Section 1 - Abstract

Our concept is simple, and arguably the future: Open Source Pharma. Very simply, it is a new, high-tech way to create affordable cures, and represents a possible paradigm shift for the pharmaceutical industry. In four words: Affordable Medicine for All. In three words: Linux for drugs.

Inspired by Linux, and leveraging radical advances in computing power, crowdsourcing, and alternative approaches to intellectual property, we can catalyze and generate new cures, to be manufactured by the existing generics industry at an affordable price.

Open source pharma represents an alternative, comprehensive pharmaceutical innovation model that can generate treatments for multiple diseases quickly and cheaply, tackle areas of public health need, and help vindicate the human right to health.

Section 2 - Call for contributions

The Need

The current regulatory and policy environment for drug development and distribution has created significant problems. Too few medicines. Too slow. Too expensive. Too many neglected realms.

As the High Level Panel is well aware, the traditional approach to pharma R&D has failed to deliver in multiple ways,

- Efficiency. As measured by cost per new molecular entity, efficiency is by some counts declining exponentially as reflected by eroom’s law, or Moore’s law in reverse. (1)

- Health needs. The basic health needs of billions of people in countries both rich and poor, in areas such as infectious tropical disease in low-income counties and antibiotics globally, are neglected, leaving millions to die each year for want of effective medicine. The Global Forum for Health Research adopted the term “The 10/90 Gap” to draw attention towards the concern that only 10% of global health research is devoted to conditions that account for 90% of the global disease burden. (2)

- Affordability. Drug prices are out of the reach of many, and can be higher than $80,000 per patient annually.
• Absolute expenditure. R&D costs on a risk-adjusted basis for a new drug are now estimated to exceed $1.3B. (3)

• Value for public money. Public funds go into proprietary pharma R&D, with arguably insufficient guarantees of open access and affordability.

A new path is needed to vindicate the human right to health and access to essential medicines.

**Open Source: A Remedy to Policy Incoherence**

Open source thinking could help remedy the policy incoherence in pharma.

Open source thinking has transformed the software and publishing industries. Its principles include leveraging the global brain, common intellectual property, and transparent development processes.

Common examples of products developed though open source thinking are Android, Wikipedia, Mozilla, and Linux.

Open source software dominates major markets, with over 80% market share for mobile phone operating systems (Android), 65% of web servers (Apache and others), and is used by 97% of the top 500 supercomputer companies (Linux). (4)

Also intriguing is the LAMP stack (Linux – Operating System, Apache- Web Server, MySQL- Database, PHP/Perl – Web Scripting), the set of open source software that has literally powered much of the Web (e.g. Facebook, Amazon, Twitter, and more). The robustness and low price and common accessibility of the LAMP Stack is arguably what enabled the Web to bloom. Startups (and large companies) did not need to pay for expensive Web technology infrastructure, which radically reduced the price of innovation. Could there be a LAMP Stack for pharma? (5).

A common saying in software: with enough eyes, all bugs are shallow.

**Open Source Pharma: The Approach**

Over the last few years there have been increasing calls for open source thinking to be applied to pharmaceuticals. (6)

It is important to distinguish “open innovation”, which could mean two companies collaborating on a product, from “open source”, where the effort is open to, and leverages, the entire world (7).

Some approaches focus on early stage discovery. We propose a comprehensive Open Source Pharma approach that covers drug discovery, development and manufacture.

**OPEN SOURCE DISCOVERY** – the early stages of drug discovery, which are often conducted via computer modelling of targets and drug candidates - to wit virtual, or *in silico* drug discovery - are highly amenable to computational and crowd-sourcing methods, and thus to an open source approach.

**OPEN SOURCE DEVELOPMENT** – pre-clinical and clinical trials are the most expensive stage and a principal bottleneck. By utilizing IT, crowdsourcing, and open data, we can open up the process, reduce duplication, and bring down costs by a factor of 2.
or more. A key project of Open Source Pharma will be the creation of the World’s First Open Source Clinical Trial, leveraging the power of repurposing, as described below.

OPEN SOURCE MANUFACTURE – the last stage, affordable manufacture, is already in place. The generics industry can be conceived of as an open source manufacturing industry. It is built on principles of being patent free and can produce affordable cures for pennies a pill.

**Impact on Public Health**

An Open Source Pharma approach has tremendous potential for public health. Public health is in fact our focus.

One third of humanity, for example, is infected with the tuberculosis bacteria (with 10% to fall ill from TB, the leading infectious disease killer in the world). And yet the most widely used TB drug is over 50 years old, and requires an 18 month course of arduous treatment.

Low revenue/high public health need areas such neglected disease or antibiotics are insufficiently lucrative for the conventional pharmaceutical industry, and structurally out of reach.

We will seek to develop new and lower cost methodologies. If we are effective in our efforts to apply open source principles to create new cures for neglected disease, we will improve public health for millions.

**Impact on Human Rights**

Economic and social rights are enshrined, albeit, neglected. As so-called “positive rights”, they can be more complex to attain than the “negative” political rights, and thus behoove creative approaches.

Economic and social rights include the right to health, which in turn includes access to medicine. Household and national budgetary strains to purchase expensive medicines impact other economic and social rights, such as the rights to housing, education and food. Impoverished and marginalized populations suffer these violations disproportionately.

If we are successful in our effort to generate in new treatments for neglected disease, we will vindicate the right to health and other human rights for many.

**Why Open Source Pharma is Different**

Open Source Pharma is of course a radical departure from the conventional pharma approach.

A number of powerful and worthy alternative approaches to the conventional approach are being pursued, including biotech startups, nonprofit product development partnerships (PDPs), private sector crowdsourcing platforms, and open innovation partnerships. An important distinction is that that some lack open approaches to IP (and thus the affordability component), openness to the global brain, and openness of data. Open source pharma seeks to include and support existing alternative initiatives.

There are several visionary open source-type efforts in pharma. Prominent among these are the pioneering Open Source Drug Discovery (OSDD) initiative of the
Government of India, founded by Professor Samir Brahmachari (8), and Professor Mat Todd’s innovative Open Source Malaria, based at the University of Sydney (9). These should be extended and amplified in multiple ways: to additional participants, from beyond early stage discovery to all stages of the drug value chain, to other parts of the globe, and to beyond government (in the case of OSDD).

IMPLEMENTATION

Vision

To implement a global Open Source Pharma model will require the collaboration of multiple stakeholders. In July 2014, a diverse group of stakeholders met and unanimously adopted, in their individual or organizational capacities, a statement of vision, mission, and operating principles. (10)

Importantly, the adopters of the Open Source Pharma statement come from across sectors (national government lab systems, multilaterals, big and small pharma, universities, NGOs, think tanks), geographies (Asia, Africa, North America, Europe), and stages of the pipeline.

Traction and Achievements to Date

Achievements to date by the broader movement include creating a network of hundreds of open source drug researchers; enabling of crowds of student to use a national supercomputer system- in this case to conduct open source research into neglected disease; using Facebook, Twitter, and gamification to annotate the tuberculosis genome; awarding scores of research fellowships for open source research into neglected disease; the formation, by OSDD, of a women scientists group, providing, among other things an avenue for women who by choice or constraint work from home; and holding the world’s first open source pharma global conferences (11). The open source pharma movement has been mentioned in leading tech news outlets, Forbes.com, The Times of India, and The Economist magazine (12).

With the attention and support of the global health community across sectors, Open Source Pharma can inspire and encourage a global commitment to address health disparities.

Functioning Mechanism

Open Source Pharma functions as a meme, encapsulating an alternative approach to pharma, and as a movement, a collection of individuals and groups that are working diligently with an open source vision.

As a new legal entity, the Open Source Pharma Foundation, based in Bangalore, India, but a global effort, and with subsequent offices in other countries, will play both a catalytic role and a supportive role, akin to the Linux Foundation, working in education, outreach, crowdsourced science, and scientific collaborations.

Our overarching aim is to build the aforementioned end-to-end open source pharma system dedicated to delivering breakthrough affordable medicines, particularly in areas of public health need. We will do so by applying open source techniques and
principles, at each stage of the value chain, from discovery to development to manufacture, attempting to address each bottleneck or piece of the puzzle.

Financial Support to Date

The Tata Trusts, via action of their Board, chaired by Mr. Ratan Tata, the chair emeritus of the Tata group, have committed $3M ($1M per year for three years) to establish the Open Source Pharma Foundation in India (13). Other funders for the Open Source Pharma movement have included the Rockefeller Foundation and the Open Society Foundations.

The Project: The World’s First Open Source Drug

In what could be called a “moonshot” venture, we seek to create the world’s first open source drug, with a focus on neglected disease, via a set of catalytic and collaborative activities, as outlined below. The result would be not only a new cure for neglected disease, but the development an alternative open source innovation model, and capacity to pursue that model. In its most exalted form, it is an Apollo project for human health, updated for a globally collaborative age.

A. Education, Community, Movement Building

1. Open source pharma research fellowships for students and faculty
2. Establishing chairs in Open Source Pharma at universities
3. Undergraduate crowdsourced research programs (e.g. phages/ Univ of Delhi)
4. Patient-community organizing, in conjunction with other groups.
5. White papers, policy papers, thought leadership
6. Social media to spread open source pharma ideas and build community
7. Conferences (e.g. OSP1 and OSP2)
8. Citizen-science/gamification
   i. Analog to the popular SETI (Search for Extra-Terrestrial Intelligence): donated screensaver/computer processing for computational drug discovery (e.g. quantum chemical descriptors)
   ii. Analog to Fold-It (protein-folding game), for neglected disease

Estimated needed funding: $4M.

B. Drug Discovery

1. Facebook for Small Molecules
   i. Allowing exchange between those with differing resources and needs.
2. Big Data + Neglected Disease
   i. Utilize massive public datasets (PubChem: 50+ million synthesized molecules, GDB-17: 100+ billion theoretical molecular structures)
   ii. Utilize artificial intelligence, machine learning, and other computational techniques to conduct virtual screening
   iii. Develop candidates for drugs for neglected disease
3. Air BnB for Open Source Pharma
   i. Platform enabling fallow in-kind resources to be obtained at donated, marginal, or lower cost
4. Wireframe
i. Coordinating platform for those working in open source research, with auto-notifications (skeleton complete, via University of Paris, Centre De Recherches Interdisciplinaires)

5. Other software/platform development
Estimated needed funding: $7M.

C. Drug Development

1. World’s First Developing Country PDP (Product Development Partnership, or nonprofit drug development company)
   i. Based in Bangalore, India.
   ii. Led by TB scientist Dr. Tanjore Balganesh (former head of rAstra Zeneca India and former Project Head of the OSDD)
iii. Points of distinction:
   1. Dedicated to open source techniques
   2. World’s first PDP to be based in India, or indeed outside the OECD
iv. In India, it would help fill a large vacuum. By law, new drugs must undergo clinical trials in India and there are a dearth of entities or NGOs to fill that role.
v. Prior PDP’s have typically been launched with $20M+ in funding, typically to support core operations, as opposed to the project costs of the clinical trials.
Estimated needed funding: $10M.

2. World’s First Open Source Clinical Trial/ Repurposing Initiative
i. Partners and Funders: OSPF, EDCTP (European Developing Countries Clinical Trials Partnership - 600M Euro clinical trials fund), Cures Within Reach (Chicago-based repurposing NGO), Tata Trusts (one of India’s oldest and largest philanthropies)
ii. The Stages of an Open Source Clinical Trial:
   1. an open call to the global community for drug candidates to take forward (initial focus: already approved generic drugs, with demonstrated repurposing potential against neglected disease)
   2. open crowd commentary on submitted candidates
   3. open crowd commentary on clinical trial protocols (via groups such as OSP collaborator Transparency Life Sciences)
   4. Use of IT and mobiles for clinical data gathering and management (such as via Apple’s Research Kit, co-developed by OSP partner Sage Bionetworks),
   5. crowdsourcing of volunteers and in-kind assistance
   6. open anonymized data available for global public analysis;
   7. having the ensuing drug itself be generic, and in a way open source.
   8. all working within existing regulatory parameters
iii. virtual clinical trials
   1. near zero cost retrospective analysis
   2. ultra-low cost prospective observational studies
iv. potential for off-label use (using approved drugs for new diseases) by physicians, based on clinical data, and bypassing the need for new full regulatory approvals.

v. cost comparison:
   1. $1.3B (Tufts figure for current R&D cost to deliver one new drug
   2. vs <$12M to create one or more new off label use, or more than 99% cost savings.
   3. possible option for full confirmatory regulatory clinical trials
      Additional needed funding: $15M.

D. Distribution
   1. “Amazon/Uber” for drugs
      i. Explore developing nonprofit Amazon-style comparison shopping web site allowing for price comparisons and importation of low cost generic drugs, e.g. from India to US or Mexico, and launch if feasible
      ii. Prepare for and fight any legal challenge (akin to Uber)
   2. “Red Hat” for drugs
      i. As Red Hat, a private sector company, is to Linux, this company, provisionally named STB (Steal This Book) Pharmaceuticals, would commercialize open source drugs, albeit on a mandated affordable basis
      ii. Follow traditional biotech path: software development and licensing, then develop in-house drug assets
   3. “Inverse Turing”
      i. Pursue inverse of Valeant or Turing/Martin Shkreli path
      ii. Private sector social business that would repurpose already approved generic drugs at affordable prices
      iii. Potential to deliver more drugs faster than traditional pharma, by using public domain materials that others have no incentive to pursue

Additional needed funding, from private sector/social business investment sources: $10M

E. Innovative Finance
   1. Q-AMC
      i. A Quasi Advance Market Commitment for open source/repurposed drugs
      ii. Analogous to G-20 $1.3 billion pneumococcal vaccine AMC, and $100M AgResults, (14) (an OSPF person advised on the latter), but cheaper, more elegant, and more impactful
      iii. Basic structure:
         1. Results-based financing model
         2. participants: offer open source/repurposed drug candidates, in specific areas of public health need
3. criteria: objective scientific thresholds for activity, toxicity, etc.

4. winners receive: clinical trial funding, in exchange for affordability guarantees

5. production by generics manufacturers

6. estimated $30M in funding could yield 3+ new drugs, for exponential cost savings

7. OSPF has relations with the UN Multi-Partner Trust Fund Office, which could serve as a fiduciary.

2. Open source grant model- a new alternative to the NIH grant model, with more openness and affordability guarantees built in, with grant decisions made by a rigorous and acclaimed panel. Estimated $20M.

3. Open Source Pharma Investment Fund

   i. Tiered self sustaining fund
   
   ii. Investment from philanthropy, government, big pharma
   
   iii. Focus on developing and marketing cures for low, medium, and high revenue diseases, with cross subsidization, and open approaches
   
   iv. Estimated needed seed investment for proof of concept: $100k
   
   v. Potential project champion and partners identified

Funding Envelope
Indicatively, for all the projects: $100M.

Financial Sustainability
Financial sustainability and leverage can be achieved in multiple ways:

- Crowdsourcing volunteers. In the first instance, the crowdsourcing of scientific volunteers is radically inexpensive. OSDD has shown that scores and even hundreds of researchers can be coordinated with a core scientific staff of 2-5.

- Revenues. Revenues can be generated via consultancies, cross subsidisation via software and services in more lucrative disease areas, goodwill payments from OECD markets for any new drugs, and, if achievable, priority review vouchers, which have garnered in some cases hundreds of millions of dollars.

- In kind. Via leveraging the in-kind resources of academic and government and pro bono private sector scientific institutions, existing distribution systems, fallow resources available at marginal cost, and the business model of the generic industry.

- Inexpensive public goods. Delivering public goods at a fraction of conventional cost structures provides tremendous value for money for public and philanthropic funding sources.
Submission Support

Cures Within Reach, a Chicago-based NGO focused on the repurposing of generic drugs, a radically cost effective way to generate affordable cures, is a supporter of this brief, and a collaborator. Conversely, the Open Source Pharma Foundation is honored to be a collaborator and supporter of the brief from Cures Within Reach.

Post 5-Year Plan

After a five year period, we hope to see Open Source Pharma physically established both in India and in North America, with influence worldwide, as well as to have it become a growing movement and model demonstrating an urgently needed alternate approach for creating affordable new cures.

We may expand from a focus on neglected diseases, to other low-revenue areas such as antibiotics, and even to affordable drugs for lucrative diseases such as cancer, to disrupt pharma as a whole, with the aim of “medicine for all”.

We would see a transformation in subject matter - from a focus on education, awareness, and purely computational work, into wet lab and further downstream work. As the model catches on, commercial and revenue possibilities would mature, as happened in the Internet space.

Most critically, the world’s first open source drugs would be on or well on their way to the market, demonstrating a new open source pharma ecosystem. They would save millions of lives and ameliorate untold suffering. And along the way, we would hope to have inspired and guided thousands of young scientists and researchers, reaching beyond the elite institutions to the immense untapped talents. And we would have trained them in actual scientific inquiry in service of grand human challenges.

References


