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ANDREW W. LO
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February 27, 2016

Senator Ron Wyden
Senator Chuck Grassley
Committee on Finance
United States Senate
Washinton, DC 20510–6200

Dear Senators Wyden and Grassley,

I am writing in response to your letter of January 21, 2016 soliciting feedback regarding the pricing of breakthrough drugs like Sovaldi and Harvoni and how to ensure patient access to such therapies.

I am a financial economist by training and profession, and the director of the MIT Laboratory for Financial Engineering. I have several other industry and government affiliations, all of which are disclosed publicly at http://alo.mit.edu/. Although I am not a healthcare economist, for the last several years my research has been focused on developing financial engineering solutions to address healthcare challenges such as the decline in funding for early stage biomedical research and translational medicine.

On behalf of all patients and their family members and friends, thank you for conducting the study on the pricing strategy of Gilead Sciences and shining a spotlight on the issue of drug pricing. When access to life-saving therapies is limited by affordability, important moral and ethical issues must be considered in addition to economic and political ones. For too long, we in the United States have ignored these issues for fear of "death panels" and difficult end-of-life decisions. But the growing number of breakthrough therapies and the rising cost of healthcare will soon force us to confront these issues directly. Your report and is an important step in helping us to develop a rational, ethical approach to dealing with this looming challenge.

With regard to the cost of Sovaldi and Harvoni, there are at least three distinct issues to consider: (1) the budgetary impact of these drugs on payers and patients; (2) whether the value of these drugs justifies their cost; and (3) the moral and ethical obligations of society to offer life-saving therapies to all. Although all three issues are critically important, I have little unique expertise in (2) and (3); hence, my remarks will address only the first issue.

Perhaps the single biggest financial impact on insurers and patients of the development of a cure to a serious illness is the large upfront payment for the therapy. Unlike drugs that must be taken in perpetuity to maintain health, which generates a stream of revenues for the drug developer, cures are, by definition, administered to patients only once. Therefore, from an economic perspective, the one-time fee for such therapies should, in equilibrium, be directly related to the cumulative value of additional health they provide over the remainder of the patient's life. From this perspective, a one-time cure should be worth considerably more than "disease mitigators," drugs that offer relief for short periods of time and must be administered repeatedly to maintain symptom-free health. In other words, even if all drugs were priced perfectly accurately to reflect only the actual value that they delivered to patients, cures would be much more expensive than mitigators. The challenge for both payers and patients is how to cover the cost of cures. This challenge is likely to become more common thanks to the recent progress in immunotherapy in oncology and gene therapy for certain rare genetic disorders.

To address the mismatch between the upfront payment and the duration of health benefits offered by cures, my co-authors Vahid Montazerhodjat and David Weinstock and I recently proposed a private-sector solution consisting of healthcare loans (HCLs).[1] The idea is straightforward: turn a large upfront payment into a more affordable sequence of much smaller payments over a longer horizon. In short, we propose the equivalent of a mortgage to cover the cost of cures. In our publication, we show that financial techniques such as portfolio theory, securitization, and credit default swaps can be applied to raise substantial amounts of capital from private investors to help patients and insurance companies pay for cures. Although our analysis is entirely hypothetical and based on statistical simulations of the risks and rewards of a portfolio of HCLs, these types of simulations often serve as the basis for launching new investment products and services. Our simulated results show that, under plausible assumptions for rates of consumer default, patient mortality, and other economic variables, investors could earn attractive rates of return by investing in pools of HCLs (in our simulations, senior and junior tranche bonds yield market rates of 2.1% and 2.5%, respectively, and the average simulated return of the equity tranche is 12.5%). And by investing in these securities, investors would be providing capital to help patients get access to expensive one-time healthcare co-payments at reasonable interest rates.

Securitized HCL funds have several other advantages. Their returns are not likely to be highly correlated with the stock market, making them good sources of diversification for large institutional investors such as pension funds, mutual funds, and life insurance companies. By pooling a large number of diverse HCLs, the fund lowers the overall risk to investors which, in turn, reduces the cost of capital charged by investors, leading to lower borrowing costs for consumers. Also, the very structure of HCLs can create a tighter link between price and value—if a cure does not really cure, then the payments stop. And HCLs would likely accelerate the pace of biomedical innovation. If drug developers are able to recoup the cost of their investment in scientists, laboratories, and expensive clinical trials, they have much a greater incentive to develop cures rather than mitigators.

[1] V. Montazerhodjat, D. M. Weinstock, A. W. Lo, Buying cures versus renting health: Financing health care with consumer loans. **Sci. Transl. Med.** 8, 327ps6 (2016).

Our proposal does not directly address the question of who is the borrower. Currently, many health insurance companies are unwilling to reimburse patients for the cost of these expensive therapies. Therefore, in the short run, patients would be the borrowers under our proposal. However, this is a temporary solution—the more permanent, and economically more efficient, solution is for health insurance to cover such expenses. This will likely require new healthcare legislation which we describe in our publication. While we wait for such legislation to be enacted, many lives can be saved by offering HCLs to consumers now.

Our proposal is far from ideal (see Table 1 of our publication for a list of its limitations). The very idea of mortgaging one's health is distasteful, and many stakeholders may find the discussion of rates of return in the context of life-and-death issues to be offensive and obscene. However, the alternative of the status quo—possessing the scientific means and the financial resources for curing patients with mortal illnesses, and not making use of both—seems even more troubling.

Another objection to HCLs is that they are based on the same techniques involved in the recent financial crisis. However, the financial crisis occurred not because these techniques did not work, but rather because they worked far too well, raising enormous amounts of capital for U.S. homebuyers in a very short period of time. Like any powerful tool, securitization can be abused, causing great harm; hence, there must be strict regulatory oversight to prevent such abuses in the case of HCL funds, including risk transparency for investors, risk-retention policies for issuers, and greater supervision by regulators. But we would be doing more harm than good by rejecting these tools just because of past mistakes.

One of the consequences of a robust and liquid HCL market may be an increase in the prices of certain drugs, which seems counter to the motivation and spirit of your report and recent Senate hearings. While I am no expert on drug pricing issues, and our proposal and research article have nothing to say about pricing, I would like to make a few general observations about this issue from my perspective as an economist.

First, there is a difference between price-gouging, which is reprehensible behavior that every industry has faced and eschews, and expensive but highly effective therapies, and we should be mindful not to conflate the two. Imposing arbitrary price caps or threatening to invalidate patents and expropriate intellectual property—solutions that have been proposed in the cases of Sovaldi and Harvoni—would have a chilling effect on biomedical innovation, especially for cures. This unintended consequence serves no one's interests.

A more productive approach from the patient perspective is to link prices more closely to value. This is easier said than done for several reasons: measuring value can be challenging, pricing is influenced not just by market forces but also by various government controls and incentives, and drug developers operate in a multi-national setting with regulated pricing structures often at odds with our own competition-driven system. Nevertheless, we can do much more to encourage "pay for performance" in the pharmaceutical industry and stimulate the development of breakthrough therapies while not condoning price gouging.

Second, prices are determined by many factors (as your report amply illustrates), including: the amount of funding for supporting basic life sciences research; the financial risks and rewards of drug development; the type of healthcare system in which drugs are

administered and the incentives they create for patients, doctors, and payers; and the legal, political, and cultural environments in which drugs are developed, administered, and paid for. Therefore, addressing the problem of the high cost of drugs may require addressing a number of related problems in the drug-development production, distribution, and reimbursement chain. One of the most commonly cited reasons for high drug prices is to justify the cost of developing a successful drug (most recently estimated to be $2.6 billion), and the financial risk to investors (in oncology, the estimated probability of FDA approval for an anti-cancer drug from Phase 1 is just 6.7%).[2] If we can reduce the costs and the risks of drug development, prices should follow suit. New approaches to clinical trial design and execution such as the I-SPY breast cancer and GBM AGILE brain cancer initiatives show great promise in bringing down the cost and increasing the efficiency of drug development,[3] and new financing and business models for funding multiple drug development programs simultaneously can reduce the financial risks to investors and draw more private-sector funding into the industry.[4]

Finally, unlike the prices of many other consumer goods, drug prices cannot be analyzed by economic logic alone because, in some cases, affordability is a matter of life and death, raising moral and ethical issues that are well outside the purview of economists. Humans are rarely motivated solely by economic incentives. However, incentives should never be disregarded as irrelevant or unimportant. Although the executives of Gilead Sciences are no doubt motivated by a genuine desire to help hepatitis C patients, they also have an obligation to manage their for-profit company to benefit Gilead shareholders, which, in standard economic theory, consists of maximizing corporate profits. If, as a society, we find this single-minded pursuit of financial success repugnant when it involves certain products and services, we should address this gap in our social contract through political discourse and legislative action.

To further that discourse and facilitate the implementation of practical solutions, MIT and the Dana Farber Cancer Institute are co-hosting a conference later this year on this subject. Representatives from all stakeholder groups will gather to explore the financial and ethical issues surrounding the pricing of breakthrough therapies, and we hope you and your staff members will be able to join our meeting and continue to provide the kind of thought leadership that your report exemplifies.

Thank you for your time and consideration.

Sincerely,

Andrew W. Lo

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[2] See http://csdd.tufts.edu/news/complete_story/pr_tufts_csdd_2014_cost_study for the most recent estimate of drug development costs, and for estimated drug-development success rates, see M. Hay, D. Thomas, J. Craighead, C. Economides, and J. Rosenthal, Clinical development success rates for investigational drugs, **Nat. Biotech.** 32, 40–51 (2014) doi:10.1038/nbt.2786.

[3] See http://ispy2.org and http://nbdabiomarkers.org/gbm-agile.

[4] J-M. Fernandez, R. Stein, A. Lo, Commercializing biomedical research through securitization techniques, **Nat. Biotech.** 30, 964–975 (2012) doi:10.1038/nbt.2374.