Pre-competitive Collaboration in Pharma

An Overview Study

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EXECUTIVE SUMMARY

The pharmaceutical industry has turned to industry-wide collaboration as a way to share the cost burden of basic research tasks. According to the Pistoia Alliance, a group of industry experts, pre-competitive collaboration in pharma involves "aggregating, accessing, and sharing data that are essential to innovation, but provide little competitive advantage."[1] Currently, there are not enough new drugs being developed because of rising costs of drug development stemming from increasing biological complexity and high levels of development failure. This is compounded further in emerging markets, where oftentimes the need for new drugs is greatest; companies are hesitant to invest because of low margins and unstable markets. Through precompetitive collaboration, there are a number of successful examples in which stakeholders have been successfully incentivized to work together for mutual benefit.

Biomarkers Consortium
Launched by Foundation for NIH with the FDA and pharmaceutical and biotechnology companies with the goal to develop biomarkers for diagnosis and treatment – i.e., discover which molecules indicate which biological processes. For example, they received in-kind contributions from Roche, GSK, and Merck to find a biomarker that would indicate a response to a class of drugs called PPAR agonists. Pooled data was analyzed by statisticians at Quintiles and National Institute of Diabetes and Digestive and Kidney Diseases, and found that adiponectin is a robust predictor.

Innovative Medicines Initiative
The European Federation of Pharmaceutical Industry Associations (EFPIA) and the European Commission put in 2 billion euros to fund this initiative whose aim is to solve the bottlenecks in drug discovery and development across diseases. One example - the NEWMEDS project developed better trial designs for schizophrenia to save time and costs. Data from genetic studies has also been pooled to allow correlations of genotype with phenotype which will be important for target validation.

TransMART
This public-private partnership develops an open-source and open-data knowledge management platform that enables scientists to develop and refine research hypotheses by investigating correlations between genetic and phenotypic data, and assess their analytical results in the context of published literature and other work. The platform has been deployed by 30+ organizations including academic medical centers, non-profit foundations and leading pharmaceutical companies. Members provide technical and financial support, with differing levels for for-profits and non-profits. Benefits of membership include participation in sustaining the open-source community, the opportunity to serve on the board of directors and membership on operating committees.

Despite these successes, there are a number of challenges in propagating such collaborations. One of the biggest is balancing interests amongst different types of stakeholders. For example, what happens when new members come into a consortium, especially if their level of support is not equivalent to that of other members? Also, there are distinct motivations amongst different types of stakeholders such as academics, industry, and NGOs. Other

[1] http://www.pistoiaalliance.org/about/

challenges include anti-trust and IP issues. It is difficult for companies to guard against inadvertently sharing trade secrets and to come to agreement with the stakeholders as to how IP developed by the collaborations is assigned.

In overcoming these challenges, there have been common themes across successful collaborations. Such consortiums have kept membership fees for industry participants low compared to benefits by leveraging academic research and/or raising funds from other sources. They have also found a way to minimize IP conflict, often by channeling the work and IP through the consortium itself; members can then license IP directly from the initiative without having to deal with each other. Impartial and structured facilitation has also been important to ensure that conflicts amongst stakeholders are resolved quickly and fairly. Finally, it has proven important to build in incentives for stakeholders to identify and prioritize key gaps.

Going forward, there are a number of ideas that have been suggested that could overcome the above challenges. These include - establishment of "IP-free" zones, creating entities specifically to support early research, open-source projects, prizes to incentivize collaboration, and having patients themselves drive the collaboration.

The takeaway for FLI is that research into AI safety (or safety of other technological concerns) can be thought of as a public good for the industry, similar to basic academic research in life sciences that need to be translated to industry. The costs to develop safety research can be decreased for each participant by pooling financial and in-kind resources together and sharing the results. In this light, for-profit companies can participate and contribute to these efforts for self-interested reasons. Although it would probably be preferable to create an IP-free zone around safety research, this conflict can be dealt with by having the initiative own the IP and license it out to members. FLI should also strongly consider prizes as an alternative mechanism to grants for incentivizing research.

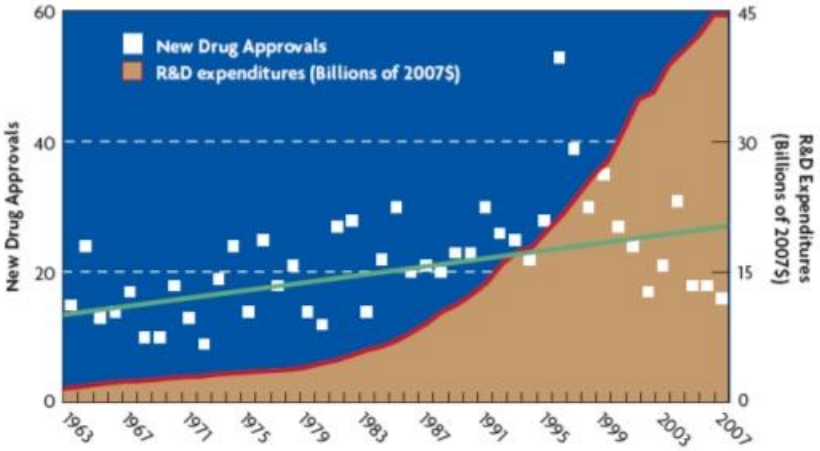
INTRODUCTION

NEED – IMPACT PERSPECTIVE

As identified in the project briefing, there is a need from a social impact perspective to increase the efficiency of drug development because the current model of operating is not meeting increasing demands for innovative products. There is a decreasing number of innovative new drugs in the pipeline and the very closely related increasing cost of development. In recent years, the number of new drugs in the pipeline has been dropping, and the biotechnology industry is producing very few new candidate drugs.[2] Approval rates for new molecular entities in the pharmaceutical industry have been flat or declining over the past two decades (Booth and Zemmel, 2004; CBO, 2009). The number of drugs coming out of the pharmaceutical industry is declining while research costs are going up. It is taking too long to develop drugs and R&D costs are not covering new drug delivery. According to Garry Neil, the high costs of drug development—between $1.2 billion and $1.8 billion per drug—are being driven by biological complexity and by the high rate of failure during development. Only one out of ten drugs pays back its development costs.[3]

[2] http://www.ncbi.nlm.nih.gov/books/NBK54323/

[3] http://www.ncbi.nlm.nih.gov/books/NBK54328/



Source: Tufts Center for the Study of Drug Development, PhRMA[4]

The need for increased efficiency and cost-effectiveness in drug development is especially compounded by the attractiveness of markets in developing economies.

Globally, most new health technologies come from the research and development efforts of private industry. Commercial enterprises not only have the expertise, capacity, and resources to carry a product forward to market, they also have strong market-driven incentives to do so. Unfortunately, this drive to pursue projects with the highest potential profit means that private companies usually do not put a high priority on products and services for developing countries. Markets in those countries are often unstable, and so perceived risks diminish projected return on investment. Pharmaceutical companies, for example, would rather invest in products that are targeted to large, lucrative therapeutic markets than pour research dollars into malaria or AIDS vaccines.[5]

CURRENT CHALLENGES

Many commentators have identified barriers to innovation in pharma, including Warren Kaplan, who compiled the following list in 2004/5:[6]

- Inadequate understanding of basic science for certain diseases and the identification of targets amenable to manipulation.
- Regulatory authority 'rituals' with regard to preclinical and clinical testing procedures that may, or may not, have basis in empirical evidence.
- Differences in perception of risk among different stakeholders.
- Uncertainty about the timing and level of reimbursement decisions leading to uncertainty among stakeholders.
- General business uncertainties in drug development.

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[4] http://www.slideshare.net/wallerc/precompetitive-collaborations Slide 6

[5] http://www.iphandbook.org/handbook/ch17/p17/

[6] Kaplan, Warren. Benefit, Risk and Innovation in Pharmaceutical Research and Development: Opportunities and Issues – JD, MPH 7 October 2004

- Potential increases in the cost of doing business due to intellectual property concerns.[7]

Other challenges include

- Increasing cost of research coupled with abysmal rates of clinical success
- Expiration of patent protection leading to loss of exclusivity (the so-called patent cliff)
- Competition from biosimilars and generics

EXISTING MODELS – PHARMA

INNOVATIVE MEDICINES INITIATIVE (IMI)

OVERVIEW

IMI is a 2 billion euro partnership between the members of the European Federation of Pharmaceutical Industry Associations (EFPIA) and the European Commission whose aim is to work pre-competitively to solve the bottlenecks in drug discovery and development across diseases that are relevant to both the developed and the developing world.

Projects range from new patient-reported outcomes in chronic obstructive pulmonary disease to expert systems for in silico toxicological prediction, and from new animal models in neurodegeneration to education and training programs. There are also infrastructure building partnerships such as the Open Pharmacological Space project. This project aims to build open access public informatics resources to support drug discovery. It will focus on developing and applying common data standards to improve the integration of data relevant to drug discovery and also develop tools and web services to aid access and mining of the data. This will enable the transfer of expertise in the use of data for drug discovery from industry into the public domain and will also expand the connectivity between the existing public databases.

HOW IT WORKS

- Each partner contributes 1 billion euro.
- There are over 25 different companies collaborating on different projects both with each other and with academia and small- and medium-sized enterprises.
- All EFPIA companies provide matching funding through in-kind contribution, which can be people, samples, assays, etc.
- Call topics announced each year for funding proposals are formulated initially by the EFPIA members and so represent real barriers to drug development in a particular disease area. This ensures a high level of industry engagement in the resulting consortia.[8]

SAMPLE OUTCOMES

[7] http://www.ddw-online.com/business/p149291-what-are-the-obstacles-to-innovation-in-the-pharmaceutical-industrysummer-11.html

[8] http://rsta.royalsocietypublishing.org/content/369/1942/1817

- The NEWMEDS project in schizophrenia has pooled data from clinical trials and this data has enabled a better and shorter trial design thus saving time and costs. Data from genetic studies has also been pooled to allow correlations of genotype with phenotype which will be important for target validation.
- To date more than 4,500 researchers are involved in IMI projects from private and public organizations , including SMEs and patient groups.
- European Lead Factory will continue to expand the impact on the whole R&D continuum (http://www.imi.europa.eu) – *see next section*

EUROPEAN LEAD FACTORY

OVERVIEW

In 2013, IMI launched a project called the European Lead Factory (http://www.europeanleadfactory.eu). The aim is to build a Joint European Compound Library which can be accessed by both private and publically funded institutions. It has 30 public and private partners, including seven pharmaceutical companies and will establish a European Screening Centre. It is hoped that this will act as a catalyst for further drug discovery in Europe.[9]

KEY TAKEAWAYS

- European Lead Factory is unique in that this pushes the traditional boundaries of what is considered precompetitive by bringing collaborative activity to compound generation and sharing.

PISTOIA ALLIANCE

http://www.pistoiaalliance.org/

OVERVIEW

Primary purpose is to streamline non-competitive elements of the life science workflow by the specification of common standards, business terms, relationships, and purposes

During a meeting in Pistoia, Italy in 2007, a group of senior pharmaceutical industry R&D IT directors concluded that many of the activities carried out by researchers in bioscience organizations were remarkably similar. For example, the activities to determine a gene sequence, identify a signal transduction pathway, search a chemical repository or keep abreast of the scientific literature were all of course necessary, but remarkably common. They identified that much replication of effort by their respective R&D IT organizations might be minimized if they shared thinking about, defined and then documented the best practices for these precompetitive research activities. This would enable expert, third-party organizations to build and deliver such services to many

[9] http://www.ddw-online.com/business/p217613-collaboration-for-innovation-is-the-new-mantra-for-the-pharmaceutical-industry-spring-14.html

companies. The money saved by sharing the costs of provision of precompetitive scientific services could be redeployed for company-specific, strategic, transformational, innovative initiatives.[10]

HOW IT WORKS

Part of the modus operandi of the Pistoia Alliance is to encourage the cross-company conversations that identify the most pernicious examples of resource-wasting replication of pre-competitive research activities – and then to launch project teams to address these challenges.

SAMPLE OUTCOMES

At its founding in 2009, The Pistoia Alliance set out a program of work around the following technology pilots:

- Sequence Services: Defining and documenting an externally hosted service where organizations can securely store and mine both in-house derived gene/sequence information as well as the public domain gene databases.
- SESL (Scientifically Enriched Scientific Literature): Exploring the feasibility of an Amazon.com-like 'brokering service' that scientists can use rapidly to gather information on disease causing genes.
- Electronic Lab Notebook (ELN): Defining a common standard that would enable scientists to use the same query across any and multiple ELNs.
- VSI (Vocabulary Standards Initiative): Defining and publishing a standard, vocabulary-based methodology for querying the scientific literature and bioinformatics databases such that all hits are found against molecular drug target search criteria rather than a subset.[11]

The Sequence Services Project exemplifies how precompetitive collaboration can produce useful solutions. Life science R&D needs access to both public and proprietary gene sequence data. Historically, each lifescience R&D function has taken a copy of the public domain data and mounted it safely behind the company firewall. In this self-evident security, scientists have used similar or the same software tools to compare and contrast their corporate-specific gene sequence data with public domain data in order to make scientific decisions.

Phase 1 of the Sequence Services project brought together bioinformaticians from several pharma companies under the aegis of the Pistoia Alliance to formulate the business, scientific and functional requirements for a common, shared, externally hosted sequence service. Performance, availability and security capabilities were all considered. Four technology vendor companies or consortia were then selected to build functional and testable sequence service installations: Constellation Technologies and Microsoft, Eagle Genomics and Cognizant, Infosys and Thomson Reuters. The working group then checked the security robustness of these systems through an independent 'ethical hack' carried out by AT&T. The resulting proofs of concept are publicly available from the vendors for evaluation.

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[10] http://www.ddw-online.com/business/p149291-what-are-the-obstacles-to-innovation-in-the-pharmaceutical-industrysummer-11.html

[11] http://www.ddw-online.com/business/p149291-what-are-the-obstacles-to-innovation-in-the-pharmaceutical-industrysummer-11.html

Phase 2 of the project will supplement these already demonstrable businesses and scientific capabilities with an enhanced, cross-company, commonly-defined scientific toolkit including open source codes as well as workflow. These requirements will be published as an RFP in mid- 2011 and the vendor community will have the opportunity to display its technical and business prowess in meeting these requirements cost-effectively and securely.

KEY TAKEAWAYS

- Created benefits that apply across a broad section of the industry. For example, with the Sequence Services project, the larger lifescience R&D companies are looking to reduce their cost of sequence services by at least 50% thereby liberating resources for innovative, transformational projects. Smaller lifescience R&D companies – who so far have been unable to afford the technology to perform these sequence services – envisage a future where they too will have access to this fundamental, non-discretionary, scientific toolkit through the cloud. The Sequence Service providers see the opportunity to generate revenue.[12]

BIOMARKERS CONSORTIUM

http://www.biomarkersconsortium.org/

OVERVIEW

In the area of biomarkers, four years ago the Foundation for NIH launched the Biomarkers Consortium as a joint effort with the Food and Drug Administration (FDA) and pharmaceutical and biotechnology companies. The consortium, which now has a large number of for-profit and not-for-profit partners, is organized around four steering committees in the areas of neuroscience, cancer, metabolic disorders, and other disease or scientific areas. The goals of the consortium are to develop biomarkers for diagnosis and treatment.

HOW IT WORKS

Funding has come largely from industry, with NIH providing samples or other support.[13]

SAMPLE OUTCOMES

To date, the Biomarkers Consortium is implementing seven projects in areas such as Alzheimer's disease, cardiovascular disease and cancer imaging; a number of other promising projects are also moving forward for implementation. The Biomarkers Consortium completed its first project, Adiponectin, in 2009.

Results from the Biomarkers Consortium's first completed project, "Evaluate the Utility of Adiponectin as a Biomarker Predictive of Glycemic Efficacy by Pooling Existing Clinical Trial Data from Previously Conducted Studies," were published in June 2009. Conducted entirely via in-kind contributions from F. Hoffman LaRoche,

[12] http://www.ddw-online.com/business/p149291-what-are-the-obstacles-to-innovation-in-the-pharmaceutical-industrysummer-11.html

[13] http://www.ncbi.nlm.nih.gov/books/NBK54323/

GlaxoSmithKline, Merck & Co and Quintiles Translational Corporation, the project involved aggregating data from clinical trials of peroxisome proliferator-activated receptor (PPAR) agonists at GlaxoSmithKline, Eli Lilly, Merck and Roche. These pooled data were then subjected to analysis by statisticians at Quintiles and at the National Institute of Diabetes and Digestive and Kidney Diseases.

Among the project's results was evidence that adiponectin is a robust predictor of glycemic response to PPAR agonists in Type II diabetes patients and that adiponectin has potential utility across the spectrum of glucose tolerance. In addition, this project established that cross-company collaboration is a feasible and powerful approach to biomarker qualification[14]

COALITION AGAINST MAJOR DISEASES (CAMD)

OVERVIEW

CAMD is a consortium under the auspices of the Critical Path Institute. CAMD members – which include biopharmaceutical companies, academic institutions, global regulatory agencies, patient advocacy groups, research foundations, scientific associations, and consultant groups – work collaboratively to accelerate the development of therapies for neurodegenerative diseases. CAMD is working toward creating common data sharing standards, establish databases of standardized clinical trial data, develop disease models, and identify biomarkers.

The CAMD's focus is to develop new tools (biomarkers and disease progression models) and methods that can be applied during the development of new treatments for neurodegenerative diseases. Specific goals include:

- Establishing a database of pooled data from controls in industry clinical trials.
- Developing quantitative disease progression models for Parkinson's disease and Alzheimer's disease and making them available for scientists worldwide.
- Defining common data element standards (Clinical Data Interchange Standards Consortium [CDISC]) for neurodegenerative diseases.
- Identifying imaging, biochemical, genetic, and molecular biomarkers that have the greatest potential to identify patient populations.
- Submitting the evidence necessary for the FDA and EMA to officially designate such tools as "qualified for use" in drug development.
- Obtaining commitment from major pharmaceutical companies to utilize CDISC standards for all medical products for neurodegenerative disease.[15]

HOW IT WORKS

CAMD was formed by the non-profit Critical Path Institute (C-Path), in cooperation with the U.S. Food and Drug Administration (FDA), patient organizations, the medical products industry and the Engelberg Center for Health Care Reform at the Brookings Institution. As a 501(c)(3), the Critical Path Institute serves as a recognized and respected neutral third party convener.

[14] http://www.fnih.org/work/key-initiatives/biomarkers-consortium

[15] http://www.fda.gov/AboutFDA/PartnershipsCollaborations/PublicPrivatePartnershipProgram/ucm231134.htm

C-Path, with support from the FDA and the State of Arizona, provides a Director, Assistant Directors and staff who manage the Consortium, coordinate planning and implementation of all projects, and provide financial oversight of research expenditures. The consortium members contribute expertise, data, information and the necessary research funding to implement each consortium's research activities. Academic, government and non-profit experts provide technical advice.[16]

CENTER FOR THERAPEUTIC TARGET VALIDATION (CTTV)

OVERVIEW

GlaxoSmithKline formed a precompetitive collaboration with the Wellcome Trust Sanger Institute and the European Bioinformatics Institute to establish the Center for Therapeutic Target Validation (CTTV). The three organizations will pool resources to discover new potential drug targets that all of the partners will be able to access.

The CTTV aims to use the almost daily advances in cutting-edge genetic research to help researchers in that crucial first step in exploring new medicines – finding where to start. Target validation is about clearly defining the role that a biological process plays in disease before developing a new drug to tackle it. Currently, an estimated 90 per cent of compounds entering clinical trials fail to demonstrate the necessary efficacy and safety requirements, never reaching patients as medicines. This is often because the biological target for a drug is not well understood.[17]

HOW IT WORKS

CTTV scientists will combine their expertise to explore and interpret large volumes of data from genomics, proteomics, chemistry and disease biology. The new approach will complement existing methods of target validation, including analysis of published research on known biological processes, preclinical animal modelling and studying disease epidemiology.

This new collaboration draws on the diverse, specializedskills from scientific institutes and the pharmaceutical industry. Scientists from the Wellcome Trust Sanger Institute will contribute their unique understanding of the role of genetics in health and disease and EMBL-EBI, a global leader in the analysis and dissemination of biological data, will provide bioinformatics-led insights on the data and use its capabilities to integrate huge streams of different varieties of experimental data. GSK will contribute expertise in disease biology, translational medicine and drug discovery.

A cornerstone of the collaboration is an agreement among the collaborators that sequence data and information gathered within the CTTV will be shared to benefit the broader scientific community, after basic quality control checks to ensure consistency with the data-sharing guidelines of both institutes. The centre will also seek publication of data and information arising from CTTV projects in peer-reviewed scientific journals. Once the centre is fully established, the collaborators will actively seek to attract new interest from other companies and academic institutions in the centre with the aim of expanding its activities.

[16] http://www.fda.gov/AboutFDA/PartnershipsCollaborations/PublicPrivatePartnershipProgram/ucm231134.htm
[17] http://www.ebi.ac.uk/about/news/press-releases/CTTV-launch

KEY TAKEWAYS

Why did industry join?

CCTV will share its sequencing data publicly, potentially providing a platform for drug development at GSK and its competitors. "If you can double the base knowledge then you've de-risked things enormously, though you've still got to make your judgement in your invention. It is not going to give you all the answers but it is going to increase the chance of getting it right," GSK's pharma R&D head Patrick Vallance told Reuters.

GSK and its Big Pharma peers have become increasingly receptive to such precompetitive partnerships as the magnitude of early stage drug discovery in the genomics era has become clear. The Wellcome Trust and GSK are both also involved with the Structural Genomics Consortium, and the whole of the European healthcare system is contributing to the Innovative Medicines Initiative. GSK wants CCTV to follow the lead of these initiatives by bringing together more drugmakers and academic institutes.

"I fully expect others to join. But it seemed sensible to get started right away rather than spend two or three years trying to get lots of other people involved," Vallance said. Eli Lilly ($LLY), Johnson & Johnson ($JNJ) and Merck ($MRK) took a similar approach to their clinical trial investigator database, which began as a three-company project but soon became one of Big Pharma consortium TransCelerate BioPharma's initiatives.[18]

ACCELERATING MEDICINES PARTNERSHIP (AMP)

OVERVIEW

US National Institutes of Health (NIH) launched a precollaborative effort called the Accelerating Medicines Partnership (AMP) to identify efficacy and safety issues for compound collections that serve as the starting points for many new drug discovery projects. By working precompetitively to identify compound liabilities early in the research process, it is hoped that everyone will benefit from reduced clinical failure rate.

AMP is a venture between NIH, 10 biopharmaceutical companies and several non-profit organizations to transform the current model for developing new diagnostics and treatments by jointly identifying and validating promising biological targets of disease. The ultimate goal is to increase the number of new diagnostics and therapies for patients and reduce the time and cost of developing them.

AMP will begin with three to five year pilot projects in three disease areas:

- Alzheimer’s disease
- type 2 diabetes
- autoimmune disorders of rheumatoid arthritis and systemic lupus erythematosus (lupus)

HOW IT WORKS

[18] http://www.fiercebiotechit.com/story/gsk-teams-apply-big-data-target-validation/2014-03-30

For each pilot, scientists from NIH and industry have developed research plans aimed at characterizing effective molecular indicators of disease called biomarkers and distinguishing biological targets most likely to respond to new therapies.

Through this cross-sector partnership, which will be managed through the Foundation for the NIH (FNIH), NIH and industry partners are sharing expertise and resources — $230 million — in an integrated governance structure that enables the best informed contributions to science from all participants. A critical component of the partnership is that industry partners have agreed to make the AMP data and analyses publicly accessible to the broad biomedical community. These pilot projects will set the stage for broadening AMP to other diseases and conditions.

The 10 companies, which include giants like GlaxoSmithKline, Merck, Eli Lilly, and Sanofi, will put up about one-half of the $230 million; NIH is providing the other half. AMP, which will also involve patients groups, will be overseen by the Foundation for the NIH.

FOR MORE INFORMATION

http://news.sciencemag.org/funding/2014/02/nih-10-drug-companies-partner-study-four-diseases

TRANSMART FOUNDATION

OVERVIEW

Non-profit organization providing a global, open-source knowledge management platform for scientists to share their pre-competitive data. tranSMART is an open-source and open-data knowledge management platform that enables scientists to develop and refine research hypotheses by investigating correlations between genetic and phenotypic data, and assess their analytical results in the context of published literature and other work. The tranSMART Foundation is a global non-profit organization devoted to realizing the promise of translational bio-medical research through development of the tranSMART knowledge management platform. The platform has since been deployed by more than 30 different organizations including academic medical centers, non-profit foundations and leading pharmaceutical companies; the platform is also under evaluation at the Food and Drug Administration (FDA).

The University of Michigan is an early tranSMART adopter. The Department of Computational Medicine and Bioinformatics is enhancing tranSMART by 1) assisting in the support of tranSMART as an open source community as a co-founder of the tranSMART Foundation (Athey, Co-CEO); 2) incorporating National Center for Integrative Biomedical Informatics (NCIBI) tools and data into tranSMART, 3) implementing metabolomic and academic/industry pre-competitive data sharing (glomerular disease) pilot projects; and 4) Overseeing a major personalized medicine demonstration project utilizing tranSMART at Johns Hopkins University.

HOW IT WORKS

As an open source solution, several leading U.S. and European-based academic, pharmaceutical and service provider organizations have contributed to this release through code development, quality assurance, testing, scientific data contribution, and hosting services for “demo” instances.

Members not only become integral parts of the Foundation's community, they also provide the financial support necessary to sustain the organization and continually enhance the tranSMART open-source platform.

The benefits of membership include participation in sustaining the tranSMART open-source community, the opportunity to serve on the board of directors and membership on the 3C operating committees (Code, Content and Community). The work of the Foundation is directed by the board and carried out by the 3C Committees, their component Working Groups and the Foundation management team.

KEY TAKEAWAYS

Interesting part of this initiative is how industry players are joining and contributing to the software and paying to do so. In return for their membership, they get to shape how tranSMART is developed.

FOR MORE INFORMATION

- http://lifesciences.ieee.org/publications/newsletter/april-2013/310-transmart-a-year-of-innovation-and-growth-of-an-open-source-community

GOING FORWARD

CHALLENGES

BALANCING INTERESTS AND ASSETS

A core challenge of precompetitive collaboration is balancing each party's interests and assets with the advantages possible from collaboration.

Setting up consortia can also be labor intensive. As Aidan Power, VP and global head of Molecular Medicine for Pfizer, pointed out, *"The political science precedes the real science. Consortia such as the Biomarkers Consortium and the Serious Adverse Events Consortium took at least 18 months to get off the ground. To establish a contract, the views of multiple parties need to be reconciled."* [19]

Stephen Friend, president and chief executive officer (CEO) of Sage Bionetworks, summarized the key points from an Institute of Medicine (IOM) workshop on precompetitive collaboration: *"Importantly, all the participants in a collaboration need to benefit. Patients need to have an opportunity to contribute to the development of more effective and ultimately personalized treatments. FDA needs to receive data and other input for evidence-based regulatory policy. Pharmaceutical companies need to see opportunities for more efficient drug development and approval. The device industry needs to benefit from larger markets and less risk. Academic researchers need to receive better clinical data and be able to work toward more effective treatments. Altruism is a great philosophical concept, but someone's got to feel there's something in it for them."* [20]

[19] http://www.ncbi.nlm.nih.gov/books/NBK54320/
[20] http://www.ncbi.nlm.nih.gov/books/NBK54325/

BUREAUCRACY

Size and bureaucratic nature of large research partners

IP

IP is one of the areas where there is the most active debate and tension when an organization is trying to create a more open, innovative ecosystem. [21]

DEFINING THE DOMAIN

According to Aidan Power, VP and global head of Molecular Medicine for Pfizer: "*A major challenge is defining the domain of precompetitive research. The basic biology, the understanding of disease, biomarkers of prognosis, and even drug responses all can be areas of precompetitive R&D. Pharmaceutical companies have recognized that they cannot develop a full understanding of these different facets of drug development on their own. Instead, they need to leverage the capabilities of many organizations, including government and academia. A few years ago, Pfizer would have considered the chemistry, the execution, and the quality of products to fall into the competitive arena, but even these areas may not be inviolate. Proposals to establish consortia that cover at least part of this territory have generated interest from pharmaceutical companies. However, some stakeholders may still view this research as strictly competitive. The line may be drawn differently between academia, diagnostic companies, and pharmaceutical companies*."[22]

DECISION-MAKING AND PARTICIPATION

More from Aidan Power: "*Establishing consortia also raises issues about decision-making and participation criteria. For example, what happens when new members come into a consortium? What do they receive? What if their support is not equivalent to the other members? How can rules governing such events be established in advance?*"[23]

CULTURE CLASH

According to Thomas Insel, the director of the National Institute of Mental Health*: "One [barrier to progress] has been a clash of cultures. The academics are looking for papers, the industry reps are looking for products, and the NIH folks are often arguing about whether there's public health impact."*[24]

CONFLICT OF INTERESTS

From NCBI Bookshelf, NIH Frameworks for Collaboration workshop summary:
Conflict of interest also poses a problem, said Insel. NIH has been thinking about whether there "are issues about

[21] http://blog.assaydepot.com/
[22] http://www.ncbi.nlm.nih.gov/books/NBK54320/
[23] http://www.ncbi.nlm.nih.gov/books/NBK54320/
[24] http://www.ncbi.nlm.nih.gov/books/NBK54320/

how academia and government scientists interact with industry that need to be managed in a different way going forward, because this has been a source of real despair for the last couple of years, both I think on the industry side and on the NIH side." Kelly Edwards, associate professor of bioethics and humanities at the University of Washington School of Medicine added that, in terms of conflicts of interest in partnerships between government and industry, people need to trust the institutions set up to develop new knowledge, which may require an "honest broker" for data interpretation and management. Insel agreed that ensuring public trust is "a really serious problem." NIH has been developing and instituting new regulations governing conflicts of interest, although other issues also have to be resolved. "This needs to involve more than just industry, academia, and NIH and really needs to bring the public into the conversation." When the research enterprise fails to deliver cures, people begin to wonder who is working for the public good as opposed to personal gain, Insel said.[25]

ANTI-TRUST ISSUES

Many precompetitive collaborations concentrate upon developing standards and processes rather than on projects that could involve conflicts of interest or IP issues. Nonetheless, it is important to be cognizant of the risks.

"Antitrust issues are a particular concern with precompetitive collaborations," agrees Chad Landmon, cochair of IP practice and chair of the FDA Practice Group, Axinn, Veltrop & Harkrider LLP. "There are ways to engage in precompetitive agreements without antitrust coming into play, but be very careful who your collaborators are and how data is shared. You don't want to be accused of either sharing or stealing trade secrets." Therefore, when possible, Landmon suggests separating the team actively collaborating from the rest of the corporation to minimize the opportunity for inadvertent release of sensitive information. For example, the individuals actively engaged in a collaborative agreement on, say, Alzheimer's Disease therapies, shouldn't be actively working on the company's own in-house Alzheimer's therapeutics.[26]

BEST PRACTICES

KEEP RESOURCES REQUIRED LOW COMPARED TO BENEFITS

It is important to ensure that companies view returns as much larger than the resources that they would commit risk of being involved in such arrangements.

"Precompetitive agreements are a creative way to share risks," Springer (Barry Springer, Ph.D., senior director, Biotechnology Center of Excellence, Janssen Research & Development, LLC, of the Janssen Pharmaceutical Companies of Johnson & Johnson) says. Financially, the funds required to participate typically are low. The Massachusetts Neuroscience Consortium, for example, is funded by seven companies contributing $250,000 each. The low contribution is possible because much of the work is done in academic labs. [27]

MINIMIZE IP CONFLICT

[25] http://www.ncbi.nlm.nih.gov/books/NBK54320/

[26] http://www.bioprocessonline.com/doc/the-rise-of-precompetitive-collaboration-0001

[27] http://www.bioprocessonline.com/doc/the-rise-of-precompetitive-collaboration-0001

It is clear that minimizing the conflict over IP is key to getting industry participation. A few points of advice below:

To minimize patent squabbles, Landmon recommends listing the collaborative entity as the patent holder. Members then license the IP from that entity just as they would any other company. Having such a formal structure for sharing IP is important when there are many collaborators, because it minimizes any confusion regarding IP ownership, Landmon says. That said, a clear understanding of exactly what is contained in the resulting patent pool is necessary to avoid disputes.

Enlight Biosciences uses a similar approach. In it, members work directly through Enlight rather than collaborating directly with each other. That helps create a degree of separation among collaborators that protects members' own trade secrets. "We have a lot of flexibility regarding the level and extent of each collaboration, so we can accommodate varying levels of trust," Harris says.[28]

PROVIDE INCENTIVES FOR IDENTIFYING AND PRIORITIZING KEY GAPS

Effective collaborations may require the identification and prioritization of "bottleneck" knowledge gaps that can be addressed more effectively through precompetitive collaboration, the development of information "utilities" such as data standards and infrastructures, less regulatory uncertainty, and more head-to-head evaluations of collaborative models to identify key features and best practices. For example, Friend suggested that Clinical and Translational Science Awards could provide a mechanism for greater collaboration, as the institutions that have received these awards are working on ways to share data that could provide a template for many other kinds of partnerships. [29]

BRAINSTORM

IDEAS

- New ways of measuring achievement would provide incentives for more researchers to participate in precompetitive collaborations.
- Establishing IP-free zones would open new areas of R&D to precompetitive collaboration[30]
    - A lot of issues facing the field today are transactional in nature, said Geoff Ginsburg. When potential collaborative agreements enter into the legal department, the process slows noticeably. There is a disconnect which needs to be addressed where IP protections can be overvalued while the value of the collaboration itself may be overlooked. Ginsburg supported the idea that studies of disease biology and biospecimens should be IP-free. "There's nothing in a biospecimen that is worth patenting. It's what you do with them," he said. "If we could lay down ground rules and say getting specimens and data out into collaboration or to the public domain is not an IP event, to me that changes the dynamics of the transaction." Terry also called attention to the cultural dimensions of change, which means putting new incentives in place.

[28] http://www.bioprocessonline.com/doc/the-rise-of-precompetitive-collaboration-0001
[29] http://www.ncbi.nlm.nih.gov/books/NBK54325/
[30] http://www.ncbi.nlm.nih.gov/books/NBK54328/

- Open source
  In some collaborations, the use of open source principles can enable distributed innovation. "Tasks do not have to be built out of centralized efforts run from a single point," said Friend. "The real power in the twenty-first century will come from distributing tasks." Open source collaborations can require novel intellectual property provisions, a resource model that can support such work, and the establishment of conditions for entering, exiting, and ending a collaborative effort.
- Prizes
  Use of prizes to motivate collaborative research. "You do not have to have two years of going through a grant review process and then pay people to do certain tasks. Prizes [offer] a much more effective way to fund things." Any organization could use such a mechanism, said Friend, including the National Institutes of Health (NIH). He contended that "the sole emphasis on the grant structure the way it is misses an opportunity to have prizes drive some of those opportunities." Friend also suggested that perhaps one-third of R01 funds could be distributed in different ways than through traditional grants. For example, large, infrastructure-driven projects could produce faster results for patients and reduce repetitive work. "I think it's going to go in that direction . . . as the government has less money," said Friend. Though he added that he did not know whether alternative funding mechanisms would be easy to institute, he said they are "worth considering."