Dendreon bankrupt

Dendreon, the Seattle-based biotech that pioneered a therapeutic cancer vaccine, filed for bankruptcy protection November 10. The company's Provenge (sipuleucel-T) was the first immunotherapy to treat patients with advanced-stage prostate cancer and its approval in 2010 was hailed as a landmark (*Nat. Biotechnol.* **28**, 531–532, 2010). The autologous cellular vaccine involves incubating a patient's own antigen-presenting cells with a fusion of prostatic acid phosphatase and granulocyte-macrophage colony-stimulating factor to stimulate an immune response. But Provenge never took off. The drug is cumbersome to produce, expensive at $93,000 for a course, and shows limited benefits over standard therapies. Sales have been disappointing at $283.7 million in 2013, well below analysts' projected $4.3 billion in annual sales by 2020. Dendreon, whose market value once topped $7 billion, unsuccessfully sought a buyer last year. The company cut 750 positions in 2012 and 2013 from a total 1,500, and sold a New Jersey plant. Now, the company will either sell itself or its assets, or if no buyers are forthcoming, the noteholders will take ownership and Dendron will become a private company.

New drug costs soar to $2.6 billion

The Tufts Center for the Study of Drug Development issued their latest estimate for the cost of developing a new drug: an eye-popping $2.6 billion. The estimate, made by the independent, nonprofit research group, is based on data provided by ten pharma companies on 106 randomly selected drugs. It includes out-of-pocket costs of $1.4 billion and another $1.1 billion in time costs—"the expected returns that investors forego while a drug is in development." Post-approval costs add another $312 million. The 145% increase from their previous estimate, done in 2003, is attributed to the increased complexity of clinical trials and health assessments, not to regulatory delays.

Nagoya Protocol takes effect—without Japan

The United Nations protocol for biodiversity protection and benefit sharing from genetic resources went into effect on October 12. But Japan, which hosted the meeting that produced the agreement, failed to ratify it in time as domestic changes necessary for the country to become a contracting party stalled due to opposition from business groups. Japan's environment minister Yoshio Mochizuki has said that Japan will aim to ratify the protocol as soon as possible and to implement the necessary domestic measures in 2015.

> **"Eight Ebola products on the market with no one knowing how they work is not helpful."** Mark Perkins, CSO of FIND, or the Foundation for Innovative New Diagnostics, commenting on the scramble to develop faster, easier tests for Ebola. (*The New York Times*, 4 November 2014)

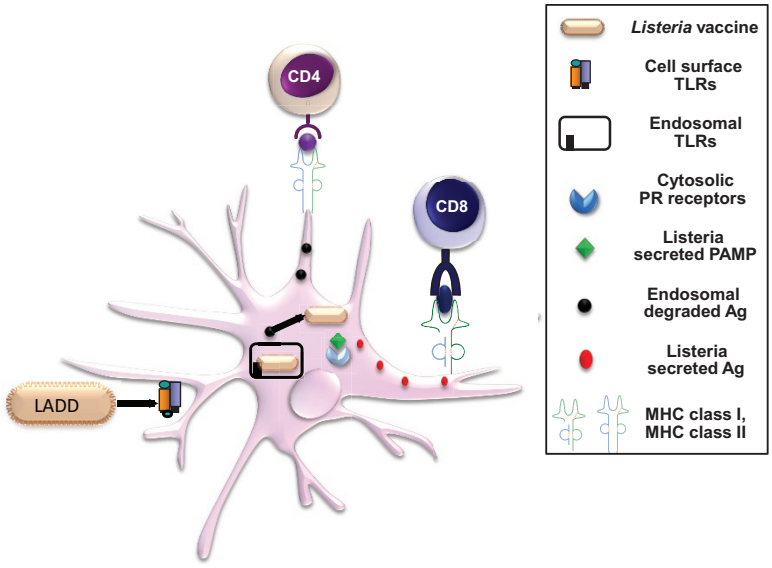
Listeria vaccines join the checkpoint frenzy

Cancer vaccines using live *Listeria* platforms have finally lured big pharma, judging by a flurry of licensing deals. In October, Berkeley, California–based Aduro Biotech announced a pact with Janssen Biotech worth up to $817 million, with $30 million upfront, based on Aduro's bioengineered *Listeria monocytogenes* platform to treat lung and other cancers. Aduro signed its first deal with the Horsham, Pennsylvania–based Janssen in May for $365 million to test the platform in prostate cancer. Also in the summer, Princeton, New Jersey–based Advaxis signed an agreement with Merck of Whitehouse Station, New Jersey, to evaluate Advaxis' *Listeria*-based immunotherapy combined with the big pharma's programmed cell death 1 immune checkpoint inhibitor Keytruda (pembrolizumab). Advaxis inked an earlier deal with MedImmune in July to test their *Listeria*-based platform with MedImmune's MEDI4736, a programmed cell death ligand 1–blocking antibody, in cervical cancer and squamous cell carcinoma of the head and neck. Interest from big pharma is a "huge deal," says Laurence Wood, assistant professor in the Department of Immunotherapeutics and Biotechnology at the Texas Tech University Health Sciences Center in Abilene. Down the road, "there will likely be even greater interest in getting bacterial-based cancer vaccines through clinical trials" alone or in combination with other drugs, he says.

The idea that bacteria could fight cancer dates back to the 1890s. William B. Coley, at Memorial Hospital in New York, noticed that infections in patients with cancer appeared to shrink tumors. The *Listeria* bacterium was known for decades to induce powerful innate and adaptive immune responses. But it was only in 2002, with the help of genetic engineering to eliminate virulence determinants, that Cerus of Concord, California, developed a safe treatment. (Aduro bought Cerus in 2009.)

Both Aduro and Advaxis are developing cancer immunotherapies that use *Listeria* strains as vectors to enhance an anti-tumor response. Aduro's vaccine technology uses live, attenuated, double-deleted *Listeria* strains in which two virulence genes, *actA* and *inlB*, have been deleted. Researchers further modify the noninfectious strain to express different tumor antigen genes. Once infused into a patient, the bacterial constructs are taken up by dendritic cells, in which the tumor antigens are processed and expressed on the cell surface and thus activate the innate and T cell–specific immune responses.

The company's lead pancreatic cancer vaccine, CRS-207, is engineered to express human mesothelin, a common antigen on



Aduro Biotech

Live, attenuated, double-deleted (LADD) *Listeria* strains are taken up by dendritic cells. *Listeria* delivers disease antigens to the cytosol, where they are processed and presented to the immune system. TLR, toll-like receptor; PR, progesterone receptor; PAMP, pathogen-associated molecular pattern; Ag, antigen.