The price of priority review: $67.5 million

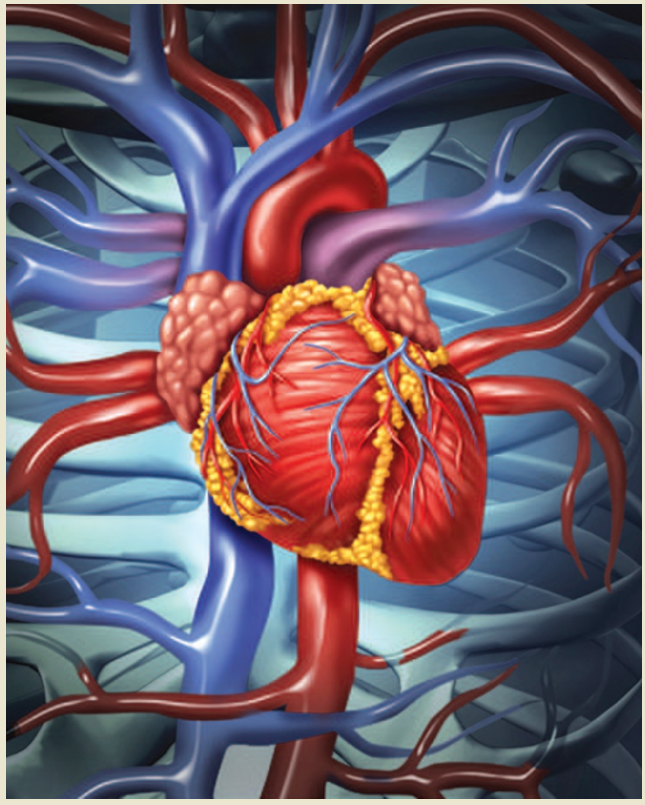
For the first time, a price has emerged for speedier US Food and Drug Administration review (FDA): $67.5 million. BioMarin Pharmaceuticals of San Rafael, California, in August 2014, became the first company to publicly sell a priority review voucher, which provides a four-month shortcut through the US drug approval pathway. Tarrytown, New York–based Regeneron Pharmaceuticals and partner Paris-based Sanofi purchased the voucher for their biologic to treat hypercholesterolemia: proprotein convertase subtilisin kexin 9 (PCSK9)-inhibitor alirocumab. With the voucher, the partners intended to gain ground over rival antibody elocuzumab from Amgen of Thousand Oaks, California, which submitted a New Drug Application on August 28. BioMarin's coup may be tricky for other voucher holders to repeat, however.

BioMarin secured its priority review voucher (PRV) in February 2014 when its rare diseases drug Vimizim (elosulfase alfa) was approved for Morquio A syndrome, a lysosomal storage disorder. These vouchers were conceived as tools to give incentives for drug development in underserved areas; they can be traded and their value lies in their potential to accelerate the review of mainstream drugs, potentially adding millions in sales for the drug's sponsor. BioMarin's is the first—and remains the only—voucher issued for a drug to treat a pediatric rare disease, under FDA's Safety and Innovation Act of 2012. Before BioMarin earned theirs, the agency issued three other PRVs under the rare tropical diseases program, created under 2007 legislation.

But until now, the tropical diseases program has been viewed with skepticism. Novartis, the first company to deploy a PRV in 2011, used it on gouty arthritis candidate ACZ885 (canakinumab). The Basel-based pharma paid a higher user fee in the process and found that it simply got rejected faster (*Nat. Biotechnol.* **29**, 958, 2011).

Now Montreal, Quebec–headquartered Knight Therapeutics wants to sell its tropical disease voucher, encouraged by BioMarin's trade. Knight secured its voucher when leishmaniasis drug Impavido (miltefosine) was approved in March. Knight's voucher may not fetch as much as BioMarin's. Tropical disease vouchers require a year's notice ahead of redemption, against just 90 days for the pediatric voucher. That limits the circumstances under which a voucher would be worth paying for. A year in advance, "how can you be sure that your pivotal trials will succeed, or that you won't win priority review anyway?" asks Mike McCaughan, co-founder of Washington, DC–based health policy analysis firm Prevision Policy. FDA already grants priority review to first-in-class and/or breakthrough candidates, without any need to purchase a voucher.

For a voucher to be worth paying for, there has to be a close race to market in a huge drug class where a four-month saving could translate into large commercial rewards. The PCSK9 race meets those criteria. Sales in this new class of cholesterol-lowering drugs are forecast to reach multiple billions of dollars. With the PRV voucher, Sanofi/Regeneron are hoping to beat Amgen to market. (The partners released promising alirocumab trial data on August 31 at the European Society of Cardiology meeting in Barcelona, Spain.)



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Sanofi will use Biomarin's voucher to get alirocumab to market quickly, in the race to make it the next blockbuster cardiovascular drug.

Knight's CFO Jeff Kadanoff thinks there could be another buyer from the PCSK9 race, though "we need a buyer that's planning ahead, and with a fair degree of certainty about the phase 3 outcome" of its drug candidate, he concedes. Pfizer, whose anti-PCSK9 antibody bococizumab is about a year behind the leaders, may want to close the gap. Kadanoff also points to verbal guidance from FDA offering flexibility for tropical disease voucher owners to change their mind after giving the 12 months' notice, and instead use the voucher on another program.

Still, "I would not view BioMarin's sale as a sign that there will be more voucher sales at these prices," says McCaughan. BioMarin had a unique ticket that fitted Regeneron's needs; the seller says it may use its share of the proceeds to expand its California headquarters or invest in an Irish manufacturing facility.

FDA may award two more pediatric priority review vouchers before reporting back to Congress to determine whether the scheme should be renewed. "I would anticipate that FDA will encourage Congress to look at different incentives, such as added exclusivity, rather than expand the priority review voucher approach," says McCaughan.

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