Harvard Global Health Institute - Open Source Pharma Foundation
Virtual Dinner
March 31, 2020, 6pm EDT
Open Source Approaches to Pharma R&D

Minutes

<u>Introduction</u>

Welcome: Ashish Jha, Director, Harvard Global Health Institute, K.T. Li Professor, Harvard School of Public Health, Professor of Medicine, Harvard Medical School, soon to be Dean of the School of Public Health at Brown University.

- Couldn't have an in person meeting, owing to pandemic
- But important to push this forward.
- At HGHI, the idea is to use open source methods to conduct R&D for neglected diseases, to bring people together.
- This meeting builds on prior meeting at HGHI on open source approaches to pharma R&D in Dec 2019.
- Where else can this go---is it only for neglected diseases?
- In addition, a focus on Covid-19
- Will be a longer conversation, beyond tonight, and also hopefully in person.
- Looks forward to continuing to stay in touch and to working on open source pharma

Welcome: Jaykumar Menon, Chair and Co-Founder, Open Source Pharma Foundation; Senior Fellow, Harvard Global Health Institute; Visiting Scientist, Harvard School of Public Health.

- Really great assemblage.
- Extraordinary situation.
- Dire circumstances in NYC, with hospitals overwhelmed.
- Housekeeping
    - Chatham House rule in effect.
    - (*Minutes note: Those who have been named in these minutes have agreed to attribution*)

- Covid-19: and open: The open approach is moving from fringe to the center.
- What is open pharma?
  - Linux for Drugs.
  - What does that mean concretely? One version:
    - Virtual early stage drug discovery
    - Distributed/pro bono wet labs
    - Open source-style clinical trials, with open data, open IP, and open commentary, and standard regulatory endpoints
    - Generic drug manufacturing and distribution.
  - OSPF is a global non profit, nurturing an OSP movement. Launching opencovid.care. Working on tuberculosis/neglected disease, and now on covid.

Opening Remarks: Bernard Munos, Co-Founder, Open Source Pharma Foundation. Author of an influential paper in Nature on open source approaches to pharma R&D.
- Open Source Pharma is inspired by software.
- In the software arena, the open source idea received a lot of early emotional pushback. Called anti IP etc.
- Today, in the Covid-19 crisis, major players such as the Gates Foundation, the Wellcome Trusts, the WHO, Microsoft, have now embraced open source ways of thinking. Only way to address the scale of problem at hand, with the speed needed.

Strategy Session #1: Which Disease Area of Focus?

Jaykumar Menon:
- This call is not so much about the basics of an OSP model, which has been covered in prior meetings. See, e.g. https://www.opensourcepharma.net/conferences.html
- It is more about strategy - how it could work?
- One area where OSP could focus is where traditional models are insufficient, due to either the lack of commercial incentive, or the difficultly of the disease (too hard for one company to solve).
- These include
  - Neglected/tropical
  - Rare
  - Rapidly cured (antibiotic)
  - Epidemic/pandemic
  - Difficult diseases (e.g Alzheimer's--little progress there)
- The question to the group: Does this focus feel right to people?

Group response: Assent, or at the least, non-objection.

Comment: Problem is that knowledge stuck in many different places; requires coordination between firms and educational institutions who don't traditionally know how to coordinate.

Strategy Session #2: Which Approaches?

Jaykumar: What approaches should be pursued? Options include the following:
- Drug repurposing (NIH's NCATS in December 2019 held a great conference on off patent drug repurposing)
- Gene therapy
- Virtual drug R&D (Massive Open Online Research)
- Vaccine

Repurposing

Comment from a scientist:

- Repurposing is indeed potentially cheaper and faster.
- Huge emphasis being placed here now
- Indeed, if you haven't tried repurposing, why bother looking into new drugs first?
- Issues to tackle:
  - What percentage of repurposing turns out to be not cheaper and not faster
  - Sometimes a repurposing effort is on the way and a few years on and some challenges come up. Like needing toxicology data that is not available
  - Dosage and duration issues
- The way the ecosystem is handling repurposing seems like one off projects till now. And not systematically. Need a global systematic effort.

Jaykumar: Entrepreneurs' perspective: We commenced a phase 2b clinical trial - for repurposing a generic drug (metformin) for TB - having spent less than, ballpark, 50k dollars. Including partner Govt of india expenditure, total outlay of less than million dollars to conduct the phase 2b. Ballpark figures; could vary with accounting methods.

Comment: Why can't all projects work that way? How can we collectively figure out entrepreneurial systematic ways to get these done?

Gene Therapy:

Jay: What is open source gene therapy? Also what is NCATS?

Comment: NCATS mission in broader sense- the translational process is rife with pitfalls. Targeted on specific diseases; there wasn't a group that could look at translational process in systematic way. To find exemplary case studies and projects, to show one could get over these problems in smarter and faster way. Ranging from evaluation and clinical setting, and how to convert that to a glimmer of hope and translate that into an actual drug candidate with efficacy and safety.

Comment: Gene therapy work shares that mission and vision. Shouldn't be so expensive and time-consuming to do this. Looking at how to make gene therapies in a faster cheaper way. And this shares values with open science.

Part of the reason gene therapy is hard is : IP barrier in some segments is high. We're making a general commercialisable vector that is publicly shared and that anyone can use. It can be used for a variety of gene therapy applications across different diseases. Rather than being the Porsche or Ferrari of gene therapy, one can try to be the Chevy Truck of gene therapy. You can just add a payload, which can come from any player, and drive through. Looking to make a sort of open science manual.

Comment:: Gene therapy effort has gotten off the ground because we clearly articulated that scope of work was those diseases for which no one else can make a business case. If we make that case for OSP - neglected diseases are in this domain- there will be less pushback. One of NCATS products is a new way of doing things. New partnerships, structures etc. that have just not been done. And new science and new toxicology too.

MOOR- Massive Open Online Research

Jaykumar: What's your impression of MOOR, and of OSP generally?

Comment: This open source is a great idea; why hasn't it happened yet? If we get into this, we get into it to win? So need to understand, why everyone else has lost? Who is going to support it long term? ROI? Or Govt model. Govt model works really well for acute needs for western world. Like covid. Govt. allocated a very large amount; isn't sustained. Govt doesn't have this kind of attention span. Opiod is an example. Why isn't it getting attention now - it's an acute crisis now? Govt. doesn't have the attention span; so hard to work with that model, and if the ROI model doesn't work then what's the model? Venture philanthropy? Doesn't scale and doesn't last? With stock market collapse, a lot of philanthropy will dry out. So we need to think of novel financing along with novel science.

Jaykumar: That was a rousing call. Necessity is the mother of invention..

Vaccines

Jaykumar: Does an OSP approach work for vaccines?

Comment: Access to knowledge and methods are not the limiting factor. Takes an extraordinarily long time. 10-15 years. Billion dollars. Generic production approach doesn't work in vaccines. Clinical equivalency needs to be shown when you change facilities. You actually need the human readout. Can't show chemical equivalency. Having access to sufficient capital is critical, as is risk tolerance.

Jaykumar: are there sub-divisions within vaccines that can be addressed by an OSP model? For example adjuvants?

Comment: Common adjuvants among different vaccines doesn't matter. Same adjuvant + new antigen = new process altogether.

Comment: If stability of financing is an issue, then there is a possible route? GIve traditional pharma something they want in exchange. Pre-identification of end points that FDA will agree to. Bayesian trials perhaps?

Comment: Acknowledging one should try to create something where pharma industry can find value and participate. David Bloom from MIT published a paper. (https://stm.sciencemag.org/content/11/497/eaaw2888.full) We have to develop a sustainable business model we have not been able to in the past, may take government commitments.

Comment: Foundation for NIH is 501 c 3 .

Comment: Struggle to do gene therapy for rare diseases. Very small numbers afflicted, one would have to treat everyone living for FDA approval. So no opportunity for pharma. No business case. So we could do. Everything open. But pharma was interested. Why? Because the regulatory pathway,and technologies developed to do this would be useful to them.

Jaykumar. OSP movement has people from big pharma. They want to learn about the open ways of doing things.

Comment; There's a publicity play, too but there has to be something in the business interest to be sustainable.

Jaykumar: Maybe doesn't need to be interesting to pharma. One can take forward ideas without them.

Jaykumar: Recap: for now we'd focus on low revenue diseases, vaccines seem difficult, MOOR seems fruitful.

Strategy Session #3: IT Platform

Jaykumar;   Heart of open source is a person with an idea without necessarily a ton of resources. They need somewhere to go.   What would an IT platform have? Clinical data? 'Omics data? User experience (UX)/templates? Community? How to make it real? What can they do there?

Bernard: I'd like tp summarize. One: someone mentioned right now we're constantly reinventing the wheel. Everything in covid is one off. There's no point where scientist with right idea can go and register and recruit other scientists and investors. We need to make a platform where

scientists can meet scientists, patients and investors. Like a github for pharma. Hope people can build that capacity.

Comment: I keep coming back to the financing question. How should we think about it to make it sustainable?

Bernard: Venture Philanthropy. Lot of money sitting to find the place to invest. Ageing billionaires. We need to facilitate those connections between those who have the idea and those have the resources.

Jaykumar: People build platforms but no one comes there. Let's have inexpensive open source software there, as an attraction. Charge for cancer. Free for malaria. Video game model-- if you want to use it, give up some share of profit later. Also, maybe it's just not that expensive.

Mike Stebbins: We have a massive market failure.   We're missing tools and ways to address this crisis and it shows the huge weakness of the biomedical industry. We're rapidly approaching a time where government. will need to come up to solve the market failures.

Constant push back from politics! Need to spend money on doing these things. Maybe after covid we'll see more appetite but we need to leverage those ideas and projects. At opportune moment to see those steps through. Maybe we can make white paper saying we can go from here to better state and it will cost X and be done in N steps.

"Public dollars for public goods"

We do government sponsored/run development in defense, why not health care?

Wrap Up and Next Steps

Jaykumar: OSP4 - 4tth global open source pharma conference, planned for 2021 in DC or San Francisco, with intervening meetings.

Group; Several interested in pitching in for white paper. Could be a short preview/op-ed as well.

Bernard: Enormously productive. If we look at COVID, one month ago, none of this would've existed. A grassroots open source movement has emerged. We need to harness this energy. Very excited and very encouraged.