make efforts to reduce or remove them. "But you can't remove them after the product is produced from the cell because they're inside the viral particle," Gray says. That's why his lab group has developed a stable cell line that expresses all the requisite genes involved in lentiviral vector construction without the need for constant retransfection with these components (*Blood* **113**, 5104–5110, 2009).

A stable job

This took "a lot of elbow grease" to achieve, Gray says. But, ultimately, such a stable cell line allows researchers to get away with fewer copies of the introduced viral helper genes, which translates into fewer impurities, he notes. According to Scott Burger, principal of Advanced Cell & Gene Therapy, a consulting firm based in Chapel Hill, North Carolina, stable producer cells also yield less variable vectors from batch to batch. "It becomes much easier to maintain consistency if you can have a master cell bank of the producer cell line and all you do is go back to the liquid nitrogen tank, pick out a cell vial and grow it up," he says.

In October, as part of an ongoing phase 2 trial of gene therapy for X-linked severe combined immunodeficiency, an inherited disorder of the immune system that affects around one in 100,000 boys, researchers at the US National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, treated the first patient with a vector generated using Gray's team's stable cell platform. Gray says he's now in the latter stages of characterization a similar stable cell line for manufacturing vectors to treat Wiskott-Aldrich syndrome, another rare X-linked disease.

In a similar vein, Sam Wadsworth, head of gene therapy research and development at Genzyme in Framingham, Massachusetts, says that the his company (a subsidiary of France's Sanofi) has an advanced stable cell system for AAV vectors that he thinks is ready for the therapeutic prime time. Genzyme currently has AAV-based gene therapy products in clinical trials for the treatment of Parkinson's disease and age-related macular degeneration, with other vectors in various stages of preclinical development. "It's a complex milieu, but it can be controlled and it can be scaled," Wadsworth says. "Suffice it to say that we believe that production of tens of thousands of patient doses can be readily undertaken."

By early 2013, Mavilio hopes that Généthon Bioprod, a new €30 million ($38 million) production site for clinical-grade gene therapy medicines, will be up and running. However, this facility is intended mainly to enable larger clinical trials for rare diseases. Ultimately, Mavilio says, commercial development must still fall on the private sector, and "if industry doesn't get serious about this type of technology, this will never happen."

Elie Dolgin

Greek drug shortage brings call for cost-effective approach

ATHENS — Ten years after entering the eurozone, Greece is faced with the herculean challenge of persuading pharmaceutical companies to strike a bargain and lower the cost of the medicines they sell in the country. At present, there are fears of drug shortages in certain hospitals as a result of unpaid bills. And concerns that the problem could grow have led to a call for the country to reevaluate the cost-effectiveness of drugs distributed in its public health system.

"If hard decisions are to be made, do what the British did: cover all major needs and let drugs with no substantial effect go uncovered," says Kostas Syrigos, head of the oncology unit at the Sotiria General Hospital in Athens. "We used to mock the British for not using expensive drugs, but it is our health system in danger now, not theirs."

During the last two decades Greece became a paradise for branded-drug producers, with generic medicines constituting only 12% of the drugs consumed in the country. Between 1997 and 2007, the amount of health spending per Greek citizen grew annually by 6.6%, bringing the country to fourth place worldwide, after South Korea, Turkey and Ireland, in terms of this growth.

The crisis comes, in part, as a result of the Greek National Health System racking up debts by treating pensioners and poorer locals with expensive branded drugs instead of generics. The government paid the pharmaceuticals mostly with state bonds that lost substantial value in the fiscal crisis, and, in response, they started turning off the faucet. The latest twist came on 3 November, when Germany's Merck KGaA formally announced that it had stopped providing Greek hospitals with the cancer drug Erbitux (cetuximab).

"Whatever temporary shortages appear in the Greek market are of branded drugs only," notes Argiris Efstratiadis, scientific director of the Biomedical Research Foundation of the Academy of Athens, adding that the situation has not affected clinical trials.

For many months, pharmacies have been reporting shortages of medicines as some distributors have reexported comparatively cheap drugs from Greece over to Germany and other European markets, achieving monetary gains of as much as 600%. But the situation at hospitals is more complicated. Panos Minogiannis, president and chief executive of the St. Savvas Athens Oncology Center, says his clinic has not yet seen any shortages.

My big fat Greek debt

Pharmaceutical expenditures at Minogiannis's hospital dropped from €35 million ($45 million) in 2009 to €20 million in 2011 at the same time that patient volume increased by 13%. Overall, Minogiannis remains optimistic, but he has concerns about the immediate future as a result of cash flow issues: "We have paid pharmaceutical suppliers up to April of 2012," he says. "But we have not received any payment from social insurance so far this year, and this places us at a very difficult spot."

Since the beginning of this year, the Greek Ministry of Health has published four consecutive versions of a price list setting reduced price tags for state-insurance–covered medicines. But Syrigos insists that if these price limitations prove insufficient the national health system should take a more aggressive approach by more rigorously evaluating whether it should cover all of the drugs it currently distributes at hospitals.

"Our Balkan neighbors do not use expensive drugs in their hospitals, and this is the reason why many of their patients were coming to Greece for treatment," he says. "We wouldn't like to get there, but maybe we'll be forced to."

Anastasios Kafantaris