DBN employees charged with agricultural espionage

The US government has charged six Chinese nationals with conspiring to steal trade secrets worth tens of millions of dollars from three US biotech seed companies. The men over the course of almost two years pilfered ears of corn and dug up newly planted corn seeds from test plots and other key fields in the Midwest grown for St. Louis–based Monsanto, Johnston, Iowa–based DuPont Pioneer and Elmwood, Illinois–based LG Seeds, the US Attorney's Office alleges. The men were caught trying to take the seeds back to China, it is claimed, to benefit their Chinese conglomerate employer Beijing Dabeinong Technology Group Company (DBN Group) and its subsidiary Beijing Kings Nower Seed. At press time, only one of the accused, Mo Hailong, had been arrested. The other five remained fugitives. Mo was released from custody in May after posting a $50,000 cash bond. He will live under home confinement while he awaits a trial set to begin on December 1.

Commercial hybrid seeds sold to farmers contain a small percentage of inbred or parent lines that carry engineered traits developed by seed companies.

US prosecutors say the men were after the seed companies' 'inbred' or 'parent' lines of corn, which can take five to eight years and millions of dollars to develop. Inbred lines exhibit precise performance characteristics and engineered traits such as insect resistance and drought tolerance. Seed companies use them in production fields to cross pollinate with other superior inbred lines, and generate robust offspring known as first-generation hybrid seeds. The hybrid seeds are sold to farmers, but the parent seeds stay with the companies.

Seed companies take every reasonable precaution to protect their inbred lines, including monitoring sensitive field locations and limiting the information given to contract growers who manage production fields. In addition, they patent proprietary technology and require anyone who buys commercial hybrid seed to sign a technology agreement that restricts how the seed is used and transported. Beyond that, "There's not much you can do," says Drew Kershen, who teaches agricultural biotech law at the University of Oklahoma College of Law in Norman. "You can't grow it all in greenhouses," and it's not practical to station guards at every field, he says. "There's no cost-effective way to provide absolute security," adds Alan McHughen, a plant biotechnologist at University of California, Riverside.

Someone could even take inbred lines straight out of a bag of commercial hybrid seed. Nearly every bag sold contains a small percentage of inbred seed—usually less than 1%. The inbred lines, once they are grown, are usually two to three feet shorter in height than the hybrids, so a grower could simply plant the seed and see what comes up. Or someone could use PCR (polymerase chain reaction) to identify inbred seeds if he or she knew the specific genetic markers of the parent lines, suggests McHughen. Doing any of this is prohibited by the technology agreements that seed buyers have to sign. But enforcing every agreement, and preventing distributors from selling to people who haven't signed agreements, isn't always possible.

Once someone has the inbred seeds, the technology is theirs. "If you have the parent lines all you have to do is start growing it," says Kershen. "You now have the parental genetics to make your first-generation hybrid." But that may not be as simple as it sounds, says Thomas Helscher, a spokesperson

Green light for Janssen's IL-6 blocker

Regulators have backed Janssen's first-in-class, anti-interleukin-6 (IL-6) Sylvant (siltuximab) for multicentric Castleman's disease, a rare B-cell lymphoproliferative disorder. Sylvant, a chimeric IL-6–neutralizing monoclonal antibody, is the first drug approved in the US and EU to treat this rare disease, although Roche's first-in-class anti-IL-6 receptor (IL-6R) Actemra (tocilizumab) similarly targeted Castleman's. Actemra achieved blockbuster status last year, driven by its sales in rheumatoid arthritis, but it was first approved to treat Castleman's disease in Japan in 2005. Janssen, a Beerse, Belgium–based subsidiary of Johnson & Johnson (J&J), is now developing its antibody for smoldering multiple myeloma, an early stage of the blood cancer. "Our ongoing phase 2 trial is important not just from the drug development point of view, but also in terms of studying the hypothesis that IL-6 is an important driver of the development of multiple myeloma," says Helgi van de Velde, senior director of oncology R&D at Janssen. Basel-based Roche's Actemra was also studied in multiple myeloma, with little success. "But I'm not sure that you can extrapolate from these results," says van de Velde, because Sylvant targets the IL-6 ligand rather than its receptor. Most firms have focused their IL-6 and IL-6R efforts on autoimmune and inflammatory indications. AbbVie's ALX-0061, Bristol-Myers Squibb's clazakizumab, J&J's sirukumab, Regeneron's sarilumab, Pfizer's PF-04236921 and other related candidates are in clinical trials for rheumatoid arthritis, psoriatic arthritis, Crohn's disease and lupus. *Asher Mullard*

Novartis' lung cancer ALK inhibitor approved

The US Food and Drug Administration has granted an accelerated approval to Novartis for its metastatic lung cancer treatment Zykadia (ceritinib) less than three and a half years after the first patient entered a clinical trial. On April 29, the agency gave Zykadia accelerated approval for patients with non-small cell lung cancer (NSCLC) who have progressed on Pfizer's first-line treatment Xalkori (crizotinib). Zykadia is an anaplastic lymphoma kinase (ALK) tyrosine kinase inhibitor that is intended for the approximately 4% of NSCLC patients who have a chromosomal rearrangement of the ALK gene that renders the tumor dependent on that signaling pathway. Most ALK$^+$ patients initially respond to New York–based Pfizer's c-Met/ALK inhibitor Xalkori, but within a year, the majority progress, owing to drug resistance. Although the Pfizer drug blocks both c-Met and ALK, it more potently inhibits c-Met. By contrast, the new drug from Basel-based Novartis, which differs structurally from Xalkori, is many times more potent against ALK. This allows it to overcome certain secondary mutations in ALK that cause resistance to Xalkori, says Gregory Riely of Memorial Sloan-Kettering Cancer Center in New York. "Zykadia has been very important to show us that these tumors are still ALK-dependent," says Alice Shaw of Massachusetts General Hospital in Boston. *Malini Guha*

Faster approval for breakthrough devices

The US Food and Drug Administration is proposing to expedite approval of certain medical devices. The agency has issued a draft guidance for a new, voluntary program delineating how the agency intends to accelerate approval of high-risk devices, diagnostics included, that address unmet public health needs. Under the proposed Expedited Access for PreMarket Approval, or EAP, the agency would offer device developers earlier and more interactive engagement with its staff—including the involvement of senior management and greater collaboration on collecting the requisite scientific and clinical data to support approval. Notably, under the EAP, companion diagnostics for a drug reviewed under the accelerated drug approval pathway may be considered for EAP. In a related new draft guidance, the agency addresses pre- and post-market data collection for class III medical devices, which are those with highest risk, to place a greater reliance on post-market collection as a basis for approval, where appropriate. "Both documents illustrate the FDA's continued efforts to work earlier and closer with device developers in order to expedite the introduction of new technologies in the US market," notes ADVI, a Washington, DC–based healthcare advisory services firm. Manufacturers often turn to the EU, which has fewer hurdles in the regulatory process, for device commercialization. *Mark Ratner*

NIH 'hubs' aid translation

In April, the National Institutes of Health (NIH) in Bethesda, Maryland, launched the NIH Research Evaluation and Commercialization Hub (REACH) program. The initiative will support proof-of-concept centers, or hubs, through grants of up to $1 million a year for three years. The focus for the REACH hubs, modeled in part on the Innovation Corps program of the National Science Foundation, is on converting research innovations into drugs, devices, vaccines or other products that help meet healthcare needs. Initially, NIH expects to fund three such hubs with a total of $9 million drawn from funds already appropriated to the agency. The program also provides access to expertise in regulatory, reimbursement, business, legal and project management. "That could serve to ensure these innovators are better equipped to advance their research projects and launch the next generation of biotech companies," says Cartier Esham, executive vice president, Emerging Companies Section for the Biotechnology Industry Organization (BIO) in Washington, DC. High-level impetus for the NIH program comes from the President's Council of Advisors on Science and Technology (PCAST) and its 2012 report on lagging drug development. "These are encouraging signs," says Garry Neil, who heads R&D at Medgenics in Wayne, Pennsylvania, and whose focus is rare diseases. "But much more needs to be done if we are going to reach the ambitious goals set in the PCAST report." *Jeffrey L Fox*

for Monsanto. A breeder would need to know a great deal about the characteristics of the particular plants he or she is working with, such as maturity, root strength, stalk strength and disease resistance characteristics. "Without this information, seed from a random corn plant wouldn't be immediately useful to a breeder trying to develop hybrids that will meet the needs of particular growers," Helscher adds. Deducing this information about the plant would be daunting and would take several years of work, but it can be done, he says.

The accused men, however, seemed to have some knowledge of the plants' characteristics, given that they were apparently targeting seed with elite properties. They were first seen acting suspiciously on May 3, 2011. Mo Hailong, director of international business at DBN, was found on his knees, presumably digging up seeds in a field in remote Iowa where inbred seeds belonging to DuPont Pioneer had been planted the day before. Pioneer officials later told the FBI that that particular field was growing "one of the company's two or three most highly anticipated inbred corn seed products" not yet on the market, according to the criminal complaint.

If he is found guilty, Mo faces up to ten years in prison and a $5 million fine. Mo's attorney, Mark Beck, a partner at Orrick, Herrington & Sutcliffe in Los Angeles, told *Nature Biotechnology* he was in the process of preparing the case for trial and could not comment on it at this stage. DBN and Kings Nower Seed declined to comment for this story.

The FBI is investigating several potential insiders at US seed companies who are suspected of providing the men with the locations of important fields, according to documents filed with the US District Court in the Southern District of Iowa.

The Mo case is not Pioneer's first encounter with trade secret theft. In a case decided in 1991, Pioneer sued rival Williamsburg, Iowa–based Holden Foundation Seeds for developing some of its seed products using one of Pioneer's inbred lines. The US District Court decided in favor of Pioneer and ordered Holden to pay Pioneer $46.7 million. The decision was upheld by an appellate court in 1994, but shortly after, the two parties settled out of court for an undisclosed amount, according to Kershen. Holden was later acquired by Monsanto.

Emily Waltz *Nashville, Tennessee*

"We could have as many as five states by the end of this year with mandatory labeling. Is the FDA going to allow them [the states] to dictate national policy, or will they step in with a federal blueprint?" Colin O'Neil, director of government affairs at the Center for Food Safety in Washington, DC. The war over GMO food labeling goes on. (*Los Angeles Times*, 6 June 2014)

"If we don't change the basic pricing structure of pharmaceuticals, this system will collapse." Steve Miller, CMO for Express Scripts, America's largest pharmacy benefit manager, on the pricing ruckus that erupted with the approval of Gilead's $89,000 HCV treatment Sovaldi. (*The Economist,* 7 June 2014)

"Does anyone think Merck will introduce a drug with an advantage and then price it at significantly less than Sovaldi?" Matthew Herper of *Forbes* predicts no relief in sight for high-priced drugs following the news that Merck bought Idenix, a maker of HCV drugs, for $3.9 billion in cash. (*Forbes,* 10 June 2014)

"Cloud computing is the great leveler. It opens up new avenues for talent development." Mark DeLong, director of research computing at Duke University, on an agreement between Google and the foundation Autism Speaks to house 10,000 complete genomes of children with autism. (*The Wall Street Journal*, 9 June 2014)

"This is probably the biggest phase 1 trial ever conducted in oncology. We were excited to see that pembrolizumab [anti-PD-1 antibody] was effective in previously untreated patients as well as in those who had multiple prior therapies, including ipilimumab [Yervoy, anti CTLA-4 antibody]." Antoni Ribas of UCLA Jonsson Comprehensive Cancer Center on trial in patients with advanced melanoma. (*MedPage Today*, 5 June 2014)

"The question is, can you extend the person's life with quality? That's what you're trying to achieve." Paul DiSilvestro of Women and Children's Hospital of Rhode Island in Providence. DiSilvestro was commenting on data presented at ASCO in June, showing that combining PARP inhibitors extends progression-free survival in ovarian cancer patients, but with additional toxicities. (*BioCentury*, 9 June 2014)