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AMPlifying targets

By C. Simone Fishburn, Senior Editor

Although small- and medium-sized biotechs are absent from the NIH's new Accelerating Medicines Partnership with industry and not-for-profit organizations, consortium leaders expect that making results publicly available on their search for new targets and biomarkers in four diseases will benefit all players. However, it is unclear whether the $230 million, 5-year fund is adequately financed to meet the partnership's goal of accelerating target discovery.

The public-private partnership (PPP) includes 10 companies, 5 disease-oriented not-for-profit organizations and the **Pharmaceutical Research and Manufacturers of America** (PhRMA) (*see* **Table 1, "Participants in the NIH AMP consortium"**). The operations and governance of the PPP will be managed by the **Foundation for the National Institutes of Health** (FNIH), a not-for-profit entity set up in the early 1990s to support the NIH by forming and facilitating PPPs for biomedical research and training.

The NIH and industry partners are contributing equally to the total fund for the Accelerating Medicines Partnership (AMP). In addition, some not-for-profit organizations are giving financial support, and all parties are making in-kind contributions such as scientists, expertise, technology and access to patient samples.

The NIH's share of the AMP budget is coming from the NIH institutes responsible for the therapeutic areas being investigated—Alzheimer's disease (AD), type 2 diabetes, rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) (*see* **Table 1, "Participants in the NIH AMP consortium"**).

About $130 million will go to AD projects, $58 million to type 2 diabetes and $42 million to the autoimmune diseases RA and SLE.

AMP will fund research that uses DNA sequencing, proteomics, single-cell analysis, bioengineered cells and imaging, and it will use big data tools to integrate information from human tissue and blood samples, clinical trials and demographic studies.

NIH director Francis Collins hopes AMP will help reduce the more than 50% failure rate of Phase II and Phase III trials. According to Collins, the failure rate results largely from poor target selection and preclinical experiments in cell-based or animal models that do not properly represent human disease.

"We want to learn about how to place the right bets on targets, to give you a higher likelihood of success," said Collins in an interview with *BioCentury This Week* television.

Elias Zerhouni noted that although there is considerable industry activity in some of the selected disease areas, AMP is focused on elucidating underlying mechanisms of those diseases. Zerhouni is president of global R&D at **Sanofi** and was director of the NIH from 2002 to 2008.

"We're hitting a wall in terms of the understanding of biology of many diseases," he told *SciBX*. "In diabetes, we know the consequences of the disease but not the causes. The same is true with Alzheimer's disease. There is no clear-cut understanding at the mechanistic level. The methodologies in the lab don't represent the human situation. We need solutions for precision medicine to generate targets that relate to human diseases."

The European **Innovative Medicines Initiative** (IMI) is another translational PPP involving government and academic organizations. David Wholley noted that the IMI is much larger in scale than AMP and, unlike AMP, also aims to spur the development of new companies and provide a regional economic stimulus.

Wholley is director of the Biomarkers Consortium at FNIH.

Bill Chin, EVP of science and regulatory affairs at PhRMA, agreed that the scope and focus of AMP set it apart from the many other PPPs in the translational space.

"There is much basic science and science in the clinical realm, but not much in the area of target development. This is a rare combination of academics, NIH, nonprofits and industry," he told *SciBX*. "AMP seeks to look at the critical bottleneck in the industry, which is to find out what we need to target."

Coalition of the willing

According to Zerhouni, the idea for AMP was seeded many years ago when the NIH concluded that something needed to be done to speed the development of new drugs.

In the past two years, NIH leaders held numerous one-on-one meetings with pharma R&D heads as well as workshops to define the goals, structure and scope of AMP. The concept of a precompetitive alliance focused on target validation was the idea from the outset,[1] but reaching agreement on disease areas and research strategies took many discussions.

"We brought industry in from the beginning to increase the chance we'll ask the right questions and bring the right answers," Chin told *SciBX*.

"What took time in building this alliance was reaching consensus on the research approach. Getting agreement on the numbers and the plan before the companies would commit was difficult—people had to agree on the costs and the timelines before signing up," said George Vradenburg, who is cofounder and chairman of the not-for-profit **USAgainstAlzheimer's** and a member of the AD steering committee of AMP.

"There's a real evolution from the industry perspective in what's competitive and what's not," Wholley said on *BioCentury This Week*. "It used to be that products of the genome were considered competitive. The line has now moved to be around the therapy and the compound."

One sticking point for AMP was whether or not to include schizophrenia.

Roche had been interested in collaborating on schizophrenia but did not join AMP when that disease was dropped. A company spokesperson said that Roche is open to joining if another opportunity arises.

"I would like to get schizophrenia back in," said Collins. "We did have

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a whole design together—about how we'd go after it—but ultimately there was not a critical mass of companies that felt it was a high enough priority for them. Without that we couldn't include it in AMP. I hope we'll be able to add schizophrenia in another year as we see some success for the model."

Something for everyone

Chin said that it was important to have multiple companies in AMP engaged in each disease area. "Once you have five to six companies, you get a diversity of opinions that adds texture and wisdom," he said.

Douglas Williams, EVP of R&D at **Biogen Idec Inc.**, said that the AD project was the impetus for joining. Biogen Idec is the lone biotech member of AMP.

"We think it's a very effective way of partnering with academia to move forward the process of target validation and disease biology," he told *SciBX*. "We needed the catalyst of the NIH stepping forward with increased financial commitment—that's what sets this apart and gives this the critical mass of resources and expertise to the problem."

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> ***—Douglas Williams, Biogen Idec Inc.***

According to Wholley, the open access to AMP results should level the playing field—even for companies that do not participate.

"Biotechs wouldn't put their money into this—nor should they. They need to preserve their resources," Zerhouni told *SciBX*.

Chin wants to see more companies join the consortium. He said that he is talking with other members of PhRMA and will provide them with updates as the AMP programs move forward.

UPPPing the ante

The precise contribution of each organization has not been disclosed, but on average each company will give $1–2 million per year. The average annual R&D budget of the participating companies is about $5 billion.

Magali Haas said that the consortium is a step in the right direction but likely needs a bigger budget.

"We have to ask: what's the appropriate level of investment?" she said. "It's the right approach, has all the right players and the right focus—on biomarkers and mechanisms—but this is woefully underfunded for the magnitude of what's needed for Alzheimer's disease. It will be difficult to accelerate the pace with that amount of funding. They'll have to make trade-offs—for example, by limiting the number of markers they can assess. I'd rather they make the appropriate investment now as this is the first step in a long process."

Haas is founder and CEO of **Orion Bionetworks**, a not-for-profit alliance of public and private partners developing predictive computerized models for CNS diseases. Orion is not a member of AMP.

Like Haas, Sandra Raymond, president and CEO of the **Lupus Foundation of America Inc.**, supports the AMP model and is concerned about funding.

"$20 million buys a lot of basic science, but it doesn't buy the huge cohorts and databanking or biobanking that you'd like to see," she told *SciBX*.

Collins and Wholley both said that AMP is a pilot program that they hope to grow in the future. They would like to add new therapeutic areas and recruit new participants once they have data to show the current plan is working.

Targets and biomarkers

According to Wholley, there are three tracks for distributing AMP funds.

The NIH will disburse its 50% contribution via the normal NIH grant process. The FNIH holds the remaining money from industry and the not-for-profit entities. A portion will go to supplement the NIH grants, and the rest will be disbursed directly by the FNIH. The grants will all go to extramural scientists, Wholley told *SciBX*.

A portion of the AD funds will go to embedding biomarker screening into several existing disease-prevention studies sponsored by the NIH, companies and not-for-profit organizations. In addition, three ongoing NIH-funded studies to identify and validate new targets will receive

Table 1. Participants in the NIH AMP consortium. The NIH has formed a public-private partnership, called the Accelerating Medicines Partnership (AMP), with industry and not-for-profit organizations to accelerate discovery of targets and biomarkers in Alzheimer's disease (AD), type 2 diabetes, rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). The not-for-profit Foundation for the National Institutes of Health will manage the funds and operations.

Government	Industry	Not-for-profit organizations
FDA	**AbbVie Inc.** (NYSE:ABBV)	**Alzheimer's Association**
NIH Office of the Director	**Biogen Idec Inc.** (NASDAQ:BIIB)	**American Diabetes Association**
National Institute on Aging	**Bristol-Myers Squibb Co.** (NYSE:BMY)	**Foundation for the National Institutes of Health**
National Institute of Diabetes and Digestive and Kidney Diseases	**GlaxoSmithKline plc** (LSE:GSK; NYSE:GSK)	**Geoffrey Beene Foundation Alzheimer's Initiative**
National Institute of Arthritis and Musculoskeletal and Skin Diseases	**Johnson & Johnson** (NYSE:JNJ)	**Lupus Foundation of America Inc.**
National Institute of Allergy and Infectious Diseases	**Eli Lilly and Co.** (NYSE:LLY)	**Pharmaceutical Research and Manufacturers of America**
	Merck & Co. Inc. (NYSE:MRK)	**Rheumatology Research Foundation**
	Pfizer Inc. (NYSE:PFE)	**USAgainstAlzheimer's**
	Sanofi (Euronext:SAN; NYSE:SNY)	
	Takeda Pharmaceutical Co. Ltd. (Tokyo:4502)	

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further money to support screening of RNA and proteomics panels. This funding will create network models using systems biology to validate targets involved in disease progression.

Williams hopes that the AMP funding will lead to the development of new biomarkers to track AD patient progression that are better than the currently used β-amyloid (Aβ). If the project proves successful, the studies could identify new pathways that drive pathogenesis in all or a subset of patients with AD, he told *SciBX*.

According to Meryl Comer, the emphasis on biomarkers reflects a paradigm shift toward understanding the need for early diagnosis of AD, especially in presymptomatic populations.

"If we can get better at characterizing the early signs and getting treatments, we could change the current mindset of physicians, which is to shy away from diagnosing Alzheimer's," she told *SciBX*. Comer is president of the **Geoffrey Beene Foundation Alzheimer's Initiative**, which is a member of AMP.

Comer said that her organization is providing in-kind assistance, for example, by launching registries and helping recruit subjects for clinical trials.

The type 2 diabetes program also aims to capitalize on data from previous or ongoing NIH studies.

Wholley told *SciBX* that the goal is to have a disease portal within two years that will integrate genomewide association studies, sequencing and other data from NIH studies in type 2 diabetes. Following that, he said, AMP will sponsor deep sequencing or further analysis of genes that show significant correlation with disease.

Robert Ratner said that the project holds the potential to find diabetes biomarkers that can predict toxic outcomes such as cardiovascular side effects in addition to finding new targets for treating the disease.

He added that **FDA** requirements for cardiovascular outcomes trials for diabetes compounds have created a need to look for rare adverse effects and find predictors of positive and negative responses to medication.

Ratner is CSO and CMO of the **American Diabetes Association**.

For SLE and RA, Collins and Chin said that the goal is to understand the molecular players that go awry in the immune system. In SLE, patients have widely varying symptoms, and the disease can affect different organs in different individuals.

According to Raymond, AMP will fund genomewide association studies and will support studies on single cells, tissues and blood subsets from patients.

"We will throw -omics at this disease: genomics, proteomics, metabolomics. This technology is not available to everyone, so it will be done in an integrated fashion between the partners," she told *SciBX*.

Wholley said that when the AMP projects do yield new targets, "companies will then have to take on an awful lot of work to take things forward from there. We are not a drug company; we're not producing treatments. There's an area in the middle [of basic research and therapeutic development] to make the whole ecosystem more efficient, and that's what AMP is," he said.

A more in-depth discussion can be viewed at the full *BioCentury This Week* interview with Collins, Wholley, Chin and Raymond.

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REFERENCES

1. Cain, C. *BioCentury* **20**(45), A8–A10; Nov. 5, 2012

COMPANIES AND INSTITUTIONS MENTIONED

American Diabetes Association, Alexandria, Va.
Biogen Idec Inc. (NASDAQ:BIIB), Weston, Mass.
Food and Drug Administration, Silver Spring, Md.
Foundation for the National Institutes of Health, Bethesda, Md.
Geoffrey Beene Foundation Alzheimer's Initiative, Washington, D.C.
Innovative Medicines Initiative, Brussels, Belgium
Lupus Foundation of America Inc., Washington, D.C.
National Institutes of Health, Bethesda, Md.
Orion Bionetworks, Cambridge, Mass.
Pharmaceutical Research and Manufacturers of America, Washington, D.C.
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Sanofi (Euronext:SAN; NYSE:SNY), Paris, France
USAgainstAlzheimer's, Washington, D.C.

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