said Kathy Hudson, PhD, NIH deputy director for science, outreach, and policy, in testimony before the Committee on Energy and Commerce.

Although the bill's provisions to increase funding for research and drug development have met with widespread support, proposed changes to the drug approval process have sparked some controversy. A recent commentary in *The New England Journal of Medicine*, for example, takes issue with the bill's directive that the FDA develop criteria for considering nontraditional data sources—including observational studies and patient registries—instead of large, randomized clinical trials when reviewing new uses for existing drugs (N Engl J Med 2015;372:2473–5).

"Although such data can provide important information about drug utilization and safety once a medication is in use, there is considerable evidence that these approaches are not as rigorous or valid as randomized trials in assessing efficacy," wrote Jerry Avorn, MD, and Aaron Kesselheim, MD, JD, MPH, both of Harvard Medical School and Brigham and Women's Hospital in Boston, MA.

The bill would also encourage the FDA to rely more on biomarkers rather than clinical endpoints in assessing drug efficacy, the researchers said, a strategy that can be faster and cheaper but not always accurate in predicting patient outcomes.

FDA officials have expressed concern over insufficient funding in the bill, which may force the agency to generate more revenue through user fees or shift funding away from other priorities.

"A total of $550 million was added to accomplish certain activities called for in the bill," said Stephen Ostroff, MD, acting commissioner of the FDA, at a meeting of the Alliance for a Stronger FDA. "But it is not enough. The biggest concern I have is ending up with yet another unfunded, or partially funded, mandate." ■

Revving Up the Immune Therapy Business

As checkpoint inhibitors and other cancer immune therapies continue to advance in the clinic, giant pharmaceutical companies and nascent biotechs are positioning themselves to make the most of these agents.

Merck and Bristol-Myers Squibb both have FDA-approved checkpoint inhibitors on the market to treat melanoma—pembrolizumab (Keytruda) and nivolumab (Opdivo), respectively—and are pushing to expand their approved uses. (For example, nivolumab was approved in March to treat advanced squamous non–small cell lung cancer.) Novartis has gained ground on competitors by buying GlaxoSmithKline's cancer portfolio, investing in Aduro Biotech (Berkeley, CA), and hiring a leader in the field, Glenn Dranoff, MD, PhD, this past spring from Dana-Farber Cancer Institute in Boston, MA, to head their efforts.

These companies are also developing first-line therapies, as well as reexamining their portfolios to find other drugs—some already FDA-approved, others not—that might prove effective in combination with checkpoint inhibitors. Research presented at major conferences this year supported the idea that patients will see greater benefits if checkpoint inhibitors are given together or in combination with targeted therapies, chemotherapies, or cancer vaccines. Companies are testing many combinations to determine which are most effective against which types of cancer.

"The trend toward consolidation in cancer—where a single pharma company can offer a suite of agents covering a range of cancers and combinations—is definitely real," says Bruce Booth, a partner in Atlas Venture, a Cambridge, MA–based venture capital firm specializing in life sciences and technology.

Dranoff agrees, saying it makes sense to have a wide range of therapies in-house that can be tested in combination. He notes that Novartis now has programs in checkpoint inhibitors, cancer vaccines, and CAR T cells, in addition to treatments such as imatinib (Gleevec) that are directed at specific genetic defects.

"I think there's enormous potential for coupling," Dranoff says. "That's going to be a theme of the work we'll be doing."

Large companies are also buying and partnering with start-ups to augment their pipelines, says Booth, referring to a flurry of recent sales, including AbbVie's $21 billion purchase of Pharmacyclics (Sunnyvale, CA) to acquire the hematologic oncology drug ibrutinib (Imbruvica). In June, Celgene and Juno Therapeutics of Seattle, WA, announced a 10-year collaboration to develop CAR T-cell therapies, a deal that will net Juno about $1 billion. In addition, Novartis has invested $250 million in Aduro Biotech, an immune therapy company developing small molecules to activate the STING pathway, which may detect tumor cells and trigger an aggressive antitumor response.

Meanwhile, young biotechs, such as Jounce Therapeutics of Cambridge, MA, are advancing the science on other immune modulators. However, these biotechs have to be more selective, says Jounce CEO Richard Murray, PhD. They cannot cast a wide net, testing many compounds, like large pharmaceutical companies can.

"Biotech probably has to really start pushing the boundaries of where some of these new pieces of biology and therapeutic paradigms might emerge," says Murray, whose company is pursuing T cell–directed therapy, as well as therapies aimed at macrophages and other cell types that may initiate or improve the immune system's antitumor response.

"A balancing approach between the more established space and the new frontier ... makes sense," he says. ■

Gene "Switch" Stops Colon Cancer in Mice

Reactivating a tumor suppressor gene that is mutated in the majority of human colorectal cancers led to rapid tumor regression and restoration of normal cell function in mice, according to findings from a recent study that may help spur development of targeted treatments (Cell 2015;161:1539–52).

Researchers used RNAi to generate transgenic mice in which they could alternately silence and restore expression of the tumor suppressor gene adenomatous polyposis coli (APC) by administering or withdrawing doxycycline. As expected, they found that APC suppression produced tumors in the small intestine and colon triggered by deregulation of the Wnt signaling pathway, which controls cell proliferation and survival. Within 2 weeks of APC restoration, the tumors completely regressed, and there were no signs of relapse over a 6-month follow-up period, even in tumors containing p53 or KRAS mutations.

"We've known that the *APC* gene is important to drive the initial events of