a receptor expressed on NK cells, macrophages and mast cells, which triggers NK-cell-mediated killing of tumor cells, and CD16B, which is expressed on granulocytes and which does not trigger cell killing (*mAbs* **6**, 727–738, 2014). "It's technically extremely challenging because there are only a couple of amino acid differences between them," he says.

The appeal of bispecific antibodies has a commercial as well as a clinical dimension, given the wave of patent expirations about to break over many lucrative antibody franchises and ongoing progress in the development of a regulatory pathway for complex biosimilar products. For some firms, bispecific molecules are now center stage in their early-stage development. About 65% of Genmab's preclinical programs—both in-house and partnered—are based on its Duobody bispecific technology, for example. "I believe this is going to be the single biggest driver of future income in the antibody space," says van de Winkel.

AbbVie is actively developing a bispecific successor to its rheumatoid arthritis drug Humira (adalimumab). Although now the world's best-selling drug—sales topped $12.5 billion in 2014—the tumor necrosis factor alpha (TNF-α) inhibitor is by no means a cure. About 40% of patients on long-term therapy attain a 50% reduction in their symptoms (ACR50), as measured by the American College of Rheumatology disease activity score. Just 20% attain ACR70. Several firms, moreover, are developing biosimilar versions.

By adding an interleukin-17 (IL-17)-inhibiting capability to an anti-TNF-α inhibitor, AbbVie hopes to develop a next-generation successor to Humira. Preclinical studies in cellular systems and animal models provide the rationale. The IL-17 inhibitors [used as single agents or on their own] in rheumatoid arthritis have not been very competitive," says Lisa Olson, vice president of discovery at AbbVie. Johnson & Johnson, of New Brunswick, New Jersey, which has a multiproduct, bispecific alliance with Genmab, is also exploring, having acquired Schlieren, Switzerland–based Covagen last year. The latter firm had begun early-stage trials of COVA-322, a bispecific based on Covagen's Fynomer scaffold technology, which targets IL-17A and TNF-α.

Bispecific antibodies are so far aimed mainly at the same indications in which monoclonal antibodies have been successful, particularly cancer and autoimmune disease. The technology development effort is, however, based on a wider assumption that in complex diseases bispecifics will have effects that go beyond what monoclonal antibodies are capable of. AbbVie's sole clinical program in osteoarthritis involves a bispecific antibody, ABT-981, which targets the β- and α-isoforms of IL-1. "We're one of the last companies doing clinical development in osteoarthritis," Olson says. It's been a challenging indication for drug firms, as the clinical development process is difficult, and the regulatory approval pathway is unclear. "It follows you may need to do combination therapy or unite the two, as we've done in the DVD, to get the clinical effect that can be recognized," says Olson. "We feel the same way about lupus."

The field is still too immature to predict the likely winners—and losers—in the big push to make bispecific antibodies a mainstream therapeutic modality. Although the BiTE format is the first to win a US Food and Drug Administration (FDA) approval, the technology is far from optimized. The short half-life of BiTE molecules necessitates intravenous infusion, which could limit their utility. Macrogenics, Genmab, Vancouver, Canada–based Zymeworks and San Francisco–based Cytomx Therapeutics are among the firms that have made much of the recent running, in terms of winning multiple big pharma deals. If bispecifics deliver on their promise, the market will be big enough to accommodate multiple players. "There's no single platform that's necessarily going to take over everything," Koenig says. "It's a little too early to dogmatically say platform A is going to win out over all the others."

Cormac Sheridan

Tassaneewan Laksanasopin/ Columbia University

Smartphone HIV test. Sam Sia and colleagues at Columbia University in New York coupled microfluidics with consumer electronics to create a smartphone app that simultaneously detects HIV and syphilis. The dongle, attaches to a smartphone by the headphone jack to perform a triplexed miniature immunoassay: HIV antibody, treponemal-specific antibody for syphilis and nontreponemal antibody for active syphilis infection. The test requires a single prick of blood and uses less than 4% of the smartphone battery. Healthcare workers in Rwanda tested 96 women at a clinic for preventing mother-child transmission. Using the app, workers obtained results in 15 minutes, with 92–100% sensitivity and 79–100% specificity. It costs $34 to manufacture the dongle, and $1.44 to run the test.

Myriad settles BRCA disputes and moves on

In February, GeneDx of Gaithersburg, Maryland, and Myriad Genetics of Salt Lake City, Utah, settled their patent dispute over BRCA testing, the final chapter of Myriad's losing battle to retain its dominance in breast cancer diagnosis. Five other companies similarly engaged in litigation over BRCA 1 and BRCA 2 testing—Ambry Genetics of Aliso Viejo, California; Gene by Gene of Houston; Quest Diagnostics of Madison, New Jersey; LabCorp of Burlington, North Carolina; and Invitae of San Francisco—had settled earlier this year. Myriad's attempt to retain its dominance in BRCA testing seemed like a losing proposition since the US Supreme Court ruled in 2013 that natural gene sequences are unpatentable (*Ambry vs. Myriad Genetics*). However, the court left open the possibility of patenting engineered molecules (cDNAs or oligos), which Myriad attempted to exploit to stop its competitors from offering BRCA tests. But in December 2014, the US Court of Appeals for the Federal Circuit upheld an earlier ruling by the US District Court for Utah, denying Myriad's request for an injunction against its competitors. District Court Judge Selby had found last March that the company's primers and probes are not patentable because they have the same sequence as the natural gene. Once the appeal was denied, Myriad forged agreements with Ambry, Quest, LabCorp and Invitae (Gene by Gene and Myriad had settled earlier in 2014) and now GeneDx. Under the terms of the settlements, Myriad agrees not to pursue any further litigation over the patents mentioned in the suit, but will not be compensating anyone for legal costs incurred, (which some view as a small victory for Myriad). The company has been working on gene panels for various diseases and signaled its interest in protein diagnostics with a recent acquisition of Crescendo Bioscience.

"**I don't have any crow's feet anymore, and I don't have any wrinkle lines above my nose. Now I can say I'm not just the CEO, I'm a user.**" Brenton Saunders, the 44 year old CEO of Parsippany, New Jersey–based generic drug company Actavis, which, in January, acquired Allergan, and along with it, the company's blockbuster product, Botox. (*Forbes*, 9 February 2015)

"**I'm not against the use of those tools [multiple herbicide–resistant crops]. I'm against their poor use. I want as big a tool chest as possible—and having all of them be effective, using them in a wise way, is ultimately where we want to go.**" Bruce Maxwell, an agroecologist at Montana State University in Bozeman, on two new crop approvals. In January, the USDA approved the use of Monsanto's cotton resistant to three herbicides, and its soybean, resistant to two, worrying some environmentalists that their overuse will lead to resistance. (*Wired,* 2 February 2015)