HealthAffairs

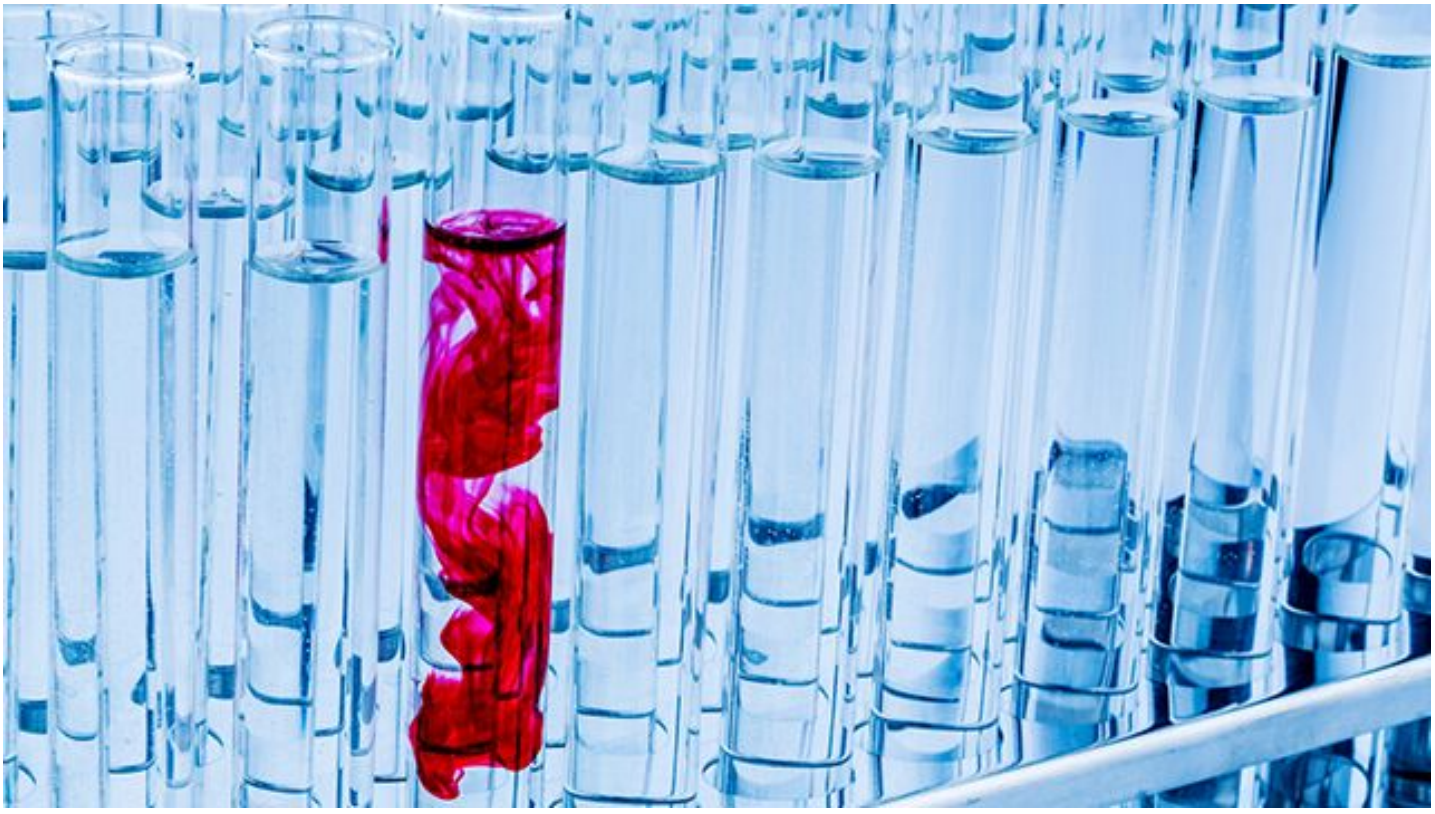
HEALTH AFFAIRS BLOG

RELATED TOPICS:
RESEARCH AND DEVELOPMENT | PHARMACEUTICALS | GENE THERAPY | PAYMENT | GRANTS | TAX CREDITS | PATIENT CARE | INTELLECTUAL PROPERTY | PRESCRIPTION DRUG COSTS | CANCER PATIENTS

Innovation Prizes To Support Cell And Gene Therapy

James C. Robinson

JULY 2, 2019 **DOI:** 10.1377/hblog20190626.554362



Personalized cell and gene therapy represent a fundamental therapeutic revolution. However, with research and development (R&D) costs for these therapies spread over far fewer patients than for traditional treatments, the revolution is arriving with eye-watering prices that shock even payers inured to the prices for targeted cancer and orphan drugs.

The payment controversy for cell and gene therapy highlights the erosion of patent-protected prices as a mechanism to finance pharmaceutical innovation. Industry prices work well for financing the development of drugs used by many patients over many years. In these cases, the fixed costs of research can be spread thinly across the large number of units sold. Even blockbusters that earn

billions annually impose modest costs on each patient. However, this mechanism has come under ever-growing strain as innovation has shifted from blockbusters to personalized, targeted, and orphan drugs.

Manufacturers now need to amortize their R&D investments over ever-smaller populations. One-time cell and gene therapies just take this to the logical extreme. R&D for tomorrow's drugs now is being financed by today's sickest patients and whichever insurers are unlucky enough to enroll them. Adverse selection is being taken to new extremes.

Rather than fund R&D for cell and gene therapy primarily through patent-protected prices, this is the moment to acknowledge the shortcomings of the conventional financing framework and to consider expanding it to a portfolio of alternatives.

Alternatives Mechanisms For Financing R&D

Patent-protected prices are by no means the only mechanism for financing pharmaceutical R&D. The price mechanism already is supplemented by research grants, tax credits for research expenditures, special regulatory considerations, and innovation prizes that reward the achievement of important developmental milestones. Each of these mechanisms has its strengths and limitations, and the mix varies across therapeutic areas. The most successful piece of public policy supporting pharmaceutical innovation, the Orphan Drug Act of 1984, uses several. It does not include innovation prizes, but this funding mechanism has gained considerable attention in recent years.

How do innovation prizes differ from patent-protected prices, as a means for financing pharmaceutical R&D?

The price mechanism generates a post-launch series of payments to manufacturers that is proportional to the number of patients initiating treatment and the number of treatments per patient. When based on comparative clinical effectiveness, these payments are titrated to the size of the benefit to the individual patient.

In contrast, the innovation prize mechanism generates a pre-launch series of payments to manufacturers that is proportional to the number of developmental milestones achieved. These payments are titrated to the importance of the scientific and clinical insights gained along the way, as measured through predefined developmental milestones, without needing to quantify benefits to individual patients. Thus, innovation prizes delink payments from the downstream treatment of the patient and move them forward.

Prize mechanisms in health care have been structured to reward new products (such as a tuberculosis test for low-resource settings), enhanced processes (such as improvements or replacements for kidney dialysis), and novel ideas not yet linked to any product or process (such as causal mechanisms for Alzheimer's disease). They are funded by federal and state governments, charitable organizations, internet-based crowd sourcing, and wealthy philanthropists.

From Prices To Prizes

Payers and manufacturers of cell and gene therapies are experimenting with annuity-based and outcomes-based pricing, but expectations should remain modest. These pricing initiatives implicitly assume that the patients using a drug receive the full value of its R&D. However, many forms of R&D create spillover benefits to future generations through the discovery of new scientific insights, engineering methods, and modes of administration. These benefits are not captured by the first set of patients to use the drugs and should not be the sole financial responsibility of those patients and their insurers.

The level of a drug's price is determined, in principle, by an estimate of the product's clinical value to the patient, sometimes measured through an incremental cost-effectiveness ratio. In contrast, the size of an innovation prize is determined by estimating how much needs to be paid to stimulate the needed research investment, accounting for the risks of failure and often-lengthy time between investment and output. No one calculates an incremental cost-effectiveness ratio to decide how much prize money to put on the table. These financial calculations are supplemented by estimates of potential non-financial rewards, including reputational enhancement, the intellectual joy of addressing complex scientific problems, and the intrinsic reward of accelerating a cure. The greater the potential for non-financial rewards, the less the need for financial rewards.

Innovation prizes could be used to stimulate and reward key milestones in the development of cell and gene therapies. They could target improvements in the processes by which patients are identified and engaged, cells are extracted and re-inserted, outcomes are monitored, and follow-on treatments are coordinated, as well as the actual manipulation of the cells themselves.

These prizes would be combined with existing mechanisms for supporting R&D, including research grants, tax credits, and supportive Food and Drug Administration policies. And, of course, insurers would continue to contribute by paying for each prescription. Through this lens, the price paid by the insurer to the manufacturer could be conceptualized as a prize linked to the milestone of successfully applying the new therapy to the new patient. But this price-as-prize would not need to support, by itself, the full investment in the underlying R&D. That investment would already have been financed in part through other mechanisms. And the prize would not be determined by estimating the number of quality-adjusted life years gained.

Three challenges face the use of prize mechanisms for stimulating research into cell and gene therapies.

First, prize mechanisms need to define in advance the milestones that will be considered as worthy of the prize payment. This already is done by governmental granting agencies, venture capitalists, and others who put their money to work conditional on the recipient being able to specify the interim outcomes that are to be achieved.

Second, prize mechanisms need to specify which entity will own the patents and other intellectual property generated by the prize-winning products, if any. At one extreme, acceptance of the prize could be conditional on the developer donating the intellectual property to a charitable organization

or making it freely available for all to use, thereby ensuring that prices will not be able to be pushed significantly above the costs of production. At the other extreme, the entity winning the prize could be allowed to retain any and all intellectual property, in which case the prize would resemble a grant or tax incentive. Blended options could well be imagined between these polar extremes. But generally prizes would be considered when conventional price mechanisms do not generate sufficient revenue to sustain R&D.

Third, of course, prize mechanisms need to find governments, organizations, or individuals willing to contribute to the funding. R&D for cell and gene therapy is expensive, and prize purses would need to be large if they were to substitute to a meaningful effect for today's painfully high prices. But just as society is being expected to find the funds to pay today's high prices, it could be expected to find funds to more directly reward milestones and thereby reduce pressures on prices.

No one says this will be simple. But reliance on the status quo, with 60 percent of pharmaceutical R&D funded by industry prices and profits, thereby generating a growing backlash on the part of patients, physicians, purchasers, and policy makers, will also not be an easy matter. In particular, the ultra-high, per-patient prices for cell and gene therapies make them the poster child of drug pricing gone amok and consequent need for greater governmental controls.

The revolution in orphan drug innovation was spurred by the prospect of enhanced prices but also by research grants, tax credits, and supportive regulatory policies. The revolution in cell and gene therapy requires its own mix of funding mechanisms, this time with a greater role for innovation prizes.