BURPA or Bust!
How to build a Bio-Unified Research Project Agency? (Extended Abstract)

Bud Mishra[1]
In collaboration with: Q. Qi, L. Rudolph, F. Savas, and M. Weill

Courant Institute, NY 10012, USA,
mishra@nyu.edu

Abstract. A specter of sky rocketing drug prices is haunting the global health care. A novel market micro-structure in alliance with theories from financial engineering, smart contracts, systems biology and information asymmetric games can exorcise this specter, thus enabling lower per-patient costs for both curative and non-curative therapies for acute and chronic diseases, respectively, while accelerating research on drug discoveries.

Here, we formalize our and others' earlier design of mega-funds via an information-asymmetric signaling game model and then implement it with verifiable smart contracts. The model not only elucidates how the stakeholders strategically interact in this market using deception, adverse selection, moral hazards, etc. but also how to tame their interactions to improve the overall performance. In particular, we suggest and rigorously evaluate an embodiment built on a scalable implementation of smart contracts and crypto-currencies. Using extensive simulations, we show that, in the smart-contract-based mega-fund both senior and junior tranche investors get their principals fully repaid in 99.9%of the time.

In costly signals, we trust; it's BURPA or bust!

Keywords: Smart Contracts, Information Asymmetric Games, Cancer Megafund

1 Problem with Current Bio-Research Project Models

The pharmaceutical industry faces a significant barrier against accelerating research for drug discovery: specifically, for cancer. The average cost of new drug development in the U.S. was around USD 2.6 billion in the past ten years – up from an average of USD 1 billion in the 1990s. Such extraordinarily high costs for drug development are not only reflected in skyrocketing prices of approved cancer drugs, which thus places a substantial burden on U.S. households, but also in discouraging the pharmaceutical industry from allocating research-and-development (R&D) resources to projects with narrow profit margins. This state of affairs leaves many cancer subtypes, rare genetic disorders or third-world infectious diseases, all but neglected. Subsequently, it can result in critical medical needs remaining largely unmet. According to many scholars, such high costs, and by inference, the declining efficiency of R&D investment in biomedical industry, is a major indicator that the current biomedical business model is flawed, relying too heavily on the incentive provided by patents to rationalize the risk of investing in biomedical R&D.

1.1 Four Stages of Bio-Research Projects

Specifically, there are four stages for each biotechnological research: (*i*) funding; (*ii*) innovation and research; (*iii*) clinical trials and regulation approval; (*iv*) pricing and marketing (See Figure 1). Based on these stages, we categorize all the current research processes into two major approaches:

1. Not-for-profit approach: Government agencies (or charity and other nongovernmental organizations) collect funds from tax payers (or general public), and then distribute them to researchers in the university labs or research institutions based on peer review process. If a researcher makes a breakthrough, he either starts up an enterprise through a technology transfer office or licenses it to pharmaceutical companies.
2. Market approach: Pharmaceutical companies collect funds from venture capitalists or the capital market and hire researchers to work on promising projects. If a drug is approved by FDA, companies price it and sell it in the market or to the hospitals.

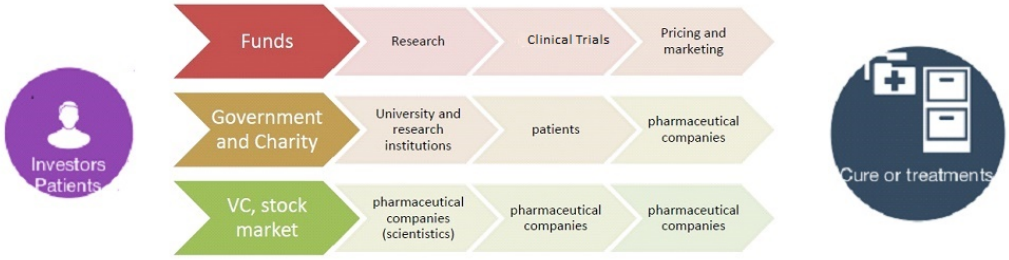

Fig. 1: *Stages of traditional biotechnology research.* The resulting market microstrucrures struggle with various forms of adverse selection, deception and moral hazards, which result from information asymmetry, exacerbated by mis-aligned utilities, lack of a community wide social norms and enforceable complete contracts.

In both of these approaches, participants from each stage usually have conflicts of interest, leading to fragmented strategies and agenda, which stifle information sharing across research teams necessary to advance treatments and cures.

Specifically, the not-for-profit approach suffers from the following three problems. First, government or non-profit organizations end up inefficiently allocating resources. For example, politicians may steer taxpayers money away from drug development to serve their own interests. As a result, under-investment is always an issue for not-for-profit drug development. Second, the interests of researchers and patients are not fully aligned. Purely academic competition among researchers, while beneficial in basic science research, prohibits them from sharing research results transparently and only a small percentage of NIH-funded medical research yields positive results that end up in publications. Third, the drug price is determined by pharmaceutical companies, therefore there is no control by the taxpayer or patients (who through charity invest their money in the first place) to rationally but strategically interact with the other key players.

1.2 Information Asymmetry and its Effects

Although the market approach is more efficient in allocating resources, pharmaceutical companies have traditionally taken advantage of its inherent information asymmetry to maximize corporate profit by charging high drug prices for the patients. In addition, they may only focus on disease groups that promise blockbuster returns and leave many rare diseases untreated. Powerful Big Pharmas also hold patents, trade secrets, know how, copyright, etc. for processes associated with actionable biomarkers and molecules. They are able to charge significant licensing fees to researchers who use or work on these intellectual assets, imposing barriers to information sharing within the drug development community. Thus, for instance, while personalized therapies are touted as the future of biomedicine, it is practically impossible to motivate a cohort to participate with their genomic data, as it will only deliver mostly equivocal, uninterpretable or non-actionable biomarkers, but not much else.

2 Combining with Crypto-currency and Smart Contracts

Given a biomedical research question (Example: "Can a drug [e.g., Avastin] be developed that will target hypoxic breast tumor cells by inhibiting angiogenesis?"), at least three types of resources are needed for the necessary research to gain momentum. These resources are: (*i*) research efforts from researchers (who understand angiogenesis pathways), (*ii*) capital provided by investors (who perform due diligence on suitability, safety and efficacy of Avastin ([Bevacizumab]) and (*iii*) data from patients attending clinical trials (who suffer from advanced breast cancer with VEGF mutation). Now, suppose a type of contract (possibly associated with a currency) existed and represented the ownership of all the pharmaceuticals, as well as the intellectual properties produced during this drug development process (henceforth, biomedical-research-based crypto-currency shortened, crypto-currency). This currency could then be earned by patients if they attend clinical trials, could be earned by researchers if they conduct experiments for this research question, and could be bought by investors. We may then conclude that the currency's versatility will lead to patients, researchers and investors from everywhere identifying themselves and noncoercively contributing to this drug development processes. In addition, if every participant in the drug development process owned part of the final products, their interests would be automatically aligned, as they receive nothing if the drug development process fails.

In order for this currency to serve as the norm, we need to make sure that all participants in the drug development believe this currency has value.

2.1 Institutions

Therefore, we propose the following three (virtual) institutions to facilitate the drug discovery process and honor the commitment by the cryptocurrency.

1. **A cryptocurrency mega-fund** that sets predetermined rules for the open innovation research process, constructs diversified portfolios of these research projects, issues cryptocurrency to represent the ownership of these portfolios and honors the commitment of the cryptocurrencies. It is worth noting parenthetically that the organizational structure of this cryptocurrency mega-fund is fundamentally different from that of the mega-fund proposed by Fagnan et al.(2013)(henceforth, centralized mega-fund). In the centralized mega-fund, the fund managers need to optimize decisions of capital structure, through buying and selling compounds for each

experiment, as well as by hiring and contracting with researchers in each stage of the drug development. The possibility of a misalignment of interests between fund managers and investors – one of the primary reasons behind 2007-2009 financial crisis – could significantly reduce the profitability of such a mega-fund. The crypto-market mega-fund would overcome this concern by using a decentralized, transparent, and market-based solution for drug development. All the activities during the open innovation research process follows predetermined rules. By avoiding a central authority governing the market and other transitional institutions, it avoids non-transparency and deception associated with the market manipulation. It also globalizes the system and encourages scaling with liquidity.

2. **A blockchain ledger** ensuring that all predetermined rules will be implemented as contracts with minimum costs. Specifically, the mega-fund manages each research project through smart contracts and real-time accounting. For investors, the costs of collecting accounting information and of enforcing the contracts are almost zero. For researchers, the funds for each stage of research will be distributed automatically if they meet predetermined milestones, their use of the cryptocurrency will be recorded in a real-time accounting system, and their discoveries will be time stamped on the blockchain. Now they have a cheaper and faster way to protect their intellectual property rights, alternative to patenting them. By compensating innovation with the cryptocurrency, researchers contributions will subsequently find their way into a commercial product, and they are then entitled to a statutory share of the products revenues.
3. **A secondary exchange market** of the cryptocurrency which would give liquidity to patients, investors and researchers. Encouraged by the cost-efficient feature of the cryptocurrency mega-fund, pharmaceutical companies would want to collaborate, instead of competing, with this mega-fund. They, along with health insurance companies, public health organizations (e.g. CDC) and charities could join the exchange market as market makers. Namely they could buy big blocks of these cryptocurrency based on their estimation of the demand, and subsequently sell it to future patients. New occupations would then emerge and will include data analysts, who will estimate returns and risks using translational systems biology and machine learning and then price the cryptocurrency to help investors better understand the research feasibility and progress.

3 The Importance of Smart Contracts

In our approach, more productive researchers will get much more research funds and higher compensation than current system. In fact, there are three design goals for the new funding system: (*i*) more innovative, efficient and productive researchers will get more funds; (*ii*) the researchers will be paid based on their performance, therefore the return to researchers with breakthrough discoveries under the new system will be significantly higher than those under the current system; (*iii*) the researchers are encouraged to take risks. In other words, they need not fear of being punished for failure when trying innovative approaches.

To design a funding system with these features, we need a better understanding of the following two questions: (*i*) *What is the production function of knowledge*? (*ii*) *What is the best way to motivate researchers*? These are questions that have been studied for decades, yet no consensus has been reached. Here we just want to borrow some recent development from the mechanism design literature and present a new funding scheme that can generate better returns to the researchers and investors than the current system.

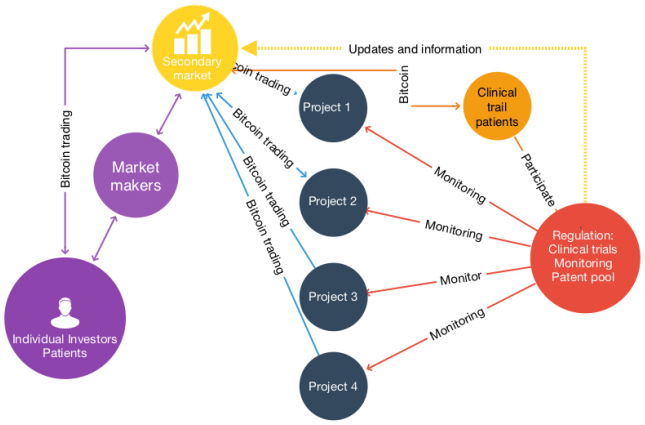

Fig. 2: *Crypto-currency system.* It tames the information asymmetry with flows of information balanced by reciprocating flows of obligations and rights (via investments and smart-contracts). Furthermore, it seamlessly includes all stake-holders: patients, researchers, investors and regulators. For example, patients invest on research based on disease risks, receive crypto-currencies and acquire the rights to buy drugs from research upon disease onset.

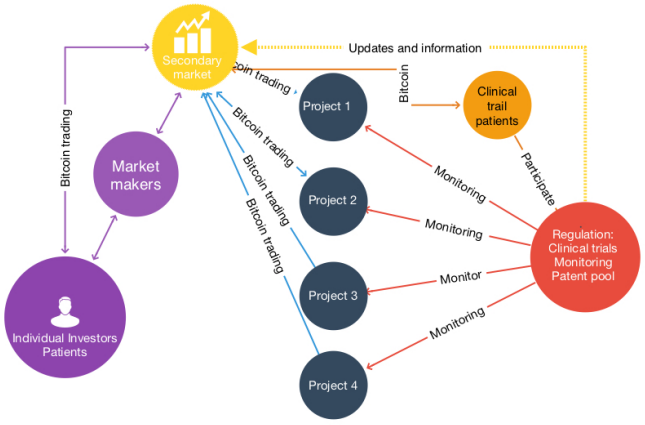

Fig. 3: *Secondary market of crypto-currency.* It brings liquidity by inviting additional market participants, who may have access to better informatics (e.g., systems and synthetic biology) for monitoring, pricing and arbitraging.

Smart contracts are important in the context of this principal-agent problem, in which investors (the principal) delegate the researchers (the agents) to search for a solution of the targeted disease. Researchers have private information about the distribution of potential outcome and their own abilities (adverse selection), as well as the efforts they put into researching (moral hazard). They can choose between two different approaches to finish the job: one is a routine approach and the other is an experimental approach. We then combined the findings from the dynamic mechanism design literature (see bibliography for some examples) and propose a new mechanism as follows:

1. At the creation of each SPV (special purpose vehicle, a legal entity with specific responsibilities), researchers submit their research proposals to the mega-fund. This research proposal will include estimates for deadlines, measurable milestones and budget needed for each milestone.
2. All the research proposals are analyzed by the mega-fund and ranked based on the past performance of the researcher, feasibility of the research approach, correlation of this approach to other approaches and its budget. More importantly, the mega-fund may also need to understand the interdependence among the proposals and the nature of coordination, cooperation and competition that it entails.
3. Approved research project is funded under a vesting schedule associated with a cryptocurrency account. A smart contract, imposed on the account, pays the researchers as determined by the research proposal. That is, cryptocurrency for the next stage research is paid to the researcher if and only if the targeted milestone at current stage is met within the predetermined time frame.
4. The budget has an option-like feature: the amount of cryptocurrency paid at each stage is determined by the initial price of the cryptocurrency, or the current price of cryptocurrency if it is lower than the initial price, to meet the proposed budget. In other words, if the price of the cryptocurrency appreciates, then the researchers will enjoy a higher value than his proposed budget; if the price of the cryptocurrency depreciates, then the researcher still gets his proposed budget.
5. For projects that is terminated early because of failing experiments or missing a milestone, the remaining unspent crypto-currencies are redistributed among the other ongoing projects. In this way, the successful projects are rewarded not only by the appreciation of the cryptocurrency, but also by the increasing amount of their cryptocurrency budget. This structure is reminiscent of DARPAs program continuation scheme with hurdles.
6. The results of the research (e.g., drugs) are made available for purchase using crypto currencies to an investor (e.g., a potential patient) upon disease onset. At any time, the patient may also relinquish his rights by selling the crypto currencies in a secondary market.

4 Conclusion

Ina forthcoming paper, Mishra and Qi have simulated the system with realistic parameters and obtained promising results (to be reported in details in the full paper).

At an abstract level, they have demonstrated how to structure the smart contracts in order to simultaneously improve the reputation of and rewards to each researcher, the efficient pricing of drugs via the cryptocurrency, and the liquidity in the resulting market – all made possible by this type of smart contract's ability to address the following information asymmetry problems.

Adverse selection: Since researchers are paid by their long-run performance, their motivation of producing "Lemon projects" are minimized. As in the game-theoretic literature, a "Lemon project" refers to the situation where a researcher has deceptively concealed his lack of skill

or the infeasibility of the proposed project by overstating his qualifications or by justifying the project with fraudulent non-reproducible results, respectively. These projects can only meet a few initial milestones and their fund will be shut down as soon as the flaws are detected. Such an outcome will hurt the researchers reputation and significantly reduce their chances of acquiring future research funds from the mega-fund.

Risk Taking: The option setting of the budget ensures that the researchers are protected from the downside risk in research and will be willing to explore the risky non-incremental approaches. First, if any research succeeds in the pool and the price of cryptocurrency appreciates, then the fund for all the other researchers in the pool will also be increased. Therefore the compensation to researchers not only depends on the outcome of his own experiment, but also on the SVPs pool of other experiments. Second, if many research projects in the pool fail, the secondary market may depreciate the cryptocurrency in an irrational way. The mega-fund will guarantee that other researchers project are still properly funded. In this way, the mega-fund ensures that all researchers put proper efforts into their respective projects to avoid a contagious default of the SPV.

Moral Hazard: The design of the fund also ensures that researchers who make a breakthrough in their research will be rewarded proportionately. First, if any compound in the system goes to next phase, the price of the cryptocurrency will jump significantly; second, funds from failed projects will be redistributed among the surviving projects in their funds. Suppose just one single drug gets FDA approval in an SPV, then the team which discovered this drug will get the highest amount of cryptocurrency. It is the same amount of cryptocurrency had the team conducted all the experiments in the SPV on their own. Free Riding: Note that the smart contract has two opposite effects on the researchers motivation. On one hand, the long-run income induced by their reputation motivates them to put as much efforts as they can (career concern); on the other hand, the fund they get is a function of the price of the cryptocurrency, which depends on their performance. However, because the outcome of the mega-fund (or the price of cryptocurrency) is a joint effort of all the researchers in the portfolio, researchers may want to free ride and put less than assumed efforts in research (free ride). Terms and structures of the smart contracts need to be carefully designed so that the career concern motivations dominate the free-ride incentives.

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