

Solving the Problem of New Uses

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Dormant Therapies

- New drugs must be proven safe & effective in clinical trials
- Firms generally need a lengthy exclusivity period to recoup the costs of clinical trials
- They mostly rely on the patent system for that protection
 - Especially for small molecules
- Prior disclosures of drug compounds (e.g., in a journal article or old patent) make them hard (or impossible) to patent effectively
 - Between 2000 & 2009 alone, the large drug companies disclosed 791,722 unique compounds in 14,335 drug-patents compared to the 230 NMEs approved over the same period
 - Firms pursue the compounds that they think are most promising, but drug R&D is highly unpredictable, and good drugs can be overlooked
- Consequently, firms fail to develop these potentially promising new drugs b/c of insufficient monopoly protection

An Easy Fix to the Dormant Therapy Problem

- Lengthening the existing period of data-exclusivity provided under Hatch-Waxman

The MODDERN Cures Act

- New drugs receive 15 years of market exclusivity if they:
 - contains no active moiety previously approved by the FDA
 - this excludes new uses of existing drugs
 - have less than 14 years of patent life remaining at approval, and
 - satisfy an “unmet medical need,” i.e., they offer some meaningful improvement over existing therapies for some class of patients
- In exchange, firms must agree to waive any patent rights over the drug when their exclusivity period ends

The Problem of New Uses

- Productivity Crisis
 - Tens of \$billions spent on de novo drug development annually
 - This money generates about 30 NME approvals annually
 - Costs viewed as unsustainable
 - Industry is cutting back on R&D; VCs are fleeing biotech
- Meanwhile, there are around 2000 FDA approved off-patent drugs
 - Drugs hit multiple targets
 - New uses often discovered through serendipity
 - Long recognized as a promising avenue for research
- There is essentially zero industry investment in testing old drugs for new uses
- And limited public funding available for clinical trials on new uses for off-patent drugs: particularly for large phase III trials

In Silico Screening

- Advances in screening technologies enable sophisticated in silico screening of drug compounds for therapeutic activity
- Stunning results
 - “[A] statistics-based chemoinformatics approach [has been used] to predict new off-targets for 878 purchasable FDA-approved small-molecule drugs.”
Michael J. Keiser et al., *Predicting New Molecular Targets for Known Drugs*, 462 NATURE 175 (2009)
 - Authors review several repurposing studies over the prior 6 years, and report that “a conservative estimate indicates at least 109 previously approved drugs have shown activity in vitro against additional diseases different than those for which the drugs were originally approved.”
Sean Ekins & Antony J. Williams, *Finding Promiscuous Old Drugs for New Uses*, 28 PHARM RES. 1785 (2011)

A Wealth of New Therapies for Unmet Medical Needs?

- “Recent academic enthusiasm in this field has resulted in the publication of relatively long lists of drugs that could potentially be repurposed for a variety of indications, including tuberculosis, breast and prostate cancer, and myelogenous leukemia.”
Tudor I. Oprea & J. Mestres, *Drug Repurposing: Far Beyond New Targets for Old Drugs*, 14 AAPS J. 759, 762 (2012)
- Expressing the hope that developing new uses for existing drugs could “convert cancer into a treatable chronic disease.”
Carlos M. Telleria, *Drug Repurposing for Cancer Therapy*, 4 J. CANCER SCI. THER. ix (2012)
- There is a growing “expectation that a substantial percentage of rare diseases if not all 8000 rare diseases might be treatable with drugs in the current pharmacopeia.”
Ramaiah Muthyala, *Orphan/Rare Drug Discovery Through Drug Repositioning*, 8 DRUG DISCOV TODAY THER STRATEG. 71 (2011)

A Better Economic Model

- Repurposing vs De Novo Drug Development
 - 3-12 years v. 12-16 years (Dudley, et al. 2011)
 - Substantially lower risk of failure (DiMasi et al. 2013)
 - \$300 million v. \$1.2 billion, rough estimate (Sahoo 2007)
- Pharma could tackle higher-risk drug candidates (e.g., new drug targets) and pursue drugs for smaller markets
- Helping to overcome the productivity prices
- Spanning the “valley of death” in biomedical research
 - For public-sector researchers, working with generic drugs is much cheaper and easier
 - The public sector can move right into Phase I or IIa studies, and then find an industry sponsor to pay for Phase IIb or III studies

The Enforcement Problem

- Pharma's business model hinges on the ability to block generic entry for long enough to recoup their R&D investments
- Once the FDA approves a new drug for one indication, the gov't generally does not allow firms to extend or renew their market exclusivity period by developing a secondary indication for that drug
- We grant temporary monopoly rights over new uses of old drugs
- But pharmaceutical companies do not know when Drs. have prescribed an old drug for a patented new indication as opposed to an older off-patent indication
- Without that information, pharmaceutical companies cannot charge payers when Drs. prescribe an old drug for a new use
 - Or require pharmacists to dispense the expensive brand-name drug instead of a low-cost generic if prescribed for a patented indication

The Solution:

E-Prescribing & Medical Records

- Insurers already monitor indications through prior authorization
 - Physicians often must report indications to patient's PBM for expensive brand-name drugs
 - Insurers can check the accuracy of reported indications with patients' health records, which is said to deter most false reporting
- We need indication-reporting capabilities in our e-prescribing software
 - Already present and used (successfully) in Quebec (Egualé et al 2010)
- Give pharmaceutical companies limited access to (de-identified) health records to police the accuracy of reported indications
 - We could expand HIPAA to address privacy concerns
 - Only works when payers & pharma can detect true indications through health records
 - But that space will expand as diagnostic technology and personalized medicine advances