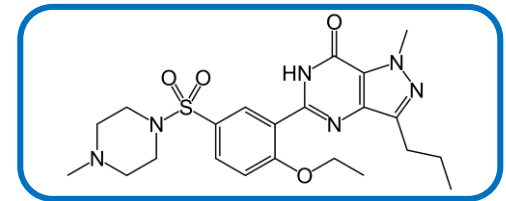
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Sildenafil – A PDE5 inhibitor



- PDE5 inhibition vasodilates via smooth muscle
- Initially targeted for angina
- Clinical studies led to repositioning for erectile dysfunction and launch as Viagra in 1998
- Subsequently investigated, and registered as Revatio for Pulmonary Arterial Hypertension



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Pulmonary Arterial Hypertension (PAH)



- Increase in pressure in the lung vasculature
- Mechanisms poorly understood
- Survival <10yrs
- Vascular fibrosis and heart failure

Sildenafil in Primary Pulmonary Hypertension

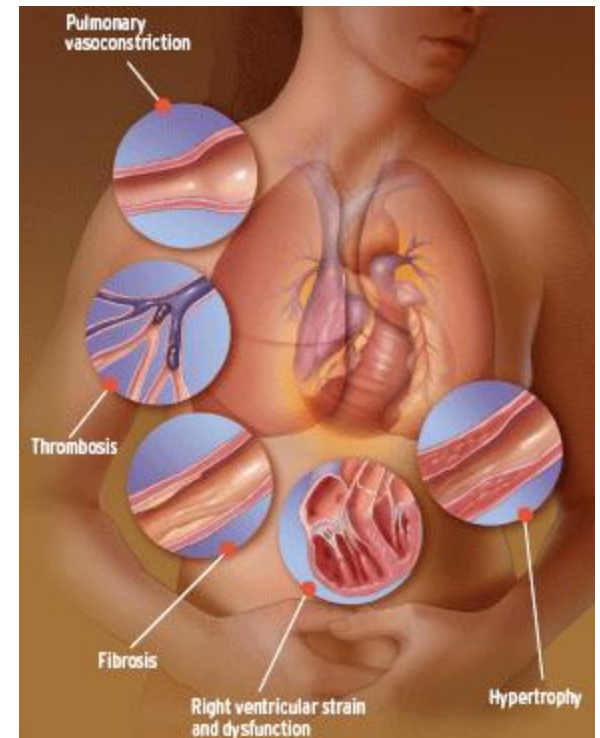
SANJAY PRASAD, M.R.C.P.

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NEJM (2000), 343, 1341



JAAPA May 2011



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Sildenafil in pulmonary arterial hypertension



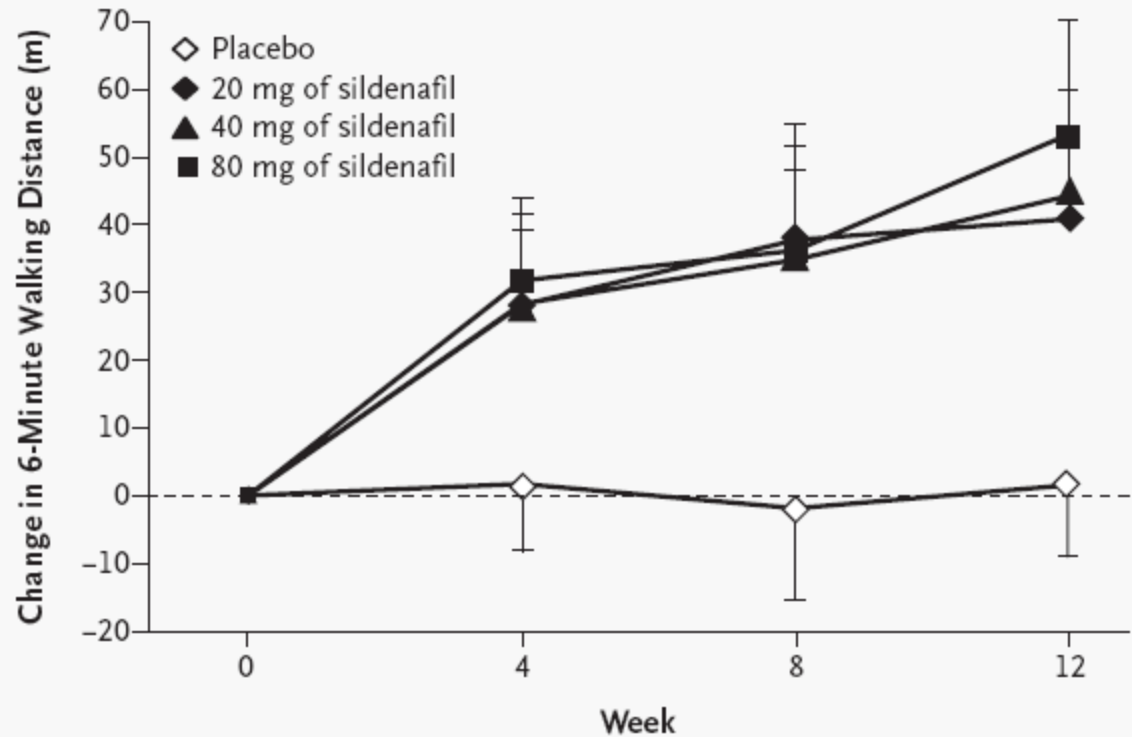
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Sildenafil Citrate Therapy for Pulmonary Arterial Hypertension

Nazzareno Galiè, M.D., Hossein A. Ghofrani, M.D., Adam Torbicki, M.D., Robyn J. Barst, M.D., Lewis J. Rubin, M.D., David Badesch, M.D., Thomas Fleming, Ph.D., Tamiza Parpia, Ph.D., Gary Burgess, M.D., Angelo Branzi, M.D., Friedrich Grimminger, M.D., Marcin Kurzyna, M.D., and Gérald Simonneau, M.D., for the Sildenafil Use in Pulmonary Arterial Hypertension (SUPER) Study Group

NEJM (2005), 353, 2148



- Viagra for Erectile Dysfunction – 25mg, 50mg or 100mg not more than once daily
- Revatio for Pulmonary Arterial Hypertension – 20mg three times daily



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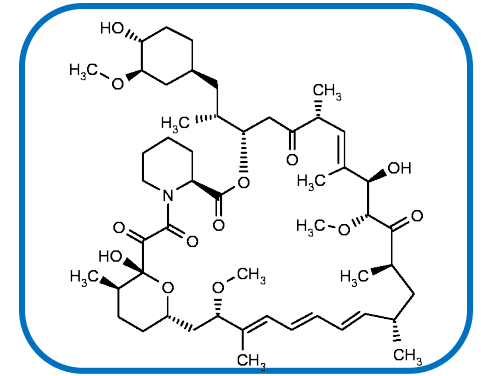
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Sirolimus – mTor inhibitor



- mTor inhibitor - immunosuppressive
- Developed for prophylaxis in organ rejection in renal transplantation
- Launched as Rapamune in 1999
- Biological knowledge led to investigation in Lymphangiomyomatosis (LAM)



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Lymphangiomyomatosis (LAM)

- Slowly progressing neoplasm that targets lungs
- Emerging mechanisms implicate mTor1 pathway
- Cystic destruction and respiratory failure over 1-2 decades

Sirolimus for Lymphangiomyomatosis Lesions

Jim J. Egan, M.D.

Kaspar Friedrich Remund, M.D.

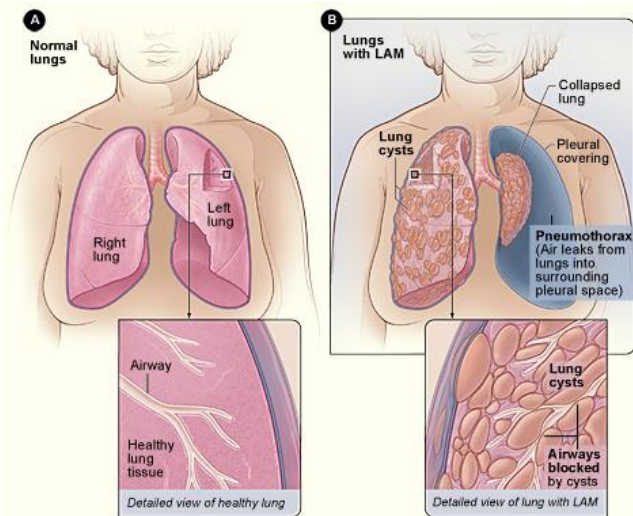
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NEJM (2008), 358, 1963

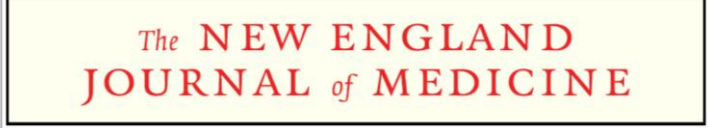


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Multicentre International LAM Efficacy and Safety of Sirolimus Study (MILES)

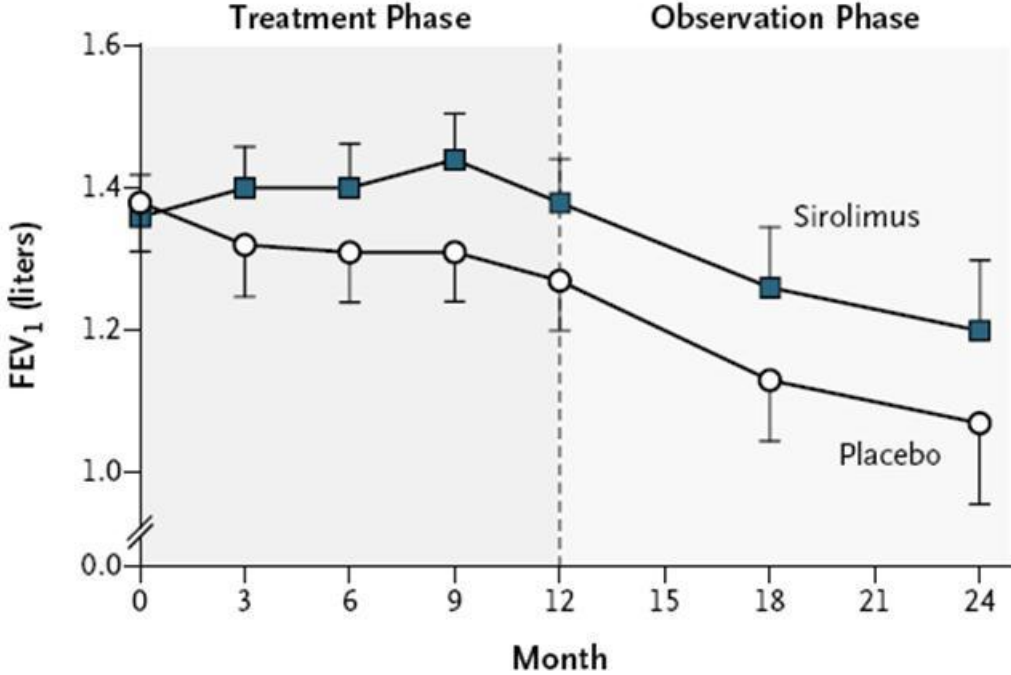


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Efficacy and Safety of Sirolimus in Lymphangioleiomyomatosis

Francis X. McCormack, M.D., Yoshikazu Inoue, M.D., Ph.D., Joel Moss, M.D., Ph.D., Lianne G. Singer, M.D., Charlie Strange, M.D., Koh Nakata, M.D., Ph.D., Alan F. Barker, M.D., Jeffrey T. Chapman, M.D., Mark L. Brantly, M.D., James M. Stocks, M.D., Kevin K. Brown, M.D., Joseph P. Lynch, III, M.D., Hilary J. Goldberg, M.D., Lisa R. Young, M.D., Brent W. Kinder, M.D., Gregory P. Downey, M.D., Eugene J. Sullivan, M.D., Thomas V. Colby, M.D., Roy T. McKay, Ph.D., Marsha M. Cohen, M.D., Leslie Korbee, B.S., Angelo M. Taveira-DaSilva, M.D., Ph.D., Hye-Seung Lee, Ph.D., Jeffrey P. Krischer, Ph.D., and Bruce C. Trapnell, M.D., for the National Institutes of Health Rare Lung Diseases Consortium and the MILES Trial Group*

NEJM (2011), 364, 1595



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Key Learnings



- Knowledge of the biological pathway can lead to new opportunities
- Early clinical pharmacology underpins successful repositioning
- Partnerships can define outcome



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Pfizer/NIH/NCATS Repositioning program



- Pfizer has made available to the NCATS program 17 molecules covering a range of molecular mechanisms
- Academic physician-scientists have career-long, hands-on insight into disease mechanisms and gaps in medical care
- Pfizer and 6 other companies making available 58 clinically ready compounds
- Call for proposals to investigate molecules in investigator-led studies
- Awards announced in May



National Center
for Advancing
Translational Sciences



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Summary



- Pfizer commitment to rare disease therapeutics
- Expedite delivery through partnership
- Repositioning is one mechanism
- Actively pursuing a number of collaborative models



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