Repositioning Existing Drugs for Rare Diseases

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Rare Disease: A key focus for Pfizer

• Scientific opportunity

• Future therapeutic strategy

• Unmet need
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

Opportunity exists to speed rate of delivery

Current rate of approval


At the current rate of approval, it will take more than 500 years to deliver therapies for all rare diseases.
We must work together if we are to deliver new medicines for rare diseases.
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
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
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.
James Wilkinson, M.R.C.P.
Michael A. Gatzoulis, M.D., Ph.D.

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NEJM (2000), 343, 1341

JAAPA May 2011
Sildenafil in pulmonary arterial hypertension

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

Sildenafil Citrate Therapy for Pulmonary Arterial Hypertension

Nazzareno Galié, 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., Tanmica Parpia, Ph.D., Gary Burgess, M.D., Angelo Branzi, M.D., Friedrich Griminger, M.D., Marcin Kurzyna, M.D., and Gérard Simonneau, M.D., for the Sildenafil Use in Pulmonary Arterial Hypertension (SUPER) Study Group

NEJM (2005), 353, 2148
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 Lymphangioleiomyomatosis (LAM)
Lymphangioleiomyomatosis (LAM)

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

*Sirolimus for Lymphangioleiomyomatosis Lesions*

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Kaspar Friedrich Remund, M.D.
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Paul Corris, M.D.
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NEJM (2008), 358, 1963
Multicentre International LAM Efficacy and Safety of Sirolimus Study (MILES)

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. Cello, M.D., Roy T. McKay, Ph.D., Marsha M. Cohen, M.D., Leslie Korbee, B.S., Angelo M. Tavares-Dasilva, M.D., Ph.D., Hye-Seung Lee, Ph.D., Jeffrey P. Krash, 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
Key Learnings

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

• Pfizer commitment to rare disease therapeutics

• Expedite delivery through partnership

• Repositioning is one mechanism

• Actively pursuing a number of collaborative models