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COMMENTARIES

# There is something rotten in the state of the Pharma Industry

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**Commentary on**
Cole, AH, 2018, Why Is Pfizer Giving Up on Parkinson's and Alzheimer's?, *Fortune*, Jan 16.

## 1. Throw in the towel

Recently, Pfizer - the third largest pharmaceutical company in the world - announced that it will stop funding research carried out up to now on Alzheimer and Parkinson's treatment. "As a result of a recent comprehensive review, we have made the decision to end our neuroscience discovery and early development efforts and re-allocate [spending] to those areas where we have strong scientific leader-ship and that will allow us to provide the greatest impact for patients", the Company stated in a press release (Novak, 2018). This statement sounds like a sentence that suppresses the expectations of the community of patients suffering from neurodegenerative diseases, and decrees at the same time the dismissal of about 300 researchers of the company.

The story has caused an uproar due to the obvious social implications that it entails but, unfortunately, it has not been accompanied by an equally courageous analysis of the true meaning behind this decision.

First of all, we have to remember that, in a capitalist society, whether you like it or not, a drug is still subject to the laws of the market. For a new drug, costs of research, development and production are inevitably huge (on average between 300 and 900 million €), and if that drug does not produce useful clinical results – as frequently happens –in the long run the endeavor will result in a definite failure. This has already happened with other companies, including Merck, which decided to withdraw from the neuro-science sector a few years ago. Pfizer implicitly recognized that there are actually no hopes of finding any effective remedies for such neurodegenerative disorders in the medium period. Hence the obvious conclusion: better to sell Viagra (or something similar), playing it safe and investing in those fields in which the economic return is already assured.

Nothing to complain about here. Moreover, this logic has already conditioned the dynamics of other sectors - such as that related to antibiotics. Identifying and producing new antibiotics is difficult, costly and amortization expenses will hardly be amortized within a reasonable time. Result: no new antibiotics have been produced during the last twenty years, despite the fact that resistance to common antibiotics has become so widespread that the emergence of an epidemic sustained by potentially unstoppable microbes has now become fearful.

Faced with this scenario, the State – the metaphorical figure that, by now, has disappeared in the 'advanced' nations and even from the lexicon of politicians - should take charge of the task. Scientific academic research should be financed and promoted, leaving private Companies to develop and market drugs and

devices proposed by the Academy. For example, there are alternatives for the treatment of Alzheimer that focus on the (preventive) use of natural molecules, for which, however, patenting possibilities are scant.

## 2. New solutions?

One of these solutions has been developed at Sapienza University of Rome, and it is based on the use of S-adenosyl-methionine (SAM), which has already yielded important results in the pre-clinical setting (Fuso, 2012). However, no one has ever investigated its usefulness in a randomized clinical trial simply because the possibility of 'transforming' it into a drug (that is, 'merchandise') amounts to almost zero, since the drug will have a hard time getting a patent. In short: if a solution exists, but cannot enter the patent-protected marketing, it is almost impossible to adopt it. A potentially life-saving drug - according to the prevailing logic - would thus end up in oblivion precisely because it could not become "merchandise". Therefore, from a logical point of view, the state should take responsibility for it. If a state does still exist.

However, Pfizer's choice cannot be explained solely by addressing financial and economic aspects, however important these may be. Economy is not the whole story. Indeed, Pfizer could also afford to bet on the future, perhaps risking losing a few billion dollars. In fact, its third-quarter accounts closed with a more than doubled profit. In the period under consideration, the pharmaceutical giant reported a net profit of 2.84 billion dollars, more than double from 1.35 billion in the same period of the previous year, while revenues rose, for the same interval of time, from 13.05 to 13.17 billion. Furthermore, the neuroscience sector is among the most promising in the long-term perspective. Let us consider the epidemiological scenario in the USA: about 10 million people are affected by Parkinson's, and 44 by Alzheimer's, data that will probably increase in a significant manner in the next decade (the estimates foresee a multiplication by three!), coinciding with the increase in the population's mean age. The cost of pharmaceutical spending for Alzheimer's alone is currently $ 259 billion. We can estimated that in 2050, the expenditure will grow to nearly one trillion dollars (Cole, 2018).

Therefore, why give up a very appetizing market? To answer the question it is necessary to take a step backwards, and try to translate the difficulties inherent in the setting of scientific research into understandable terms. The treatments used today in the treatment of Parkinson's and Alzheimer's have been developed between the end of the '60s and' 70s. For Parkinson's, just look at the wonderful movie Awakenings, with R. de Niro and R. Williams, where it is clearly shown how 'discovery' proceeds - as usually happens - from personal intuition to a recurring comparison of empirical phenomena, framed in a theoretical model.

Since then, unfortunately, we have not really made any substantial progress in the field, in spite of the trumpeted victory bulletins issued at regular intervals by the revolving shoppers. "Current Alzheimer's drugs - as one of the leading scientists in the industry, Joseph Jebelli recently pointed out - have only been approved because they are 'better than nothing'. And at the moment we do not have anything else" (Jebelli, 2018a).

## 3. Inadequacy of theoretical premises

Why then did research arrive at a cul de sac? Francis Bacon or no Francis Bacon, the so-called 'inductive' method could only lead to disappointing results in Biology, when data acquisition and classification are not regulated by robust (and correct) scientific theory, however provisional that theory may be. Empirical data does not explain anything by itself, unless you have a theoretical tool able to frame raw data within an explanatory model. As widely recognized, the model that hitherto led experimentation in neuroscience is based on the so-called 'central dogma of Biology' (Francis Crick dixit!)(Crick, 1970), for which – ultimately - every disease is determined by the altered function of a gene.

Yet, it is not so, as evidenced by the case of Alzheimer's and Parkinson's, at least. Indeed, in these diseases, no 'mutated gene' or 'altered' gene has been found so far. Definitely, a clear genetic predisposition, deemed to increase the risk of developing Alzheimer (with a chance of about 50%), has been ascertained in only a 5-10% of individuals (Jebelli, 2018b).

Consequently, it is futile to look for a drug – a magic bullet - that can target a specific gene segment. Over the years, on the other hand, the evidence for which the disease "emerged" from an altered regulation of the relationship between the neuronal cell and the microenvironment has gained momentum (Cotman et al., 2000; Fuso, 2018). Thereby, efforts must be concentrated on identifying those drugs that can change the framework of cell/environment mutual relationships.

Something similar also happens in the oncological field, as recently mentioned - with great courage - by Ermanno Leo, eminent scientist of the IRCCS of Milan.

"Even in oncology, claims do not match the facts: "research continues to come out announcing sensational discoveries against cancer, but cancer deaths are still more than 180 thousand a year [in Italy]. Something's wrong, isn't it? [...] Chemotherapy is not the solution. We must change the register" (Leo, 2018).

A verdict that Pharmaceutical Companies can hardly digest. Oncology is a fruitful business. The average cost of treatment for a cancer patient, in Europe, now ranges between 50 and 135,000 euros/year/patient (Dolgin, 2018). Clinical outcomes? Almost worthless. It is suffice to see the mortality data published by Atlanta's Center for Disease Control. Why? Simply because you continue to believe in a theory that denies (or severely underestimates) the existence of contradictory facts. It is not enough to hit 'genetic/enzymatic targets', since not only are they unspecific, but they become irrelevant once a tumor deviates towards 'alternative pathways' of functional activation.

In conclusion, I think Pfizer understood all of this. There is no hope in the short to medium term to find a drug that works, precisely because the scientific theory on which this research is based is 'bankrupt'. And yet no one has the courage to say it openly.

How long will we have to wait (and what cost will we have to sustain unnecessarily) before we radically change our perspective?

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