Box 1 ASCO launches historic off-label trial

ASCO is taking its own approach to personalized medicine with the first clinical trial that aims to test molecularly targeted cancer drugs outside indications approved by the US Food and Drug Administration. The TAPUR (Targeted Agent and Profiling Utilization Registry) will use tumor genomic profiling to guide off-label uses of targeted therapies already used in oncology practice, and collect the information into a registry to guide oncologists' treatment decisions.

Treating physicians will initially screen patients' tumors to identify genomic variations and, based on these results, they will select a drug from those available in the TAPUR study protocol. This prospective, nonrandomized study will operate "in a real world setting, but off-label," and include advanced cancer patients who have exhausted other treatments, says Richard Schilsky, ASCO's chief medical officer. Enrollment should begin by year's end.

TAPUR will test for 20 genomic variants in the same cancers as NCI-MATCH and use at least 13 targeted therapies donated by five companies, including London-based AstraZeneca; S. San Francisco, California–based Genentech; Indianapolis-based Eli Lilly; and New York–based Bristol-Myers Squibb and Pfizer. Another important difference between the TAPUR and NCI-MATCH trials is that researchers will process TAPUR's biopsies at any Clinical Laboratory Improvement Amendments–certified laboratory, and that TAPUR will be conducted initially at three clinical sites, including the Michigan Cancer Research Consortium, the Cancer Research Consortium of West Michigan and the Carolinas HealthCare System, and then will expand nationally. It will operate in parallel with the Netherlands Center for Personalized Cancer Treatment (Utrecht, the Netherlands), which is using a similar protocol, with objective tumor response as the primary endpoint and progression-free survival, overall survival and duration of treatment as the secondary endpoint.

according to molecular abnormalities in their tumors. And in June, the American Society for Clinical Oncology (ASCO) will launch a trial of its own to test targeted drugs for off-label uses (**Box 1**).

What is truly unique about the NCI-MATCH approach is it will explore drug efficacy independent of where the tumor originates. "That we are now looking at cancers by what drives them rather than the site of origin is truly novel, and in my opinion, the future of the field," says Herbst. However, Frederic de Sauvage, vice president and staff scientist, molecular oncology, at Genentech, writing in a company blog in May, noted that it might be a mistake not to take into consideration the tissue of origin. Although 50% of melanomas carry a BRAF mutation, so do 5–8% of colorectal cancers, and BRAF inhibitors have been disappointing so far in that indication, he noted. The NCI-MATCH could help shed light on some of these questions.

Vicki Brower *New York*

"People are starting to look over their shoulder now, and it won't take much of a scare to cool down investors' ardor." Michael Gilman, CEO of Cambridge, Massachusetts' Padlock Therapeutics, addressing the concern that the biotech 'bubble' could burst at any time. (*The Boston Globe*, 15 June 2015)

"How do we think about consent on behalf of someone who hasn't been born? Those are the types of questions that need to be…addressed." Jeffrey Kahn, a Johns Hopkins University bioethicist, testifying before the US Congressional Research and Technology Subcommittee about the conundrum raised by the prospect of using gene editing technologies on embryos. (*Fusion* 17 June 2015)

"I have in my bag a kidney and a brain." Francis Collins, NIH director, shows Bio2015 attendees on June 17 the prototypes of 3-D printed human cell biochips derived from induced pluripotent stem cells, which he hopes will eventually replace animal testing to assess drug toxicity. (@Bio convention, 17 June 1015)

"This not about patients but about participants, it is not a disease model but what works in maintaining wellness." Francis Collins, NIH director, tells how volunteers, armed with smart phones and mobile health apps, are joining the proposed National Research Cohort of 1 million or more US citizens to advance human health. (@Bio convention, 17 June 2015)

"The worst thing we could ever do is throw these patients a great lifeline out there, and have it be frayed by the issue of access." Robert Beall, president and CEO of the Cystic Fibrosis Foundation in Bethesda, Maryland, which sold its royalty rights to the Vertex drug Kalydeco for $3.3 billion. Beall is concerned about patients who are facing a $300,000/year price tag.

Alnylam, Dicerna tussle over RNAi tech

In June, Alnylam Pharmaceuticals sued Dicerna Pharmaceuticals in the Superior Court of Middlesex County, Massachusetts, for misappropriation of trade secrets relating to the *N*-acetylgalactosamine conjugate technology for delivering RNA therapeutics. The dispute between the Cambridge, Massachusetts–based companies stems from Alnylam's $175-million purchase of Sirna Therapeutics from Merck, of Kenilworth, New Jersey, in 2014. Alnylam claims that after the acquisition, Dicerna hired several laid-off Merck researchers who "collected and took to Dicerna proprietary materials and confidential trade secret information relating to Sirna's siRNA delivery technologies," which rightfully belonged to Alnylam in accordance with its asset acquisition. Dicerna has denied the claims, calling many of the insinuations in the Alnylam complaint simply false and others, unfounded speculation. "Our RNAi-based therapeutics utilize our proprietary RNAi [RNA interference] technologies, and not prior Merck research. We stand behind these technologies, and the company's record and practices for respecting IP [intellectual property] rights, in order to develop and deliver life-changing therapies as efficiently as possible," said Dicerna CEO Douglas Fambrough in a statement. Given the different nature of trade secrets compared with patents, and what "reasonable protective measures" Alnylam took as the trade secret holder, industry watchers expect the companies to settle before the court reaches its decision.

Court invalidates Sequenom's prenatal test patent

The US Court of Appeals for the Federal Circuit has dealt Sequenom a setback, ruling that the San Diego–based company's patent for its noninvasive prenatal test is invalid. The case has implications for innovation incentives and access to an important new technology. The decision upholds a ruling by a California district court in favor of Basel-based Roche's Ariosa Diagnostics unit, San Jose, California, against Sequenom in 2013. Sequenom's test, which uses DNA found in maternal blood samples to determine certain fetal characteristics, avoids the risk of more invasive tests, such as taking samples from the fetus or placenta. The court ruled that detecting DNA in blood falls under the US Supreme Court's rule against patenting natural phenomena (*Nat. Biotechnol.* **32**, 403–404, 2014). While calling the test "a positive and valuable contribution to science…[e]ven such valuable contributions can fall short of statutory patentable subject matter, as it does here." Another judge wrote in a concurring opinion that though he was obligated to invalidate the patent claims, "[b]ut for the sweeping language in the Supreme Court's *Mayo* opinion, I see no reason, in policy or statute, why this breakthrough invention should be deemed patent ineligible."