Denise Myshko

Public-Private Partners *for* Innovation

Pharma and the National Institutes of Health are teaming up in new ways to bring increased understanding and knowledge to drug discovery and development.

Partnerships with academics and the public sector have always played a significant role in research. In fact, successful private-public partnerships have led to private sector growth and innovation, job creation, and a strengthened national economy, according to a recent report by United for Medical Research.

Public-private partnerships are not new. What is new is that the definition of precompetitive space continues to expand, says David Wholley, director, The Biomarkers Consortium at the Foundation for the National Institutes of Health.

"There is a tremendous amount of research and early-phase development, such as with biomarkers, that focuses on something outside of the main line of compound development that can be the subject of these public-private partnerships," he says. "One of the earliest of these was the Human Genome Project, which helped to establish rules about what is precompetitive and how intellectual property should be handled."

In the past, public-private partnerships were largely a funding vehicle, says Lon Cardon, Ph.D., senior VP, alternative discovery and development at GlaxoSmithKline.

"Now, the partnerships that are successful have a genuine recognition of the strength of all parties," he says.

Public-private partnerships have changed because the nature of the research questions has changed, says Jonathan Zalevsky, Ph.D., head of the inflammation drug discovery unit, at Takeda.

"Studies that are epidemiological in nature and that collect the characteristics of disease are very helpful, but they are primarily addressing descriptive features of the disease," he says.

Accelerating Medicines

One such public-private partnership is the Accelerating Medicines Partnership (AMP), which was launched in February 2014. The initiative is a venture between the NIH, 10 biopharmaceutical companies — AbbVie, Biogen Idec, Bristol-Myers Squibb, GlaxoSmithKline, Johnson & Johnson, Lilly, Merck, Pfizer, Sanofi, and Takeda — and several nonprofit organizations to jointly identify and validate promising biological targets of disease. AMP will begin with three-to-five year pilot projects in three disease areas: Alzheimer's disease, type 2 diabetes, and autoimmune disorders of rheumatoid arthritis and lupus.

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

Through this partnership, which is managed through the Foundation for the NIH (FNIH), NIH and industry partners are contributing a total of $230 million over five years.

The AMP effort focuses on target validation and was initially called the Target Validation Consortium, says Kathy Hudson, Ph.D., deputy director for science, outreach, and policy at the NIH.

"The partnership got started several years ago when NIH and industry were talking about the fairly high failure rate for chemical compounds entering the drug development pipeline with failures both for safety and efficacy," she says. "That meeting looked at what was needed to improve the quality of the biological targets that are being pursued in the drug development pipeline."

Dr. Hudson says, over time, it became clear that successfully addressing this challenge was context specific.

"To test this, three pilots were identified that would be adopted initially," she says. "At the time that we launched, we had a robust set of partners for these three pilot projects, including 10 pharmaceutical companies, the FDA, and patient advocacy groups."

The focus on target validation is an important area in research, says William Chin, M.D., executive VP of scientific and regulatory affairs, at the Pharmaceutical Research and Manufacturers of America (PhRMA), which is also a participant in the AMP program.

"The industry has gotten more proficient

in making molecules but a key challenge has been to ask whether we have the right molecule targets for drug discovery and development," he says. "Often we don't know until we've tested the molecules in patients in a Phase III trial. This is inefficient."

AMP is the first major example where companies are working with the NIH to solve an important upstream problem, Dr. Chin says.

"Historically people who had uniquely solved a problem would have true competitive advantage," he says. "The truth is that R&D leaders have realized that the work that we are doing is very similar in the early stages to work being done at other companies."

A critical component of the partnership is that industry partners have agreed to make the AMP data and analyses publicly accessible to the broader research community.

"The partners are involved in putting together large information resources about targets and disease pathways, and we're making everything as broadly available to the scientific community as possible, including to the companies," Mr. Wholley says.

One company participating in the AMP program is Takeda. The company is involved in the rheumatoid arthritis and lupus part of the program, which will receive $20.7 million in contributions from industry partners and $20.9 million from the NIH.

"The goal put forward in AMP is to apply cutting-edge research and systems biology to take into account all of the different features of local and distal diseases, and synthesize these together to characterize and define patients better using molecular phenotypes," Dr. Zalevsky says. "As soon as we learned that this was one of the goals of the NIH, we very quickly agreed that it would be in our best interest to participate."

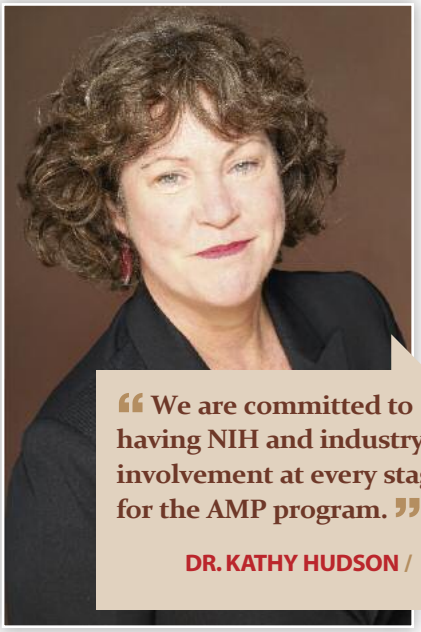
Dr. Zalevsky says the industry partners had the opportunity to shape the research plans in each of the areas.

"This is one of the differences of the AMP compared with other consortia," he says. "Since the aim is to accelerate medicines and to decrease the failure rate in the clinic, it's important that industry could help shape the goals and deliverables of the consortium, influencing the kinds of data we will collect, the kinds of biomarkers and diagnostics that can come from that data, and helping to focus the progression of the project including milestones and go/no go criteria."

GlaxoSmithKline is another pharmaceutical company participating in the AMP program. The company is involved in the Alzheimer's disease pilot, which has a five-year budget of $129.5 million, of which $61.9 million was contributed by the participating companies and the remainder from NIH.

"There is great emphasis at the NIH to find innovative ways to work with small and large companies and patient groups to develop new cures and therapies."

LILI PORTILLA / NCATS



"We are committed to having NIH and industry involvement at every stage for the AMP program."

DR. KATHY HUDSON / NIH

"GSK had largely exited from neurological disorders, not because we weren't interested or because we didn't recognize the importance of them; we didn't feel we could make great headway independently of others," Dr. Cardon says. "These disorders are very heterogeneous, and the science is difficult. The end points are often not the clearest. We want to make a difference to help patients in these areas but we don't feel like we can win if we go it alone."

GlaxoSmithKline wanted to help advance scientific knowledge and gain insight into Alzheimer's, Dr. Cardon says. And while intellectual property is important, he says working together is the best way to capitalize on that knowledge.

Dr. Cardon says historically pharma companies viewed genes and targets as competitive intellectual property.

"This view is changing," he says. "We believe that the targets themselves and some of the annotation around these are precompetitive. What we learn about the genome should be shared by all. Where we should compete is on making medicine, which is what pharma does best. Members of AMP have come to this realization; so we are able to join forces on the basic science."

GlaxoSmithKline also participates in the Innovative Medicines Initiative, Europe's largest public-private initiative. This initiative supports collaborative research projects and builds networks of industrial and academic experts in order to boost pharmaceutical innovation in Europe.

One project the company supports is on antibacterial research, which began in May 2012. The New Drugs for Bad Bugs program brings together the EU, industry, and academia with a total budget of about €224 million (about $307 million). GlaxoSmithKline, along with AstraZeneca, Janssen, Sanofi, and Basilea Pharmaceutica, are working alongside public research organizations and scientific experts to address several aspects of resistance and stimulate new antibiotic research.

"In this effort, the different groups work together and develop medicines and even to co-develop medicines because the need is so great for antibacterials," Dr. Cardon says. "Antibiotics are important, but so few companies are working in this area anymore."

Included in this program is GSK's antibiotic, GSK1322322, which targets multi-drug resistant respiratory and skin infections including MRSA and is in Phase II development.

Research highlights of AMP

ALZHEIMER'S DISEASE

- Five-year budget: $129.5 million
- Identify biomarkers that can predict clinical outcomes by incorporating an expanded set of biomarkers into four major NIH-funded clinical trials, which include industry support, designed to delay or prevent disease.
- Conduct large-scale, systems biology analyses of human patient brain tissue samples with Alzheimer's disease to validate biological targets that play key roles in disease progression, and increase understanding of molecular networks involved in the disease, to identify new potential therapeutic targets.

TYPE 2 DIABETES

- Five-year budget: $58.4 million
- Build a knowledge portal of DNA sequence, functional genomic, and epigenomic information, and clinical data from studies on type 2 diabetes and its heart and kidney complications. The portal will include existing data and new data from studies involving 100,000 to 150,000 individuals. The rich collection of curated and collated information in this portal will provide an opportunity to identify the most promising therapeutic targets for diabetes from the growing mountain of potentially relevant data.
- Focus on DNA regions that might be critical for the development or progression of type 2 diabetes and search for natural variations in targeted populations that might predict the likelihood of success of drug development aimed at these targets.

RHEUMATOID ARTHRITIS AND LUPUS

- Five-year budget: $41.6 million
- Collect and analyze tissue and blood samples from people with rheumatoid arthritis and lupus to pinpoint biological changes at the single cell level, to allow comparisons across the diseases and provide insights into key aspects of the disease process.
- Identify differences between rheumatoid arthritis patients who respond to current therapies and those who do not, and provide a better systems-level understanding of disease mechanisms in RA and lupus.

Source: National Institutes of Health

"AMP is the first major example where companies are working with the NIH to solve an important upstream problem."

DR. WILLIAM CHIN / PhRMA

New Therapeutic Uses

Another important public-private partnership is the Discovering New Therapeutic Uses for Existing Molecules pilot through the NIH's National Center for Advancing Translational Sciences. This program, launched in May 2012, matches researchers with a selection of molecular compounds from the industry to test ideas for new therapeutic uses, with the goal of identifying promising new treatments for patients.

Eight companies — AbbVie, AstraZeneca, Bristol-Myers Squibb, Eli Lilly & Company, GlaxoSmithKline, Janssen Research & Development, Pfizer, and Sanofi — provided 58 compounds for the pilot program.

This program developed from a workshop that was held with the NIH, several pharmaceutical companies, and academic researchers about repurposing drugs that pharmaceutical companies already have, says Christine Colvis, Ph.D., program director of the New Therapeutic Uses program.

"These compounds and biologics had already been tested in humans but the projects were discontinued either because they failed to show efficacy in the original indication or were deprioritized for business reasons," she says. "But since they had already been tested in humans, the safety profile was well-known and characterized."

The workshop participants wanted to address how they could make discontinued compounds available to the research community. The program asked researchers to submit proposals for projects with the scientific rationale and proposed team.

"We were particularly interested in answering three questions: is this an unmet medical

need, is the scientific rationale sound, and is this the right team," Dr. Colvis says. "We received almost 160 applications, and we put those through a peer-review process here at NCATS. We selected the most promising projects, and put the investigators in touch with the pharmaceutical companies. The investigator and the company shared data and then made a decision about whether the project was something worth pursuing and, if so, a full application was submitted to the NIH."

In June 2013, NIH awarded $12.7 million to fund nine projects through this program. These cooperative agreement awards will be valid for two or three years and pair academic research groups with a selection of pharmaceutical industry compounds to explore new treatments for patients in eight disease areas, including Alzheimer's, Duchenne muscular dystrophy, and schizophrenia.

The NIH will support studies through Phase IIa trials. The pharmaceutical company will have the first option to license the academic research partners' new intellectual property arising out of the research.

While the NIH provides the research funds to investigators, the pharmaceutical companies are obligated then to provide at no cost the preclinical and clinical supply of the drug, as well as the matched placebo that is needed for trials.

"This strategy of crowd sourcing — going to the broader research community and soliciting ideas for how to use these compounds — has potential because no pharmaceutical company can have the breadth of knowledge of the entire research community," Dr. Colvis says.

One unique aspect of this partnership was the development of template agreements that were used for negotiations between the companies and investigators. The template agreements streamlined and limited the amount of negotiation that was required, which is often a bottleneck.

"The NIH and the pharma partners developed templates that would be used to kick start negotiations with the investigators' institutions," says Lili Portilla, director, Strategic Alliances Group, at NCATS. "The template agreements were instrumental in quickly implementing this program. Investigators were given an 11-week period from initial contact with pharma companies to the point of submitting for a grant. This is a learning that NCATS is interested in disseminating to the larger research community. It's really important for these large public-private partnerships to consider having these preset templates because they can shorten negotiation time."

Best Practices

Dr. Cardon says successful public-private partnerships require strong leadership with clear mandates.

"It's important to define clear accountability at the outset and spend time on what the goals are so that arguments don't come later," he says. "There is a tendency of bureaucratic creep, which gives everyone fatigue. To avoid consortium fatigue, it's important to maximize the effort, energy, and resources that go into the science."

Mr. Wholley says one challenge is finding the sweet spot where all of the stakeholders' interests are served.

"One of the key factors to evaluate is whether a problem could be addressed more effectively and more efficiently than could be done by any one of the stakeholders individually," he says. "If companies have a research program that they would be better off doing within their own development units, then they are probably not going to end up lasting long as a public-private partnership. Finding that sweet spot is a lot more difficult than people think."

Ms. Portilla says it's important to set expectations of all parties early in any public-private partnership.

> "There is a tremendous amount of research and early-phase development outside of the main line of compound development that can be the subject of public-private partnerships."
>
> **DAVID WHOLLEY** / FNIH

> "We want to help generate a foundation of disease-specific knowledge that all researchers can ideally use to shape the future of medicine."
>
> **DR. JONATHAN ZALEVSKY**
> Takeda

"Having those discussions early on helps to prevent misconceptions that could potentially delay the project," she says.

Antoinette Konski, partner at Foley & Lardner, says both parties have to be aware of what their expectations are when they start a new partnership.

"The partners need to work out up front who is going to be preparing the IP and how disagreements are handled," she says.

Dr. Colvis says one of the reasons that the New Therapeutic Uses program is working well is that everybody sees value in it.

"The companies have been committed, engaged, and collaborative with the NIH as well as with the academic investigators," she says. "We are strengthening our level of trust and understanding. All sides are listening to each other." PV

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Public-Private Partnerships

Partnerhips are win-win-win, when:

- Institutes and centers at NIH can pursue high-risk/high-reward research and advance their missions more quickly and cost-effectively.
- Regulatory agencies can draw upon a robust body of research to inform domestic and international regulatory decision-making.
- The pharmaceutical industry can more efficiently develop new interventions, diagnostics, devices and therapies.
- Academia can increase its access to federal and industry experts, technology and resources, and opportunities for research and training.
- Advocacy organizations can access resources and research data that they could not obtain on their own.
- Patients gain earlier access to improvements in diagnostics, preventive strategies, drugs, interventions and therapies.

Source: Foundation for the National Institutes of Health

Supporting *the* NIH

The Foundation for the National Institutes of Health complements the work of the NIH, raising private sector funds for research.

The Foundation for the National Institutes of Health was established by the U.S. Congress in 1990 to support the mission of the National Institutes of Health. The nonprofit organization began its work in 1996 raising private-sector funds for a broad portfolio of unique programs that complement and enhance NIH priorities.

The partnerships that the FNIH create combine the expertise and resources of NIH with those of industry, the public and philanthropic communities, sparking research that is more innovative, collaborative, complex, and efficient.

The Foundation for NIH manages several large biomedical research partnerships. These partnerships leverage the resources of the National Institutes of Health with the public and private sectors.

> **"The FNIH provides a mechanism for public-private partnerships to be convened in a way that's both ethical and efficient, and we can represent the interest of donors."**
>
> **DAVID WHOLLEY** / FNIH

The FNIH has seven strategic initiatives: raise awareness of the FNIH, diversify funding streams, identify areas of special interest, expand its global health portfolio, emphasize translation research, develop programs for comparative effectiveness research, and continue efforts to partner for research education and training.

Public-private partnerships — in many different forms — are the hallmark of the foundation's work. An independent nonprofit evaluator ranks the Foundation for NIH among the top five charities in health/medical research with budgets of $13.5 million and above.

The FNIH has raised about $750 million since its founding, most of it in the last 10 years, says David Wholley, director of The Biomarkers Consortium at the FNIH.

"We have a very large portfolio of programs in global health, much of which is funded by the Bill and Melinda Gates Foundation, that addresses diseases of the developing world, malaria, HIV, and malnutrition."

Key initiatives include:

- The Biomarkers Consortium is an initiative that expands the science of personalized medicine.
- Grand Challenges in Global Health, funded by the Gates Foundation, encompasses 43 projects across 33 countries, working toward scientific breakthroughs to prevent, treat, and cure diseases that kill millions each year.
- MAL-ED: A Global Network for the Study of Malnutrition and Enteric Diseases, funded by the Gates Foundation, draws together an international group of science investigators to study the inter-relationship between enteric infections and malnutrition to reduce its devastating effects.
- HIV Vaccine Development is working to expedite development of an effective AIDS vaccine and is part of Gates Foundation's Collaboration for AIDS Vaccine Discovery.
- The Sports and Health Research Program (SHRP) is a partnership among the NIH, the National Football League, and the FNIH to help accelerate the pursuit of research to enhance the health of athletes at all levels. The program aims to extend the impact of that research beyond the playing field to benefit others in the general population, including members of the military. PV

FNIH by the Numbers

- 94 cents on every dollar directly supports programs
- Received 4-star Charity Navigator ratings for the past seven years
- 15 years of proven scientific expertise and leadership
- In support of more than 400 projects
- More than 100 current active programs
- Raised more than $700 million
- Ranked among Top 10 charities in medical research organizations
- Ranked among Top 30 in health category organizations

Source: Foundation for the National Institutes of Health

"You're Only As Good As Your Data" is a Half-Truth

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