IN brief

NextCODE to mine Icelandic genetic wealth

A team of venture capitalists has launched NextCODE Health to provide a diagnostics service to researchers—and, later, physicians providing routine care—by tapping into the genomics platform developed by deCODE Genetics. Arch Venture Partners of Seattle, and Waltham, Massachusetts–based Polaris Ventures founded NextCODE October 23, inking a 5-year exclusive license to access the platform developed by Reykjavik-based deCODE, the pioneering genetics firm, now a wholly owned Amgen subsidiary. Amgen paid $415 million for deCODE in 2012 to mine the detailed genetic profiling and genealogical data of the Icelandic population for use in discovery research (*Nat. Biotechnol.* **31**, 87–88, 2013). NextCODE will offer genome interpretation, data analysis and next-generation clinical sequencing services to enable researchers and clinicians to more quickly, accurately and cheaply decipher whole-genome sequence data and diagnose conditions. Michael A. Patton, professor of medical genetics at St. George's, University of London, says NextCODE "is competing with many other companies in offering exome sequencing and genomics analysis and may find it difficult to create a commercial market." Jeff Gulcher, NextCODE's president and CSO and deCODE's co-founder, says that, unlike relational databases, which cannot efficiently handle the trillions of data points associated with even several dozen genomes, NextCODE's sequence analysis platform has been used to successfully manage data from more than 350,000 whole genomes. Additionally, "we have access to the largest and most successful clinical genetics reference database in the world," he says. NextCODE has already struck service agreements, focusing on oncology and pediatrics, with Queensland University in Brisbane, Australia, Boston Children's Hospital, Newcastle University in the UK and Saitama University in Japan.

Emma Dorey

IN their words

"Sadly, this guidance is the biggest step the FDA has taken in a generation to combat the overuse of antibiotics in corporate agriculture, and it falls woefully short of what is needed to address a public health crisis." Representative Louise Slaughter (D-NY), the only microbiologist in the Congress, commenting on the recent FDA guidance on antibiotic use in agriculture. (*USA Today*, 11 December 2013)

"This suit is nothing more than an attempt to change the venue of existing litigation against Invitae away from Utah." Myriad Genetics reaction to a countersuit by Invitae over BRCA1/2 testing in breast cancer. (*Genome Web Daily News*, 2 December 2013)

Genentech's glyco-engineered antibody to succeed Rituxan

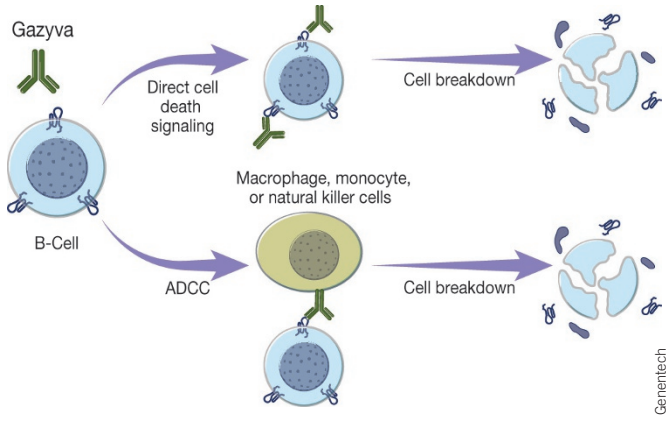
On November 1, Gazyva (obinutuzumab), Genentech's successor to its own long-time blockbuster drug Rituxan (rituximab), gained US approval—the first under the Food and Drug Administration (FDA)'s breakthrough therapy designation. It is the first glyco-engineered antibody drug to reach the Western market; only Tokyo-based Kyowa Hakko Kirin's Poteligeo (mogamulizumab), which was approved in Japan in 2012 to treat a form of T-cell lymphoma, a rare cancer, has preceded it. Gazyva (also known as GA101) is noteworthy for several reasons: the molecule's glyco-engineered origins, the use of the breakthrough drug pathway, its large market and Genentech's clinical trial aimed at showing its superiority to Rituxan. But Gazyva may prove to be a one-of-a-kind tale of drug development because the extent to which glyco-engineering contributes to its apparent potency over Rituxan is unclear.

The agency's go-ahead for Gazyva to treat people with previously untreated chronic lymphocytic leukemia (CLL) is for use in combination with the chemotherapy drug chlorambucil. The approval was based on results from a randomized, open-label, multicenter trial where study participants receiving the combination regimen showed significantly improved, progression-free survival: an average of 23 months compared with 11.1 months with chlorambucil alone. A second element of the trial design, for which data were not ripe at the time of the March 2013 decision to file a biologics license application (BLA), compared Gazyva with Rituxan, each combined with chlorambucil, head to head. In July, when the second portion of the study achieved its primary endpoint, Genentech stopped the trial.

"We had our answer, that GA101 was superior to Rituxan," says Nancy Valente, head of global hematology development for San Francisco–based Genentech, a member of the Basel-based Roche Group. In addition to extending progression-free survival, the Gazyva-chlorambucil combination showed a greater depth of remission compared with Rituxan-chlorambucil, which "would translate into improved outcome in the long run for patients," she says. "We are trying to induce a deep remission with a minimum of treatment, so they can have long periods in remission, progression free and off therapy." In addition, Genentech has three large randomized phase 3 trials in lymphoma, two of which are head to head against Rituxan.

Because Genentech petitioned FDA only for breakthrough therapy status for Gazyva late in the development process, at the time of the BLA filing, it did not receive all of the potential benefits of the program, such as a speedy review (*Nat. Biotechnol.* **31**, 374, 2013). Nonetheless, the process enabled "a richer interaction with the FDA," Valente says, in terms of both the medical and manufacturing reviews. It provided more frequent dialog "and also allowed us to have multiple divisions present at the same time," she says, which improved coordination.

Gazyva is a fully humanized monoclonal antibody directed, like Rituxan, against CD20 found on B cells. Its development began a few years after Rituxan's initial approval in late 1997 for the treatment of CD20-positive B-cell non-Hodgkin's lymphoma (NHL). By that time, there was evidence—both preclinical and indirectly from the clinic—that ADCC (antibody-dependent cellular cytotoxicity, an immune effector function mediated through Fcγ receptors) was at least partly responsible for the activity of Rituxan in NHL patients, says Pablo Umaña, head of the Roche GlycArt biotech research site in Schlieren, Switzerland.



Gazyva's dual mechanism of action: the antibody binds directly killing B cells, and through antibody dependent cytotoxicity it recruits the immune system to attack B cells.

Roche acquired GlycArt, a spin-out of the Swiss Federal Institute of Technology (ETH) and founded by Umaña, in 2005. By then, GlycArt had begun development of Gazyva, a