
Patents, Partnerships, and the Pre-Competitive Collaboration Myth in Pharmaceutical Innovation

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Public-private partnerships offer a promising alternative paradigm for pharmaceutical innovation in complex disease areas where there are both strong commercial interests and significant public need. They have the potential to reduce the tremendous waste associated with duplicative unsuccessful drug development efforts and to encourage the sharing of knowledge essential to accelerate pharmaceutical innovation. Patents threaten the potential of partnership strategies, however, by making it harder to sustain robust systems of knowledge sharing. Policymakers have tried to avoid this problem by focusing partnership strategies on areas deemed to be pre-competitive — areas of collaboration without competition and typically also without patents.

This Article suggests that the current pre-competitive approach to partnership strategies in pharmaceutical innovation is fundamentally flawed for two reasons. First, it ignores the competitive market pressures that both shape what is deemed to be pre-competitive and fuel tensions

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within partnerships between sharing knowledge and staking out proprietary rights to gain competitive advantage. Second, it limits partnerships to areas where sharing already occurs instead of concentrating them in areas where greater sharing is badly needed but unlikely to occur.

Instead of a pre-competitive partnership strategy, we need a partnership strategy that works in areas of competitive collaboration. To support such a strategy, we need to recalibrate the balance of access and exclusion to knowledge that patents and other sources of exclusivity provide in the drug discovery and development process. The Article concludes that a targeted statutory patent fair use may begin to push the pharmaceutical industry towards more collaborative innovation, and that public and private efforts to accelerate cures for Alzheimer's disease provide a natural area for such an experiment.

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INTRODUCTION

Disease don't care if you're black or white, disease don't care if you're left or right, disease don't care if you're rich or poor, disease will find a way to come a-knocking at your door. So come on people won't you join me please? Let's get it all together and knock out disease¹

Progress in keeping our bodies alive has not been matched by progress in keeping our minds functioning as we live longer. As a result, a recent study suggests that Alzheimer's disease, the most common form of dementia, may now be the third rather than the sixth leading cause of death in the United States, just after heart disease and cancer.² Of the top ten leading causes of death, Alzheimer's disease stands alone as the only disease with no effective treatment.³ While Alzheimer's disease is ultimately fatal, the average patient can expect to live for as long as a decade after the onset of symptoms in a state of debilitating decline requiring extensive long-term care.⁴ This makes the disease one of the nation's most costly.⁵ The magnitude of the global economic costs imposed by Alzheimer's and related dementias is even more daunting.⁶ The burdens that this disease imposes on the

¹ See *A Conversation with Dr. Francis Collins, Director of the NIH*, DIANE REHM SHOW (Feb. 10, 2014, 10:00 AM ET), <http://thedianerehmshow.org/shows/2014-02-10/conversation-dr-francis-collins-director-nih>.

² See Bryan D. James et al., *Contribution of Alzheimer Disease to Mortality in the United States*, 82 *NEUROLOGY* 1045, 1045, 1049 (2014) (suggesting that number of deaths caused by Alzheimer's in the United States is higher than previously thought); Tara Bahrapour, *New Study Ranks Alzheimer's as Third Leading Cause of Death, After Heart Disease and Cancer*, WASH. POST (Mar. 5, 2014), http://www.washingtonpost.com/local/new-study-ranks-alzheimers-as-third-leading-cause-of-death-after-heart-disease-and-cancer/2014/03/05/8097a452-a48a-11e3-8466-d34c451760b9_story.html.

³ See Allan S. Vann, *The National Alzheimer's Project Act . . . Missed Opportunities from a Caregiver's Perspective*, 62 *J. AM. GERIATRICS SOC'Y* 966, 966 (2014).

⁴ See Gary W. Small et al., *Diagnosis and Treatment of Alzheimer Disease and Related Disorders: Consensus Statement of the American Association for Geriatric Psychiatry, the Alzheimer's Association, and the American Geriatrics Society*, 278 *J. AM. MED. ASS'N* 1363, 1364 (1997).

⁵ See *Alzheimer's Facts and Figures*, ALZHEIMER'S ASS'N, http://www.alz.org/alzheimers_disease_facts_and_figures.asp (last visited Jan. 3, 2014) (estimating direct costs to American society of caring for Alzheimer's patients at \$214 billion).

⁶ While international aspects are beyond the scope of this paper, the findings I reach here are considered in light of and are consistent with international treaty obligations and with the public interest in sharing knowledge. See Jerome H. Reichman, *Rethinking the Role of Clinical Trial Data in International Intellectual Property Law: The Case for a Public Goods Approach*, 13 *MARQ. INTELL. PROP. L. REV.* 1, 9 (2009) [hereinafter *Rethinking the Role*] (making the case for treating clinical trials

U.S. economy and its population will continue to grow as its population ages unless effective treatments are found.⁷

The substantial public interest in finding a way of preventing, delaying, or even just slowing the progression of Alzheimer's disease is matched by significant private sector interest in finding and commercializing an Alzheimer's drug.⁸ The profit to be reaped from producing an effective treatment for Alzheimer's is immense.⁹ Yet even with strong public and private incentives in place, and despite billions of dollars in public and private investment and scientific and technological advances that generate new ways of understanding the brain and its malfunctioning,¹⁰ traditional modes of proprietary commercial drug development have failed to produce effective treatments.¹¹ While these costly failures are often blamed on the complexity of the disease and the research challenges that it poses, this Article suggests that they are symptomatic of broader problems with the existing system of drug discovery and development.¹²

as public goods on national and international basis instead of treating them as private goods to improve pharmaceutical innovation).

⁷ See Ron Brookmeyer, Elizabeth Johnson, Kathryn Ziegler-Graham & H. Michael Arrighi, *Forecasting the Global Burden of Alzheimer's Disease*, 3 *ALZHEIMER'S & DEMENTIA* 186, 190 (2007) (estimating that by 2050, one in eighty-five persons worldwide could be living with Alzheimer's disease unless more effective interventions are found); Ryan McBride, *Pharma Counts Just 3 Alzheimer's Drug Wins in 13 Years (101 Losses!)*, *FIERCEBIOTECH* (Sept. 14, 2012), <http://www.fiercebiotech.com/story/pharma-counts-just-3-alzheimers-drug-wins-13-years-101-losses/2012-09-14> (estimating the disease cost \$200 billion in medical expenses alone, with a rise to \$1 trillion by 2050).

⁸ *But see* SOEREN MATTKE ET AL., RAND CORP., *THE NEW NEGLECTED DISEASES?: POLICY INTERVENTIONS ARE NEEDED TO ENCOURAGE CNS DRUG DEVELOPMENT* 1, 3 (2013), available at http://www.rand.org/content/dam/rand/pubs/perspectives/PE100/PE117/RAND_PE117.pdf (suggesting that the huge costs and high failure rates in disease areas like Alzheimer's are deterring pharmaceutical companies and that more private incentives are needed).

⁹ See Bertha Coombs, *The Race for Next-Generation Alzheimer's Drugs*, *CNBC* (Sept. 5, 2013, 2:30 PM ET), <http://www.cnn.com/id/101011893> (suggesting that profits could be as high as \$20 billion for a drug that can treat the disease itself, as opposed to simply treating the symptoms).

¹⁰ For a glimpse into the immense amount of data that can now be generated about the human brain, see, for example, Carl Zimmer, *Secrets of the Brain*, *NAT'L GEOGRAPHIC*, Feb. 2014, at 31.

¹¹ See Karen Chiang & Edward H. Koo, *Emerging Therapeutics for Alzheimer's Disease*, 54 *ANN. REV. PHARMACOLOGY & TOXICOLOGY* 381, 381 (2014) (noting that the failure of several recent large-scale Phase III trials suggests the need to reexamine mainstream hypotheses about the disease and "the need to explore alternatives in both clinical testing strategies and drug discovery targets").

¹² See Eduardo Porter, *A Dearth in Innovation for Key Drugs*, *N.Y. TIMES* (July 22, 2014), <http://www.nytimes.com/2014/07/23/business/a-dearth-of-investment-in-much-needed->

For decades, drugs for ailments such as Alzheimer's, diabetes, and cancer that have large commercial markets have been developed pursuant to a model that moves from largely publicly-funded and publicly-disseminated research on the nature of disease and ways of modifying the disease¹³ to a private, proprietary development process for promising drug candidates.¹⁴ Drug development has been primarily the domain of large and intensely secretive pharmaceutical companies.¹⁵ These companies have relied heavily on patent protection and trade secrecy to stake their claims in promising drug candidates as they push them through the long, expensive, and risky drug development process.¹⁶

drugs.html (suggesting that the economics of drug development are not aligned well with public health needs).

¹³ Basic research and early stage drug discovery has been largely the domain of non-commercial, publicly-funded academic research institutions and government labs, where researchers have shared their ideas and results openly through publications and other academic networks — although increasingly they have also patented drug-related discoveries. See, e.g., Arti K. Rai & Rebecca S. Eisenberg, *The Public Domain: Bayh-Dole Reform and the Progress of Biomedicine*, 66 LAW & CONTEMP. PROBS. 289 (2003) (discussing the negative impact of upstream shift in patenting on tradition of open science).

¹⁴ Researchers identify biological characteristics of disease that can be targeted by a drug in efforts to modify the disease, referred to as “drug targets,” and sometimes discover potential drugs, or “drug candidates” that impact drug targets in desired ways. Pharmaceutical companies focus on potential drug candidates and move them through the drug development and regulatory approval process. Biotechnology companies, often with close ties to research institutions, have also played an important role in research and discovery efforts, complicating the non-commercial practices of knowledge sharing that had dominated academic research in this area. See, e.g., Iain M. Cockburn, *The Changing Structure of the Pharmaceutical Industry*, 23 HEALTH AFF., 10 (2004) (explaining the impact of changes in organization of the pharmaceutical industry on R&D).

¹⁵ This paradigm of pharmaceutical innovation has never worked well for neglected diseases or for many rare diseases, where the commercial returns are too low to attract the interest of large pharmaceutical companies. In the past, however, it has seemed to work well for diseases with significant commercial markets. Blockbuster drugs such as Lipitor, which lowers cholesterol, and Plavix, a blood thinner, have addressed medical problems for millions of people while also racking up hefty profits for pharmaceutical companies. See, e.g., Alex Kandybin & Vessela Genova, *Big Pharma's Uncertain Future*, STRATEGY+BUS. (Feb. 28, 2012), <http://www.strategy-business.com/article/00095> (suggesting era of blockbuster drugs that solve medical problems for large parts of the population, like Lipitor, Zyprexa, and Plavix is coming to an end).

¹⁶ Development efforts include applied research to identify and investigate the properties of promising drug candidates, testing the potential drugs in clinical trials to see if they are safe and effective in patients, and moving to large-scale production and marketing of the drugs if they are approved by the U.S. Food and Drug Administration

The approach has persisted with relatively little change. Even as research and development costs have soared, the number of costly failures of drug candidates in late stages of development has increased, and the number of new drugs reaching the market has dropped.¹⁷ It is estimated that bringing a new drug to the market now costs over one billion dollars, and only 20% of approved drugs make enough money to recover their research and development costs.¹⁸ The chance, when starting a drug development program, of actually getting a drug approved for sale by the Food and Drug Administration (“FDA”) ten or more years later is now well under 1%, and many of the failures occur in late stages of development after much time and money has been wasted.¹⁹ The costs and the odds for success of drug development programs targeting Alzheimer’s disease are even worse.²⁰ While

(“FDA”) for use to treat the specified disease(s). For a good summary of the development process, see, for example, Gregory A. Petsko, *When Failure Should Be the Option*, 8 BMC BIOLOGY 61 (2010). Before a drug can be sold, it must be approved by the FDA. Obtaining regulatory approval requires extensive clinical testing, including Phase I trials that test the experimental drug for safety on a small group of people, Phase II trials that test for safety and efficacy of the drug on a larger group, and Phase III trials that test the drug for efficacy on a large group of people. See *FAQ: ClinicalTrials.gov — Clinical Trial Phases*, U.S. NAT’L LIBRARY OF MED., NAT’L INSTS. OF HEALTH, <http://www.nlm.nih.gov/services/ctphases.html> (last visited Jan. 4, 2015). For an interesting and more detailed discussion of the traditional paradigm and how it has changed, see R.L. Juliano, *Pharmaceutical Innovation and Public Policy: The Case for a New Strategy for Drug Discovery and Development*, 40 SCI. & PUB. POL’Y 393, 393-94 (2013).

¹⁷ See Chris Cain, *Making the Case for Precompetitive Clinical Development*, 4 SCI.-BUS. EXCHANGE, no. 20 (May 19, 2011), <http://www.nature.com/scibx/journal/v4/n20/full/scibx.2011.562.html> [hereinafter *Making the Case*] (“Globally, the industry is spending \$160 billion a year on R&D and only getting 3–5 novel drugs targeting pioneer mechanisms per year.”); Fabio Pammolli, Laura Magazzini & Massimo Riccaboni, *The Productivity Crisis in Pharmaceutical R&D*, 10 NATURE REVIEWS DRUG DISCOVERY 428, 428 (2011). There is also a shift in the focus of pharmaceutical companies away from areas of large public health impact like antibiotics and Alzheimer’s and towards rare diseases. See, e.g., MATTKE ET AL., *supra* note 8 (investigating the disconnect between unmet health needs and private investment in drug development).

¹⁸ See Ish Khanna, *Drug Discovery in Pharmaceutical Industry: Productivity Challenges and Trends*, 17 DRUG DISCOVERY TODAY 1088, 1089 (2012).

¹⁹ See Anna Edney, *Alzheimer’s Therapy May Come from New Look at Old Drugs*, BLOOMBERG (Apr. 11, 2014, 10:11 AM PT), <http://www.bloomberg.com/news/2014-04-11/alzheimer-s-therapy-may-come-from-new-look-at-old-drugs.html> (estimating about 60% of mid-stage clinical trials and about 40% of final-stage trials are not successful, with significantly worse odds in areas such as Alzheimer’s).

²⁰ See Matthew Herper, *How a Failed Alzheimer’s Drug Illustrates the Drug Industry’s Gambling Problem*, FORBES (Aug. 8, 2012, 4:17 PM), <http://www.forbes.com/sites/matthewherper/2012/08/08/how-a-failed-alzheimers-drug-illustrates-the-drug->

inadequacies in existing approaches to drug discovery and development are easy to identify,²¹ industry incumbents show little interest in restructuring their role in the drug development process and policymakers have been slow to intervene.²² Things are only slowly starting to change.

Public-private partnerships²³ have emerged as among the most promising, and certainly the most popular, strategies for improving innovation outcomes in complex major disease areas such as Alzheimer's, diabetes, and cancer.²⁴ By pooling resources and expertise, increasing knowledge sharing, and reducing duplication of efforts and mistakes, public-private partnerships have the potential to reach public health goals that have eluded each sector acting independently.²⁵

industrys-gambling-problem/.

²¹ See, e.g., Daniel J. Chandler, *Something's Got to Give: Psychiatric Disease on the Rise and Novel Drug Development on the Decline*, 18 *DRUG DISCOVERY TODAY* 202 (2013) (discussing factors contributing to the decline in R&D for psychiatric illnesses); Peter T. Lansbury, Jr., *Back to the Future: The 'Old-Fashioned' Way to New Medications for Neurodegeneration*, 5 *NATURE REVIEWS NEUROSCIENCE* S51 (2004) (identifying obstacles to effective drug discovery for neurodegeneration); Kandybin & Genova, *supra* note 15 ("It is doubtful whether big pharmaceutical companies will be able to pursue these goals [of alleviating disease] within the old model of developing exclusive new pills that they can sell under patent protection.").

²² See Juliano, *supra* note 16, at 395.

²³ Public-private partnerships, as defined in this Article, are formal contractual arrangements between at least one public (government) and at least one private (commercial) party to share risk, costs, knowledge, and decision-making in joint projects to achieve agreed upon public health goals.

²⁴ See Michel Goldman, Carolyn Compton & Barbara B. Mittleman, *Public-Private Partnerships As Driving Forces in the Quest for Innovative Medicines*, *CLINICAL & TRANSLATIONAL MED.*, Jan. 2013, at 1, 2; see also WORLD HEALTH ORG., *PRIORITY MEDICINES FOR EUROPE AND THE WORLD: 2013 UPDATE – NEW APPROACHES TO PROMOTING INNOVATION* 185-207 (2013), available at <http://apps.who.int/medicinedocs/documents/s20222en/s20222en.pdf>. Indeed, public-private partnerships between government agencies such as the National Institutes of Health ("NIH") and the FDA, pharmaceutical companies, biotech companies, academic institutions, and other stakeholders, now form a critical part of current U.S. innovation strategies to combat Alzheimer's disease. See, e.g., *The BRAIN Initiative: Public-Private Partnership to Map the Function of the Human Brain*, *BRAIN & BEHAV. RES. FOUND. Q.*, Summer 2013, at 7, 7, available at https://bbrfoundation.org/sites/bbrf.civicaactions.net/files/file-downloads/the-quarterly-summer-2013_0.pdf (describing the purpose of President Barack Obama's BRAIN Initiative); *NIH and Other Public Private Partnerships to Research Treatments for Multiple Diseases*, *POLY & MED.* (Oct. 4, 2013), <http://www.policymed.com/2013/10/nih-and-other-public-private-partnerships-to-research-treatments-for-multiple-diseases.html> (describing a number of public-private collaborations involving the NIH); see also *BRAIN Initiative*, WHITE HOUSE (Sept. 30, 2014), <http://www.whitehouse.gov/share/brain-initiative>.

²⁵ See Maria C. Carrillo, *Leveraging Global Resources to End the Alzheimer's*

Unfortunately, current knowledge of how to make these partnerships work effectively in environments where commercial interests are strong is limited.²⁶ Wary of the challenges that patents and other market-based incentives can create for public-private partnerships, policymakers have focused their efforts on areas of drug discovery and development deemed to be pre-competitive — areas of collaboration without competition. This typically confines partnerships to limited areas of early stage research where the knowledge, results, and materials that are shared do not — at least purportedly — confer a competitive advantage by being shared. In many cases the collaborators agree not to patent in these areas. This approach has the effect of segmenting the pharmaceutical innovation process into areas deemed by private participants to be pre-competitive, often with contractual restrictions on patenting and requirements to share information, and areas that are driven by competitive market forces.²⁷

This Article addresses a gap in the innovation law and policy literature by exposing two fundamental flaws with the reliance on pre-

Pandemic, 9 ALZHEIMER'S & DEMENTIA 363, 363 (2013) (“[C]ooperation and collaborative research development offer the most expedient and efficient option to organize research teams moving forward.”); Bernard H. Munos & William W. Chin, *A Call for Sharing: Adapting Pharmaceutical Research to New Realities*, SCI. TRANSLATIONAL MED., Dec. 2, 2009 at 1, 1 (2009).

²⁶ Public-private partnerships have been used extensively in the discovery and development of drugs for neglected diseases and many orphan diseases, areas that have been largely ignored by the private sector, but they are relatively new in disease areas that have major economic markets and significant pharmaceutical company interest. See MARY MORAN ET AL., LONDON SCH. OF ECON. & POLITICAL SCI., *THE NEW LANDSCAPE OF NEGLECTED DISEASE DRUG DEVELOPMENT* 1, 13-14 (2005), available at http://www.policycures.org/downloads/The_new_landscape_of_neglected_disease_drug_development.pdf; Roy Widdus, *Public-Private Partnerships for Health: Their Main Targets, Their Diversity, and Their Future Directions*, 79 BULL. WORLD HEALTH ORG. 713, 718 (2001), available at <http://www.scielosp.org/pdf/bwho/v79n8/v79n8a06.pdf> (noting the need for development of good practices for public-private partnerships for health); see, e.g., Constance E. Bagley & Christina D. Tvarno, *Pharmaceutical Public-Private Partnerships in the United States and Europe: Moving from the Bench to the Bedside* 1 (Yale Law Sch. Lecturer & Other Affiliate Scholarship Series, Paper No. 12, 2013), available at <http://digitalcommons.law.yale.edu/ylas/12> (discussing recent public-private initiatives to accelerate drug development in the pharmaceutical industry).

²⁷ See Chris Cain, *A Mind for Precompetitive Collaboration*, 5 SCI.-BUS. EXCHANGE, no. 19 (May 17, 2012), <http://www.nature.com/scibx/journal/v5/n19/full/scibx.2012.483.html>; STEVE OLSON & ADAM C. BERGER, INST. OF MED. OF THE NAT'L ACADS., *ESTABLISHING PRECOMPETITIVE COLLABORATIONS TO STIMULATE GENOMICS-DRIVEN PRODUCT DEVELOPMENT: WORKSHOP SUMMARY* 13-15 (2011), available at <http://www.ncbi.nlm.nih.gov/books/NBK54322/pdf/TOC.pdf>.

competitive partnerships to spur pharmaceutical innovation.²⁸ First, the pre-competitive approach to public-private partnerships ignores both the competitive ways in which the boundaries of these partnerships are fashioned and the inevitable tensions within them between cooperative and competitive mechanisms for the production and sharing of knowledge. Second, this approach limits partnerships to areas of intellectual production where knowledge sharing is already likely to occur rather than concentrating them in areas where greater sharing of knowledge is badly needed.

Instead of trying to segment the innovation process into competitive areas that are left to the market and seemingly pre-competitive areas where partnerships play a role, policymakers should encourage public-private partnerships in areas of drug discovery and development that are inherently competitive but also in need of greater collaboration. In order to do so, they need to find ways of mitigating the negative effects of market incentives on cooperation without removing market incentives altogether from this process. This requires strategies for confronting and reducing the tensions between private and public incentives to create and share knowledge.²⁹ The Article suggests that these tensions can be reduced by recalibrating the balance of access to and exclusion from knowledge that patents and other intellectual property rights, along with data exclusivity rules, provide in areas where both cooperative and competitive approaches to the production and sharing of knowledge are important.³⁰ It proposes a modest change in patent law — a limited statutory patent fair use — as one

²⁸ For a definition of pharmaceutical innovation, see, for example, Steven Morgan, Ruth Lopert & Devon Greyson, *Toward a Definition of Pharmaceutical Innovation*, 2 OPEN MED. E4, E4-E5 (2008).

²⁹ This focus on public-private partnerships as alternatives to other forms of transacting has natural analogues in theories of the firm and the roles that intellectual property can play in shaping firm boundaries. For a few of the many contributions, see, for example, Dan L. Burk, *Intellectual Property and the Firm*, 71 U. CHI. L. REV. 3 (2004); Dan L. Burk & Brett H. McDonnell, *The Goldilocks Hypothesis: Balancing Intellectual Property Rights at the Boundary of the Firm*, 2007 U. ILL. LAW REV. 575; Paul J. Heald, *A Transaction Costs Theory of Patent Law*, 66 OHIO ST. L.J. 473 (2005); Robert P. Merges, *Of Property Rules, Coase, and Intellectual Property*, 94 COLUM. L. REV. 2655 (1994).

³⁰ Tania Bubela, Garret A. FitzGerald & E. Richard Gold, *Recalibrating Intellectual Property Rights to Enhance Translational Research Collaborations*, SCI. TRANSLATIONAL MED., Feb. 2012, at 1, 3-4. See generally Arti K. Rai, “Open and Collaborative” Research: A New Model for Biomedicine, in INTELLECTUAL PROPERTY RIGHTS IN FRONTIER INDUSTRIES 131 (2005) (exploring models of open and collaborative biomedical innovation, and tensions between open systems and need for downstream market incentives to develop products).

way of beginning a process of recalibration that could facilitate an industry shift towards more collaborative drug discovery and development.³¹

This Article proceeds as follows. Part I shows how the traditional drug development paradigm has failed for Alzheimer's disease and describes the emergence of public-private partnerships for drug discovery and development as innovation strategies to address the failure.³² It identifies unique features of public-private partnerships that enable them to increase knowledge sharing and reduce waste, but also notes the challenges that patents can create for these partnership strategies. Part II describes the policy focus on pre-competitive public-private partnerships as a response to patent challenges.³³ It goes on to expose two fundamental flaws with the current pre-competitive partnership strategy. Part III suggests that instead of focusing on pre-competitive strategies, policymakers need to confront the challenges that patents create for partnerships directly.³⁴ It proposes a targeted statutory patent fair use as one way of beginning to rebalance access to and exclusion from knowledge in ways that promote collaborative innovation in areas that are inherently competitive.³⁵ The Article concludes that the concerted public-private efforts to cure Alzheimer's disease provide a natural area to experiment with a statutory patent fair use as a component of partnership strategies.

³¹ This incremental approach is not without risks. Relying on this kind of incremental change in patent rules may have the unintended consequence of deterring a more radical shift in the ways in which knowledge is shared and the benefits of contributions to the innovation process distributed. In addition, allowing for a limited patent fair use might serve to reinforce the patent owner's rights outside of permitted fair uses, and patent owners might extract additional protections outside of the area of permitted fair use in return.

³² See *infra* Part I.

³³ See *infra* Part II.

³⁴ See *infra* Part III. While I focus on challenges that patents may create for public-private partnerships, I recognize that patents may also play facilitating roles in creating and sustaining partnerships. The policy experiment that I explore seeks to mitigate the negative effects of patents on certain kinds of cooperation in a way that preserves other beneficial functions that patents may play in sustaining collaborative innovation.

³⁵ This is clearly not the only way in which we could start to recalibrate both access rights to knowledge and benefits from the fruits of knowledge, and I am not claiming that this is the best way. While a comparative analysis of alternative mechanisms is beyond the scope of this paper, it is part of my larger project. For now, I simply claim that this is a potentially feasible intervention that could improve upon the status quo.

I. PUBLIC-PRIVATE PARTNERSHIPS AS INNOVATION STRATEGIES

Alzheimer's is the cleverest thief, because she not only steals from you, but she steals the very thing you need to remember what's been stolen.³⁶

Therapies remain as elusive as memories for people with Alzheimer's disease.³⁷ As a result, Alzheimer's disease continues to claim a growing number of people as the U.S. population ages. This Part provides a picture of how the traditional drug discovery and development paradigm has failed in a striking way to combat Alzheimer's disease, and describes the emergence of public-private partnerships as key innovation strategies. It focuses attention on a critical function that public-private partnerships can play in the discovery and development process, and patent barriers that may impede them from performing this function.

A. *Failure of Traditional Paradigm*

Ten years ago people talked confidently of stopping Alzheimer's disease in its tracks. Now, they realise they have no idea how to do that.³⁸

Alzheimer's disease is an irreversible, progressive brain disease that slowly destroys brain function.³⁹ The incidence of the disease increases dramatically with age, which means that as growing populations age the burden of Alzheimer's disease increases.⁴⁰ By 2030 as many as 7.7

³⁶ JAROD KINTZ, *THIS BOOK HAS NO TITLE* (2012).

³⁷ See, e.g., Liesi E. Hebert et al., *Alzheimer Disease in the United States (2010–2050) Estimated Using the 2010 Census*, 80 *NEUROLOGY* 1778, 1778 (2013) (estimating the total number of people with AD dementia in the United States in 2050 projects to be 13.8 million, with 7 million aged eighty-five or older); Dennis J. Selkoe, *The Therapeutics of Alzheimer's Disease: Where We Stand and Where We Are Heading*, 74 *ANNALS NEUROLOGY* 328, 328 (2013) (“[R]esearch funding from all sources will need to increase dramatically and soon to stave off the approaching tsunami of AD.”).

³⁸ *Alzheimer's Disease: No End to Dementia*, *ECONOMIST* (June 17, 2010), <http://www.economist.com/node/16374470>.

³⁹ Alzheimer's disease as used in this paper refers to Alzheimer's disease and closely related dementias based on the approach followed in the National Plan. The disease leads to decline in cognitive functions such as memory, language functioning and ability to make decisions, along with behavioral and psychiatric disorders and general decline in the ability to function independently. See U.S. DEP'T OF HEALTH & HUMAN SERVS., *NATIONAL PLAN TO ADDRESS ALZHEIMER'S DISEASE: 2013 UPDATE 4* (2013), available at <http://aspe.hhs.gov/daltcp/napa/NatlPlan.pdf>.

⁴⁰ Alzheimer's disease is already the sixth leading cause of death in the United States and it threatens to one day become the leading cause of death and disability. In

million people in the United States may have Alzheimer's disease, and by 2050 this number may increase to as many as 16 million people.⁴¹ On a global level, approximately 44 million people worldwide have Alzheimer's or some other dementia, with that number expected to reach a projected 135 million people in 2050.⁴² There is no cure and the disease ultimately results in death, but the average patient may live in a state of continual decline requiring long-term care for a decade after the initial appearance of symptoms.⁴³ This makes Alzheimer's not only one of the most frightening, but also one of the most costly, diseases. Indeed, the disease burden in the United States alone is estimated to cost over \$200 billion annually with projections to reach \$1.2 trillion by 2050.⁴⁴

The urgency of finding an effective treatment is clear. Unfortunately, how to find an effective treatment is much less clear. Alzheimer's disease was first documented in 1906 by Dr. Alois Alzheimer, a German doctor who discovered abnormal clumps and tangled bundles of fibers in the brain tissue of a woman who had memory loss and other signs of cognitive decline.⁴⁵ These clumps, now referred to as

2012 there were an estimated 5.3 million Americans with Alzheimer's disease, with an associated annual cost of more than \$150 billion. John Q. Trojanowski et al., *A Model for Improving the Treatment and Care of Alzheimer's Disease Patients Through Interdisciplinary Research*, 8 *ALZHEIMER'S & DEMENTIA* 564, 565 (2012). While estimates vary, current studies suggest that about one out of every nine Americans who are sixty five or older have Alzheimer's disease, and about one third of Americans who are eighty five or older have Alzheimer's disease. See, e.g., *ALZHEIMER'S ASS'N, 2013 ALZHEIMER'S DISEASE FACTS AND FIGURES 15* (2013), available at http://www.alz.org/downloads/facts_figures_2013.pdf (reporting Alzheimer's statistics in the United States).

⁴¹ Trojanowski et al., *supra* note 40, at 565; see also *ALZHEIMER'S ASS'N, supra* note 40, at 20.

⁴² See Press Release, Alzheimer's Ass'n, G8 Countries Collectively Agree to Goals Including Mirroring the U.S. National Alzheimer's Plan to Find a Cure and Treat Dementia by 2025, at 2 (Dec. 11, 2013), available at http://www.alz.org/documents_custom/g8_summit_121113.pdf. See generally *September Is World Alzheimer's Month*, CTRS. FOR DISEASE CONTROL & PREVENTION, <http://www.cdc.gov/features/worldalzheimersday/> (last visited Jan. 9, 2015) (providing facts and other information about Alzheimer's).

⁴³ See, e.g., Small et al., *supra* note 4, at 1364 ("The average course of AD is approximately a decade, with a range of 3 to 20 years duration from diagnosis to death . . .").

⁴⁴ *Record \$122 Million Increase for Alzheimer's Disease Signed into Law by President Obama*, *ALZHEIMER'S ASS'N* (Jan. 17, 2014), http://www.alz.org/news_and_events_law_by_Obama.asp.

⁴⁵ Dr. Alzheimer described the "haunting case of Auguste D., a patient who had profound memory loss, unfounded suspicion about her family, and other worsening psychological changes. In her brain at autopsy, he saw dramatic shrinkage and

amyloid or brain plaques, and tangled bundles, now known as neurofibrillary tangles, along with loss of connections between neurons in the brain, remain the central known features of Alzheimer's disease.⁴⁶ By 1976 Alzheimer's was already recognized not only as the most common form of dementia but also as a major public health challenge, but the first clinical trial for an Alzheimer's drug did not occur until 1987.⁴⁷ Drug discovery and development efforts have ramped up since then, but with no success in finding an effective treatment for the disease.⁴⁸

The failure to find effective therapies for Alzheimer's disease is not due to a lack of private market development efforts. Since 1998 there have been more than 100 failed attempts by pharmaceutical companies to find effective treatments for Alzheimer's disease, many failing only in late stages of clinical testing.⁴⁹ As of 2010 there were a reported seventy-nine potential new therapies for Alzheimer's in development.⁵⁰ Recent expensive and disappointing clinical trial results include the failures of two experimental drugs in late stages of clinical testing, one developed by Pfizer, one of the largest pharmaceutical companies, and the other by Eli Lilly.⁵¹ Pfizer has subsequently halted its research efforts on this failed new drug, while Eli Lilly remains optimistic that its drug might work if tried on patients at earlier stages of the disease.⁵² Despite disappointing results, and expectations of more

abnormal deposits in and around nerve cells." *Major Milestones in Alzheimer's and Brain Research*, ALZHEIMER'S ASS'N, http://www.alz.org/research/science/major_milestones_in_alzheimers.asp (last visited Jan. 9, 2015).

⁴⁶ NAT'L INST. ON AGING, ALZHEIMER'S DISEASE: FACT SHEET (2011), available at http://www.nia.nih.gov/sites/default/files/alzheimers_disease_fact_sheet_1.pdf.

⁴⁷ See, e.g., *Major Milestones in Alzheimer's and Brain Research*, *supra* note 45 (naming tacrine as the first Alzheimer's-specific drug to go through clinical trials).

⁴⁸ For an overview of the search for treatments for Alzheimer's, including current research directions, see, for example, Jonathan S. Bor, *The Search for Effective Alzheimer's Therapies: A Work in Progress*, 33 HEALTH AFF. 527 (2014).

⁴⁹ Maria Thompson, *Alzheimer's Drug Development Costs Soar to a New High*, OPEN EXCHANGE: AN ASSAY DEPOT BLOG (May 30, 2013, 10:17 PM), <http://blog.assaydepot.com/2013/05/drug-development-costs-alzheimers/>.

⁵⁰ See Neil S. Buckholtz et al., *NIA Commentary: Translational Issues in Alzheimer's Disease Drug Development*, 37 NEUROPSYCHOPHARMACOLOGY REVIEWS 284, 284 (2012).

⁵¹ See, e.g., Susan Fitzgerald, *Two Large Alzheimer's Trials Fail to Meet Endpoints: What's Next?*, NEUROLOGY TODAY, Mar. 6, 2014, at 12 (discussing implications of the failure of phase 3 trials for new drugs that had been hoped to provide a much needed breakthrough in Alzheimer's).

⁵² See, e.g., Melissa Healy, *Two Proposed Alzheimer's Drugs Show Disappointing Results*, L.A. TIMES (Jan. 22, 2014, 5:27 PM), <http://www.latimes.com/science/sciencenow/la-sci-alzheimers-drugs-disappointing-20140122-story.html> (noting that Eli Lilly shifted its focus to testing their drug in people at earlier stages of the disease);

disappointing results, some pharmaceutical companies continue to gamble. They are lured by the large profits that any approved drug for Alzheimer's can generate — as much as \$5 billion annually for a drug with limited impact on symptoms, or \$20 billion or more for a drug that can treat the disease itself.⁵³

The main problem with the current paradigm of pharmaceutical innovation does not seem to be the lack of private market incentives, but rather the ways in which the private market incentives reinforce a proprietary drug discovery and development process that is expensive, wasteful, and prone to error when applied to complex diseases.⁵⁴ This is nowhere more clearly illustrated than in the current efforts to find therapies for Alzheimer's disease. Pharmaceutical companies are looking for the small molecule drug candidates that they are familiar with, drug candidates that they can stake proprietary claims in through patenting, secrecy in the development process, and exclusivity rights over data used in the regulatory process required to approve the drug for sale.⁵⁵ Scientists still do not know what causes the disease, although it is now thought that a combination of genetic and environmental factors trigger the process of brain nerve cell destruction and that the process may begin long before the manifestation of symptoms.⁵⁶ When placing their large bets on

Dennis Thompson, *2 Alzheimer's Drugs Found Ineffective in Clinical Trials*, HEALTHDAY (Jan. 22, 2014), <http://consumer.healthday.com/cognitive-health-information-26/alzheimer-s-news-20/alzheimer-s-drugs-684115.html> (“Dashing hopes, bapineuzumab and soanezumab did not improve patient's ability to think or perform daily activities.”).

⁵³ See, e.g., Michelle Fay Cortez & Drew Armstrong, *Alzheimer's Theory That's Been Drug Graveyard Facing Test*, BLOOMBERG (Dec. 12, 2013, 1:16 PM PST), <http://www.bloomberg.com/news/2013-12-12/merck-s-bid-to-treat-alzheimer-s-tests-fundamental-cause.html> (showing that while reward is high, so is the cost); see also Coombs, *supra* note 9.

⁵⁴ See, e.g., Munos & Chin, *supra* note 25, at 3 (explaining how “the fear of jeopardizing intellectual property” has increased the costs of innovation).

⁵⁵ Historically drug development has focused on small molecule drugs — drugs based on small (low molecular weight) chemically manufactured compounds, such as acetylsalicylic acid, the active ingredient in aspirin, that can regulate a biological process. This can be contrasted with biologics, a class of drugs based on large protein molecules that are found to have a therapeutic effect. See, e.g., *Small and Large Molecules: Drugs on a Chemical and Biological Basis*, BAYER HEALTHCARE, <http://www.bayerpharma.com/en/research-and-development/technologies/small-and-large-molecules/index.php> (last visited Jan. 9, 2015). This Article focuses only on small molecule drugs, which still make up the vast majority of drugs on the market today. I leave for an important follow-up project the question of what changes, if any, are needed to support development of biologic drugs for Alzheimer's.

⁵⁶ See *Alzheimer's Disease Background*, N.Y. TIMES, <http://www.nytimes.com/>

potential drugs, the pharmaceutical companies must thus rely on a very imperfect understanding about a complex disease and its causes. They continue to jump too quickly from perceived advances in isolated aspects of the disease to narrowly-focused drug development projects in their race to be the first to build proprietary rights in potential drug candidates.⁵⁷ They focus on shorter-term clinical studies of patients in advanced stages of the disease in their rush to reap rewards from their patented drug candidates before patent terms expire.⁵⁸ Strong patent rights at early stages of the discovery and development process reinforce the model of placing early and secret bets on potential drug candidates that are pushed through a proprietary development process.⁵⁹ These commercial pressures affect earlier phases of research and discovery, as academic research institutions become more focused on engaging in and protecting the fruits of translational research efforts and less focused on creating and sharing more basic scientific research.⁶⁰

It should thus come as no surprise that the five Alzheimer's drugs currently on the market and many of the drugs now being tested in clinical trials all focus on closely related and similarly incomplete and imperfect theories about the disease, none of which have as of yet produced successful results.⁶¹ Pharmaceutical companies continue to

health/guides/disease/alzheimers-disease/in-depth-report.html (last visited Jan. 9, 2015) (summarizing the disease and what is known about it); see also Pam Belluck, *For Edge on Alzheimer's, Testing Early Treatments*, N.Y. TIMES, http://www.nytimes.com/ref/health/healthguide/alzheimers_ess.html (last visited Jan. 9, 2015).

⁵⁷ See, e.g., Buckholtz et al., *supra* note 50, at 284 (citing the "inability of pre-clinical studies to correctly characterize and identify good clinical candidates" as a major reason to explain high rate of clinical failures).

⁵⁸ See, e.g., Eric Budish, Benjamin N. Roin & Heidi Williams, *Do Fixed Patent Terms Distort Innovation? Evidence from Cancer Clinical Trials* (Univ. of Chi. Booth Sch. of Bus. Research Paper Series. Paper No. 97, 2013), available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2353471 (exploring the distortionary effect that limited patent terms can have on R&D in context of cancer R&D).

⁵⁹ See, e.g., Lansbury, *supra* note 21 (identifying patenting, particularly at early stages of research, as an obstacle to drug discovery for Alzheimer's).

⁶⁰ See, e.g., *id.* (arguing that academic research institutions should disseminate rather than patent general knowledge that allows for discovery of chemical entities); see also Lorelei Ritchie de Larena, *What Copyright Teaches Patent Law About "Fair Use" and Why Universities Are Ignoring the Lesson*, 84 OR. L. REV. 779, 806 (2006) (explaining that technology transfer, which focuses largely on patenting, has become a multi-billion dollar industry for universities).

⁶¹ See, e.g., Andrew W. Lo et al., *Parallel Discovery of Alzheimer's Therapeutics*, SCI. TRANSLATIONAL MED., June 18, 2014, at 1 (suggesting the need for a portfolio approach to drug development efforts in Alzheimer's); Cortez & Armstrong, *supra* note 53 (discussing Merck's study of an experimental drug that tests the so far unsuccessful

rely heavily on the amyloid theory of the disease, which holds that beta-amyloid plaques are the chief sources of the disease, and they search for drugs that might interfere with or remove plaques. All five of the drugs that have been approved for Alzheimer's seek to remove amyloid plaques from the diseased brain.⁶² Four out of the five drugs focus on the same mechanism for addressing plaques.⁶³ None of these drugs change the underlying disease process — at best, they slow the progression of the disease to a very modest extent.⁶⁴ The proprietary nature of the development process, with much of the development and testing conducted in secret, means that some companies may even pursue essentially the same drug candidates into late stages of clinical testing, sometimes engaging in clinical trials for candidates that competitors have already rejected.⁶⁵ Greater sharing of information at all stages of drug discovery and development could reduce this waste and accelerate pharmaceutical innovation, but pharmaceutical companies are reluctant to compromise their proprietary intellectual property positions on potential drug candidates by sharing data and results more freely.

To add to the problems besetting the traditional paradigm, many industry experts hypothesize that the “low hanging fruit” — small molecules that are safe and effective at modulating a particular disease on their own — have been picked. They suggest that further progress on finding new drugs will require research on a number of different mechanisms of disease that must be jointly explored and developed into combination drug therapies that are tailored to patient sub-groups.⁶⁶ As prevention becomes a more promising strategy than

prevailing theory on the cause of Alzheimer's).

⁶² John Gever, *No Surprises in Report on Failed Alzheimer's Drug*, MEDPAGE TODAY (July 25, 2013), <http://www.medpagetoday.com/Neurology/AlzheimersDisease/40680>.

⁶³ See, e.g., H.M. Fillit et al., *Barriers to Drug Discovery and Development for Alzheimer Disease*, 16 ALZHEIMER DISEASE & ASSOCIATED DISORDERS S1, S1 (2002) (reporting that four drugs for Alzheimer's are all in the same class of cholinesterase inhibitors, focusing on the same mechanism, but none of them modify the disease).

⁶⁴ The five drugs approved for Alzheimer's by the FDA are Aricept, Cognex, Razadyne, Namenda, and Exelon. See Bor, *supra* note 48, at 532; McBride, *supra* note 7; Thompson, *supra* note 49.

⁶⁵ See, e.g., Daniel Cressey, *Traditional Drug-Discovery Model Ripe for Reform*, 471 NATURE 17 (2011) (noting that a key problem with the current drug development system is the fact that pharmaceutical companies tend to work in parallel, often on the same or identical target molecules, not knowing that these molecules may have already been tested and discarded by competitors).

⁶⁶ See, e.g., Edney, *supra* note 19 (reporting that NIH Director Francis Collins suggests that many of the well-characterized and comparatively easy drug candidates have already been discovered, leaving us in a space that is more complex and

treating patients who already have the disease, the road to drug development becomes even longer and more reliant on the cumulative innovation strategies that patents do a poor job of supporting.⁶⁷ Pharmaceutical companies are reluctant to make the necessary shift from drug programs focused on a single drug that will impact a particular disease target to programs that requires collaborative development of combination therapies targeting smaller patient populations. The greater cooperation and sharing of intellectual production, control, and rewards that multi-factor, multi-drug approaches require fit poorly with the development models and profits pharmaceutical companies demand.⁶⁸

Despite the intransigence of industry incumbents, it is becoming hard to dispute that complex diseases like Alzheimer's, diabetes, and cancer require greater collaborative use of knowledge across specialty areas and between competing drug development programs.⁶⁹ Sharing of knowledge, data, and research materials is needed to gain a better understanding of which biological aspects of the disease to target and with what combination of therapies. Sharing of costs and risks is needed to keep the many private sector participants that are needed engaged in development efforts. Without such collaboration, the costs and risks of drug development efforts in Alzheimer's and other complex disease areas will continue to rise, private and public funding will stagnate, and progress will remain slow.⁷⁰ These conditions have fueled support for public-private partnership strategies. Policymakers are hoping that public-private partnerships will promote the sharing of knowledge and collaborative development that is needed to reduce the waste in and increase the productivity of pharmaceutical innovation.

difficult); Thompson, *supra* note 52 (stating it is likely that there will not be one single mechanism that works against Alzheimer's, but rather a variety of different approaches that will need to be tailored to particular manifestations and stages of the disease, requiring combination drug therapies and making greater cooperation and data sharing among companies essential). While this Article focuses on small molecule drugs, attention also needs to be paid to the potential of biologics for Alzheimer's. Analysis of the innovation process for biologics to treat Alzheimer's is left for subsequent study.

⁶⁷ Sam Gandy & Steven DeKosky, *Toward the Treatment and Prevention of Alzheimer's Disease: Rational Strategies and Recent Progress*, 64 ANN. REV. MED. 367, 378-79 (2013).

⁶⁸ See Buckholtz et al., *supra* note 50, at 284-85.

⁶⁹ For a definition of complex drugs, see *supra* note 28.

⁷⁰ See, e.g., Thompson, *supra* note 49 (describing continuing increase in costs of R&D directed at Alzheimer's disease).

B. *Public-Private Partnerships as Policy Response*

Public actors such as the National Institutes of Health (“NIH”), which continues to be the world’s largest single funder of biomedical research, and the FDA, which controls the regulatory process by which drugs receive marketing approval, are actively promoting public-private partnerships as new pathways for engaging in drug discovery and development for complex major market diseases like Alzheimer’s, cancer, and diabetes.⁷¹ The NIH Public-Private Partnership Program was initiated as an important outgrowth of the NIH strategic roadmap, and it is designed to encourage and support partnerships between industry, academic institutions, and government actors at varying levels of drug discovery and development in a variety of disease areas.⁷² The FDA established the Critical Path Initiative to encourage collaborative innovation in the process of developing, evaluating, and manufacturing medical products.⁷³ Their shared approach has been to create partnership opportunities and make them attractive to private partners in the hope of encouraging voluntary private sector shifts towards collaborative innovation.⁷⁴

⁷¹ See, e.g., *Accelerating Medicines Partnership*, NAT’L INSTS. OF HEALTH, <http://www.nih.gov/science/amp/index.htm> (last reviewed Aug. 15, 2014) (describing partnership between NIH, biopharmaceutical companies, and non-profit organizations aimed at increasing new diagnostics and therapies); *About*, CRITICAL PATH INST., <http://c-path.org/about/> (last visited Jan. 16, 2015) (describing its creation under auspices of FDA’s Critical Path Initiative program and Alzheimer’s initiatives); NAT’L INST. ON AGING, THE NATIONAL PLAN TO ADDRESS ALZHEIMER’S DISEASE, <http://www.nia.nih.gov/alzheimers/publication/2012-2013-alzheimers-disease-progress-report/national-plan-address-alzheimers> (last visited Jan 16, 2015) (describing NIH activities and strategies focused on achieving Plan goals).

⁷² See *NIH Public-Private Partnership Program*, NAT’L INSTS. OF HEALTH, <http://ppp.od.nih.gov> (last updated Dec. 4, 2013). The NIH Public-Private Partnership includes general partnerships like the Biomarkers Consortium, partnerships in emergent areas of study such as nanobiology, and disease-specific initiatives in areas such as neglected tropical diseases, Alzheimer’s, lupus, and osteoarthritis. For examples of partnerships, see *Partnership Examples*, NAT’L INSTS. OF HEALTH, <http://ppp.od.nih.gov/pppinfo/examples.asp> (last updated Oct. 6, 2010). See also Meredith Wadman, *NIH Gambles on Recycled Drugs*, 499 NATURE 263, 263 (2013) [hereinafter *NIH Gambles*] (describing NIH partnership strategy targeting Alzheimer’s disease and reporting the national cost of Alzheimer’s disease was estimated to be at least \$200 billion in 2013).

⁷³ See *FDA’s Critical Path Initiative*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/ucm076689.htm> (last updated Dec. 28, 2012).

⁷⁴ There have been related public pressures to convince pharmaceutical companies to share clinical data, but companies have been resistant, moving only slowly and when pressured by concerns that disclosure will ultimately be required by law, as has

A collaborative approach to curing Alzheimer's disease was hard wired into federal law with the passage of the National Alzheimer's Project Act ("NAPA") in December 2010.⁷⁵ NAPA established the first-ever framework for a national strategic plan to address the Alzheimer's crisis.⁷⁶ It required relevant federal agencies, health care providers, researchers, and other stakeholders to work together through a National Alzheimer's Advisory Council to assess the current challenges and resources available to manage and combat the disease and to develop recommendations for a national plan to address gaps and exploit opportunities in research, care, and services.⁷⁷ The Act requires a national plan and annual updates of the plan to be presented to Congress for the fifteen-year duration of the law.⁷⁸ The first National Plan, released by the Department of Health and Human Services in May 2012, included among its five goals: "the development of effective prevention and treatment approaches for Alzheimer's disease and related dementias by 2025."⁷⁹ NAPA was not accompanied

happened in Europe. See, e.g., Ed Silverman, *On Data Sharing, Pharmaceutical Companies Finally Open Up*, WALL ST. J. BLOG (Mar. 18, 2014, 4:50 PM ET), <http://blogs.wsj.com/corporate-intelligence/2014/03/18/access-to-pharma-trial-data-how-open-is-open/> (discussing some drug makers' plans for providing access to clinical data). Europe has adopted a harder stance, requiring that drug clinical trials be publicly registered and results reported. See, e.g., *Europe Votes for Clinical Trial Transparency*, ALLTRIALS (Apr. 2, 2014), <http://www.alltrials.net/news/europe-votes-for-clinical-trial-transparency/> (describing Europe's new clinical trial regulations requiring that clinical trials be publicly registered and results reported).

⁷⁵ National Alzheimer's Project Act, Pub. L. No. 111-375, 124 Stat. 4100 (2011). For project plans and advisory council meetings related to the Act, see *National Alzheimer's Project Act*, OFFICE OF THE ASSISTANT SEC'Y FOR PLANNING & EVALUATION, U.S. DEP'T OF HEALTH & HUMAN SERVS., <http://aspe.hhs.gov/daltcp/napa/> (last updated Dec. 16, 2014).

⁷⁶ NAPA included a mandate to the Department of Health and Human Services to establish a National Plan that includes ways of meeting the ambitious research goals of slowing the progression, delaying the onset, and ultimately preventing Alzheimer's. See Meredith Wadman, *Fleshing Out the US Alzheimer's Strategy*, NATURE NEWS (Jan. 19, 2012), <http://www.nature.com/news/fleshing-out-the-us-alzheimer-s-strategy-1.9856>.

⁷⁷ See David Hoffman, *Alzheimer's Disease Legislation and Policy — Now and in the Future*, 33 HEALTH AFF. 561, 562 (2014).

⁷⁸ See Robert Egge, *The Alzheimer's Study Group's Recommendations Five Years Later: Planning Has Advanced, but Agenda Remains Unfinished*, 33 HEALTH AFF. 555, 556-57 (2014) (providing overview of what the act requires).

⁷⁹ Press Release, U.S. Dep't of Health & Human Servs., Obama Administration Presents National Plan to Fight Alzheimer's Disease (May 15, 2012), available at <http://www.nia.nih.gov/newsroom/2012/05/obama-administration-presents-national-plan-fight-alzheimers-disease>; see also U.S. DEP'T OF HEALTH & HUMAN SERVS., NATIONAL PLAN TO ADDRESS ALZHEIMER'S DISEASE 9 (2012) [hereinafter HHS NATIONAL PLAN], available at <http://alzheimers.gov/pdf/NationalPlanToAddressAlzheimersDisease.pdf>.

by an appropriation of funds, however, and while the NIH has shifted funds from other research areas to Alzheimer's disease, funding for Alzheimer's still remains far lower than spending for cancer and diabetes research.⁸⁰ As a result, the National Plan must rely heavily on encouraging better use of existing resources through national and international partnerships among public and private stakeholders to meet its goals.⁸¹

One of the primary roles of the National Plan has thus been to establish a framework for the pooling of public and private resources and the coordination of public and private efforts to combat Alzheimer's.⁸² "By enhancing collaboration between the public and private sectors," we are told, "the [National Alzheimer's] Plan is breaking down walls that have prevented the sharing of expertise, data and resources needed to combat the disease and provide the best care possible."⁸³ Details on what the walls are, how they should be broken, and with what consequences, remain limited however, and partnership strategies remain in flux. While the National Plan sets a goal of 2025 for finding an effective therapy for Alzheimer's, the details on how to reach this goal have been left largely to the NIH.⁸⁴

As part of NIH efforts to develop a research and development plan, an Alzheimer's Disease Research Summit was convened by the U.S. Department of Health and Human Services and its operating division NIH in 2012 to bring together researchers, clinicians, and other stakeholders to provide strategies and action steps for accelerating discovery and development efforts.⁸⁵ The proceedings resulted in forty recommendations, with the need for public-private collaboration figuring prominently in many of these recommendations.⁸⁶ The

⁸⁰ According to NIH figures, Alzheimer's disease receives about a tenth of the money allocated to cancer. See *Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC)*, NAT'L INSTS. OF HEALTH, http://report.nih.gov/categorical_spending.aspx (last updated Mar. 7, 2014).

⁸¹ U.S. DEP'T OF HEALTH & HUMAN SERVS., HHS NATIONAL PLAN, *supra* 79, at 1, 6, 12.

⁸² See National Alzheimer's Project Act, Pub. L. No. 111-375, § 2(c), 124 Stat. 4100, 4100 (2011); see also U.S. DEP'T OF HEALTH & HUMAN SERVS., HHS NATIONAL PLAN, *supra* note 79, at 6-7.

⁸³ Press Release, U.S. Dep't of Health & Human Servs., HHS Releases 2013 Alzheimer's Disease Update (June 14, 2013), available at <http://aspe.hhs.gov/daltcp/napa/PR-061413.pdf>.

⁸⁴ See Egge, *supra* note 78, at 555-56.

⁸⁵ See *Alzheimer's Disease Summit Suggests National Research Priorities*, NAT'L INST. ON AGING, <http://www.nia.nih.gov/about/links/2012/12/alzheimers-disease-summit-suggests-national-research-priorities> (last visited Jan. 13, 2014).

⁸⁶ *Id.*

participants in the Summit highlighted the need to enable partnerships for: “data sharing, creating, validating and sharing tools for translational research . . . and expanding the precompetitive space using new models of public-private partnerships . . .”⁸⁷ These recommendations informed the NIH’s research and development plan that was presented to the public in 2013 as “Charting NIH Milestones to Implement the Recommendations from the Alzheimer’s Disease Research Summit,” and later incorporated into the National Plan.⁸⁸

While innovative ideas for new models of public-private partnerships emerged at the Summit and were included in the NIH Milestones document, a significant gap between ideas and practical implementation persists and an attachment to traditional models of drug discovery and development remains. When formulating recommendations for NAPA’s scientific agenda, the NAPA working group report focuses mainly on the need to increase funding of basic research and early stage drug discovery within the traditional model of pharmaceutical innovation.⁸⁹ While the NIH Milestones includes a section on “New Models of Public Private Partnerships” that suggests in broad brushstrokes the need to promote and enable partnerships across all sectors, the focus remains on research-focused initiatives involving traditional forms of data sharing, creating, validating and sharing research tools, and expanding precompetitive spaces of collaboration.⁹⁰

A more detailed framework for how public-private partnership strategies will accelerate innovation to meet the 2025 deadline has yet to be developed as part of the National Plan, and public efforts to adjust the legal framework to support partnership strategies are largely absent. Instead, both the efforts of relevant government agencies and the plans that have followed NAPA rely primarily on promoting voluntary collaborative arrangements between public and private actors, with a focus on pre-competitive partnerships that promote sharing of early stage data and research materials. Since participation

⁸⁷ *Alzheimer’s Disease Research Summit Offers Research Recommendations*, NAT’L INST. ON AGING (May 18, 2012), <http://www.nia.nih.gov/newsroom/announcements/2012/05/alzheimers-disease-research-summit-offers-research-recommendations>.

⁸⁸ U.S. DEP’T OF HEALTH & HUMAN SERVS., CHARTING NIH MILESTONES TO IMPLEMENT THE RECOMMENDATIONS FROM THE ALZHEIMER’S DISEASE RESEARCH SUMMIT (Apr. 2013) [hereinafter CHARTING NIH MILESTONES], available at <http://aspe.hhs.gov/daltcp/napa/042913/Mtg8-Handout1.pdf>.

⁸⁹ See Alzheimer’s Ass’n Expert Advisory Workgroup on NAPA, *Workgroup on NAPA’s Scientific Agenda for a National Initiative on Alzheimer’s Disease*, 8 ALZHEIMER’S & DEMENTIA 357, 357-59 (2012).

⁹⁰ CHARTING NIH MILESTONES, *supra* note 88, at 21.

by the private sector is voluntary, much of the momentum for shifting to a new more collaborative mode of drug development remains contingent on private sector interests, particularly the pharmaceutical companies, making any significant paradigm shift unlikely. To realize the potential of the national framework that NAPA provides, policymakers need both a clearer understanding of what role public-private partnerships should play in pharmaceutical innovation and a better strategy for supporting this role.

C. *What Public-Private Partnerships Offer*

True partnership is really about combining different skills, expertise and resources to achieve a common goal that is unattainable by independent action within a framework of defined responsibilities, transparency and accountability.⁹¹

Public-private partnerships can play unique roles in the drug discovery and development process if they are properly designed and supported. In this section, I identify the advantages that public-private partnerships offer over alternative arrangements, such as private sector collaborations, improved technology transfer from research institutions, or purely public sector initiatives. In the following sections, I identify some key impediments in both patent law and innovation policy that may limit the realization of these functions.

Public-private partnerships, as defined earlier in this Article, are contractual agreements between one or more public (government) and one or more private (industry) organizations to combine their resources, data, and knowledge to perform a jointly governed project in pursuit of shared goals, in this case effective treatments for disease.⁹² These partnerships are to be distinguished from privatization arrangements in which the private sector provides public health services pursuant to public regulations and directives. They should also be distinguished from public funding of private sector projects, much of it in the form of competitive grants awarded to researchers at academic institutions who share their results with industry via

⁹¹ WORLD ECON. FORUM, DEVELOPMENT-DRIVEN PUBLIC-PRIVATE PARTNERSHIPS IN HEALTH: EMERGING PRIORITIES FROM ROUNDTABLE DISCUSSIONS 2-3 (2005), available at http://www.weforum.org/pdf/ppp_health_summary.pdf.

⁹² This definition accords roughly with the definitions used by the WHO in their public-private partnerships report and the NIH definition. See, e.g., Widdus, *supra* note 26 (overview of public private partnerships that address global health needs); NIH Policy Manual: 1167 — *Public-Private Partnerships*, NAT'L INSTS. OF HEALTH (Sept. 25, 2007), <http://oma1.od.nih.gov/manualchapters/management/1167/>.

publication, consulting, or licensing.⁹³ The participants in public-private partnerships rely on a combination of contract, informal rules and norms, and internal governance structures to engage in joint projects that serve joint interests.⁹⁴ To achieve their goals, these partnerships require participants to share knowledge and project results within the partnership and, in most cases, beyond the partnership as well.

The combination of distinct public and private capabilities, incentives, and modes of intellectual production make public-private partnerships for pharmaceutical innovation uniquely conducive to collaborative knowledge creation and sharing.⁹⁵ The distinctive features of public-private partnerships include: (1) the sharing of costs and risks between public and private entities; (2) the pooling of different kinds of expertise; (3) the balancing of public health and private commercial objectives through joint decision making; (4) the integration of market and non-market based approaches to producing and sharing knowledge; and (5) the role that public actors can play as trusted intermediaries. These features offer the following advantages in promoting knowledge sharing and collaborative product development.⁹⁶

First, the sharing of costs and risks between the public and private sector can make knowledge sharing arrangements both more attractive for private participants and more sustainable. Public funds can be used to subsidize projects where shared infrastructure to support research and development activities, such as systems for facilitating data access

⁹³ See Suzanne Scotchmer & Stephen Maurer, *Innovation Today: A Public-Private Partnership*, in *INNOVATION AND INCENTIVES* 227, 231 (2004). The NIH invests nearly \$30.1 billion annually in medical research, and about 80% of this is used to support almost 50,000 competitive grants to research institutions, with another 10% to fund its own labs. See *NIH Budget*, NAT'L INSTS. OF HEALTH, <http://www.nih.gov/about/budget.htm> (last reviewed Mar. 11, 2014).

⁹⁴ See, e.g., Bagley & Tvarno, *supra* note 26 (suggesting strategies for the design of efficient public-private partnerships between government, universities and industry in the translation of academic research into products).

⁹⁵ In thinking about these partnerships as systems of institutionalized knowledge sharing, I draw on a growing body of work on the knowledge commons. See, e.g., BRETT FRISCHMANN, MICHAEL MADISON & KATHERINE STRANDBURG, *GOVERNING KNOWLEDGE COMMONS* (2014) (providing research framework for studying various knowledge commons).

⁹⁶ See, e.g., Bubela et al., *supra* note 30, at 3 (examining interplay between formal and informal rules, particularly intellectual property rights, in the design and effectiveness of collaborative models for drug discovery); Munos & Chin, *supra* note 25 (arguing that public and private participants have much to gain from widespread collaboration in pharmaceutical R&D and that greater sharing is needed).

and sharing or shared physical facilities useful in drug development activities, are required.⁹⁷ Public funds can also be used to subsidize projects where knowledge spillovers are important.⁹⁸ Where projects have high risk and/or very long time horizons, public cost sharing can lower the risk and magnitude of the investments needed from the private sector. The use of public resources to push early stage discoveries further along a path of development is referred to in the innovation policy literature as the “de-risking” of drug development projects.⁹⁹ In these ways, public funding can make participating in a collaborative project, and in downstream development efforts, more attractive to private firms.

Private funds also play an important role in making these partnerships work well. Private cost sharing can reduce the incentive problems that arise when public funds are provided to finance private parties with imperfect public information about costs and outcomes in at least four ways.¹⁰⁰ The private participants have less incentive to inflate costs or shirk on effort when they are helping to pay for the project. Sharing costs can also allow for alternative incentive schemes that do not rely as heavily on exclusive rights to the results of the project.¹⁰¹ Private parties will pay closer attention to project selection

⁹⁷ See, e.g., BRETT FRISCHMANN, *INFRASTRUCTURE: THE SOCIAL VALUE OF SHARED RESOURCES* (2012) (examining how society benefits from infrastructure resources); Peter Lee, *The Evolution of Intellectual Infrastructure*, 83 WASH. L. REV. 39, 102-20 (2008) (exploring concept of infrastructure in intellectual property law, offers view of IP laws as ensuring wide access to productivity-enabling intellectual infrastructure, where infrastructure is defined in terms of widespread appropriation of intellectual assets).

⁹⁸ Knowledge spillovers refer to the positive external effects of knowledge. See, e.g., Joseph Stiglitz & Scott Wallsten, *Public-Private Technology Partnerships: Promises and Pitfalls*, 43 AM. BEHAV. SCIENTIST 52 (1999) (discussing concept of knowledge spillovers); see also Brett Frischmann & Mark Lemley, *Spillovers*, 107 COLUM. L. REV. 257, 257-58 (2007) (exploring complex interaction between law, property rights in particular, and positive externalities).

⁹⁹ See, e.g., Asher Mullard, *An Audience with Francis Collins*, 10 NATURE REVIEWS DRUG DISCOVERY 14 (2011) (discussing NIH director's views about the importance of translational medicine).

¹⁰⁰ The private sector may inflate costs or invest too little effort, or may focus on goals other than those identified by the public funders. See, e.g., Scotchmer & Maurer, *supra* note 93 (examining public private partnerships and their relative merits as producers of innovation).

¹⁰¹ Where both the costs and the value of innovation are known, for example, direct public funding without the use of intellectual property rights may be the best scheme from a public welfare standpoint. When there is asymmetric information, or uncertainty, about the costs and the outcome, private firms may distort costs or underinvest effort, and intellectual property becomes more attractive as an incentive

and design and will care more about the efficiency of the project if they are sharing in the cost. Finally, public funds for research are shrinking, and public investments need to be leveraged in ways that can attract matching private funds.¹⁰²

Second, these partnerships combine different and complementary kinds of expertise and knowledge. The high rate of clinical trial failures is due largely to a poor understanding of the disease and its causes, which makes it hard for pharmaceutical companies to identify good clinical drug candidates.¹⁰³ Public sector participants, along with academic researchers who are largely publicly funded, provide the necessary expertise to generate a better understanding of the disease. They also have access to facilities and tools that can be used to further research efforts. Although much of this expertise is already shared informally through consulting, publications, and conferences, there are additional benefits from continuous work on shared projects. Public participants can influence the research questions that are asked in joint projects and can share ideas and know-how on an ongoing basis as projects unfold. Pharmaceutical companies have expertise in drug development, including designing and running clinical trials to test drug candidates. They also have valuable research materials, such as libraries of compounds that might contain potential drug candidates, drug development tools, and valuable data generated from development efforts.¹⁰⁴ The data that drug companies obtain from their drug development efforts, including their development failures,

scheme for attracting and rewarding private sector participants. See Scotchmer & Maurer, *supra* note 93, at 242-47; see, e.g., Nancy Gallini & Suzanne Scotchmer, *Intellectual Property: When Is It the Best Incentive System?*, in 2 *INNOVATION POLICY AND THE ECONOMY* 51 (Adam Jaffe et al. eds., 2002) (emphasizing that the ideal design of an intellectual property system depends on ease with which rightsholders can enter into licensing).

¹⁰² Mixing public and private funds has advantages over purely private funding of science as well, since it preserves a role for public interest determinations of which projects to fund and which areas to pursue.

¹⁰³ See, e.g., Buckholtz et al., *supra* note 50, at 285 (discussing reasons for clinical failures); Francis Collins, *Introducing AMP: The Accelerating Medicines Partnership*, NAT'L INSTS. OF HEALTH DIRECTOR'S BLOG (Feb. 14, 2014), <http://directorsblog.nih.gov/2014/02/04/introducing-amp-the-accelerating-medicines-partnership/> (discussing introduction of AMP, a public-private effort that will strive to identify better targets in order to develop better drugs at a faster pace).

¹⁰⁴ For an innovative partnership strategy that focuses on making greater use of pharmaceutical company compound libraries, see Arti K. Rai, Jerome H. Reichman, Paul F. Uhler & Colin Crossman, *Pathways Across the Valley of Death: Novel Intellectual Property Strategies for Accelerated Drug Discovery*, 8 *YALE J. HEALTH POL'Y L. & ETHICS* 1, 4-5 (2008).

can provide researchers with important insights into the nature of the disease. By working together on shared projects, and by increasing the flow of knowledge, materials, and data both within the partnership and outside of the partnership, public and private sector participants may make discoveries that would not otherwise have been made. They may also be able to identify problems in existing drug development programs at a much earlier stage, reducing cost and waste and accelerating discovery.¹⁰⁵

Third, the public participant will, or at least should, internalize both the total social welfare benefits from knowledge sharing and the total social costs that stem from a lack of knowledge sharing.¹⁰⁶ The public interest in finding any cure, rather than focusing only on one particular cure, can prompt partnership decisions that are not based solely on whether efforts will advance one particular drug development effort or theory but rather on the success of any drug in the partnership portfolio.¹⁰⁷ The public participant will also consider the value of everyone's wasted resources when drug development mistakes are duplicated. Since the public and private participants must agree on the goals and governance of the partnership, the public participant will push the private participants to take a broader range of costs and benefits into account when making project decisions. Since partnership rules are decided up front before any one private partner knows whether it will be the net beneficiary or net loser from a particular rule, each private party may be willing to accept rules, such as broader sharing requirements or flexibility in project direction, that are advocated by the public partner, as long as they are confident that others will to do the same.

Although sharing rules and related intellectual property ownership issues are and will likely continue to be heavily negotiated, the process of negotiating can sometimes be productive. It can facilitate learning by each participant about the needs, abilities, and constraints of other participants, and it may encourage joint problem solving to find alternative ways of balancing competing interests and incentives. Since the public participants are typically also either regulators, such as the FDA, or agencies that influence the flow of public funding, such as the

¹⁰⁵ See, e.g., Petsko, *supra* note 16 (describing valuable information that Phase II failures can provide for biomedical research and arguing for greater sharing of this information).

¹⁰⁶ The advantages of a public-private partnership depend at least in part on the competence and integrity of the public participants.

¹⁰⁷ See, e.g., Lo et al., *supra* note 61 (describing portfolio approach to drug development for Alzheimer's).

NIH, these negotiations can and do have the additional beneficial effect of prompting regulatory and funding innovations.¹⁰⁸

A fourth and closely related advantage of the partnerships is the integration of market based and non-market based approaches to intellectual production.¹⁰⁹ Public sector and academic research institutions rely largely on non-market approaches to intellectual production that encourage the open dissemination and sharing of knowledge.¹¹⁰ Publication is an important part of public intellectual production. Private commercial parties, in contrast, are driven by market-based incentives and are used to pursuing proprietary development strategies in which sharing of knowledge and research materials is restricted. Public-private partnerships are a departure from both purely public and purely private approaches to intellectual production. They operate partially through contract, but since contracts are inevitably incomplete and decisions about whether and what to share are hard to observe, the partnerships must rely at least in part on voluntary compliance of participants with shared

¹⁰⁸ Where partnerships come up with new tools for drug development, for example, the FDA can work with the partners to find ways of acceptable validation and incorporation into clinical trials. *See, e.g.*, Goldman, Compton & Mittleman, *supra* note 24, at 1 (describing positive impact of public-private partnerships on drug development process); *see also FDA Offers New Guidance on Developing Drugs for Alzheimer's Disease*, U.S. FOOD & DRUG ADMIN. (Feb. 7, 2013), <http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm338659.htm>; *NIH and FDA Announce Collaborative Initiative to Fast-track Innovations to the Public*, NAT'L INSTS. OF HEALTH (Feb 24, 2010) <http://www.nih.gov/news/health/feb2010/od-24.htm>.

¹⁰⁹ *See, e.g.*, Bagley & Tvarno, *supra* note 26 (stating that public-private partnerships must include mechanisms for cooperation, which involves combination of contract and relational norms that promote cooperative outcomes).

¹¹⁰ The role of norms of sharing in academic science and in government labs, as well as the pressures that patents may create on these norms, have been widely discussed. *See, e.g.*, Rebecca Eisenberg & Arti Rai, *Property Considerations*, in 1 HANDBOOK ON STEM CELLS 793 (Robert Lanza et al. eds., 2004) (discussing general problem of proprietary research tools in universities); Robert Merges, *Property Rights Theory and the Commons: The Case of Scientific Research*, in SCIENTIFIC INNOVATION, PHILOSOPHY, AND PUBLIC POLICY 145 (Ellen Frankel Paul et al. eds., 1996) (discussing property rights in scientific research and arguing for patent infringement exception and exclusion of some areas of research from patentability); Arti K. Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 NW. U. L. REV. 77 (1999) (employing a law-and-norms theory to argue that norms should militate against securing intellectual property rights in scientific research); Katherine Strandburg, *User Innovator Community Norms: At the Bounds Between Academic and Industry Research*, 77 FORDHAM L. REV. 2237 (2009) [hereinafter *User Innovator Community Norms*] (discussing how policy initiatives can promote "ignoring patents" and materials sharing norms). *But see, e.g.*, Rick Mullin, *Cracking the Tough Ones*, CHEMICAL & ENGINEERING NEWS, Feb. 22, 2010, at 12, 12.

commitments. Trust that others will honor project goals and rules plays an important role in supporting the sharing of knowledge and resources that the partnerships require.¹¹¹ Since the partnership must remain attractive to its different participants, reciprocity in the exchange of knowledge and other resources is also important. Norms that support sharing of knowledge may be easier to establish and reinforce in collaborations that include a strong role for public sector participants, since they are already accustomed to such norms, and these norms can reinforce mechanisms of trust and reciprocity. A hybrid system of governance in which intellectual property rights are moderated, norms of sharing are promoted, and trust and reciprocity are relied upon to sustain systems of cooperative intellectual production may be useful in supporting open and cumulative innovation within and beyond these partnerships.¹¹² Private sector competition also has an important role to play in the partnerships, however. Private sector competition can bring with it market-based discipline and project management skills that public sector projects sometimes lack. The combination of market and non-market mechanisms can offer unique benefits for pharmaceutical innovation, provided that the tensions between them can be moderated.

A final feature of public-private partnerships is the ability of the government actor(s) to act as trusted intermediaries in collaborations that typically involve market competitors.¹¹³ Having an influential government actor such as the NIH who convenes the partnership and invites private sector participants to join can be useful in addressing collective action problems among private participants. The public actor can more credibly commit to enforcing group rules of sharing and can facilitate the building of trust and the sharing of information

¹¹¹ See, e.g., H. Stevens, G. Van Overwalle, B. Van Looy & I. Huys, *Perspectives and Opportunities for Precompetitive Public-Private Partnerships in the Biomedical Sector*, 32 BIOTECHNOLOGY L. REP. 131 (2013) (examining characteristics of and opportunities for public-private partnerships in biomedical sector). For a longer discussion of the role of non-market mechanisms in sustaining cooperative innovation, see, for example, Liza Vertinsky, *Making Room for Cooperative Innovation*, 41 FLA. ST. U. L. REV. 1067 (2014).

¹¹² See Vertinsky, *supra* note 111, at 1094-95; see also Stephen M. Maurer & Suzanne Scotchmer, *Open Source Software: The New Intellectual Property Paradigm* 19 (Nat'l Bureau Econ. Research, Working Paper No. 12148, 2006).

¹¹³ See, e.g., Rai, Reichman, Uhler & Crossman, *supra* note 104 (proposing a public-private partnership model for drug development built around the use of a trusted intermediary which involves pooling of pre-competitive small molecule libraries and explores compensation schemes). *But see, e.g.,* OLSON & BERGER, *supra* note 27, at 49-54 (noting the intermediary doesn't have to be any entity in particular so long as they can look at the big picture and solve disputes).

among competitors. While the private parties may all be better off if everybody joins the partnership, each individual company may be better off by not joining when others do, free riding on the benefits from the group. Also, no company may want to be the first to join. A public actor such as the NIH, in contrast, is always better off by joining, and might even be willing to make its contributions regardless of whether others participate. The NIH can act as the first to enter the collaboration, getting the process started, and its presence can increase the odds that other private actors will join. The NIH can put pressure on those who do not participate, making not joining less attractive than it might otherwise be. This dynamic has been evident in programs such as the NIH's Discovering New Therapeutic Uses for Existing Molecules program, where private actors were content to leave failed drug candidates sitting on their shelves until the NIH stepped in and prompted them to contribute their candidates to a partially public funded and public monitored drug repurposing program.¹¹⁴ Having public oversight can also mitigate some of the antitrust concerns that naturally arise when market rivals get together to coordinate their activities.

D. Patent Challenges

Despite the advantages they seem to offer in increasing knowledge sharing and reducing waste, public-private partnerships in drug discovery and development remain limited in size, number, and scope.¹¹⁵ Large-scale partnerships in particular have been confined to a few areas involving development of large data sets comprised of pieces of information which, on their own, offer minimal competitive value.¹¹⁶

The limited scope and number of public-private partnerships in drug discovery and development can be explained in part by the reluctance of private parties, particularly the large pharmaceutical

¹¹⁴ See *Repurposing Drugs*, NAT'L CTR. FOR ADVANCING TRANSLATIONAL SCIS, <http://www.ncats.nih.gov/research/reengineering/rescue-repurpose/rescue-repurpose.html> (last visited Jan. 11, 2015); see also Wadman, *NIH Gambles*, *supra* note 72, at 263-64. But see, e.g., Derek Lowe, *The NIH's Drug Repurposing Program Gets Going*, CORANTE (July 22, 2013), http://pipeline.corante.com/archives/2013/07/22/the_nih_drug_repurposing_program_gets_going.php (expressing concern over the way NIH has talked about drug repurposing versus its chances for success).

¹¹⁵ See, e.g., Barbara Mittleman, Gary Neil & Joel Cutcher-Gershenfeld, *Precompetitive Consortia in Biomedicine — How Are We Doing?*, 31 NATURE BIOTECHNOLOGY 979 (2013) (noting too few consortia being formed).

¹¹⁶ See Bruce Pratt, *Collaborative Models in the Pharmaceutical and Biotechnology Sectors*, 4 DRUG DEV. 61, 62 (2009), available at http://www.touchophthalmology.com/sites/www.touchoncology.com/files/migrated/articles_pdfs/bruce-m-pratt.pdf.

companies that dominate drug development, to relinquish control and forgo proprietary rights at any but the very earliest stages of research.¹¹⁷ Pharmaceutical companies typically rely on patent protection of early stage discoveries, such as a promising drug candidate, along with trade secrecy for related information, to exclude competitors from pursuing similar drug development paths. They are reluctant to share any information or discoveries that would reveal their development strategies or otherwise confer a competitive advantage on their rivals. Since sharing of resources and knowledge lies at the heart of the public-private partnership strategy, pharmaceutical companies are interested in participating only where they don't see any competitive advantages for themselves in keeping the required contributions private.

The pharmaceutical company focus on proprietary development can be contrasted with the interests of public-sector participants in an open, public domain approach to knowledge.¹¹⁸ Public-sector participants and, although perhaps to a lesser extent, academic research participants, operate in a culture, and with norms, that encourage the open dissemination of knowledge.¹¹⁹ There is a public

¹¹⁷ See, e.g., Thea C. Norman et al., *Leveraging Crowdsourcing to Facilitate the Discovery of New Medicines*, SCI. TRANSLATIONAL MED., June 22, 2011, at 1 (describing challenges (and benefits) of moving to an open access model of drug discovery and development).

¹¹⁸ Public sector participants like the NIH do sometimes obtain patents for their discoveries, of course, but the motivation for doing so is generally to provide incentives for private parties to develop the technology. This is the heart of technology transfer legislation such as the Bayh-Dole Act, for universities, and the Stevenson-Wydler Technology Innovation Act, for government labs.

¹¹⁹ While academic research institutions are interested in the public dissemination of knowledge, they are also concerned about patent protection for even their early stage discoveries, which can lead to conflicting interests in how knowledge is shared. There is also increasing evidence that academic researchers are reluctant to share research materials, a trend that is no doubt exacerbated by increasing competition over research funding. This may make public sector participation all the more important. See, e.g., Eisenberg & Rai, *supra* note 110 (reporting the role of NIH and reserved government rights particularly important in combatting proprietary pressures on upstream discoveries); Strandburg, *User Innovator Community Norms*, *supra* note 110 (demonstrating concerns about erosion of sharing norms in academic research); Patrick L. Taylor, *Research Sharing, Ethics, and Public Benefit*, 25 NATURE BIOTECHNOLOGY 398 (2007) (arguing that other areas of biomedical research should emulate the ethical guidelines promoting sharing of research materials, data and discoveries adopted by the International Society for Stem Cell Research); John Walsh, Wesley Cohen & Charlene Cho, *Where Excludability Matters: Material Versus Intellectual Property in Academic Biomedical Research*, 36 RESEARCH POL'Y 1184 (2007) (examining impact of patents on access to inputs used in follow-on research and identify factors leading to restricted access).

interest in maximizing the social value of knowledge, including the value of reducing waste from duplication of failed projects through greater sharing of project results. This divergence in goals and practices makes it difficult for public and private parties to reach agreement even when they are both interested in doing so. Often the public participants are in the position of sharing more of the background intellectual property for the project and the private participants are most likely to make new patentable discoveries through the use of this knowledge, making negotiations over ownership and benefit sharing difficult. Failure to agree on how intellectual property rights should be handled within public-private partnerships, as well as the conflicting incentives that intellectual property rights, particularly patent rights, can create, are frequently cited as roadblocks to public-private partnerships.¹²⁰ The policy focus on pre-competitive partnerships discussed in Part II is largely a reflection of efforts to avoid the problems that patents and other forms of exclusive rights in knowledge create.

Patents may create two kinds of problems for establishing and sustaining public-private partnerships in disease areas such as Alzheimer's where public health and commercial interests are both strong and collaborative production and sharing of knowledge is essential.¹²¹ The first problem is that patents can reduce the willingness of private sector participants to join the partnership. Where a company has or may discover something that could provide it with a competitive advantage if not shared, patents increase the benefits of not sharing by allowing the company to obtain exclusive rights over its discovery. If a company shares information that could enable a competitor to make a patentable invention, this also makes sharing less attractive since there is a risk that the competitor may acquire exclusive rights over something useful. Patents thus change the relative benefits of sharing information and discoveries to further a general platform of knowledge as compared to keeping information and discoveries private. If exclusive rights over discoveries were limited, then a company would be giving up less by joining the

¹²⁰ See, e.g., Stevens, Van Overwalle, Van Looy & Huys, *supra* note 111 (discussing how much access should be given to background intellectual property).

¹²¹ I acknowledge that the converse may also be true in some cases — patents may sometimes facilitate the ability of public and private parties to collaborate. See, e.g., Paul J. Heald, *supra* note 29 (discussing how patents can ameliorate significant team production problems); F. Scott Kieff, *Coordination, Property, and Intellectual Property: An Unconventional Approach to Anticompetitive Effects and Downstream Access*, 56 EMORY L.J. 327 (2006) (discussing how intellectual property coordination matters a great deal).

partnership and committing to sharing knowledge.¹²² The incentive problems that patents create for partnerships also lead to higher transaction costs in the negotiation of partnership agreements, particularly provisions concerning intellectual property ownership and use, and increase the possibility that no agreement will be reached.¹²³ Participants who must share existing intellectual property with other participants worry about how to share in the fruits of the patentable discoveries that are made by others using this background intellectual property. Disagreements about the value of these existing intellectual property contributions, and about how to handle claims of ownership and use of future intellectual property generated using partnership resources, can lead to a breakdown in negotiations and decisions not to enter the partnership.

Second, patenting may interfere with the non-market mechanisms needed to sustain robust sharing of information and results within the partnership.¹²⁴ Patents can create private market-based incentives that crowd out non-market incentives to cooperate and disrupt cooperative mechanisms of knowledge sharing. Given the inevitable incompleteness of contracts and the inability to identify in advance what will be produced, along with challenges in monitoring adherence to sharing, participants in public-private partnerships must rely at least in part on mechanisms of trust and reciprocity to sustain the partnership. Trust that group members will continue to honor the obligations of the partnership becomes more important where adherence to sharing commitments is hard to monitor and punishments for defectors are limited. Reciprocity, both in terms of relatively balanced contributions of expertise and resources from the different partners and adherence to norms and rules governing access and use of results to support shared goals, is also critical to the sustainability of public-private partnerships.¹²⁵

Where the benefits of hiding information and/or the ability to appropriate the work of the group for private gain increases, there will be less trust that partners are working towards the agreed upon

¹²² There is an underlying assumption here that trade secrecy cannot serve the same role as patent protection, either because of the likelihood of independent discovery, or because of disclosure requirements (which ideally would be increased) or other reasons why disclosure might become necessary.

¹²³ See, e.g., Stevens, Van Overwalle, Van Looy & Huys, *supra* note 111 (discussing issues that arise during negotiations amongst partners over intellectual rights).

¹²⁴ The tensions between patents and cooperative mechanisms based on trust and reciprocity are explored in more detail in Vertinsky, *supra* note 111.

¹²⁵ See Widdus, *supra* note 26, at 718 (“Partnerships appear to be most justified where . . . the contributions of expertise and resources are reasonably balanced.”).

common goal and less likelihood that contributions of knowledge will be reciprocated, lowering the incentives of participants to continue making their own contributions to the partnership. To illustrate, if one partner can appropriate the benefits of the partnership without a return benefit to the group, other members will be less willing to share their information. Participants who contribute non-patentable information and results that increase the likelihood of a patentable discovery will not get rewarded, but the entity that makes the patentable discovery will. This lack of benefit sharing will reduce the motivation of any one participant to share. In addition, participants may have incentives to limit their own contributions of non-patentable information in the hopes that they will be the first to make a patentable discovery that they can then exclude others from using. Even where the information or results being shared cannot themselves be patented, the ability to patent the tools that generate this information or to use the information to increase the likelihood of discovering something patentable change the incentives of participants in ways that may impact both trust and reciprocity within the group.¹²⁶

In these ways patents make it harder to sustain the trust and reciprocity that the partnerships rely upon. For the partnerships, “their impact and performance can be at stake when there is a lack of trust among the stakeholders, which lack may find its origin in the IP hurdles — especially the access to background IP and information sharing.”¹²⁷ While contractual obligations to share information may reduce this problem, monitoring contributions of knowledge and specifying what needs to be shared in advance are often difficult. Moreover, getting agreement on broader sharing obligations up front will be hard, and partners will generally be free to exit from the partnership if they don’t want to comply with contractual obligations to share knowledge. None of the private actors will want to be the last to exit the sharing arrangement, which can lead to an unraveling of the partnership even when all of the participants would still benefit from continuing to participate. Patents thus exacerbate a collective action problem — everybody would be better off if everyone shared data and discoveries that ultimately do not get shared.¹²⁸

¹²⁶ See, e.g., Rebecca S. Eisenberg & Arti K. Rai, *Harnessing and Sharing the Benefits of State-Sponsored Research: Intellectual Property Rights and Data Sharing in California’s Stem Cell Initiative*, 21 BERKELEY TECH. L.J. 1187 (2006) [hereinafter *Harnessing and Sharing*] (discussing the disadvantages that the free sharing of data can create).

¹²⁷ Stevens, Van Overwalle, Van Looy & Huys, *supra* note 111, at 137.

¹²⁸ See, e.g., Bagley & Tvarno, *supra* note 26 (providing a game theoretic approach to public-private partnerships and sharing equilibrium).

To provide a concrete example of these problems, suppose that the NIH forms a partnership with pharmaceutical companies to find biomarkers that can be used to measure the progression of the disease¹²⁹ and to identify and validate the right biological targets for the disease.¹³⁰ This is exactly what it has done in the Accelerating Medicines Partnership described below. A pharmaceutical company will not want to join if it thinks that it is ahead of its competitors in the discovery process based on knowledge it would have to share or if it thinks that it will give its competitors an advantage in evaluating their own proprietary drug candidates. Similarly, companies that have entered into a partnership will have incentives to limit their knowledge sharing or even leave the partnership once they think that they have made more progress in identifying a disease target or ways of modifying that target. The opportunity to overtake collaborators may serve as a disincentive to share knowledge right from the beginning of the process.¹³¹ Patents exacerbate the challenges that these kinds of partnerships face in ways that are difficult to avoid.

II. THE MYTH OF PRE-COMPETITIVE COLLABORATION

Competition has been shown to be useful up to a certain point and no further, but cooperation, which is the thing we must strive for today, begins where competition leaves off.¹³²

A. Policy Focus on Pre-Competitive Partnerships

Policymakers have tried to avoid the tensions between competition and cooperation that patents and other intellectual property and

¹²⁹ See, e.g., Bor, *supra* note 48, at 531 (describing the requirements of a biomarker for AD).

¹³⁰ By drug target I mean a substance in the body, such as a protein, which is modified by a drug resulting in a desired therapeutic effect. Much of the current debate in Alzheimer's is focused on whether to target beta amyloid, a protein that tends to collect in plaques outside neurons, or altered tau protein, which is thought to form tangles inside the cells. "Among the questions bedeviling researchers is when to interrupt the chain of events, and with what." *Id.* at 529.

¹³¹ For a discussion of some of these concerns in the AMP context, see, for example, Aaron Kesselheim & Yongtian Tan, *Accelerating Medicines Partnership: A New Public-Private Collaboration for Drug Discovery*, HEALTH AFFAIRS BLOG (Apr. 8, 2014, 9:26 AM), <http://healthaffairs.org/blog/2014/04/08/accelerating-medicines-partnership-a-new-public-private-collaboration-for-drug-discovery/> (describing concerns regarding intellectual property affecting collaboration in research).

¹³² NATHAN MILLER, *FDR: AN INTIMATE HISTORY* 89 (1983) (quoting President Franklin Delano Roosevelt) (internal quotation marks omitted).

regulatory exclusivities foster by focusing public-private partnerships in areas that are deemed to be pre-competitive.¹³³ These are areas in which participants can purportedly collaborate without competition, typically preceding product development phases during which they will compete. Pre-competitive public-private partnerships have played an important role in other industries suffering from productivity challenges, such as the semi-conductor industry in the 1990s.¹³⁴ They have been concentrated in areas in which competitors can work together on broadly enabling technologies or standards that advance the interests of the industry as a whole.¹³⁵ The legal framework has been modified to support these kinds of arrangements by clarifying and limiting the application of anti-trust law to cooperative research ventures.¹³⁶

In the drug discovery and development context, pre-competitive partnerships generally refer to collaborations in which public and

¹³³ See, e.g., R.A. Barratt et al., *The Critical Path Initiative: Leveraging Collaborations to Enhance Regulatory Science*, 91 *CLINICAL PHARMACOLOGY & THERAPEUTICS* 380 (2012) (noting “precompetitive collaborative model described above offers unprecedented opportunities to leverage pooled data and to develop knowledge critical to the improvement of the drug development process”); Ben Sidders et al., *Precompetitive Activity to Address the Biological Data Needs of Drug Discovery*, 13 *NATURE REVIEWS DRUG DISCOVERY* 83 (2014) (describing areas that would benefit from pre-competitive collaboration); Stevens, Van Overwalle, Van Looy & Huys, *supra* note 111, at 131-39 (describing the role of public-private partnerships in the pharmaceutical industry).

¹³⁴ See, e.g., Elias G. Carayannis & Jeffrey Alexander, *Strategy, Structure, and Performance Issues of Precompetitive R&D Consortia: Insights and Lessons Learned from SEMATECH*, 51 *IEEE TRANSACTIONS ON ENG'G MGMT.* 226 (2003) (describing the evolution of pre-competitive collaboration in the semiconductor industry); Stiglitz & Wallsten, *supra* note 98 (discussing the role of public-private partnerships in the semiconductor industry).

¹³⁵ See, e.g., Stiglitz & Wallsten, *supra* note 98 (asserting that public private partnerships work best when there is a shared objective in the industry). For questions that relate to the concerns of protecting cooperation that are the focus of this paper, see generally Suzanne E. Majewski, *How Do Consortia Organize Collaborative R&D? Evidence from the National Cooperative Research Act (Apr. 10, 2008)* (unpublished manuscript), available at <http://web.mit.edu/is08/pdf/majewski.pdf> (examining how firms structure R&D agreements to extract the benefits of collaborative R&D while avoiding problems of free riding and unintentional spillovers).

¹³⁶ See National Cooperative Research and Production Act of 1993, Pub. L. No. 103-42, § 3, 107 Stat. 117, 119-20 (codified as amended at 15 U.S.C. §§ 4301-06 (2006)) (extending similar protections to joint production activities); National Cooperative Research Act of 1984, Pub. L. No. 98-462, § 2, 98 Stat. 1815, 1815-16 (codified as amended at 15 U.S.C. §§ 4301-06 (2006)) (clarifying the application and limiting the risk of anti-trust law to cooperative research ventures); see also Pratt, *supra* note 116, at 62.

private actors can share resources, human capital, and data freely and openly without impinging on the competitive market interests of the private participants.¹³⁷ They are considered to be pre-competitive because they involve the sharing of very early stage research results that do not — at least purportedly — confer any particular competitive advantage on the discloser. Typically this means that the collaborations are limited to the pooling and sharing of information and discoveries made at very early stages of biomedical research.¹³⁸ By limiting partnerships to areas that are pre-competitive, typically also areas in which the private participants are willing to forego the right to patent, policymakers hope to avoid some of the more challenging issues of ownership and control that arise when project contributions and results have dual roles as enabling inputs for collaborative discovery and as sources of private competitive advantage and/or commercial value. Policymakers seek to avoid the negative impact of patents on both decisions to enter a partnership and on the willingness of participants to share knowledge once in the partnership by focusing on areas in which patenting by the desired participants would be unlikely to occur. Private actors will be comfortable participating in these collective, cooperative modes of intellectual production, it is assumed, because there are no competitive pressures to limit the sharing that is required. Data about biomarkers, which are characteristics that can be used as indicators of biological conditions or states, and genomics data, are good examples of knowledge that is presumed to be pre-competitive. These partnerships are often, if not almost always, created as IP-free zones with limited participants but free and open access to the project results.¹³⁹

¹³⁷ For a discussion of non-competitive, pre-competitive, and competitive collaborations in the pharmaceutical industry, see, for example, Pratt, *supra* note 116.

¹³⁸ As further discussed in Part III, recent Supreme Court decisions limiting patentable subject matter may have helped to reinforce and even expand areas deemed to be pre-competitive by limiting the ability to patent the fruits of early stage research. See, e.g., *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013) (holding that naturally occurring “isolated” DNA not patent eligible subject matter); *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2011) (holding that claims to the diagnostic method in question were unpatentable because they merely observed a correlation that was the result of a law of nature).

¹³⁹ See, e.g., OLSON & BERGER, *supra* note 27, at 49-53 (discussing the role of IP-free zones to open new areas to precompetitive collaboration).

B. Examples

Three prominent examples of pre-competitive public-private partnerships are described below. They illustrate both the distinctive features of public-private partnerships and the policy efforts to expand partnership strategies by pushing the boundaries of what is deemed pre-competitive further into the drug development process.¹⁴⁰ The first, the Alzheimer's Disease Neuroimaging Initiative ("ADNI"), is largely an extension of traditional academic collaborations between academic medical centers. The second, the Accelerating Medicines Partnership ("AMP"), is a limited collaboration between ten large pharmaceutical companies, the NIH, and some additional public and non-profit participants. This is an example of a publicly initiated and monitored collaboration among private participants designed to push the boundaries of collaboration further along in the drug discovery and development process. The third example, Arch2POCM, is a partnership that tries to establish a much broader zone of pre-competitive activity in which competition among firms is limited.

1. Alzheimer's Disease Neuroimaging Initiative

ADNI, first launched in 2004, is the largest public-private partnership to date in Alzheimer's research.¹⁴¹ It is used as the poster child for the partnership strategies that the Alzheimer's Act wants to encourage.¹⁴² The goal of ADNI is to find biological markers of the disease, referred to as biomarkers,¹⁴³ that can be used both to detect

¹⁴⁰ See *id.* at 49; see also Editorial, *Expanding Precompetitive Space*, 10 NATURE REVIEWS DRUG DISCOVERY 883, 883 (2011). But see proposals such as those made in Rai, Reichman, Uhlir & Crossman, *supra* note 104, at 8.

¹⁴¹ See *Supporting Infrastructure and Initiatives*, NAT'L INST. ON AGING, <http://www.nia.nih.gov/alzheimers/publication/2011-2012-alzheimers-disease-progress-report/supporting-infrastructure-and> (last visited Jan. 8, 2015) (describing programs in Alzheimer's Disease research); see also Giovanni B. Frisoni & Michael W. Weiner, *Alzheimer's Disease Neuroimaging Initiative Special Issue*, 31 NEUROBIOLOGY OF AGING 1259, 1259 (2010); Stephen Salloway, *New Lessons from the Alzheimer's Disease Neuroimaging Initiative*, 68 ARCHIVES OF NEUROLOGY 19, 19 (2011) (describing that the ADNI was founded with the goal of developing biomarkers to predict progression from normal aging and mild cognitive impairment through to dementia phases of AD, "ADNI has created the infrastructure to conduct a longitudinal observational trial, standardized methods for multicenter biomarker analysis, and established a widely available data repository").

¹⁴² See U.S. DEP'T OF HEALTH & HUMAN SERVS., ADVISORY COUNCIL ON ALZHEIMER'S RESEARCH, CARE, & SERVS., OPPORTUNITIES AND GAPS, *available at* <http://aspe.hhs.gov/daltcp/napa/092711/Mtg1-Slides3.pdf>.

¹⁴³ A biomarker is, in general terms, any substance, measurement, or indicator of a

the disease and its progression and to measure the effectiveness of alternative therapies in clinical trials.¹⁴⁴ In Alzheimer's, biomarkers may include the level of protein in a person's blood or spinal fluid or a particular gene expression profile or may be imaging-based. It is hoped that ADNI will be able to validate biomarkers as surrogates for Alzheimer's disease that can be used for clinical trials.¹⁴⁵ A biomarker is validated as a "surrogate" for the disease by proving that it reliably tracks disease severity and that treatments that improve the biomarker also treat the underlying disease.¹⁴⁶ Cholesterol is a well-known biomarker for heart disease and has been validated as a surrogate for heart disease — meaning that it has been accepted by regulators as reliably tracking the severity of heart disease and that treatments that improve cholesterol levels also treat heart disease.

ADNI is one of several pre-competitive public-private biomarker research consortiums.¹⁴⁷ Two thirds of its original funding came from the NIH, in the form of a six-year grant, and one third came from the pharmaceutical industry and several foundations.¹⁴⁸ The project funding has been renewed and ADNI is now in its third phase. It is governed by a board that includes academic, public, and private industry members, but it is largely operated by investigators at academic medical research institutions.¹⁴⁹ It is a multisite, longitudinal study of a patient population. The study is conducted primarily in academic research institutions and medical centers that are responsible for enrolling clinical trial volunteers and collecting the

biological state that can be used as an indicator of disease or its progression.

¹⁴⁴ See ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE, <http://adni.loni.usc.edu> (last visited Jan. 8, 2015).

¹⁴⁵ See *Study Design*, ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE, <http://adni.loni.usc.edu/study-design/> (last visited Jan. 8, 2015).

¹⁴⁶ See, e.g., Alan Dove, *Choose Your Marker*, DRUG DISCOVERY & DEV. (Feb. 3, 2009, 7:45 AM), <http://www.dddmag.com/articles/2009/02/choose-your-marker> (noting that complex diseases blur the boundaries between biomarker discovery, drug development and diagnosis since biomarkers provide useful information in research, can be used as tools to segment patient populations for clinical testing, but can also become endpoints in clinical trials).

¹⁴⁷ Other examples of such consortiums include the Predictive Safety and Testing Consortium, the NIH Biomarker's Consortium, and several consortiums supported by Europe's Innovation Medicine's Initiative. See, e.g., Editorial, *Biomarkers Unbound*, 30 NATURE BIOTECHNOLOGY 372 (2012) (listing various research consortium).

¹⁴⁸ See *ADNI Sponsors and Partners*, ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE, <http://www.adni-info.org/Scientists/ADNISponsorsAndPartners.aspx> (last visited Jan. 8, 2015).

¹⁴⁹ See *ADNI Overview*, ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE, <http://www.adni-info.org/Scientists/ADNIOverview.aspx> (last visited Jan. 8, 2015).

required data over time from these volunteers. ADNI participants are required to make the de-identified patient data they collect available to the general scientific community within a very short time frame. All ADNI images, data, and test samples are stored in a central repository that is administered by ADNI.¹⁵⁰ These test results and electronically stored images are made available to all qualified researchers worldwide as soon as the data becomes available for the purpose of “scientific investigation, teaching, or planning clinical research studies.”¹⁵¹ ADNI biological samples are also made available to qualified scientists, again at no cost, but on a more limited basis after determining the scientific merit of the request. ADNI has been described as “a leader in open data sharing, having provided clinical, imaging and biomarker data to over 4,000 qualified scientists around the world, which has generated over 700 scientific manuscripts.”¹⁵²

ADNI performs the important function of identifying and validating neuroimaging data and other biomarkers that have useful functions in the drug discovery and development process. There has been significant public and private investment in research to invent, qualify, and use biomarkers to improve success rates in drug discovery and development, but the need for greater standardization and validation of biomarkers remains immense.¹⁵³ The huge biological data needs for drug discovery in areas such as Alzheimer’s make collaborative efforts to gather, organize, and disseminate this biological data imperative to further research as well as to the improved design of clinical trials.¹⁵⁴

ADNI illustrates the value of having a public participant step forward with initial funding for what is essentially required infrastructure for private drug developers. While no one company was

¹⁵⁰ See *Data & Samples*, ALZHEIMER’S DISEASE NEUROIMAGING INITIATIVE, <http://adni.loni.usc.edu/data-samples/> (last visited Jan. 8, 2015).

¹⁵¹ See ALZHEIMER’S DISEASE NEUROIMAGING INITIATIVE, ALZHEIMER’S DISEASE NEUROIMAGING INITIATIVE (ADNI) DATA SHARING AND PUBLICATION POLICY (2013), available at http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_DSP_Policy.pdf.

¹⁵² *Big Data from Alzheimer’s Disease Whole Genome Sequencing Will Be Available to Researchers Due to Novel Global Research Database*, BIOMARKER COMMONS (July 24, 2013), <http://www.biomarkercommons.org/biomarker-news/big-data-from-alzheimers-disease-whole-genome-sequencing-will-be-available-to-researchers-due-to-novel-global/>.

¹⁵³ See, e.g., H. Salter & R. Holland, *Biomarkers: Refining Diagnosis and Expediting Drug Development — Reality, Aspiration and the Role of Open Innovation*, 276 J. INTERNAL MED. 215 (2014) (evaluating results of biomarker research efforts and their impact).

¹⁵⁴ See, e.g., Sidders et al., *supra* note 133 (arguing for the need of accessible, standardized, integrated biological reference data sets, role of precompetitive collaborations in making them available).

interested in funding the project to develop standards for acquiring and assessing biomarkers, all of the major drug companies have been happy to participate.¹⁵⁵ ADNI clearly benefits from the sharing of costs and risks between public and private sector participants. It provides important infrastructure for development efforts, with public benefits from the results and their use that exceed the private benefits. The combination of public and private sector expertise is also important, as the projects involve a combination of scientific knowledge and clinical trial expertise. The public infrastructure aspects of this project, the positive externalities from the research, the need for pooling of expertise and resources from public and private sectors, and the benefits of harnessing public science modes of collecting and disseminating research to support improvements in private sector clinical trials, make this a natural area for a public-private partnership.

ADNI also fits relatively easily into the pre-competitive category since it relies heavily on public funding and is run largely by academic research investigators and their teams. It is in many ways a natural extension of the kinds of work that academic medical centers are used to performing. ADNI serves as a platform for collecting, standardizing, and making available to the scientific community data that can support research and development in the area of Alzheimer's disease. The scientific community then publishes its results, making them available for general use. Biomarker research has for the most part been considered by academics, the government, and the pharmaceutical companies as pre-competitive, because it precedes work by pharmaceutical companies on specific drug candidates, although this view is not necessarily shared by companies interested in developing commercial applications such as diagnostic tests.

While ADNI performs a vital function in advancing Alzheimer's R&D, it is inherently limited in both scope and the nature of private sector participation. The shared information comes only from ADNI trials, rather than including useful data from privately run clinical trials. It is limited to the slow accumulation of information necessary to validate those biomarkers that are publicly known. ADNI also does not tackle the problem of benefit sharing between the upstream investments in biomarkers and biomarker research and any downstream profits from product sales. Greater benefit sharing might further the financial resources for this kind of project and fuel the incentives of upstream participants.

¹⁵⁵ See, e.g., Mullin, *supra* note 110 (discussing how drug firms seek to accelerate their R&D efforts through partnerships).

2. Accelerating Medicines Partnership

In contrast to the well-established and academically dominated ADNI, AMP is a new experiment with expanding the domain of public-private partnerships into areas that pharmaceutical companies have traditionally treated as proprietary.¹⁵⁶ It is described by the NIH as “a bold new venture . . . to transform the current model for developing new diagnostics and treatments by jointly identifying and validating promising biological targets of disease.”¹⁵⁷ AMP was formed in early 2014 as a five-year agreement between ten large pharmaceutical companies, the NIH, and some additional participants, to collaborate in identifying targets for new drugs to treat four diseases: Alzheimer’s, Type 2 diabetes, rheumatoid arthritis, and lupus.¹⁵⁸

This collaboration encompasses some of the pharmaceutical industry’s largest competitors such as Johnson & Johnson, GlaxoSmithKline, and Eli Lilly, along with the NIH and philanthropic foundations such as the Alzheimer’s Association.¹⁵⁹ The NIH has agreed to contribute \$119 million to the initiative over the next five years, with the ten pharmaceutical companies providing \$111 million and patient advocacy groups providing \$1 million.¹⁶⁰ The participants will pool not just funds, but also expertise, data, and other resources.¹⁶¹ The partnership clearly benefits from the pooling of public and private resources and expertise, efforts to increase knowledge sharing to satisfy both public and private goals, and the role of the public participant as a trusted intermediary.

Previous drug company failures have been largely attributable to drug development programs that focus on the wrong biological targets, and therefore fail to effectively modify the disease. Poor clinical trial performance has also been attributed to a failure to separate out different patient groups, such as including patients who have different kinds of dementias in a clinical test for an Alzheimer’s drug. In response to these problems, scientists from both the NIH and industry have developed joint research plans for each of the targeted

¹⁵⁶ See, e.g., *Accelerating Medicines Partnerships*, *supra* note 71 (describing AMP).

¹⁵⁷ *Id.*

¹⁵⁸ See, e.g., Monica Langley & Jonathan D. Rockoff, *Drug Companies Join NIH in Study of Alzheimer’s, Diabetes, Rheumatoid Arthritis, Lupus*, WALL ST. J. (Feb 3, 2014), <http://www.wsj.com/articles/SB10001424052702303519404579353442155924498> (describing the AMP initiative).

¹⁵⁹ *Accelerating Medicines Partnerships*, *supra* note 71.

¹⁶⁰ *Id.*

¹⁶¹ *Id.*

disease areas aimed at finding and validating effective biomarkers and biological targets most likely to respond to new treatments.¹⁶² AMP efforts in the area of Alzheimer's include: (1) incorporating promising biomarkers into four NIH-funded clinical trials to identify reliable markers of the disease that can be used to predict clinical outcomes; and (2) conducting large-scale analysis of human brain tissue samples from Alzheimer's patients to validate biological targets that are important in disease progression.¹⁶³ Research has already added new disease targets such as measures of brain inflammation and immune function to traditional targets such as beta-amyloid, and validation of this broader range of targets will help drug companies to refocus their development efforts in areas where they are more likely to find effective therapies.

AMP is pre-competitive in the sense that it involves sifting through massive piles of data in the search for useful biomarkers and the right biological targets. There are so many potential targets that nobody knows which one to begin with, so sharing data and resources about targets at this stage does not convey any proprietary information or confer any competitive advantage — at least not for the pharmaceutical companies. A key part of this arrangement is an agreement by the parties to restrict the use of any discovery made pursuant to the collaboration for proprietary research until the project has made data on that discovery public.¹⁶⁴ This includes making the data, methods, and analyses from AMP's early-stage clinical trials publicly available to the biomedical community before companies resume their proprietary drug development.¹⁶⁵

The potential for this project to shift quickly into areas that are unquestionably competitive is high, however. While AMP has been described as “the first national cross-sector partnership of its size and scale” and “the latest initiative in the drug development market to

¹⁶² See *id.* As previously defined, a drug target is some aspect of the biological disease process, such as an existing cellular or molecular structure associated with the disease, which a drug candidate is meant to act on and modify. See, e.g., Peter Imming et al., *Drugs, Their Targets and the Nature and Number of Drug Targets*, 5 NATURE REVIEWS DRUG DISCOVERY 821 (2006) (discussing the large number and nature of drug targets, and the consequent need to collaborate).

¹⁶³ NIH, *Industry and Non-profits Join Forces to Speed Validation of Disease Targets*, NAT'L INSTS. OF HEALTH (Feb. 4, 2014), <http://www.nih.gov/news/health/feb2014/od-04.htm>.

¹⁶⁴ See Langley & Rockoff, *supra* note 158.

¹⁶⁵ See, e.g., Sara Reardon, *Pharma Firms Join NIH on Drug Development*, NATURE NEWS (Feb. 4, 2014), <http://www.nature.com/news/pharma-firms-join-nih-on-drug-development-1.14672> (describing the AMP initiative).

embrace open data exchange, encouraging collaboration over competition as pathways for promoting innovation,”¹⁶⁶ it has also been referred to as a process of herding lions, who with the right bait will then hunt in packs.¹⁶⁷ The difficulty of hammering out a pre-competitive arrangement between competitive pharmaceutical companies is evidenced by the fact that the AMP arrangement took more than two years of intense negotiations to conclude. Moreover, it remains focused heavily in areas that pharmaceutical companies are generally not that interested in patenting, such as biomarkers.¹⁶⁸ Publicly available details on the projects remain limited, and there is clearly ample room for the participants to obtain proprietary rights over drug candidates and to otherwise stake out proprietary positions in the downstream areas that they care most about. While AMP has received a great deal of attention, including a statement from President Obama highlighting this new public-private partnership,¹⁶⁹ its transformative impact on current models of drug development is unlikely to be large.

3. Arch2POCM

Arch2POCM is a public-private partnership that aims to test a new approach to drug discovery and development, with the goal of making the drug development process for potential drug candidates open, cooperative, and IP-free until drug targets have been validated in patients. Arch2POCM has been advanced by policymakers, including those involved in setting the agenda for the National Plan required by NAPA, as an innovative model for tackling the inefficiencies in the drug development process.

Pharmaceutical companies have traditionally competed both on the selection of drug targets and drug design.¹⁷⁰ Many potential drug

¹⁶⁶ See, e.g., Kesselheim & Tan, *supra* note 131 (describing AMP and identifying opportunities and challenges of this approach).

¹⁶⁷ See, e.g., Reardon, *supra* note 165 (relating collaboration among drug companies to “herding lions”).

¹⁶⁸ See NIH, *Industry and Non-profits Join Forces to Speed Validation of Disease Targets*, *supra* note 163.

¹⁶⁹ See Press Release, Office of the Press Sec’y, White House, Statement by the President on the Accelerated Medicines Partnership (Feb. 4, 2014), available at <http://www.whitehouse.gov/the-press-office/2014/02/04/statement-president-accelerated-medicine-partnership>. Interestingly, the focus of this statement was on the combination of government resources with private sector innovation rather than on the combined effort at intellectual production.

¹⁷⁰ See, e.g., Sidders et al., *supra* note 133 (discussing opportunities for increasing efficiency and effectiveness of drug development through greater sharing of previously

candidates fail mid-way through clinical testing because the clinical results suggest that the drugs are not effective in treating the disease, frequently because of problems with the drug target selected. These failures are repeated because each pharmaceutical company pursues its own secretive discovery and development program without sharing the results.¹⁷¹

The Arch2POCM model seeks to avoid this waste and accelerate discovery efforts by pushing the boundaries of pre-competitive collaboration all the way up to mid-stage “proof of concept” clinical trials, known as Phase II clinical trials.¹⁷² Under the Arch2POCM model, a network of researchers drawn largely from academic research institutions but also from industry would identify and develop safe and unpatented test drug candidates against novel drug targets and make the data generated publicly available. All of the research would be open-access and IP-free prior to Phase II clinical trials, providing information useful in evaluating promising drug targets.¹⁷³ These projects would move from ideas to proof of clinical mechanism (“POCM”) in an IP-free environment. A mix of public and private funding would fund the activities needed to reach the Phase II clinical trial, and all data on prospective drug candidates would be published openly until this point. After that, companies would be allowed to compete. Companies could compete either by bidding for exclusive rights to the data generated from any successful unpatented drug or by using the research results to develop their own proprietary drug candidates.¹⁷⁴ The incentives

unshared biological data).

¹⁷¹ See, e.g., Cressey, *supra* note 65 (describing the failures of the traditional model of drug development).

¹⁷² See, e.g., Norman et al., *supra* note 117 (“The new [public-private partnership] Arch2POCM hopes to foster biomedical innovation through precompetitive validation of pioneer therapeutic targets for human diseases.”). For a description of how Arch2POCM is supposed to work, see Ben Hirschler, *Factbox: How to Develop a Patent-free Medicine*, REUTERS (Sept. 28, 2011, 12:09 PM EDT), <http://www.reuters.com/article/2011/09/28/us-pharmaceuticals-research-fb-idUSTRE78R3S320110928>.

¹⁷³ See Sidders et al., *supra* note 133, at 85 (discussing kinds of biological data needed in drug discovery, “fundamental need for accessible, standardized and integrated biological data sets” for evaluating drug targets); Stephen Strauss, *Open Access Consortium*, 29 NATURE BIOTECHNOLOGY 298, 298 (2011) (describing the initiative designed to move high-risk disease targets to the point of proof of clinical mechanism before any patenting takes place).

¹⁷⁴ See, e.g., Ben Hirschler, *Analysis: Open-Access R&D One Answer to Drug Industry Woes*, REUTERS (Sept. 28, 2011, 12:09 PM EDT), <http://www.reuters.com/article/2011/09/28/us-pharmaceuticals-research-idUSTRE78R3RP20110928> (describing participation by pharmaceutical companies in International Structural Genomics Consortium and proposals for a more ambitious experiment with openness in drug development as part of Arch2POCM).

necessary for this final commercialization process for the drug would thus come either from product exclusivity regulations or from development of alternative proprietary drug candidates.

The idea that lies at the core of Arch2POCM is that there are too many barriers to the sharing of materials and data and discoveries, and that these barriers lead to duplication of mistakes and the demise of potentially fruitful collaborative efforts. Intellectual property rights, patents in particular, are seen as barriers to the kind of sharing that needs to take place at even relatively late stages of drug development.¹⁷⁵ The model borrows heavily from open-innovation models that have been used to advance cures for neglected diseases, areas in which intellectual property restrictions have been limited or even removed.¹⁷⁶ The proponents of Arch2POCM see their project as an important experiment in moving from disease to therapy in an IP-free zone.¹⁷⁷ Related efforts to shift from a proprietary to an open paradigm of drug discovery and development include the Structural Genomics Consortium, a pre-competitive public-private partnership focusing on making genomics information freely and publicly available,¹⁷⁸ and the newer Neurocommons project, which builds on open source software models and endeavors to create an open source platform for biological research.¹⁷⁹

This IP-free approach to drug development has met with limited practical success to date, due largely to the reluctance of

¹⁷⁵ But see, for example, the interesting idea proposed in Sean B. Seymore, *The Null Patent*, 53 WM. & MARY L. REV. 2041, 2047-48 (2012). Seymore suggests that researchers be not only allowed, but encouraged, to publish their negative scientific results in a “null patent” that would resemble patents but without patent claims. These null patents could be used to help solve the problem of unpublished negative scientific results.

¹⁷⁶ See, e.g., Cressey, *supra* note 65 (discussing advantages of more collaborative models of drug discovery and development, and an increased role for academics as part of these collaborative models).

¹⁷⁷ See, e.g., Stephen Friend, *Crowdsourcing Drug Discovery*, THE SCIENTIST (Sept. 1, 2010), <http://www.the-scientist.com/?articles.view/articleNo/29220/title/Crowdsourcing-Drug-Discovery/> (soliciting views on how to improve on current system for finding drugs from experts).

¹⁷⁸ See, e.g., Elie Dolgin, *Patent-free Pact Pushes the Boundaries of Precompetitive Research*, 20 NATURE MED. 564 (2014) (discussing IP-free initiatives such as Structural Genomics Consortium and Arch2POCM).

¹⁷⁹ See, e.g., *Background Briefing*, SCI. COMMONS, <http://sciencecommons.org/projects/data/background-briefing/> (last visited Jan. 8, 2015) (describing one of its three goals “to demonstrate that scientific impact is directly related to the freedom to legally reuse and technically transform scientific information — that Open Access is an essential foundation for Innovation”).

pharmaceutical companies to forgo intellectual property protection and the closely related challenges of raising funding to support the project.¹⁸⁰ Arch2POCM would achieve its IP-free status through contractual agreement by participating members, and to be effective it therefore needs to achieve buy-in from the private sector.¹⁸¹ Most private sector participants have been unwilling to go beyond the negotiation of limited intellectual property arrangements on a project-by-project basis in areas that are deemed pre-competitive, and few of the large pharmaceutical companies have been willing to endorse the Arch2POCM model.¹⁸² The slow progress of the Arch2POCM model from concept to practice suggests that if we rely solely on voluntary participation through contract we will not move that far away from the current drug discovery and development model.

C. *The Problem with Pre-Competitive Strategies*

In fundamental ways, the processes, structures and cultures current in the [pharmaceutical] industry are inadequate to meet the demands of biomedicine in the twenty-first century.¹⁸³

Policymakers have continued to focus on pre-competitive public-private partnerships as the preferred partnership strategy for accelerating pharmaceutical innovation, seeking to enlarge the role of the partnerships by expanding pre-competitive boundaries.¹⁸⁴ Both

¹⁸⁰ See, e.g., Dolgin, *supra* note 178 (stating the reluctance of Big Pharma to support Arch2POCM's vision, but growth of smaller-scale initiatives trying to limit patent protection).

¹⁸¹ See, e.g., Cain, *Making the Case*, *supra* note 17 (“A newly established public-private partnership called the Archipelago to Proof of Clinical Mechanism (Arch2POCM) hopes to improve the efficiency and lower the costs of drug development by generating a portfolio of small molecules that hit new therapeutic targets and by carrying out early clinical work — up to Phase II clinical trials.”).

¹⁸² See Dolgin, *supra* note 178, at 564.

¹⁸³ Mittleman, Neil & Cutcher-Gershenfeld, *supra* note 115, at 979 (“Too few precompetitive consortia are being formed to mitigate lost opportunities and deliver on other potential mutual gains for public and private stakeholders in drug development.”).

¹⁸⁴ See, e.g., Pratt, *supra* note 116 (discussing pre-competitive collaboration models in the biotechnology and pharmaceutical industries); Stevens, Van Overwalle, Van Looy & Huys, *supra* note 111 (discussing the different types of biopharmaceutical public-private partnerships and their areas of focus; empirical study of biopharmaceutical R&D public-private partnerships). Efforts are being made to push collaborations into new areas, generally out of necessity in the face of steep discovery costs and declining productivity. See, e.g., Ted Agres, *Policy & Projections: More to*

AMP and Arch2POCM are examples of efforts to expand what is considered pre-competitive into later stages of drug development. I suggest that this policy focus on pre-competition is fundamentally flawed for two reasons. The first reason is that it ignores both the competitive market pressures that determine what is deemed to be pre-competitive and the tensions that competitive market pressures create within partnerships between sharing knowledge and staking out proprietary rights to gain competitive advantage. The second reason is that it limits partnerships to areas where sharing already occurs instead of concentrating them in areas where greater sharing is badly needed. These flaws in the pre-competitive approach can lead to the following three kinds of problems which collectively undermine the effectiveness of the partnerships that are created.

First, the strategic interests of some industry members may be favored over others in the design of pre-competitive partnerships. Assuming that a particular partnership is pre-competitive ignores the competitive ways in which the boundaries of the partnership are fashioned. Rival pharmaceutical and biotechnology companies are intensely competitive with each other and with other industry participants that have competing business interests, such as diagnostic companies, and their decisions and actions will reflect their own private commercial interests. The ways in which pre-competitive boundaries are designed, the areas of research that they target, and the limits on patenting and requirements for data sharing that are adopted, will be guided by private strategic interests and informed by competitive goals. Pharmaceutical companies play a critical role in deciding what is considered pre-competitive because their voluntary participation is generally needed to make the partnership a success. Pharmaceutical companies may have an interest in limiting patent protection for certain kinds of discoveries that they use as inputs into their own proprietary research, such as biomarkers, whereas other companies, such as diagnostic companies, may rely on patent protection for these discoveries as part of their core business.¹⁸⁵

Share, DRUG DISCOVERY & DEV. (Dec. 20, 2013, 10:40 AM), <http://www.dddmag.com/articles/2013/12/policy-projections-more-share> (examining recent efforts by pharma to expand areas of collaboration, including deal between Roche and AstraZeneca to share data and test results from a specified group of early-stage small chemical drug candidates and Pfizer's decision to make large-molecule software available on an open-source basis to competitors through a nonprofit collaborative entity).

¹⁸⁵ Questions about the patentability of biomarkers in recent U.S. case law coincide with pressures from some biomedical industry stakeholders to limit patent protection for biomarkers and other diagnostics. The implications for developing innovative

Pharmaceutical companies may be interested in limiting patent protection and increasing sharing of discoveries and materials that they use as research tools, but the developers of the tools, including universities, will have very different interests.¹⁸⁶

When deciding to make certain kinds of discoveries and data freely available but not others, public-private partnerships are influencing the research and development landscape in ways that may have negative consequences both for those excluded from the partnership and for those with less control over the partnership terms. In doing so, they might be creating advantages for some development strategies and industry actors while disadvantaging others.¹⁸⁷ Selective voluntary limits on intellectual property rights could also be used by large industry incumbents to discourage entry into the industry, limiting the viability of start-up companies to develop and promote new technologies.¹⁸⁸ The competitive effects of what is considered pre-competitive thus need to be carefully considered.

diagnostics need to be carefully considered. See, e.g., Michael M. Hopkins & Stuart Hogarth, *Biomarker Patents for Diagnostics: Problem or Solution?*, 30 NATURE BIOTECHNOLOGY 498 (2012) (describing implications of limiting patents on genes and other biomarkers for diagnostic innovation); A. Kesselheim & N. Shiu, *The Evolving Role of Biomarker Patents in Personalized Medicine*, 95 CLINICAL PHARMACOLOGY & THERAPEUTICS 127 (2014) (examining how courts have approached patents covering biomarkers).

¹⁸⁶ Patenting of research tools has created concerns and made the R&D process more complex. See, e.g., John P. Walsh et al., *Effects of Research Tool Patents and Licensing on Biomedical Innovation*, in PATENTS IN THE KNOWLEDGE-BASED ECONOMY 285, 285-340 (Wesley M. Cohen & Stephen A. Merrill eds., 2003) (describing the effects of patenting research tools). But the environment for drug discovery is changing, and the nature of research tools and cost of developing them is also changing, raising important questions about when and how to incentivize the development of these tools. See, e.g., Tanuja V. Garde, *Supporting Innovation in Targeted Treatments: Licenses of Right to NIH-Funded Research Tools*, 11 MICH. TELECOMM. & TECH. L. REV. 249, 249-84 (2005) (highlighting that much of the success of new drugs in complex disease areas depends on discovery and validation of new targets using new and existing research tools).

¹⁸⁷ Private actors with bargaining power, such as the larger pharmaceutical companies, might be effective in excluding partnerships in areas of data and research tools that are broadly enabling in efforts to squeeze out a competitive advantage. They might also be effective in concentrating partnerships, and corresponding requirements to make certain kinds of data and results open and accessible, in areas where they gain strategic interests from limiting proprietary rights. Diagnostic companies and universities may be less enthusiastic about partnerships that focus on making certain kinds of research tools open source, for example, because their ability to patent may be concentrated at earlier stages of drug discovery.

¹⁸⁸ See, e.g., Jonathan Barnett, *Dynamic Analysis of Intellectual Property: Theory, Evidence and Policy* 59 (Univ. of S. Cal. Gould Sch. of Law Legal Studies Research

A second problem is the failure to confront and address the inevitable tensions within these partnerships between cooperative and competitive mechanisms for intellectual production. Public-private partnership strategies cannot avoid the influence of market-based incentives on their cooperative modes of intellectual production. Even early stages of research and discovery are influenced by competitive concerns.¹⁸⁹ Without measures to mitigate these tensions, partnerships will be unable to achieve optimal levels of knowledge sharing. These tensions are particularly problematic for collaborations like AMP that seek to move cooperation among competing pharmaceutical companies and greater public knowledge access downstream into later stages of drug development. The AMP collaboration agreement requires participating companies to publish their results before they can resume competition and pursue proprietary development strategies. How this time point for publishing and resuming competitive strategies will be decided remains unclear, however. The participants will each want to resume competition at a point where they are ahead of their competitors. This incentive to stay ahead may limit their incentives to share earlier in the collaboration, and may lead to delay in projects as a company with a potential advantage waits for the end of the agreement.¹⁹⁰ Public and private participants are also likely to have different views about what should happen after the required disclosure of project results and about how benefits from the project should be shared. Given that public funds are being invested in lowering the risk of drug discovery and development efforts, making the cost of development lower, some have argued that the public should share in the economic benefit of resulting products as well.¹⁹¹ The AMP does not appear to restrict private participants from pursuing proprietary development paths once they have shared the

Paper Series, No. 13-4, 2013) (showing that limiting public IP rights can sometimes enhance entry barriers and reduce the size of the public domain where some firms have lower cost access to private forms of intellectual protection than others).

¹⁸⁹ See, e.g., Rai & Eisenberg, *supra* note 13, at 289-90 (discussing the competition in the biomedical industry to get patents).

¹⁹⁰ See, e.g., Kesselheim & Tan, *supra* note 131 (evaluating opportunities and challenges that AMP offers).

¹⁹¹ See, e.g., Jerry Avorn & Aaron S. Kesselheim, *The NIH Translational Research Center Might Trade Public Risk for Private Reward*, 17 *NATURE MED.* 1176 (2011) (suggesting that if NIH is going to absorb more of the early stage development costs it should share in the downstream rewards from the products developed); Ron Bouchard & Trudo Lemmens, *Privatizing Biomedical Research — A ‘Third Way,’* 26 *NATURE BIOTECHNOLOGY* 31, 31 (2008) (arguing for a change in how risks and benefits are allocated in federally funded medical science).

project data, and they will retain the ability to patent results that they have developed as a result of the project, leaving the pharmaceutical companies as the likely beneficiaries from the public investment of resources and knowledge.¹⁹²

A third problem resulting from the pre-competitive policy focus is the restriction of the innovation strategy to areas where sharing is already likely to occur rather than focusing on areas where greater sharing is badly needed. In many areas of drug discovery and development, data and research tools that have value as broadly enabling industry research and development efforts can also provide sources of private competitive advantage. There are few areas where the shared data and tools confer no private competitive advantage and there are significant opportunities to benefit from the pooling of public and private resources and data in areas where the information shared has competitive aspects. The FDA, for example, has been actively trying to encourage more sharing of information and greater public participation in areas of clinical testing that have long been regarded as proprietary.¹⁹³ Sharing of information about which drug candidates are being studied and tested, along with knowledge derived from clinical trial failures, can be a critical part of reducing duplicative discovery efforts and avoiding later stage drug candidate failures. By limiting partnership strategies to areas deemed pre-competitive instead of pushing for collaboration in areas that are recognized as inherently competitive, policymakers are failing to promote broader experimentation with alternatives to the existing proprietary drug development model.¹⁹⁴

This problem is compounded where decisions about what is pre-competitive are endogenous to the design of the innovation system. Defining narrow areas as pre-competitive reinforces the treatment of activities that fall outside of these areas as competitive and may fuel proprietary strategies and discourage more open systems of intellectual production. If certain kinds of data and tools are made broadly available, the areas and ways in which industry players compete will change and their views as to what confers an important competitive advantage are also likely to change. Arch2POCM tries to advance a related concept, seeking to construct an area that is pre-

¹⁹² See Kesselheim & Tan, *supra* note 131.

¹⁹³ See, e.g., *Learning from Failure*, 9 NATURE REVIEWS DRUG DISCOVERY 499 (2010) (describing a new initiative to share data from clinical trials of drugs for Alzheimer's disease); Petsko, *supra* note 16 (showing the critical importance of sharing information about drug candidate failures in Phase II stages of clinical testing).

¹⁹⁴ See Petsko, *supra* note 16, at 61; see also Herper, *supra* note 20.

competitive all the way through to clinical testing by limiting proprietary rights in drug candidates and the data that they generate. The underlying strategy is to identify and validate potential drug targets in an environment where data is shared freely, leaving companies to engage in drug development programs only after successful validation of the target.¹⁹⁵ Although the Arch2POCM model has not adequately resolved challenges of attracting sufficient private sector investment and participation, it has confronted the need for collaboration in competitive environments head on. Policymakers need to do the same.

These problems with the focus on pre-competitive need to be acknowledged and addressed by refocusing partnership strategies on ways of supporting cooperation in competitive environments. Policymakers must confront the tensions between cooperative and competitive approaches to innovation directly and must locate partnerships more centrally in the competitive drug discovery and development process. Finding ways to mitigate the negative effects of market incentives on cooperation without removing market incentives altogether is a critical part of making public-private partnership strategies more effective in drug discovery and development. Acknowledging the role of competition even in early research stages will allow more appropriate policy interventions where needed to protect the public interest.

III. MOVING BEYOND “PRE-COMPETITIVE”

A. *Rebalancing Knowledge Access and Exclusion*

Researchers are now looking at not just one kind of change in the brain, but at the many different ways in which the diseased brain changes over time, as well as variance in how those changes occur across different people. Research increasingly supports the view of Alzheimer’s disease as a process of shifting from “normal to pathological networks” in the brain, not an isolated response to a change in a single target.¹⁹⁶ This means that successful therapies for

¹⁹⁵ The creation of Arch2POCM is an exception to the mainstream public-private partnerships in the area. It focuses on identifying and validating potential drug targets pursuant to a partnership arrangement that restricts patenting and requires disclosure of results. Whether the model will ultimately succeed and be replicated more broadly remains to be seen. See, e.g., Norman et al., *supra* note 117, at 1 (“The new [public-private partnership] Arch2POCM hopes to foster biomedical innovation through precompetitive validation of pioneer therapeutic targets for human diseases.”).

¹⁹⁶ See Buckholtz et al., *supra* note 50, at 285 (“There is a growing realization that

Alzheimer's are unlikely to take the form of a single drug that targets a single disease pathway. Instead, they will take the form of combination therapies that address different aspects of the disease and that are tailored to different patient groups. Developing these therapies will require innovations at many different parts of the discovery and development process, including a variety of diagnostic tools to separate patient groups and identify early stages of the disease and advances in identifying and validating novel drug targets.

As a result, all of the participants in the drug discovery and development process need to be more willing to share their advances and the tools they use to make those advances even when the knowledge and tools that they share have competitive value. Greater knowledge sharing must be accompanied by greater benefit sharing. Those who reap the largest commercial returns from the cumulative results of research and development, typically those selling therapies that have received regulatory approval, must be willing to share their benefits equitably with other contributors to the research and development process.

In essence, the problem that policymakers must confront is how to reduce waste and increase collective production and sharing of knowledge in areas that are both cooperative and competitive.¹⁹⁷ While patents may impede incentives to share and may make public-private partnerships harder to sustain, removing the private incentives that patents create may deter private sector participation — as evidenced by the failure to secure sufficient private backing for the Arch2POCM model.¹⁹⁸ Rather than advocating patent-free approaches

AD [Alzheimer's disease] is a disorder affecting a large number of neuronal cell types organized into functionally connected networks across many brain regions, and not just a disease of discrete brain lesions isolated in specific brain regions Many in the AD field now view the disease as a response to a shift from normal to pathological networks, not a response to a pathogenic change in a single target, and this poses a special challenge to the selection of truly disease-relevant therapeutic targets. Furthermore, the focus of AD therapy development has been a target-centric drug discovery, with target selection based on genetic studies and pathological features of the disease").

¹⁹⁷ This focus on the boundaries between cooperative activities that occur outside of the market and competitive activities that rely on the market builds upon the rich foundations laid by work done on intellectual property and theories of the firm. *See supra* note 29.

¹⁹⁸ *But see* Scott Woolley, *Prizes Not Patents*, FORBES (Apr. 19, 2006, 9:00 AM), http://www.forbes.com/2006/04/15/drug-patents-prizes_cx_sw_06slate_0418drugpatents.html (arguing for using prizes instead of patents to incentivize the pharmaceutical industry). There is an active debate over alternatives to patent protection, such as prizes. *See, e.g.*, Daniel J. Hemel & Lisa Larrimore Ouellette, *Beyond the Patents-Prizes Debate*, 92 TEX. L.

to pharmaceutical innovation, this Article instead explores ways of recalibrating patent rights to balance competing interests of users and patent owners in the innovation process. The goal of the recalibration is to enable greater sharing of knowledge and rewards between the various contributors to a successful therapy without overly deterring private sector participation.¹⁹⁹ Patent law does not currently have the flexibility to explicitly balance interests and incentives in this way, but it could.

In contrast to patent law, copyright law does include a doctrine that is designed to balance the competing interests of owners and users of copyright protected materials with the public interest goals of the copyright statute in mind: the doctrine of fair use.²⁰⁰ Patent scholars have from time to time suggested importing a similar concept of fair use into patent law. This Article suggests that a patent fair use may be particularly useful in the context of pharmaceutical innovation, where it can be used to reinforce public sector efforts to promote greater sharing and utilization of knowledge in drug discovery and development. This proposal is introduced as a way of beginning, rather than completing, the conversation about how to recalibrate intellectual property rights and other sources of exclusivity to support collaborative development efforts. While an incremental change such as this will have little impact on its own, requiring supporting adjustments in other parts of the legal framework such as regulatory data disclosure requirements, it provides a promising and potentially feasible starting point for moving the law, and the industry, in the right direction.²⁰¹ The following section outlines what a limited

REV. 303, 304-05 (2013) (providing overview of alternative mechanisms); Brian D. Wright, *The Economics of Invention Incentives: Patents, Prizes, and Research Contracts*, 73 AM. ECON. REV. 691, 691 (1983) (discussing alternatives to patents); see also Tracy Lewis, Jerome Reichman & Anthony So, *The Case for Public Funding and Public Oversight of Clinical Trials*, 4 ECONOMIST'S VOICE (Jan. 2007), http://www.researchgate.net/publication/4985804_The_Case_for_Public_Funding_and_Public_Oversight_of_Clinical_Trials.

¹⁹⁹ See, e.g., Garrett FitzGerald, *Can Intellectual Property Save Drug Development?*, 338 SCIENCE 483, 483 (2012) (“[R]adical reform of the iron rules of intellectual property (IP) worldwide will be necessary if we are to harvest and integrate the efforts of scientists and clinicians scattered across companies, universities, and countries, best qualified to generate new therapies.”).

²⁰⁰ See Wendy Gordon, *Fair Use As Market Failure: A Structural and Economic Analysis of the Betamax Case and Its Predecessors*, 82 COLUM. L. REV. 1600, 1601 (1982).

²⁰¹ For fully developed patent fair use proposals, see, for example, Maureen A. O'Rourke, *Toward a Doctrine of Fair Use in Patent Law*, 100 COLUM. L. REV. 1177, 1180 (2000) (discussing fair use for patents); Katherine Strandburg, *Patent Fair Use 2.0*, 1 UC IRVINE L. REV. 265, 266-68 (2011) [hereinafter *Patent Fair Use*] (arguing for “a fair-

statutory patent fair use targeted at collaborative drug discovery and development might look like and illustrates how it might work in the context of partnership strategies targeting treatments for Alzheimer's disease.

B. A Proposal for Patent Fair Use

In a seminal article on patent fair use Professor O'Rourke explores the applicability of a copyright-like fair use defense to patent law in response to market failures in the patent system.²⁰² The copyright fair use doctrine provides unauthorized users of a work protected by copyright with affirmative defenses to infringement where their use is considered to be a fair use under the doctrine.²⁰³ It operates like a limited compulsory license with a royalty rate of zero,²⁰⁴ providing a mechanism for ensuring that socially desirable transfers and uses of information occur when they otherwise might not.²⁰⁵ Professor O'Rourke argues that a similar mechanism is needed in patent law to respond to the breakdown of the traditional assumption that "market incentives will, more often than not, lead patentees to exploit their innovations efficiently."²⁰⁶ While borrowing the concept of fair use from copyright law, O'Rourke rejects the specific features of the

use type infringement exemption" in patent law). See also Joshua I. Miller, *Towards a Doctrine of Fair Use in Some of Patent Law*, 2 INTELL. PROP. BRIEF 56, 56-63 (2011); Ritchie de Larena, *supra* note 60, at 784-85.

²⁰² See O'Rourke, *supra* note 201, at 1188 (describing concerns that include making sure that patentees do not have an overly broad ability to hamper follow on innovation).

²⁰³ See 17 U.S.C. § 107 (2012) (codifying the following factors to determine whether a use is fair use: (1) the purpose and character of the use; (2) the nature of the copyrighted work; (3) the amount and substantiality of the portion used in relation to the copyrighted work as a whole; and (4) the effect of the use on the potential market for or value of the copyrighted work).

²⁰⁴ See, e.g., Dan Burk, *Patenting Speech*, 79 TEX. L. REV. 99, 158-59 (2000) [hereinafter *Patenting Speech*] (examining alternatives to patent fair use, such as compulsory licensing).

²⁰⁵ See Gordon, *supra* note 200, at 1626 (illustrating how courts have employed fair use to remedy market failure, focusing on three concerns — whether use can be appropriately purchased through the market, whether transferring control over use to the infringer serves the public interest, and whether copyright owner's interests will be substantially impaired); see also Steven J. Grossman, *Experimental Use or Fair Use As a Defense to Patent Infringement*, 30 IDEA 243, 263 (1990); Miller, *supra* note 201, at 56-63; O'Rourke, *supra* note 201, at 1180.

²⁰⁶ See, e.g., O'Rourke, *supra* note 201, at 1179 (arguing for patent fair use to address market failures).

copyright fair use doctrine, instead developing a model of fair use tailored to the different concerns and needs of patent law.

Increasing evidence of market failure in a number of contexts supports the case for this kind of patent fair use doctrine.²⁰⁷ Professor Strandburg builds on and modifies Professor O'Rourke's patent fair use analysis to incorporate additional concerns for patent law raised by changing innovation paradigms such as user innovation and open collaborative innovation.²⁰⁸ Strandburg begins with specific contexts in which patent infringement exemptions are likely to be socially desirable and uses these contexts as the basis for her fair use proposal. She makes the important point that an infringement exemption such as patent fair use will be a beneficial addition to patent law because it "can account for the fact that different uses of patented technology have different social costs and benefits. Neither social nor private costs and benefits are all-or-nothing quantities."²⁰⁹ Both O'Rourke and Strandburg explain at length why existing patent scope-limiting doctrines and defenses to infringement are inadequate to address the problems that a patent fair use is suited to respond to.²¹⁰ What patent law needs, and a fair use tailored to the patent context offers, is the flexibility to define protected uses in terms of the relationship of the use and user to the broader system of innovation.

The areas of pharmaceutical innovation discussed in this Article exhibit both the market failure emphasized by Professor O'Rourke and the importance of alternative innovation paradigms and incentives emphasized by Professor Strandburg. As discussed, in Part I, the current system of drug discovery and development is characterized by too little sharing of knowledge, resulting in the duplication of expensive mistakes and a slower rate of innovation. The public interest in advancing any breakthrough in drug discovery, regardless of its source, while minimizing the total cost of making it, is not

²⁰⁷ O'Rourke points to three kinds of market failure that justify fair use: high transaction costs that interfere with private bargaining, the inability of the infringer to pay licensing costs, and the failure of a market to develop for a particular use. *See id.* at 1188.

²⁰⁸ *See* Strandburg, *Patent Fair Use*, *supra* note 201, at 299 ("[T]he availability of non-patent-motivated innovation paradigms for a particular technology weakens the argument for patent exclusivity because it changes the cost-benefit tradeoffs.").

²⁰⁹ *Id.* at 277; *see also* Dan Burk, *Intellectual Property in the Cathedral 1* (UC Irvine Sch. of Law Legal Studies Research Paper Series, Paper No. 2012-77, 2012) (suggesting that liability rules, along with other related allocation rules, should play more regular parts in intellectual property cases).

²¹⁰ *See* O'Rourke, *supra* note 201, at 1204; Strandburg, *Patent Fair Use*, *supra* note 201, at 266-73.

adequately captured in private patenting and licensing decisions. Public-private partnerships provide alternative ways of organizing innovation designed to overcome these limitations and to encourage broader sharing and use of knowledge, including both patentable and unpatentable discoveries. Part I.D described two kinds of problems that patents might create for at least some kinds of public-private partnerships — the negative effects of patents on the willingness of private sector participants to join the partnership, and the negative impact of patents on non-market mechanisms needed to sustain robust sharing of knowledge and benefits within the partnerships.²¹¹ As discussed in Part II, the incentives that patents create may make those public-private partnerships that rely on voluntary participation and knowledge sharing more difficult to create and sustain.

A patent fair use defense to infringement could, if properly designed and implemented, reduce the negative effects of patents on public-private partnerships and other collaborations in drug discovery and development.²¹² It could provide a way for courts to balance the interests of users and infringers in situations where exempting uses from infringement might be needed to support socially beneficial partnership strategies.²¹³ In the remainder of this section, this Article

²¹¹ See *supra* Part I.D. This is not to suggest that patents are never useful in supporting collaborations, they may indeed serve a variety of beneficial functions in supporting collaborations. See, e.g., *supra* note 121 (explaining that patents may sometimes facilitate the ability of public and private parties to collaborate). I am arguing only that the private incentives that patents provide may interfere with mechanisms of cooperative production and sharing of knowledge that are essential to the kinds of public-private partnerships we need in pharmaceutical innovation.

²¹² This approach is not without risks, including the risk of deterring more radical shifts in the ways in which knowledge is shared and the benefits of contributions to the innovation process distributed and the risk that it might reinforce the patent owner's rights outside of permitted fair uses. The benefits of this approach will depend heavily on whether this adjustment in patent law is accompanied by other legal and regulatory changes, as well as private sector changes, designed to promote greater knowledge and benefit sharing among public and private participants in pharmaceutical innovation. See *supra* text accompanying note 31.

²¹³ O'Rourke provides a general set of factors for this balancing. See O'Rourke, *supra* note 201, at 1205 (proposing five factors as basis for patent fair use: "i) the nature of the advance represented by the infringement; ii) the purpose of the infringing use; iii) the nature and strength of the market failure that prevents a license from being concluded; iv) the impact of the use on the patentee's incentives and overall social welfare; and v) the nature of the patented work"). Strandburg identifies different situations in which an infringement exemption might be socially desirable, distinguishing between those for independent inventors and those for infringers who have copied from the patent. These distinct situations support three factors for a court to consider: justifiable failures to purchase or license; whether there is a substantial improvement over the invention or some reason for blocking patent failure; and

describes what a fair use doctrine designed for this purpose might look like and suggests how it might support the broader partnership strategies that are needed to advance a cure for Alzheimer's and other complex diseases.²¹⁴

Unlike prior proposals for a general patent fair use, this Article proposes a limited fair use targeted at mitigating problems that patents create for collaborative drug discovery and development where the public and private sector are necessary participants working together in realms characterized by uncertainty, conflicting incentives and interests, and incomplete contracts.²¹⁵ The reason for this is pragmatic — a limited fair use proposal targeted at an area of political and public interest may succeed where broader efforts at patent law change have failed. While the patent fair use doctrine could be established through statute or developed by the courts as part of common law patent doctrine,²¹⁶ the close connection between the goal of this fair use proposal and existing legislation prompting national partnership strategies makes a statutory fair use more practical. A statutory change might have the additional benefit of prompting additional coordinated legislative measures designed to support more collaborative pharmaceutical innovation.

whether alternative innovation paradigms reduce the importance of patent incentives. See Strandburg, *Patent Fair Use*, *supra* note 201, at 305.

²¹⁴ The benefits of this incremental change will only be realized if they are part of a much larger concerted effort to increase access to and sharing of data, materials, and discoveries in drug discovery and development. This proposal will only be useful in so far as it supports a cumulative increase in legal and non-legal measures designed to increase the balancing of interests and sharing of benefits in the R&D process. Relying on an incremental strategy such as this could backfire, however. See *supra* text accompanying note 31.

²¹⁵ While contracts play an important part in managing public-private partnerships, contracts are inevitably incomplete and must be tailored to attract the participation of private sector participants. See, e.g., GORDON RAUSSER & HOLLY AMEDEN, *INCOMPLETE CONTRACTS AND PUBLIC-PRIVATE PARTNERSHIPS* (2013) (discussing incomplete contracting theory and public-private partnerships); Bagley, *supra* note 26 (examining public-private partnerships as contractual arrangements that rely in part on social norms for success). The patent fair use proposed here is designed to enhance the contracting opportunities between public and private sector participants.

²¹⁶ The fair use doctrine in copyright law began as common law and was later codified. Both Strandburg and O'Rourke propose a statutory fair use exemption. See, e.g., O'Rourke, *supra* note 201, at 1210 (suggesting Congress is the best to implement fair use doctrine because it has the resources to make empirical studies, can provide guidance on interpretation through legislative history, and has the power to adopt it); Strandburg, *Patent Fair Use*, *supra* note 201, at 305 (arguing statutory fair use type exemptions are more likely to occur).

In contemplating the design of a statutory patent fair use, Congress can look to two existing statutory changes to the Patent Act that were designed to balance public and private interests relevant to pharmaceutical innovation. The first is the patenting requirements and limits on exclusivity, including government use and march-in rights, that attach to inventions developed with public funding.²¹⁷ The second is the limited patent use exemption for uses of patented discoveries by potential generic drug manufacturers as part of the regulatory approval process in order to facilitate the entry of generic drugs into the market quickly upon expiration of the patent. This second modification to the Patent Act, a patent use exemption that was incorporated into section 271 of the Patent Act as 35 U.S.C. § 271(e)(1), provides the closest reference point for the kind of balancing of interests advocated here. Section 271(e)(1) provides an exemption from infringement for uses of patent inventions that are “reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.”²¹⁸ This provision, along with other statutory changes, was the product of a balancing of the private interests of incumbent pharmaceutical companies and generic competitors with public interests in having robust innovation and cheaper drugs.²¹⁹ While section 271(e)(1) does not sufficiently capture

²¹⁷ The Patent Act already includes some examples of restrictions on patent rights that are tied to specific national policies. The Bayh-Dole Act, which deals with patent rights for inventions made with federal assistance, is one of them, providing for restrictions on patenting and reserved government use rights where inventions are made pursuant to federal funding. See 35 U.S.C. § 200 (2012). Other examples include provisions concerning the secrecy of certain inventions in which the government might have a national security interest, 35 U.S.C. § 181, and 35 U.S.C. § 271(e)(1), allows uses of patented inventions that are “reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.” 35 U.S.C. § 181 (2012); 35 U.S.C. § 271(e)(1) (2012).

²¹⁸ 35 U.S.C. § 271 is the section of the Patent Act that deals with infringement of patents, defining what constitutes an infringement along with exemptions from infringement. 35 U.S.C. § 271 (2012). Section 271(e) deals with the exemption from infringement for specified uses that are reasonably related to the regulatory approval process for drugs. *Id.* For a discussion of what this exemption encompasses, and does not encompass, see *Merck KGAA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 202-03 (2005).

²¹⁹ See *Drug Price Competition & Patent Term Restoration (Hatch-Waxman) Act*, Pub. L. No. 98-417, § 202, 98 Stat. 1585, 1603 (1984). For a statement of FDA counsel explaining the public policies behind the Act, see *Drug Price Competition and Patent Term Restoration Act of 1984: Hearing Before the S. Comm. on the Judiciary*, 108th Cong. (2003) (statement of Daniel E. Troy, Chief Counsel, U.S. Food & Drug

the balancing of interests that are needed to promote collaborative innovation, it provides a good starting point for modeling a patent fair use exception to infringement.

With this model in mind, this Article proposes a patent fair use provision that takes the form of a new subsection to section 271 of the Patent Act. This subsection would limit what constitutes infringement under section 271 by making the fair use defense available for uses of patented inventions that “are reasonably related to the public health objectives of public-private collaborations in drug discovery and development.” If the potentially infringing use of a discovery satisfied this hurdle, it would have to be further evaluated by the courts to determine if the use was fair under the statute and thus should be exempt from infringement.²²⁰ Since maintaining private incentives to participate and encouraging benefit sharing are important components of the policy goal, the fair use provision would include a mechanism for providing compensation for ongoing use of discoveries under specified circumstances.

This proposed patent fair use thus involves two steps, the first a determination of whether the use falls within the statute, the second an application of fair use factors to determine whether the use in question is a “fair” one and, if so, whether compensation should be provided for continued infringing use.²²¹ Whether use of a patented invention is fair under this provision will be based on four fair use factors designed to mitigate the negative impact of patents on sharing of knowledge and benefits in public-private partnerships. The four proposed factors are: (1) whether there is a justifiable failure to license, such as the social value of use exceeding the private value;²²²

Admin.), available at <http://www.fda.gov/newsevents/testimony/ucm115033.htm>.

²²⁰ Some but not all of the infringing uses of discoveries that would fall under my proposed fair use provision might also fall under § 271(e)(1). In this case, the potential infringer would have two alternative defenses available.

²²¹ These problems and the ideas for how to resolve them draw from and share important similarities to proposals for a general compensatory liability scheme in response to the problems that alternative exclusivity regimes create in the drug discovery and development environment. See Rai, Reichman, Uhler & Crossman, *supra* note 104, at 25-26; see also J.H. Reichman, *Of Green Tulips and Legal Kudzu: Repackaging Rights in Subpatentable Innovation*, 53 VAND. L. REV. 1743, 1746-47 (2000).

²²² This reference to market failure incorporates the ideas suggested by O'Rourke and Strandburg, who are both concerned with justifiable failures to license. For Strandburg, the justifiable failure to purchase or license could be due to: (a) social value of making invention available to market that patentee will be unable to serve; (b) an “anti-patent” license failure for strategic anti-competitive interests, or a failure due to an anti-commons hold up. Strandburg, *Patent Fair Use*, *supra* note 201, at 305.

(2) whether the use is necessary to advance the public health goals of a public-private partnership;²²³ (3) whether the patented invention was made within the scope of a public-private partnership, or builds directly on the results provided by the public-private partnership;²²⁴ and (4) how allowing the infringing use would impact both incentives to innovate and social welfare.²²⁵ These fair use factors build upon the fair use factors considered by O'Rourke²²⁶ and Strandburg,²²⁷ sharing the same overall purpose of allowing welfare improving patent uses, but they diverge by focusing specifically on challenges that patents create in the particular context of public-private collaboration in drug discovery and development. The definition of public-private partnership for this statutory provision could be the same general one used throughout the Article. With these factors in place, the fair use

²²³ Both Strandburg and O'Rourke consider whether the infringing use is a significant improvement or "major step" forward, with the underlying idea that a major advancement will have more impact on public welfare. O'Rourke also considers the nature of the use, with fair use favoring non-commercial uses. In my case, public welfare is tied to the system of pharmaceutical innovation as a whole, so I focus on uses that further the goals of the institutions designed to improve this innovation process. See O'Rourke, *supra* note 201, at 1206.

²²⁴ This factor focuses on limiting opportunism by private actors who benefit from knowledge sharing and the fruits of collective intellectual production but do not want to share their benefits in return. It reflects the need to support reciprocity and benefit sharing and to reinforce informal norms of sharing in areas where public-private partnerships and other cooperative systems are important.

²²⁵ This factor is similar to the fourth factor proposed by O'Rourke, capturing the need to balance potential negative incentive effects on the patent owner against the social benefits of allowing this kind of infringing use. O'Rourke suggests that this is "the most important fair use factor because it focuses on ensuring that the goals of the patent system are adequately protected." O'Rourke, *supra* note 201, at 1207-08. This factor will require consideration of the investments made and the ability of the patent owner and the infringer to recoup on their investments.

²²⁶ See *id.* at 1180. Under O'Rourke's proposal, courts would use the following five factors in determining whether a particular use is considered fair: (1) the nature of the advance made by the infringement (with more significant advances favored); (2) the purpose of the infringing use (with non-commercial use favored); (3) nature and strength of the market failure, including reason for failure and its impact on innovation; (4) impact of use on incentives to invent and social welfare (use leading to commercial product that directly infringes invention disfavored); and (5) nature of the patented work (where patented invention is minor advance, fair use favored). *Id.* at 1206-08.

²²⁷ Under Strandburg's proposal, fair use factors weigh heavily in favor for independent inventors, but factors for even those who knowingly copy from the patentee include: (1) excusable licensing failure (e.g. underserved market, anti-patent refusal to license, or ant-commons type hold up); (2) substantial improvements to patented invention; and (3) alternative innovation paradigms which provide alternative incentives. Strandburg, *Patent Fair Use*, *supra* note 201, at 299-305.

provision would encompass some uses of patented discoveries for commercial purposes, but it would not include use of the patented invention as part of a final product, such as a combination therapy. It would also exclude uses that are not intended or designed to advance an area of research and development targeted by a public-private partnership focused on drug discovery and development.²²⁸

These fair use factors would help the courts to determine not just whether the infringing use was fair, but also whether compensation should be paid to the patent owner for continuing infringing use.²²⁹ Where the infringing uses are directly related to commercial development and there are no prohibitive barriers to establishing a compensation scheme, policy goals may be best served by providing compensation for some kinds of fair uses.

To see how the fair use provision might work, consider its application to the growing role of biomarkers in discovery and development efforts for Alzheimer's. Establishing a biomarker as a reliable indicator of a particular phase of Alzheimer's disease, particularly one that can identify the presence of disease before symptoms manifest themselves, may be instrumental in both early stage discovery efforts and clinical testing of a potential drug. Knowledge about this biomarker at even early stages, as well as tools for detecting this biomarker, have tremendous value to researchers and drug companies, suggesting the importance of making this knowledge and related diagnostic tools widely available. Suppose that a private company has private information about a biomarker and develops and patents a diagnostic test to detect this biomarker.²³⁰ If the company is a pharmaceutical company, or is working with a pharmaceutical company, this test will likely confer a competitive advantage and the company may not license it widely, or even at all, although the social use of making it available is significant. Although other companies and academic researchers may want to use the diagnostic, and although there may be large social benefits from

²²⁸ While a broader fair use such as that proposed by Professor O'Rourke or by Professor Strandburg may indeed be a good idea, this determination is beyond the scope of this Article. Moreover, keeping the proposal relatively narrow and tailored to an important public health problem may increase the chances that it is adopted.

²²⁹ See O'Rourke, *supra* note 201, at 1205.

²³⁰ See, e.g., *Biomarkers in Alzheimer's Disease*, GLOBALDATA (June 2013), http://www.pharmavision.co.uk/uploads/tp_174.pdf (providing an overview of emerging Alzheimer's disease biomarker market). But for a discussion of limits on the ability to patent diagnostics, see, for example, *Biomarkers Unbound*, *supra* note 147. See also Arti Rai, *Diagnostic Patents at the Supreme Court*, 18 MARQ. INTELL. PROP. L. REV. 1, 3 (2014).

allowing such use, these unlicensed users may be unable to obtain a license to use the patented diagnostic. Access to the diagnostic clearly implicates the proposed fair use provision — a variety of different uses of the diagnostic will be “reasonably related to the public health objectives of public-private collaborations in drug discovery and development.”²³¹ Many of the fair use factors would support a variety of different uses relating to drug discovery and development for the following reasons. The use is clearly important to the advancement of the goals of partnerships such as ADNI and AMP. Given the focus of partnerships on advancing the development and testing of biomarkers, it is likely that this company benefits at least indirectly from partnership results. Significant public investment in supporting biomarker research and development may offset the impact on private incentives, and the social welfare from allowing widespread use of the diagnostic is likely to be significant. The intensity of public funding and public incentive schemes would be an important consideration in this fair use analysis.²³² While further details would be needed for the courts to determine whether uses of the patented test were fair uses, the initial application of factors would suggest that unauthorized uses would be considered fair uses — particularly if there was no acceptable alternative and there was a refusal to make the test available at reasonable cost.

While we want to maximize the availability of this biomarker and tools that employ it for use in a variety of ways, we also want to ensure that adequate incentives are in place for those who discover and develop the diagnostic. This is where the compensation aspect of the fair use proposal becomes important. Discovery will require research time, interest, and money. It will also be time consuming and expensive to engage in the testing and validation of the biomarker and to develop a diagnostic that is accepted by regulators for use in clinical trials. In cases like this, it may be in the public interest to provide compensation for permitted fair uses.²³³ In this respect, the fair use

²³¹ See *supra* Part III.B (describing proposed language for fair use provision).

²³² Strandburg points out the need to consider the availability of alternative innovation paradigms which would suggest that patent incentives are less important. Strandburg, *Patent Fair Use*, *supra* note 201, at 299.

²³³ O’Rourke’s proposal includes compensation for some kinds of uses, with the same fair use factors used to determine whether the fair use should be royalty free or royalty bearing. See O’Rourke, *supra* note 201, at 1209-10, 1234-35. The idea that certain otherwise infringing uses should be permitted, but with compensation, has been raised by others, both in the context of fair use and also in the context of research use or experimental use. See, e.g., Rochelle Dreyfuss, *Protecting the Public Domain of Science: Has the Time for an Experimental Use Defense Arrived?*, 46 ARIZ. L.

provision would operate in ways that are analogous to the more general compensatory liability rules that Professor Reichman has proposed.²³⁴

The four proposed factors for determining whether a particular use of a patented invention is a fair use would also guide determinations of compensation. The nature of the failure to license would be an important factor in determining when and how much compensation should be paid for uses of a patented invention that are permitted as fair uses. Where the discovery is motivated by some alternative incentive scheme, such as public funding or academic research, this would weigh against compensation. If the patented invention required significant investment and alternative means for recouping this investment are inadequate, or if development and testing costs need to be recouped, compensation at or near fair market value should be considered. Where the patent owner has also benefited from the partnership, as referenced in the third fair use factor, this reciprocal benefit should be taken into account and the compensation adjusted downward. Where this is a discovery developed within the partnership

REV. 457 (2004) (proposing a waiver and buy out system for experimental use by universities and non-profits, with buyout acting like a retroactive compulsory licensing scheme); Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017 (1989) (proposing experimental use exemption, but with reasonable royalties to patentees in some cases to ensure adequate return on investment); Ritchie de Larena, *supra* note 60 (favoring patent fair use and suggesting that compulsory licensing scheme may make sense, with compensation in the form of a reasonable royalty where transaction costs are high and patentee has invested significant resources in technology); Katherine J. Strandburg, *What Does the Public Get? Experimental Use and the Patent Bargain*, 2004 WIS. L. REV. 81 [hereinafter *What Does the Public Get?*] (stating that where experimenting with a research tool, compensation may be necessary). It has also been raised in other contexts, such as the doctrine of equivalents. *See, e.g.*, Timothy Holbrook, *Equivalency and Patent Law's Possession Paradox*, 23 HARV. J.L. & TECH. 1, 1 (2009) (suggesting a way of resolving conflict between idea that patents protect what the inventor possessed and the greater protection that patents provide through doctrine of equivalents, and proposing limits on injunctions to mitigate the negative consequences of this greater protection).

²³⁴ *See, e.g.*, Jerome H. Reichman, A Compensatory Liability Regime to Promote the Exchange of Microbial Genetic Resources for Research and Benefit Sharing, in *Designing the Microbial Research Commons: Proceedings of an International Symposium* 43-53 (Paul F. Uhler ed., 2011), available at Available at: http://scholarship.law.duke.edu/faculty_scholarship/2620 (proposing a general compensatory liability approach in context of cumulative and sequential innovation where sub-patentable contributions are important, pragmatic approach to duty to pay could be to use royalties levied on a fixed percentage of offender's gross revenue); *see also* Rai, Reichman, Uhler & Crossman, *supra* note 104, at 26-27.

or relying heavily on the partnership, this would weigh against compensation.

The issue of how, if at all, the government should be compensated by private firms that benefit from publicly-funded research and development efforts has been a topic of recurrent interest in Congress. One appealing aspect of fair use that includes compensation is the ability to recoup public investments that result in the downstream discovery and development of a drug.²³⁵ This raises a host of other questions, however, such as whether public participants should be patenting discoveries used as inputs and whether this might skew public incentives in ways that distort research agendas. Decisions to compensate should not be made lightly or without thought to the incentive effects associated with payment.²³⁶

While there may be important benefits to a patent fair use, particularly one targeted at supporting collaborative drug discovery and development, introducing even a modest change in patent law is not without costs. The fair use that this Article proposes needs to be evaluated in light of these costs and compared to alternative measures that might achieve the same goal at less cost.²³⁷ Five main concerns with the patent fair use proposal are discussed below, and the potential costs weighed against the potential benefits of the fair use proposal.

One potential cost of the fair use proposal is the potential increase in the use of trade secrecy where private companies want to avoid the infringing uses that a patent fair use would permit. While the growing need for private parties to engage in collaboration and the ability to compel at least some kinds of disclosure through contractual requirements as a condition of joining the collaboration or using its results may reduce these concerns, they remain significant. For this

²³⁵ See, e.g., David Korn & Stephen Heinig, *Recoupment Efforts Threaten Federal Research*, 20 ISSUES IN SCI. & TECH., Summer 2004, at 26, available at http://issues.org/20-4/p_korn/ (showing that recoupment would injure private sector innovation, in an alternative view); Bhaven N. Sampat & Frank R. Lichtenberg, *What Are the Respective Roles of the Public and Private Sectors in Pharmaceutical Innovation?*, 30 HEALTH AFF. 332 (2011), available at <http://content.healthaffairs.org/content/30/2/332.full.pdf> (finding the direct role of government funding most important for priority-review drugs, but that government funding has played an indirect role in almost half of drugs approved and almost two-thirds of priority review drugs).

²³⁶ I explore comparative policy interventions in pharmaceutical innovation, including alternative recoupment strategies, in a follow-up project.

²³⁷ While a comparative analysis of alternative policy interventions is beyond the scope of this paper, it forms an important part of a larger project on public-private partnerships in biomedical innovation.

reason, a patent fair use provision should not be seen as a stand-alone change in the legal framework. Instead, it should be one of a number of complementary legal and regulatory changes designed to rebalance access and exclusion in intellectual production. Policies that could usefully supplement this patent fair use include greater incentives or requirements to disclose clinical data,²³⁸ and guidelines for making research data and materials available where public funding has been provided.²³⁹

A second potential cost is the diversion of private sector efforts into other areas. A diversion of pharmaceutical development efforts away from complex diseases like Alzheimer's is occurring already, even without the change proposed here, and the diversion may increase if private incentives are weakened.²⁴⁰ The patent fair use provision is tied to increased opportunities for sharing public and private resources, however, and if the fair use can help to solve bottlenecks in the drug discovery and development process, the odds of finding a successful drug may increase and the costs of doing so may fall — making the expected profits higher even if some of the upside has to be shared. The opportunities for private sector gain in Alzheimer's remain significant, even with some increased fair-use enabled competition along the way. Overall, it is not at all clear that flight from this disease area would be smaller with patent fair use and more collaboration than it already is with less collaboration and the daunting risks of private efforts to find a cure for Alzheimer's disease.

A third area of concern is the difficulty of implementing a fair use measure such as this in a way that is cost effective and predictable. While the proposed patent fair use will be statutory in nature, courts will be tasked with its application, and different courts may have different views about what the fair use factors require. Where courts

²³⁸ See, e.g., Reichman, *Rethinking the Role*, *supra* note 6, at 1 (suggesting a rule in which generic manufacturers can use original manufacturers' data in return for reasonable compensation, and other shifts in balance of exclusivity and access to clinical data); T. Lewis et al., *Treating Clinical Trials as a Public Good: The Most Logical Reform* (Sept. 1, 2006) (unpublished manuscript), available at <http://www.escholarship.org/uc/item/3cn7258n> (arguing that mandatory disclosures are helpful but do not address the root of the problem).

²³⁹ See, e.g., Eisenberg & Rai, *Harnessing and Sharing*, *supra* note 126 (noting the limited role of statutory IP law in data sharing and providing a case study of California's stem cell initiative that shows ways of balancing competing interests in sharing of biomedical data and knowledge).

²⁴⁰ See, e.g., MATTKE ET AL., *supra* note 8 (suggesting that the huge costs and high failure rates in disease areas like Alzheimer's are deterring pharmaceutical companies and that more private incentives are needed).

are asked to consider whether and how much compensation to award for fair uses of a patented invention, the challenges and uncertainty will be even higher. Calculating appropriate compensation will require an investment of time and resources on the part of the courts and private party litigants. Private party expectations about whether and how much compensation might be awarded by the courts will influence *ex ante* decisions about whether to license and/or use a patented invention, with mixed effects on the costs and outcomes of licensing transactions. These challenges are not unique to the patent fair use proposal, however, and there are many areas of patent law and copyright law where courts are already dealing with similar issues. This patent fair use operates in many ways like a compulsory license with a royalty set at zero or, in some cases, at above zero.²⁴¹ Analogies can be drawn with a court's decision to deny injunctive relief where public interests in use trump private interests in preventing use. Where courts denying injunctive relief go on to award damages for continuing use at a reasonable royalty rate, they effectively shift patent enforcement from a property rule approach to a liability rule approach.²⁴² A similar shift occurs when courts determine what "FRAND" (fair, reasonable and non-discriminatory) obligations mean and what royalties are appropriate in the context of obligations to make standard essential patents available on fair, reasonable and non-discriminatory terms. While these calculations are not without challenges, in many cases the patent fair use may simply operate as an *ex ante* prompt to encourage licensing. Where fair use encourages transactions that would not occur in the absence of the threat of fair use, uncertainty might even play a positive role in making private parties reconsider their private benefits from opting out of collaboration.

While we may be able to overcome some of the costs, or they may be outweighed by social benefits, there may be other better ways to accomplish the desired balancing of interests of users and patent owners. Courts are already required to take the public interest into account when awarding injunctive relief,²⁴³ and are sometimes called

²⁴¹ See Burk, *Patenting Speech*, *supra* note 204, at 158 ("An alternative approach to patent fair use might be to look to forms of compulsory licensing. Both fair use and experimental use might be characterized as a type of compulsory license at a royalty of zero.").

²⁴² See *id.* at 160.

²⁴³ See James Boyle, *Open Source Innovation, Patent Injunctions, and the Public Interest*, 11 DUKE L. & TECH. REV. 30, 41 (2012) (discussing the role of the public interest in decisions on whether to award injunctions in patent cases after *eBay v.*

upon to determine royalties for ongoing infringing uses where injunctive relief is denied.²⁴⁴ While some of the fair use considerations might play a role in this analysis, however, it would essentially require importing the fair use factors into the court's determination of whether to award injunctive relief. This would be more costly and less effective than having a separate targeted provision. We could reinvigorate a broad research or experimental use exemption, but this would be a poor fit for activities that are focused explicitly on commercial drug development.²⁴⁵ We could try to stretch section 271(e)(1) to fit the needs of collaborative pharmaceutical innovation, but this safe harbor is tied to the regulatory process in ways that might be both over and under-inclusive.²⁴⁶ Some participants in collaborative

MercExchange).

²⁴⁴ See, e.g., Lisa M. Tittlemore, *The Controversy over "Ongoing Royalty" Awards in the Evolving Landscape of Remedies for Patent Infringement*, FED. LAW., Nov.-Dec. 2009, at 29, 29-30 (examining court decisions awarding ongoing royalties for patent infringement where injunctive relief was denied).

²⁴⁵ Patent scholars have proposed a variety of different research use and experimental use exemptions, all of them focused primarily on exempting non-commercial research activities. See, e.g., Dreyfuss, *supra* note 233 (proposing a waiver and buy out system for experimental use by universities and non-profits, with buyout acting like a retroactive compulsory licensing scheme); Eisenberg, *supra* note 233 (proposing experimental use exemption, but with reasonable royalties to patentees in some cases to ensure adequate return on investment); Henrik Holzapfel & Joshua Sarnoff, *A Cross-Atlantic Dialog on Experimental Use and Research Tools*, 48 IDEA 123 (2008) (discussing the role of research tools in experimental use); Janice M. Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1 (2001) (arguing that scientists should be permitted to use patented research tools but must pay the patent owner a royalty); Joshua D. Sarnoff & Christopher M. Holman, *Recent Developments Affecting the Enforcement, Procurement, and Licensing of Research Tool Patents*, 23 BERKELEY TECH. L. J. 1299 (2008) (discussing patent law developments regarding research tool inventions); Strandburg, *What Does the Public Get?*, *supra* note 233, at 90 (stating that when experimenting with a research tool, compensation may be necessary).

²⁴⁶ 35 U.S.C. § 271(e)(1) creates an exemption from patent infringement for use of a patented invention "solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs." 35 U.S.C. § 271(e)(1) (2012). The parameters of this exemption were clarified by the Supreme Court in *Merck KGAA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 206-08 (2005), where the Court broadly interpreted scope of the safe harbor provision, 35 U.S.C. § 271(e)(1), to include uses of patented inventions reasonably related to the development and submission of any information under the Federal Food, Drug, and Cosmetic Act, including preclinical studies of patented compounds that are appropriate for submission to the FDA as part of the regulatory process even if they are not ultimately included in a submission to the FDA. See also Harold Wegner, *Post-Merck Experimental Use and the "Safe Harbor"*, 15 FED. CIR. B.J. 1, 18 (2005).

drug discovery and development may be engaging in activities that are not reasonably related to the regulatory process but nonetheless are valuable in the overall process of drug discovery and development, and they should have the benefits of the fair use defense. Some participants may be making uses that are directly related to drug development, but in ways that should be compensated under a fair use analysis rather than permitted without charge under a 271(e)(1) analysis. In addition, one of the purposes of pushing for this fair use provision is to interject a way of balancing the interests of users and owners of patented discoveries. Trying to fit it into a provision that is targeted at something different would defeat the expressive function of this change. Patent law is not well equipped to deal with infringing uses that have a direct or indirect commercial purpose but are also socially valuable, and fair use would improve the flexibility of the law in this context.²⁴⁷

If the benefits are likely to outweigh the costs, as this Article suggests, then why do we not already have a patent fair use? There are a variety of reasons why this may be the case, many of which have been explored and discussed in commentary advocating for research use and experimental use exemptions.²⁴⁸ Reasons include the traditional focus of patent law on the incentives of the patent owner and the public interest in protecting these incentives, rather than on the interests of the users and the ways in which the inventions are used.²⁴⁹ It could also be due to the challenges of drawing lines between protected uses and infringing uses in ways that are both clear and not overly burdensome to patent owners. Most likely it is due to a lack of support for such a measure both in the legislature and in the judiciary and, perhaps with some exceptions, among the practicing members of the patent bar. At a pragmatic level, tying a limited statutory patent fair use to an area in which there is both political will and private sector interest in collaboration may reduce opposition to such a measure, making this an opportunity not to be missed.

The more that we rely upon alternative innovation paradigms, such as the public-private partnership strategies discussed in this Article, the greater the need to explore proposals such as the limited patent

²⁴⁷ See O'Rourke, *supra* note 201, at 1204.

²⁴⁸ See Dreyfuss, *supra* note 233, at 472; Eisenberg, *supra* note 233, at 1086; Mueller, *supra* note 245, at 1.

²⁴⁹ See, e.g., Gaia Bernstein, *The Rise of the End User in Patent Litigation*, 55 B.C. L. REV. 1443, 1443 (2014) (arguing that the patent system focuses on the interests of the patentee and its competitor, to the exclusion of the interests of users, even as end users begin to play a bigger role in patent law disputes).

fair use advocated for here. Public policy concerns with the growing burden of Alzheimer's disease and the lack of effective therapies can be harnessed to garner support for a limited patent fair use that might help to improve the rate and reduce the waste of discovering and developing an Alzheimer's drug. Success in this context could provide support for a broader patent fair use, as well as other complementary changes in the legal framework needed to support a new collaborative paradigm of pharmaceutical innovation.

C. Application to Alzheimer's Disease

The concerted national effort to accelerate innovation through public-private partnerships in this area, as reflected by NAPA and recent high profile partnerships such as AMP, provide a natural opportunity to test out the patent fair use proposal in a limited way. As an initial experiment with patent fair use, the fair use proposal could be limited specifically to partnerships directed at Alzheimer's disease and related dementias. If the fair use approach proved to be workable and beneficial, it could be extended to other areas in which patents may undermine the goals of concerted public and private efforts to solve public health challenges. The following examples illustrate how the patent fair use proposal might work to address the patent problems that arise in public-private partnerships for drug discovery and development, with specific applications to ADNI, AMP, and Arch2POCM. The market failure that these factors address include the failure of private parties to take the social benefits of access into account in their licensing and contracting decisions, particularly when making decisions about whether and how much to participate in public-private partnerships. Application of this fair use provision could help to reduce the patent challenges for public-private partnerships discussed earlier in the following ways.

First, having a robust patent fair use provision with clear parameters would reduce the free rider problem, in which private companies decline to participate and share their knowledge and materials while benefiting from the results of the partnership. Since a patent owner's patented discoveries could be used for R&D purposes by unauthorized users regardless of whether the patent owner was a participant in a partnership or not, there would be less advantage to staying out of the partnership. In addition, since certain uses of the patented invention would be exempt from patent infringement liability, there would be less incentive to patent the kinds of early stage, broadly enabling inventions that would have uses either mostly or entirely covered by the fair use provision. Finally, the company would be less worried

about sharing knowledge that might help another company to obtain a patent, since the patent would not block the company from research and development using that patented invention. Since there would be less to gain by staying out of the partnership, more parties might participate. Essentially, the fair use requirement narrows the gap between what the patent owner can do outside of the partnership and what the patent owner can do inside the partnership.

Second, the fair use provision would reduce opportunities for participants to act opportunistically once inside of the partnership, either by limiting disclosure of information or results in the hope of obtaining a patent on the results or on a discovery enabled by the results or by appropriating the results shared by the group. There would also be less incentive for a participant with a patentable discovery to leave the partnership to avoid disclosure and sharing since sharing would be enabled through the statutory fair use.

Suppose, for example, that Company A and Company B are participants in AMP, and they have both contributed biomarkers to AMP which have no known or expected commercial use. The AMP proposal calls for participants to identify biomarkers that can predict clinical outcomes by incorporating them into NIH-funded clinical trials. Suppose Company A, using Company B's biomarker validated by the publicly-funded trials and building on Company B's work in validating a target for the disease, learns something about a drug candidate that Company A has not disclosed, leading Company A to patent that drug candidate and secretly try to turn it into a drug. Suppose that Company B's materials and results were essential tools enabling Company A to make its patentable discovery. In this case, Company A can limit Company B's efforts to experiment on A's drug candidate, and the commercial benefits if the drug is successful will accrue only to Company A. With this scenario in mind, both Company A and Company B will have incentives to limit their sharing of information about drug candidates and will limit their disclosure of knowledge that might give the other company an advantage in discovering a drug candidate. Company B will not be able to experiment with the drug candidate and learn the information that Company A learns. Company B will not know if Company A's efforts are successful or not, at least not without a significant delay, leaving Company B to make similar mistakes with similar drug candidates. With a patent fair use, along with disclosure requirements, Company B would be able to experiment with drug candidates and drug targets for the purposes of informing its own drug discovery and development efforts, but would not be able to sell any products that include the

compound patented by Company A. Company A might learn from B's efforts, and Company B might learn from A's efforts, so they will stay together in the collaboration for longer.

Largely as a result of the effects described above, the fair use provision might help to reinforce the non-market mechanisms of trust and reciprocity on which public-private partnerships rely. It would do so by reducing the incentives of private participants to act opportunistically and either limit their knowledge sharing or defect from the group if they thought they might make a patentable discovery, since the benefits to them from sharing might now outweigh the more limited benefits from obtaining proprietary rights. The lower the probability that any one party will act opportunistically and not share, the easier it will be to sustain systems of sharing that rely on reciprocal commitments to share by the participants.

This kind of patent fair use may also be helpful in reducing the antitrust concerns that might otherwise arise in partnerships that include competitors with market power and limited entry, such as the AMP. If the patent fair use enables general use of project results and discoveries arising from the partnership, regardless of whether the partnership specifies such use, it may reduce the anti-competitive effects that might otherwise arise.

CONCLUSION

Things seem to take on a sudden shimmer before vanishing: the polished black loafers he wore yesterday, the reason for climbing the stairs, even the names of his own children are swallowed like spent stars against the dark vault of memory.

— *Losing Solomon*, Sean Nevin, 2005.

There are many fears associated with Alzheimer's disease.²⁵⁰ As we age, we fear getting the disease, families fear the challenges of caring for relatives incapacitated by the disease, and the nation fears the tremendous economic burden of disease that will continue to grow as the baby boomers age. These fears will not diminish, and indeed are likely to increase, unless and until we can find better ways of supporting the innovations needed to curtail this and other complex and pervasive diseases. This Article has argued that progress towards a cure for Alzheimer's will continue to be slow, uncertain, and

²⁵⁰ See Hoffman, *supra* note 77, at 561 (“[A] recent Marist Institute poll . . . indicates [that] Alzheimer's is the most-feared disease in America — with the level of fear progressing with age.”).

expensive unless dramatic shifts are made towards collaborative innovation across disciplines and across the public and private sectors. Changes in the legal framework are needed to facilitate and promote these shifts. Similar changes are needed in how we approach other important complex diseases such as cancer and diabetes.

Strategies for encouraging public-private partnerships and other forms of collaborative innovation are beginning to move the pharmaceutical industry in the right direction. The push for concerted change in the process of drug discovery and development has not been hard enough, however. While experiments are occurring among industry, government, and academia, the experiments have been limited primarily to areas deemed by the pharmaceutical companies to be pre-competitive. This Article has argued that if the current policy focus on pre-competitive partnerships is not changed, the benefits of partnership strategies may be limited. Partnerships that encourage the sharing of disease and drug-related knowledge, data and materials must occur broadly across many stages of drug discovery and development in order to be effective. Sustaining the partnerships that are needed will require policymakers to address the tensions between private market incentives and public non-market incentives within and around these partnerships directly, and in ways that encourage private participation while at the same time achieving public health goals in areas of R&D that are both cooperative and competitive.

Finding the right mix of cooperation, competition, and regulation at various parts of the drug discovery and development process, and with different combinations of stakeholders, is no easy task. It is an essential one, however, if we are to come closer to finding the cures that we so desperately need. Perhaps proposals such as the one advanced here, for a limited patent fair use with compensation, can begin to recalibrate the incentives and rewards of drug discovery and development in ways that promote the sharing of knowledge and benefits that we need. They will, however, only be effective if they serve as a starting point for broader changes in the legal and regulatory framework designed to promote the alternative innovation paradigms that we need.