

4. a. Paul, S. M.; Mytelka, D. S.; Dunwiddie, C. T.; Persinger, C. C.; Munos, B. H.; Lindborg, S. R.; Schacht, A. L. How to Improve R&D Productivity: The Pharmaceutical Industry's Grand Challenge. *Nat. Rev. Drug Discov.* **2010**, *9*, 203–214.
b. Munos, B. Lessons from 60 Years of Pharmaceutical Innovation. *Nat. Rev. Drug Discov.* **2009**, *8*, 959–968.
5. a. DiMasi, J. A.; Hansen, R. W.; Grabowski, H. G. The Price of Innovation: New Estimates of Drug Development Costs. *J Health Econ.* **2003**, *22*, 151–185.
b. *Research and Development in the Pharmaceutical Industry*; The Congress of the United States Congressional Budget Office, October 2006.
6. Exntance, A. Alzheimer's Failure Raises Questions about Disease-modifying Strategies. *Nat. Rev. Drug Discov.* **2010**, *9*, 749–751.
7. Berenson, A. *Pfizer Ends Studies on Drug for Heart Disease*; The New York Times, December 3, 2006.
8. a. Nissen, S. E.; Tardif, J. C.; Nicholls, S. J.; Revkin, J. H.; Shear, C. L.; Duggan, W. T.; Ruzyllo, W.; Bachinsky, W. B.; Lasala, G. P.; Tuzcu, E. M. Effect of Torcetrapib on the Progression of Coronary Atherosclerosis. *N. Engl. J. Med.* **2007**, *356* (13), 1304–1316.
9. a. Furberg, C. D.; Pitt, B. Withdrawal of Cerivastatin from the World Market. *Curr. Controlled Trials Cardiovas. Med.* **2001**, *2*, 205–207.
b. Psaty, B. M.; Furberg, C. D.; Ray, W. A.; Weiss, N. S. Potential for Conflict of Interest in the Evaluation of Suspected Adverse Drug Reactions: Use of Cerivastatin and Risk of Rhabdomyolysis. *J. Am. Med. Assoc.* **2004**, *292* (21), 2622–2631.
10. Karha, J.; Topol, E. J. The Sad Story of Vioxx, and What We Should Learn from it. *Cleveland Clin. J. Med.* **2004**, *71* (12), 933–939.
11. National Institutes of Health, RFA-RM-07-007. Clinical and Translational Science Award (U54), Part II: Full Text of Announcement, Section I: Funding Opportunity Description, Subsection 1: Research Objectives, Definitions. <http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-007.html>.
12. a. Rubio, D. M.; Schoenbaum, E. E.; Lee, L. S.; Schteingart, D. E.; Marantz, P. R.; Anderson, K. E.; Platt, L. D.; Baez, A.; Esposito, K. Defining Translational Research: Implications for Training. *Acad. Med.* **2010**, *85* (3), 470–475.
b. Houry, M. J.; Gwinn, M.; Yoon, P. W.; Dowling, N.; Moore, C. A.; Bradley, L. The Continuum of Translation Research in Genomic Medicine: How Can We Accelerate the Appropriate Integration of Human Genome Discoveries into Healthcare and Disease Prevention? *Genet. Med.* **2007**, *9* (10), 665–674.
13. a. Fischl, M. A.; Richman, D. D.; Grieco, M. H.; Gottlieb, M. S.; Volberding, P. A.; Laskin, O. L.; Leedom, J. M.; Groopman, J. E.; Mildvan, D. The Efficacy of Azidothymidine (AZT) in the Treatment of Patients with AIDS and AIDS-related Complex. A Double-blind, Placebo-controlled Trial. *N. Engl. J. Med.* **1987**, *317* (4), 185–191.
b. Brook, I. Approval of Zidovudine (AZT) for Acquired Immunodeficiency Syndrome. *J. Am. Med. Assoc.* **1987**, *258* (11), 1517.
14. a. Drusano, G. L.; Yuen, G. J.; Lambert, J. S.; Seidlin, M.; Dolin, R.; Valentine, F. T. Relationship between Dideoxyinosine Exposure, CD4 Counts, and P24 Antigen Levels in Human Immunodeficiency Virus Infection. A Phase 1 Trial. *Ann. Intern. Med.* **1992**, *116*, 562–566.
b. Kahn, J. O.; Beall, G.; Sacks, H. S.; Merigan, T. C.; Beltangady, M.; Smaldone, L.; Dolin, R.; Lagakos, S. W.; Richman, D. D.; Cross, A.; et al. A Controlled Trial Comparing Continued Zidovudine with Didanosine in Human Immunodeficiency Virus Infection. *N. Engl. J. Med.* **1992**, *327* (9), 581–587.
15. Atkinson, A. J.; Colburn, W. A.; DeGruttola, V. G.; DeMets, D. L.; Downing, G. J.; Hoth, D. F.; Oates, J. A.; Peck, C. C.; Schooley, R. T.; Spilker, B. A.; et al. Biomarkers and Surrogate Endpoints: Preferred Definitions and Conceptual Framework. *Clin. Pharmacol. Ther.* **2001**, *69* (3), 89–95.