**PEOPLE**

**Epigenetics pioneer C. David Allis, PhD**, will be awarded the 2014 Japan Prize in Life Sciences in April. The Japan Prize Foundation bestows the prize, worth about $500,000, annually to scientists and researchers who have made substantial contributions to their field and to “the peace and prosperity of mankind.” Allis discovered that histone proteins are chemically modified in order to activate or silence nearby genes. He is a professor at The Rockefeller University in New York, NY.

**Hervé Hoppenot**, former president of Novartis Oncology, has been named president and CEO of Incyte (Wilmington, DE), which develops small-molecule drugs for oncology and inflammation. At Novartis, Hoppenot was responsible for translational medicine, development, and approval and commercialization, which included $11 billion in global sales. He also helped introduce new indications for Afinitor (everolimus) and Tasigna (nilotinib), and launched two new drugs, Signifor (pasireotide) for Cushing’s disease and the JAK inhibitor Jakavi (ruxolitinib) for myelofibrosis.

Roche has promoted **Sandra Horning, MD**, to chief medical officer and head of global product development. Most recently, she served as head of clinical development for the company’s oncology and hematology business and helped shepherd several cancer drugs through development, including Zelboraf (vemurafenib), Erivedge (vismodegib), and Perjeta (pertuzumab). Before joining Roche in 2009, Horning worked as a practicing oncologist, clinical investigator, and professor of medicine at Stanford University School of Medicine in Palo Alto, CA.

**Combination Therapy Approved for Melanoma**

In January, the U.S. Food and Drug Administration (FDA) approved the targeted drug combination of trametinib (Mekinist; GlaxoSmithKline) and dabrafenib (Tafinlar; GlaxoSmithKline) for treating patients with metastatic or unresectable melanoma with BRAF V600K or V600E mutations. Both drugs received approval as monotherapies in May 2013.

Trametinib and dabrafenib inhibit kinases in the RAS/RAF/MEK/ERK pathway. In clinical trials, patients treated with either of these single-agent therapies develop resistance to the drugs and have disease progression within 6 or 7 months, but their combined effect extends that time.

Keith Flaherty, MD, an oncologist at the Massachusetts General Hospital Cancer Center in Boston, says combination therapies expand the efficacy of the first generation of targeted drugs, the earliest of which entered treatment regimens more than a dozen years ago. “Numerous two-drug combinations are being evaluated in ongoing drug trials now,” he says, representing the beginning of a coming wave of multi-drug therapies. “I think 2014 will witness the first wave of triplet targeted regimens as well.”

Targeted therapies often benefit only a small fraction of a cancer population, but combination therapies may prolong response times and benefit additional patient subgroups.

In the approval statement, the FDA cited results from a phase II open-label clinical trial, led by Flaherty, involving 162 patients with metastatic melanoma that expressed a BRAF mutation, most of whom were previously untreated. Participants received either dabrafenib alone or dabrafenib in combination with trametinib. Patients who received the highest combination dose—150 mg of dabrafenib twice daily with 2 mg of trametinib once daily—had an objective response rate of 76% and a median progression-free survival (PFS) of 9.4 months, compared with 54% and 5.8 months in patients treated only with dabrafenib. Overall survival data are not yet available.

On January 24, after FDA approval was granted, GlaxoSmithKline announced that the combination met its primary endpoint of PFS in a phase III trial that compared the combination to dabrafenib plus a placebo. PFS, response rate, and interim overall survival results were consistent with those seen in earlier studies, according to the company. Full results will be presented at an upcoming scientific meeting.

When targeted therapy is appropriate for a patient, the newly approved combination clearly has some advantages over single agents and “should be considered as an option for standard of care,” says Mario Sznol, MD, an oncologist at the Yale Cancer Center in New Haven, CT. Data from the phase II trial, which was published in 2012, “really showed a dramatic improvement in progression-free survival for the combination,” with tolerable toxicity.

The next difficult decision clinicians will face, says Sznol, is determining whether to offer the combination targeted therapy or immunotherapy to a patient with a BRAF mutation—or offer both, one after the other.

“We may need a randomized trial to determine which sequence of therapies, if sequencing is indeed the best approach, would lead to the best outcome in the majority of patients.”

**$540 Million Gift Boosts Cancer Research**

In one of the largest single philanthropic gifts ever made to support cancer research, Ludwig Cancer Research, based in New York, NY, announced that it will disburse $540 million from the estate of the late shipping magnate Daniel K. Ludwig equally to six institutions.

In its January 6 announcement, the organization said that the money would fund cancer research at Ludwig Centers at Harvard University, Johns Hopkins University, the Massachusetts Institute of Technology, Memorial Sloan-Kettering Cancer Center, Stanford University, and the University of Chicago, based on stipulations Ludwig made before his death in 1992.

“Daniel Ludwig viewed cancer as a major challenge to mankind, which requires a comprehensive and concerted...”
We're not restricted in how incredible opportunity," says Geoffrey Greene, PhD, codirector of the Ludwig Institute for Cancer Research worldwide. To date, Ludwig Cancer Research has a collaborative network of acclaimed scientists with an endowment of $1.2 billion.

The centers combined with the Institute make up Ludwig Cancer Research, a nonprofit, international, collaborative network of acclaimed scientists with an endowment of $1.2 billion. To date, Ludwig Cancer Research has dedicated more than $2.5 billion to cancer research worldwide.

"The donation provides us an incredible opportunity," says Geoffrey Greene, PhD, codirector of the Ludwig Center at the University of Chicago in Illinois. "We're not restricted in how we use it, so we can be creative, innovative, and use as much 'out-of-the-box' thinking as we want to."

Greene and his colleagues plan to use the funds to recruit senior investigators and fund new initiatives to bolster their effort to better understand the genesis, progression, and management of cancer metastasis. Other centers are focused on areas ranging from immunotherapy and stem cell research to cancer prevention and early detection.

**Budgets Up at NIH, NCI, and FDA**

After a fiscally challenging year, scientific and medical research will feel some budgetary relief with the new federal spending bill signed into law in mid-January by President Obama, totaling $1.1 trillion for fiscal year 2014. Under the new budget, the U.S. Food and Drug Administration (FDA) will receive $2.552 billion, $166 million more than its post-sequestration 2013 budget, a 7% increase. Funding for the NIH will increase by $1 billion to $29.9 billion, a 3.5% increase, and funding for the National Cancer Institute (NCI) will increase by $140 million to $4.923 billion, a 2.9% increase.

Sequestration, which amounted to a 5% reduction of the NIH FY2013 budget applied evenly across all programs, projects, and activities, had wide-ranging effects. According to NIH Director Francis Collins, MD, PhD, the cuts not only increased competition for new grants, making it harder for new investigators and new ideas to be funded, but also slashed funds from existing grants that were already operating on tight budgets.

For the FDA, the bill goes beyond restoration of budget losses due to sequestration, although a large portion of the increase will cover food-safety activities mandated by a 2011 law. However, other agencies weren’t as lucky. The NIH budget falls $714 million short of pre-sequestration funding levels. The NCI budget increase makes up only about half of sequestration losses. In fact, in real dollars, NCI’s FY2014 budget falls short of its FY2009 budget of $4.968 billion.

"We should clearly express our appreciation to the Congress for being able to do that much in an incredibly difficult environment,” says Edward J. Benz Jr., MD, president of Dana-Farber Cancer Institute in Boston, MA. “On the other hand, it’s a partial make-up. It is not a solution to the fundamental weakening of the research enterprise that has resulted from a long history of dwindling funding that was exacerbated by sequestration."

At Dana-Farber, sequestration delayed recruitment and indefinitely postponed development of various research centers. “Money that might have been used for new projects, new ideas, or for recruiting new investigators had to be diverted toward making up for the losses to existing labs,” says Benz.

The sequestration cuts of FY2013 came on top of budget cuts for the NIH and NCI that began in FY2011. Even without taking into account outright budget cuts, the NIH budget had not kept pace with biomedical inflation, an estimated increase in the prices of research equipment and supplies, in a decade. In January 2013, the NIH projected biomedical inflation levels of 2.7% for FY2014 and 2.9% for FY2015.

"Resources are constrained, but there is still a lot of federal and non-federal money being spent on cancer research,” says Benz. “It’s incumbent on us to find the best way to use existing funding to make the biggest impact on patients."

**Report Links Smoking to Poor Cancer Outcomes**

Fifty years ago, the landmark 1964 report Smoking and Health, issued by U.S. Surgeon General Luther Terry, MD, first linked smoking to lung cancer. The latest report, issued in January by Acting Surgeon General Boris Lushniak, MD, MPH, and available at www.surgeongeneral.gov, highlights successes of the resulting anti-tobacco movement and expands the long list of smoking-related health problems to include colorectal and liver cancers, diabetes, and rheumatoid arthritis, among others.

The comprehensive new report—the 32nd such document—is also the first to offer evidence documenting the harms of continued smoking for people with cancer. It notes that smoking increases all-cause mortality by at least 50% and cancer-specific mortality by 61% in cancer patients. Cancer survivors who...
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