## Does IHU Mediterranean Infection influence Gilead stock price?

2 Chabriere Eric<sup>1\*</sup>

- <sup>1</sup>Aix Marseille Université, IRD, APHM, MEPHI, IHU-Méditerranée Infection, Marseille, France
- 4 \* correponding author : eric.chabriere@univ-amu.fr

5

1

6

7

## Abstract

- 8 During Covid-19 pandemic the Gilead stock prices rose sharply with large variations. These
- 9 fluctuations have been tentatively related to communications, publications or leaks about Remdesivir
- 10 or hydroxychloroquine/azithromicin treatment .

11

12

25

26

In December 2019, an outbreak of an emerging disease (COVID-19) caused by a novel 13 14 coronavirus (named SARS-CoV-2 later) started in Wuhan (China) and rapidly spread in China and outside <sup>1,2</sup>. The WHO declared the epidemic of COVID-19 as a pandemic on March 12th 2020<sup>3</sup>. Two 15 promising drugs against covid-19 rapidly emerged: Remdesivir and Chloroquine<sup>4</sup>. Remdesivir, a new 16 antiviral drug developed by Gilead Science in 2017, is currently under clinical investigation as a 17 treatment against Ebola virus infection<sup>5</sup>. Chloroquine is a very old, widely used and safe generic 18 antimalarial drugs<sup>6</sup>. 19 20 Some early clinical Chinese studies suggested efficiency of chloroquine<sup>7</sup>. From this, IHU 21 Mediterranean Infection (IHU-MI) chose to evaluate the association of hydroxychloroquine, a closely 22 related molecule to chloroquine better tolerated, and azithromycin drugs. Azithromyin is a generic classical antibiotic, chosen for prevention of bacterial complications and also for these antiviral 23 properties<sup>8</sup>. Despite some promising results, with a first clinical trial including 24 patients<sup>9</sup> and 24

another one including 80 patients<sup>10</sup>, the treatment associating hydroxychloroquine and azithromycin

was strongly attacked. The first argument was that Clinical trials were not performed as conventional

RCT design. The second argument was the toxicity and side effects of these two molecules<sup>11</sup>. Such debate was surprising considering that these two generic drugs have been widely prescribed for a longtime, are very safe and their side effects are well documented and limited<sup>12</sup>. Conversely, investors seem more optimistic with Remdesevir although there is still no publication demonstrating efficiency about Remdesivir treatment and Remdesivir presents toxicity side effects. Meanwhile, stock exchange of Gilead, the biopharmaceutical company developing Remdesivir molecule, increased significantly in a period where numerous stock market prices fall including pharmaceutical companies. Consequently, we decided to analyze the reasons and consequences.

We compared the market trading price from January first to May 6<sup>th</sup> of several pharmaceutical

companies: Gilead, Sanofi, Roche, GlaxoSmithKline and Abbvie (figure 1). With the exception of Gilead, all companies suffered from the COVID-19 crisis with a drastic decrease at the end of March 2020 followed by a steady increase thereafter. The absolute cumulated fluctuations day by day of the stock price for these companies represent 2.4, 1.71, 1.65, 1.57, 1.29 times its value for Gilead, Abbvie Sanofi, Roche and GSK respectively. Cleary, Gilead stock price presented the most variations. They were also most exceptional as they were not due to the drastic drop and catching up as other companies.

The capitalization of Gilead is about 100G\$. The share market trading price of Gilead from January first 2020 is represented in figure 1<sup>13</sup>. It increased regularly from the end of January. The minimum price of the share was 62.83\$ January 21<sup>st</sup> and reached up to 85.19\$ on April 17<sup>th</sup>. This corresponds to a capitalization increase of about 35.6G€ in 3 months. The curve shows also large fluctuations showing a quasi-perfect synchronization with declarations or publications about Remdesivir and IHU-FMI (figure 1). Forces that increase the market price of Gilead are journal publications or leaks related to the performance of the Remdesivir and information about the start of clinical trials. The

Remdesivir competitive hydroxychloroquine/azithromycine treatment, politic support or journal

54 publications about inefficiency of Remdesivir.

The main fluctuation was observed on March 16<sup>th</sup> with a market price increase of 13.7\$ in three days,

corresponding to an increase of the companies value of 21.8G\$. This huge increase followed Dr.

Fauci's lecture announcing, despite the scientific use and without any documentation, that

Remdesivir was only effective for the duration of hospitalization but not for mortality or clinical

improvement.

60

53

55

56

57

58

59

6162

63

64

65

66

67

68

69

70

71

Publications about the efficiency of Remdesivir as a treatment againstCOVID-19 are not convincing

neither from a methodological nor from a medical point of view<sup>14,15</sup>. Furthermore, a Chinese team

recently reported the absence of benefit of Remdesivir treatment against placebo<sup>16</sup>. Consequently,

the value of Gilead based on the potentially of Remdesivir is overestimated as it was pointed by

Gilead analyst<sup>17</sup>. Furthermore, we estimated from the ABC bourse<sup>13</sup> that the total exchange of shares

from January first to May 6th represents 10.7G\$, a very high-level. Communication about Remdesvir

considerably influences stock change of Gilead. Given that, we can raise the issue of insider trading<sup>14</sup>.

Prior knowledge by certain Gilead shareholders of the publication of articles written by Gilead itself

or of statements or leaks from various institutions would allow them to obtain enormous benefits.

72

73

74

## Materials and Methods.

- Cotation of pharmaceutical companies and volume shares exchanged from January first to May 6th
- have been uploaded from ABC bourse website<sup>13</sup>
- The total sum exchanged of share was calculated by multiplying the opening price of the share by the
- 77 number of share exchanged and sum over the period.

The cumulated fluctuations were the absolute difference between the price (D<sub>i</sub>-D<sub>i-1</sub>) and sum over the period. This Sum was divided by the average price of the share over the period to compare the cumulated fluctuations with the share value. Acknowledgements This work was supported by "Investissements d'avenir" program (Méditerranée Infection 10-IAHU-03) of the French Agence Nationale de la Recherche (ANR). Competing interests Author declare to have no conflict of interest Reference. Lai CC, Shih PS, Ko WC, Tang HJ, Hsueh PR. "Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges". Int J Antimicrob Agents 55 (2020). 105924 Wang LS, Wang YR, Ye DW, Liu A QQ. "Review of the 2019 Novel Coronavirus (COVID-19) based on current evidence". Int J Antimicrob Agents (2020), in press WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. [https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—11-march-2020]. Google Scholar

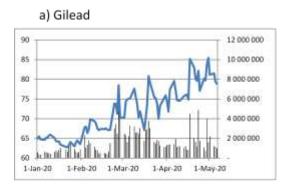
Wang M, Cao R, Zhang, L. et al. "Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro". Cell Res (2020). 30, 269-271. Mulangu S, Dodd LE, Davey RT et al." A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics" N Engl J Med (2019). 381, 2293-2303. Solomon VR, Lee H. "Chloroquine and its analogs: A new promise of an old drug for effective and safe cancer therapies". European Journal of Pharmacology (2009). 625, 220-233 Gao J Tian Z, Yang X"Breakthrough: Chloroquine Phosphate Has Shown Apparent Efficacy in Treatment of COVID-19 Associated Pneumonia in Clinical Studies." Bioscience Trend (2020). 14, 72-73. Min JY, Jang YJ. "Macrolide therapy in respiratory viral infections. Mediators Inflamm". Mediators Inflamm (2012). 2012, 649570 Gautret P, Lagier JC, Parola P, et al. "Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial". International Journal of Antimicrobial Agents (2020). 105949, in press Gautret P, Lagier JC, Parola P, et al. "Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: A pilot observational study." Travel Medicine and Infectious Disease (2020). 101663, 1477-8939 https://www.nbcnews.com/health/health-news/man-dies-after-ingesting-chloroquine-attempt-prevent-coronavirus-n1167166 Hache G, Jean Marc Rolain JM, Gautret P, et al. (2020). https://www.mediterranee-infection.com/wp-content/uploads/2020/04/azithroquine\_manuscript-soumis.pdf. Preprint ABC bourse. https://www.abcbourse.com/download/historiques.aspx

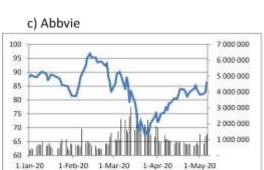
https://www.reuters.com/article/us-health-coronavirus-gilead-sciences-op-idUSKBN23828D

- 128 Grein J, Ohmagari N, Shin D et al. "Compassionate Use of Remdesivir for Patients with Severe Covid-
- 129 19". n engl j med (2020). DOI: 10.1056/NEJMoa2007016
- 130 16 IHU news. https://www.mediterranee-infection.com/actualite-du-traitement/
- 131 17 Whang Y, Zhang D, Guanhua D et et al. (2020). "Remdesivir in adults with severe COVID-19: a
- randomised, double-blind, placebo-controlled, multicentre trial". The lancet (2020).
- 133 https://doi.org/10.1016/S0140-6736(20)31022-9
- 134 18 https://www.bloomberg.com/news/articles/2020-03-05/gilead-analyst-sees-only-50-chance-that-
- 135 coronavirus-drug-works
- 136 19 Remuzzi. "COVID-19 and Italy: what next?" The lancet (2020). 395: 1225–28
- De Wit E, Feldmann F, Cronin J et al. "Prophylactic and therapeutic remdesivir (GS-5734) treatment in
- the rhesus macaque model of MERS-CoV infection". PNASS 117, 6771-6776.
- 139 21 https://www.nih.gov/news-events/news-releases/nih-clinical-trial-remdesivir-treat-covid-19-begins
- Holshue M, Debolt C, Linsquist S et al . « First Case of 2019 Novel Coronavirus in the United States". N
- 141 Engl J Med (2020). 382, 929-936
- 142 23 https://fr.wikipedia.org/wiki/Discovery\_(essai\_clinique)
- 143 24 https://www.nbcnews.com/health/health-news/man-dies-after-ingesting-chloroquine-attempt-
- 144 prevent-coronavirus-n1167166
- 145 25 https://www.clinicaltrialsarena.com/news/gilead-remdesivir-covid-19-uk-trials/
- 146 26 https://www.statnews.com/2020/04/16/early-peek-at-data-on-gilead-coronavirus-drug-suggests-
- 147 patients-are-responding-to-treatment/
- 148 27 https://www.japantimes.co.jp/news/2020/05/03/national/science-health/japan-health-ministry-
- approve-remdesivir/#.XrLkl0QzZOQ

150	28	https://www.niaid.nih.gov/news-events/nih-clinical-trial-shows-remdesivir-accelerates-recovery-
151	advanced-covid-19	
152	29	IHU-MI communication (February 25th). "CORONAVIRUS : VERS UNE SORTIE DE CRISE ?"
153	https://www.mediterranee-infection.com/coronavirus-vers-une-sortie-de-crise/	
154	30	IHU-MI Communication (March 9th). "CORONAVIRUS : PEUR VS DATA / CHLOROQUINE : RECHERCHE
155	CLINIQ	JE" https://www.mediterranee-infection.com/coronavirus-peur-vs-data-chloroquine-recherche-
156	clinique/	
157	31	IHU-FMI press release (March 22). https://www.mediterranee-infection.com/epidemie-a-coronavirus
158	covid-19/	
159	32	https://www.theguardian.com/world/2020/apr/23/high-hopes-drug-for-covid-19-treatment-failed-in-
160	full-tria	I
161		
162		
163		
164		
165	Legeno	d figure 1
166	Cotatio	on of some pharmaceutical companies (Opening price). Curves is the price of the stock price
167	left axi	s. Histogram is the volume of shares exchanged, right axis. a) Gilead, b) Sanofi, c) Abbvie, d)
168	Roche,	e) Glaxosmithkline.
169		
170		
171	Legeno	I figure 2. Cotation of Gilead science. Opening price.

172 + Corresponds to elements susceptible to explain increase of the market price of Gilead 173 - Corresponds to elements susceptible to explain decrease of the market price of Gilead 174 Increases 175 +a. COVID-19 reaches Europe<sup>19</sup> 176 +b. February 13<sup>th</sup> first publication of "Prophylactic and therapeutic remdesivir (GS-5734) treatment in the rhesus macaque 177 model of MERS-CoV infection." In PNASS<sup>20</sup> 178 +c. Clinical trial of remdesivir to treat COVID-19 begins<sup>21</sup> 179 +d. Publication of the First patient healed with Remdesivir. <sup>22</sup> 180 +e. Start of the European trial discovery 23 181 +f. Fake news about chloriquine toxicity 24 +g. Gilead initiates two studies of remdesivir for Covid-19 in UK  $^{25}$ 182 183 +h. Publication of the first clinical trial about Remdesivir. 16 184 +i. A leak from Chicago hospital suggests patients are responding to Remdesivir <sup>26</sup>. 185 +j. The health ministry is moving to approve the antiviral drug Remdesivir to treat domestic coronavirus patients<sup>27</sup>. 186 +k. NIH claims Remdesivir Accelerates Recovery from Advanced COVID-19<sup>28</sup> 187 188 Decreases 189 -a IHU-MI suggest that hydroxycholoroquine is a treatment for COVID-19<sup>29</sup> 190 -b. IHU-FMI announce the beginning of the clinical trial with hydroxycholoroquine<sup>30</sup> 191 -c. IHU-FMI announce that it will treat COVID patient with hydroxychloroquine and azithromycine invocating Hyppocratic Oath<sup>31</sup> 192 -d. Publication of First clinical trial of the IHU-MI<sup>9</sup> 193 -e. French president E Macron visits IHU-FMI (April 9<sup>th</sup>). 194 -f. WHO Leak "First trial for potential Covid-19 drug shows it has no effect" 32. 195 -g A clinical trial published by the lancet show no benefit for the Remdesivir<sup>15</sup>



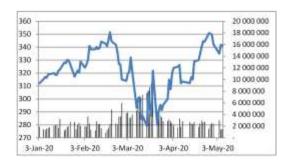








## d) Roche



200 Figure 2

