UNIVERSITY OF CAMBRIDGE

Faculty of Politics, Psychology, Sociology, and International Studies

March 2, 2016

Re: New evidence for Senate Finance Committee study on Sovaldi and Gilead Sciences

To the Senate Finance Committee:

Our research team at the University of Cambridge has been investigating the innovation system behind Hepatitis C science and drug development between the 1970s and present, and we have two preliminary findings that we believe would make a valuable contribution to your study on Sovaldi and Gilead Sciences. A more comprehensive version of our findings, which rely on documentary analysis of the scientific and medical literature, interviews with leading scientists and executives involved in Hepatitis C, as well as earnings call transcripts between investment analysts and firm executives, are currently being developed into papers for peer review. However, we wanted to share these two features of the innovation process because they may bring to light aspects of the Hepatitis C debate not previously considered.

First, Hepatitis C drug development required early public financing from a network of public research institutes and federal grant programs.

- The discovery of the virus – first reported in the journal *Science* in 1989 - required a network of public and private actors, featuring scientists at the Centers for Disease Control, National Institutes of Health, and Chiron Pharmaceuticals[1,2,3].
- But drug development could not proceed for over a decade after the virus' discovery because scientists could not grow Hepatitis C in cell culture and thus could not test whether potential drug compounds had an anti-viral effect[4,5,6].
- Furthermore, Chiron's Hepatitis C related patents further discouraged firms from investing in Hepatitis C[7]. In fact, Gilead Sciences itself dropped their Hepatitis C program in the late 1990s, only returning to invest in Hepatitis C research after further public investments led to necessary research tools and Chiron's loosening of their intellectual property hold[8].
- Publicly financed scientists in Germany and the U.S. – the labs of Ralf Bartenschlager and Charlie Rice – developed the *replicon*, a research tool that generated the parts of the Hepatitis C virus necessary for potential drugs to be tested[9,10]. This replicon was commercialized by Apath LLC, which received further NIH funding from the Small Business Innovation Research Program (SBIR) as a spin-off from the Charlie Rice's lab (Washington University in St. Louis and then Rockefeller University)[11]. The replicon gave small biotechnology companies and large firms interested in Hepatitis C a major tool to spur drug development[12].
- One of the companies to use the replicon was Pharmasset, which ultimately developed *sofosbuvir.* Pharmasset emerged in 1998 from a lab at Emory University funded

Free School Lane
Cambridge
CB2 3RQ

primarily through the U.S. Veterans Administration and National Institutes of Health[13]. The company also received funding from the NIH's SBIR program for its early drug development programs, including for Hepatitis C (further information available upon request).

Second, Gilead Sciences has directed most of their windfall Hepatitis C revenues back into share buybacks and dividends.

- Pharmaceutical companies have been criticized in the past for spending more money on marketing than research and development. Yet a growing trend is for firms to direct their retained earnings into share buy backs and dividends rather than research and development[14].
- Gilead Science's near monopoly on the Hepatitis C market has allowed it to accrue over $31 billion in revenue from Hepatitis C medicines since their launch in December of 2013[15]. In 2015, the company's revenue from Hepatitis C alone exceeded $19 billion, representing nearly 2/3rd of the entire $30.4 billion annual budget of the U.S. National Institutes of Health. As of the first quarter of 2016, Gilead held nearly $25 billion in cash and debt primarily driven by their windfalls from Hepatitis C.
- What are the uses of this money? The company has announced $27 billion in 'share buy backs' since the beginning of 2015, a strategy through which a company purchases its own shares to increase its stock price[16,17]. In addition to $1.9 billion in dividends, increases in share repurchases far outpace additions to their R&D budget, which rose from $2.5 billion to $3 billion between 2014 and 2015.
- Gilead's senior management, with the encouragement and pressure of Wall Street analysts, has publicly indicated that they are looking for acquisitions with assets deemed sufficiently 'de-risked' by reaching late stage of clinical development, much as they did with Pharmasset[18]. In September of 2015, the company took on an additional $10 billion in debt to ensure the strength of their financial position as an acquirer of future assets[19]. Meanwhile, as the Senate Finance Committee report documented, many patients continue to wait with state Medicaid programs restricting access.

These two features of the innovation process – early public financing as well as late-stage financial market speculation – should raise further questions about how risks and rewards are distributed in drug development. The important issues which the Senate Finance Committee report documents around price, value, and access should be considered in light of this evidence.

We would welcome further discussion on this crucial case study of Hepatitis C, and what it might tell us for future breakthrough medicines.

Sincerely,

Victor Roy (vr260@cam.ac.uk) ***Corresponding author***
MD candidate, Northwestern University, Feinberg School of Medicine (Chicago, IL)
PhD candidate, University of Cambridge, Gates Cambridge Scholar (Cambridge, UK)

Dr. Lawrence King
Professor of Sociology and Political Economy
Fellow, Emmanuel College
University of Cambridge (Cambridge, UK)

[1] Choo Q, Kuo G, Weiner A, Overby L, Bradley D, Houghton M. Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. Science. American Association for the Advancement of Science; 1989 Apr 21;244(4902):359–62.
[2] Alter HJ. The road not taken or how I learned to love the liver: A personal perspective on hepatitis history. Hepatology. 2013 Nov 22;59(1):4–12.
[3] Houghton M. Discovery of the hepatitis C virus. Liver Int. 2009 Jan;29:82–8.
[4] Nair P. Profile of Charles M. Rice. Proceedings of the National Academy of Sciences. National Acad Sciences; 2011 May 24;108(21):8541–3.
[5] Cohen J. The Scientific Challenge of Hepatitis C. Science. 1999 Jul 2;285(5424):26–30.
[6] Bartenschlager R. Hepatitis C virus replicons: potential role for drug development. Nat Rev Drug Discov. 2002 Nov;1(11):911–6.
[7] Cohen J. Chiron Stakes Out Its Territory. Science. 1999 Jul 2;285(5424):28–8.
[8] Pollack A. H.I.V. Lessons Used in Hepatitis C Treatment. New York Times. 2003 Mar 11.
[9] Lohmann V. Replication of Subgenomic Hepatitis C Virus RNAs in a Hepatoma Cell Line. Science. American Association for the Advancement of Science; 1999 Jul 2;285(5424):110–3.
[10] Blight KJ. Efficient Initiation of HCV RNA Replication in Cell Culture. Science. American Association for the Advancement of Science; 2000 Dec 8;290(5498):1972–4.
[11] Company Profile [Internet]. Apath. [cited 2016 Feb 2]. Available from: http://www.apath.com/Company.htm
[12] Marshall, E. (2000). Hepatitis C - New "replicon" yields viral proteins. *Science*, *290*(5498), 1870–1871.
[13] Cohen J. King of the pills. Science. American Association for the Advancement of Science; 2015 May 7;348(6235):622–5.
[14] Booth B. Big BioPharma Stock Buybacks: Are There Better Alternatives?[Internet]. Forbes. 2012 [cited 2016 Mar 2]. Available from: http://www.forbes.com/sites/brucebooth/2012/08/22/big-biopharma-stock-buybacks-are-there-better-alternatives/#748561f9340f

[15] Gilead Sciences. Quarterly Financial Reports. 2014-2016. http://www.gilead.com/news/press-releases
[16] Gilead Sciences Announces Declaration of Q1 Cash Dividend and Increases to Shareholder Return Programs [Internet]. Gilead Sciences; 2016. Available from: http://www.gilead.com/news/press-releases/2016/2/gilead-sciences-announces-declaration-of-q1-cash-dividend-and-increases-to-shareholder-return-programs
[17] Gilead Sciences Announces 43 Cents Quarterly Dividend Program and $15 Billion Share Buyback Program [Internet]. 2015. Available from: http://www.gilead.com/news/press-releases/2015/2/gilead-sciences-announces-43-cents-quarterly-dividend-program-and-15-billion-share-buyback-program#sthash.m2ebZoSG.dpuf
[18] Crow D. Cash-rich Gilead hits acquisition trail. Financial Times [Internet]. 2015 Dec 7. Available from: http://www.ft.com/cms/s/0/8a8e383e-9abc-11e5-a5c1-ca5db4add713.html
[19] Grant C. Gilead's Big Borrowing Raises Deal Talk. Wall Street Journal [Internet]. Money Beat. 2015 Sep 9. Available from: http://blogs.wsj.com/moneybeat/2015/09/09/gileads-big-borrowing-raises-deal-talk/